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### Concise synthesis of $\alpha$ -substituted 2-benzofuranmethamines and other 2-substituted benzofurans via $\alpha$ -substituted 2-benzofuranmethyl carbocation intermediates

Nikhom Wongsa  
*University of Wollongong*

Ubonta Sommart  
*University of Wollongong*

Thunwadee Ritthiwigrom  
*University of Wollongong, tr379@uow.edu.au*

Arife Yazici  
*University of Wollongong, arife@uow.edu.au*

Somdej Kanokmedhakul  
*Khon Kaen University*

*See next page for additional authors*

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## Concise synthesis of $\alpha$ -substituted 2-benzofuranmethamines and other 2-substituted benzofurans via $\alpha$ -substituted 2-benzofuranmethyl carbocation intermediates

### Abstract

Propargyl amines **4**, where R<sub>3</sub> is aryl, undergo 5-exo-dig cyclization reactions under relatively mild conditions (AgNO<sub>3</sub>, DMF, 60 °C, 1 h) to give 3-amino-2,3-dihydro-2-arylmethylidenebenzofurans **5** (R<sub>3</sub> = aryl). In contrast, substrates where R<sub>3</sub> is alkyl undergo competing 6-endo-dig and 5-exo-dig cyclization processes. The hydroxymethyl substrate **4** (R<sub>3</sub> = CH<sub>2</sub>OH), however, was smoothly converted to its corresponding 5-exo-dig cyclization product **5**, likely due to the assistance of the primary hydroxyl group in the 5-exo-dig cyclization process by silver cation coordination. Under more enforcing conditions (AgNO<sub>3</sub>, DMF, 100 °C, 18 h), the initially formed products **5** undergo a 1,3-allylic rearrangement to their corresponding 2-substituted benzofuran derivatives **6**. This rearrangement can also be effected by treating **5** with AgNO<sub>3</sub> in DMF at 100 °C for 18 h or BF<sub>3</sub>·Et<sub>2</sub>O at rt. 2-(3-Butenyl)benzofurans **7** (Nu = allyl) can be prepared by treatment of **5** with BF<sub>3</sub>·Et<sub>2</sub>O and allyltributylstannane. Furan and MeOH could also be employed as external nucleophiles in these BF<sub>3</sub>·Et<sub>2</sub>O-promoted reactions.

### Keywords

via, benzofurans, substituted, 2, concise, synthesis, benzofuranmethamines, substituted, other, intermediates, carbocation, benzofuranmethyl, CMMB

### Disciplines

Medicine and Health Sciences | Social and Behavioral Sciences

### Publication Details

Wongsa, N., Sommart, U., Ritthiwigrom, T., Yazici, A., Kanokmedhakul, S., Kanokmedhakul, K., Willis, A. C. & Pyne, S. G. (2013). Concise synthesis of  $\alpha$ -substituted 2-benzofuranmethamines and other 2-substituted benzofurans via  $\alpha$ -substituted 2-benzofuranmethyl carbocation intermediates. *Journal of Organic Chemistry*, 78 (3), 1138-1148.

### Authors

Nikhom Wongsa, Ubonta Sommart, Thunwadee Ritthiwigrom, Arife Yazici, Somdej Kanokmedhakul, Kwanjai Kanokmedhakul, Anthony C. Willis, and Stephen G. Pyne

# Concise Synthesis of $\alpha$ -Substituted 2-Benzofuranmethamines and Other 2-Substituted Benzofurans via $\alpha$ -Substituted 2-Benzofuranmethyl Carbocation Intermediates

Nikhom Wongsa,<sup>†,‡</sup> Ubonta Sommart,<sup>†,§</sup> Thunwadee Ritthiwigrom,<sup>†,||</sup> Arife Yazici,<sup>†</sup> Somdej Kanokmedhakul,<sup>‡</sup> Kwanjai Kanokmedhakul,<sup>‡</sup> Anthony C. Willis,<sup>⊥</sup> and Stephen G. Pyne<sup>\*,†</sup>

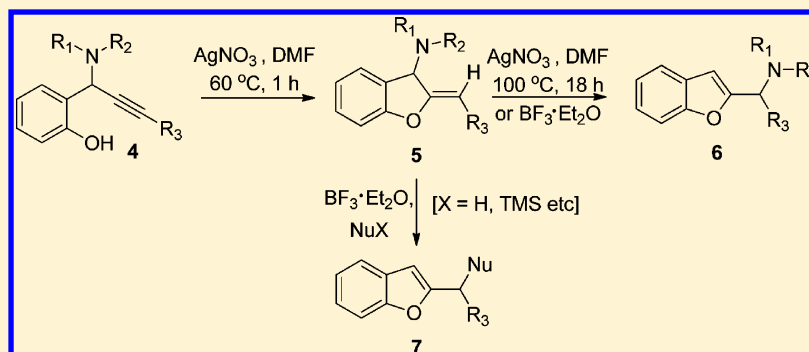
<sup>†</sup>School of Chemistry, University of Wollongong, Wollongong, New South Wales, 2522, Australia

<sup>‡</sup>Natural Products Research Unit, Department of Chemistry and Center of Excellence for Innovation in Chemistry, Faculty of Science, Khon Kaen University, Khon Kaen 40002, Thailand

<sup>§</sup>Department of Chemistry, Prince of Songkla University, Songkhla, 90112, Thailand

<sup>⊥</sup>Research School of Chemistry, Australian National University, Canberra, ACT, 0200, Australia

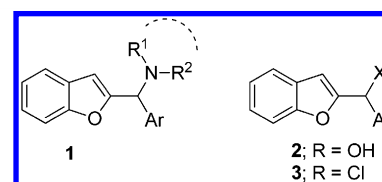
## Supporting Information



**ABSTRACT:** Propargyl amines **4**, where  $R^3$  is aryl, undergo *5-exo-dig* cyclization reactions under relatively mild conditions ( $\text{AgNO}_3$ , DMF,  $60^\circ\text{C}$ , 1 h) to give 3-amino-2,3-dihydro-2-arylmethylidenebenzofurans **5** ( $R^3 = \text{aryl}$ ). In contrast, substrates where  $R^3$  is alkyl undergo competing *6-endo-dig* and *5-exo-dig* cyclization processes. The hydroxymethyl substrate **4** ( $R^3 = \text{CH}_2\text{OH}$ ), however, was smoothly converted to its corresponding *5-exo-dig* cyclization product **5**, likely due to the assistance of the primary hydroxyl group in the *5-exo-dig* cyclization process by silver cation coordination. Under more enforcing conditions ( $\text{AgNO}_3$ , DMF,  $100^\circ\text{C}$ , 18 h), the initially formed products **5** undergo a 1,3-allylic rearrangement to their corresponding 2-substituted benzofuran derivatives **6**. This rearrangement can also be effected by treating **5** with  $\text{AgNO}_3$  in DMF at  $100^\circ\text{C}$  for 18 h or  $\text{BF}_3\cdot\text{Et}_2\text{O}$  at rt. 2-(3-Butenyl)benzofurans **7** (Nu = allyl) can be prepared by treatment of **5** with  $\text{BF}_3\cdot\text{Et}_2\text{O}$  and allyltributylstannane. Furan and MeOH could also be employed as external nucleophiles in these  $\text{BF}_3\cdot\text{Et}_2\text{O}$ -promoted reactions.

## INTRODUCTION

$\alpha$ -Aryl-2-benzofuranmethamines have valuable medicinal chemistry properties. For example, compounds of the general structure **1** have been reported to be s-1 receptor ligands,<sup>1</sup> have analgesic<sup>2</sup> and  $\text{Ca}^{2+}$  antagonist<sup>3</sup> properties, and applications in the treatment of arrhythmic, histaminic, and tussive conditions (Figure 1).<sup>4</sup> These compounds have been prepared from the corresponding carbinols **2** via amine substitution reactions of the corresponding chlorides **3**.<sup>4</sup> The prerequisite carbinols **2** are generally prepared from 2-lithiobenzofuran and an arylaldehyde (Figure 1).<sup>4</sup> More recently, the Petasis, boronic acid Mannich reaction has been used to prepare a single  $\alpha$ -aryl-2-benzofuranmethamine, 4-(2-benzofuranylphenylmethyl)-morpholine (**1**, where  $\text{NR}^1\text{R}^2 = \text{morpholino}$  and  $\text{Ar} = 2$ -hydroxyphenyl), in yields varying from 23<sup>5</sup> to 95%.<sup>6</sup> This reaction, however, will be limited to the preparation of 2-



**Figure 1.**  $\alpha$ -Aryl-2-benzofuranmethamines (**1**) and their synthetic precursors **2** and **3**.

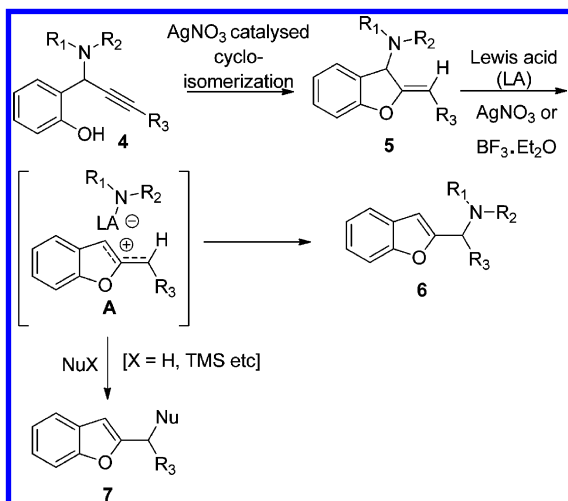
hydroxyaryl derivatives. We report here a new method for preparing  $\alpha$ -aryl (or  $\alpha$ -alkyl)-2-benzofuranmethamines **6** via a novel Lewis-acid-catalyzed 1,3-allylic rearrangement of 3-amino-2,3-dihydro-2-arylmethylidenebenzofurans **5** (Scheme

**Received:** November 27, 2012

**Published:** January 4, 2013

1). These compounds are readily obtained from propargyl amines **4** via  $\text{AgNO}_3$ -catalyzed *5-exo-dig* cycloisomerization

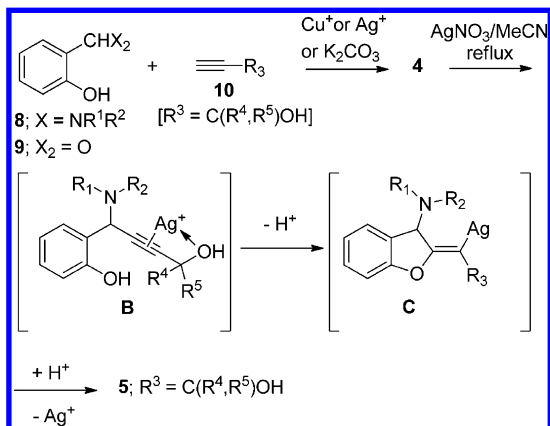
Scheme 1



reactions without the need to prepare reactive and sensitive organolithium or aryl halide reagents. We also report the isolation of novel products from unexpected *6-endo-dig* cyclization processes and the preparation of other 2-substituted benzofurans **7** via trapping of the intermediate  $\alpha$ -aryl (or  $\alpha$ -alkyl) 2-benzofuranmethyl carbocation **A** with other, nonamine, nucleophiles (Scheme 1).

In 2002, Ukhin et al.<sup>7</sup> reported the synthesis of 2-methylidenebenzofurans **5**, from the cyclization reactions of propargyl amines **4**, prepared from animal **8** of salicylaldehyde **9** and propargyl alcohols **10** according to Scheme 2. Cyclization

Scheme 2



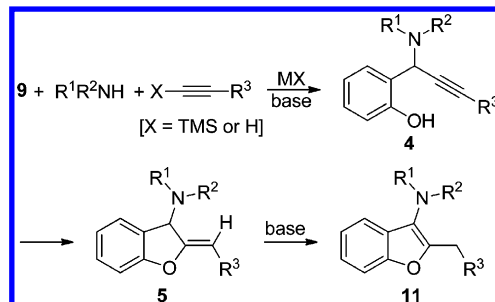
of **4** ( $X = \text{piperidino}$ ,  $R^3 = R^4 = \text{Me}$ ) with either  $\text{AgNO}_3$  (10 mol %) in MeCN at reflux temperature for 15 min or by treatment with KOH in MeOH at reflux temperature for 40 min gave **5** ( $R^1/R^2 = \text{piperidino}$ ,  $R^4 = R^5 = \text{Me}$ ) in yields of 63 and 74%, respectively. Treatment of animal **8** ( $X = \text{morpholino}$ ,  $R^4/R^5 = \text{cyclohexyl}$ ) with the propargylic alcohol **10** ( $R^4/R^5 = \text{cyclohexyl}$ ) and a stoichiometric amount of CuI in MeCN at reflux temperature for 30 min gave **5** ( $R^1/R^2 = \text{morpholino}$ ,  $R^4/R^5 = \text{cyclohexyl}$ ) directly in 39% yield (Scheme 2).

These results were supported by a study by Li et al.,<sup>8</sup> who reported that treatment of salicylaldehyde with a cyclic amine (2 equiv) and a propargyl alcohol (2 equiv) or an alkyne having

a remote OH (or a propargylic NHTs group in one case) in the presence of 5 mol % of CuI with microwave heating at 130 °C for 30 min gave 3-amino-2,3-dihydro-2-arylmethylidenebenzofurans **5** ( $R^3 = \text{CR}^4, \text{R}^5(\text{OH})$ ), or their corresponding analogues, in yields ranging from 44 to 88%. Conditions employing 5 mol % of  $\text{AgCl}/\text{MeCN}/80\text{ }^\circ\text{C}/16\text{ h}$  were also effective but provided **5** ( $R^3 = \text{CR}^4, \text{R}^5(\text{OH})$ ) in slightly lower yields. Importantly, they demonstrated that this reaction did not work with 3,3-dimethylbut-1-yne, which suggested that the hydroxyl (or NHTs) group on the alkyne component **10** was important to assist cyclization via a metal coordination process in intermediate **B** (Scheme 2).

In 2008, Sakai et al.<sup>9</sup> demonstrated that these multi-component reactions can be performed on 1-TMS-alkynes, without the requirement of a propargylic hydroxyl group. They employed salicylaldehyde (1.5 equiv), a cyclic or acyclic secondary amine (1 equiv), 1-TMS-alkyne (1.5 equiv), 5 mol % of  $\text{Cu}(\text{OTf})_2$ , and 5 mol % of CuCl with 1 molar equiv of DMAP in MeCN at reflux temperature for 6 h. Under these conditions, poor to excellent yields (22–99%) of 2-alkyl-3-aminobenzofuran products **11** resulted from a base-catalyzed isomerization of the initially formed, but never isolated, 3-amino-2,3-dihydro-2-aryl- (or alkyl-) methylidenebenzofurans **5** (Scheme 3).

Scheme 3



A subsequent study by Li et al.<sup>10</sup> found similar results using salicylaldehyde (2 equiv), a cyclic or acyclic secondary amine (1 equiv), and a terminal alkyne (1.5 equiv) using 20 mol % of CuI,  $\text{K}_2\text{CO}_3$  (1 equiv), and  $\text{Bu}_4\text{NBr}$  (1 equiv) in toluene at 110 °C for 2–3 h. Of significance, to our study, was their singly reported finding that in the absence of  $\text{K}_2\text{CO}_3$  and  $\text{Bu}_4\text{NBr}$  the propargyl amine **4** ( $R^1/R^2 = \text{morpholine}$ ,  $R^3 = \text{phenyl}$ ) was obtained in 84% yield. Further, in one other example, using 1-octyne, a separable mixture (ca. 1:1) of **5** and **11** ( $R^1/R^2 = \text{morpholine}$ ,  $R^3 = \text{hexyl}$ ) was obtained, suggesting to us that our targeted compounds of general structure **5** might be isolatable in better yields under less basic conditions. A related study by Zhang and Fan<sup>11</sup> demonstrated that these reactions to give compounds **11** could be performed efficiently using salicylaldehyde (1 equiv), a cyclic or acyclic secondary amine (1.2 equiv), and a terminal alkyne (1.5 equiv), CuI (10 mol %), and [bmim]OAc (20 mol %) in [bmim]PF<sub>6</sub> at 80 °C for 6–9 h.

The cyclization reactions of the propargyl alcohol analogues of the propargyl amines **4** ( $R^3 = \text{H}$  or aryl but not alkyl) have been previously studied. These reactions give the analogous 3-hydroxy-2,3-dihydro-2-arylmethylidenebenzofurans (the 3-hydroxy analogues of **5**) which undergo rearrangement to 2-hydroxymethyl benzofurans or 2-alkoxybenzofurans upon exposure to acid or an alcohol and acid, respectively.<sup>12</sup>

## RESULTS AND DISCUSSION

The prerequisite propargyl amines **4**, required for the synthesis of compounds **5** and then **6**, were prepared using the method of Li<sup>10</sup> (method A, Table 1), or a modification of this method

**Table 1. Synthesis of Propargyl Amines 4a–i and 5g and 12 (Schemes 1 and 4)**

entry	NR <sup>1</sup> /R <sup>2</sup>	R <sup>3</sup>	method <sup>a</sup>	products (% yield) <sup>b</sup>
1	morpholino	Ph	A	<b>4a</b> (63)
2	morpholino	Ph	B	<b>4a</b> (84)
3	piperidino	Ph	B	<b>4b</b> (87)
4	pyrrolidino	Ph	B	<b>4c</b> (47)
5	morpholino	4-FC <sub>6</sub> H <sub>4</sub>	B	<b>4d</b> (86)
6	morpholino	4-MeOC <sub>6</sub> H <sub>4</sub>	B	<b>4e</b> (92)
7	morpholino	<i>n</i> -pentyl	A	<b>4f</b> (50)
8	morpholino	<i>n</i> -pentyl	B	<b>4f</b> (13), <b>12</b> (0.7)
9	morpholino	<i>n</i> -pentyl	C	<b>4f</b> (97)
10	piperidino	CH <sub>2</sub> OH	B	<b>4g</b> (43), <b>5g</b> (44)
11	piperidino	CH <sub>2</sub> OH	C	<b>4g</b> (0), <b>5g</b> (73)
12	piperidino	(CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub> OH	C	<b>4h</b> (98)
13	dibutylamino	Ph	C	<b>4i</b> (90)
14	dibenzylamino	Ph	B or C	<b>4j</b> (0)
15	diallylamino	Ph	B or C	<b>4k</b> (0)
16	<i>N</i> -methylanilino	Ph	B or C	<b>4l</b> (0)

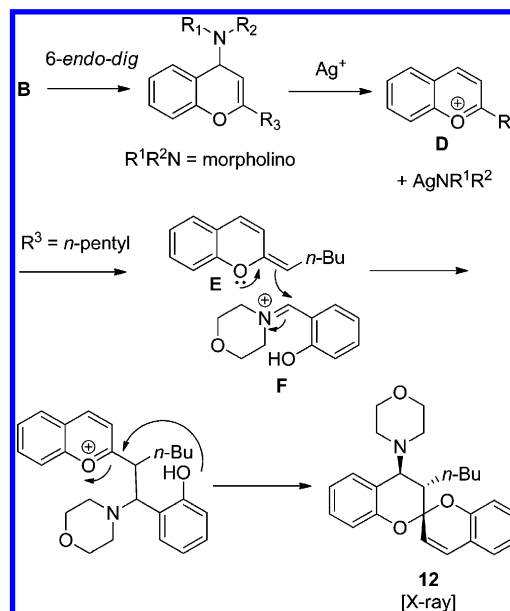
<sup>a</sup>Method A (from Li et al.):<sup>10</sup> **9** (2 equiv), HNR<sup>1</sup>R<sup>2</sup> (1 equiv) and HC≡CR<sup>3</sup> (1.5 equiv), CuI (20 mol %), 110 °C, 24 h. Method B: **9** (2 equiv), HNR<sup>1</sup>R<sup>2</sup> (1 equiv) and HC≡CR<sup>3</sup> (1.5 equiv), AgNO<sub>3</sub> (20 mol %), 110 °C, 24 h. Method C (from Adapa et al.):<sup>13</sup> **9** (1 equiv), HNR<sup>1</sup>R<sup>2</sup> (1.3 equiv) and HC≡CR<sup>3</sup> (1.5 equiv), Zn(OAc)<sub>2</sub>·2H<sub>2</sub>O (10 mol %), 120 °C, 24 h. <sup>b</sup>After purification by column chromatography.

using AgNO<sub>3</sub> instead of CuI (method B) or the method of Adapa<sup>13</sup> (method C, Table 1) from the one-pot reactions of salicylaldehyde **9**, a cyclic or acyclic secondary amine (HNR<sup>1</sup>R<sup>2</sup>), and a terminal alkyne (HC≡CR<sup>3</sup>) in toluene solution using either CuI (20 mol %), AgNO<sub>3</sub> (20 mol %), or Zn(OAc)<sub>2</sub>·2H<sub>2</sub>O (10 mol %) as catalysts, respectively, at 110–120 °C (Table 1).

Method A provided the propargyl amine **4a** in 63% yield (Table 1, entry 1). However, we found that a better yield of **4a** could be obtained using AgNO<sub>3</sub> as the catalyst rather than CuI. Method B provided the propargyl amines **4a–4e** (Table 1, entries 2–6), all in good yields (84–92%) except for the pyrrolidino adduct **4c** (47% yield). While method C was more efficient (97% yield) in giving the propargyl amine **4f** from heptyne when compared to method A or B (Table 1, entries 7–9). Interestingly, method B (Table 1, entry 8) also provided a small amount (0.7%) of the novel spirocyclic compound **12** whose structure was determined by a single-crystal X-ray analysis (Supporting Information). A possible mechanism for the formation of **12** is shown in Scheme 4. This mechanism involves formation of the flavylum ion intermediate **D**,<sup>14</sup> formed from cyclization of the intermediate **B** (Scheme 2) via a 6-*endo-dig* process<sup>15</sup> (Scheme 4). Coupling of intermediates **E** and **F** followed by an intramolecular spirocyclization process gives the spirocyclic compound **12**.

In the reactions involving salicylaldehyde **9**, piperidine, and propargyl alcohol (Table 1, entries 10 and 11), method B gave a separable mixture of **4g** and the 2-methylidenebenzofuran **5g**, while method C gave only **5g** in 73% yield. These results were consistent with those of Li<sup>8</sup> and the assistance of the primary

**Scheme 4**



hydroxyl group in the 5-*exo-dig* cyclization process by metal coordination in intermediate **B** (Scheme 2). In contrast, the reaction of **9**, piperidine, and 4-pentyn-1-ol gave only the propargyl amine product **4h** in 98% yield (Table 1, entry 10, method B). Clearly, the hydroxyl group in **4h** is too remote to assist in cyclization to **5h**. Method B also provided **4i** in 90% yield from the reaction of **9** with the acyclic amine, dibutylamine, and phenylacetylene (Table 1, entry 14). The amines, dibenzylamine, diallylamine, or *N*-methylaniline, were not effective (Table 1, entries 14–16).

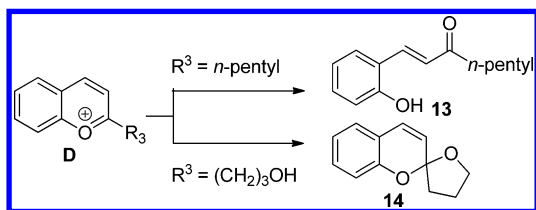
For the cyclization reactions of **4a** to **5a** (Scheme 1), several metal salt catalysts were examined (CuI, AgNO<sub>3</sub>, Au(Ph<sub>3</sub>P)<sub>3</sub>Cl, or PdCl<sub>2</sub>(Ph<sub>3</sub>P)<sub>2</sub>/CuI) in various solvents (CH<sub>2</sub>Cl<sub>2</sub>, THF, MeCN, DMF) and at several temperatures (60–120 °C). Of these, 20 mol % of AgNO<sub>3</sub>/DMF proved to be the most efficient. These results are summarized in Table 2. Treatment of **4a** with 20 mol % of AgNO<sub>3</sub> at 60 °C for 1 h gave the 2-phenylmethylidenebenzofuran **5a** in 90% yield (Table 1, entry 1). When this reaction was performed at 100 °C for 18 h, the 1,3-allylic rearrangement product **6a** was produced in 60% yield along with a small amount (5%) of **5a** (Table 1, entry 2). The former, milder conditions also worked well for the substrates **4b–d** and **4g** and **4i** (Table 2, entries 3, 5, 7, 13, and 15), providing the corresponding 2-methylidenebenzofurans **5b–d** and **5g** and **5i** in yields ranging from 65 to 85%. The more electron-rich 4-methoxyphenyl-substituted derivative **4e**, however, gave the 1,3-allylic rearrangement product **6e** in 68% yield (Table 2, entry 9). This product was also formed exclusively under the harsher (100 °C for 18 h) reaction conditions (Table 2, entry 10). The reactions of the *n*-pentyl derivative **4f** at 60 or 100 °C gave **5f** in low yields (32 and 23%, Table 2, entries 11 and 12). These low yields were most likely due to a competing 6-*endo-dig* cyclization process that resulted in the formation of many colored unidentifiable products apart from the (*E*)-enone **13**, which was isolated in 6% yield (Scheme 5). Similarly, the cyclization reaction of **4h** resulted in mixtures from competing 6-*endo-dig* and 5-*exo-dig* processes. The major product (51% yield) was the known spirocyclic compound **14**<sup>16</sup> formed by intramolecular trapping of the flavylum ion intermediate **D**<sup>14</sup> (Scheme 5). The 5-*exo-dig* products **5h** (32%) and **6h** (7%)

**Table 2.** Synthesis of 3-Amino-2,3-dihydro-2-arylmethylidenebenzofurans **5** and/or  $\alpha$ -Aryl (or  $\alpha$ -Alkyl) 2-Benzofuranmethammines **6** from the  $\text{AgNO}_3$ -Catalyzed Cyclization Reactions of Propargyl Amines **4** (Schemes 1 and 5)<sup>a</sup>

entry	propargyl amine <b>4</b> (NR <sup>1</sup> R <sup>2</sup> /R <sup>3</sup> )	AgNO <sub>3</sub> (20 mol %), DMF temp (°C)/time (h)	products (% yield) <sup>a</sup>
1	<b>4a</b> (morpholino/Ph)	60/1	<b>5a</b> (90)
2	<b>4a</b> (morpholino/Ph)	100/18	<b>5a</b> (5), <b>6a</b> (60)
3	<b>4b</b> (piperidino/Ph)	60/1	<b>5b</b> (78)
4	<b>4b</b> (piperidino/Ph)	100/18	<b>5b</b> (17), <b>6b</b> (53)
5	<b>4c</b> (pyrrolidino/Ph)	60/1	<b>5c</b> (65)
6	<b>4c</b> (pyrrolidino/Ph)	100/18	<b>5c</b> (2), <b>6c</b> (36)
7	<b>4d</b> (morpholino/4F-C <sub>6</sub> H <sub>4</sub> )	60/1	<b>5d</b> (81)
8	<b>4d</b> (morpholino/4F-C <sub>6</sub> H <sub>4</sub> )	100/18	<b>5d</b> (13), <b>6d</b> (52)
9	<b>4e</b> (morpholino/4MeO-C <sub>6</sub> H <sub>4</sub> )	60/1	<b>6e</b> (68)
10	<b>4e</b> (morpholino/4MeO-C <sub>6</sub> H <sub>4</sub> )	100/18	<b>6e</b> (69)
11	<b>4f</b> (morpholino/ <i>n</i> -pentyl)	60/1	<b>5f</b> (32), <b>13</b> (6)
12	<b>4f</b> (morpholino/ <i>n</i> -pentyl)	100/18	<b>5f</b> (23)
13	<b>4g</b> (piperidino/CH <sub>2</sub> OH)	60/1	<b>5g</b> (84)
14	<b>4h</b> (piperidino/(CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub> OH)	60/1	<b>5h</b> (32), <b>14</b> (51)
15	<b>4i</b> (dibutylamino/Ph)	60/1	<b>5i</b> (85)

<sup>a</sup>After purification by column chromatography.

**Scheme 5**



were also obtained (Table 2, entry 13). The hydroxymethyl substrate **4g** ( $\text{R}^3 = \text{CH}_2\text{OH}$ ), however, was smoothly converted to the 5-*exo-dig* cyclization product **5g** in 84% yield (Table 2, entry 13), for the reasons discussed above.

Heating a solution of **5a** with  $\text{AgNO}_3$  (20 mol %) in DMF at 100 °C for 24 h also provided the rearranged benzofuran **6a** in 68% yield. No detectable (TLC or NMR analysis) amount of **6a** was formed when a DMF solution of **5a** was heated at 100 °C for 24 h in the absence of  $\text{AgNO}_3$ .

Table 3 provides a summary of our study on the  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ -catalyzed 1,3-allylic rearrangements of **5** to **6** and the preparation of other 2-substituted benzofurans **15–17** via trapping of the assumed ion pair intermediate **A** (Scheme 1) with an external nucleophile (Scheme 6).

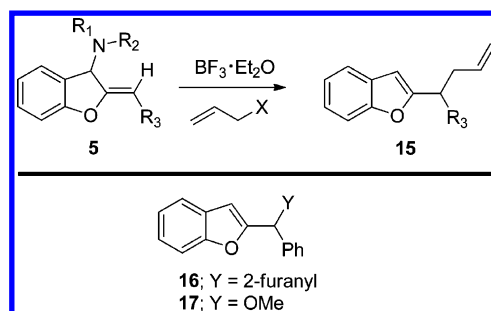
Treatment of a  $\text{CH}_2\text{Cl}_2$  solution of **5a** with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (1.5 equiv) at rt for 2 h gave the rearranged benzofuran **6a** in 87% yield (Table 3, entry 1). In contrast, the rearrangement reactions of the corresponding piperidino and pyrrolidino derivatives, **5b** and **5c**, were considerably slower and required reaction times of 18–24 h to obtain close to 50% conversions.

**Table 3.** Synthesis of **6** and **13–15** from the  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ -Catalyzed Reactions of **5** with or without an External Nucleophile (Schemes 1 and 6)<sup>a</sup>

entry	benzofuran <b>5</b> (NR <sup>1</sup> R <sup>2</sup> /R <sup>3</sup> )	time (h)/temp (°C)/external nucleophile (equiv)	products (% yield) <sup>a</sup>
1	<b>5a</b> (morpholino/Ph)	2/rt/–	<b>6a</b> (87)
2	<b>5b</b> (piperidino/Ph)	18/rt/–	<b>6b</b> (58), <b>5b</b> (41)
3	<b>5c</b> (pyrrolidino/Ph)	24/rt/–	<b>6c</b> (43), <b>5c</b> (56)
	<b>5d</b> (morpholino/4F-C <sub>6</sub> H <sub>4</sub> )	2/rt/–	<b>6d</b> (96)
4	<b>5f</b> (morpholino/ <i>n</i> -pentyl)	6/rt/–	<b>6f</b> (22), <b>5f</b> (66)
5	<b>5i</b> (morpholino/ <i>n</i> -pentyl)	24/rt/–	<b>6i</b> (87)
6	<b>5a</b> (morpholino/Ph)	2/rt/allylBF <sub>3</sub> K (3)	<b>15a</b> (0), <b>6a</b> (96)
7	<b>5a</b> (morpholino/Ph)	2/rt/allylTMS (3)	<b>15a</b> (46), <b>6a</b> (53)
8	<b>5a</b> (morpholino/Ph)	2/rt/allylSnBu <sub>3</sub> (3)	<b>15a</b> (73), <b>6a</b> (26)
9	<b>5a</b> (morpholino/Ph)	2/rt/furan (10)	<b>16</b> (43), <b>6a</b> (54)
10	<b>5a</b> (morpholino/Ph)	2/rt/MeOH (10)	<b>17</b> (52), <b>6a</b> (48)
11	<b>5b</b> (piperidino/Ph)	18/rt/allylSnBu <sub>3</sub> (3)	<b>15a</b> (87)
12	<b>5d</b> (morpholino/4F-C <sub>6</sub> H <sub>4</sub> )	2/rt/allylSnBu <sub>3</sub> (3)	<b>15d</b> (69), <b>6d</b> (30)
13	<b>6e</b> (morpholino/4MeO-C <sub>6</sub> H <sub>4</sub> )	2/rt/allylSnBu <sub>3</sub> (3)	<b>15e</b> (36)
14	<b>5f</b> (morpholino/ <i>n</i> -pentyl)	2/rt/allylSnBu <sub>3</sub> (3)	<b>15f</b> (87)

<sup>a</sup>After purification by column chromatography.

**Scheme 6**



This resulted in lower yields of **6b** and **6c**, respectively, due to reisolations of unreacted starting materials (Table 3, entries 2 and 3). Compound **6b** was more readily prepared from the cyclization of **4b** with  $\text{AgNO}_3$  at 100 °C (Table 2, entry 4). The morpholino derivative **5d**, having a deactivating 4-fluorophenyl substituent, also underwent smooth conversion to its rearranged product **6d** in 96% yield. The *n*-pentyl derivative **5f** was found to react even more sluggishly than **5b** or **5c** and provided **6f** in only 22% yield along with 66% yield of recovered unreacted starting material (Table 3, entry 4). The dibutylamino compound **5i**, however, provided the rearranged product **6i** in 87% yield (Table 3, entry 5). Clearly, the morpholino derivatives **5a** and **5d** underwent  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ -promoted rearrangements to their corresponding benzofurans **6a,d** more readily than their piperidino and pyrrolidino analogues **5b** and **5c**. These results are in accord with the relative basicities ( $K_b$  values)<sup>17</sup> of these amino groups, where

the less basic morpholino group would be expected to be a better leaving group (form a more stable  $\text{BF}_3$ -coordinated incipient amide ion in the ion pair A) and more readily form the carbocation ion pair A (Scheme 1). However, the observed similar reactivity of the morpholino and dibutylamino substrates, **5a** and **5i**, suggests that other factors are important in controlling the rates of these reactions. Indeed, very few examples are known for unactivated allylic amines undergoing 1,3-allylic rearrangements.<sup>18</sup> In our cases, the driving force for rearrangement of **5** to **6** is clearly the formation of a more stable benzofuran product **6**.

In an attempt to form the allylated derivative **15a**, we treated a  $\text{CH}_2\text{Cl}_2$  solution of **5a** with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (1.5 equiv) and potassium allyltrifluoroborate (3 equiv). This gave only the rearranged product **6a** (Table 3, entry 6). Allyltrimethylsilane gave a 46% yield of **15a** while allyltributylstannane gave **15a** in a much improved yield of 73%. In each case, the rearranged benzofuran **6a** was also formed (Table 3, entries 7 and 8). Under similar reaction conditions, **15a** could be prepared in high yield from **5b** and allyltributylstannane; however, the reaction time was 18 h (Table 3, entry 8). Similarly, compounds **5d** and **5f** could be converted to their corresponding allylated derivatives, **15d** and **15f**, respectively (Table 3, entries 12 and 14). The methoxy-activated derivative **6e** could also be converted to its allylated derivative **15e** but in low yield (36%, Table 3, entry 13). The furan and methanol adducts, **16** and **17**, respectively, could be prepared from the  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (1.5 equiv)-promoted reactions of **5a** in the presence of furan (10 equiv) and MeOH (10 equiv), respectively. These products were separated from nearly equal amounts of **6a** (Table 3, entries 9 and 10).

In summary, the propargyl amines **4**, where  $\text{R}^3$  is aryl, undergo cyclization under relatively mild conditions ( $\text{AgNO}_3$ , DMF, 60 °C, 1 h) to give ready access to 3-amino-2,3-dihydro-2-arylmethylidenebenzofurans **5** ( $\text{R}^3 = \text{aryl}$ ). These reactions proceed through a 5-*exo-dig* cyclization process. Under these nonbasic conditions, the corresponding 2-alkyl-3-aminobenzofuran products **11**, as reported previously,<sup>10</sup> are not observed. In contrast, the substrates **4f** and **4h**, where  $\text{R}^3$  is alkyl, undergo competing 6-*endo-dig* and 5-*exo-dig* cyclization processes as evident of the isolation of compounds **13** and **14**. The hydroxymethyl substrate **4g** ( $\text{R}^3 = \text{CH}_2\text{OH}$ ), however, was smoothly converted to the 5-*exo-dig* cyclization product **5g** in 84% yield, likely due to the assistance of the primary hydroxyl group in the 5-*exo-dig* cyclization process by metal coordination in intermediate **B** ( $\text{R}^3 = \text{CH}_2\text{OH}$ ) (Scheme 2). Under more enforcing conditions ( $\text{AgNO}_3$ , DMF, 100 °C, 18 h), the initially formed 2,3-dihydro-2-substituted methylidenebenzofurans **5** undergo a 1,3-allylic rearrangement to their corresponding 2-substituted benzofuran derivatives **6**. This rearrangement can also be effected by treating **5** with  $\text{AgNO}_3$  in DMF at 100 °C for 18 h or  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (1.5 equiv) at rt. 2-(3-Butenyl)-benzofurans **15** can be prepared by treatment of **5** with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  and allyltributylstannane; however, compound **6** is often also formed as a minor product. Furan and MeOH could also be employed as external nucleophiles in the  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ -promoted reactions of **5a**.

## EXPERIMENTAL SECTION

Melting points were determined on a capillary tube melting point apparatus and are uncorrected. All IR spectra were run as neat samples.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were obtained in  $\text{CDCl}_3$  solution using TMS and residual  $\text{CHCl}_3$  as an internal standard ( $\delta_{\text{H}}$  0.00,  $\delta_{\text{C}}$  77.16).  $^1\text{H}$

NMR data were listed in order of the number of protons, multiplicity [singlet (s), broad singlet (brs), doublet (d), triplet (t), quartet (q), quintet (quint), and multiplet (m)], coupling constants ( $J$ ) in hertz, and assignment of nuclei concerned. NMR assignments are based upon gCOSY, HSQC, HMBC, and, sometimes, gNOESY experiments. High-resolution ESI mass spectra were obtained on a QTOF (ESI) mass spectrometer. Thin layer chromatography (TLC) was performed with precoated Merck silica gel 60  $\text{PF}_{254}$  aluminum sheets, and the spots were visualized under UV light (254 and 366 nm) and further by spraying with an acidified aqueous solution of ammonium molybdate and cerium(IV) sulfate then heating until charred. Column chromatography (CC) was performed with Merck silica gel 60 (40–60  $\mu\text{m}$ ) and under pressure from compressed air. All air-sensitive reactions were carried out in predried glassware apparatus under a dry nitrogen atmosphere.

**2-(1-Morpholino-3-phenylprop-2-ynyl)phenol (4a).** *Method A:* A mixture of  $\text{CuI}$  (762 mg, 4.0 mmol), salicylaldehyde (4.88 g, 40 mmol), phenylacetylene (3.07 g, 30 mmol), and morpholine (1.75 g, 20 mmol) in anhydrous toluene (20 mL) was heated under  $\text{N}_2$  at 110 °C for 48 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) and then crystallization with EtOAc/petrol to give product **4a** (3.68 g, 63%) as colorless crystals: mp 96–98 °C;  $R_f = 0.34$  (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\text{max}}$  3053, 2961, 2848, 2230, 1588, 1488, 1245, 1115, 1095, and 690  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  10.81 (1H, brs, ArOH), 7.57–7.53 (3H, m, ArH), 7.37–7.35 (3H, m, ArH), 7.25 (1H, t,  $J = 7.2$  Hz, ArH), 6.89–6.86 (2H, m, ArH), 5.09 (1H, s, CHN), 3.80 (4H, brs,  $2 \times \text{CH}_2\text{O}$ ), 2.79 (4H, brs,  $2 \times \text{CH}_2\text{N}$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  157.1 (ArCO), 132.0 ( $2 \times \text{ArCH}$ ), 129.9 (ArCH), 128.89 (ArCH), 128.88 (ArCH), 128.6 (ArCH), 122.4 (ArC), 120.7 (ArC), 119.6 (ArCH), 116.6 (ArCH), 90.5 ( $\text{C}\equiv\text{CAr}$ ), 81.7 ( $\text{C}\equiv\text{CAr}$ ), 67.0 ( $2 \times \text{CH}_2\text{O}$ ), 60.9 (CHN) (due to line broadening signals for ( $2 \times \text{CH}_2\text{N}$ ) were not observed); HRESIMS calcd for  $\text{C}_{19}\text{H}_{20}\text{NO}_2$  ( $\text{M} + \text{H}$ )<sup>+</sup> 294.1494; found, 294.1504.

*Method B:* A mixture of  $\text{AgNO}_3$  (679 mg, 4.0 mmol), salicylaldehyde (4.88 g, 40 mmol), phenylacetylene (3.07 g, 30 mmol), and morpholine (1.75 g, 20 mmol) in anhydrous toluene (20 mL) was heated under  $\text{N}_2$  at 110 °C for 48 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) and then crystallization with EtOAc/petrol to give product **4a** (4.903 g, 84%).

**2-(3-Phenyl-1-(piperidin-1-yl)prop-2-yn-1-yl)phenol (4b).** A mixture of  $\text{AgNO}_3$  (68 mg, 0.4 mmol), salicylaldehyde (489 mg, 4.0 mmol), phenylacetylene (306 mg, 3.0 mmol), and piperidine (170 mg, 2.0 mmol) in anhydrous toluene (10 mL) was heated under  $\text{N}_2$  at 110 °C for 48 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:19)) to product **4b** (511 mg, 87%) as a yellow solid: mp 60–62 °C; IR (neat)  $\nu_{\text{max}}$  3062, 3037, 2942, 2837, 2211, 1603, 1583, 1459, 1319, 1242, 671, and 634  $\text{cm}^{-1}$ ;  $R_f = 0.24$  (EtOAc/petrol (1:19));  $^1\text{H}$  NMR (300 Hz)  $\delta$  7.53 (3H, brs, ArH), 7.34 (3H, brs, ArH), 7.20 (1H, t,  $J = 7.2$  Hz, ArH), 6.82 (2H, d,  $J = 7.2$  Hz, ArH), 5.07 (1H, s, CHN), 2.70 (4H, brs,  $2 \times \text{CH}_2\text{N}$ ), 1.65 (4H, brs,  $2 \times \text{CH}_2$ ), 1.49 (2H, brs,  $\text{CH}_2$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  157.7 (ArCOH), 132.0 ( $2 \times \text{ArCH}$ ), 129.5 (ArCH), 128.7 ( $2 \times \text{ArCH}$ ), 128.5 ( $2 \times \text{ArCH}$ ), 122.7 (ArC), 121.4 (ArC), 119.1 (ArCH), 116.4 (ArCH), 89.9 ( $\text{C}\equiv\text{CAr}$ ), 82.4 ( $\text{C}\equiv\text{CAr}$ ), 61.2 ( $2 \times \text{CH}_2\text{N}$ ), 52.9 ( $\text{CH}_2\text{N}$ ), 26.1 ( $\text{CH}_2$ ), 24.1 ( $2 \times \text{CH}_2$ ); HRESIMS calcd for  $\text{C}_{20}\text{H}_{22}\text{NO}$  ( $\text{M} + \text{H}$ )<sup>+</sup> 292.1701; found, 292.1708.

**2-(3-Phenyl-1-(pyrrolidin-1-yl)prop-2-yn-1-yl)phenol (4c).** A mixture of  $\text{AgNO}_3$  (68 mg, 0.4 mmol), salicylaldehyde (489 mg, 4.0 mmol), phenylacetylene (306 mg, 3.0 mmol), and pyrrolidine (143 mg, 2.0 mmol) in anhydrous toluene (10 mL) was heated under  $\text{N}_2$  at 110 °C for 48 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (5% EtOAc/petrol (1:19)) to give the product **4c** (532 mg, 47%) as a yellow viscous oil:  $R_f = 0.33$  (EtOAc/petrol (1:5)); IR (neat)  $\nu_{\text{max}}$  3053, 2967, 2840, 2219, 1590, 1465, 1348, 1257, 690, and 633  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  10.99 (1H, brs, ArOH), 7.55–7.50 (3H, m, ArH), 7.34–7.31 (3H, m, ArH), 7.20 (1H, dt,  $J = 7.2, 0.9$  Hz,

ArH), 6.87–6.81 (2H, m, ArH), 5.25 (1H, s, CHN), 2.87–2.76 (4H, m, 2 × CH<sub>2</sub>N), 1.86–1.82 (4H, m, 2 × CH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz) δ 157.6 (ArCOH), 131.9 (2 × ArCH), 129.4 (ArCH), 128.6 (2 × ArCH), 128.4 (ArCH), 127.9 (ArCH), 122.6 (ArCH), 122.2 (ArC), 119.0 (ArCH), 116.3 (ArCH), 89.1 (C≡CAr), 83.0 (C≡CAr), 57.0 (CHN), 48.9 (2 × CH<sub>2</sub>N), 23.9 (2 × CH<sub>2</sub>); HRESIMS calcd for C<sub>19</sub>H<sub>20</sub>NO (M + H)<sup>+</sup> 278.1545; found 278.1546.

**2-(3-(4-Fluorophenyl)-1-morpholinopro-2-yn-1-yl)phenol (4d).** A mixture of AgNO<sub>3</sub> (68 mg, 0.4 mmol), salicylaldehyde (489 mg, 4.0 mmol), 1-ethynyl-4-fluorobenzene (391 mg, 3.0 mmol), and morpholine (174 mg, 2.0 mmol) in anhydrous toluene (5 mL) was heated under N<sub>2</sub> at 110 °C for 48 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) and then crystallization with EtOAc/petrol to give the product **4d** (572 mg, 91.9%) as a pale yellow solid: mp 104–106 °C; R<sub>f</sub> = 0.33 (EtOAc/petrol (1:4)); IR (neat) ν<sub>max</sub> 3050, 2961, 2851, 2232, 1600, 1586, 1506, 1454, 1397, 1232, 1115, 1094, 660, and 635 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz) δ 10.71 (1H, brs, ArOH), 7.54–7.50 (3H, m, ArH), 7.23 (1H, t, J = 7.5 Hz, ArH), 7.04 (2H, t, J = 7.5 Hz, ArH), 6.88–6.86 (2H, m, ArH), 5.05 (1H, s, CHN), 3.77 (4H, brs, 2 × CH<sub>2</sub>O), 2.75 (4H, brs, 2 × CH<sub>2</sub>N); <sup>13</sup>C NMR (125 MHz) δ 162.8 (d, J = 248 Hz, ArCF), 157.05 (ArCO), 133.8 (d, J = 8.6 Hz, ArCH), 129.8 (ArCH), 128.7 (ArCH), 120.5 (ArC), 119.5 (ArCH), 118.4 (d, J = 3.9 Hz, ArC), 116.6 (ArCH), 115.8 (d, J = 22 Hz, ArCH), 89.3 (C≡CAr), 81.0 (C≡CAr), 66.9 (2 × CH<sub>2</sub>O), 60.7 (CHN), 52.1 (2 × CH<sub>2</sub>N); HREIMS calcd for C<sub>19</sub>H<sub>19</sub>FNO<sub>2</sub> (M + H)<sup>+</sup> 312.1400; found 312.1397.

**2-(3-(4-Methoxyphenyl)-1-morpholinopro-2-yn-1-yl)phenol (4e).** A mixture of AgNO<sub>3</sub> (68 mg, 0.4 mmol), salicylaldehyde (489 mg, 4.0 mmol), *p*-ethynylanisole (396 mg, 3.0 mmol), and morpholine (174 mg, 2.0 mmol) in anhydrous toluene (5 mL) was heated under N<sub>2</sub> at 110 °C for 48 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (10% EtOAc/petrol (1:9)) and then crystallization with EtOAc/petrol to give product **4e** (559 mg, 86%) as a pale yellow solid: mp 144–146 °C; R<sub>f</sub> = 0.24 (EtOAc/petrol (1:4)); IR (neat) ν<sub>max</sub> 3058, 3034, 2937, 2845, 2208, 1603, 1508, 1467, 1248, 1112, 829, and 803 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz) δ 10.87 (1H, brs, OH), 7.57 (1H, d, J = 7.5 Hz, ArH), 7.49–7.46 (2H, m, ArH), 7.24 (1H, t, J = 7.5 Hz, ArH), 6.90–6.85 (3H, m, ArH), 5.07 (1H, s, CHN), 3.83 (3H, s, OCH<sub>3</sub>), 3.80 (4H, brs, 2 × CH<sub>2</sub>O), 2.78 (4H, brs, 2 × CH<sub>2</sub>N); <sup>13</sup>C NMR (75 MHz) δ 160.0 (ArCOCH<sub>3</sub>), 157.1 (ArCOH), 133.5 (2 × ArCH), 129.8 (ArCH), 129.0 (ArCH), 120.9 (ArC), 119.5 (ArCH), 116.6 (ArCH), 114.4 (ArC), 114.2 (2 × ArCH), 90.4 (C≡CAr), 80.2 (C≡CAr), 67.0 (OCH<sub>3</sub>), 60.9 (2 × CH<sub>2</sub>O), 55.5 (2 × CH<sub>2</sub>N); HRESIMS calcd for C<sub>20</sub>H<sub>22</sub>NO<sub>2</sub> (M + H)<sup>+</sup> 324.1600; found 324.1597.

**2-(1-Morpholinoct-2-yn-1-yl)phenol (4f) and 4-(3-(pentan-2-yl)spiro[chroman-2,2'-chromen]-4-yl)morpholine (12).** *Method A:* A mixture of AgNO<sub>3</sub> (68 mg, 0.4 mmol), salicylaldehyde (489 mg, 4.0 mmol), 1-heptyne (289 mg, 3.0 mmol), and morpholine (174 mg, 2.0 mmol) in anhydrous toluene (5 mL) was heated under N<sub>2</sub> at 110 °C for 48 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:19)) and then crystallization with EtOAc/petrol to give compound **4f** (75 mg, 13.0%) and compound **12** (6 mg, 0.7%). **Compound 4f:** colorless viscous oil; R<sub>f</sub> = 0.24 (EtOAc/petrol (1:9)); IR (neat) ν<sub>max</sub> 3041, 2956, 2852, 2234, 1587, 1455, 1275, 1242, 1116, 1093, and 753 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz) δ 10.93 (1H, brs, OH), 7.48 (1H, dt, J = 7.5, 1.2, ArH), 7.21 (1H, ddd, J = 7.5, 1.8, 0.6 Hz, ArH), 6.88–6.81 (3H, m, ArH), 4.84 (1H, s, CHN), 3.76 (4H, brs, 2 × CH<sub>2</sub>O), 2.67 (4H, brs, 2 × CH<sub>2</sub>N), 2.34 (2H, t, J = 7.2 Hz, C≡CCH<sub>2</sub>), 1.61 (2H, quint, J = 7.2 Hz, C≡CCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.50–1.30 (4H, m, 2 × CH<sub>2</sub>), 0.93 (3H, t, J = 6.9 Hz, CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz) δ 157.1 (ArCOH), 129.6 (ArCH), 128.9 (ArCH), 121.2 (ArC), 119.3 (ArCH), 116.4 (ArCH), 91.2 (C≡CCH<sub>2</sub>), 72.2 (C≡CCH<sub>2</sub>), 66.9 (2 × CH<sub>2</sub>O), 60.4 (CHN), 31.2 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 28.6 (C≡CCH<sub>2</sub>CH<sub>2</sub>), 22.3 (CH<sub>2</sub>CH<sub>3</sub>), 18.8 (C≡CCH<sub>2</sub>), 14.1 (CH<sub>2</sub>CH<sub>3</sub>) [signals for 2 × CH<sub>2</sub>N were not observed due to line broadening]; HRESIMS calcd for C<sub>18</sub>H<sub>26</sub>NO<sub>2</sub> (M + H)<sup>+</sup> 288.1964; found 288.1959. **Compound 12:** colorless crystals; mp 125–127 °C; R<sub>f</sub> = 0.48

(EtOAc/petrol (1:4)); IR (neat) ν<sub>max</sub> 3069, 3031, 2930, 2855, 1641, 1582, 1482, 1451, 1230, 1194, 1108, and 757 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz) δ 7.51 (1H, d, J = 7.8 Hz, ArCH), 7.17–7.05 (3H, m, ArCH), 6.97–6.92 (2H, m, ArCH), 6.82 (1H, d, J = 9.6 Hz, CH=CHAr), 6.71 (1H, d, J = 8.1 Hz, ArCH), 6.66 (1H, d, J = 8.1 Hz, ArCH), 5.88 (1H, d, J = 9.6 Hz, CH=CHAr), 4.12 (1H, d, J = 10.5 Hz, CHN), 3.71–3.69 (4H, m, 2 × CH<sub>2</sub>O), 2.95–2.70 (4H, m, 2 × CH<sub>2</sub>N), 2.22–2.16 (1H, m, CH), 1.80–1.60 (2H, m, CH<sub>2</sub>), 1.55–1.40 (2H, m, CH<sub>2</sub>), 1.30 (2H, sext, J = 7.2 Hz, CH<sub>2</sub>CH<sub>3</sub>), 0.89 (3H, t, J = 7.2 Hz, CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz) δ 152.2 (ArCO), 151.1 (ArCO), 129.5 (ArCH), 128.3 (ArCH), 128.2 (ArCH), 127.1 (CH=CHAr), 127.0 (ArCH), 124.5 (ArC), 123.2 (CH=CHAr), 121.8 (ArCH), 121.1 (ArCH), 120.1 (ArC), 117.5 (ArCH), 116.7 (ArCH), 100.8 (C(O)<sub>2</sub>), 68.2 (2 × CH<sub>2</sub>O), 61.6 (CHN), 50.2 (2 × CH<sub>2</sub>N), 44.1 (CH), 30.6 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 23.4 (CH<sub>2</sub>CH<sub>3</sub>), 14.2 (CH<sub>2</sub>CH<sub>3</sub>); HRESIMS calcd for C<sub>25</sub>H<sub>30</sub>NO<sub>3</sub> (M + H)<sup>+</sup> 392.2226; found 392.2231.

*Method B:* A mixture of CuI (381 mg, 2.0 mmol), salicylaldehyde (2.44 g, 20 mmol), 1-heptyne (1.44 g, 15 mmol), and morpholine (872 mg, 10 mmol) in anhydrous toluene (10 mL) was heated under N<sub>2</sub> at 110 °C for 48 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (5% EtOAc/petrol (1:19)) and then crystallization with EtOAc/petrol to give compound **4f** (1.44 g, 50%) as a colorless oil.

*Method C:* A mixture of Zn(OAc)<sub>2</sub>·2H<sub>2</sub>O (88 mg, 0.2 mmol), salicylaldehyde (489 mg, 4.0 mmol), 1-heptyne (577 mg, 6.0 mmol), and morpholine (453 mg, 5.2 mmol) in anhydrous toluene (10 mL) was heated under N<sub>2</sub> at 120 °C for 24 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:19)) and then crystallization with EtOAc/petrol to give compound **4f** (1.13 g, 97%) as a colorless oil.

**2-(4-Hydroxy-1-(piperidin-1-yl)but-2-yn-1-yl)phenol (4g) and 2-(3-(Piperidin-1-yl)benzofuran-2(3H)-ylidene)ethanol (5g).** A mixture of AgNO<sub>3</sub> (68 mg, 0.4 mmol), salicylaldehyde (489 mg, 4.0 mmol), phenylacetylene (306 mg, 3.0 mmol), and piperidine (170 mg, 2.0 mmol) in anhydrous toluene (10 mL) was heated under N<sub>2</sub> at 110 °C for 24 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:1)) to give compound **4g** (211 mg, 43%) and compound **5g** (216 mg, 44%).

**Compound 4g:** a brown viscous oil; R<sub>f</sub> = 0.24 (EtOAc/petrol (1:1)); IR (neat) ν<sub>max</sub> 3405, 3042, 2934, 2854, 2234, 1608, 1589, 1664, 1366, 1275, 1245, 1060, and 753 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz) δ 7.56 (1H, brs, ArOH), 7.45 (1H, d, J = 7.5 Hz, ArH), 7.15 (1H, t, J = 7.5 Hz, ArH), 6.82 (2H, d, J = 7.5 Hz, ArH), 6.79 (1H, t, J = 7.5 Hz, ArH), 4.83 (1H, s, CHN), 4.12 (2H, s, CH<sub>2</sub>OH), 2.59 (4H, brs, 2 × CH<sub>2</sub>N), 1.59 (4H, brs, 2 × CH<sub>2</sub>), 1.45 (2H, brs, CH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz) δ 157.0 (ArCOH), 129.2 (ArCH), 128.2 (ArCH), 120.9 (ArC), 119.0 (ArCH), 116.1 (ArCH), 88.2 (C≡CCH<sub>2</sub>), 77.8 (C≡CCH<sub>2</sub>), 60.3 (CHN), 50.4 (CH<sub>2</sub>OH), 45.5 (2 × CH<sub>2</sub>N), 25.7 (2 × CH<sub>2</sub>), 23.6 (CH<sub>2</sub>); HRESIMS calcd for C<sub>15</sub>H<sub>20</sub>NO<sub>2</sub> (M + H)<sup>+</sup> 246.1494; found 246.1506.

**Compound 5g:** a brown viscous oil; R<sub>f</sub> = 0.24 (EtOAc/petrol (1:1)); IR (neat) ν<sub>max</sub> 3332, 3051, 2934, 2807, 1699, 1595, 1463, 1322, 1229, 1086, 969, 750, and 729 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz) δ 7.38 (1H, d, J = 7.8 Hz, ArH), 7.20 (1H, dt, J = 8.1, 0.9 Hz, ArH), 6.97 (1H, dt, J = 7.2, 0.9 Hz, ArH), 6.93 (1H, d, J = 8.1 Hz, ArH), 4.87 (1H, s, CHN), 4.46–4.41 (2H, m, CH<sub>2</sub>OH), 3.15 (1H, brs, OH), 2.60–2.35 (4H, m, 2 × CH<sub>2</sub>N), 1.55–1.51 (4H, brs, 2 × CH<sub>2</sub>), 1.40–1.38 (2H, m, CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 157.7 (OC=C), 154.7 (ArCO), 129.4 (ArCH), 126.2 (ArCH), 125.5 (ArC), 121.9 (ArCH), 109.6 (ArCH), 105.2 (C=CH), 67.0 (CHN), 56.9 (CH<sub>2</sub>OH), 49.4 (2 × CH<sub>2</sub>N), 26.2 (CH<sub>2</sub>), 24.4 (CH<sub>2</sub>); HRESIMS calcd for C<sub>15</sub>H<sub>20</sub>NO<sub>2</sub> (M + H)<sup>+</sup> 246.1494; found 246.1486.

**2-(6-Hydroxy-1-(piperidin-1-yl)hex-2-yn-1-yl)phenol (4h).** A mixture of Zn(OAc)<sub>2</sub>·2H<sub>2</sub>O (88 mg, 0.4 mmol), salicylaldehyde (489 mg, 4.0 mmol), 4-pentyn-1-ol (505 mg, 6.0 mmol), and piperidine (443 mg, 5.2 mmol) in anhydrous toluene (10 mL) was heated under N<sub>2</sub> at 120 °C for 24 h. The solvent was removed under reduced



pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:1)) to give product **4h** (1.076 g, 98%) as a colorless viscous oil:  $R_f = 0.44$  (EtOAc/petrol (1:1)); IR (neat)  $\nu_{\max}$  3397, 3042, 2934, 2852, 2234, 1607, 1589, 1464, 1368, 1274, 1246, 1154, 1058, 981, 858, and 805  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz)  $\delta$  7.44 (1H, d,  $J = 8.00$  Hz, ArH), 7.18 (1H, t,  $J = 8.00$  Hz, ArH), 6.84–6.80 (2H, m, ArH), 4.82 (1H, s, CHN), 3.81 (2H, t,  $J = 6.0$  Hz,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 2.63–2.58 (4H, m,  $2 \times \text{CH}_2\text{N}$ ), 2.50–2.47 (2H, m,  $\text{CH}_2$ ), 1.86 (2H, quint,  $J = 6.5$  Hz,  $\text{CH}_2$ ), 1.64 (4H, brs,  $2 \times \text{CH}_2$ ), 1.50 (2H, brs,  $\text{CH}_2$ );  $^{13}\text{C}$  NMR (125 MHz)  $\delta$  157.7 (ArCOH), 129.3 (ArCH), 128.4 (ArCH), 121.9 (ArC), 119.0 (ArCH), 116.3 (ArCH), 89.5 ( $\text{C}\equiv\text{CCH}_2$ ), 73.4 ( $\text{C}\equiv\text{CCH}_2$ ), 61.8 ( $\text{CH}_2\text{OH}$ ), 60.8 (CHN), 31.8 ( $\text{CH}_2$ ), 26.0 ( $2 \times \text{CH}_2$ ), 24.1 ( $\text{CH}_2$ ), 15.5 ( $\text{CH}_2$ ), [signals for  $2 \times \text{CH}_2\text{N}$  were not observed due to line broadening]; HRESIMS calcd for  $\text{C}_{17}\text{H}_{24}\text{NO}_2$  ( $M + \text{H}^+$ ) 274.1807; found 274.1796.

**2-(1-(Dibutylamino)-3-phenylprop-2-yn-1-yl)phenol (4i).** A mixture of  $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$  (88 mg, 0.4 mmol), salicylaldehyde (489 mg, 4.0 mmol), phenylacetylene (613 mg, 6.0 mmol), and dibutylamine (672 mg, 5.2 mmol) in anhydrous toluene (10 mL) was heated under  $\text{N}_2$  at 120 °C for 18 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:19)) to give product **4i** (1.20 g, 90%) as a yellow viscous oil:  $R_f = 0.20$  (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\max}$  3054, 2961, 2848, 2232, 1588, 1473, 1257, 1245, 1115, 1072, 689, and 636  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  11.35 (1H, brs, ArOH), 7.60 (1H, d,  $J = 7.5$  Hz, ArH), 7.55–7.52 (2H, m, ArH), 7.34–7.32 (3H, m, ArH), 7.23 (1H, t,  $J = 7.5$  Hz, ArH), 6.88–6.83 (4H, m,  $2 \times \text{CH}_2\text{N}$ ), 5.30 (1H, s, CHN), 2.72–2.52 (4H, m,  $2 \times \text{CH}_2\text{N}$ ), 1.68–1.49 (4H, m,  $2 \times \text{CH}_2$ ); 1.48–1.21 (4H, m,  $2 \times \text{CH}_2$ ), 0.90 (6H, t,  $J = 7.5$  Hz,  $2 \times \text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  157.4 (ArCO), 131.9 ( $2 \times \text{ArCH}$ ), 129.4 (ArCH), 128.6 ( $2 \times \text{ArCH}$ ), 128.4 ( $2 \times \text{ArCH}$ ), 122.7 (ArC), 122.0 (ArC), 119.1 (ArCH), 116.4 (ArCH), 89.2 ( $\text{C}\equiv\text{CAr}$ ), 82.8 ( $\text{C}\equiv\text{CAr}$ ), 57.1 (CHN), 51.0 ( $2 \times \text{CH}_2\text{N}$ ), 30.0 ( $2 \times \text{CH}_2\text{CH}_2\text{CH}_2$ ), 20.7 ( $2 \times \text{CH}_2\text{CH}_3$ ), 14.0 ( $2 \times \text{CH}_2\text{CH}_3$ ); HRESIMS calcd for  $\text{C}_{23}\text{H}_{30}\text{NO}$  ( $M + \text{H}^+$ ) 336.2327; found 336.2343.

**4-(2-Benzylidene-2,3-dihydrobenzofuran-3-yl)morpholine (5a).** A mixture of  $\text{AgNO}_3$  (240 mg, 1.41 mmol) and **4a** (2.00 g, 6.82 mmol) in anhydrous DMF (30 mL) was heated under  $\text{N}_2$  at 60 °C for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:4)) and then crystallization with EtOAc/petrol to give product **5a** (1.80 g, 90%) as colorless crystals: mp 104–106 °C;  $R_f = 0.23$  (EtOAc/petrol (1:19)); IR (neat)  $\nu_{\max}$  3035, 2939, 2849, 1681, 1608, 1447, 1339, 1229, 1209, 1109, 727, and 690  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.70 (2H, d,  $J = 8.0$  Hz, ArH), 7.35 (1H, d,  $J = 7.0$  Hz, ArH), 7.34 (2H, t,  $J = 7.5$  Hz, ArH), 7.25 (1H, t,  $J = 7.5$  Hz, ArH), 7.17 (1H, t,  $J = 7.0$  Hz, ArH), 7.00 (1H, d,  $J = 8.0$  Hz, ArH), 6.99 (1H, d,  $J = 7.5$  Hz, ArH), 5.85 (1H, s,  $\text{C}=\text{CHAr}$ ), 4.95 (1H, s, CHN), 3.75–3.65 (4H, m,  $2 \times \text{CH}_2\text{O}$ ), 2.80–2.66 (2H, m,  $\text{CH}_2\text{N}$ ), 2.60–2.50 (2H, m,  $\text{CH}_2\text{N}$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  158.2 (ArC), 153.8 ( $\text{C}=\text{CHAr}$ ), 135.0 (ArC), 129.7 (ArCH), 128.5 ( $2 \times \text{ArCH}$ ), 128.46 ( $2 \times \text{ArCH}$ ), 126.4 (ArCH), 126.2 (ArCH), 124.4 (ArC), 122.3 (ArCH), 110.3 (ArCH), 105.7 ( $\text{C}=\text{CHAr}$ ), 68.2 (CHN), 67.4 ( $2 \times \text{CH}_2\text{O}$ ), 48.8 ( $2 \times \text{CH}_2\text{N}$ ); HRESIMS calcd for  $\text{C}_{19}\text{H}_{20}\text{NO}_2$  ( $M + \text{H}^+$ ) 294.1494; found 294.1490.

**1-(2-Benzylidene-2,3-dihydrobenzofuran-3-yl)piperidine (5b).** A mixture of  $\text{AgNO}_3$  (161 mg, 0.95 mmol) and **4b** (1.385 g, 4.75 mmol) in anhydrous DMF (25 mL) was heated under  $\text{N}_2$  at 60 °C for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) to give product **5b** (1.086 g, 78%) as a pale yellow solid: mp 78–80 °C;  $R_f = 0.25$  (EtOAc/petrol (1:9)); IR (neat)  $\nu_{\max}$  3050, 2942, 2808, 1686, 1606, 1590, 1459, 1331, 1227, 1209, 753, and 691  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.73 (2H, d,  $J = 8.0$  Hz, ArH), 7.42–7.33 (3H, m, ArH), 7.26–7.19 (2H, m, ArH), 7.04–7.01 (2H, m, ArH), 5.85 (1H, s,  $\text{C}=\text{CHAr}$ ), 4.96 (1H, s, CHN), 2.72–2.63 (2H, m,  $\text{CH}_2\text{N}$ ), 2.52–2.42 (2H, m,  $\text{CH}_2\text{N}$ ), 1.59–1.50 (4H, m,  $2 \times \text{CH}_2$ ), 1.43–1.34 (2H, m,  $\text{CH}_2$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  158.2 (ArCO), 154.9 (OC=CH), 135.4 (ArC), 129.4 (ArCH), 128.5 ( $2 \times \text{ArCH}$ ), 126.2 ( $2 \times \text{ArCH}$ ), 125.4 (ArC), 122.1 (ArCH), 110.1 (ArCH), 105.0 ( $\text{C}=\text{CHAr}$ ), 68.8 (CHN), 49.8 ( $2 \times \text{CH}_2\text{N}$ ), 26.6 ( $2 \times \text{CH}_2$ ), 24.6 ( $\text{CH}_2$ ); HRESIMS calcd for  $\text{C}_{20}\text{H}_{22}\text{NO}$  ( $M + \text{H}^+$ ) 292.1701; found 292.1710.

**1-(2-Benzylidene-2,3-dihydrobenzofuran-3-yl)pyrrolidine (5c).** A mixture of  $\text{AgNO}_3$  (229 mg, 1.35 mmol) and **4c** (1.883 g, 6.79 mmol) in anhydrous DMF (30 mL) was heated under  $\text{N}_2$  at 60 °C for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:19)) to give product **5c** (1.221 g, 65%) as a brown viscous oil:  $R_f = 0.23$  (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\max}$  3053, 2965, 2811, 1686, 1611, 1594, 1461, 1347, 1228, 1210, 1069, 748, and 692  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.72 (2H, d,  $J = 7.5$  Hz, ArH), 7.41 (1H, d,  $J = 7.0$  Hz, ArH), 7.35 (2H,  $J = 7.5$  Hz, d, ArH), 7.25 (1H, t,  $J = 7.5$  Hz, ArH), 7.04 (1H, d,  $J = 7.5$  Hz, ArH), 7.00 (1H, t,  $J = 7.0$  Hz, ArH), 5.83 (1H, s,  $\text{C}=\text{CHAr}$ ), 5.16 (1H, s, CHN), 2.77–2.62 (4H, m,  $2 \times \text{CH}_2\text{N}$ ), 1.78–1.72 (4H, m,  $2 \times \text{CH}_2$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  158.3 ( $\text{C}=\text{CHAr}$ ), 154.8 (ArCO), 135.2 (ArC), 129.5 (ArCH), 128.6 ( $2 \times \text{ArCH}$ ), 128.5 ( $2 \times \text{ArCH}$ ), 126.3 (ArCH), 126.2 (ArCH), 125.6 (ArC), 122.2 (ArCH), 110.3 (ArCH), 105.7 ( $\text{C}=\text{CHAr}$ ), 63.9 (CHN), 48.2 ( $2 \times \text{CH}_2\text{N}$ ), 23.5 ( $2 \times \text{CH}_2$ ); HRESIMS calcd for  $\text{C}_{19}\text{H}_{20}\text{NO}$  ( $M + \text{H}^+$ ) 278.1545; found 278.1544.

**1-(2-Benzylidene-2,3-dihydrobenzofuran-3-yl)pyrrolidine (5c) and 1-(Benzofuran-2-yl(phenyl)methyl)pyrrolidine (6c).** A mixture of  $\text{AgNO}_3$  (35 mg, 0.21 mmol) and **4c** (285 mg, 1.03 mmol) in anhydrous DMF (5 mL) was heated under  $\text{N}_2$  at 100 °C for 18 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (5% EtOAc/petrol) to give **5c** (102 mg, 35.8%) and **6c** (6 mg, 2.1%). **Compound 6c:** a viscous yellow oil;  $R_f = 0.38$  (20% EtOAc/petrol); IR (neat)  $\nu_{\max}$  3052, 3029, 2965, 2874, 2786, 1584, 1492, 1452, 1251, 1134, 801, 744, and 701  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  7.56 (2H, d,  $J = 7.50$  Hz, ArH), 7.46 (2H, t,  $J = 7.50$  Hz, ArH), 7.34–7.16 (5H, m, ArH), 6.63 (1H, s,  $\text{C}=\text{CH}$ ), 4.42 (1H, s, CHN), 2.52 (4H, brs,  $2 \times \text{CH}_2\text{N}$ ), 1.80 (4H, brs,  $2 \times \text{CH}_2$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  158.8 (OC=CH), 154.9 (ArCO), 140.6 (ArC), 128.5 ( $2 \times \text{ArCH}$ ), 128.3 (ArC), 128.3 ( $2 \times \text{ArCH}$ ), 127.7 (ArCH), 123.8 (ArCH), 122.7 (ArCH), 120.8 (ArCH), 111.5 (ArCH), 103.6 (OC=CH), 69.4 (CHN), 53.5 ( $2 \times \text{CH}_2\text{N}$ ), 23.5 ( $2 \times \text{CH}_2$ ); HRESIMS calcd for  $\text{C}_{19}\text{H}_{20}\text{NO}$  ( $M + \text{H}^+$ ) 278.1545; found 278.1553.

**4-(2-(4-Fluorobenzylidene)-2,3-dihydrobenzofuran-3-yl)morpholine (5d).** A mixture of  $\text{AgNO}_3$  (22 mg, 0.13 mmol) and **4d** (203 mg, 0.65 mmol) in anhydrous DMF (5 mL) was heated under  $\text{N}_2$  at 60 °C for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (15:85)) and then crystallization with EtOAc/petrol to give product **5d** (165 mg, 81%) as a pale yellow solid: mp 128–130 °C;  $R_f = 0.15$  (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\max}$  3063, 2973, 2932, 2823, 1690, 1593, 1508, 1457, 1340, 1228, 1210, 1106, 909, and 850  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.71–7.66 (2H, m, ArH), 7.43 (1H, d,  $J = 7.8$  Hz, ArH), 7.30 (1H, t,  $J = 7.8$  Hz, ArH), 7.09–7.02 (4H, m, ArH), 5.84 (1H, s,  $\text{C}=\text{CHAr}$ ), 4.98 (1H, s, CHN), 3.71–3.68 (4H, m,  $2 \times \text{CH}_2\text{O}$ ), 2.79–2.72 (2H, m,  $\text{CH}_2\text{N}$ ), 2.58–2.51 (2H, m,  $\text{CH}_2\text{N}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  161.4 (d,  $J = 245$  Hz, ArCF), 158.2 (ArCO), 153.5 ( $\text{C}=\text{CHAr}$ ), 131.2 (ArC), 130.2 (ArCH), 130.1 (ArCH), 129.8 (ArCH), 126.3 (ArCH), 124.5 (ArC), 122.4 (ArCH), 115.5 (d,  $J = 21$  Hz, ArCH), 115.2 (ArCH), 110.3 (ArCH), 104.6 ( $\text{C}=\text{CHAr}$ ), 68.2 (CHN), 67.5 ( $2 \times \text{CH}_2\text{O}$ ), 48.8 ( $2 \times \text{CH}_2\text{N}$ ); HRESIMS calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_2\text{F}$  ( $M + \text{H}^+$ ) 312.1400; found 312.1413.

**4-(Benzofuran-2-yl(4-methoxyphenyl)methyl)morpholine (6e).** A mixture of  $\text{AgNO}_3$  (21 mg, 0.12 mmol) and **4e** (203 mg, 0.63 mmol) in anhydrous DMF (5 mL) was heated under  $\text{N}_2$  at 60 °C for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) to give product **6e** (137 mg, 68%) as a viscous yellow oil:  $R_f = 0.28$  (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\max}$  3065, 3035, 2956, 2851, 2806, 1607, 1509, 1452, 1247, 1172, 1114, 1032, 1005, 811, and 746  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.50–7.42 (4H, m, ArH), 7.23–7.14 (2H, m, ArH), 6.86 (2H, d,  $J = 8.7$  Hz, ArH), 6.63 (1H, s,  $\text{C}=\text{CHAr}$ ), 4.45 (1H, s, CHN), 3.76 (3H, s,  $\text{OCH}_3$ ), 3.72 (4H, t,  $J = 4.5$  Hz,  $2 \times \text{CH}_2\text{O}$ ), 2.52–2.38 (2H, m,  $2 \times \text{CH}_2\text{N}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ,

75 MHz)  $\delta$  159.3 (ArCO), 157.3 (C=CHAr), 155.0 (ArCO), 130.7 (ArC), 129.8 (2  $\times$  ArCH), 128.2 (ArC), 123.9 (ArCH), 122.8 (ArCH), 120.8 (ArCH), 119.0 (2  $\times$  ArCH), 111.5 (ArCH), 105.0 (C=CHAr), 69.2 (OCH<sub>3</sub>), 67.1 (2  $\times$  CH<sub>2</sub>O), 55.3 (CHN), 52.3 (2  $\times$  CH<sub>2</sub>N); HRESIMS calcd for C<sub>20</sub>H<sub>22</sub>NO<sub>3</sub> (M + H)<sup>+</sup> 324.1600; found 324.1612.

**4-(2-Hexylidene-2,3-dihydrobenzofuran-3-yl)morpholine (5f) and (E)-1-(2-Hydroxyphenyl)oct-1-en-3-one (13).** A mixture of AgNO<sub>3</sub> (51 mg, 0.30 mmol) and 4f (432 mg, 1.50 mmol) in anhydrous DMF (10 mL) was heated under N<sub>2</sub> at 60 °C for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (NH<sub>3</sub>/EtOAc/petrol (1:2.5:44)) to give 5f (136 mg, 31.5%) and 13 (21 mg, 6.4%).

**Compound 5f:** Light yellow viscous oil;  $R_f$  = 0.30 (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\max}$  3048, 2956, 2924, 2853, 1604, 1596, 1460, 1378, 1232, 1114, 898, and 751 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz)  $\delta$  7.36 (1H, dd,  $J$  = 7.5, 0.6 Hz, ArH), 7.22 (1H, dt,  $J$  = 7.5, 0.9 Hz, ArH), 6.96 (1H, dt,  $J$  = 7.5, 0.9 Hz, ArH), 6.90 (2H, d,  $J$  = 8.4 Hz, ArH), 4.87 (1H, dt,  $J$  = 7.2, 1.5 Hz, C=CHCH<sub>2</sub>), 4.76 (1H, s, CHN), 3.68–3.65 (4H, m, 2  $\times$  CH<sub>2</sub>O), 2.68–2.59 (2H, m, CH<sub>2</sub>N), 2.49–2.42 (2H, m, CH<sub>2</sub>N), 2.28 (2H, appr q,  $J$  = 7.8 Hz, C=CHCH<sub>2</sub>), 1.46–1.31 (6H, m, 3  $\times$  CH<sub>2</sub>), 0.90 (3H, t,  $J$  = 6.6 Hz, CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  158.3 (ArCO), 151.9 (OC=CH), 129.6 (ArCH), 126.3 (ArCH), 125.5 (ArC), 121.6 (ArCH), 109.7 (ArCH), 107.0 (C=CHCH<sub>2</sub>), 67.5 (2  $\times$  CH<sub>2</sub>O), 66.5 (CHN), 48.5 (2  $\times$  CH<sub>2</sub>N), 31.7 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 25.3 (C=HCH<sub>2</sub>), 22.7 (CH<sub>2</sub>), 14.3 (CH<sub>2</sub>CH<sub>3</sub>); HRESIMS calcd for C<sub>18</sub>H<sub>26</sub>NO<sub>2</sub> (M + H)<sup>+</sup> 288.1964; found 288.1959.

**Compound 13:** pale yellow solid; mp 72–74 °C;  $R_f$  = 0.25 (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\max}$  3160, 2934, 2859, 1665, 1600, 1453, 1250, 1179, 975, and 745 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz)  $\delta$  8.11 (1H, brs, ArOH), 7.69 (1H, d,  $J$  = 16.5 Hz, ArCH=CH), 7.47 (1H, dd,  $J$  = 8.0, 1.5 Hz, ArH), 7.24 (1H, dt,  $J$  = 8.0, 1.5 Hz, ArH), 7.02 (1H, d,  $J$  = 16.5 Hz, ArCH=CH), 6.96 (1H, d,  $J$  = 7.5 Hz, ArH), 6.89 (1H, t,  $J$  = 7.5 Hz, ArH), 2.71 (2H, t,  $J$  = 7.5 Hz, CH<sub>2</sub>C=O), 1.69 (2H, quint,  $J$  = 7.5 Hz, CH<sub>2</sub>), 1.36–1.31 (2H, m, CH<sub>2</sub>CH<sub>3</sub>), 0.90 (3H, t,  $J$  = 6.5 Hz, CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz)  $\delta$  204.1 (C=O), 156.5 (ArCO), 140.2 (ArCH=CH), 130.0 (ArCH), 129.5 (ArCH), 126.6 (ArCH=CH), 121.8 (ArC), 120.6 (ArCH), 116.8 (ArCH), 40.3 (CH<sub>2</sub>C=O), 31.7 (CH<sub>2</sub>), 24.6 (CH<sub>2</sub>), 22.6 (CH<sub>2</sub>CH<sub>3</sub>), 14.1 (CH<sub>2</sub>CH<sub>3</sub>); HRESIMS calcd for C<sub>14</sub>H<sub>19</sub>O<sub>2</sub> (M + H)<sup>+</sup> 219.1385; found 219.1392.

**2-(3-(Piperidin-1-yl)benzofuran-2(3H)-ylidene)ethanol (5g).** A mixture of AgNO<sub>3</sub> (235 mg, 1.38 mmol) and 4g (1.695 g, 6.61 mmol) in anhydrous DMF (40 mL) was heated under N<sub>2</sub> at 60 °C for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:1)) to give product 5g (1.426 g, 84%) as a viscous yellow oil. See above for physical and spectroscopic data.

**4-(3-(Piperidin-1-yl)benzofuran-2(3H)-ylidene)butan-1-ol (5h) and 4',5'-Dihydro-3'H-spiro[chromene-2,2'-furan] (14).** A mixture of AgNO<sub>3</sub> (138 mg, 0.81 mmol) and 4h (1.113 mg, 4.07 mmol) in anhydrous DMF (20 mL) was heated under N<sub>2</sub> at 60 °C for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (50% EtOAc/petrol) to give 12a (393 mg, 51.3%) and 5h (356 mg, 32.0%).

**Compound 14:** colorless oil;  $R_f$  = 0.20 (5% EtOAc/petrol (1:19)); IR (neat)  $\nu_{\max}$  3046, 2981, 2886, 1642, 1605, 1487, 1189, 1121, 1063, 984, 949, 842, and 754 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz)  $\delta$  7.20–7.09 (2H, m, ArH), 6.92–6.88 (2H, m, ArH), 6.68 (1H, d,  $J$  = 9.6 Hz, ArCH=CH), 5.72 (1H, d,  $J$  = 9.6 Hz, ArCH=CH), 4.20–3.85 (2H, m, CH<sub>2</sub>O), 2.37–2.32 (2H, m), 2.04–1.98 (2H, m); <sup>13</sup>C NMR (75 MHz)  $\delta$  151.8 (ArCO), 129.2 (ArCH), 126.88 (ArCH), 126.85 (ArCH=CH), 122.6 (ArCH=CH), 121.2 (ArCH), 120.4 (ArC), 116.5 (ArCH), 105.3 (C(O)<sub>2</sub>), 68.3 (CH<sub>2</sub>O), 39.2 (CH<sub>2</sub>), 24.5 (CH<sub>2</sub>); ESIMS  $m/z$  189 (M + H)<sup>+</sup>. Spectroscopic data are identical to those in the literature.<sup>16</sup>

**Compound 5h:** brown viscous oil;  $R_f$  = 0.27 (50% EtOAc/petrol); IR (neat)  $\nu_{\max}$  3336, 2934, 2853, 1699, 1612, 1595, 1462, 1323, 1227, 1086, 750, and 729 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz)  $\delta$  7.36 (1H, d,  $J$  = 7.5 Hz, ArH), 7.20 (1H, t,  $J$  = 8.0 Hz, ArH), 6.95 (1H, t,  $J$  = 7.5 Hz, ArH), 6.87 (1H, d,  $J$  = 8.0 Hz, ArH), 4.89 (1H, dt,  $J$  = 7.5, 1.5 Hz, C=CH),

4.75 (1H, s, CHN), 3.69 (2H, t,  $J$  = 6.5 Hz, CH<sub>2</sub>OH), 2.75 (1H, brs, OH), 2.54–2.52 (2H, m, CH<sub>2</sub>N), 2.41–2.34 (4H, m, CH<sub>2</sub>N and C=CHCH<sub>2</sub>), 1.73 (2H, quint,  $J$  = 7.0 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.56–1.48 (4H, m, 2  $\times$  CH<sub>2</sub>), 1.40–1.36 (2H, m, CH<sub>2</sub>); <sup>13</sup>C NMR (125 MHz)  $\delta$  158.0 (ArCO), 153.3 (OC=CHAr), 129.3 (ArCH), 126.3 (ArCH), 125.9 (ArC), 121.6 (ArCH), 109.5 (ArCH), 105.1 (C=CHAr), 66.9 (CHN), 62.1 (CH<sub>2</sub>OH), 49.4 (2  $\times$  CH<sub>2</sub>N), 32.5 (CH<sub>2</sub>), 26.3 (2  $\times$  CH<sub>2</sub>), 24.5 (CH<sub>2</sub>), 21.5 (C=CHCH<sub>2</sub>); HRESIMS calcd for C<sub>17</sub>H<sub>24</sub>NO<sub>2</sub> (M + H)<sup>+</sup> 274.1807; found 274.1807.

**2-Benzylidene-N,N-dibutyl-2,3-dihydrobenzofuran-3-amine (5i).** A mixture of AgNO<sub>3</sub> (109 mg, 0.64 mmol) and 4i (1.080 g, 3.22 mmol) in anhydrous DMF (20 mL) was heated under N<sub>2</sub> at 60 °C for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:49)) to give product 5i (1.086 g, 84.5%) as a viscous yellow oil;  $R_f$  = 0.70 (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\max}$  3055, 3024, 2955, 2929, 2865, 2820, 1685, 1610, 1595, 1460, 1341, 1228, 1209, 1083, 917, 747, and 693 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz)  $\delta$  7.70 (2H, d,  $J$  = 7.5 Hz, ArH), 7.38–7.33 (3H, m, ArH), 7.25–7.15 (2H, m, ArH), 7.03–7.95 (2H, m, ArH), 5.80 (1H, s, C=CHAr), 5.19 (1H, s, CHN), 2.63–2.44 (2H, m, 2  $\times$  CH<sub>2</sub>N), 1.45 (4H, quint,  $J$  = 7.5 Hz, 2  $\times$  CH<sub>2</sub>), 1.30 (4H, sext,  $J$  = 7.2 Hz, 2  $\times$  CH<sub>2</sub>CH<sub>3</sub>), 0.86 (6H, t,  $J$  = 7.2 Hz, 2  $\times$  CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz)  $\delta$  158.0 (ArCO), 156.2 (OC=CHAr), 135.5 (ArC), 129.2 (ArCH), 128.5 (2  $\times$  ArCH), 128.4 (2  $\times$  ArCH), 126.4 (ArC), 126.1 (ArCH), 125.9 (ArCH), 122.1 (ArCH), 110.3 (ArCH), 104.2 (C=CHAr), 64.3 (CHN), 50.9 (2  $\times$  CH<sub>2</sub>N), 31.1 (2  $\times$  CH<sub>2</sub>), 20.5 (2  $\times$  CH<sub>2</sub>CH<sub>3</sub>), 14.2 (2  $\times$  CH<sub>2</sub>CH<sub>3</sub>); HRESIMS calcd for C<sub>23</sub>H<sub>30</sub>NO (M + H)<sup>+</sup> 336.2327; found 336.2332.

**4-(Benzofuran-2-yl(phenyl)methyl)morpholine (6a).** Method A: A mixture of AgNO<sub>3</sub> (12 mg, 0.07 mmol) and 5a (97 mg, 0.33 mmol) in anhydrous DMF (5 mL) was heated under N<sub>2</sub> at 100 °C for 24 h. The solvent was removed under reduced pressure, and the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:5)) to give 6a (66 mg, 68%) as a yellow viscous oil;  $R_f$  = 0.40 (20% EtOAc/petrol (1:4)); IR (neat)  $\nu_{\max}$  3061, 3030, 2956, 2852, 2807, 1584, 1492, 1451, 1393, 1251, 1114, 870, 746, and 701 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz)  $\delta$  7.53 (2H, d,  $J$  = 7.5 Hz, ArH), 7.49 (1H, d,  $J$  = 8.0 Hz, ArH), 7.45 (1H, d,  $J$  = 8.5 Hz, ArH), 7.33 (2H, t,  $J$  = 8.0 Hz, ArH), 7.26 (1H, t,  $J$  = 7.5 Hz, ArH), 7.22 (1H, t,  $J$  = 7.0 Hz, ArH), 7.18 (1H, t,  $J$  = 7.0 Hz, ArH), 6.65 (1H, s, C=CH), 4.50 (1H, s, CHN), 3.73 (4H, t,  $J$  = 5.0 Hz, 2  $\times$  CH<sub>2</sub>O), 2.52–2.42 (4H, m, 2  $\times$  CH<sub>2</sub>N); <sup>13</sup>C NMR (75 MHz)  $\delta$  157.0 (C=CO), 155.1 (ArCO), 138.7 (ArC), 128.7 (2  $\times$  ArCH), 128.6 (2  $\times$  ArCH), 128.2 (ArC), 127.9 (ArCH), 124.0 (ArCH), 122.8 (ArCH), 120.9 (ArCH), 111.5 (ArCH), 105.3 (C=CH), 69.9 (CHN), 67.1 (2  $\times$  CH<sub>2</sub>O), 52.3 (2  $\times$  CH<sub>2</sub>N); HRESIMS calcd for C<sub>19</sub>H<sub>20</sub>NO<sub>2</sub> (M + H)<sup>+</sup> 294.1494; found 294.1501.

**Method B in MeCN:** To a solution of 5a (89 mg, 0.30 mmol) in anhydrous CH<sub>3</sub>CN (5 mL) at rt was added BF<sub>3</sub>·Et<sub>2</sub>O (60  $\mu$ L, 0.46 mmol) dropwise under N<sub>2</sub>, and the mixture was stirred at rt for 4 h. The solution was treated with saturated NaHCO<sub>3</sub> solution (10 mL) and extracted with EtOAc (2  $\times$  15 mL). The combined EtOAc extract was washed with brine, dried (MgSO<sub>4</sub>), filtered, and evaporated under reduced pressure. The crude mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) to give product 6a (86 mg, 97%).

**Method B in CH<sub>2</sub>Cl<sub>2</sub>:** To a solution of 5a (100 mg, 0.34 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (5 mL) at rt was added BF<sub>3</sub>·Et<sub>2</sub>O (63  $\mu$ L, 0.51 mmol) dropwise under N<sub>2</sub>, and the mixture was stirred at rt for 2 h. After a workup procedure similar to that described above, the crude mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) to give 6a (87 mg, 87%).

**1-(Benzofuran-2-yl(phenyl)methyl)piperidine (6b).** The title compound was prepared according to method B above from 5b (102 mg, 0.35 mmol) using CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and BF<sub>3</sub>·Et<sub>2</sub>O (65  $\mu$ L, 0.53 mmol). After stirring the solution at rt for 18 h, the reaction mixture was worked up as described above. The crude mixture was purified using flash column chromatography (EtOAc/petrol (1:23)) to give 6b (59 mg, 58%) and starting material (5b) (42 mg, 41%). Compound 6b was obtained as a brown viscous oil;  $R_f$  = 0.28 (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\max}$  3062, 3029, 2932, 2852, 2796, 1583, 1491, 1450, 1252,

1160, 807, 744, and 699  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.51–7.42 (4H, m, ArH), 7.34–7.12 (5H, m, ArH), 6.61 (1H, s, OC=CH), 4.55 (1H, s, CHN), 2.41 (4H, brs,  $2 \times \text{CH}_2\text{N}$ ), 1.58 (4H, brs,  $2 \times \text{CH}_2$ ), 1.41 (2H, brs,  $\text{CH}_2$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  157.9 (OC=CH), 155.0 (ArCO), 139.4 (ArC), 128.6 ( $2 \times \text{ArCH}$ ), 128.4 ( $2 \times \text{ArCH}$ ), 127.5 (ArCH), 123.7 (ArCH), 122.7 (ArCH), 120.7 (ArCH), 111.5 (ArCH), 105.0 (OC=CH), 69.9 (CHN), 52.9 ( $2 \times \text{CH}_2\text{N}$ ), 26.2 ( $2 \times \text{CH}_2$ ), 24.6 ( $\text{CH}_2$ ); HRESIMS calcd for  $\text{C}_{20}\text{H}_{22}\text{NO}$  ( $M + \text{H}$ ) $^+$  292.1701; found 292.1708.

**1-(Benzofuran-2-yl(phenyl)methyl)pyrrolidine (6c).** The title compound was prepared according to method B above from **5c** (100 mg, 0.36 mmol) using  $\text{CH}_2\text{Cl}_2$  (5 mL) and  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (66  $\mu\text{L}$ , 0.54 mmol). After stirring the solution at rt for 24 h, the reaction mixture was worked up as described above. The crude mixture was purified using flash column chromatography (EtOAc/petrol (1:23)) to give **6c** (43 mg, 43%) and recovered starting material (**5c**) (56 mg, 56%). The physical and spectroscopic data for **6c** are described above.

**4-(Benzofuran-2-yl(4-fluorophenyl)methyl)morpholine (6d).** The title compound was prepared according to method B above from **5d** (105 mg, 0.30 mmol) using  $\text{CH}_2\text{Cl}_2$  (5 mL) and  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (55  $\mu\text{L}$ , 0.45 mmol). After stirring the solution at rt for 1 h, the reaction mixture was worked up as described above. The crude mixture was purified using flash column chromatography (20% EtOAc/petrol (1:4)) to give **6d** (101 mg, 96%) as a pale yellow solid: mp 56–58  $^\circ\text{C}$ ;  $R_f$  = 0.35 (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\text{max}}$  3061, 3039, 2931, 2874, 2853, 2823, 1689, 1592, 1508, 1458, 1227, 1209, 1107, 1007, 909, 849, and 758  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.55–7.44 (4H, m, ArH), 7.27–7.16 (2H, m, ArH), 7.02 (2H, appr t,  $J$  = 15 Hz, ArH), 6.64 (1H, d,  $J$  = 0.9 Hz, C=CH), 4.49 (1H, s, CHN), 3.73 (4H, t,  $J$  = 4.8 Hz,  $2 \times \text{CH}_2\text{O}$ ), 2.52–2.38 (4H, m,  $2 \times \text{CH}_2\text{N}$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  162.4 ( $J$  = 245 Hz, ArCF), 156.6 (OC=C), 155.1 (ArCO), 134.5 (d,  $J$  = 3.8 Hz, ArC), 130.3 (d,  $J$  = 8.0 Hz, ArCH), 128.1 (ArC), 124.2 (ArCH), 122.9 (ArCH), 120.9 (ArCH), 115.5 (d,  $J$  = 21.5 Hz, ArCH), 111.5 (ArCH), 105.4 (CH=C), 69.0 (CHN), 67.1 ( $2 \times \text{CH}_2\text{O}$ ), 52.3 ( $2 \times \text{CH}_2\text{N}$ ); HRESIMS calcd for  $\text{C}_{19}\text{H}_{19}\text{FNO}_2$  ( $M + \text{H}$ ) $^+$  312.1400; found 312.1397.

**4-(1-(Benzofuran-2-yl)hexyl)morpholine (6f).** The title compound was prepared according to method B above from **5f** (101 mg, 0.35 mmol) using  $\text{CH}_2\text{Cl}_2$  (5 mL) and  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (65  $\mu\text{L}$ , 0.53 mmol). After stirring the solution at rt for 6 h, the reaction mixture was worked up as described above. The crude mixture was purified using flash column chromatography (EtOAc/petrol (1:23)) to give **6f** (22 mg, 22%) and recovered starting material (**5f**) (67 mg, 66%). Compound **6f** was obtained as a light yellow oil;  $R_f$  = 0.28 (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\text{max}}$  3064, 3036, 2954, 2929, 2853, 1613, 1577, 1452, 1251, 1116, 1004, and 743  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.52 (1H, d,  $J$  = 7.5 Hz, ArH), 7.46 (1H, d,  $J$  = 7.5 Hz, ArH), 7.24–7.20 (2H, m, ArH), 6.51 (1H, s, OC=CH), 3.71–3.68 (4H, m,  $2 \times \text{CH}_2\text{O}$ ), 3.58 (1H, t,  $J$  = 6.5 Hz, CHN), 2.62–2.50 (4H, m,  $2 \times \text{CH}_2\text{N}$ ), 1.95–1.85 (2H, m,  $\text{CH}_2$ ), 1.49–1.22 (6H, m,  $3 \times \text{CH}_2$ ), 0.85 (3H, t,  $J$  = 6.5 Hz,  $\text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  156.9 (OC=CH), 154.8 (ArCO), 128.2 (ArC), 123.8 (ArCH), 122.7 (ArCH), 120.8 (ArCH), 111.4 (ArCH), 105.2 (OC=CH), 67.4 ( $2 \times \text{CH}_2\text{O}$ ), 63.6 (CHN), 50.5 ( $2 \times \text{CH}_2\text{N}$ ), 31.9 ( $\text{CH}_2$ ), 30.4 ( $\text{CH}_2$ ), 26.4 ( $\text{CH}_2$ ), 22.6 ( $\text{CH}_2$ ), 14.1 ( $\text{CH}_2\text{CH}_3$ ); HRESIMS calcd for  $\text{C}_{18}\text{H}_{26}\text{NO}_2$  ( $M + \text{H}$ ) $^+$  288.1964; found 288.1967.

**N-(Benzofuran-2-yl(phenyl)methyl)-N-butylbutan-1-amine (6i).** The title compound was prepared according to method B above from **5i** (107 mg, 0.32 mmol) using  $\text{CH}_2\text{Cl}_2$  (5 mL) and  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (59  $\mu\text{L}$ , 0.48 mmol). After stirring the solution at rt for 24 h, the reaction mixture was worked up as described above. The crude mixture was purified using flash column chromatography (EtOAc/petrol (1:49)) to give **6i** (99 mg, 87%) as a light yellow viscous oil;  $R_f$  = 0.70 (EtOAc/petrol (1:4)); IR (neat)  $\nu_{\text{max}}$  3062, 3030, 2956, 2928, 2865, 1600, 1579, 1452, 1377, 1251, 1165, 1071, 744, and 698  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.54–7.45 (4H, m, ArH), 7.343–7.18 (5H, m, ArH), 6.60 (1H, s, C=CHAr), 5.12 (1H, s, CHN), 2.62–2.53 (2H, m,  $\text{CH}_2\text{N}$ ), 2.49–2.40 (2H, m,  $\text{CH}_2\text{N}$ ), 1.52–1.41 (4H, m,  $2 \times \text{CH}_2$ ), 1.34–1.18 (4H, m,  $2 \times \text{CH}_2\text{CH}_3$ ), 0.85 (6H, t,  $J$  = 7.5 Hz,  $2 \times \text{CH}_2\text{CH}_3$ );  $^{13}\text{C}$  NMR (75 MHz)  $\delta$  157.7 (OC=CHAr) 155.0

(ArCO), 140.2 (ArC), 128.7 ( $2 \times \text{ArCH}$ ), 128.4 (ArCH), 128.2 ( $2 \times \text{ArCH}$ ), 127.3 ( $2 \times \text{ArCH}$ ), 123.7 (ArCH), 122.7 (ArCH), 120.8 (ArCH), 111.5 (ArCH), 105.8 (C=CHAr), 63.6 (CHN), 50.5 ( $2 \times \text{CH}_2\text{N}$ ), 30.0 ( $2 \times \text{CH}_2$ ), 20.6 ( $2 \times \text{CH}_2\text{CH}_3$ ), 14.3 ( $2 \times \text{CH}_2\text{CH}_3$ ); HRESIMS calcd for  $\text{C}_{23}\text{H}_{30}\text{NO}$  ( $M + \text{H}$ ) $^+$  336.2327; found 336.2318.

**2-(1-Phenylbut-3-en-1-yl)benzofuran (15a).** *Method A: Using Allyl Trimethylsilane.* To a solution of **5a** (103 mg, 0.35 mmol) and allyl trimethylsilane (168  $\mu\text{L}$ , 1.05 mmol) in anhydrous  $\text{CH}_2\text{Cl}_2$  (5 mL) at rt was added  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (65  $\mu\text{L}$ , 0.53 mmol) dropwise under  $\text{N}_2$ . After stirring at rt for 2 h, the reaction mixture was treated with saturated  $\text{NaHCO}_3$  solution (10 mL) and extracted with  $\text{CH}_2\text{Cl}_2$  ( $2 \times 15$  mL). The combined  $\text{CH}_2\text{Cl}_2$  extract was washed with brine, dried ( $\text{MgSO}_4$ ), filtered, and evaporated under reduced pressure. The crude reaction mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) to give **6a** (55 mg, 53%) and **15a** (40 mg, 46%). Compound **15a** was obtained as a colorless viscous oil;  $R_f$  = 0.50 (EtOAc/petrol (1:23)); IR (neat)  $\nu_{\text{max}}$  3064, 3030, 1638, 1581, 1451, 1252, 916, 744, and 698  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz)  $\delta$  7.48–7.46 (1H, m, ArH), 7.42–7.38 (1H, m, ArH), 7.32–7.26 (4H, m, ArH), 7.24–7.16 (3H, m, ArH), 6.46 (1H, s, OC=CH), 5.82–5.69 (1H, m, CH=CH<sub>2</sub>), 5.11–4.96 (2H, m, CH=CH<sub>2</sub>), 4.15 (1H, t,  $J$  = 7.5 Hz, CHCH<sub>2</sub>), 3.08–2.41 (2H, m, CH<sub>2</sub>);  $^{13}\text{C}$  NMR (125 MHz)  $\delta$  160.5 (OC=CH), 154.9 (ArCO), 141.5 (ArC), 135.9 (CH=CH<sub>2</sub>), 128.7 ( $2 \times \text{ArCH}$ ), 128.2 ( $2 \times \text{ArCH}$ ), 127.0 (ArCH), 123.6 (ArCH), 122.6 (ArCH), 120.6 (ArCH), 117.0 (CH=CH<sub>2</sub>), 111.1 (ArCH), 103.0 (OC=CH), 45.9 (CHCH<sub>2</sub>), 38.9 (CH<sub>2</sub>); HRESIMS calcd for  $\text{C}_{18}\text{H}_{17}\text{O}$  ( $M + \text{H}$ ) $^+$  249.1279; found 249.1275.

*Method B: Using Allyl Tributylstannane.* To a solution of **5a** (100 mg, 0.34 mmol) and allyl tributylstannane (316  $\mu\text{L}$ , 1.02 mmol) in anhydrous acetonitrile (5 mL) at rt was added  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (62  $\mu\text{L}$ , 0.51 mmol) dropwise under  $\text{N}_2$ . After stirring for 2 h at rt, the reaction mixture was treated with saturated  $\text{NaHCO}_3$  solution (10 mL) and extracted with  $\text{CH}_2\text{Cl}_2$  ( $2 \times 15$  mL). The combined  $\text{CH}_2\text{Cl}_2$  extract was washed with brine, dried ( $\text{MgSO}_4$ ), filtered, and evaporated under reduced pressure. The crude reaction mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) to give **6a** (26 mg, 26%) and **15a** (61 mg, 73%).

*Method C: From Allylation of 1-(2-Benzylidene-2,3-dihydrobenzofuran-3-yl)piperidine (5b) with Allyl tributylstannane.* The title compound was prepared according to method B above from **5b** (100 mg, 0.34 mmol) and allyl tributylstannane (316  $\mu\text{L}$ , 1.02 mmol) using  $\text{CH}_2\text{Cl}_2$  (5 mL) and  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (63  $\mu\text{L}$ , 0.51 mmol). After stirring the solution at rt for 18 h, the reaction mixture was worked up as described above. The crude reaction mixture was purified using flash column chromatography (5% EtOAc/petrol (1:23)) to give **15a** (73 mg, 87%) as a colorless oil.

*Method D: From Allylation of 1-(2-Benzylidene-2,3-dihydrobenzofuran-3-yl)pyrrolidine (5c) with Allyl tributylstannane.* The title compound was prepared according to method B above from **5c** (105 mg, 0.38 mmol) and allyl tributylstannane (353  $\mu\text{L}$ , 1.14 mmol) using  $\text{CH}_2\text{Cl}_2$  (5 mL) and  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (70  $\mu\text{L}$ , 0.57 mmol). After stirring the solution at rt for 18 h, the reaction mixture was worked up as described above. The crude reaction mixture was purified using flash column chromatography (5% EtOAc/petrol (1:23)) to give **15a** (36 mg, 38%), **6c** (4 mg, 3.8%), and recovered starting material (**5c**) (60 mg, 57%).

**2-(1-(4-Fluorophenyl)but-3-en-1-yl)benzofuran (15d).** The title compound was prepared according to method B above from **5d** (99 mg, 0.32 mmol) and allyl tributylstannane (298  $\mu\text{L}$ , 0.96 mmol) using  $\text{CH}_2\text{Cl}_2$  (5 mL) and  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  (59  $\mu\text{L}$ , 0.48 mmol). After stirring the solution at rt for 2 h, the reaction mixture was worked up as described above. The crude reaction mixture was purified using flash column chromatography (EtOAc/petrol (1:23)) to give **6d** (30 mg, 30%) and **15d** (59 mg, 69%). Compound **15d** was obtained as a colorless viscous oil;  $R_f$  = 0.50 (EtOAc/petrol (1:23)); IR (neat)  $\nu_{\text{max}}$  3070, 2925, 1641, 1602, 1507, 1452, 1253, 1224, 1161, 917, and 744  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz)  $\delta$  7.50–7.47 (1H, m, ArH), 7.41–7.38 (1H, m, ArH), 7.27–7.17 (4H, m, ArH), 7.04–6.96 (2H, m, ArH), 6.45 (1H, s, C=CH), 5.80–5.68 (1H, m, CH=CH<sub>2</sub>), 5.10–4.97 (2H, m, CH=CH<sub>2</sub>), 4.13 (1H, t,  $J$  = 8.1 Hz, CHCH<sub>2</sub>), 3.00–2.91

(1H, m, CHCH<sub>2</sub>), 2.75–2.67 (1H, m, CHCH<sub>2</sub>); <sup>13</sup>C NMR (75 MHz) δ 161.9 (d, J = 244 Hz, ArCF), 160.2 (OC=CH), 154.9 (ArCO), 137.2 (d, J = 3.2 Hz, ArC), 135.6 (CH<sub>2</sub>CH=CH<sub>2</sub>), 129.7 (d, J = 7.7 Hz, ArCH), 128.6 (ArC), 123.7 (ArCH), 122.7 (ArCH), 120.7 (ArCH), 117.3 (CH<sub>2</sub>CH=CH<sub>2</sub>), 115.5 (d, J = 21.2 Hz, ArCH), 111.1 (C=CCO), 103.0 (CHAr), 45.1 (CHCH<sub>2</sub>), 38.9 (CH<sub>2</sub>CH=CH<sub>2</sub>); HRESIMS calcd for C<sub>18</sub>H<sub>16</sub>O<sub>2</sub> (M + H)<sup>+</sup> 267.1185; found 267.1187.

**2-(1-(4-Methoxyphenyl)but-3-en-1-yl)benzofuran (15e).** The title compound was prepared according to method B above from **6e** (80 mg, 0.25 mmol) and allyltributylstannane (233 μL, 0.75 mmol) using CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and BF<sub>3</sub>·Et<sub>2</sub>O (47 μL, 0.38 mmol). After stirring the solution at rt for 18 h, the reaction mixture was worked up as described above. The crude reaction mixture was purified using flash column chromatography (EtOAc/petrol (1:23)) to give **15e** (25 mg, 36%) as a colorless viscous oil: R<sub>f</sub> = 0.35 (EtOAc/petrol (1:23)); IR (neat) ν<sub>max</sub> 3069, 3034, 2931, 2835, 1610, 1582, 1510, 1453, 1248, 1175, 1034, 915 803 and 745 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz) δ 7.47 (1H, d, J = 8.0 Hz, ArH), 7.39 (1H, d, J = 8.0 Hz, ArH), 7.23–7.13 (4H, m, ArH), 6.85 (2H, d, J = 8.7 Hz, ArH), 6.43 (1H, s, OC=CH), 5.82–5.68 (1H, m, CH=CH<sub>2</sub>), 5.07 (1H, d, J = 17.1 Hz), 4.98 (d, J = 10.2 Hz), 4.10 (1H, t, J = 7.8 Hz, CHCH<sub>2</sub>), H<sub>4</sub>), 3.77 (3H, s, OCH<sub>3</sub>), 3.00–2.91 (1H, m), 2.78–2.66 (1H, m); <sup>13</sup>C NMR (75 MHz) δ 160.9 (OC=CH), 158.6 (ArCO), 154.9 (ArCO), 136.0 (CH=CH<sub>2</sub>), 133.6 (ArC), 129.1 (2 × ArCH), 128.7 (ArC), 123.5 (ArCH), 122.6 (ArCH), 120.6 (ArCH), 117.0 (CH=CH<sub>2</sub>), 114.0 (2 × ArCH), 111.1 (ArCH), 102.7 (OC=CH), 55.4 (OCH<sub>3</sub>), 45.0 (CHCH<sub>2</sub>), 39.0 (CH<sub>2</sub>); HRESIMS calcd for C<sub>19</sub>H<sub>19</sub>O<sub>2</sub> (M + H)<sup>+</sup> 279.1385; found 279.1376.

**2-(Non-1-en-4-yl)benzofuran (15f).** The title compound was prepared according to method B above from **5f** (101 mg, 0.35 mmol) and allyltributylstannane (326 μL, 1.05 mmol) using CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and BF<sub>3</sub>·Et<sub>2</sub>O (65 μL, 0.53 mmol). After stirring the solution at rt for 2 h, the reaction mixture was worked up as described above. The crude reaction mixture was purified using flash column chromatography (100% petrol) to give **15f** (74 mg, 87.1%) as a colorless oil: R<sub>f</sub> = 0.60 (5% EtOAc/petrol (1:23)); IR (neat) ν<sub>max</sub> 3072, 2926, 2857, 1641, 1586, 1451, 1251, 1171, 913, 798, and 742 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz) δ 7.50–7.41 (2H, m, ArH), 7.23–7.17 (2H, m, ArH), 6.38 (1H, s, C=CH), 5.81–5.67 (1H, m, CH=CH<sub>2</sub>), 5.06–4.95 (2H, m, CH=CH<sub>2</sub>), 2.95–2.83 (1H, m, CH(CH<sub>2</sub>)<sub>2</sub>), 2.58–2.38 (2H, m, CH<sub>2</sub>CH=CH<sub>2</sub>), 1.80–1.60 (2H, m, CH<sub>2</sub>), 1.27 (6H, brs, 3 × CH<sub>2</sub>), 0.85 (3H, brs, CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz) δ 161.9 (OC=C), 154.7 (ArCO), 136.4 (CH=CH<sub>2</sub>), 128.9 (ArC), 123.1 (ArCH), 122.5 (ArCH), 120.4 (ArCH), 116.5 (CH=CH<sub>2</sub>), 111.0 (ArCH), 102.3 (CH=CO), 39.6 (CH(CH<sub>2</sub>)<sub>2</sub>), 38.3 (CH<sub>2</sub>CH=CH<sub>2</sub>), 33.3 (CH<sub>2</sub>), 31.9 (CH<sub>2</sub>), 27.0 (CH<sub>2</sub>), 22.7 (CH<sub>2</sub>), 14.2 (CH<sub>2</sub>CH<sub>3</sub>); HRESIMS calcd for C<sub>17</sub>H<sub>22</sub>O (M + H)<sup>+</sup> 243.1749; found 243.1741.

**2-(Furan-2-yl(phenyl)methyl)benzofuran (16).** To a solution of **5a** (101 mg, 0.34 mmol) and furan (248 μL, 3.40 mmol) in anhydrous acetonitrile (5 mL) at rt was added BF<sub>3</sub>·Et<sub>2</sub>O (62 μL, 0.51 mmol) dropwise under N<sub>2</sub>. After stirring for 2 h at rt, the reaction mixture was treated with saturated NaHCO<sub>3</sub> solution (10 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 15 mL). The combined CH<sub>2</sub>Cl<sub>2</sub> extract was washed with brine, dried (MgSO<sub>4</sub>), filtered and evaporated under reduced pressure. The crude reaction mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) to give **6a** (54 mg, 54%) and **16** (40 mg, 43%). Compound **16** was obtained as a brown viscous oil; R<sub>f</sub> = 0.60 (EtOAc/petrol (1:5)); IR (neat) ν<sub>max</sub> 3062, 3030, 1583, 1499, 1452, 1165, 1009, 736, and 697 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz) δ 7.56–7.18 (9H, m, ArH), 6.41 (1H, m, furanyl-H), 6.35 (1H, brs, furanyl-H), 6.11 (1H, brs, furanyl-H), 5.59 (1H, s, CH); <sup>13</sup>C NMR (75 MHz) δ 157.6 (OC=CH), 155.1 (ArCO), 153.8 (furanyl-C), 142.3 (OC=CH), 138.9 (ArC), 128.8 (2 × ArCH), 128.6 (2 × ArCH), 128.5 (ArC), 127.6 (ArCH), 124.0 (ArCH), 122.8 (ArCH), 120.9 (ArCH), 111.3 (ArCH), 110.5 (furanyl-C), 108.1 (furanyl-C), 104.9 (furanyl-C), 45.6 (CH); HRESIMS calcd for C<sub>19</sub>H<sub>15</sub>O<sub>2</sub> (M + H)<sup>+</sup> 275.1072; found 275.1064.

**2-(Methoxy(phenyl)methyl)benzofuran (17).** To a solution of **5a** (100 mg, 0.34 mmol) and methanol (139 μL, 3.40 mmol) in anhydrous acetonitrile (5 mL) at rt was added BF<sub>3</sub>·Et<sub>2</sub>O (62 μL, 0.51 mmol) dropwise under N<sub>2</sub>. The mixture was stirred at rt for 2 h and

then treated with saturated NaHCO<sub>3</sub> solution (10 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 15 mL). The combined CH<sub>2</sub>Cl<sub>2</sub> extract was washed with brine, dried (MgSO<sub>4</sub>), filtered, and evaporated under reduced pressure. The crude reaction mixture was purified using flash column chromatography (EtOAc/petrol (1:9)) to give **6a** (48 mg, 48%) and **17** (42 mg, 52%). Compound **17** was obtained as a light yellow oil: R<sub>f</sub> = 0.58 (EtOAc/petrol (1:4)); IR (neat) ν<sub>max</sub> 3062, 3032, 2931, 1822, 1600, 1451, 1252, 1087, 745, and 698 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz) δ 7.50–7.14 (9H, m, ArH), 6.52 (1H, s, C=CH), 5.39 (1H, s, Ar(OCH<sub>3</sub>)CH), 3.45 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (75 MHz) δ 157.1 (C=CO), 155.3 (ArCO), 138.6 (ArC), 128.6 (2 × ArCH), 128.4 (ArCH), 128.1 (ArC), 127.4 (2 × ArCH), 124.4 (ArCH), 122.8 (ArCH), 121.2 (ArCH), 111.5 (ArCH), 105.1 (C=CH), 79.5 [(OCH<sub>3</sub>)CAr], 57.4 (OCH<sub>3</sub>); HRESIMS calcd for C<sub>16</sub>H<sub>15</sub>O<sub>2</sub> (M + H)<sup>+</sup> 239.1072; found 239.1092.

## ■ ASSOCIATED CONTENT

### 📄 Supporting Information

Copies of the <sup>1</sup>H and <sup>13</sup>C NMR spectra of all synthesized compounds and the X-ray crystallographic details of compound **12** (CCDC no 911817). This material is available free of charge via the Internet at <http://pubs.acs.org>.

## ■ AUTHOR INFORMATION

### ✉ Corresponding Author

\*E-mail: [spyne@uow.edu.au](mailto:spyne@uow.edu.au).

### 📍 Present Address

<sup>†</sup>Department of Chemistry, Chiang Mai University, Chiang Mai, Thailand.

### 📄 Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

We thank the University of Wollongong for partial support. N.W. was supported by a grant under the program, Strategic Scholarships for Frontier Research Network for the Joint Ph.D. Program Thai Doctoral Degree from the Office of the Higher Education Commission, Thailand. U.S. thanks the Royal Golden Jubilee Ph.D. Program of the Thailand Research Fund (Grant No. PHD/0232/2549) and the Center of Excellence for Innovation in Chemistry (PERCH-CIC) for a scholarship.

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