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# Sequential one-pot method for oxy-Michael addition, Heck coupling, and degradation followed by condensation: facile synthesis of 2-benzoxepin-3(1*H*)-ones

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Dedicated to the memory of my teacher Professor P.V. Subba Rao, Department of Chemistry, Andhra University, Visakhapatnam

*Keywords:*
Oxy-Michael addition
Heck coupling
Pd-catalysis
*retro*-Oxy-Michael addition
Condensation
2-Benzoxepin-3(1*H*)-ones

ABSTRACT

A sequential one-pot intermolecular oxy-Michael addition, intermolecular Heck coupling, and intramolecular degradation (*retro*-oxy-Michael addition) followed by condensation method has been developed for the synthesis of interesting 2-benzoxepin-3(1*H*)-ones. Significantly, the 2-benzoxepin-3(1*H*)-ones form the core quantum of biologically vital natural products. The initial oxy-Michael addition and Heck coupling steps involve a straight forward construction of C–O and C–C bonds, whereas, the final condensation step follows a novel mechanistic path via intramolecular degradation, double bond isomerization, and intramolecular condensation. Notably, a remarkable solvent effect has been observed in-order to promote the final intramolecular condensation.



## 1. Introduction

Synthetic practices like one-pot/sequential one-pot are treated as the most useful techniques/methods for synthesizing organic compounds as they do not involve the intermediate isolation.[1] These one-pot processes involve multiple reactions to be catalyzed sequentially by a metal complex or sequential addition of reagents to drive a set of reactions.[2] Such processes can be categorized as pseudo domino strategies, cascade reactions,[3] and tandem catalysis and they are advantageous over the conventional methods, like in, less waste generation, saving time, energy, resources, and eventually resulting in more efficiency.[4] Also, it has been noticed that, generally, the overall yields of one-pot processes are higher than those obtained from the corresponding step-wise reactions. Therefore, one-pot processes that involve construction of multiple bonds, particularly cyclic structures are of utmost importance, as this form the significant core/part-structures in many biologically active natural products.

The transition metal mediated one-pot methods have gained much recognition lately, because of their procedural advantages.[5,6] Among them, the Heck type of reaction is of particular importance, especially the Pd-catalyzed domino Heck reactions are well documented.[1g,7–9] Though reports on Heck coupling followed by a consequent cyclization (e.g., Michael addition) are limited. Pd-catalyzed Heck–Michael,[11] Heck-aza-Michael,[12] and Heck-aldol condensation are some of the notable reactions in one-pot processes. Since most of the Pd-catalyzed reactions administer a base; it is advantageous to perform such one-pot processes where both base and palladium would involve individually and affect each reaction of the process.[10–12] As continuation of our contemporary interest in the development of synthetic methods by palladium-catalysis,[13] recently we reported a sequential one-pot intermolecular oxy-Michael addition and subsequent intermolecular Heck reaction with the Michael acceptor for the synthesis of functionalized cinnamates.[14] Herein, we report a successful application involving a sequential one-pot intermolecular oxy-Michael addition, subsequent intermolecular Heck coupling with the Michael acceptor followed by intramolecular lactonization for the synthesis of 2-benzoxepin-3(1*H*)-ones. Most significantly, the 2-benzoxepin-3(1*H*)-ones are not only present as major skeletal structure in antibiotics xylarinol (**A**) and xylarinol (**B**),[15] but also as the part structure of new tyrosine kinase (p56lck) inhibitor ulocladol[16] and cytotoxic alterlactone[17]

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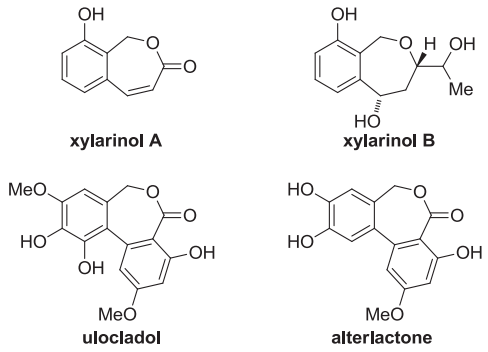
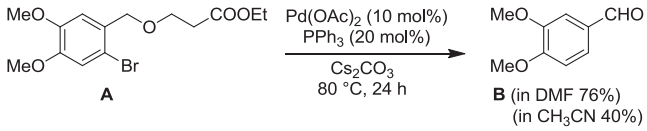



**Fig. 1.** 2-Benzoxepin-3(1*H*)-one is present as core/part-structure of natural products.

(Fig. 1). Moreover, analogues of 2-benzoxepin-3(1*H*)-ones have been identified to exhibit good analgesic activities.[18]

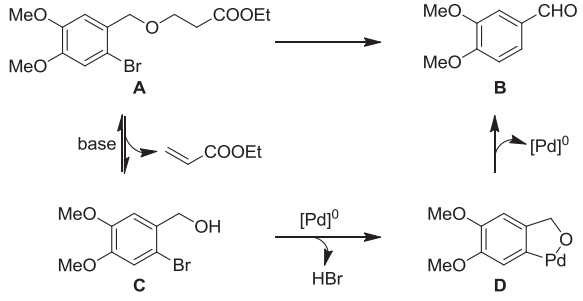
## 2. Results and discussion

In our initial studies we have come across with an interesting observation that the bromoester **A** in the presence of Pd-catalyst and a base gave back the very first starting material benzaldehyde **B** as depicted in Scheme 1. This interesting reaction takes



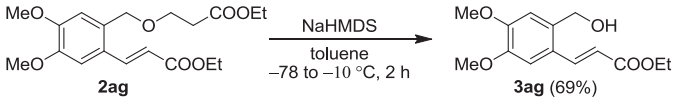

**Scheme 1.** Oxidative degradation of **A** to **B** under Pd-catalysis.

place particularly in the presence of polar solvents, such as DMF and $CH_3CN$ (for details see Ref. 14). The formation of **B** can be justified via base triggering *retro*-oxy-Michael addition on bromoester **A** to set-up an equilibration with the starting *ortho*-bromobenzyl alcohol **C**, which in turn in the presence of Pd-catalyst turned back to the very first starting material benzaldehyde **B** as depicted in Scheme 2.[13c] The formation of benzyl alcohol **C** as an




**Scheme 2.** Plausible routes for the oxidative degradation of **A** to **B**.

intermediate followed by Pd-catalyzed transformation to **B** is justified based on the reaction of a strong base with the diester **2ag** at low temperature, which has yielded alcohol enoate **3ag** as shown in Scheme 3 (this reaction of the diester **2ag** with strong base has



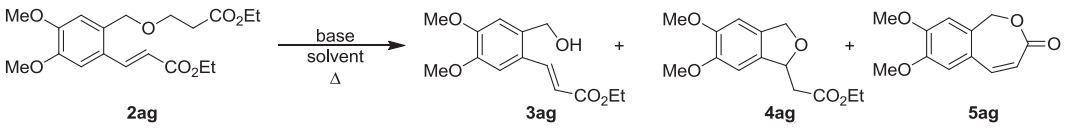

**Scheme 3.** Degradation of **2ag** to **3ag** via *retro*-oxy-Michael addition.

been suggested by one of the reviewer to observe the possible formation of five membered cyclic ether via intramolecular cyclization).

Nevertheless, this interesting observation inspired us to explore different conditions promoted by base, for intramolecular cyclizations for the formation of isobenzofuran cyclic systems.[19] Since the alcohol enoate **3ag** was the exclusive product in the presence of strong base NaHMDS at the low temperature range (Scheme 3, Table 1, entry 1), the diester **2ag** was treated with the same base but at 50 °C in order to form isobenzofuran via an intramolecular oxy-Michael addition. However, the reaction was found to be unclear under these conditions (Table 1, entry 2). The diester **2ag** was subjected for the same kind of degradation under previous conditions[14] with base $Cs_2CO_3$ at 80 °C in toluene in order to check the stability of the diester **2ag**. As expected, there was no progress in the reaction with base $Cs_2CO_3$ at 80 °C (Table 1 entry 3), which is obvious otherwise the diester **2ag** would not have been yielded at all in our previous report. We thought that the temperature change might activate the diester towards degradation (*retro*-oxy-Michael addition) followed by cyclization under the same conditions. As expected, it gave the cyclic ether **4ag** albeit in poor yield along with the unexpected lactenone **5ag** (Table 1, entry 4). The possible reaction mechanism for the formation of **5ag** is described in Scheme 4. Fortunately, changing the solvent proved beneficial to generate exclusively the lactenone product **5ag**, in good yield (Table 1, entries 5 & 6).

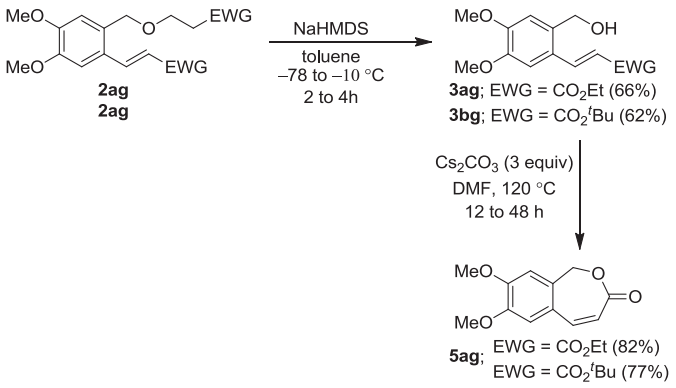
After successful formation of interesting cyclic ester **5ag** by performing the reaction on an isolated diester **2ag**, we aimed to make the method more efficient by synthesizing target lactenone **5** in a sequential one-pot fashion by directly starting from *ortho*-bromobenzyl alcohols **1** [i.e., a sequential one-pot intermolecular oxy-Michael addition, intermolecular Heck coupling, and intramolecular degradation (*retro*-oxy-Michael addition) followed by condensation]. Toluene, reported as suitable solvent for oxy-Michael addition and subsequent Heck coupling,[14] however, was not suitable for the final cyclization. Instead, DMF was observed to be an ideal solvent for the cyclization to give the lactenone **5ag** (entries 5 & 6, Table 1) while it impedes the formation of diester **2ag**.[14] Therefore, we decided to play safe in a way by

**Table 1**
Screening reaction conditions for the synthesis of **5ag** starting from **2ag**




| Entry | Base [2 equiv] | Solvent [2 mL] | Temp [°C] | Time [h] | Yield **3ag** [%][a] | Yield **4ag** [%][a] | Yield **5ag** [%][a] |
|---|---|---|---|---|---|---|---|
| 1 | NaHMDS | toluene | −78 to −10 | 12 | 69 | 0 | 0 |
| 2 | NaHMDS | toluene | 50 | 12 | 0 | 0 | 0 |
| 3 | $Cs_2CO_3$ | toluene | 80 | 48 | 0 | 0 | 0 |
| 4 | $Cs_2CO_3$ | toluene | 120 | 24 | 0 | 16 | 23 |
| **5** | **$Cs_2CO_3$** | **DMF** | **120** | **12** | **0** | **0** | **77** |
| 6 | $Cs_2CO_3$ | DMF | 80 | 24 | 0 | 0 | 78 |

[a] Yields of chromatographically isolated pure products.

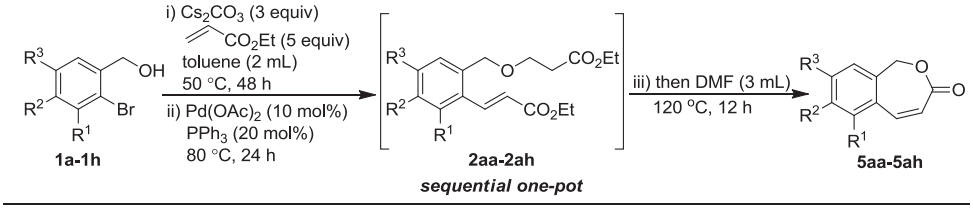


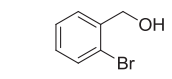
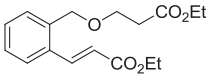
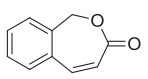
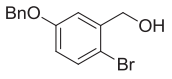
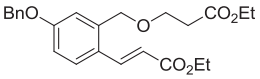
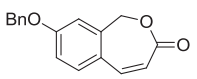
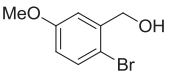
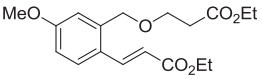
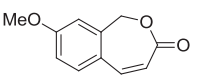
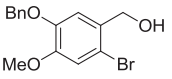
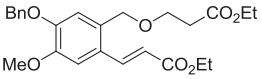
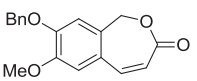
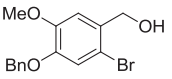
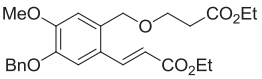
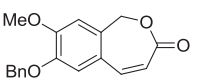
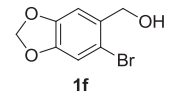
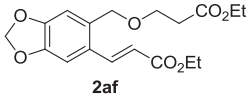
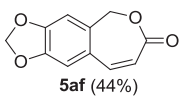
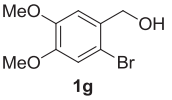
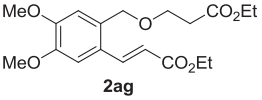
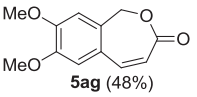
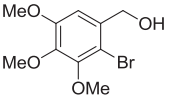
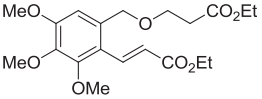
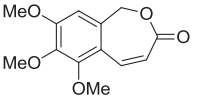

**Scheme 4.** Formation of lactenone **5ag** from isolated *retro*-Michael precursors **3ag** and **3bg**.

choosing toluene as the first solvent up-to the formation of diester **2** and then DMF as the second solvent system to promote the final cyclization of the diester **2** to yield the lactenone **5**. Since, the lactenone **5ag** formation was initiated at 120 °C in toluene (entry 4, Table 1), the final cyclization was also performed at the same temperature after addition of DMF to the diester **2**. Delightfully, the reaction was successful and furnished cyclic lactenone in moderate yields (Table 2). Though the yield is moderate, but the overall yield is still in an acceptable range after three individual transformations (i.e., each individual step approximately accounts for 75%), since such systems have been achieved in not less than three individual transformations. It is noteworthy that, when the reaction carried out on the 2-bromobenzyl alcohol **1g**, in a mixture of solvents, such as DMF and toluene (1:1 mixture), the initial Michael addition followed by Heck coupling itself was found unclear along with the formation of unwanted degradative aldehyde **B** (8%). Indeed, this is in good agreement to that of our previous results reported for the synthesis of diesters where DMF was not a suitable solvent.[14]

Since it was well established that the sequential one-pot method was quite successful to produce the diester **2** in excellent yields with the bulky tertiarybutyl acrylate as the Michael acceptor, we anticipated the subsequent intramolecular cyclization in sequential one-pot would also be amenable to give the lactenone **5** in the similar fashion. However, under optimized conditions, in

**Table 2**
Sequential one-pot formation of lactenones **5aa**–**ah** starting from *ortho*-bromobenzyl alcohols **1a**–**h**




| | | |
|---|---|---|
|  **1a** |  **2aa** |  **5aa** (46%) |
|  **1b** |  **2ab** |  **5ab** (40%) |
|  **1c** |  **2ac** |  **5ac** (46%) |
|  **1d** |  **2ad** |  **5ad** (42%) |
|  **1e** |  **2ae** |  **5ae** (44%) |
|  **1f** |  **2af** |  **5af** (44%) |
|  **1g** |  **2ag** |  **5ag** (48%) |
|  **1h** |  **2ah** |  **5ah** (47%) |

[a] Yields of chromatographically isolated pure products.

sequential one-pot, the reaction was unaffected and led to isolation of the diester **2bg**. While, the reaction on isolated diester **2bg**, particularly, at slightly higher temperature, was also unable to produce the lactenone **5ag** as an exclusive product, rather unexpectedly furnished three possible products (Table 3). This can be explained as, it might release of strong base CsO$^t$Bu, after the formation of lactenone **5ag**, might revert back the cyclic ether **4bg** intermediate to the acyclic alcohol enoate **3bg**. In an alternative way, it may be due to the bulky tertiarybutyl group might impede final cyclization, after initial cyclization and ring opening through the isomerization of the double bond. Delightfully, longer reaction times in DMF forced the reaction to furnish **5ag** as an exclusive product in good yield (entry 6, Table 3).

Nevertheless, these step-wise optimized conditions (entry 6, Table 3), particularly in case of ditertiarybutyl diester **2bg**, failed to furnish the lactenone **5ag**, when applied to the optimized sequential one-pot method as in the case of diethyl diesters **2** (Table 2). Similar problem has been encountered with the diethyl/ditertiarybutyl diesters **2aj**, **2ak**, **2bi**, and **2bl**; those have been originated from the corresponding secondary alcohols **2i**–**l**. Therefore, separate base induced (entry 6, Table 3) cyclization was applied to these diesters (**2aj**, **2ak**, **2bi**, and **2bl**). As a result, the corresponding lactenones **5** have been obtained in fair yields (Table 4). However, the reaction of diester **2bm** with electron withdrawing group on the aromatic ring was found unclear.

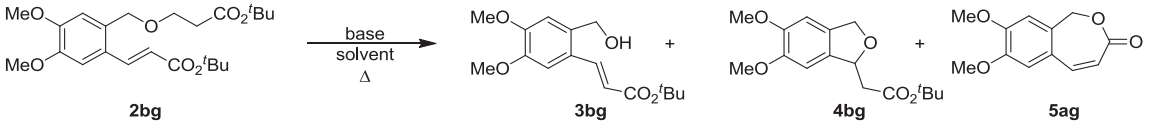
On the other hand, in order to well understand the reaction mechanism for the lactenones formation **5**, we have separately treated the isolated alcohol esters **3ag** & **3bg** for cyclization. In parallel to our expectation, the lactenone **5ag** was obtained in good yields (Scheme 4).

To further confirm the path of the reaction, it was also performed on the isolated cyclic ether **4ag** (i.e., employed the reaction conditions of entry 4 in Table 1). Similarly, the reaction furnished cyclic lactenone **5ag** (Scheme 5).

Also, **2bg** was subjected to base mediated cyclization (Table 3, entry 3). And when the isolated cyclic ether **4bg** (i.e., employed the reaction conditions of entry 3 in Table 3) and an inseparable mixture of **3bg** & **5ag** were separately treated with the base under the same reaction conditions, gave the lactenone **5ag** as expected (Scheme 6).

Based on the above studies, the possible reaction mechanism for the formation of **5ag** from **2ag** is as depicted in Scheme 7. After the formation of oxy-Michael product **A** and subsequent Heck coupling to give **2ag**, the base may trigger *retro*-oxy-Michael addition ($E_2$-elimination) of **2ag** and an intramolecular oxy-Michael addition of the resulted alkoxide would lead to cyclic enolate **H**. Now, the cyclic enolate **H** can equilibrate back to acyclic alkoxide **I** through possible *E* to *Z*-isomerization of cinnamate double bond. Finally, an

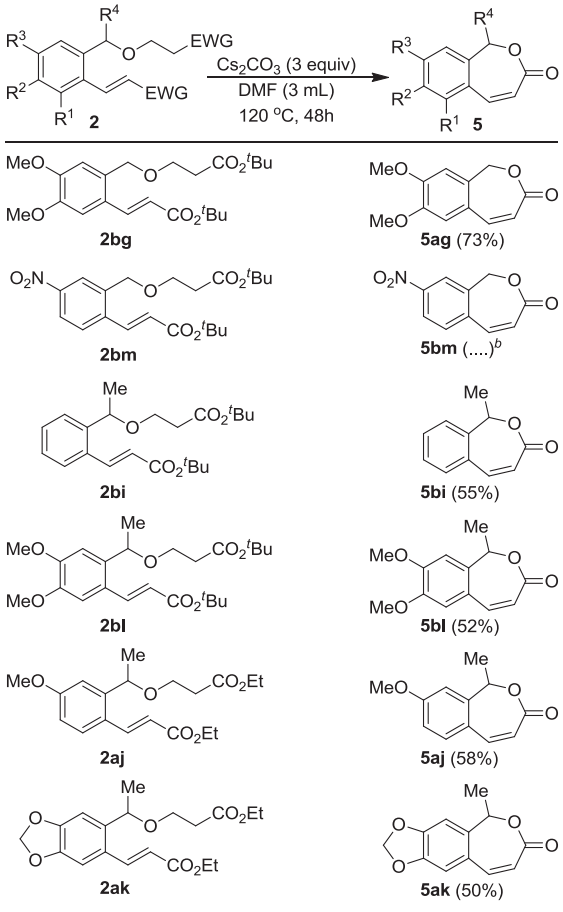
**Table 3**
Screening reaction conditions, for the synthesis of **5ag** starting from **2bg**



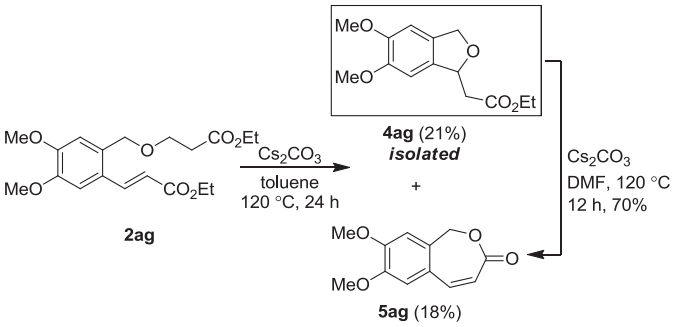

| Entry | Base [equiv] | Solvent [mL] | Temp [°C] | Time [h] | Recovery of **2bg** [%] | Yield **3bg** [%][a] | Yield **4bg** [%][a] | Yield **5ag** [%][a] |
|---|---|---|---|---|---|---|---|---|
| 1 | $Cs_2CO_3$ [2] | toluene [2] | 80 | 48 | 93 | 0 | 0 | 0 |
| 2 | $Cs_2CO_3$ [2] | toluene [2] | 100 | 48 | 83 | 0 | 0 | 0 |
| 3 | $Cs_2CO_3$ [3] | DMF [2] | 80 | 24 | — | 9[b] | 28 | 18[b] |
| 4 | $Cs_2CO_3$ [3] | $CH_3CN$ [3] | 80 | 24 | — | 0 | 20 | 16 |
| 5 | $Cs_2CO_3$ [3] | DMF [2] | 140 | 3 | — | 15[b] | 23 | 40[b] |
| **6** | **$Cs_2CO_3$ [3]** | **DMF [2]** | **120** | **48** | — | — | — | **73** |
| 7[c] | $Cs_2CO_3$ [1.5] | xylene [2] | 130 | 48 | 30 | 0 | 24 | 10 |
| 8 | $Cs_2CO_3$ [3] | DMA [2] | 160 | 12 | —[d] | 0 | 0 | 0 |
| 9 | $Cs_2CO_3$ [3] | DMSO [2] | 160 | 12 | —[d] | 0 | 0 | 0 |
| 10 | NaHMDS [4] | toluene [2] | 50 | 12 | —[d] | 0 | 0 | 0 |

[a] Yields of chromatographically isolated pure products.
[b] Yields of the products based on $^1$H NMR.
[c] Yields based on the recovery of the starting material (30%).
[d] Reaction was not clean.

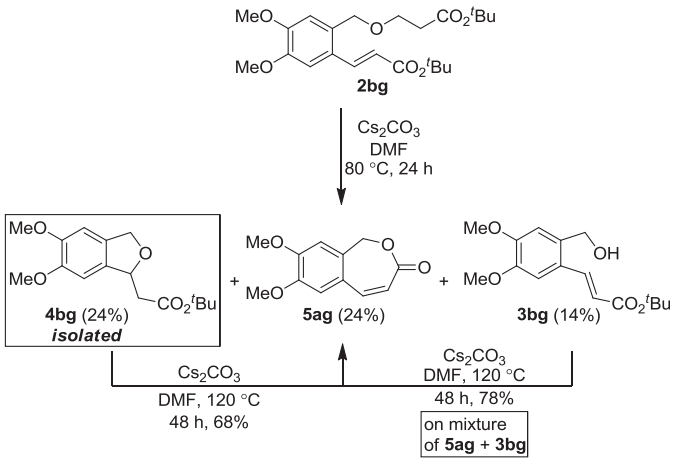
**Table 4**
Step-wise conversion of diesters **2** to lactenones **5**



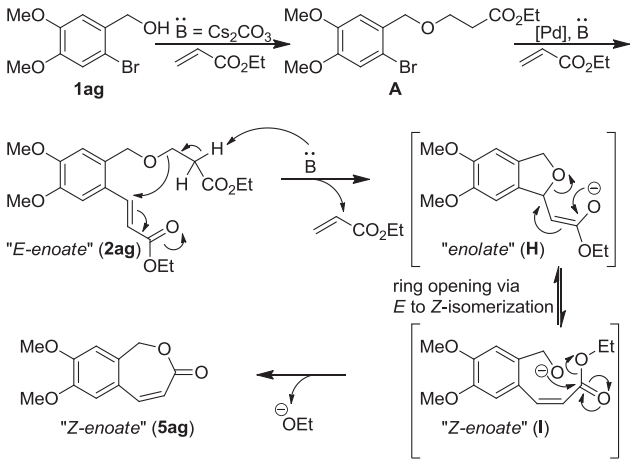

[a] Yields of chromatographically isolated pure products.
[b] Unclear reaction that niether yield any product nor the recovery of **2bm**.




**Scheme 5.** Conversion of isolated cyclic ether **4ag** to the lactenone **5ag**.




**Scheme 6.** Transformation of isolated cyclic ether **4bg** to the lactenone **5ag**.




**Scheme 7.** Plausible mechanistic path for the conversion of **2ag** into **5ag**.

intramolecular degradation followed by condensation yields lactenone **5ag**.

In addition to the NMR spectroscopic structural elucidation, the structure of lactenone **5** was further unambiguously confirmed by single crystal X-ray diffraction analysis on **5ac** (Fig. 2).

## 3. Conclusion

In summary, we have developed a novel sequential one-pot method for the synthesis of functionalized 2-benzoxepin-3(1*H*)-ones via an intermolecular oxy-Michael addition, intermolecular Heck coupling, and intramolecular degradation (*retro*-oxy-Michael addition) followed by condensation. Notably, a remarkable solvent effect has been observed in-order to promote the final intramolecular degradation followed by condensation. Initial two steps involve a straight forward construction of C–O and C–C bonds, whereas the final cyclization involves a novel base promoted intramolecular degradation, double bond isomerization and condensation mechanistic path.

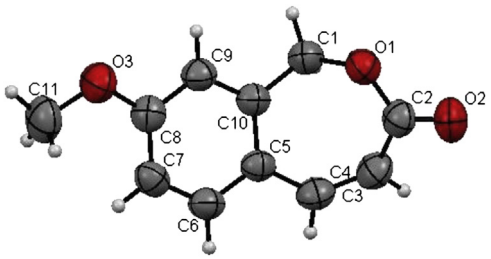



**Fig. 2.** X-ray crystal structure of **5ac**. Thermal ellipsoids are drawn at 50% probability level.[20]

## 4. Experimental section

### 4.1. General

IR spectra were recorded on a Bruker Tensor 37 (FTIR) spectrophotometer. $^1$H NMR spectra were recorded on Bruker Avance 400 (400 MHz) spectrometer at 295 K in $CDCl_3$; chemical shifts ($\delta$ in parts per million) and coupling constants ($J$ in Hertz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) ($\delta_H$=0.00 ppm) or $CHCl_3$ ($\delta_H$=7.25 ppm). $^{13}$C NMR spectra were recorded on Bruker Avance 400 (100 MHz) spectrometer at rt in $CDCl_3$; chemical shifts ($\delta$ in ppm) are reported relative to $CHCl_3$ [$\delta_C$=77.00 ppm (central line of triplet)]. In the $^{13}$C NMR, the nature of carbons (C, CH, $CH_2$ and $CH_3$) was determined by recording the DEPT-135 spectra, and is given in parentheses and noted as s=singlet (for C), d=doublet (for CH), t=triplet (for $CH_2$), and q=quartet (for $CH_3$). In the $^1$H NMR, the following abbreviations were used throughout: s=singlet, d=doublet, t=triplet, q=quartet, qui=quintet, m=multiplet, and br s=broad singlet. The assignment of signals was confirmed by $^1$H, $^{13}$C CPD, and DEPT spectra. High-resolution mass spectra (HR-MS) were recorded on an Agilent 6538 UHD Q-TOF using multimode source. All small scale dry reactions were carried out using Schlenk tube technique. Reactions were monitored by TLC on silica gel using a mixture of petroleum ether and ethyl acetate as eluents. Reactions were generally run under an argon or nitrogen atmosphere. Solvents, petroleum ether, ethyl acetate, and dichloromethane were distilled prior use. Petroleum ether with a boiling range of 60–80 °C was used. Diethyl ether and toluene were dried over benzophenone/sodium. DMF was dried over calcium hydride. 2-Bromo benzaldehyde and other aromatic aldehydes were purchased from local commercial sources and used as received. Acme's silica gel (60–120 mesh) was used for column chromatography (approximately 20 g per one gram of crude material).

### 4.2. General procedure-1 (for the sequential one-pot reaction)

In an oven dried Schlenk tube, were added alcohol **1** (100.0 mg, 0.31–0.53 mmol), ethyl acrylate [155.1–265.3 mg, (i.e., 1.55–2.65 mmol)], and $Cs_2CO_3$ [303.0–518.0 mg, (i.e., 0.93–1.59 mmol)] followed by the addition of toluene (2 mL) at rt under nitrogen

atmosphere. The resulted reaction mixture was stirred at 50 °C in an oil bath for 48 h. After the completion of Michael addition (monitored by TLC) and to the cooled reaction mixture at rt, were added $Pd(OAc)_2$ (6.9–11.9 mg, 10 mol %) and $PPh_3$ (16.3–27.8 mg, 20 mol %) under nitrogen atmosphere. The reaction mixture was then heated at 80 °C in an oil bath for 24 h. Once after formation intermolecular Heck coupling product, (monitored by TLC) and then to the cooled reaction mixture at rt, was added DMF (3 mL) and heated to 120 °C, in an oil bath for 12 h (monitored by TLC). The reaction mixture at rt was quenched by the addition of aqueous $NH_4Cl$ and extracted with DCM (3×15 mL). The organic layers were washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the lactenones **5** (40–48%).

Diesters **2ag**, **2bg**, and **2cg** and the alcohol ester **3ag** are known in the literature.[14]

### 4.3. *tert*-Butyl (2*E*)-3-{2-[1-(3-*tert*-butoxy-3-oxopropoxy) ethyl]phenyl}acrylate (2bi)

In an oven dried Schlenk tube, were added alcohol **1i** (200.0 mg, 0.99 mmol), tertiarybutyl acrylate (637.0 mg, 4.97 mmol), and $Cs_2CO_3$ (972.0 mg, 2.98 mmol) followed by addition of toluene (4 mL) at rt under nitrogen atmosphere. The stirred reaction mixture was heated in an oil bath at 50 °C for 48 h. Progress of the Michael addition was monitored by TLC till the reaction is completed. To the cooled reaction mixture at rt, were added $Pd(OAc)_2$ (22.0 mg, 10 mol %) and $PPh_3$ (52.0 mg, 20 mol %) under nitrogen atmosphere. The stirred reaction mixture was then heated in an oil bath at 80 °C for 24 h and monitored by TLC. Then, the mixture was cooled to rt, treated with aqueous $NH_4Cl$ solution, and then extracted with $CH_2Cl_2$ (3×10 mL). The organic layer was washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 95:5 to 90:10) furnished the diester **2bi** (220.0 mg, 59%) as yellow viscous oil. [TLC control (petroleum ether/ethyl acetate 90:10), $R_f$ (**1i**)=0.35, $R_f$ (**2bi**)=0.45, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2922, 1730, 1709, 1632, 1367, 1319, 1149, 1105, 954, 762 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.98 (d, 1H, $J$=15.6 Hz, C*H*=CHCOO$^t$Bu), 7.52 (d, 1H, $J$=7.3 Hz, Ar–H), 7.48 (d, 1H, $J$=7.8 Hz, Ar–H), 7.38 (dd, 1H, $J$=7.8 and 7.3 Hz, Ar–H), 7.25 (dd, 1H, $J$=7.8 and 7.8 Hz, Ar–H), 6.27 (d, 1H, $J$=15.6 Hz, CH=*CH*COO$^t$Bu), 4.81 (q, 1H, $J$=6.4 Hz, Ar–*CH*$CH_3$), 3.55 (t, 2H, $J$=6.4 Hz, O*CH*$_2$$CH_2$COO$^t$Bu), 2.48 (td, 2H, $J$=6.4 and 1.5 Hz, $OCH_2CH_2$COO$^t$Bu), 1.55 [s, 9H, OC$(CH_3)_3$], 1.45 [s, 9H, OC$(CH_3)_3$], 1.40 (d, 3H, $J$=6.4 Hz, Ar–CH*CH*$_3$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=170.8 (s, O=C–O), 166.1 (s, O=C–O), 142.8 (s, Ar–C), 140.3 (d, *C*H=CHCOO$^t$Bu), 132.4 (s, Ar–C), 130.0 (d, Ar–CH), 127.3 (d, Ar–CH), 126.6 (d, Ar–CH), 126.0 (d, Ar–CH), 122.0 (d, CH=*C*HCOO$^t$Bu), 80.5 [s, O*C*$(CH_3)_3$], 80.4 [s, O*C*$(CH_3)_3$], 74.7 (d, Ar–*C*H$CH_3$), 64.5 (t, O$CH_2CH_2$COO$^t$Bu), 36.4 (t, $CH_2$*C*$H_2$COO$^t$Bu), 28.1 [q, 3C, OC$(CH_3)_3$], 28.0 [q, 3C, OC$(CH_3)_3$], 23.7 (q, Ar–CH*C*$H_3$) ppm. HR-MS (APCI$^+$) $m/z$ calculated for $[C_{22}H_{31}O_5]^+$=$[M+H]^+$: 375.2166; found 375.2171.

### 4.4. Ethyl (2*E*)-3-{2-[1-(3-ethoxy-3-oxopropoxy)ethyl]-4-methoxyphenyl}acrylate (2aj)

In an oven dried Schlenk tube, were added alcohol **1j** (200.0 mg, 0.86 mmol), ethyl acrylate (433.0 mg, 4.32 mmol), and $Cs_2CO_3$ (846.0 mg, 2.58 mmol) followed by addition of toluene (4 mL) at rt under a nitrogen atmosphere. The stirred reaction mixture was heated in an oil bath at 50 °C for 48 h. Progress of the Michael addition was monitored by TLC till the reaction is completed. To the cooled reaction mixture at rt, were added $Pd(OAc)_2$ (19.4 mg, 10 mol %) and $PPh_3$ (45.0 mg, 20 mol %) under nitrogen atmosphere. The stirred reaction mixture was then heated in an oil bath at 80 °C for 24 h and monitored by TLC. Then, the mixture was cooled to rt, treated with aqueous $NH_4Cl$ solution, and then extracted with $CH_2Cl_2$ (3×10 mL). The organic layer was washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the diester **2aj** (200.0 mg, 57%) as a yellow viscous oil. [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**1j**)=0.45, $R_f$ (**2aj**)=0.45, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2923, 1735, 1712, 1631, 1603, 1493, 1252, 1179, 1162, 1107, 1034, 731 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.94 (d, 1H, $J$=15.6 Hz, C*H*=CHCOOEt), 7.50 (d, 1H, $J$=8.3 Hz, Ar–H), 7.02 (d, 1H, $J$=2.4 Hz, Ar–H), 6.79 (dd, 1H, $J$=8.3 Hz and 2.4 Hz, Ar–H), 6.23 (d, 1H, $J$=15.6 Hz, CH=*CH*COOEt), 4.80 (q, 1H, $J$=6.4 Hz, Ar–C*H*$CH_3$), 4.24 (q, 2H, $J$=7.3 Hz, O*CH*$_2$$CH_3$), 4.12 (qd, 2H, $J$=7.3 and 1.9 Hz, O*CH*$_2$$CH_3$), 3.83 (s, 3H, Ar–$OCH_3$), 3.70–3.45 (m, 2H, O*CH*$_2$$CH_2$COOEt), 2.56 (t, 2H, $J$=6.8 Hz, $OCH_2$*CH*$_2$COOEt), 1.37 (d, 3H, $J$=6.4 Hz, Ar–CH*CH*$_3$), 1.31 (t, 3H, $J$=7.3 Hz, $OCH_2$*CH*$_3$), 1.23 (t, 3H, $J$=7.3 Hz, $OCH_2$*CH*$_3$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=171.4 (s, O=C–O), 167.1 (s, O=C–O), 161.5 (s, Ar–C), 145.0 (s, Ar–C), 140.5 (d, *C*H=CHCOOEt), 128.2 (d, Ar–CH), 124.6 (s, Ar–C), 117.7 (d, CH=*C*HCOOEt), 113.6 (d, Ar–CH), 110.7 (d, Ar–CH), 74.7 (d, Ar*C*H$CH_3$), 64.3 (t, O$CH_2CH_2$COOEt), 60.4 (t, O$CH_2CH_3$), 60.3 (t, O$CH_2CH_3$), 55.3 (q, Ar–$OCH_3$), 35.2 (t, O$CH_2$*C*$H_2$COOEt), 23.9 (q, Ar*C*H*C*$H_3$), 14.3 (q, O$CH_2$*C*$H_3$), 14.1 (q, O$CH_2$*C*$H_3$) ppm. HR-MS (APCI$^+$) $m/z$ calculated for $[C_{19}H_{26}NaO_6]^+$=$[M+Na]^+$: 373.1622; found 373.1630.

### 4.5. Ethyl (2*E*)-3-{6-[1-(3-ethoxy-3-oxopropoxy)ethyl]-1,3-benzodioxol-5-yl}acrylate (2ak)

In an oven dried Schlenk tube, were added alcohol **1f** (200.0 mg, 0.82 mmol), ethyl acrylate (408.0 mg, 4.10 mmol), and $Cs_2CO_3$ (798.0 mg, 2.46 mmol) followed by addition of toluene (4 mL) at rt under a nitrogen atmosphere. The stirred reaction mixture was heated in an oil bath at 50 °C for 48 h. Progress of the Michael addition was monitored by TLC till the reaction is completed. To the cooled reaction mixture at rt, were added $Pd(OAc)_2$ (18.0 mg, 10 mol %) and $PPh_3$ (42.0 mg, 20 mol %) under nitrogen atmosphere. The stirred reaction mixture was then heated in an oil bath at 80 °C for 24 h and monitored by TLC. Then, the mixture was cooled to rt, treated with aqueous $NH_4Cl$ solution and then extracted with $CH_2Cl_2$ (3×10 mL). The organic layer was washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the diester **2ak** (178.0 mg, 60%) as a yellow viscous oil. [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**1f**)=0.50, $R_f$ (**2ak**)=0.50, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2958, 2921, 2852, 1732, 1618, 1482, 1285, 1254, 1180, 1103, 1038, 934 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.92 (d, 1H, $J$=15.6 Hz, C*H*=CHCOOEt), 6.99 (s, 1H, Ar–H), 6.97 (s, 1H, Ar–H), 6.20 (d, 1H, $J$=15.6 Hz, CH=*CH*COOEt), 5.98 (d, 1H, $J$=6.4 Hz, $OCH_2O$), 5.97 (d, 1H, $J$=6.4 Hz, Ar–H), 4.79 (q, 1H, $J$=6.8 Hz, Ar–C*H*$CH_3$), 4.24 (q, 2H, $J$=7.3 Hz, O*CH*$_2$$CH_3$), 4.14 (q, 2H, $J$=7.3 Hz, O*CH*$_2$$CH_3$), 3.65–3.50 (m, 2H, O*CH*$_2$$CH_2$COOEt), 2.55 (t, 2H, $J$=6.4 Hz, $OCH_2$*CH*$_2$COOEt), 1.34 (d, 3H, $J$=6.8 Hz, Ar–*CH*$CH_3$), 1.32 (t, 3H, $J$=7.3 Hz, $OCH_2$*CH*$_3$), 1.25 (t, 3H, $J$=7.3 Hz, $OCH_2$*CH*$_3$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=171.5 (s, O=C–O), 167.0 (s, O=C–O), 149.9 (s, Ar–C), 147.2 (s, Ar–C), 140.3 (d, *C*H=CHCOOEt), 138.9 (s, Ar–C), 125.8 (s, Ar–C), 118.2 (d, CH=*C*HCOOEt), 106.1 (d, Ar–CH), 105.6 (d, Ar–CH), 101.4 (t, $OCH_2O$), 74.1 (d, Ar*C*H$CH_3$), 64.2 (t, O$CH_2CH_2$COOEt), 60.5 (t, O$CH_2CH_3$), 60.4 (t, O$CH_2CH_3$), 35.3 (t, O$CH_2$*C*$H_2$COOEt), 24.0 (q, Ar*C*H*C*$H_3$), 14.3 (q, O$CH_2$*C*$H_3$), 14.2 (q,

$OCH_2CH_3$) ppm. HR-MS ($APCI^+$) *m/z* calculated for $[C_{19}H_{25}O_7]^+=[M+H]^+$: 365.1595; found 365.1603.

### 4.6. *tert*-Butyl (2*E*)-3-[2-(hydroxymethyl)-4,5-dimethoxyphenyl]acrylate (3bg)

To a cold (−78 °C), magnetically stirred solution of a diester **2bg** (100 mg, 0.24 mmol), under argon atmosphere, in dry toluene (2 mL), was added 1 M solution of NaHMDS (0.96 mL, 0.96 mmol) in toluene. Then the reaction mixture was allowed to stir at −78 °C for 1 h and allowed to −10 °C for 3 h. The reaction mixture was quenched with aqueous $NH_4Cl$ solution and extracted with ethyl acetate (3×15 mL). The organic layer was washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the filtrate under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate 70:30 to 50:50) furnished the hydroxy ester **3bg** (43.4 mg, 62%) as a pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 70:30), $R_f$ (**2bg**)=0.50, $R_f$ (**3bg**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=3432, 2975, 1702, 1629, 1601, 1514, 1457, 1274, 1146, 1104, 977, 845 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.87 (d, 1H, *J*=15.6 Hz, C*H*=CHCOO$^t$Bu), 7.07 (s, 1H, Ar–H), 6.94 (s, 1H, Ar–H), 6.22 (d, 1H, *J*=15.6 Hz, CH=C*H*COO$^t$Bu), 4.78 (s, 2H, Ar–$CH_2$OH), 3.90 (s, 3H, Ar–$OCH_3$), 3.89 (s, 3H, Ar–$OCH_3$), 1.89 (br s, OH), 1.52 [(s, 9H, C($CH_3$)$_3$] ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=166.6 (s, O=C–O), 150.6 (s, Ar–C), 148.6 (s, Ar–C), 139.8 (d, *C*H=CHCOO$^t$Bu), 133.4 (s, Ar–C), 125.3 (s, Ar–C), 119.6 (d, Ar–CH), 111.6 (d, Ar–CH), 109.0 (d, CH=*C*HCOO$^t$Bu), 80.5 [(s, *C*($CH_3$)$_3$] 62.3 (t, Ar–$CH_2$OH), 56.0 (q, Ar–$OCH_3$), 55.9 (q, Ar–$OCH_3$), 28.2 [(q, 3C, C(*C*H$_3$)$_3$] ppm.

### 4.7. Ethyl (5,6-dimethoxy-1,3-dihydro-2-benzofuran-1-yl)acetate (4ag)

In an oven dried Schlenk tube, were added diester **2ag** (50.0 mg, 0.14 mmol) and $Cs_2CO_3$ (133.5 mg, 0.72 mmol) followed by the addition of toluene (2 mL) at rt under nitrogen atmosphere. The resulted reaction mixture was stirred at 120 °C in an oil bath for 24 h. Progress of the reaction was monitored by TLC. The reaction mixture at rt was quenched by the addition of aqueous $NH_4Cl$ and extracted with DCM (3×15 mL). The organic layers were washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the ether **4ag** (5.6 mg, 16%), as a pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 75:25), $R_f$ (**2ag**)=0.45, $R_f$ (**4ag**)=0.46, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2917, 1728, 1602, 1505, 1464, 1266, 1220, 1163, 1107, 1037, 855, 729 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=6.72 (s, 1H, Ar–H), 6.70 (s, 1H, Ar–H), 5.65–5.55 (m, 1H, ArC*H*CH$_2$COOEt), 5.08 (dd, 1H, *J*=11.7 and 2.9 Hz, ArC*H*$_a$H$_b$O), 5.00 (dd, 1H, *J*=11.7 and 1.5 Hz, ArCH$_a$*H*$_b$O), 4.18 (q, 2H, *J*=7.3 Hz, O*C*H$_2$CH$_3$), 3.86 (s, 3H, $ArOCH_3$), 3.85 (s, 3H, $ArOCH_3$), 2.72 (dd, 2H, *J*=7.3 and 6.4 Hz, ArCHC*H*$_2$COOEt), 1.25 (t, 3H, *J*=7.3 Hz, $OCH_2CH_3$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=170.9 (s, O=C–O), 149.3 (s, Ar–C), 148.9 (s, Ar–C), 132.2 (s, Ar–C), 130.6 (s, Ar–C), 104.2 (d, Ar–CH), 103.9 (d, Ar–CH), 80.6 (d, Ar*C*HCH$_2$COOEt), 72.8 (t, Ar$CH_2$O), 60.6 (t, O*C*H$_2$CH$_3$), 56.1 (q, Ar–$OCH_3$), 56.0 (q, Ar–$OCH_3$), 41.8 (t, ArCH*C*H$_2$COOEt), 14.2 (q, OCH$_2$*C*H$_3$) ppm. HR-MS ($APCI^+$) *m/z* calculated for $[C_{14}H_{18}NaO_5]^+=[M+Na]^+$: 289.1046; found 289.1052. Further elution of crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 70:30) yielded Michael addition product **5ag** (10.2 mg, 23%). [TLC control (petroleum ether/ethyl acetate 75:25), $R_f$ (**2ag**)=0.45, $R_f$ (**5ag**)=0.30, UV detection].

### 4.8. *tert*-Butyl (5,6-dimethoxy-1,3-dihydro-2-benzofuran-1-yl)acetate (4bg)

In an oven dried Schlenk tube, were added diester **2bg** (50.0 mg, 0.12 mmol) and $Cs_2CO_3$ (117.3 mg, 0.36 mmol) followed by the addition of $CH_3CN$ (3 mL) at rt under nitrogen atmosphere. The resulted reaction mixture was stirred at 80 °C in an oil bath for 24 h. Progress of the reaction was monitored by TLC. The reaction mixture at rt was quenched by the addition of aqueous $NH_4Cl$ and extracted with DCM (3×15 mL). The organic layers were washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the ether **4bg** (5.9 mg, 16%) as pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**2bg**)=0.45, $R_f$ (**4bg**)=0.47, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2975, 1723, 1603, 1503, 1464, 1391, 1274, 1220, 1146, 1108, 1036, 844, 766 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=6.71 (2× s, 2H, Ar–H), 5.60–5.48 (m, 1H, ArC*H*CH$_2$COO$^t$Bu), 5.06 (dd, 1H, *J*=11.7 and 2.9 Hz, ArC*H*$_a$H$_b$O), 4.98 (dd, 1H, *J*=11.7 and 1.5 Hz, ArCH$_a$*H*$_b$O), 3.85 (s, 3H, $ArOCH_3$), 3.84 (s, 3H, $ArOCH_3$), 2.65 (dd, 2H, *J*=6.8 and 1.5 Hz, ArCHC*H*$_2$COOEt), 1.44 [s, 9H, OC($CH_3$)$_3$] ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=170.2 (s, O=C–O), 149.2 (s, Ar–C), 148.8 (s, Ar–C), 132.6 (s, Ar–C), 130.7 (s, Ar–C), 104.3 (d, Ar–CH), 103.9 (d, Ar–CH), 80.8 [s, O*C*($CH_3$)$_3$], 80.7 (d, Ar*C*HCH$_2$COO$^t$Bu), 72.8 (t, Ar$CH_2$O), 56.1 (q, Ar–$OCH_3$), 56.0 (q, Ar–$OCH_3$), 42.9 (t, ArCH*C*H$_2$COOEt), 28.0 [q, 3C, OC(*C*H$_3$)$_3$] ppm. HR-MS ($APCI^+$) *m/z* calculated for $[C_{16}H_{20}O_4]^+=[M-(H_2O)]^+$: 276.1356; found 276.1352.

### 4.9. 2-Benzoxepin-3(1*H*)-one (5aa)

**GP-1** was carried out with alcohol **1a** (100.0 mg, 0.53 mmol), ethyl acrylate (265.3 mg, 2.65 mmol), $Cs_2CO_3$ (518.0 mg, 1.59 mmol), toluene (2 mL) for Michael addition at 50 °C for 48 h, then with $Pd(OAc)_2$ (11.9 mg, 10 mol %), $PPh_3$ (27.8 mg, 20 mol %) for Heck coupling at 80 °C for 24 h and finally with DMF (3 mL) at 120 °C for 12 h. Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 95:5 to 85:15) furnished the lactenone **5aa** (39.5 mg, 46%) as a pale yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10), $R_f$ (**1a**)=0.50, $R_f$ (**5aa**)=0.38, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2921, 1707, 1602, 1457, 1273, 1209, 1157, 1106, 1034, 818, 741 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.55–7.30 (m, 4H, Ar–H), 7.21 (d, 1H, *J*=11.7 Hz, C*H*=CHCO), 6.35 (d, 1H, *J*=11.7 Hz, CH=C*H*CO), 5.06 (s, 2H, Ar$CH_2O$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=167.6 (s, O=C–O), 140.6 (d, *C*H=CHCO), 135.4 (s, Ar–C), 135.1 (s, Ar–C), 130.2 (d, Ar–CH), 129.8 (d, Ar–CH), 129.7 (d, Ar–CH), 128.6 (d, Ar–CH), 122.7 (d, CH=*C*HCO), 68.6 (t, Ar$CH_2O$) ppm. HR-MS ($APCI^+$) *m/z* calculated for $[C_{10}H_7O]^+=[(M+H)-H_2O]^+$: 143.0491; found 143.0496.

### 4.10. 8-(Benzyloxy)-2-benzoxepin-3(1*H*)-one (5ab)

**GP-1** was carried out with alcohol **1b** (100.0 mg, 0.34 mmol), ethyl acrylate (170.2 mg, 0.17 mmol), $Cs_2CO_3$ (332.3 mg, 1.03 mmol), toluene (2 mL) for Michael addition at 50 °C for 48 h, then with $Pd(OAc)_2$ (7.6 mg, 10 mol %), $PPh_3$ (17.8 mg, 20 mol %) for Heck coupling at 80 °C for 24 h and finally with DMF (3 mL) at 120 °C for 12 h. Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the lactenone **5ab** (36.2 mg, 40%) as a pale yellow semi-solid. [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**1b**)=0.48, $R_f$ (**5ab**)=0.41, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2925, 1701, 1605, 1501, 1283, 1178, 1040, 835, 737 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.46–7.30 (m, 6H, Ar–H), 7.14 (d, 1H,

$J$=12.2 Hz, C*H*=CHCO), 7.03 (dd, 1H, $J$=8.3 and 2.4 Hz, Ar–H), 7.01 (d, 1H, $J$=2.4 Hz, Ar–H), 6.22 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 5.12 (s, 2H, $PhCH_2O$), 5.00 (s, 2H, $ArCH_2O$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=168.0 (s, O=C–O), 160.1 (s, Ar–C), 140.6 (d, *C*H=CHCO), 137.1 (s, Ar–C), 136.0 (s, Ar–C), 131.7 (d, Ar–CH), 128.7 (d, 2C, Ar–CH), 128.5 (s, Ar–C), 128.3 (d, Ar–CH), 127.4 (d, 2C, Ar–CH), 120.2 (d, CH=*C*HCO), 115.7 (d, Ar–CH), 115.1 (d, Ar–CH), 70.3 (t, $PhCH_2O$), 68.7 (t, $ArCH_2O$) ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{17}H_{15}O_3]^+$=$[M+H]^+$: 267.1016; found 267.1020.

### 4.11. 8-Methoxy-2-benzoxepin-3(1*H*)-one (5ac)

**GP-1** was carried out with alcohol **1c** (100.0 mg, 0.46 mmol), ethyl acrylate (230.3 mg, 2.30 mmol), $Cs_2CO_3$ (449.6 mg, 1.38 mmol), toluene (2 mL) for Michael addition at 50 °C for 48 h, then with $Pd(OAc)_2$ (10.3 mg, 10 mol %), $PPh_3$ (24.1 mg, 20 mol %) for Heck coupling at 80 °C for 24 h and finally with DMF (3 mL) at 120 °C for 12 h. Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 80:20) furnished the lactenone **5ac** (40.4 mg, 46%) as a pale brown solid, recrystallized from dichloromethane/hexane (mp 96–98 °C). [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**1c**)=0.45, $R_f$ (**5ac**)=0.40, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2926, 1699, 1605, 1503, 1453, 1284, 1251, 1160, 1034, 909, 805, 727 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.34 (d, 1H, $J$=8.3 Hz, Ar–H), 7.14 (d, 1H, $J$=12.2 Hz, C*H*=CHCO), 6.96 (dd, 1H, $J$=8.3 and 2.4 Hz, Ar–H), 6.92 (d, 1H, $J$=2.4 Hz, Ar–H), 6.21 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 5.01 (s, 2H, $ArCH_2O$), 3.85 (s, 3H, $Ar–OCH_3$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=168.1 (s, O=C–O), 161.0 (s, Ar–C), 140.7 (d, *C*H=CHCO), 137.0 (s, Ar–C), 131.7 (d, Ar–CH), 128.3 (s, Ar–C), 120.0 (d, CH=*C*HCO), 114.8 (d, Ar–CH), 114.2 (d, Ar–CH), 68.7 (t, $ArCH_2O$), 55.5 (q, $Ar–OCH_3$) ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{11}H_{11}O_3]^+$=$[M+H]^+$: 191.0703; found 191.0704.

### 4.12. 8-(Benzyloxy)-7-methoxy-2-benzoxepin-3(1*H*)-one (5ad)

**GP-1** was carried out with alcohol **1d** (100.0 mg, 0.31 mmol), ethyl acrylate (155.2 mg, 1.55 mmol), $Cs_2CO_3$ (303.0 mg, 0.93 mmol), toluene (2 mL) for Michael addition at 50 °C for 48 h, then with $Pd(OAc)_2$ (6.9 mg, 10 mol %), $PPh_3$ (16.3 mg, 20 mol %) for Heck coupling at 80 °C for 24 h and finally with DMF (3 mL) at 120 °C for 12 h. Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 75:25) furnished the lactenone **5ad** (38.6 mg, 42%) as white solid, recrystallized from dichloromethane/hexane (mp 159–160 °C). [TLC control (petroleum ether/ethyl acetate 75:25), $R_f$ (**1d**)=0.45, $R_f$ (**5ad**)=0.38, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2924, 1702, 1603, 1519, 1368, 1275, 1165, 1025, 740 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.42 (d, 2H, $J$=7.8 Hz, Ar–H), 7.38 (dd, 2H, $J$=7.8 and 7.3 Hz, Ar–H), 7.32 (t, 1H, $J$=7.3 Hz, Ar–H), 7.11 (d, 1H, $J$=12.2 Hz, C*H*=CHCO), 6.91 (s, 1H, Ar–H), 6.89 (s, 1H, Ar–H), 6.25 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 5.20 (s, 2H, $PhCH_2O$), 4.92 (s, 2H, $ArCH_2O$), 3.91 (s, 3H, $Ar–OCH_3$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=167.9 (s, O=C–O), 150.3 (s, Ar–C), 149.5 (s, Ar–C), 140.5 (d, *C*H=CHCO), 136.2 (s, Ar–C), 129.0 (s, Ar–C), 128.7 (d, 2C, Ar–CH), 128.6 (s, Ar–C), 128.2 (d, Ar–CH), 127.2 (d, 2C, Ar–CH), 121.0 (d, CH=*C*HCO), 113.7 (d, Ar–CH), 112.7 (d, Ar–CH), 71.1 (t, $PhCH_2O$), 68.3 (t, $ArCH_2O$), 56.2 (q, $Ar–OCH_3$) ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{18}H_{17}O_4]^+$=$[M+H]^+$: 297.1121; found 297.1121.

### 4.13. 7-(Benzyloxy)-8-methoxy-2-benzoxepin-3(1*H*)-one (5ae)

**GP-1** was carried out with alcohol **1e** (100.0 mg, 0.31 mmol), ethyl acrylate (155.2 mg, 1.55 mmol), $Cs_2CO_3$ (303.0 mg, 0.93 mmol), toluene (2 mL) for Michael addition at 50 °C for 48 h, then with $Pd(OAc)_2$ (6.9 mg, 10 mol %), $PPh_3$ (16.3 mg, 20 mol %) for Heck coupling at 80 °C for 24 h and finally with DMF (3 mL) at 120 °C for 12 h. Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 75:25) furnished the lactenone **5ae** (40.5 mg, 44%) as colorless solid, recrystallized from dichloromethane/petroleum ether (mp 160–161 °C). [TLC control (petroleum ether/ethyl acetate 75:25), $R_f$ (**1e**)=0.45, $R_f$ (**5ae**)=0.38, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2925, 1694, 1602, 1517, 1453, 1354, 1275, 1164, 1106, 1031, 987, 864, 733, 698 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.42 (d, 2H, $J$=7.8 Hz, Ar–H), 7.37 (dd, 2H, $J$=7.8 and 7.3 Hz, Ar–H), 7.31 (t, 1H, $J$=7.3 Hz, Ar–H), 7.04 (d, 1H, $J$=12.2 Hz, C*H*=CHCO), 6.91 (s, 1H, Ar–H), 6.89 (s, 1H, Ar–H), 6.22 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 5.16 (s, 2H, $PhCH_2O$), 4.97 (s, 2H, $ArCH_2O$), 3.93 (s, 3H, $Ar–OCH_3$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=168.0 (s, O=C–O), 150.9 (s, Ar–C), 148.7 (s, Ar–C), 140.6 (d, *C*H=CHCO), 136.3 (s, Ar–C), 129.2 (s, Ar–C), 128.6 (d, 2C, Ar–CH), 128.4 (s, Ar–C), 128.1 (d, Ar–CH), 127.2 (d, 2C, Ar–CH), 120.7 (d, CH=*C*HCO), 114.7 (d, Ar–CH), 111.7 (d, Ar–CH), 71.1 (t, $PhCH_2O$), 68.3 (t, $ArCH_2O$), 56.2 (q, $Ar–OCH_3$) ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{18}H_{17}O_4]^+$=$[M+H]^+$: 297.1121; found 297.1120.

### 4.14. [1,3]Dioxolo[4,5-*h*][2]benzoxepin-7(5*H*)-one (5af)

**GP-1** was carried out with alcohol **1f** (100.0 mg, 0.43 mmol), ethyl acrylate (215.2 mg, 2.15 mmol), $Cs_2CO_3$ (423.0 mg, 1.30 mmol), toluene (2 mL) for Michael addition at 50 °C for 48 h, then with $Pd(OAc)_2$ (9.6 mg, 10 mol %), $PPh_3$ (22.5 mg, 20 mol %) for Heck coupling at 80 °C for 24 h and finally with DMF (3 mL) at 120 °C for 12 h. Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 80:20) furnished the lactenone **5af** (38.6 mg, 44%) as colorless solid, recrystallized from dichloromethane/petroleum ether (mp 149–150 °C). [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**1f**)=0.45, $R_f$ (**5af**)=0.40, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2921, 1698, 1617, 1504, 1490, 1387, 1267, 1238, 1147, 1023, 928, 879 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.06 (d, 1H, $J$=12.2 Hz, C*H*=CHCO), 6.86 (s, 1H, Ar–H), 6.83 (s, 1H, Ar–H), 6.24 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 6.03 (s, 2H, $O–CH_2–O$), 4.93 (s, 2H, $ArCH_2O$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=167.8 (s, O=C–O), 149.0 (s, Ar–C), 148.7 (s, Ar–C), 140.3 (d, *C*H=CHCO), 130.2 (s, Ar–C), 130.0 (s, Ar–C), 121.0 (d, CH=*C*HCO), 109.3 (d, Ar–CH), 109.0 (d, Ar–CH), 101.9 (t, $O–CH_2–O$), 68.2 (t, $ArCH_2O$) ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{11}H_9O_4]^+$=$[M+H]^+$: 205.0495; found 205.0493.

### 4.15. 7,8-Dimethoxy-2-benzoxepin-3(1*H*)-one (5ag)

**GP-1** was carried out with alcohol **1g** (100.0 mg, 0.40 mmol), ethyl acrylate (202.6 mg, 2.02 mmol), $Cs_2CO_3$ (395.6 mg, 1.21 mmol), toluene (2 mL) for Michael addition at 50 °C for 48 h, then with $Pd(OAc)_2$ (9.1 mg, 10 mol %), $PPh_3$ (21.0 mg, 20 mol %) for Heck coupling at 80 °C for 24 h and finally with DMF (3 mL) at 120 °C for 12 h. Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 70:30) furnished the lactenone **5ag** (42.8 mg, 48%) as yellow semi-solid. [TLC control (petroleum ether/ethyl acetate 75:25), $R_f$ (**1g**)= 0.45, $R_f$ (**5ag**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2924, 1693, 1603, 1519, 1463, 1356, 1274, 1247, 1164, 1107, 1029, 988, 840, 731 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.12 (d, 1H, $J$=12.2 Hz, C*H*=CHCO), 6.90 (s, 1H, Ar–H), 6.87 (s, 1H, Ar–H), 6.26 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 4.98 (s, 2H, $ArCH_2O$), 3.93 (s, 3H, $ArOCH_3$), 3.90 (s, 3H, $ArOCH_3$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=168.0 (s, O=C–O), 150.3 (s, Ar–C), 149.7 (s, Ar–C), 140.6 (d, *C*H=CHCO), 128.7 (s, Ar–C), 128.6 (s, Ar–C), 120.9 (d, CH=*C*HCO), 112.1 (d, Ar–CH), 111.3 (d, Ar–CH), 68.3 (t, $ArCH_2O$),

56.2 (q, Ar–$OCH_3$), 56.1 (q, Ar–$OCH_3$) ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{12}H_{13}O_4]^+=[M+H]^+$: 221.0808; found 221.0804.

### 4.16. 6,7,8-Trimethoxy-2-benzoxepin-3(1*H*)-one (5ah)

**GP-1** was carried out with alcohol **1h** (100.0 mg, 0.36 mmol), ethyl acrylate (180.7 mg, 1.80 mmol), $Cs_2CO_3$ (351.9 mg, 1.08 mmol), toluene (2 mL) for Michael addition at 50 °C for 48 h, then with $Pd(OAc)_2$ (8.1 mg, 10 mol %), $PPh_3$ (18.9 mg, 20 mol %) for Heck coupling at 80 °C for 24 h and finally with DMF (3 mL) at 120 °C for 12 h. Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 75:25) furnished the lactenone **5ah** (42.3 mg, 47%) as yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**1h**)=0.45, $R_f$ (**5ah**)=0.38, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2925, 1703, 1595, 1498, 1458, 1375, 1338, 1249, 1123, 1089, 1031, 822 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.43 (d, 1H, $J$=12.2 Hz, C*H*=CHCO), 6.71 (s, 1H, Ar–H), 6.24 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 4.94 (s, 2H, $ArCH_2O$), 3.91 (s, 3H, $ArOCH_3$), 3.90 (s, 3H, $ArOCH_3$), 3.87 (s, 3H, $ArOCH_3$) ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=168.2 (s, O=C–O), 155.0 (s, Ar–C), 152.2 (s, Ar–C), 142.5 (s, Ar–C), 135.6 (d, *C*H=CHCO), 131.9 (s, Ar–C), 122.6 (s, Ar–C), 120.2 (d, CH=*C*HCO), 107.4 (d, Ar–CH), 68.7 (t, $ArCH_2O$), 61.7 (q, Ar–$OCH_3$), 61.0 (q, Ar–$OCH_3$), 56.2 (q, Ar–$OCH_3$) ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{13}H_{15}O_5]^+=[M+H]^+$: 251.0914; found 251.0913.

### 4.17. 1-Methyl-2-benzoxepin-3(1*H*)-one (5bi)

In an oven dried Schlenk tube, were added diester **2bi** (200.0 mg, 0.53 mmol) and $Cs_2CO_3$ (520.0 mg, 1.59 mmol) followed by the addition of DMF (4 mL) at rt under nitrogen atmosphere. The resulted reaction mixture was stirred at 120 °C in an oil bath for 12 h. Progress of the reaction was monitored by TLC. The reaction mixture at rt was quenched by the addition of aqueous $NH_4Cl$ and extracted with DCM (3×15 mL). The organic layers were washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 80:20) furnished the ether as yellow oil **5bi** (50.8 mg, 55%). [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**2bi**)=0.50, $R_f$ (**5bi**)=0.25, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2923, 2852, 1701, 1617, 1455, 1398, 1269, 1215, 1152, 1068, 1044, 1018, 972, 823, 808, 777, 731 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.60–7.30 (m, 4H, Ar–C), 7.21 (d, 1H, $J$=12.2 Hz, C*H*=CHCO), 6.39 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 5.31 [q, 1H, $J$=6.8 Hz, ArC*H*($CH_3$)O], 1.85 [d, 3H, $J$=6.8 Hz, ArCH(C*H*$_3$)O] ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=167.4 (s, O=C–O), 140.4 (d, *C*H=CHCO), 138.2 (s, Ar–C), 135.1 (s, Ar–C), 130.1 (d, Ar–CH), 129.9 (d, Ar–CH), 129.1 (d, Ar–CH), 124.9 (d, Ar–CH), 123.0 (d, CH=*C*HCO), 72.7 [d, ArC*H*($CH_3$)O], 17.3 [q, ArCH(*C*H$_3$)O] ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{10}H_9O]^+=[(M+H)-H_2O]^+$: 157.0648; found 157.0644.

### 4.18. 7,8-Dimethoxy-1-methyl-2-benzoxepin-3(1*H*)-one (5bl)

In an oven dried Schlenk tube, were added diester **2bl** (220.0 mg, 0.50 mmol) and $Cs_2CO_3$ (493.0 mg, 1.50 mmol) followed by the addition of DMF (4 mL) at rt under nitrogen atmosphere. The resulted reaction mixture was stirred at 120 °C in an oil bath for 12 h. Progress of the reaction was monitored by TLC. The reaction mixture at rt was quenched by the addition of aqueous $NH_4Cl$ and extracted with DCM (3×15 mL). The organic layers were washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 70:30 to 60:40) furnished the ether as yellow oil **5bl** (62.5 mg, 52%). [TLC control (petroleum ether/ethyl acetate 60:40), $R_f$ (**2bl**)=0.75, $R_f$ (**5bl**)=0.20, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2925, 2852, 1695, 1604, 1518, 1462, 1362, 1335, 1199, 1177, 1151, 1068, 1025, 957, 863, 812, 729, 612 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.11 (d, 1H, $J$=12.2 Hz, C*H*=CHCO), 6.96 (s, 1H, Ar–H), 6.86 (s, 1H, Ar–H), 6.30 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 5.25 [q, 1H, $J$=6.4 Hz, ArC*H*($CH_3$)O], 3.95 (s, 3H, Ar–$OCH_3$), 3.90 (s, 3H, Ar–$OCH_3$) 1.83 [d, 3H, $J$=6.4 Hz, ArCH(C*H*$_3$)O] ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=167.7 (s, O=C–O), 150.3 (s, Ar–C), 149.2 (s, Ar–C), 140.2 (d, *C*H=CHCO), 131.9 (s, Ar–C), 128.3 (s, Ar–C), 121.4 (d, CH=*C*HCO), 112.3 (d, Ar–CH), 107.9 (d, Ar–CH), 72.4 [d, ArC*H*($CH_3$)O], 56.1 (q, Ar–$OCH_3$), 56.0 (q, Ar–$OCH_3$), 17.5 [q, ArCH(*C*H$_3$)O] ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{13}H_{15}O_4]^+=[M+H]^+$: 235.0695; found 235.0694.

### 4.19. 8-Methoxy-1-methyl-2-benzoxepin-3(1*H*)-one (5aj)

In an oven dried Schlenk tube, were added diester **2aj** (150.0 mg, 0.43 mmol) and $Cs_2CO_3$ (419.0 mg, 1.29 mmol) followed by the addition of DMF (3 mL) at rt under nitrogen atmosphere. The resulted reaction mixture was stirred at 120 °C in an oil bath for 12 h. Progress of the reaction was monitored by TLC. The reaction mixture at rt was quenched by the addition of aqueous $NH_4Cl$ and extracted with DCM (3×15 mL). The organic layers were washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 80:20) furnished the ether as yellow viscous liquid **5aj** (50.8 mg, 58%). [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**2aj**)=0.60, $R_f$ (**5aj**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2923, 2852, 1697, 1605, 1562, 1501, 1460, 1399, 1382, 1236, 1218, 1178, 1073, 1035, 975, 876, 859 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.33 (d, 1H, $J$=8.3 Hz, Ar–H), 7.14 (d, 1H, $J$=11.7 Hz, C*H*=CHCO), 7.00 (d, 1H, $J$=2.4 Hz, Ar–H), 6.94 (dd, 1H, $J$=8.3 and 2.4 Hz, Ar–H), 6.25 (d, 1H, $J$=11.7 Hz, CH=C*H*CO), 5.26 [q, 1H, $J$=6.8 Hz, ArC*H*($CH_3$)O], 3.87 (s, 3H, Ar–$OCH_3$) 1.82 [d, 3H, $J$=6.8 Hz, ArCH(C*H*$_3$)O] ppm. $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$=167.8 (s, O=C–O), 161.1 (s, Ar–C), 140.5 (d, *C*H=CHCO), 140.2 (s, Ar–C), 131.8 (d, Ar–CH), 128.0 (s, Ar–C), 120.5 (d, CH=*C*HCO), 113.6 (d, Ar–CH), 111.4 (d, Ar–CH), 72.5 [d, ArC*H*($CH_3$)O], 55.5 (q, Ar–$OCH_3$), 17.3 [q, ArCH(*C*H$_3$)O] ppm. HR-MS ($APCI^+$) $m/z$ calculated for $[C_{12}H_{13}O_3]^+=[M+H]^+$: 205.0859; found 205.0862.

### 4.20. 8,9-Dihydro[1,3]dioxolo[4,5-*h*][2]benzoxepin-7(5*H*)-one (5ak)

In an oven dried Schlenk tube, were added diester **2ak** (80.0 mg, 0.22 mmol) and $Cs_2CO_3$ (214.0 mg, 0.66 mmol) followed by the addition of DMF (2 mL) at rt under nitrogen atmosphere. The resulted reaction mixture was stirred at 120 °C in an oil bath for 12 h. Progress of the reaction was monitored by TLC. The reaction mixture at rt was quenched by the addition of aqueous $NH_4Cl$ and extracted with DCM (3×15 mL). The organic layers were washed with saturated NaCl solution, dried ($Na_2SO_4$), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 85:15 to 75:25) furnished the ether as yellow oil **5ak** (24.0 mg, 50%). [TLC control (petroleum ether/ethyl acetate 80:20), $R_f$ (**2ak**)=0.50, $R_f$ (**5ak**)=0.20, UV detection]. IR (MIR-ATR, 4000–600 $cm^{-1}$): $\nu_{max}$=2921, 2851, 1694, 1505, 1489, 1385, 1261, 1156, 1036, 932 $cm^{-1}$. $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$=7.06 (d, 1H, $J$=12.2 Hz, C*H*=CHCO), 6.98 (s, 1H, Ar–H), 6.83 (s, 1H, Ar–H), 6.30 (d, 1H, $J$=12.2 Hz, CH=C*H*CO), 6.04 (d, 1H, $J$=6.3 Hz, $OCH_aH_bO$), 6.03 (d, 1H, $J$=6.3 Hz, $OCH_aH_bO$), 5.20 [q, 1H, $J$=6.3 Hz, ArC*H*($CH_3$)O], 1.79 [d, 3H, $J$=6.3 Hz, ArCH(C*H*$_3$)O] ppm. $^{13}C$ NMR ($CDCl_3$,

100 MHz): $\delta$=167.6 (s, O=C–O), 149.3 (s, Ar–C), 148.1 (s, Ar–C), 140.0 (d, CH=CHCO), 133.7 (s, Ar–C), 129.7 (s, Ar–C), 121.6 (d, CH=CHCO), 109.3 (d, Ar–CH), 105.6 (d, Ar–CH), 101.9 (t, $OCH_2O$), 72.3 (d, $ArCHCH_3$), 17.6 (q, $ArCHCH_3$) ppm. HR-MS ($APCI^+$) *m/z* calculated for $[C_{12}H_{11}O_4]^+$=$[(M+H)]^+$: 219.0652; found 219.0657.

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## Supplementary data

Copies of $^1H$ and $^{13}C$ NMR spectra related to this article are available. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.09.050.

## References and notes

1. (a) Ulaczyk-Lesanko, A.; Hall, D. G. *Curr. Opin. Chem. Biol.* **2005**, *9*, 266–276; (b) Parsons, P. J.; Penkett, C. S.; Shell, A. J. *Chem. Rev.* **1996**, *96*, 195–206; (c) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136; (d) Dounay, A. B.; Overman, L. E. *Chem. Rev.* **2003**, *103*, 2945–2963; (e) Tietze, L. F.; Ila, H.; Bell, H. P. *Chem. Rev.* **2004**, *104*, 3453–3516; (f) Domling, A. *Chem. Rev.* **2006**, *106*, 17–89; (g) Zeni, G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644–4680; (h) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174–238; (i) Touré, B. B.; Hall, D. G. *Chem. Rev.* **2009**, *109*, 4439–4486; (j) Bras, J. L.; Muzart, J. *Chem. Rev.* **2011**, *111*, 1170–1214; (k) Liégault, B.; Renaud, J.-L.; Bruneau, C. *Chem. Soc. Rev.* **2008**, *37*, 290–299; (l) Orru, R. V. A.; Greef, M. *Synthesis* **2003**, *10*, 1471–1499.
2. (a) Bruggink, A.; Schoevaart, R.; Kieboom, T. *Org. Process Res. Dev.* **2003**, *7*, 622–640; (b) Maddaford, S. P.; Andersen, N. G.; Cristofoli, W. A.; Keay, B. A. *J. Am. Chem. Soc.* **1996**, *118*, 10766–10773; (c) Overman, L. E.; Rosen, M. D. *Angew. Chem.* **2000**, *112*, 4768–4771; *Angew. Chem., Int. Ed.* **2000**, *39*, 4596–4599; (d) Grigg, R.; Fretwell, P.; Meerholtz, C.; Sridharan, V. *Tetrahedron* **1994**, *50*, 359–370; (e) Fielding, M. R.; Grigg, R.; Sridharan, V.; Thornto-Pett, M.; Urch, C. J. *Tetrahedron* **2001**, *57*, 7737–7748; (f) Shi, L.; Narula, C. K.; Mak, K. T.; Kao, L.; Xu, Y.; Heck, R. F. *J. Org. Chem.* **1983**, *48*, 3894–3900; (g) Cuny, G.; Bois-Choussy, M.; Zhu, J. *J. Am. Chem. Soc.* **2004**, *126*, 14475–14484; (h) Zhang, H.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 5132–5138; (i) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F. *Synlett* **2000**, 394–396; (j) Dyker, G. *J. Org. Chem.* **1993**, *58*, 6426–6428; (k) Xu, X.; Qian, Y.; Yang, L.; Hu, W. *Chem. Commun.* **2011**, 797–799; (l) Xu, X.; Hu, W.-H.; Zavalij, P. Y.; Doyle, M. P. *Angew. Chem.* **2011**, *123*, 11348–11351; *Angew. Chem., Int. Ed.* **2011**, *50*, 11152–11155; (m) Peter Wipf, P.; Stephenson, C. R. J.; Okumura, K. *J. Am. Chem. Soc.* **2003**, *125*, 14694–14695; (n) Nair, V.; Rajesh, C.; Vinod, A. U.; Bindu, S.; Sreekanth, A. R.; Mathen, J. S.; Balagopal, L. *Acc. Chem. Res.* **2003**, *36*, 899–907; (o) Zhu, J. *Eur. J. Org. Chem.* **2003**, *7*, 1133–1144; (p) Hu, W.; Xu, X.; Zhou, J.; Liu, W.-J.; Huang, H.; Hu, J.; Yang, L.; Gong, L.-Z. *J. Am. Chem. Soc.* **2008**, *130*, 7782–7783; (q) Truong, P.; Xu, X.; Doyle, M. P. *Tetrahedron Lett.* **2011**, *52*, 2093–2096.
3. (a) Shiri, M. *Chem. Rev.* **2012**, *112*, 3508–3549; (b) Lebel, H.; Ladjel, C.; Brthous, L. *J. Am. Chem. Soc.* **2007**, *129*, 13321–13326; (c) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Art, S.; Nomura, M. *J. Org. Chem.* **1998**, *63*, 5211–5215.
4. Negishi, E.-I.; Copéret, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365–393.
5. For some recent domino one-pot Pd-catalyzed transformations, see: (a) Chowdhury, C.; Mukherjee, S.; Chakraborty, B.; Achari, B. *Org. Biomol. Chem.* **2011**, *9*, 5856–5862; (b) Lubkoll, J.; Millemaggi, A.; Perry, A.; Taylor, R. J. K. *Tetrahedron* **2010**, *66*, 6606–6612; (c) Rao, M. L. N.; Dasgupta, P. *Tetrahedron Lett.* **2012**, *53*, 162–165; (d) Laleu, B.; Lautens, M. *J. Org. Chem.* **2008**, *73*, 9164–9167; (e) Selander, N.; Szabó, K. J. *J. Org. Chem.* **2009**, *74*, 5695–5698; (f) Cheng, Y.; Duan, Z.; Yu, L.; Li, Z.; Zhu, Y.; Wu, Y. *Org. Lett.* **2008**, *10*, 901–904; (g) Satyanarayana, G.; Maier, M. E. *Org. Lett.* **2008**, *10*, 2361–2364; (h) Kim, I.; Kim, K. *Org. Lett.* **2010**, *12*, 2500–2503; (i) Satyanarayana, G.; Maier, M. E. *Eur. J. Org. Chem.* **2008**, 5543–5552; (j) Leogane, O.; Lebel, H. *Angew. Chem.* **2008**, *120*, 356–358; *Angew. Chem., Int. Ed.* **2008**, *47*, 350–352; (k) Barluenga, J.; Mendoza, A.; Rodríguez, F.; Fañanás, F. J. *Angew. Chem.* **2009**, *121*, 1672–1675; *Angew. Chem., Int. Ed.* **2009**, *48*, 1644–1647; (l) Liang, Y.; Meng, T.; Zhang, H.-J.; Xi, Z. *Synlett* **2011**, 911–914; (m) Toyoshima, T.; Mikano, Y.; Miura, T.; Murakami, M. *Org. Lett.* **2010**, *12*, 4584–4587; (n) Schweinitz, A.; Chtchemelinine, A.; Orellana, A. *Org. Lett.* **2011**, *13*, 232–235; (o) Jafarpour, F.; Jalalimanesh, N. *Tetrahedron* **2012**, *68*, 10286–10292; (p) Cho, C. S.; Lim, D. K.; Zhang, J. Q.; Kim, T.-J.; Shim, S. C. *Tetrahedron Lett.* **2004**, *45*, 5653–5656; (q) Hashmi, A. S. K.; Ghanbari, M.; Rudolph, M.; Rominger, F. *Chem.—Eur. J.* **2012**, *18*, 8113–8119; (r) Hashmi, A. S. K.; Lothschütz, C.; Döpp, R.; Ackermann, M.; Becker, J. D. B.; Rudolph, M.; Scholz, C.; Rominger, F. *Adv. Synth. Catal.* **2012**, *354*, 133–137; (s) Hashmi, A. S. K.; Lothschütz, C.; Döpp, R.; Rudolph, M.; Ramamurthi, T. D.; Rominger, F. *Angew. Chem.* **2009**, *121*, 8392–8395; *Angew. Chem., Int. Ed.* **2009**, *48*, 8243–8246.
6. For some recent sequential one-pot Pd-catalyzed transformations, see: (a) Song, R.-J.; Liu, Y.; Li, R.-J.; Li, J.-H. *Tetrahedron Lett.* **2009**, *50*, 3912–3916; (b) Nassar-Hardy, L.; Fabre, S.; Amer, A. M.; Fouquet, E.; Felpin, F.-X. *Tetrahedron Lett.* **2012**, *53*, 338–341; (c) Zhou, Y.; Zhao, Y.; Dai, X.; Liu, J.; Li, L.; Zhang, H. *Org. Biomol. Chem.* **2011**, *9*, 4091–4097; (d) Lee, J.-Y.; Ho Lee, P. *J. Org. Chem.* **2008**, *73*, 7413–7416; (e) Matsuda, T.; Shigeno, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 5219–5221; (f) Zhao, Y.; Zhou, Y.; Liang, L.; Yang, X.; Du, F.; Li, L.; Zhang, H. *Org. Lett.* **2009**, *11*, 555–558; (g) Peng, J.; Jiang, D.; Lin, W.; Chen, Y. *Org. Biomol. Chem.* **2007**, *5*, 1391–1396.
7. For reviews on domino Heck reactions, see: (a) Negishi, E.; Copret, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365–394; (b) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009–3066; (c) Dounay, A. B.; Overman, L. E. *Chem. Rev.* **2003**, *103*, 2945–2964; (d) Dupont, J.; Consorti, C. S.; Spencer, J. *Chem. Rev.* **2005**, *105*, 2527–2572.
8. For recent domino Heck cyclizations, see: (a) Ruck, R. T.; Huffman, M. A.; Kim, M. M.; Shevlin, M.; Kandur, W. V.; Davies, I. W. *Angew. Chem.* **2008**, *120*, 4789–4792; *Angew. Chem., Int. Ed.* **2008**, *47*, 4711–4714; (b) Satyanarayana, G.; Maichle-Mössmerzb, C.; Maier, M. E. *Chem. Commun.* **2009**, 1571–1573; (c) Hu, Y.; Yu, C.; Ren, D.; Hu, Q.; Zhang, L.; Cheng, D. *Angew. Chem.* **2009**, *121*, 5556–5559; *Angew. Chem., Int. Ed.* **2009**, *48*, 5448–5451; (d) Tietze, L. F.; Düfert, A.; Lotz, F.; Sölter, L.; Oum, K.; Lenzer, T.; Beck, T.; Herbst-Irmer, R. *J. Am. Chem. Soc.* **2009**, *131*, 17879–17884.
9. For recent domino Heck couplings, see: (a) René, O.; Lapointe, D.; Fagnou, K. *Org. Lett.* **2009**, *11*, 4560–4563; (b) Lu, Z.; Hu, C.; Guo, J.; Li, J.; Cui, Y.; Jia, Y. *Org. Lett.* **2010**, *12*, 480–483; (c) Hussain, M.; Toguem, S.-M. T.; Ahmad, R.; Tùng, Đ. T.; Knepper, I.; Villinger, A.; Langer, P. *Tetrahedron* **2011**, *67*, 5304–5318; (d) Ullah, I.; Nawaz, M.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2011**, *52*, 1888–1890.
10. (a) Terao, Y.; Satoh, T.; Miura, M.; Nomura, M. *Tetrahedron* **2000**, *56*, 1315–1320; (b) Tua, S.; Shaa, Y.; Xub, L.-H.; Xiaoa, Z.-Y.; Yea, L.-Y.; Fanga, J. *J. Chem. Res.* **2010**, 254–258.
11. (a) Dyker, G.; Grundt, P. *Tetrahedron Lett.* **1996**, *37*, 619–622.
12. (a) Khan, M. W.; Reza, A. F. G. M. *Tetrahedron* **2005**, *61*, 11204–11210; (b) Rolfe, A.; Young, K.; Hanson, P. R. *Eur. J. Org. Chem.* **2008**, 5254–5262; (c) Priebbenow, L. D. L.; Stewartb, S. G.; Pfeffer, F. M. *Org. Biomol. Chem.* **2011**, *9*, 1508–1515; (d) Priebbenow, D. L.; Pfeffer, F. M.; Stewart, S. G. *Eur. J. Org. Chem.* **2011**, 1632–1635.
13. (a) Reddy, A. G. K.; Krishna, J.; Satyanarayana, G. *Synlett* **2011**, 1756–1760; (b) Krishna, J.; Reddy, A. G. K.; Mahendar, L.; Ramulu, B. V. *Synlett* **2012**, 375–380; (c) Mahendar, L.; Krishna, J.; Reddy, A. G. K.; Ramulu, B. V. *Org. Lett.* **2012**, *14*, 628–631; (d) Reddy, A. G. K.; Satyanarayana, G. *Tetrahedron* **2012**, *68*, 8003–8010; (e) Suchand, B.; Krishna, J.; Ramulu, B. V.; Dibyendu, D.; Reddy, A. G. K.; Mahendar, L.; Satyanarayana, G. *Tetrahedron Lett.* **2012**, *53*, 3861–3864.
14. Reddy, A. G. K.; Krishna, J.; Satyanarayana, G. *Tetrahedron Lett.* **2012**, *53*, 5635–5640.
15. For xylarinol (A) and xylarinol (B), see: In-Kyoung, L.; Yun-Woo, J.; Young-Sook, K.; Hun, Y. S.; Jae, L. K.; Seung-Moon, P.; Byung-Taek, O.; Jong-Chan, C.; Bong-Sik, Y. J. *Antibiotics* **2009**, *62*, 163–165.
16. For ulocladol, see: Ulrich, H.; Gabriele, K.; Anthony, D. W. *Eur. J. Org. Chem.* **1999**, *11*, 2949–2955.
17. For alterlactone, see: Aly, A. H.; Edrada-Ebel, R.; Indriani, I. D.; Wray, V.; Müller, W. E. G.; Totzke, F.; Zirrgiebel, U.; Schächtele, C.; Kubbutat, M. H. G.; Lin, W. H.; Proksch, P.; Ebe, R. *J. Nat. Prod.* **2008**, *71*, 972–980.
18. (a) Glukhov, A. A.; Kirillov, N. F.; Potapova, A. A.; Makhmudov, R. R.; Mardanova, L. G. *Pharm. Chem. J.* **2010**, *44*, 483–485; (b) Yus, M.; Soler, T.; Foubelo, F. *Tetrahedron* **2002**, *58*, 7009–7016; (c) Oh, C. H.; Park, S. J. *Tetrahedron Lett.* **2003**, *44*, 3785–3787; (d) Matsuda, T.; Shigeno, M.; Murakami, M. *J. Am. Chem. Soc.* **2007**, *129*, 12086–12087.
19. (a) Cho, C. S.; Shim, S. C. *Bull. Korean Chem. Soc.* **2006**, *27*, 776–779 For review, see: (b) Muzart, J. *Tetrahedron* **2005**, *61*, 5955–6008.
20. CCDC number for the compound **5ac** CCDC 930424.