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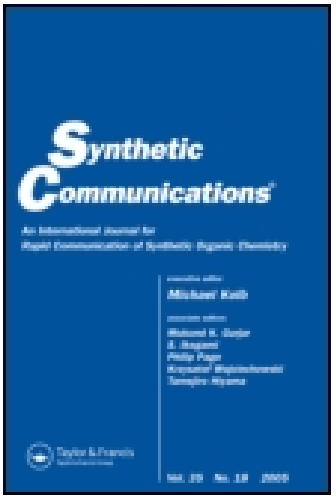


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# Water-Promoted, Silver-Phosphine Complex-Catalyzed Stereoselective Cyclization of 2-(1-Hydroxy-3-arylprop-2-ynyl)phenols Leading to a Highly Efficient Approach to Aurones

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# WATER-PROMOTED, SILVER–PHOSPHINE COMPLEX–CATALYZED STEREOSELECTIVE CYCLIZATION OF 2-(1-HYDROXY-3-ARYLPROP-2-YNYL)PHENOLS LEADING TO A HIGHLY EFFICIENT APPROACH TO AURONES

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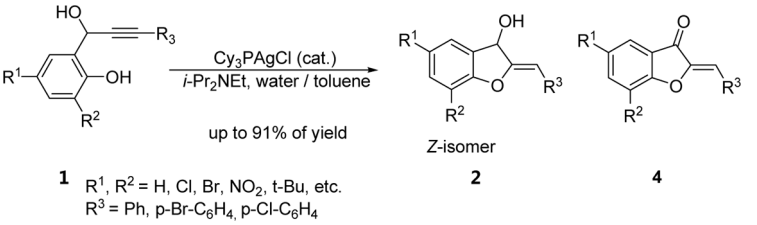
## GRAPHICAL ABSTRACT




**Abstract** *Silver–phosphine complexes can be utilized as highly efficient catalysts for the cyclization of 2-(1-hydroxy-3-arylprop-2-ynyl)phenols (**1**) to give product **2**, key intermediates to synthesize aurones (**4**), with good yields and stereoselectivities in water–toluene mixed solvent. With fluoride as the counteranion, complete* E- *or* Z- *stereoselectivities were achieved at high temperature or room temperature, respectively. Furthermore, after removing water from the reaction mixtures, the toluene solution containing crude products **2** can be treated by $MnO_2$ directly without further purification, to give aurones **4** in good yields.*

**Keywords** Catalyzed cyclization; silver–phosphine complex; syntheses of aurones; water-promoted

## INTRODUCTION

(Z)-2,3-Dihydrobenzofuran-3-ol derives (**2**) are key intermediates for the syntheses of aurones (**4**), which have exhibited a wide range of biological activities and have been used as antifungal agents, tyrosinase inhibitors, antioxidants, and

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others.[1] Wu,[2] Michael,[3] Agrawal,[4] Morimoto,[5] and others reported different synthetic methods to obtain aurones. Among the reported methods, Pale and his coworkers recently reported a three-step approach based on a gold(I)-catalyzed cyclization of 2-(1-hydroxy-3-arylprop-2-ynyl)phenols **(1)** followed by oxidation of the cyclized product **2** with $MnO_2$, which led to an efficient and expeditious synthesis of aurones.[6] However, this procedure has certain disadvantages: The formation of flavones cannot be completely prevented, the catalyst is relatively expensive and requires high loading, and usually a long reaction time is required, which sometimes limits versatility and applicability in industrial processes.

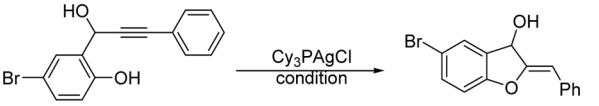
Very recently, we also reported a highly efficient water-triggered, counteranion-controlled and silver–phosphine complex–catalyzed stereoselective cascade alkynylation/cyclization of terminal alkynes with salicylaldehydes leading to substituted 2,3-dihydrobenzofuran-3-ol derivatives (**2**).[7] In the procedure, various salicylaldehydes could be utilized effectively, except for substrates with strong electron-withdrawing groups; however, long heating times were usually required. We also noted that water was the best solvent in the reaction, and introduction of other organic solvents would result in the deactivation of catalyst. To further study the detailed mechanism of the reaction, compound **1** was synthesized and some silver(I)–phosphine complexes were evaluated for the annulation of **1**. These silver(I) complexes show high efficiency in catalyzing the cyclization with good yields and stereoselectivities. A much better functional group compatibility than in the cascade process was also observed. Furthermore, in contrast to our previously reported results, the Ag(I)–phosphine complexes show the best activity for the cyclization in a water–toluene biphasic system with low catalyst loading at room temperature.

## RESULTS AND DISCUSSION

4-Bromo-2-(1-hydroxy-3-phenylprop-2-ynyl)phenol (**1b**) was selected as the representative substrate to screen the catalysts. Following the conditions described previously,[7] $Cy_3PAgCl$ was examined first in a water–phenylacetylene mixed solvent. After 3 h at 70 °C, a moderate yield of the desired cyclization product was observed (entry 1, Table 1). Some other organic solvents, instead of phenylacetylene, were then introduced as cosolvents (entries 2–6). Interestingly, any solvents that are soluble in water disfavored the reaction (entries 2–4). On the other hand, when water-insoluble toluene and dichloroethane were used as cosolvents, the catalyst showed the best activity. Even at room temperature, total conversion of the starting materials was observed within 1.5–2 h, and ca. 80% yields were achieved with 5 mol% of catalyst (entries 5 and 6). Compared with the results obtained from the corresponding reaction in pure organic solvents (entries 5 and 6 vs. entries 7–9), the Ag(I)–phosphine complex–catalyzed cyclization seems to be an on-water reaction,[8] which tends to proceed at the interface of water and organic solvent. Subsequently, the ratio of water and toluene was studied, and a 1:1 mixture of water and toluene gave the best yield (entries 5, 10, and 11). Even with 1 mol% of catalyst, 77% of yield was still achieved with a prolonged reaction time (entries 12 and 13).

Several kinds of phosphine ligands such as $PPh_3$, n-$Bu_3P$, and $Cy_3P$ were also examined. Among them, both $Cy_3P$ and $PPh_3$ gave good results (entry 5 vs. entries 14 and 15). The effect of counteranions on the reaction was then studied with $PPh_3$

**Table 1.** Silver(I)–phosphine complex–catalyzed annulation of **1b**[a]




**1b** **2b**

| Entry | Conditions | Result[b] (%) |
|---|---|---|
| 1 | $Cy_3PAgCl$ 10 mol%, water/PhC≡CH, *i*-$Pr_2NEt$ 20 mol%, 70 °C, 3 h | 71 |
| 2 | $Cy_3PAgCl$ 5 mol%, water/THF (1:1), *i*-$Pr_2NEt$ 10 mol%, 70 °C, 24 h | 46 |
| 3 | $Cy_3PAgCl$ 5 mol%, water/$CH_3CH_2OH$ (1:1), *i*-$Pr_2NEt$ 10 mol%, 70 °C, 24 h | 24 |
| 4 | $Cy_3PAgCl$ 5 mol%, water/MeCN (1:1), *i*-$Pr_2NEt$ 10 mol%, 70 °C, 24 h | 33 |
| 5 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 10 mol%, rt, 1.5 h | 80 |
| 6 | $Cy_3PAgCl$ 5 mol%, water/$CH_2ClCH_2Cl$ (1:1), *i*-$Pr_2NEt$ 10 mol%, rt, 2 h | 80 |
| 7 | $Cy_3PAgCl$ 5 mol%, MeCN, *i*-$Pr_2NEt$ 10 mol%, 70 °C, 3 h | 22 |
| 8 | $Cy_3PAgCl$ 5 mol%, toluene, *i*-$Pr_2NEt$ 10 mol%, 70 °C, 3 h | 7 |
| 9 | $Cy_3PAgCl$ 5 mol%, $CH_2ClCH_2Cl$, *i*-$Pr_2NEt$ 10 mol%, 70 °C, 24 h | 29 |
| 10 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:4), *i*-$Pr_2NEt$ 10 mol%, rt, 4 h | 81 |
| 11 | $Cy_3PAgCl$ 5 mol%, water/toluene (4:1), *i*-$Pr_2NEt$ 10 mol%, rt, 1.5 h | 78 |
| 12 | $Cy_3PAgCl$ 10 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 10 mol%, rt, 1 h | 79 |
| 13 | $Cy_3PAgCl$ 1 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 10 mol%, rt, 9 h | 77 |
| 14 | $Bu_3P$/AgCl 5 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 10 mol%, rt, 5 h[c] | 73 |
| 15 | $Ph_3PAgCl$ 5 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 10 mol%, rt, 1.5 h | 79 |
| 16 | $Ph_3PAgBr$ 5 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 10 mol%, rt, 1.5 h | 57 |
| 17 | $Ph_3PAgI$ 5 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 10 mol%, rt, 1.5 h | 9 |
| 18 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 5 mol%, rt, 2.5 h | 75 |
| 19 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 20 mol%, rt, 1.5 h | 79 |
| 20 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), no base, rt, 24 h | Trace |
| 21 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), $NaHCO_3$ 10 mol%, rt, 4 h | 78 |
| 22 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), $K_3PO_4$ 10 mol%, rt, 3 h | 78 |
| 23 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), pyridine 10 mol%, rt, 24 h | 58 |
| 24 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), aniline 10 mol%, rt, 24 h | 27 |
| 25 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), 2,6-lutidine 10 mol%, rt, 24 h | 15 |
| 26 | $Cy_3PAgCl$ 5 mol%, water/toluene (1:1), *i*-$Pr_2NEt$ 10 mol%, rt, 2. h, in air | 79 |

[a]**1b** (0.15 mmol), $Cy_3PAgCl$ (5 mol%), and base (10 mol%), solvent 3 mL, room temperature.
[b]Isolated yield.
[c]The catalyst was prepared *in situ* by mixing phosphine ligand and AgCl in toluene and stirring for 4 h.

as ligand. Chloride gave the highest yield under similar reaction condition (entries 15–17).

It is worthy noting that a catalytic amount of base is also important in the reaction. Several kinds of organic or inorganic base were studied, and *i*-$Pr_2NEt$ was found to be the most effective (entries 18–25). As shown in entries 21 and 22, an inorganic base such as $NaHCO_3$ and $K_3PO_4$ also gave good results with a slightly prolonged reaction time. Furthermore, although air-sensitive phosphine ligands were used in current studies, no significant decrease in either catalytic activity or yield was observed even when the reaction was carried out in air (entry 26).

Thus, under the optimized conditions [$Cy_3PAgCl$ 5 mol%, *i*-$Pr_2NEt$ 10 mol% in toluene–water (1:1) mixed solvent], a variety of propargylic alcohol substrates **1**, prepared from substituted salicylaldehydes and terminal alkynes, could be utilized in the

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catalytic reaction to give product **2** in moderate to good yields with high stereoselectivities (Table 2). As shown in Table 2, the substrates bearing electron-withdrawing groups such as nitro- groups (in **1f** and **1g**) furnished the cyclization products **2f** and **2g** in 83% and 79% yields, respectively (entries 6 and 7, Table 2). It is worth mentioning that in our previous study on the Ag(I)–phosphine complex–catalyzed cascade alkynylation/cyclization of terminal alkynes with salicylaldehydes, nitro-substituted salicylaldehyde **1f** could not give the desired products at all, whereas poor yield was obtained for **1g**.[7] On the other hand, when the bulky alkyl group was introduced, no obvious decrease in yields was observed except a prolonged reaction time was required (entries 8 and 9), and up to 91% of yield was achieved with **1h** as starting material.

Compared with good functional group compatibility on salicylaldehydes, the substitutes on alkynes show significant effects on the reaction. As shown by entries 10–14, the electron-donating group on arylacetylene disfavored the reaction: with Me- and MeO- as the substitutes, only about 70% of yields of the desired products were observed. In all cases, no other regio- or stereoisomer was observed.

The relationship between the $E/Z$ selectivity and counteranions was also studied (Table 3). By using AgCl as the catalyst precursor, only $Z$-isomer was observed after a long time of stirring at room temperature (entry 1, Table 3). When AgF was utilized together with $Cy_3P$ as ligand, after 24 h of stirring at room temperature, we

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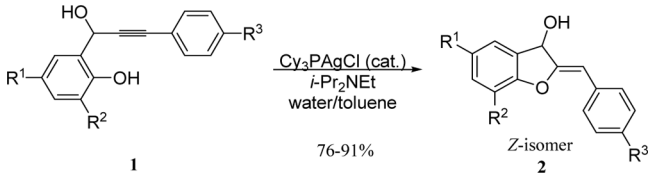
**Table 2.** $Cy_3PAgCl$-catalyzed cyclization of **2**[a]



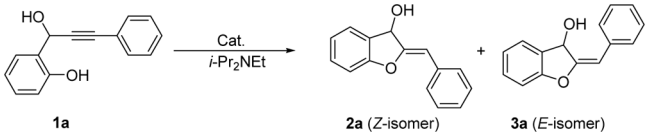

**1** **2**

| Entry | Substrate | $R^1$ | $R^2$ | $R^3$ | Conditions | Product | Yield[b] (%) |
|---|---|---|---|---|---|---|---|
| 1 | **1a** | H | H | H | rt, 3 h | **2a** | 89 |
| 2 | **1b** | Br | H | H | rt, 1.5 h | **2b** | 80 |
| 3 | **1c** | Br | Br | H | rt, 4 h | **2c** | 83 |
| 4 | **1d** | Cl | H | H | rt, 2 h | **2d** | 76 |
| 5 | **1e** | Cl | Cl | H | rt, 5 h | **2e** | 76 |
| 6 | **1f** | $NO_2$ | H | H | rt, 1.5 h | **2f** | 83 |
| 7 | **1g** | Cl | $NO_2$ | H | rt, 1 h | **2g** | 79 |
| 8 | **1h** | *t*-Bu | Br | H | rt, 6 h | **2h** | 91 |
| 9 | **1i** | *t*-Bu | $NO_2$ | H | rt, 7 h | **2i** | 88 |
| 10 | **1j** | H | H | Cl | rt, 2 h | **2j** | 89 |
| 11 | **1k** | H | H | $CH_3$ | rt, 4 h | **2k** | 65 |
| 12 | **1l** | Br | H | $CH_3$ | rt, 45 min | **2l** | 67 |
| 13 | **1m** | H | H | -$OCH_3$ | rt, 3 h | **2m** | 66 |
| 14 | **1n** | Br | H | -$OCH_3$ | rt, 1 h | **2n** | 77 |

[a]**1** (0.15 mmol), $Cy_3PAgCl$ (5 mol%), *i*-$Pr_2NEt$ (10 mol%), 1.5 mL of $H_2O$, and 1.5 mL of toluene, room temperature.

[b]Isolated yield.

**Table 3.** Counteranion and temperature-controlled $E/Z$-selectivity of the cyclization of **1a**[a]

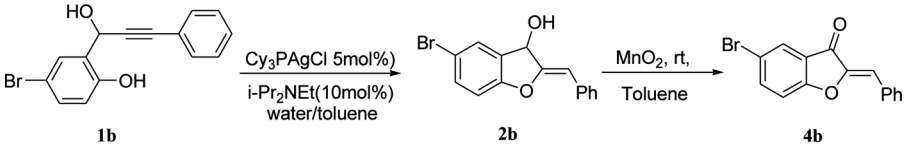



**1a** **2a** ($Z$-isomer) **3a** ($E$-isomer)

| Entry | Catalyst | Conditions | Yield of **2a:3a** (%)[b] |
|---|---|---|---|
| 1 | $Cy_3PAgCl$ (5 mol%) | $H_2O$/toluene, rt, 24 h | 85 Only $Z$ |
| 2 | $AgF/Cy_3P$ (1:1) | $H_2O$/toluene, rt, 24 h | 40 (**2a**:**3a** = 2:1) |
| 3 | $AgF/Cy_3P$ (1:1) | $H_2O$/toluene, 100 °C, 24 h | 70 (**2a**:**3a** = 2:1) |
| 4 | $AgF/Cy_3P$ (1:1) | $H_2O/CH_2Cl_2$, rt, 24 h | 83 Only $Z$ |
| 5 | $AgF/Cy_3P$ (1:1) | $H_2O/CH_2Cl_2$, 100 °C, 24 h | 81 Only $E$ |

[a]**1a** (0.15 mmol), $Cy_3P$ (5 mol%), AgF (5 mol%), $i$-$Pr_2NEt$ (10 mol%), 1.5 mL of $H_2O$, and 1.5 mL of toluene, room temperature.

[b]Yields were determined by $^1H$ NMR with 0.1 mmol of nitromethane as internal standard.




**1b** **2b** **4b**

Total yield from **1b** to **4b** : 81.3%

**Scheme 1.** The one-pot cyclization-oxidation for aurone synthesis.

noticed the formation of $E$-isomer **3a** with poor overall yield (entry 2); whereas at 100 °C for 24 h, the same ratio of $E/Z$ was observed with 70% yield (entry 3). Surprisingly, when $CH_2Cl_2$ was used as cosolvent, the temperature became the switch for $E/Z$ selectivity: at room temperature, only $Z$-isomer was obtained, while complete stereoselectivity toward $E$-isomer was achieved with 83% of yield at 100 °C. This result suggested that the formation of $Z$-isomer might be kinetically controlled and the $E$-isomer might be thermodynamically controlled.

Toluene/water mixed solvent utilized in the reaction provided a possibility to carry out a one-pot reaction to prepare aurones (**4**) directly without additional purification for compound **2**. After removing water from the reaction mixture by pipette, the crude product **2b** was oxidized effectively by adding $MnO_2$ directly to the toluene solution, and up to 81% of total yield of aurone **4b** was obtained (Scheme 1).

## CONCLUSION

In summary, silver–phosphine complexes can be used as highly efficient catalysts for the cyclization of 2-(1-hydroxy-3-arylprop-2-ynyl)phenols (**1**) in water–toluene mixed solvent at room temperature. In the reaction, both water and phosphine ligands are the key factors to activate the catalyst. A variety of substrates **1**

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could be utilized in the catalytic reaction to give product **2** in moderate to good yields and high stereoselectivities. Furthermore, by removing water from the reaction mixtures, the toluene solution containing crude product **2** could be treated by $MnO_2$ directly without further purification to give aurone **4** in good yields. The procedure provides an alterative method to synthesize aurones with high efficiency and high stereoselectivities.

## EXPERIMENTAL

All experiments were carried out under an inert atmosphere of nitrogen. Flash column chromatography was performed over silica gel 30–60 μm. $^1$H NMR and $^{13}$C NMR spectra were acquired by 400 MHz and 100 MHz, or 300 MHz and 75 MHz, respectively, and referenced to the internal solvent signals. High-resolution mass spectra (HRMS) were measured at the Shanghai Institute of Organic Chemistry, CAS. The data for all products are described.

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### Typical Reaction Procedure 1 (Entry 1 in Table 2)

2-(1-Hydroxy-3-phenylprop-2-ynyl)phenol (**1a**, 0.15 mmol), $Cy_3PAgCl$ (3.2 mg, 0.0075 mmol, 5 mol%), and 2.6 μL of *i*-$Pr_2NEt$ (0.015 mmol, 10 mol%) were added into a 10-mL Schlenk tube with 1.5 mL of toluene and 1.5 mL of distilled water under nitrogen. The mixture was stirred at room temperature for 3 h. The reaction was stopped and extracted with ether ($3 \times 3$ mL). The combined organic phase was dried with $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent 20:1 hexanes and ethyl acetate). Compound **2a** was obtained in 80% yield.

### Typical Procedure 2 (Scheme 1)

Following the procedure described in Typical Procedure 1, 2 mmol of 2-(1-hydroxy-3-phenylprop-2-ynyl)phenol (**1b**) was added into a mixed solvent of water (5 mL) and toluene (5 mL) in the presence of $Cy_3PAgCl$ (42.2 mg, 0.1 mmol, 5 mol%) and 34 μL of *i*-$Pr_2NEt$ (0.2 mmol, 10 mol%). When the reaction was over, the aqueous layer was removed by pipette. The toluene solution was then cooled in an ice bath, and $MnO_2$ (6 mmol) was added. The mixture was stirred at room temperature for 4 h and then filtered through celite. The solution was concentrated under reduced pressure, and the residue was purified by flash column chromatography on silica gel (eluent: hexanes/EtOAc 40:1). Compound **4b** was obtained in 81% yield.

### Selected Data

**(*Z*)-2-Benzylidene-2,3-dihydrobenzofuran-3-ol (2a).**[7] IR (KBr): $\nu_{max}$ 3414, 1683, 1612, 1601, 1479, 1290, 1236, 1088, 1022, 908 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.74 (d, $J = 7.9$ Hz, 2H), 7.50 (d, $J = 7.2$ Hz, 1H), 7.42–7.34 (m, 3H), 7.28–7.24 (m, 1H), 7.12–7.09 (m, 2H), 6.02 (s, 1H), 5.76 (d, $J = 12$ Hz, 1H), 2.32 (d, $J = 12$ Hz, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm) δ 157.8, 157.0, 134.5, 130.6, 128.7, 128.5, 126.9, 126.8, 125.7, 122.9, 110.7, 106.0, 72.5.

**(Z)-2-Benzylidene-5-bromo-2,3-dihydrobenzofuran-3-ol (2b).**[7] IR (KBr): $\nu_{max}$ 3434, 3058, 1644, 1608, 1470, 1236, 1097, 1005, 907 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, ppm) δ 7.70 (d, $J = 7.8$ Hz, 2H), 7.62 (s, 1H), 7.46 (dd, $J = 1.2$, 5.3 Hz, 1H), 7.40 (t, $J = 8.1$ Hz, 2H), 7.27 (dd, $J = 5.2$, 8.2 Hz, 1H), 6.99 (d, $J = 8.5$ Hz, 1H), 6.03 (s, 1H), 5.77 (d, $J = 6.6$ Hz, 1H), 2.24 (d, $J = 7.9$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz, ppm) δ 156.7, 156.5, 134.0, 133.5, 129.2, 128.5, 127.1, 115.0, 112.3, 106.6, 72.2.

**(Z)-2-Benzylidene-5,7-dibromo-2,3-dihydrobenzofuran-3-ol (2c).**[7] IR (KBr): $\nu_{max}$ 3435, 3062, 1690, 1600, 1492, 1450, 1228, 1174, 1113, 1075, 1005, 903 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, ppm) δ 7.75 (d, $J = 7.7$ Hz, 2H), 7.66 (d, $J = 1.6$ Hz, 1H), 7.56 (d, $J = 0.9$ Hz, 1H), 7.42 (t, $J = 7.5$ Hz, 2H), 7.30 (m, 1H), 6.07 (s, 1H), 5.84 (d, $J = 8.4$ Hz, 1H), 2.29 (d, $J = 9.2$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz, ppm) δ 155.2, 154.5, 135.7, 133.6, 129.9, 129.0, 128.6, 127.7, 127.4, 115.2, 107.8, 104.3, 72.9.

**(*Z*)-2-Benzylidene-5-chloro-2,3-dihydrobenzofuran-3-ol (2d).**[7] IR (KBr): $\nu_{max}$ 3425, 3054, 2923, 1690, 1611, 1475, 1237, 1100, 1022, 908 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, ppm) δ 7.71 (d, $J = 7.6$ Hz, 2H), 7.49 (s, 1H), 7.41 (t, $J = 7.6$ Hz, 2H), 7.33–7.25 (m, 2H), 7.04 (d, $J = 8.6$ Hz, 1H), 6.04 (s, 1H), 5.78 (s, 1H), 2.20 (bs, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz, ppm) δ 156.6, 156.2, 134.1, 130.6, 128.7, 128.6, 128.5, 127.9, 127.1, 125.9, 111.8, 106.6, 72.3.

**(Z)-2-Benzylidene-5,7-dichloro-2,3-dihydrobenzofuran-3-ol (2e).**[7] IR (KBr): $\nu_{max}$ 3350, 3068, 1687, 1605, 1462, 1229, 1186, 1117, 1017, 902 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, ppm) δ 7.74 (d, $J = 7.6$ Hz, 2H), 7.44–7.37 (m, 4H), 7.30 (d, $J = 7.4$ Hz, 1H), 6.08 (s, 1H), 5.82 (d, $J = 9.0$ Hz, 1H), 2.28 (d, $J = 9.5$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz, ppm) δ 156.7, 156.5, 134.1, 133.5, 129.2, 128.8, 128.7, 128.5, 127.1, 115.0, 112.3, 106.6, 72.2.

**(Z)-2-Benzylidene-7-nitro-2,3-dihydrobenzofuran-3-ol (2f).**[6] IR (KBr): $\nu_{max}$ 3288, 2927, 1601, 1520, 1471, 1338 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, ppm) δ 8.42 (s, 1H), 8.32 (d, $J = 8.9$ Hz, 1H), 7.71 (d, $J = 7.7$ Hz, 2H), 7.42 (t, $J = 7.5$ Hz, 2H), 7.32 (d, $J = 7.3$ Hz, 1H), 7.20 (d, $J = 8.9$ Hz, 1H), 6.14 (s, 1H), 5.87 (d, $J = 9.0$ Hz, 1H), 2.48 (d, $J = 9.1$ Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz, ppm) δ 162.1, 156.0, 143.7, 133.5, 129.0, 128.7, 128.4, 127.7, 127.5, 122.3, 111.0, 108.5, 71.4.

**(*Z*)-2-Benzylidene-5-chloro-7-nitro-2,3-dihydrobenzofuran-3-ol (2g).**[7] IR (KBr): $\nu_{max}$ 3537, 3100, 1693, 1625, 1597, 1527, 1449, 1350, 1220, 1199, 1126, 1050, 866, 760 $cm^{-1}$; $^1H$ NMR ($d_6$-DMSO, 400 MHz, ppm) δ 8.16 (s, 1H), 7.92 (s, 1H), 7.81 (d, $J = 7.4$ Hz, 2H), 7.42 (dd, $J = 7.3$, 7.3 Hz, 2H), 7.28 (t, $J = 7.0$ Hz, 1H), 6.14 (s, 1H), 5.82 (s, 1H; $^1H$ NMR ($CDCl_3$, 400 MHz, ppm) δ 8.14 (s, 1H), 7.83 (d, $J = 7.6$ Hz, 2H), 7.77 (s, 1H), 7.44 (dd, $J = 7.5$, 7.5 Hz, 2H), 7.33 (t, $J = 7.5$ Hz, 1H), 6.17 (s, 1H), 5.86 (s, 1H), 2.40 (bs, 1H); $^{13}C$ NMR ($d_6$-DMSO, 100 MHz, ppm) δ 157.1, 150.2, 135.6, 134.04, 132.63, 132.56, 129.1, 129.0, 127.8, 126.9, 125.0, 107.3, 69.6.

**(Z)-2-Benzylidene-7-bromo-5-*tert*-butyl-2,3-dihydrobenzofuran-3-ol (2h).**[7] IR (KBr): $\nu_{max}$ 3408, 2963, 2868, 1692, 1613, 1479, 1234, 1122, 1087, 1030, 911 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, ppm) δ 7.78 (d, $J = 7.8$ Hz, 2H), 7.51 (d,

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$J = 1.6$, 1H), 7.48 (d, $J = 0.7$ Hz, 1H), 7.42 (t, $J = 7.6$ Hz, 2H), 7.28 (m, 1H), 6.06 (s, 1H), 5.84 (d, $J = 9.3$ Hz, 1H), 2.20 (d, $J = 9.7$ Hz, 1H), 1.35 (s, 9H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm) δ 156.3, 153.0, 148.1, 134.1, 130.7, 128.9, 128.6, 127.9, 127.0, 121.5, 106.9, 102.7, 73.5, 34.8, 31.5.

**(Z)-2-Benzylidene-7-nitro-5-*tert*-butyl-2,3-dihydrobenzofuran-3-ol (2i).** IR (KBr): $\nu_{max}$ 3515, 2960, 2870, 1633, 1542, 1327, 1224, 1096, 1040, 895 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, ppm) δ 8.16 (s, 1H), 7.86–7.85 (m, 3H), 7.44 (t, $J = 7.4$ Hz, 2H), 7.32–7.27 (m, 1H), 6.15 (s, 1H), 5.84 (d, $J = 9.0$ Hz, 1H), 2.34 (d, $J = 9.5$ Hz, 1H), 1.39 (s, 9H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm) δ 155.8, 149.8, 147.2, 133.4, 132.2, 129.3, 129.1, 128.8, 127.7, 122.8, 108.7, 71.4, 35.0; GC/MS $m/z$ (%) 325 ($M^+$, 100), 324, 308, 278, 248, 206, 188, 132, 105, 77; HRMS calcd. for $C_{19}H_{19}NO_4$: 325.1314; found: 325.1316.

**(*Z*)-2-(4-Chlorobenzylidene)-2,3-dihydrobenzofuran-3-ol (2j).[7]** IR (KBr): $\nu_{max}$ 3331, 2923, 1684, 1615, 1600, 1466, 1292, 1237, 1134, 1085, 1018, 910 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, $J = 8.5$ Hz, 2H), 7.52 (d, $J = 7.2$ Hz, 1H), 7.37–7.35 (m, 3H), 7.12 (t, $J = 7.6$ Hz, 2H), 5.98 (s, 1H), 5.78 (d, $J = 6.9$ Hz, 1H), 2.21 (d, $J = 8.5$ Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) 157.6, 157.5, 133.1, 132.4, 130.8, 130.0, 128.7, 125.7, 123.1, 110.7, 104.9, 72.6.

**Z)-2-(4-Methylbenzylidene)-2,3-dihydrobenzofuran-3-ol (2k).[7]** IR (KBr): $\nu_{max}$ 3387, 3052, 2921, 1688, 1603, 1479, 1467, 1291, 1234, 1134, 1132, 1085, 1010, 906 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.64 (d, $J = 8.1$ Hz, 2H), 7.51 (d, $J = 7.2$, 1H), 7.36 (dd, $J = 0.9$, 7.6 Hz, 1H), 7.21 (d, $J = 7.9$ Hz, 2H), 7.12–7.08 (m, 2H), 6.00 (s, 1H), 5.76 (bs, 1H), 2.39 (s, 3H), 2.20 (bs, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm) δ 157.8, 156.3, 136.7, 131.7, 130.6, 129.2, 128.6, 127.0, 125.7, 122.8, 110.6, 106.0, 72.5, 21.3.

**(Z)-5-Bromo-2-(4-methylbenzylidene)-2,3-dihydrobenzofuran-3-ol (2 l).[7]** IR (KBr): νmax 3423, 3027, 1689, 1607, 1512, 1471, 1236, 1096, 1005, 906 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.61–7.58 (m, 3H), 7.46 (dd, $J = 1.6$, 8.5 Hz, 1H), 7.20 (d, $J = 7.9$ Hz, 2H), 6.98 (d, $J = 8.5$ Hz, 1H), 6.00 (s, 1H), 5.74 (s, 1H), 2.38 (s, 3H), 2.24 (bs, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz, ppm) δ 156.8, 155.8, 137.0, 133.4, 131.2, 129.2, 128.8, 128.7, 114.8, 112.3, 106.6, 72.2, 21.3.

**(*Z*)-2-(4-Methoxybenzylidene)-2,3-dihydrobenzofuran-3-ol (2m)[6].** IR (KBr): $\nu_{max}$ 3369, 3043, 2997, 2929, 2837, 1685, 1607, 1514, 1462, 1294, 1253, 1179, 1130, 1084 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz, ppm) δ 7.66 (d, $J = 8.7$ Hz, 2H), 7.49 (d, $J = 7.2$ Hz, 1H), 7.33 (t, $J = 7.8$ Hz, 1H), 7.11–7.06 (m, 2H), 6.92 (d, $J = 8.7$ Hz, 1H), 5.95 (bs, 1H), 5.74 (d, $J = 9.3$ Hz, 1H), 3.83 (s, 3H), 2.18 (d, $J = 9.3$ Hz, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz, ppm) δ 158.6, 157.9, 155.5, 130.7, 130.1, 127.5, 127.2, 125.8, 122.9, 114.1, 110.7, 105.8, 72.6, 55.4.

**(*Z*)-5-Bromo-2-(4-methoxybenzylidene)-2,3-dihydrobenzofuran-3-ol (2n).** IR (KBr): $\nu_{max}$ 3354, 3080, 2957, 2836, 1604, 1512, 1471, 1253, 1180, 1095, 1024, 904 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz, ppm) δ 7.64–7.59 (m, 2H), 7.45–7.414 (m, 2H), 6.96–6.89 (m, 2H), 5.95 (s, 1H), 5.72 (d, $J = 9.0$ Hz, 1H), 3.83 (s, 3H), 2.31 (d, $J = 9.6$ Hz, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz, ppm) δ 158.8, 157.0, 155.0, 133.5, 130.2, 129.5, 129.0, 127.0, 114.9, 114.2, 112.4, 106.4, 72.2, 55.4; MS (EI) $m/z$ (%)

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330 (100, $M^+ - 2$), 315, 301, 287, 236, 152, 132, 117, 89; HRMS calcd. for $C_{16}H_{11}O_3Br$ (M − 2H): 329.9893; found: 329.9892.

**(*E*)-2-Benzylidene-2,3-dihydrobenzofuran-3-ol (3a).**[7] IR (neat, NaCl): $\nu_{max}$ 3332, 2977, 2920, 1600, 1493, 1452, 1378, 1321, 1298, 1253, 1170, 1126, 1079, 1041, 945, 885, 843, 802, 775, 742, 698, 537 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, ppm) δ 7.54–7.36 (m, 7H), 7.28–7.22 (m, 2H), 6.53 (s, 1H), 5.94 (b, 1H), 2.77 (b, 1H); $^{13}C$ NMR ($CDCl_3$, 75 MHz, ppm) δ 158.7, 155.3, 140.5, 128.9, 128.6, 128.3, 127.1, 124.6, 123.1, 121.4, 111.6, 104.3, 70.9.

**(Z)-2-Benzylidene-5-bromobenzofuran-3(2h)-one (4b).**[6] IR (KBr): $\nu_{max}$ 3081, 1706, 1642, 1600, 1456, 1265, 1176, 1133, 959, 923 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz, ppm) δ 7.94–7.92 (m, 3H), 7.77 (d, $J = 8.7$ Hz, 1H), 7.51–7.42 (m, 3H), 7.27 (d, $J = 7.1$ Hz, 1H), 6.94 (s, 1H);$^{13}C$ NMR ($CDCl_3$, 100 MHz, ppm) δ 183.3, 164.7, 146.8, 139.4, 132.0, 131.7, 130.3, 129.0, 127.4, 123.4, 116.4, 114.7, 114.2.

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