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PAPER

# A biomass-involved strategy for the synthesis of N-arylated dibenzo[b,e][1,4]oxazepin-11(5H)-ones, acridones, 7, 12-dihydrodibenzo[b,e][1,4]oxazocin-6H-ones and dibenzo[b,f]azepin-10(11H)-ones

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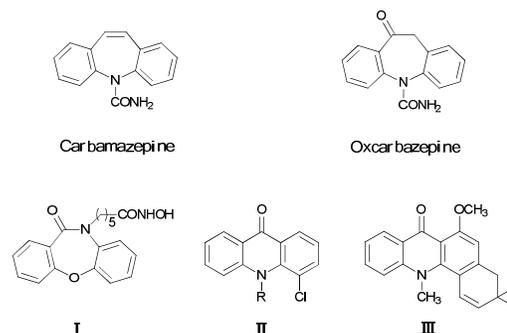
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An efficient method for the assembly of novel and diversified benzo-fused N-heterocycles mediated by the biomass-derived N-arylated 2-aminophenol (**1**) has been established. Four kinds of benzo-fused N-heterocycles with six- to eight-membered ring systems, including N-arylated dibenzo[b,e][1,4]oxazepin-11(5H)-ones (**4**), acridones (**5**), 7, 12-dihydrodibenzo[b,e][1,4]oxazocin-6H-ones (**6**) and dibenzo[b,f]azepin-10(11H)-ones (**7**) have been efficiently synthesized in good to excellent yields respectively. This process is comprised of the N-arylation reaction between N-arylated 2-aminophenols (**1**) and 2-halogenated benzoic or phenylacetic acids to afford a series of multifunctionalized triaryl amines (**3**), followed by chemo- and regio-selective intramolecular lactonization or acylation under mild conditions.

## Introduction

Benzo-fused N-heterocycles, especially those with six- to eight-membered systems such as dibenzazepines and acridones represent an intriguing class of heterocycles prevalent in various pharmaceuticals, bioactive compounds and nature products.<sup>1</sup> For instance, the most frequently used antiepileptic drugs carbamazepine<sup>2</sup> and its analogue oxcarbazepine<sup>3</sup> as well as the histone deacetylase inhibitor<sup>4</sup> (**I**) are all characterized by the dibenzazepine core structure. The cytotoxic agent chloroacridone<sup>5</sup> (**II**) and the pyranoacridone alkaloid acronycine<sup>6</sup> (**III**) also possess an acridone scaffold (**Fig. 1**). To the best of our knowledge, although great efforts have been made for the construction of these benzo-fused six- to eight-membered N-heterocycles,<sup>7</sup> the structural diversity of these compounds is still limited. Moreover, no protocol for the construction of N-aryl-dibenzo[b,e][1,4]oxazepin-11(5H)-ones (**4**), N-aryl-7, 12-dihydro-dibenzo[b,e][1,4]oxazocin-6(H)-ones (**6**) as well as N-aryl-dibenzo[b,f]azepin-10(11H)-ones (**7**) has been reported thus far (**Scheme 1**). In addition, only a few approaches for access to N-aryl acridones have been documented. Ground-breaking works leading to N-aryl acridones reported by Cheng and Deng respectively, involved the reaction of copper-catalyzed intramolecular oxidative C-H functionalization and C-N formation



**Figure 1.** Examples of drugs, biologically active compounds and nature product containing the benzo-fused N-heterocycle motif.

of phenyl-(2-phenylaminophenyl)methanone.<sup>8</sup> Another method for the synthesis of N-aryl acridones included an intermolecular insertion reaction of benzyne with amides or  $\beta$ -lactams, followed by stepwise intramolecular transformations.<sup>9</sup> Although each of these approaches represents a workable access to N-aryl acridones, novel and efficient methods are still needed. In view of the above, a practical approach that is facile, efficient and could enhance the structural diversity and complexity for these benzo-fused six- to eight-membered N-heterocycles would be genuinely attractive.

With the diminishing of fossil oil reserves and the increasing concerns about the environment and sustainability, the development of novel and efficient biomass-involved strategies to meet our needs for chemical and pharmaceutical products has drawn worldwide attention.<sup>10</sup> In the last decade, chemo- and regio-selective synthesis of intermediates and fine chemicals from renewable biomass or biomass-derived substrates represents

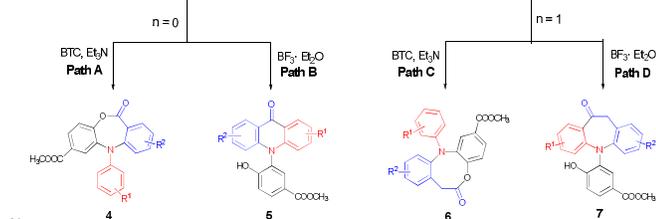
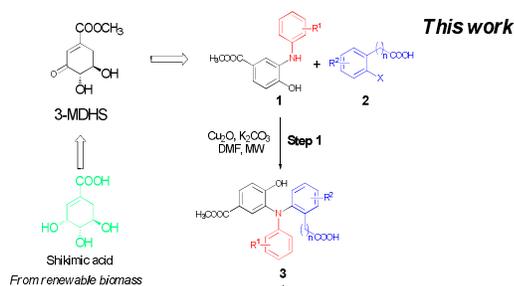
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one of the most important progress in organic chemistry.<sup>11</sup> Our recent studies showed that the methyl 3-dehydroshikimate (3-MDHS), which was readily synthesized from (-)-shikimic acid could serve as a versatile and highly efficient reagent for various N-arylation processes, and could be used to generate a series of platform compounds, namely N-substituted 2-aminophenols (**1**)<sup>12</sup> (Scheme 1). We envisioned that **1** could readily couple with 2-halogenated benzoic acids or 2-halogenated phenylacetic acids to afford the multifunctionalized triaryl amines (**3**), which could serve as successive platform compounds with great potential for further transformations. Subsequent cyclization under different conditions would give rise to a range of N-arylated benzo-fused heterocycles (Scheme 1). As a part of our continuing efforts towards biomass conversion and the biomass-involved construction of bioactive molecules,<sup>13</sup> we herein report a chemo- and regio-selective strategy for the facile synthesis of four kinds of novel six- to eight-membered, benzo-fused N-heterocycles from the renewable feedstock (-)-shikimic acid (Scheme 1).



**Scheme 1.** The strategy for the synthesis of four kinds of six- to eight-membered, benzo-fused N-heterocycles.

## Results and Discussion

Based on the well-established protocol for the preparation of N-aryl 2-aminophenols (**1**) from the abundantly available (-)-shikimic acid<sup>12</sup>, we chose the reaction of **1a** and 2-iodobenzoic acid (**2a**) as the model reaction to screen conditions for access to triaryl amine (**3a**) (Scheme 1, step 1) under microwave irradiation (Table 1). To our delight, the N-arylation reaction proceeded smoothly in the presence of Cu<sub>2</sub>O (20 mol %) in DMF with high chemo-selectivity providing the highly functionalized triaryl amine (**3a**) in good yield (87 %), whereas no O-arylated product (**3a'**) was detected (Table 1, entry 1). Other copper catalysts such as Cu(OAc)<sub>2</sub>, CuSO<sub>4</sub>, Cu(NO<sub>3</sub>)<sub>2</sub> were used, but could only afford **3a** in moderate yields (Table 1, entries 2-4). Interestingly, a blue solution was formed in the work-up procedure when we diluted the filtrate of the reaction mixture with water (20 % Cu<sub>2</sub>O was used as catalyst, Table 1, entry 1), which indicated that the more catalytically active Cu(I) species might

**Table 1.** Screening of reaction conditions for step 1<sup>a</sup>

Entry	Catalyst	Base	<i>t</i> <sub>1</sub> (min)	Yield (%) <sup>b</sup>
1 <sup>c</sup>	Cu <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	8	87
2 <sup>c</sup>	Cu(OAc) <sub>2</sub>	K <sub>2</sub> CO <sub>3</sub>	10	56
3 <sup>c</sup>	CuSO <sub>4</sub>	K <sub>2</sub> CO <sub>3</sub>	10	60
4 <sup>c</sup>	Cu(NO <sub>3</sub> ) <sub>2</sub>	K <sub>2</sub> CO <sub>3</sub>	10	53
5	Cu <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	8	95
6 <sup>d</sup>	Cu <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	8	72
7 <sup>e</sup>	Cu <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	6	95
8 <sup>f</sup>	Cu <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	6	52
9 <sup>g</sup>	Cu <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	6	69
10 <sup>h</sup>	Cu <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	300	89
11	Cu <sub>2</sub> O	Na <sub>2</sub> CO <sub>3</sub>	8	87
12	Cu <sub>2</sub> O	CS <sub>2</sub> CO <sub>3</sub>	8	95

<sup>a</sup> Reaction conditions: **1a** (0.24 g, 1 mmol), **2a** (0.25 g, 1 mmol), DMF (5 ml), catalyst (20 mol%), base (3 mmol) at 120 °C for indicated minutes under N<sub>2</sub> atmosphere. <sup>b</sup> Isolated yields. <sup>c</sup> Reaction carried out in air. <sup>d</sup> Reaction carried out in O<sub>2</sub> atmosphere. <sup>e</sup> 1 mmol Cu<sub>2</sub>O used as the catalyst. <sup>f</sup> 20 % 1,10-phenanthroline used as the ligand. <sup>g</sup> 20 % mmol 2, 2'-bipyridine used as the ligand. <sup>h</sup> Reaction carried out in an oil bath.

be partially oxidized to the less active Cu(II) species during the reaction under air conditions. Hence, control experiments were carried out with Cu<sub>2</sub>O (20 mol %) used as the catalyst under N<sub>2</sub> or O<sub>2</sub> atmosphere respectively. As shown in Table 1, an excellent yield (95 %) of **3a** was obtained when the N-arylation reaction was performed under N<sub>2</sub> atmosphere (Table 1, entry 5), while only a moderate yield was obtained when the reaction was carried out under O<sub>2</sub> atmosphere (Table 1, entry 6). Increasing the amount of catalyst to 1 equiv., no obvious improvement of the yield was observed (Table 1, entry 7). Unexpectedly, when 20 mol % 1,10-phenanthroline or 2, 2'-bipyridine were used as the ligands, a sharp decrease of the yields was observed, which might be due to side reactions such as decarboxylation reaction being accelerated by the ligands. In comparison, the reaction was also carried out in an oil bath at 120 °C for 5 hours and a slightly lower yield was obtained (89 %, Table 1, entry 10). It is worth mentioning that, although other inorganic bases such as Na<sub>2</sub>CO<sub>3</sub>, Cs<sub>2</sub>CO<sub>3</sub> were also effective for this copper catalyzed chemo-selective N-arylation reaction (Table 1, entries 11-12), we eventually chose K<sub>2</sub>CO<sub>3</sub> as the base for economic considerations. Thus, the optimized reaction conditions for the construction of the triaryl amine intermediate **3a** (Step 1) consist of **1a** (1 mmol), **2** (0.25 g, 1 mmol), DMF (5 ml), Cu<sub>2</sub>O (20 mol %), and K<sub>2</sub>CO<sub>3</sub> (3 mmol) under N<sub>2</sub> atmosphere in microwave conditions.

The thus obtained highly functionalized triaryl amines **3** which contained multiple active groups, displayed a good opportunity for further chemo-selective manipulations. We deduced that the N-aryl dibenzo[b,e][1,4]oxazepin-11(5*H*)-ones (**4**) and the N-aryl acridones (**5**) could be obtained respectively via a dehydration

**Table 2.** Screening of reaction conditions for step 2.

Entry	Catalyst (Path A)	Catalyst (Path B)	$t_2$ (h)	Yield (%) <sup>a</sup> (4a)	Yield (%) <sup>a</sup> (5a)
1 <sup>c</sup>	PTSA	--	8	30	55
2	SOCl <sub>2</sub>	--	5	76	10
3 <sup>d</sup>	DCC/DMAP	--	12	62	ND <sup>b</sup>
4 <sup>e</sup>	BTC	--	3	96	ND <sup>b</sup>
5 <sup>f</sup>	--	PPA	2	Trace	Trace
6 <sup>g</sup>	--	BF <sub>3</sub> ·Et <sub>2</sub> O	3	ND <sup>b</sup>	92
7	--	AlCl <sub>3</sub>	12	ND <sup>b</sup>	Trace

<sup>a</sup> Isolated yield. <sup>b</sup> ND: not detected. <sup>c</sup> Reaction conditions: **3a** (0.36 g, 1 mmol), PTSA (0.1 mmol), toluene (5 ml) reflux for indicated hours. <sup>d</sup> Reaction conditions: **3a** (0.36 g, 1 mmol), DCC (0.41 g, 2 mmol), DMAP (12 mg, 0.1 mmol) and THF (5 ml). <sup>e</sup> Reaction conditions: **3a** (0.36 g, 1 mmol), BTC (0.29 g, 1 mmol), Et<sub>3</sub>N (4 mmol) and DCM (5 ml). <sup>f</sup> Reaction conditions: **3a** (0.36 g, 1 mmol) and PPA (5 ml) heated at 100 °C for indicated hours. <sup>g</sup> Reaction conditions: **3a** (0.36 g, 1 mmol) in BF<sub>3</sub>·Et<sub>2</sub>O (5 ml) heated at 60 °C for 3 h.

process, one through intramolecular esterification (Scheme 1, Path A) and the other through intramolecular acylation (Scheme 1, Path B). Accordingly, **3a** was chosen as the model substrate to screen the catalysts suitable for these transformations (Table 2, entries 1-7). Results showed that treatment of **3a** with PTSA (10 %) in toluene for 8 h gave rise to the esterification product **4a** in 30 % yield and the acylation product **5a** in 55 % yield, respectively (Table 2, entry 1). The same reaction promoted by SOCl<sub>2</sub> (2 equiv.) in dichloromethane in an ice bath afforded **4a** with a higher selectivity (76 % for **4a**, 10 % for **5a**, Table 2, entry 2). We have also found that **4a** could be obtained in 62 % yield in the presence of DCC/DMAP in THF at 65 °C for 12 h, whereas **5a** was not detected in the reaction mixture (Table 2, entry 3). Gratifyingly, when bis(trichloromethyl)carbonate (BTC) was used as the catalyst, the esterification reaction was performed selectively and efficiently at room temperature, affording **4a** in 96 % yield with no **5a** obtained (Table 2, entry 4). Attempts for selective construction of **5a** were also made, we have found that, although the polyphosphoric acid (PPA) had previously proven to be an efficient catalyst for acylation reactions,<sup>14</sup> it failed to convert **3a** into **5a** in the present conditions, presumably due to the side reaction caused by the hydroxyl group (Table 2, entry 5). Much to our surprise, when BF<sub>3</sub>·Et<sub>2</sub>O was used as the catalyst, the acylation reaction proceeded efficiently with high chemo- and regio-selectivity, affording **5a** in 92 % yield, whereas no **4a** was detected (Table 2, entry 6). However, only trace amount of **5a** was obtained when **3a** was treated with 4 equiv. AlCl<sub>3</sub> in DCM for 12 h (Table 2, entry 7). Thus, the optimized reaction conditions for the selective formation of **4a** and **5a** include: treatment of **3a** (1 mmol) with BTC (0.30 g, 1 mmol) in the presence of Et<sub>3</sub>N (4 mmol) in DCM gave **4a** (Table 2, Path A), and treatment of **3a** (1 mmol) with BF<sub>3</sub>·Et<sub>2</sub>O afforded **5a** (Table 2, Path B).

With the optimized reaction conditions in hand, we

**Table 3.** Scope for the synthesis of N-aryl dibenzo[b,e][1,4]oxazepin-11(5H)-ones<sup>a</sup>

Entry	<b>1</b>	(Ar)	$t_1/t_2$ (min/h)	Product	Yield (%) <sup>b</sup>
1	<b>1a</b>	Ph	8/3	<b>4a</b>	91
2	<b>1b</b>	4-MeC <sub>6</sub> H <sub>4</sub>	8/3	<b>4b</b>	91
3	<b>1c</b>	4-OMeC <sub>6</sub> H <sub>4</sub>	8/3	<b>4c</b>	93
4	<b>1d</b>	4-FC <sub>6</sub> H <sub>4</sub>	10/4	<b>4d</b>	83
5	<b>1e</b>	4-ClC <sub>6</sub> H <sub>4</sub>	10/3	<b>4e</b>	85
6	<b>1f</b>	4-BrC <sub>6</sub> H <sub>4</sub>	10/3	<b>4f</b>	85
7	<b>1g</b>	4-AcC <sub>6</sub> H <sub>4</sub>	12/4	<b>4g</b>	78
8	<b>1h</b>	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	12/4	<b>4h</b>	80
9	<b>1i</b>	2-MeC <sub>6</sub> H <sub>4</sub>	12/4	<b>4i</b>	87
10	<b>1j</b>	2,5-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	15/5	<b>4j</b>	65
11	<b>1k</b>	3-MeC <sub>6</sub> H <sub>4</sub>	8/3	<b>4k</b>	90
12	<b>1l</b>	3-ClC <sub>6</sub> H <sub>4</sub>	10/3	<b>4l</b>	83
13	<b>1m</b>	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	12/4	<b>4m</b>	82
14	<b>1n</b>	3-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	13/4	<b>4n</b>	75
15	<b>1o</b>	1-naphthyl	17/5	<b>4o</b>	68
16	<b>1p</b>	4-(4-ClC <sub>6</sub> H <sub>4</sub> )C <sub>6</sub> H <sub>4</sub>	10/3	<b>4p</b>	85

<sup>a</sup> Reaction conditions: **1** (1 mmol), 2-iodobenzoic acid (0.25 g, 1.0 mmol), K<sub>2</sub>CO<sub>3</sub> (3 mmol), DMF (5 ml) and Cu<sub>2</sub>O (20 mol %) at 120 °C for indicated minutes ( $t_1$ ) under microwave irradiation with the protection of N<sub>2</sub> atmosphere (Step 1); the isolated intermediate **3**, BTC (0.30 g, 1 mmol) and Et<sub>3</sub>N (4 mmol) in DCM (5 ml) at room temperature for  $t_2$  hours (Step 2). <sup>b</sup> Isolated yields based on **1**.

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further investigated the substrate scope for the synthesis of N-aryl dibenzo[b,e][1,4]oxazepin-11(5H)-ones (**4**). As summarized in Table 3, a wide range of functional groups such as Me, OMe, F, Cl, Br, NO<sub>2</sub> and CF<sub>3</sub> were compatible in this two step transformation, affording the corresponding products (**4a-4p**) in very good to excellent yields. Generally, substrates possessing an electron-donating group tended to give better yields than those bearing an electron-withdrawing group. For example, **1b** and **1c**

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**Table 4.** Scope for the synthesis of N-aryl dibenzo[b,e][1,4]oxazepin-11(5H)-ones<sup>a</sup>

Entry	<b>2</b>	R <sup>2</sup>	$t_1/t_2$ (min/h)	Product	Yield (%) <sup>b</sup>
1	<b>2a</b> , X=I	H	8/3	<b>4a</b>	91
2	<b>2b</b> , X=Br	H	10/3		85
3	<b>2c</b> , X=Cl	H	20/3		62
4	<b>2d</b> , X=F	H	30/--		ND <sup>c</sup>
5	<b>2e</b> , X=Br	4-F	8/4	<b>4q</b>	87
6	<b>2f</b> , X=Cl	5-NO <sub>2</sub>	12/4	<b>4r</b>	79

<sup>a</sup> Reaction conditions: **1a** (1 mmol), 2-halogenated benzoic acids (1 mmol), K<sub>2</sub>CO<sub>3</sub> (3 mmol) and DMF (5 ml) with Cu<sub>2</sub>O (20 mol %) as catalyst for step 1; the isolated intermediate **3**, BTC (0.30 g, 1 mmol) and Et<sub>3</sub>N (4 mmol) in DCM (5 ml) for step 2. <sup>b</sup> Isolated yield. <sup>c</sup> ND: not detected.

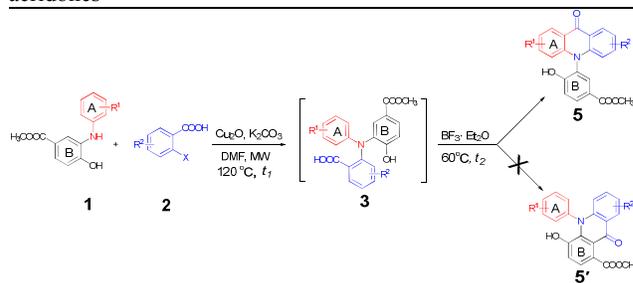
gave rise to **4b** and **4c** in excellent yields (Table 3, entries 2-3), whereas **1g** and **1h** afforded **4g** and **4h** in moderate yields (Table 3, entries 7-8). Steric effect was also observed, for substrates which were *ortho*-substituted such as **1i** and **1j** afforded the corresponding products **4i** and **4j** in relative lower yields (Table 3, entries 9-10). To our gratification, the N-naphthyl substituted substrate **1o** as well as the N-biphenyl substituted substrate **1p** were also compatible under the optimized reaction conditions and furnished the desired products **4o** and **4p** (Table 3, entries 15-16) in moderate and good yields.

Inspired by these encouraging results, we next explored the scope of substrate **2** using various 2-halogenated benzoic acids under the optimized reaction conditions (Table 4). Results showed that 2-iodobenzoic acid (**2a**), 2-bromobenzoic acid (**2b**) as well as 2-chlorobenzoic acid (**2c**) could chemo-selectively couple with **1a** to afford the corresponding triarylamine **3a**, which could subsequently undergo the intramolecular esterification to furnish the desired products **4a** in moderate to excellent yields (Table 4, entries 1-3). However, no desired product was detected when 2-fluorobenzoic acid (**2d**) was used as the reactant (Table 4, entry 4). Gratifyingly, 2-halogenated benzoic acids with an additional substituent such as -F or -NO<sub>2</sub> were also workable in this process. For example, the desired products **4q** and **4r** were obtained in 87% yield (entry 5) and 79% yield (entry 6) when 2-bromo-4-fluorobenzoic acid (**2e**) and 2-chloro-5-nitrobenzoic acids (**2f**) respectively were used as the substrate under the optimized reaction conditions.

Under the aforementioned optimal reaction conditions for the synthesis of N-aryl acridones, a wide variety of N-arylated 2-aminophenols (**1a-1f**, **1h** and **1p**) and 2-halogen benzoic acids (**2a** and **2e**) were subjected to the reaction conditions (Table 5). Intriguingly, the intramolecular acylation reaction of functionalized triarylamine intermediates **3** occurred selectively at A-ring, leading to the desired products **5** in moderate to good yields, whereas **5'** to which the acylation reaction should take place at B-ring was not detected. As expected, electron-donating groups or halogen atoms on A-ring were beneficial to the acylation reaction. Substrates bearing a Me, OMe, Cl and Br group (**1b**, **1c**, **1e** and **1f**) performed smoothly in this two-step transformations and gave rise to the desired products **5b**, **5c**, **5e** and **5f** in very good to excellent yields. Even with a strong electron-withdrawing group, such as the fluorinated substrate **1d** (R<sub>1</sub> = 4-F), a 72% yield of the desired product **5d** could still be obtained by reacting with 2-iodobenzoic acid. However, no acylation product **5h** was detected in the case of **1h** bearing the strong electron-withdrawing 4-nitro group (Scheme 2 and Table 5). Fortunately and gratifyingly, we still managed to obtain **5h** in a 75% yield when **1a** (R<sub>1</sub> = H) and **2f** (X = Cl, R<sub>2</sub> = 5-NO<sub>2</sub>) were used as the reactants (Scheme 2). This interesting result provided an alternative and effective approach towards the N-aryl acridones bearing electron-withdrawing group(s) in one of the aryl ring. It is worth noting that, biphenyl substrate **1p** was also compatible and afforded the desired product **5p** in 85% yield. Moreover, fluorine substituted 2-halogenated benzoic acid such as 2-bromo-4-fluorobenzoic acid (**2e**) could also be converted to N-arylacridone (**5q**) in good yield (83%).

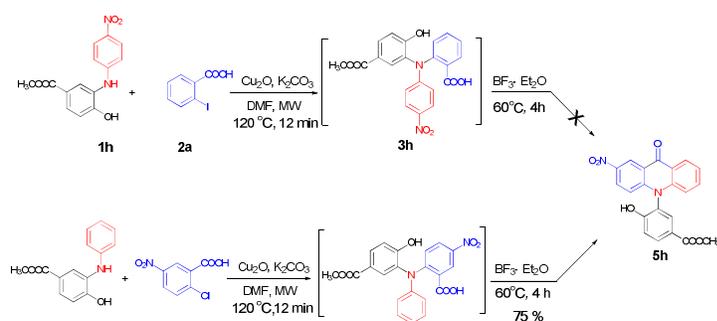
Finally, the substrate scope of this chemo- and regio-selective strategy based upon the biomass-derived N-aryl 2-aminophenols

**Table 5.** Chemo- and regio- selective synthesis of N-aryl acridones<sup>a</sup>



<i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (min/h), Yield (%) <sup>b</sup>		
 <b>5a</b> R <sub>1</sub> = H, R <sub>2</sub> = H X = I <i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (8/3), 87 %	 <b>5b</b> R <sub>1</sub> = 4-CH <sub>3</sub> , R <sub>2</sub> = H X = I <i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (8/3), 87 %	 <b>5c</b> R <sub>1</sub> = 4-OCH <sub>3</sub> , R <sub>2</sub> = H X = I <i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (8/3), 89 %
 <b>5d</b> R <sub>1</sub> = 4-F, R <sub>2</sub> = H X = I <i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (10/4), 72 %	 <b>5e</b> R <sub>1</sub> = 4-Cl, R <sub>2</sub> = H X = I <i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (10/3), 78 %	 <b>5f</b> R <sub>1</sub> = 4-Br, R <sub>2</sub> = H X = I <i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (10/3), 82 %
 <b>5h</b> R <sub>1</sub> = 4-NO <sub>2</sub> , R <sub>2</sub> = H X = I <i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (12/4), ND <sup>c</sup>	 <b>5p</b> R <sub>1</sub> = 4-(4-chlorophenyl) R <sub>2</sub> = H, X = I <i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (10/3), 85 %	 <b>5q</b> R <sub>1</sub> = H, R <sub>2</sub> = 4-F X = Br <i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (8/3), 83 %

<sup>a</sup> Reaction conditions: **1a** (1 mmol), 2-halogen benzoic acid (1.0 mmol), K<sub>2</sub>CO<sub>3</sub> (3 mmol), DMF (5 ml) and Cu<sub>2</sub>O (20 mol %) reacted at 120 °C for *t*<sub>1</sub> minutes (Step 1); the isolated intermediate **3** and BF<sub>3</sub>·Et<sub>2</sub>O (5 ml) reacted at 60 °C for *t*<sub>2</sub> h (Step 2). <sup>b</sup> Isolated yield based on **1**. <sup>c</sup> ND: not detected.



**Scheme 2.** Alternative approaches for the synthesis of **5h**

**Table 6.** Synthesis of N-aryl-7, 12-dihydrodibenzo[b,e][1,4]oxazocin-6(*H*)-ones (**6**) and N-aryl dibenzo[b,f]azepin-10(1*H*)-ones (**7**)<sup>a</sup>

Entry	X	<i>t</i> <sub>1</sub> / <i>t</i> <sub>2</sub> (min/h)	Product	Yield (%) <sup>b</sup>
1	F	10/4		85
2	Cl	8/3		89
3	F	10/3		78
4	Cl	8/3		80

<sup>a</sup> Reaction conditions: **1a** (1.0 mmol), 2-bromophenylacetic acid (1.0 mmol), K<sub>2</sub>CO<sub>3</sub> (3.0 mmol), DMF (5.0 ml) and Cu<sub>2</sub>O (20 mol %) reacted at 120 °C for *t*<sub>1</sub> minutes (Step 1); the isolated intermediate **3**, DCM (5 ml) and BTC (0.30 g, 1 mmol) using Et<sub>3</sub>N (4 mmol) for step 2 (Path C) or the isolated intermediate **3** and BF<sub>3</sub>•Et<sub>2</sub>O (5.0 ml) reacted at 60 °C for *t*<sub>2</sub> h for step 2 (Path D). <sup>b</sup> Isolated yields based on **1**.

(**1**) was also examined using 2-bromophenylacetic acid (**2g**) as the reactant. Likewise, the coupling reaction between **1** and **2g** readily afforded the key triarylamine intermediates **3** (Table 6), which would then undergo lactonization or acylation in the presence of BTC/Et<sub>3</sub>N or BF<sub>3</sub>•Et<sub>2</sub>O respectively (Scheme 1, Path C and D), and selectively provide the benzo-fused, eight-membered N-aryl lactone products **6d-6e** or seven-membered N-aryl acylation products **7d-7e** in good yields (Table 6). It is noteworthy that, high chemo- and regio-selectivity was also observed in this two step transformation, as no self-condensation products (**8**) were detected in the reaction mixture. Notably, the acylation process (Path D) provided an efficient entry for the assembly of the novel N-aryl oxcarbazepine derivatives, which had not been reported elsewhere. In addition, the structure of all of the compounds

reported in this paper were unambiguously confirmed by MS, <sup>1</sup>HNMR, <sup>13</sup>CNMR, HRMS and FT-IR.

## Conclusion

In conclusion, we have developed an efficient and practical method for the facile construction of six- to eight-membered, benzo-fused N-heterocycles from the biomass-derived N-aryl 2-aminophenols (**1**). A series of N-aryl-dibenzo[b,e][1,4]oxazepin-11(5*H*)-ones (**4**), N-aryl-acridones (**5**), N-aryl-7, 12-dihydrodibenzo[b,e][1,4]oxazocin-6(*H*)-ones (**6**) as well as N-aryl-dibenzo[b,f]azepin-10(1*H*)-ones (**7**) were efficiently synthesized via an N-arylation reaction (Step 1) and a controllable, chemo- and regio-selective intramolecular dehydration reaction (Step 2). The utilization of biomass-derived platform compounds, the operational simplicity, the controllable selectivity, the structural novelty and diversity of compounds, are notable features of this protocol and conform to the elements of green chemistry. In addition, the six- to eight-membered, benzo-fused N-heterocycles with novel structural characteristics might be beneficial in drug development.

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## Graphical Abstract

**A biomass-involved strategy for the synthesis of N-arylated dibenzo[b,e][1,4]oxazepin-11(5*H*)-ones, acridones, 7, 12-dihydrodibenzo[b,e][1,4]oxazocin-6*H*-ones and dibenzo[b,f]azepin-10(11*H*)-ones**

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A chemo- and regio-selective method for the construction of benzo-fused six- to eight-membered N-heterocycles from renewable feedstock shikimic acid is described.

