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LDA-Promoted Synthesis of 3-Amino Furans by Selective Lithiation of Enaminones

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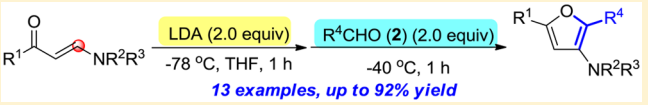
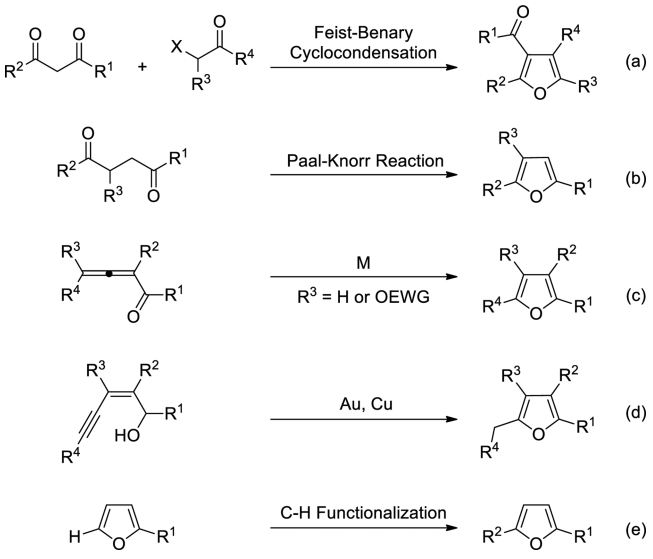
Supporting Information

ABSTRACT: An efficient cascade β-metalation/addition/cyclization reaction promoted by LDA is described in which 3-amino furans were constructed from enaminones and aldehydes. A broad range of substituents on the starting compounds was tolerated, and the polysubstituted furans were gained with moderate to excellent yields within 2 h.



Highly functionalized furans play a significant role in organic chemistry, since they, as fundamental heterocyclic motifs, are widely found in biologically active natural products, pharmaceuticals, and materials.[1] Moreover, they have also frequently been used as basic building blocks in synthetic chemistry.[2] Thus, substantial interest has been attracted toward the development of efficient methods to prepare multiply substituted furans.[3] Traditional approaches for the synthesis of furans include Feist–Bénary cyclocondensation[4] from 1,3-dicarbonyl compounds and haloketones (Scheme 1a), Paal–Knorr cyclocondensation[5] from 1,4-dicarbonyl compounds (Scheme 1b), and so on. Transition-metal-catalyzed methods have also been developed for the assembly of various multisubstituted furans, such as the cyclization of allenyl ketones (Scheme 1c),[6] Au-catalyzed cyclization of (*Z*)-enynols (Scheme 1d),[7] and Pd-catalyzed arylation of furans via C–H activation[8] (Scheme 1e).

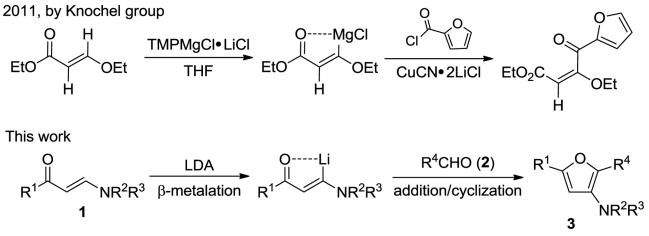
Scheme 1. Synthesis of Highly Substituted Furan



Another process to construct polysubstituted furan derivatives is ring transformation.[9] Functionalization at the 2- and 5-positions of furans is readily permitted in chemical transformations, but similar operations at the 3- or 4-position are difficult to achieve. Electron-rich furan derivatives like 3-amino furans are easy to modify by Friedel–Crafts acylation and are exceptionally useful dienes for use in Diels–Alder reactions, whereas there are only a few reports of the synthesis of substituted 3-amino furans.[10]

The functionalization of aromatic molecules and heterocyclic compounds has often been achieved by metalation using various bases.[11] However, the deprotonation of functionalized nonaromatic and olefinic systems is more difficult and sensitive compared with that of aromatic and heteroaromatic systems.[12] Excellent work by Knochel's group described the magnesiation or zincation of highly functionalized alkenes and cycloalkenes using 2,2,6,6-tetramethylpiperidyl base (Scheme 2).[12a] During the course of our continued work on the preparation of heterocycles from enaminones,[13] we developed an efficient cascade addition/cyclization reaction to synthesize 3-amino-2,5-aryl (or alkyl) furans promoted by LDA, from enaminones and aldehydes, inspired by the β-metalation of unsaturated olefins facilitated by the orientation effect on the carbonyl

Scheme 2. β-Metalation as the Key Step



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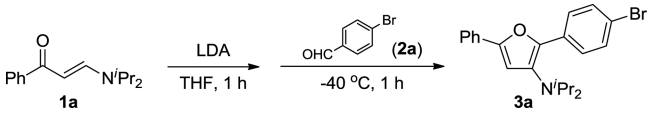
group. To our delight, only the desired products of the β-metalation process were obtained and no α-metalation products were observed in this system.

We began our investigation with enaminone **1a** and 1.4 equiv of LDA (lithium diisopropylamide) using a lithiation temperature of −78 °C under a N_2 atmosphere, followed by adding 1.5 equiv of 4-bromobenzaldehyde **2a**. 3-Amino furan **3a** was efficiently obtained in 80% isolated yield (Table 1, entry 1). To

Table 1. Optimization of Reaction Conditions[a]



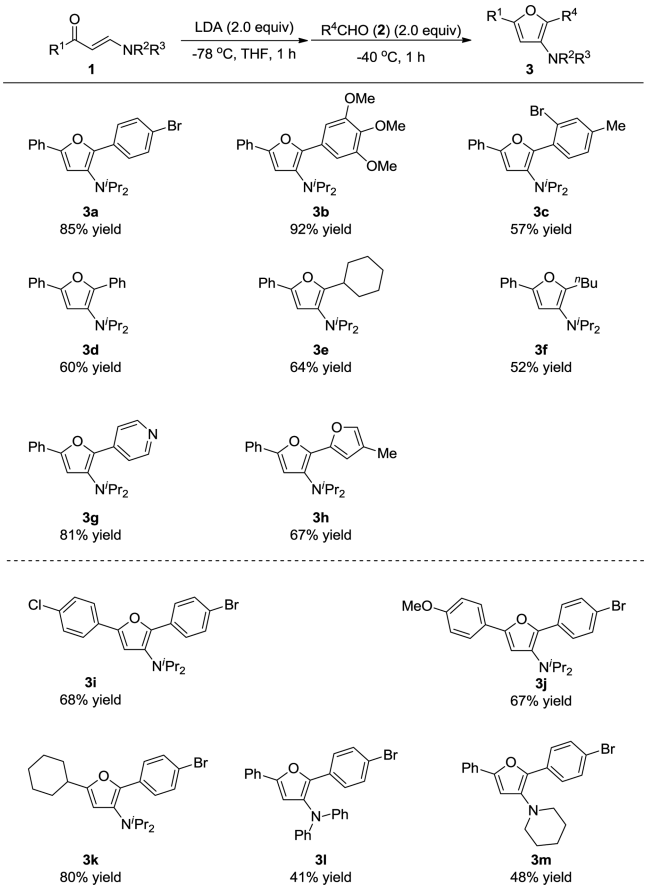
entry	LDA (equiv)	lithiation temp.	**2a** (equiv)	yield (%)[b]
1	1.4	−78 °C	1.5	80
2	1.4[c]	−78 °C	1.5	79
3	1.4[c]	−40 °C	1.5	66
4	1.2	−78 °C	1.5	24
5	2.0	−78 °C	1.5	54
6	2.0	−78 °C	2.0	85
7	1.5	−78 °C	2.0	78

[a]Unless otherwise noted, the reactions were carried out under a N_2 atmosphere on a 0.5 mmol scale. [b]Isolated yield. [c]LDA in situ.

our delight, no α-lithiation byproduct was detected. This result encouraged us to optimize the reaction conditions with **1a** and **2a** as model substrates (Table 1). First, LDA was tested in situ, and almost no difference in product yields was observed (entries 1 and 2). Because LDA is commercially available, we chose to use LDA as the organolithium reagent. When the lithiation temperature was increased to −40 °C, the yield of desired product **3a** decreased to 66% (entry 3). Next, the lithiation temperature was fixed at −78 °C and the amounts of LDA and 4-bromobenzaldehyde **2a** were screened, revealing that 2.0 equiv of LDA and **2a** was essential to this system, with 85% isolated yield of 3-amino furan **3a** (entries 4−7).

With the optimized reaction conditions (Table 1, entry 6) in hand, the substrate scope of the reaction was explored by employing a variety of enaminones **1** and aldehydes **2** (Scheme 3). High chemoselectivities and high efficiency were observed in all cases, and a series of polysubstituted 3-amino furans was gained in moderate to good yields within 2 h. The reaction tolerated aldehydes **2** with aromatic substituents with different electronic properties (**2a**−**d**), alkyl substituents (**2e**−**f**), or heteroaromatic substituents (**2g**−**h**), giving corresponding products **3** in good to excellent yields (52−92%). Among them, 3,4,5-trimethoxybenzaldehyde (**2b**), with a highly electron-donating group as substituent R^4, gave the best result in producing 3-amino furan **3b** (92% isolated yield). The data also illustrated that benzaldehyde (**2d**) offered product **3d** in a lower yield (60% yield) compared with that using aldehydes with either an electron-withdrawing (**2a**) or electron-donating (**2b**) group as substituent R^4. However, when sterically hindered aldehydes **2c** (R^4 = 2-bromo-4-methylphenyl) with an *ortho*-substituent on the benzene ring was employed, the yield of product **3c** dropped dramatically (57% yield). Alkyl aldehydes such as **2e** and **2f** yielded 3-amino furans **3** with good results (**3e**, 64% yield; **3f**, 52% yield). Furthermore, the reaction with heteroaromatic aldehydes **2g** and **2h** also went smoothly, resulting in desired products **3g** and **3h** in 81 and 67% yields, respectively. In addition, the structure of 3-amino furan **3c** was

Scheme 3. Synthesis of 3-Amino Furans 3[a,b]



[a]All reactions were carried out under a N_2 atmosphere on a 0.5 mmol scale. [b]Isolated yield.

characterized by X-ray crystallography (see Supporting Information, including a CIF file).

Next, we proceeded to extend the reaction scope to different kinds of enaminones **1**. R^1 substituents with either an electron-withdrawing (**1i**, R^1 = 4-chlorophenyl) or electron-donating (**1j**, R^1 = 4-methoxyphenyl) group on the benzene ring led to a decline in the yields of the corresponding furan products (**3i**, 68% yield; **3j**, 67% yield) with respect to that using enaminone **1a** with a phenyl group as the R^1 substituent (**3a**, 85% yield). Notably, the scope of the enaminones could be extended to simple aliphatic enaminones, such as **1k**, affording the corresponding furan **3k** in good yield (80%). Then, efforts were made to examine the N-substituents, R^2 and R^3, finding that isopropyl is sterically and electrically fit for this system. Other N-substituents like a phenyl group (**1l**) and piperidin-1-yl-substituted enaminone (**1m**) sharply impacted the yields of the desired products, resulting in **3l** in 41% yield and **3m** in 48% yield.

On the basis of the reported work,[12a,14] a plausible mechanism for this reaction is proposed in Scheme 4. The process begins with the β-metalation of enaminone **1** by LDA, which is aided by help from the orientation effect on the carbonyl group to form lithium compound **A**. Then, attack by aldehyde **2** gives intermediate **B**. The cyclization of **B** generates 2,5-dihydrofuran ring intermediate **C**. After quenching by a saturated solution of ammonium chloride, the desired 3-amino furan **3** was finally obtained by aromatization.

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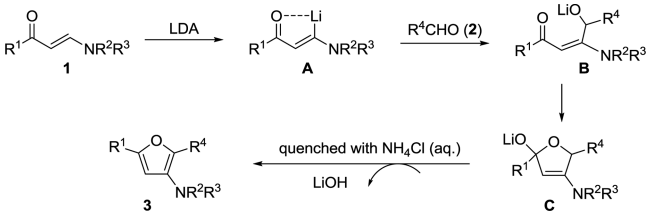
Scheme 4. Plausible Mechanisms



In conclusion, we have developed an efficient procedure for the synthesis of 3-amino furans promoted by LDA, starting with ready-in-hand reagents. This system tolerated a broad range of enaminones and aldehydes and achieved moderate to excellent yields within 2 h. It provides a new, efficient approach to prepare polysubstituted furans.

EXPERIMENTAL SECTION

General Remarks. Unless otherwise mentioned, all commercial reagents and solvents were used as purchased without further purification. THF was distilled from sodium/benzophenone. Column chromatographic purification of products was carried out using silica gel (200−300 mesh). NMR spectra were recorded at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) respectively, referenced to tetramethylsilane (δ = 0.00 ppm) and the residual solvent peak (δ = 77.00 ppm) in $CDCl_3$ (containing 0.03% TMS) solutions. J values are in hertz. High-resolution mass spectra were performed on a mass spectrometer with a TOF (for EI or ESI) or FT-ICR (for MALDI) analyzer.

General Procedure for the Preparation of (*E*)-Enaminone 1.[13e] To a solution of ynone (5.0 mmol) in toluene or methanol (5 mL) in a Schlenk tube was added secondary amine (6.0 mmol, 1.2 equiv), and the mixture was stirred at room temperature until the full conversion of ynone was observed, as monitored by thin-layer chromatography. The resulting mixture was concentrated under reduced pressure. Purification by chromatography on silica gel (petroleum ether) afforded desired compound **1**.[15] The data of new compounds **1** are given below.

(E)-1-Cyclohexyl-3-(diisopropylamino)prop-2-en-1-one. Yellow liquid, obtained in 12 h and purified by chromatography on silica gel (petroleum ether/ethyl acetate 4:1); yield: 0.75 g (63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10−1.30 (m, 15H), 1.37−1.47 (m, 2H), 1.64−1.68 (m, 1H), 1.76−1.83 (m, 4H), 2.25 (t, J = 11.2 Hz, 1H), 3.73 (br, 2H), 5.23 (d, J = 12.8 Hz, 1H), 7.74 (d, J = 12.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 22.9, 25.4, 25.5, 25.6, 29.2, 47.8, 49.9, 93.1, 146.9, 201.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{28}NO$, 238.2165; found, 238.2176.

(E)-3-(Diisopropylamino)-1-(4-methoxyphenyl)prop-2-en-1-one. Yellow solid, obtained in 25 min and purified by chromatography on silica gel (petroleum ether/ethyl acetate 3:1); yield: 1.27 g (97%); mp 77−78 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26−1.28 (m, 12H), 3.62 (m, 1H), 3.84 (s, 3H), 3.40 (m, 1H), 5.89 (d, J = 12.4 Hz, 1H), 6.91 (d, J = 9.2 Hz, 2H), 7.91 (d, J = 8.8 Hz, 2H), 7.97 (d, J = 12.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 23.3, 55.1, 91.2, 113.3, 129.5, 133.7, 148.7,162.0, 187.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{24}NO_2$, 262.1802; found, 262.1807.

General Procedure for the Preparation of 3-Amino Furans 3. To a solution of enaminone **1** (0.5 mmol) in dry THF (5 mL) in a Schlenk tube was added a 2.0 M solution of LDA in THF (1.0 mmol, 0.5 mL) dropwise, and the mixture was stirred at −78 °C for 1 h under nitrogen. Then, aldehyde **2** (1.0 mmol) was added at −78 °C, and the reaction mixture was allowed to warm to −40 °C and kept at the temperature until the full conversion of enaminone **1** was observed, as monitored by thin-layer chromatography. The resulting mixture was quenched with a saturated solution of NH_4Cl and extracted with ethyl acetate (10 mL × 3). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (petroleum ether) afforded desired compound **3**.

*2-(4-Bromophenyl)-N,N-diisopropyl-5-phenylfuran-3-amine (**3a**).* Colorless liquid, 170 mg (85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (d, J = 6.0 Hz, 12H), 3.37−3.43 (m, 2H), 6.68 (s, 1H), 7.21−7.25 (m, 1H), 7.35−7.39 (m, 2H), 7.46−7.48 (m, 2H), 7.69−7.72 (m, 2H), 8.22−8.25 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 20.6, 49.8, 108.8, 120.1, 123.5, 126.3, 127.4, 128.6, 130.5, 130.7, 131.0, 131.9, 147.4, 150.9. HRMS (EI-TOF) m/z: M^+ calcd for $C_{22}H_{24}NOBr$, 397.1041; found, 397.1038.

*N,N-Diisopropyl-5-phenyl-2-(3,4,5-trimethoxyphenyl)furan-3-amine (**3b**).* Colorless liquid, 188 mg (92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (d, J = 6.4 Hz, 12H), 3.41−3.48 (m, 2H), 3.90 (s, 3H), 3.93 (s, 6H), 6.70 (s, 1H), 7.22−7.26 (m, 1H), 7.37−7.41 (m, 2H), 7.71−7.74 (m, 2H), 7.76 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 49.5, 55.8, 55.8, 60.7, 102.0, 108.8, 123.3, 127.0, 127.1, 128.5, 130.6, 130.7, 136.7, 148.0, 150.2, 152.7. HRMS (EI-TOF) m/z: M^+ calcd for $C_{25}H_{31}NO_4$, 409.2253; found, 409.2252.

*2-(2-Bromo-4-methylphenyl)-N,N-diisopropyl-5-phenylfuran-3-amine (**3c**).* White solid, 117 mg (57% yield); mp 133−134 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (d, J = 6.4 Hz, 12H), 2.32 (s, 3H), 3.30−3.36 (m, 2H), 6.71 (s, 1H), 7.08−7.10 (m, 1H), 7.20−7.24 (m, 1H), 7.34−7.38 (m, 2H), 7.47−7.48 (m, 1H), 7.71−7.75 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 21.0, 49.6, 107.1, 122.4, 123.5, 127.2, 127.4, 128.6, 129.5, 131.1, 131.5, 131.9, 134.0, 139.2, 147.2, 151.0. HRMS (EI-TOF) m/z: M^+ calcd for $C_{23}H_{26}NOBr$, 411.1198; found, 411.1201.

*N,N-Diisopropyl-2,5-diphenylfuran-3-amine (**3d**).* Colorless liquid, 95 mg (60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (d, J = 6.4 Hz, 12H), 3.40−3.46 (m, 2H), 6.70 (s, 1H), 7.18−7.25 (m, 2H), 7.34−7.40 (m, 4H), 7.72−7.74 (m, 2H), 8.34−8.36 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 49.8, 108.9, 123.5, 124.8, 126.5, 127.2, 127.9, 128.6, 131.0, 131.3, 131.7, 148.4, 150.5. HRMS (EI-TOF) m/z: M^+ calcd for $C_{22}H_{25}NO$, 319.1936; found, 319.1932.

*2-Cyclohexyl-N,N-diisopropyl-5-phenylfuran-3-amine (**3e**).* Colorless liquid, 104 mg (64% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, J = 6.4 Hz, 12H), 1.26−1.38 (m, 4H), 1.62−1.83 (m, 6H), 2.84−2.88 (m, 1H), 3.24−3.31 (m, 2H), 6.49 (s, 1H), 7.14−7.18 (m, 1H), 7.31−7.35 (m, 2H), 7.60−7.63 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 26.1, 26.5, 31.5, 34.3, 49.6, 106.9, 123.0, 125.9, 126.4, 128.5, 131.6, 149.3, 157.4. HRMS (EI-TOF) m/z: M^+ calcd for $C_{22}H_{31}NO$, 325.2406; found, 325.2410.

*2-Butyl-N,N-diisopropyl-5-phenylfuran-3-amine (**3f**).* Colorless liquid, 78 mg (52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, J = 7.6 Hz, 3H), 0.98 (d, J = 6.4 Hz, 12H), 1.39−1.44 (m, 2H), 1.64−1.68 (m, 2H), 2.64 (t, J = 7.6 Hz, 2H), 3.27−3.30 (m, 2H), 6.51 (s, 1H), 7.17−7.19 (m, 1H), 7.31−7.35 (m, 2H), 7.60−7.63 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 21.2, 22.8, 25.2, 30.2, 49.8, 107.2, 123.0, 126.4, 127.4, 128.5, 131.6, 149.6, 153.8. HRMS (EI-TOF) m/z: M^+ calcd for $C_{20}H_{29}NO$, 299.2249; found, 299.2247.

*N,N-Diisopropyl-5-phenyl-2-(pyridin-4-yl)furan-3-amine (**3g**).* Yellow liquid, 130 mg (81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (d, J = 6.4 Hz, 12H), 3.42−3.48 (m, 2H), 6.74 (s, 1H), 7.27−7.31 (m, 1H), 7.39−7.43 (m, 2H), 7.74−7.76 (m, 2H), 8.17−8.19 (m, 2H), 8.57−8.59 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 49.8, 109.0, 118.3, 123.7, 127.9, 128.6, 130.1, 135.7, 137.9, 145.7, 149.5, 152.5. HRMS (EI-TOF) m/z: M^+ calcd for $C_{21}H_{24}N_2O$, 320.1889; found, 320.1890.

*N,N-Diisopropyl-4′-methyl-5-phenyl-[2,2′-bifuran]-3-amine (**3h**).* Yellow liquid, 109 mg (67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.029 (d, J = 6.0 Hz, 6H), 1.034 (d, J = 6.8 Hz, 6H), 2.37 (s, 3H), 3.36−3.39 (m, 2H), 6.03−6.04 (m, 1H), 6.63−6.64 (m, 1H), 6.85−6.86 (m, 1H), 7.19−7.23 (m, 1H), 7.34−7.38 (m, 2H), 7.71−7.74 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 20.9, 49.8, 107.3, 108.1, 108.6, 123.4, 127.0, 128.6, 129.2, 130.8, 143.4, 144.4, 150.6. HRMS (EI-TOF) m/z: M^+ calcd for $C_{21}H_{25}NO_2$, 323.1885; found, 323.1891.

*2-(4-Bromophenyl)-5-(4-chlorophenyl)-N,N-diisopropylfuran-3-amine (**3i**).* Colorless liquid, 148 mg (68% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (d, J = 6.4 Hz, 12H), 3.32−3.35 (m, 2H), 6.59 (s, 1H), 7.26 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 8.3 Hz, 2H), 7.54 (d, J =

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8.3 Hz, 2H), 8.11 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 49.8, 109.6, 120.6, 125.0, 126.6, 129.1, 129.5, 130.6, 131.4, 132.3, 133.3, 148.2, 150.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{23}BrClNO$, 432.0730; found, 432.0737.

*2-(4-Bromophenyl)-N,N-diisopropyl-5-(4-ethoxyphenyl)furan-3-amine (**3j**).* Yellow liquid, 144 mg (67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (d, J = 6.8 Hz, 12H), 3.39−3.42 (m, 2H), 3.80 (s, 3H), 6.56 (s, 1H), 6.92 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 8.8 Hz, 2H), 7.65 (d, J = 8.8 Hz, 2H), 8.21 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 49.8, 55.2, 107.3, 114.1, 119.7, 123.8, 125.0, 126.1, 130.6, 131.0, 132.0, 146.8, 151.0, 159.1. HRMS (EI-TOF) m/z: M^+ calcd for $C_{23}H_{26}BrNO_2$, 427.1147; found, 427.1151.

*2-(4-Bromophenyl)-5-cyclohexyl-N,N-diisopropylfuran-3-amine (**3k**).* Colorless liquid, 162 mg (80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (d, J = 6.4 Hz, 12H), 1.23−1.45 (m, 5H), 1.68−1.71 (m, 1H), 1.77−1.80 (m, 2H), 2.04−2.06 (m, 2H), 2.59−2.63 (m, 1H), 3.32−3.38 (m, 2H), 5.96 (s, 1H), 7.39−7.42 (m, 2H), 8.09−8.12 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 25.9, 26.1, 31.4, 37.4, 49.7, 106.6, 119.2, 125.9, 130.5, 130.9, 131.1, 145.5, 158.6. HRMS (EI-TOF) m/z: M^+ calcd for $C_{22}H_{30}BrNO$. 403.1511; found. 403.1506.

*2-(4-Bromophenyl)-N,N-5-triphenylfuran-3-amine (**3l**).* Colorless liquid, 96 mg (41% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (s, 1H), 6.92−6.95 (m, 2H), 7.12−7.14 (m, 4H), 7.18−7.27 (m, 5H), 7.33−7.38 (m, 4H), 7.61−7.63 (m, 2H), 7.66−7.69 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.4, 121.0, 121.1, 122.3, 123.7, 125.5, 127.9, 128.3, 128.7, 129.2, 130.0, 130.6, 131.5, 145.2, 146.1, 152.5. HRMS (EI-TOF) m/z: M^+ calcd for $C_{28}H_{20}BrNO$, 465.0728; found, 465.0725.

*1-(2-(4-Bromophenyl)-5-phenylfuran-3-yl)piperidine (**3m**).* Colorless liquid, 92 mg (48% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.53−1.56 (m, 2H), 1.67−1.73 (m, 4H), 2.83−2.86 (m, 4H), 6.71 (s, 1H), 7.20−7.26 (m, 1H), 7.35−7.38 (m, 2H), 7.48−7.50 (m, 2H), 7.66−7.69 (m, 2H), 7.83−7.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0, 26.2, 53.5, 102.2, 119.3, 123.5, 125.3, 127.4, 128.6, 130.4, 130.6, 131.4, 139.9, 140.4, 151.3. HRMS (EI-TOF) m/z: M^+ calcd for $C_{21}H_{20}BrNO$, 381.0728; found, 381.0724.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02211.

Experimental details and characterization data for all new compounds (PDF)

X-ray crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

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