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Formal [4+1] cycloaddition of camphor-derived sulfonium salts with aldimines: enantioselective synthesis of 2,3-dihydrobenzofurans

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ABSTRACT

An asymmetric formal [4+1] cycloaddition of camphor-derived sulfonium salts with aldimines has been described. The reaction allows for the efficient synthesis of *trans*-2,3-disubstituted-2,3-dihydrobenzofurans in moderate to good yields with >95:5 dr and up to 98% ee under mild reaction conditions.

1. Introduction

The 2,3-dihydrobenzofurans (DHBs) are privileged structural motifs found in many natural products and biologically active compounds.[1] These compounds have been shown to exhibit a broad range of biological activities. For example, neolignans, isolated from secondary plant metabolites, are a type of important natural products, which have exhibited high structural diversity and broad bioactivity profile.[1a–e] The furaquinocins are a class of antibiotics with antihypertensive activity, inhibition of platelet aggregation and coagulation.[1f–h] Moreover, the synthetical cell motility inhibitor shows good biological effects in cell-based assays (Fig. 1).[2] Given the significance of these valuable DHBs and their potential biological properties, the development of more efficient synthetic methods for the construction of such scaffolds represents an area of intensive research.

During the last few decades, a great deal of research efforts have been devoted to the development of asymmetric methods for their synthesis. In this context, the most procedures are mainly based on the utilization of chiral starting materials,[3] kinetic resolution,[4] or chiral auxiliaries.[5] Recently, the sporadic examples of catalytic enantioselective construction of 2,3-dihydrobenzofurans have also been documented.[6] For instance, Hashimoto and co-workers firstly developed a highly efficient catalytic method for the diastereo- and enantioselective synthesis of *cis*-2-aryl-3-methoxycarbonyl-2,3-dihydrobenzofurans via the Rh(II)-catalyzed C–H insertion reaction.[6c] Notably, the diastereoisomer products are otherwise difficult to prepare. Alternatively, the group of Jørgensen recently developed a pioneering organocatalytic one-pot reaction cascade, which provided an efficient entry to *trans*-2,3-dihydrobenzofurans bearing three contiguous stereogenic centers in a highly enantioselective manner.[6e] Despite these elegant and creative strategies toward the construction of 2,3-dihydrobenzofurans, it is still highly desirable to search for other practical asymmetric process for the synthesis of optically active *trans*-2,3-disubstituted-2,3-dihydrobenzofurans with respect to the functional tolerance and efficiency.

As part of our ongoing program on carbon- and heterocycle-oriented methodology development based on sulfur ylides,[7,8] we recently disclosed highly chemo- and stereoselective formal [4+1]

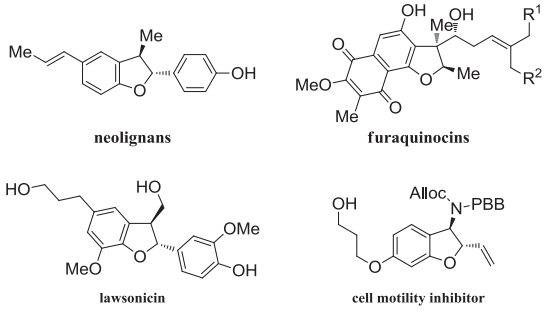

Fig. 1. Representative structures containing 2,3-dihydrobenzofuran motif.

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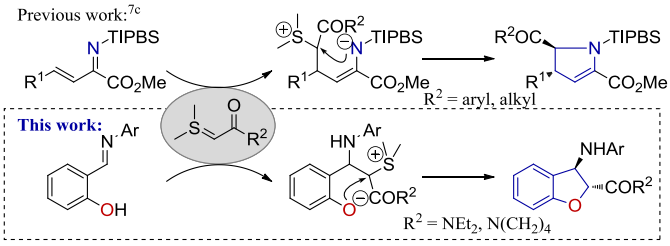
cycloaddition/rearrangement of nitroolefins,[7a] [4+1]/[3+2] cycloaddition cascade of alkene-tethered nitroolefins,[7b] [4+1] cycloaddition of α,β-unsaturated imines (Scheme 1),[7c] affording a variety of structurally diverse nitrogen-containing heterocycles in high yields. Recently, the versatility of the sulfur ylides was successfully extended to asymmetric cyclopropanation of β,γ-unsaturated α-ketoesters[9a] and [4+1] cycloaddition of in situ-generated azo-*o*-quinodimethane.[9b] During the course of these studies, we identified that the electronic and steric effects, and reaction parameters played an important role on controlling the reaction pathway and stereoselectivity.[7,9] Inspired by these achievements, we wondered about the possibility of formal asymmetric [4+1] cycloadditions of salicyl imines and sulfur ylides, which would provide an efficient approach to optically active 2,3-dihydrobenzofurans. Herein, we report a successful realization of such a strategy by a cycloaddition of camphor-derived sulfonium salts and aldimines, which gives the *trans*-2,3-disubstituted-2,3-dihydrobenzofurans with good yields and enantioselectivities (Scheme 1). Recently, the group of Huang reported a novel domino annulation between sulfur ylides and salicyl *N*-thiophosphinyl imines, in which the bulky thiophosphinyl group was used to control the reaction pathway and diastereoselectivity.[10] Notably, Bolm and co-workers recently described an enantioselective formal [4+1] cycloaddition of in situ-derived azoalkenes and sulfur ylides catalyzed by a chiral copper/Tol-BINAP complex, providing the biologically important dihydropyrazoles with high enantioselectivities in good yields.[11]

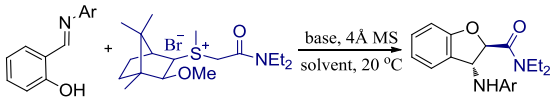


Scheme 1. Formal [4+1] cycloaddition based on sulfur ylides.

2. Result and discussion

Initially, we investigated the desired cycloaddition between camphor-derived sulfonium salt **2a**[12] with aldimine **1**[13] bearing different protecting groups (Table 1). To our delight, treating camphor-derived sulfonium salt **2a** with aldimines **1** (Ar=C_6H_5) at room temperature in dry MeCN for 12 h provided the desired enantioenriched cycloadduct with 53% yield and 54% ee (Table 1, entry 1). Then, the effects of the protecting group of the nitrogen on the reaction efficiency and stereoselectivity were further investigated under the above conditions. For example, the electron-donating substituents on the benzene ring of aldimines **1** resulted in a little of increase in the enantioselectivity (Table 1, entries 2 and 3). In contrast, the electron-withdrawing substituents on the benzene ring of aldimines **1** substantially improved the yield (Table 1, entries 4–6). Therefore, the 3,5-$(CF_3)_2C_6H_3$ was chosen as the most suitable protecting group for further optimization study in terms of the enantioselectivity and yield (Table 1, entry 6). With the use of aldimine **1** bearing 3,5-$(CF_3)_2C_6H_3$, we then simply examined a series of bases and it was found that the use of TMG as the base gave the best results (Table 1, entries 7, 9–12 vs entry 8). Further screen of the common solvents showed that the use of toluene led to positive effect on the enantioselectivity (Table 1, entry 14). Finally, the lowering the reaction temperature to 0 °C further increased the enantiomeric excess to 97% (Table 1, entry 17). Interestingly, the annulation reaction with aldimine bearing *p*-BrC_6H_4 at 0 °C afforded the corresponding product in 82% yield but with only 58% ee (Table 1, entry 18). It is noteworthy that all the reactions gave exclusively the corresponding *trans*-2,3-dihydrobenzofurans.

Table 1
Condition optimization for asymmetric cycloadditions of camphor-derived sulfonium salt **2a** with aldimines **1**[a]



1 **2a** **3**

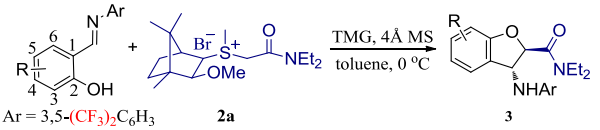
Entry	Ar	Solvent/base	Time (h)	Yield[b] (%)	ee[c,d] (%)
1	C_6H_5	MeCN/KOH	12	53	54
2	*p*-$OMeC_6H_4$	MeCN/KOH	7	66	57
3[e]	*o*-MeC_6H_4	MeCN/KOH	5	43	62
4	*p*-BrC_6H_4	MeCN/KOH	7	86	43
5	*p*-$NO_2C_6H_4$	MeCN/KOH	7	89	44
6	3,5-$(CF_3)_2C_6H_3$	MeCN/KOH	5	70	59
7	3,5-$(CF_3)_2C_6H_3$	THF/Cs_2CO_3	8	50	90
8	3,5-$(CF_3)_2C_6H_3$	THF/TMG	5	63	91
9	3,5-$(CF_3)_2C_6H_3$	THF/KOH	14	51	87
10	3,5-$(CF_3)_2C_6H_3$	THF/CsOH	14	60	88
11	3,5-$(CF_3)_2C_6H_3$	THF/$Ba(OH)_2\cdot 8H_2O$	14	54	79
12	3,5-$(CF_3)_2C_6H_3$	THF/$LiOH\cdot H_2O$	>24	Trace	—
13	3,5-$(CF_3)_2C_6H_3$	Et_2O/TMG	11	54	96
14	3,5-$(CF_3)_2C_6H_3$	Toluene/TMG	11	56	96
15	3,5-$(CF_3)_2C_6H_3$	DCM/TMG	48	60	80
16	3,5-$(CF_3)_2C_6H_3$	MeOH/TMG	48	45	47
17[f]	*3,5-$(CF_3)_2C_6H_3$*	*Toluene/TMG*	*24*	*63*	*97*
18[f]	*p*-BrC_6H_4	MeCN/KOH	21	82	58

[a] Experimental conditions: a mixture of **1** (0.1 mmol), **2a** (0.11 mmol), 4 Å MS (100 mg), and base (0.22 mmol) in solvent (0.5 mL) was stirred at 20 °C for the indicated time. TMG=1,1,3,3-tetramethylguanidine.
[b] Yield of isolated product.
[c] Determined by chiral HPLC analysis.
[d] The dr values in this table were all >95:5 and determined by chiral HPLC analysis and ^{1}H NMR analysis.
[e] In this reaction, a byproduct 3-arylaminocinnamamide **BP** was also isolated. Please see Supplementary data for more details.
[f] The reaction temperature was 0 °C.

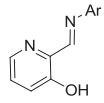
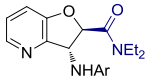
With the optimal conditions in hand (Table 1, entry 17, TMG as the base in toluene at 0 °C), we firstly investigated the substrate scope for this asymmetric cascade reaction by employing a range of aldimines. As summarized in Table 2, various aldimines proved to be suitable for this asymmetric cyclization reaction. For example, the aldimine **1b** with an electron-donating substituent on the benzene ring was well tolerated and the corresponding product was obtained in moderate isolated yield (43%) and with excellent stereoselectivity (>95:5 dr, 98% ee) (Table 2, entry 2). Surprisingly, introducing a strong electron-withdrawing group (e.g., NO_2) to the aromatic ring led to a substantial decrease in both yield and enantioselectivity due to the formation of some unknown side products (Table 2, entry 3). Note that the aldimines **1d**–**1f** bearing the weak electron-withdrawing groups on the aromatic ring can participate in this cyclization well to give the desired products in good yields with good ee's (Table 2, entries 4–6). The use of disubstituted aldimines (**1g** and **1h**) resulted in diminished enantioselectivities probably because of the steric hindrance (Table 2, entries 7 and 8). Importantly, the reaction with heteroaromatic aldimine, such as **1i**, also proceeded smoothly to give the corresponding product **3i** in 63% yield with > 95:5 dr and 21% ee (Table 2, entry 9).

Significantly, the encumbered camphor-derived sulfonium salt **2b** can also be successfully applied to the desired cycloaddition. As shown in Table 3, electron-poor and -rich aldimines with different substitution patterns on the aromatic ring reacted smoothly with camphor-derived sulfonium salt **2b** under optimal conditions, affording the corresponding cycloadducts **3j**–**l** in good yields with high diastereo- (up to >95:5 dr) and enantioselectivities (up to 93%

Table 2
Asymmetric cycloadditions of camphor-derived sulfonium salt **2a** with aldimines **1a–i**[a]

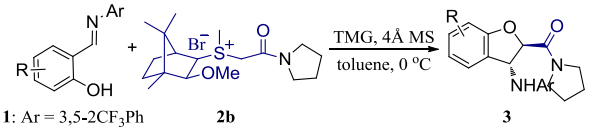


1: Ar = 3,5-$(CF_3)_2C_6H_3$ **2a** **3**

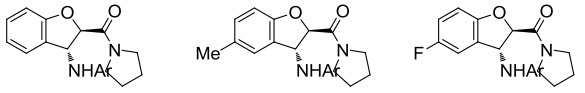
Entry	**1** (R)	Time (h)	Yield[c] (%)	dr[d]	ee[e] (%)
1	**1a** (H)	24	**3a**: 63	>95:5	97
2	**1b** (5-Me)	96	**3b**: 43	>95:5	98
3[b]	**1c** (5-NO_2)	18	**3c**: 29	>95:5	22
4	**1d** (5-F)	12	**3d**: 66	>95:5	95
5	**1e** (5-Cl)	24	**3e**: *68*	>95:5	88
6	**1f** (5-Br)	24	**3f**: 67	>95:5	86
7	**1g** (3,5-Cl_2)	12	**3g**: 46	>95:5	49
8	**1h** (3,5-Br_2)	18	**3h**: 52	>95:5	43
9	 **1i**	16	 **3i**: 63	>95:5	21

[a] Experimental conditions: a mixture of **1** (0.2 mmol), **2a** (0.22 mmol), 4 Å MS (200 mg), and TMG (0.44 mmol) in toluene (1.0 mL) was stirred at 0 °C for the indicated time.
[b] The reaction temperature was 20 °C.
[c] Yield of isolated product.
[d] Determined by chiral HPLC analysis and ^{1}H NMR analysis.
[e] Determined by chiral HPLC analysis.

Table 3
Asymmetric cycloaddition of aldimines **1** with camphor-derived sulfonium salt **2b**



1: Ar = 3,5-2CF_3Ph **2b** **3**

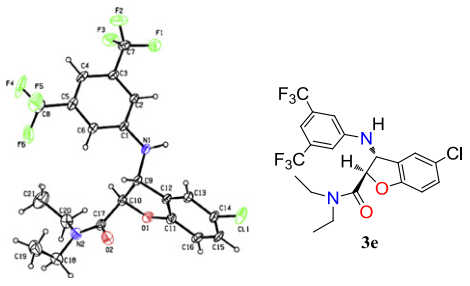


3j: 18 h, 67% yield
> 95:5 dr, 84% ee

3k: 18 h, 71% yield
> 95:5 dr, 93% ee

3l: 18 h, 78% yield
> 95:5 dr, 73% ee

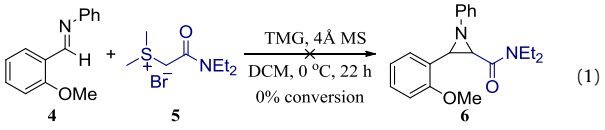
ee). In addition, we have also tried some other stable sulfur ylides such as alkyloxy- and aryl-acyl sulfur ylides.[7,9] Unfortunately, only a complex mixture was observed. Notably, the products **3a–l** were fully characterized by NMR analysis and elemental analysis. The absolute configuration of **3e** was unambiguously determined by X-ray crystal structure analysis (Fig. 2).[14]



3e

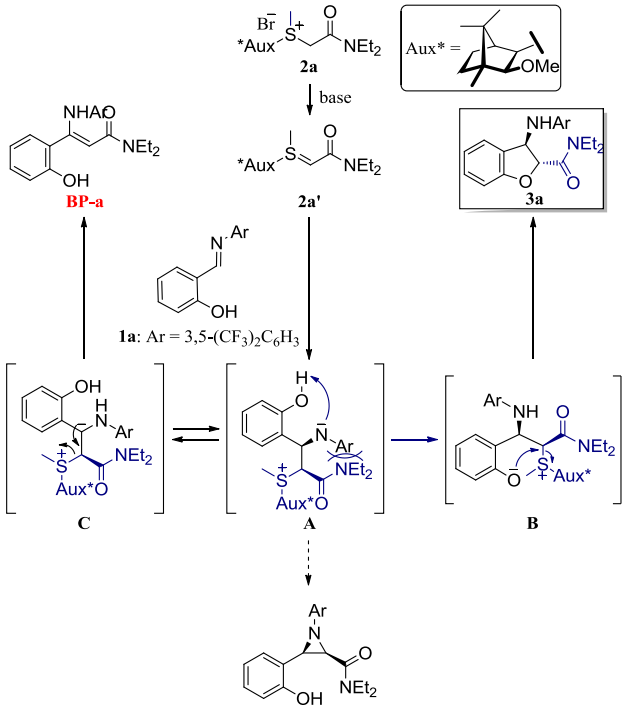
Fig. 2. ORTEP diagram of the X-ray crystal structure of **3e**. The thermal ellipsoids are drawn at the 30% probability level.

To gain some insights into the possible mechanism, we tried the reaction between *N*-phenyl imine **4** of 2-methoxybenzaldehyde and sulfonium salt **5** under the optimized conditions (Eq. 1). In accordance with Huang's observation, the imine **4** remained intact and no formation of aziridine product **6** was detected even after 22 h, which was probably because of the steric hindrance of such type of imine (Eq. 1).



4 **5** **6** (1)

Based on the X-ray structure of the product **3e** (Fig. 2) and Huang's observations,[10] we proposed a possible pathway to account for this formal [4+1] cycloaddition. As depicted in Scheme 2, for example, camphor-derived sulfonium salt **2a** was firstly transformed into the reactive sulfur ylide in the presence of TMG. The resulting sulfur ylide **2a**′ reacted with aldimine **1a** to give the intermediate **A**, whereafter the intramolecular hydrogen transfer to the nitrogen resulted in the formation of intermediate **B**. Finally, the intermediate **B** underwent an intramolecular O-alkylation (S_N2 substitution) to afford the desired product **3a** with release of the chiral sulfide. According to Speziale's previous studies on the reaction between carbonyl-stabilized sulfur ylides and Schiff bases,[15] another possible intermediate **C** might be formed through a hydride shift to nitrogen followed by the elimination of chiral sulfide to give the byproduct 3-arylaminocinnamamide **BP-a**. Notably, during our optimization studies with respect to the protecting groups on the nitrogen, we found that the reaction with aldimine bearing *o*-MeC_6H_4 on the nitrogen gave a mixture of 2,3-dihydrobenzofuran and byproduct 3-arylaminocinnamamide.[16] Accordingly, we speculated that such reaction pathway should be more favored in the cases of aldimines bearing strongly electron-withdrawing groups (e.g., 5-NO_2, 3,5-2Cl or 3,5-2Br). The possible equilibrium between the intermediates **A** and **C** might lead to the decreased enantioselectivity in the desired 2,3-dihydrobenzofuran **3a**.



Scheme 2. Proposed reaction pathway and transition state.

3. Conclusion

In conclusion, we have developed an asymmetric formal [4+1] cycloaddition of camphor-derived sulfonium salts with aldimines to construct optically active *trans*-2,3-disubstituted-2,3-dihydrobenzofuran derivatives. The process provided a complementary method to the precedented metal complex or organocatalyst catalyzed asymmetric synthesis of 2,3-dihydrobenzofurans.[6c,e] Although the full substrate scope awaits further improvement, the current methodology provides a new direction of the use of sulfur ylides in the carbon and heterocyclic chemistry.[17] Additional mechanistic studies and applications of this methodology to other functionalized heterocycle synthesis are now ongoing in our laboratory.

4. Experimental section

4.1. General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. Flash column chromatography (FC) was performed using 200–300 mesh silica gel.

^{1}H NMR spectra were recorded on 400/600 (400/600 MHz) spectrophotometer. Chemical shifts (δ) are reported in parts per million (ppm) from the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, m=multiplet, q=quarternary), coupling constants (Hz), and integration. ^{13}C NMR spectra were recorded on 400/600 (100/150 MHz) spectrophotometer ($CDCl_3$: 77.0 ppm) with complete proton decoupling. Mass spectra were measured on a Trace MS spectrometer. Elemental analysis was taken on an elementary analysis instrument.

4.2. General procedure for the synthesis of aldimines

At room temperature, 3,5-bis(trifluoromethyl)aniline (5.0 mmol) was added to a solution of 2-hydroxybenzaldehyde (5.0 mmol) in ethanol (20 mL). After stirring for 2 h, solid was precipitated. Then the solid recrystallized with ethanol to obtain the corresponding pure product **1**.

*4.2.1. (E)-2-(((3,5-Bis(trifluoromethyl)phenyl)imino)methyl) phenol (**1a**).* Yellow solid, 0.78 g, yield: 47%, mp 87–88 °C (ethanol). IR (KBr) ν 3423, 3098, 2977, 1957, 1795, 1603, 1579, 1382, 1278, 1172, 1126, 949, 759 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.44 (s, 1H), 8.66 (s, 1H), 7.79 (s, 1H), 7.69 (s, 2H), 7.46–7.43 (m, 2H), 7.05 (d, J=8.8 Hz, 1H), 6.99 (t, J=7.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 161.2, 150.1, 134.5, 133.4, 133.0, 132.7, 132.4, 124.4, 121.7, 121.5, 120.0, 119.5, 118.5, 117.5. MS: m/z=333.15 (M^+). Elemental Anal. Calcd for $C_{15}H_9F_6NO$: C, 54.07; H, 2.72; N, 4.20. Found: C, 53.93; H, 2.61; N, 4.21.

*4.2.2. (E)-2-(((3,5-Bis(trifluoromethyl)phenyl)imino)methyl)-4-methylphenol (**1b**).* Yellow solid, 0.56 g, yield: 32%, mp 74–75 °C (ethanol). IR (KBr) ν 3444, 3103, 2922, 2361, 1795, 1629, 1583, 1486, 1374, 1285, 1178, 947, 890, 784 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.22 (s, 1H), 8.61 (s, 1H), 7.78 (s, 1H), 7.68 (s, 2H), 7.27 (s, 1H), 7.24 (s, 1H), 6.96 (d, J=8.3 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.1, 150.3, 135.5, 133.0, 132.9, 132.7, 132.4, 128.7, 124.4, 121.7, 121.5, 119.9, 118.2, 117.3, 20.2. MS: m/z=347.14 (M^+). Elemental Anal. Calcd for $C_{16}H_{11}F_6NO$: C, 55.34; H, 3.19; N, 4.03. Found: C, 55.14; H, 2.99; N, 4.04.

*4.2.3. (E)-2-(((3,5-Bis(trifluoromethyl)phenyl)imino)methyl)-4-nitrophenol (**1c**).* Orange solid, 1.29 g, yield: 68%, mp 166–169 °C (ethanol). IR (KBr) ν 3446, 3090, 1804, 1632, 1604, 1579, 1372, 1339, 1279, 1180, 1128, 947 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.38 (s, 1H), 8.81 (s, 1H), 8.49 (s, 1H), 8.34 (d, J=8.8 Hz, 1H), 7.87 (s, 1H), 7.76 (s, 2H), 7.17 (d, J=8.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.2, 148.8, 140.4, 133.9, 133.4, 133.1, 132.7, 129.3, 129.1, 124.2, 121.6, 121.1, 118.6, 117.7. MS: m/z=378.20 (M^+). Elemental Anal. Calcd for $C_{15}H_8F_6N_2O_3$: C, 47.63; H, 2.13; N, 7.41. Found: C, 47.86; H, 2.07; N, 7.48.

*4.2.4. (E)-2-(((3,5-Bis(trifluoromethyl)phenyl)imino)methyl)-4-fluorophenol (**1d**).* Yellow solid, 0.70 g, yield: 40%, mp 95–97 °C (ethanol). IR (KBr) ν 3422, 3091, 2976, 1905, 1801, 1627, 1579, 1485, 1376, 1285, 1133, 947, 894, 682 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.41 (s, 1H), 8.60 (s, 1H), 7.82 (s, 1H), 7.69 (s, 2H), 7.21–7.15 (m, 2H), 7.04–7.01 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 157.4, 156.8, 154.4, 149.7, 133.5, 133.2, 132.8, 132.5, 127.0, 124.3, 121.6, 121.5, 120.4, 118.8, 118.2, 118.1, 117.7, 117.5. MS: m/z=351.11 (M^+). Elemental Anal. Calcd for $C_{15}H_8F_7NO$: C, 51.30; H, 2.30; N, 3.99. Found: C, 51.56; H, 2.52; N, 4.02.

*4.2.5. (E)-2-(((3,5-Bis(trifluoromethyl)phenyl)imino)methyl)-4-chlorophenol (**1e**).* Yellow solid, 1.27 g, yield: 69%, mp 120–123 °C (ethanol). IR (KBr) ν 3446, 1796, 1577, 1477, 1368, 1280, 1173, 947, 891, 748 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.41 (s, 1H), 8.60 (s, 1H), 7.82 (s, 1H), 7.69 (s, 2H), 7.44–7.38 (m, 2H), 7.02 (d, J=8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 159.7, 149.6, 134.2, 133.5, 133.2, 132.8, 132.5, 131.8, 127.0, 124.3, 124.2, 121.5, 120.5, 119.2, 119.1, 118.9. MS: m/z=367.12 (M^+). Elemental Anal. Calcd for $C_{15}H_8ClF_6NO$: C, 49.00; H, 2.19; N, 3.81. Found: C, 49.18; H, 2.38; N, 3.75.

*4.2.6. (E)-2-(((3,5-Bis(trifluoromethyl)phenyl)imino)methyl)-4-bromophenol (**1f**).* Orange solid, 1.79 g, yield: 87%, mp 133–135 °C (ethanol). IR (KBr) ν 3447, 1797, 1601, 1576, 1476, 1376, 1280, 1173, 1127, 947, 798, 681 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.43 (s, 1H), 8.60 (s, 1H), 7.82 (s, 1H), 7.69 (s, 2H), 7.58 (d, J=2.0 Hz, 1H), 7.52 (dd, J=8.8, 2.0 Hz, 1H), 6.97 (d, J=8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 160.2, 149.6, 137.0, 134.9, 133.5, 133.2, 132.9, 132.5, 124.3, 121.5, 120.5, 119.9, 119.5, 111.0. MS: m/z=413.05 ($[M+H]^+$). Elemental Anal. Calcd for $C_{15}H_8BrF_6NO$: C, 43.72; H, 1.96; N, 3.40. Found: C, 43.90; H, 1.72; N, 3.19.

*4.2.7. (E)-2-(((3,5-Bis(trifluoromethyl)phenyl)imino)methyl)-4,6-dichlorophenol (**1g**).* Orange solid, 1.21 g, yield: 60%, mp 128–132 °C (ethanol). IR (KBr) ν 3445, 1577, 1444, 1368, 1279, 1177, 1134, 946, 891, 738 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.20 (s, 1H), 8.63 (s, 1H), 7.85 (s, 1H), 7.71 (s, 2H), 7.54 (d, J=2.2 Hz, 1H), 7.39 (d, J=2.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 155.6, 148.8, 133.9, 133.7, 133.4, 133.0, 132.7, 130.4, 126.9, 124.2, 124.0, 123.1, 121.5, 121.0, 119.6. MS: m/z=401.13 ($[M-H]^+$). Elemental Anal. Calcd for $C_{15}H_7Cl_2F_6NO$: C, 44.80; H, 1.75; N, 3.48. Found: C, 45.02; H, 1.63; N, 3.48.

*4.2.8. (E)-2-(((3,5-Bis(trifluoromethyl)phenyl)imino)methyl)-4,6-dibromophenol (**1h**).* Orange solid, 2.14 g, yield: 87%, mp 160–162 °C (ethanol). IR (KBr) ν 3446, 3073, 1808, 1599, 1441, 1364, 1278, 1170, 1132, 937, 889, 690 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.38 (s, 1H), 8.60 (s, 1H), 7.86–7.81 (m, 2H), 7.71 (s, 2H), 7.57 (d, J=1.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 157.0, 148.6, 139.3, 134.1, 133.3, 133.0, 124.2, 121.6, 121.5, 121.0, 120.1, 112.3, 110.9. MS: m/z=491.08 (M^+). Elemental Anal. Calcd for $C_{15}H_7Br_2F_6NO$: C, 36.69; H, 1.44; N, 2.85. Found: C, 36.90; H, 1.66; N, 2.69.

*4.2.9. (E)-2-(((3,5-Bis(trifluoromethyl)phenyl)imino)methyl) pyridin-3-ol (**1i**).* Yellow solid, 0.35 g, yield: 21%, mp 91–93 °C (ethanol). IR (KBr) ν 3441, 3068, 1579, 1447, 1377, 1281, 1171, 1126, 946, 845, 808 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.30 (s, 1H), 8.90 (s, 1H), 8.35–8.32 (m, 1H), 7.84 (s, 1H), 7.77 (s, 2H), 7.43–7.37 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 158.5, 149.2, 142.0, 136.4, 133.5, 133.2, 132.8, 132.5, 127.7, 126.9, 125.3, 124.2, 121.7, 121.5, 120.8. MS:

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m/*z*=334.17 (M^+). Elemental Anal. Calcd for $C_{14}H_8F_6N_2O$: C, 50.31; H, 2.41; N, 8.38. Found: C, 50.23; H, 2.32; N, 8.14.

4.3. General procedure for asymmetric cycloaddition of camphor-derived sulfonium salts with aldimines

Aldimine **1** (0.20 mmol), camphor-derived sulfonium salts **2** (0.22 mmol), and 4 Å MS (200 mg) were mixed in dry toluene (1.0 mL). After stirring at 0 °C for 30 min, TMG (50.7 mg, 0.44 mmol) was introduced directly. The reaction mixture was stirred at 0 °C for 24 h. After the complete consumption of the aldimine **1** (as monitored by TLC), the mixture was purified by flash column chromatography on silica gel to give the corresponding pure product **3**.

*4.3.1. 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-N,N-diethyl-2,3-dihydrobenzofuran-2-carboxamide (**3a**).* White solid, 56.2 mg, yield: 63%, mp 148–150 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 97%, $[\alpha]_D^{25}$ −64.48 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=95:5, flow rate 0.7 mL/min, *T*=25 °C, 254 nm, t_R=10.42 min (major), t_R=11.55 min (minor). IR (KBr) *ν* 3323, 3076, 2987, 2938, 1642, 1545, 1479, 1398, 1277, 1187, 1124, 757 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.30 (d, *J*=7.4 Hz, 1H), 7.25–7.19 (m, 2H), 7.05 (s, 2H), 6.94 (t, *J*=7.4 Hz, 1H), 6.84 (d, *J*=8.1 Hz, 1H), 5.90 (dd, *J*=8.2, 4.4 Hz, 1H), 5.02 (d, *J*=4.4 Hz, 1H), 4.74 (d, *J*=8.3 Hz, 1H), 3.52–3.31 (m, 4H), 1.19–1.15 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 166.9, 158.7, 147.1, 133.1, 132.7, 132.4, 132.1, 130.4, 127.4, 125.7, 125.2, 124.7, 122.0, 121.7, 119.3, 112.4, 110.9, 110.2, 85.2, 58.2, 42.3, 40.9, 14.5, 12.5. MS: *m*/*z*=446.27 (M^+). Elemental Anal. Calcd for $C_{21}H_{20}F_6N_2O_2$: C, 56.50; H, 4.52; N, 6.28. Found: C, 56.59; H, 4.42; N, 6.27.

*4.3.2. 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-N,N-diethyl-5-methyl-2,3-dihydrobenzofuran-2-carboxamide (**3b**).* White solid, 39.6 mg, yield: 43%, mp 127–130 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 98%, $[\alpha]_D^{25}$ −44.12 (*c* 1.0, $CHCl_3$). Daicel Chirapak OD-H, hexane/isopropanol=95:5, flow rate 1.0 mL/min, *T*=25 °C, 254 nm, t_R=6.70 min (major), t_R=8.74 min (minor). IR (KBr) *ν* 3326, 3073, 2987, 2940, 2245, 1886, 1641, 1547, 1491, 1399, 1277, 1188, 1126, 811 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.20 (s, 1H), 7.13 (s, 1H), 7.07 (s, 3H), 6.76 (d, *J*=8.2 Hz, 1H), 5.98–5.95 (m, 1H), 5.03 (d, *J*=4.2 Hz, 1H), 4.49 (d, *J*=8.1 Hz, 1H), 3.48–3.34 (m, 4H), 2.30 (s, 3H), 1.20–1.16 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 167.0, 156.7, 147.2, 133.0, 132.7, 132.4, 132.1, 131.1, 130.9, 127.5, 125.7, 125.5, 124.7, 122.0, 119.3, 112.4, 110.7, 109.8, 85.3, 58.3, 42.2, 40.9, 20.6, 14.5, 12.5. MS: *m*/*z*=460.31 (M^+). Elemental Anal. Calcd for $C_{22}H_{22}F_6N_2O_2$: C, 57.39; H, 4.82; N, 6.08. Found: C, 57.66; H, 4.54; N, 6.11.

*4.3.3. 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-N,N-diethyl-5-nitro-2,3-dihydrobenzofuran-2-carboxamide (**3c**).* Yellow solid, 28.5 mg, yield: 29%, mp 145–147 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 22%, $[\alpha]_D^{24}$ −16.17 (*c* 1.0, $CHCl_3$). Daicel Chirapak IC-H, hexane/isopropanol=80:20, flow rate 1.0 mL/min, *T*=25 °C, 254 nm, t_R=4.84 min (minor), t_R=5.41 min (major). IR (KBr) *ν* 3322, 3084, 2991, 2944, 2911, 1634, 1548, 1526, 1475, 1398, 1340, 1277, 1172, 957 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.25–8.21 (m, 2H), 7.27 (s, 1H), 7.09 (s, 2H), 6.95 (d, *J*=8.8, 1H), 6.06 (t, *J*=4.2 Hz, 1H), 5.25 (d, *J*=4.4 Hz, 1H), 4.70 (d, *J*=8.8 Hz, 1H), 3.54–3.39 (m, 4H), 1.21–1.18 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 165.7, 163.7, 146.6, 142.7, 133.0, 132.7, 127.5, 127.3, 124.6, 121.9, 112.6, 111.7, 110.5, 87.0, 57.5, 42.4, 41.2, 14.6, 12.5. MS: *m*/*z*=491.21 (M^+). Elemental Anal. Calcd for $C_{21}H_{19}F_6N_3O_4$: C, 51.33; H, 3.90; N, 8.55. Found: C, 51.55; H, 3.72; N, 8.40.

*4.3.4. 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-N,N-diethyl-5-fluoro-2,3-dihydrobenzofuran-2-carboxamide (**3d**).* White solid, 61.3 mg, yield: 66%, mp 141–143 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 95%, $[\alpha]_D^{26}$ −64.76 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=95:5, flow rate 0.7 mL/min, *T*=25 °C, 254 nm, t_R=9.84 min (major), t_R=13.01 min (minor). IR (KBr) *ν* 3315, 3079, 2986, 2941, 1865, 1642, 1549, 1487, 1398, 1277, 1124, 819 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.23 (s, 1H), 7.08 (s, 2H), 7.04 (d, *J*=7.4 Hz, 1H), 7.00–6.95 (m, 1H), 6.80 (dd, *J*=8.7, 4.0 Hz, 1H), 6.04–6.01 (m, 1H), 5.08 (d, *J*=4.4 Hz, 1H), 4.50 (d, *J*=7.6, 1H), 3.53–3.35 (m, 4H), 1.20–1.17 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 166.8, 159.0, 156.6, 154.7, 147.1, 133.1, 132.8, 132.5, 132.1, 127.4, 127.1, 127.0, 124.7, 122.0, 119.3, 117.0, 116.8, 112.5, 112.1, 111.9, 111.1, 110.7, 110.6, 85.7, 58.4, 42.3, 41.0, 14.4, 12.4. MS: *m*/*z*=464.29 (M^+). Elemental Anal. Calcd for $C_{21}H_{19}F_7N_2O_2$: C, 54.31; H, 4.12; N, 6.03. Found: C, 54.22; H, 3.93; N, 6.05.

*4.3.5. 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-5-chloro-N,N-diethyl-2,3-dihydrobenzofuran-2-carboxamide (**3e**).* White solid, 65.4 mg, yield: 68%, mp 141–142 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 88%, $[\alpha]_D^{24}$ −48.69 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=95:5, flow rate 0.7 mL/min, *T*=25 °C, 254 nm, t_R=10.33 min (major), t_R=11.95 min (minor). IR (KBr) *ν* 3324, 3077, 2989, 2941, 1639, 1550, 1475, 1399, 1277, 1190, 1127, 817 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.31 (s, 1H), 7.23 (s, 2H), 7.07 (s, 2H), 6.81 (d, *J*=8.6 Hz, 1H), 6.03–6.00 (m, 1H), 5.08 (d, *J*=4.3 Hz, 1H), 4.47 (d, *J*=8.9 Hz, 1H), 3.52–3.35 (m, 4H), 1.18 (t, *J*=7.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 166.5, 157.3, 147.0, 133.1, 132.8, 132.5, 132.1, 130.3, 127.6, 126.3, 125.2, 124.7, 121.9, 112.4, 111.3, 85.7, 58.1, 42.3, 41.0, 14.5, 12.5. MS: *m*/*z*=480.15 (M^+). Elemental Anal. Calcd for $C_{21}H_{19}ClF_6N_2O_2$: C, 52.46; H, 3.98; N, 5.83. Found: C, 52.58; H, 3.75; N, 5.75.

*4.3.6. 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-5-bromo-N,N-diethyl-2,3-dihydrobenzofuran-2-carboxamide (**3f**).* Yellow solid, 70.4 mg, yield: 67%, mp 134–136 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 86%, $[\alpha]_D^{25}$ −36.43 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=95:5, flow rate 0.7 mL/min, *T*=25 °C, 254 nm, t_R=10.47 min (major), t_R=11.95 min (minor). IR (KBr) *ν* 3326, 3076, 2989, 2941, 1638, 1549, 1473, 1398, 1277, 1127, 956, 815, 679 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.45 (s, 1H), 7.37 (d, *J*=8.5 Hz, 1H), 7.23 (s, 1H), 7.07 (s, 2H), 6.76 (d, *J*=8.6 Hz, 1H), 6.01 (dd, *J*=8.4, 4.1 Hz, 1H), 5.07 (d, *J*=4.3 Hz, 1H), 4.52 (d, *J*=8.3 Hz, 1H), 3.521–3.35 (m, 4H), 1.18 (t, *J*=7.1 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 166.6, 157.9, 147.0, 133.2, 132.8, 132.4, 132.1, 128.2, 128.1, 124.4, 121.9, 113.3, 112.4, 111.8, 111.1, 85.6, 58.1, 42.3, 41.0, 14.5, 12.4. MS: *m*/*z*=526.28 ($[M+H]^+$). Elemental Anal. Calcd for $C_{21}H_{19}BrF_6N_2O_2$: C, 48.02; H, 3.65; N, 5.33. Found: C, 48.27; H, 3.47; N, 5.15.

*4.3.7. 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-5,7-dichloro-N,N-diethyl-2,3-dihydrobenzofuran-2-carboxamide (**3g**).* White solid, 47.4 mg, yield: 46%, mp 153–155 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 46%, $[\alpha]_D^{26}$ −28.59 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=90:10, flow rate 1.0 mL/min, *T*=25 °C, 254 nm, t_R=4.42 min (major), t_R=5.14 min (minor). IR (KBr) *ν* 3390, 3087, 2989, 1640, 1589, 1527, 1461, 1393, 1275, 1174, 993, 871, 750 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.29 (s, 1H), 7.25 (s, 1H), 7.22 (s, 1H), 7.10 (s, 2H), 6.15–6.12 (m, 1H), 5.16 (d, *J*=4.3 Hz, 1H), 4.51 (d, *J*=8.6 Hz, 1H), 3.56–3.52 (m, 2H), 3.45–3.28 (m, 2H), 1.25 (t, *J*=7.2 Hz, 3H), 1.18 (t, *J*=7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 165.8, 153.7, 146.9, 133.7, 133.4, 133.1, 132.7, 130.5, 129.1, 127.5, 127.2, 124.8, 123.8, 122.1, 116.8, 113.0, 112.0, 86.8, 59.0, 42.5, 41.2, 14.5, 12.5. MS: *m*/*z*=516.34 ($[M+H]^+$). Elemental Anal. Calcd for

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$C_{21}H_{18}Cl_2F_6N_2O_2$: C, 48.95; H, 3.52; N, 5.44. Found: C, 49.18; H, 3.76; N, 5.42.

*4.3.8. 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-5,7-dibromo-N,N-diethyl-2,3-dihydrobenzofuran-2-carboxamide (**3h**).* Yellow solid, 62.8 mg, yield: 52%, mp 167–169 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 43%, $[\alpha]_D^{26}$ −19.87 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=90:10, flow rate 1.0 mL/min, *T*=25 °C, 254 nm, t_R=4.54 min (major), t_R=5.72 min (minor). IR (KBr) *ν* 3403, 3322, 3082, 2988, 2944, 1653, 1626, 1454, 1397, 1277, 1181, 1129, 863, 681 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.58 (s, 1H), 7.40 (s, 1H), 7.25 (s, 1H), 7.11 (s, 2H), 6.19 (dd, *J*=8.6, 4.2 Hz, 1H), 5.15 (d, *J*=4.4 Hz, 1H), 4.47 (d, *J*=8.3 Hz, 1H), 3.59–3.53 (m, 2H), 3.41–3.29 (m, 2H), 1.27 (d, *J*=7.1 Hz, 3H), 1.19 (d, *J*=7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 165.7, 155.3, 146.7, 135.5, 132.9, 132.6, 128.9, 127.3, 124.6, 121.9, 113.7, 112.6, 111.5, 104.0, 86.2, 58.7, 42.5, 41.0, 14.4, 12.4. MS: *m*/*z*=604.08 (M^+). Elemental Anal. Calcd for $C_{21}H_{18}Br_2F_6N_2O_2$: C, 41.75; H, 3.00; N, 4.64. Found: C, 41.94; H, 3.29; N, 4.44.

*4.3.9. 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-N,N-diethyl-2,3-dihydrofuro[3,2-b]pyridine-2-carboxamide (**3i**).* White solid, 56.3 mg, yield: 63%, mp 182–185 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 21%, $[\alpha]_D^{24}$ 11.12 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=70:30, flow rate 1.0 mL/min, T=25 °C, 254 nm, t_R=4.88 min (minor), t_R=5.93 min (major). IR (KBr) *ν* 3319, 3078, 2989, 2941, 1635, 1580, 1473, 1397, 1278, 1188, 1125, 952, 854, 797 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.20 (d, *J*=3.3 Hz, 1H), 7.23–7.17 (m, 3H), 7.07 (s, 2H), 5.95–5.91 (m, 1H), 5.17 (d, *J*=5.3 Hz, 1H), 4.90 (d, *J*=5.8 Hz, 1H), 3.56–3.43 (m, 4H), 1.24–1.19 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 166.3, 152.8, 147.5, 147.5, 143.0, 133.0, 132.6, 132.3, 132.0, 124.7, 124.5, 122.0, 117.3, 112.4, 111.1, 85.0, 58.4, 42.3, 41.1, 14.7, 12.6. MS: *m*/*z*=447.27 (M^+). Elemental Anal. Calcd for $C_{20}H_{19}F_6N_3O_2$: C, 53.69; H, 4.28; N, 9.39. Found: C, 53.87; H, 4.12; N, 9.11.

*4.3.10. (3-((3,5-Bis(trifluoromethyl)phenyl)amino)-2,3-dihydro benzofuran-2-yl)(pyrrolidin-1-yl)methanone (**3j**).* White solid, 59.5 mg, yield: 67%, mp 163–164 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 84%, $[\alpha]_D^{25}$ −57.99 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=95:5, flow rate 1.0 mL/min, *T*=25 °C, 254 nm, t_R=13.36 min (major), t_R=14.61 min (minor). IR (KBr) *ν* 3288, 3176, 3099, 2965, 2891, 1648, 1620, 1456, 1397, 1275, 1187, 1121, 853, 753 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) *δ* 7.34 (d, *J*=7.4 Hz, 1H), 7.29 (t, *J*=7.8 Hz, 1H), 7.22 (s, 1H), 7.15 (s, 2H), 6.99 (t, *J*=7.4 Hz, 1H), 6.90 (d, *J*=8.1 Hz, 1H), 5.92–5.90 (m, 1H), 5.00 (d, *J*=3.9 Hz, 1H), 4.50 (d, *J*=8.3 Hz, 1H), 3.71–3.69 (m, 1H), 3.58–3.54 (m, 3H), 2.00–1.87 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) *δ* 166.5, 158.8, 147.1, 133.0, 132.7, 132.4, 132.1, 130.5, 125.7, 125.3, 124.7, 122.0, 121.7, 112.4, 110.9, 110.2, 86.4, 58.4, 46.9, 46.6, 26.1, 23.8. MS: *m*/*z*=444.28 (M^+). Elemental Anal. Calcd for $C_{21}H_{18}F_6N_2O_2$: C, 56.76; H, 4.08; N, 6.30. Found: C, 56.91; H, 4.25; N, 6.04.

*4.3.11. (3-((3,5-Bis(trifluoromethyl)phenyl)amino)-5-methyl-2,3-dihydrobenzofuran-2-yl)(pyrrolidin-1-yl)methanone (**3k**).* White solid, 65.1 mg, yield: 71%, mp 203–206 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 93%, $[\alpha]_D^{24}$ −49.77 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=95:5, flow rate 1.0 mL/min, *T*=25 °C, 254 nm, t_R=14.37 min (major), t_R=16.46 min (minor). IR (KBr) *ν* 3304, 3081, 2971, 2892, 1642, 1576, 1450, 1401, 1276, 1190, 1129, 815 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.21 (s, 1H), 7.14 (s, 3H), 7.08 (d, *J*=8.7 Hz, 1H), 6.78 (d, *J*=8.2 Hz, 1H), 5.87–5.84 (m, 1H), 4.98 (d, *J*=4.0 Hz, 1H), 4.46 (d, *J*=8.3 Hz, 1H), 3.71–3.67 (m, 1H), 3.57–3.53 (m, 3H), 2.31 (s, 3H), 1.97–1.89 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 166.6, 156.8, 147.1, 133.1, 132.8, 132.4, 132.1, 131.3, 131.0, 125.6, 124.7, 122.0, 112.4, 110.9, 109.9, 86.6, 58.6, 46.9, 46.7, 26.2, 23.8, 20.7. MS: *m*/*z*=458.24 (M^+). Elemental Anal. Calcd for $C_{22}H_{20}F_6N_2O_2$: C, 57.64; H, 4.40; N, 6.11. Found: C, 57.68; H, 4.15; N, 6.39.

*4.3.12. (3-((3,5-Bis(trifluoromethyl)phenyl)amino)-5-fluoro-2,3-dihydrobenzofuran-2-yl)(pyrrolidin-1-yl)methanone (**3l**).* White solid, 72.1 mg, yield: 78%, mp 144–148 °C (petroleum ether/ethyl acetate), diastereoisomer ratio: >95:5, enantiomeric excess: 73%, $[\alpha]_D^{26}$ −56.17 (*c* 1.0, $CHCl_3$). Daicel Chirapak AD-H, hexane/isopropanol=95:5, flow rate 0.7 mL/min, *T*=25 °C, 254 nm, t_R=11.99 min (major), t_R=18.27 min (minor). IR (KBr) *ν* 3292, 3085, 2988, 2888, 1644, 1559, 1484, 1453, 1400, 1277, 1194, 1129, 818 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.23 (s, 1H), 7.13 (s, 2H), 7.04–6.96 (m, 2H), 6.83–6.80 (m, 1H), 5.94–5.90 (m, 1H), 5.03 (d, *J*=4.3 Hz, 1H), 4.52 (d, *J*=8.5 Hz, 1H), 3.72–3.67 (m, 1H), 3.58–3.46 (m, 3H), 2.04–1.87 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 166.2, 159.0, 156.7, 154.7, 146.9, 132.8, 132.4, 126.9, 126.8, 124.7, 122.0, 117.1, 116.9, 112.5, 112.2, 112.0, 111.2, 110.7, 110.7, 86.9, 58.4, 46.8, 46.6, 26.0, 23.8. MS: *m*/*z*=462.44 (M^+). Elemental Anal. Calcd for $C_{21}H_{17}F_7N_2O_2$: C, 54.55; H, 3.71; N, 6.06. Found: C, 54.37; H, 3.92; N, 5.89.

*4.3.13. (Z)-N,N-Diethyl-3-(2-hydroxyphenyl)-3-(o-tolylamino) acrylamide (**BP**).* ^1H NMR (400 MHz, $CDCl_3$) *δ* 11.26 (s, 1H), 7.25–7.13 (m, 2H), 7.10–7.08 (m, 3H), 6.94–6.89 (m, 2H), 6.85–6.82 (m, 1H), 6.11 (d, *J*=12.5 Hz, 1H), 3.58 (d, *J*=5.9 Hz, 4H), 1.95 (s, 3H), 1.26–1.22 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 173.5, 156.5, 139.3, 130.9, 130.1, 129.9, 127.3, 123.8, 121.0, 120.4, 119.7, 119.2, 112.1, 105.9, 16.9, 13.8, 13.7.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.03.059.

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