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Lewis Acid Catalyzed Regiospecific Cross-Dehydrative Coupling Reaction of 2-Furylcarbinols with β-Keto Amides or 4-Hydroxycoumarins: A Route to Furyl Enols

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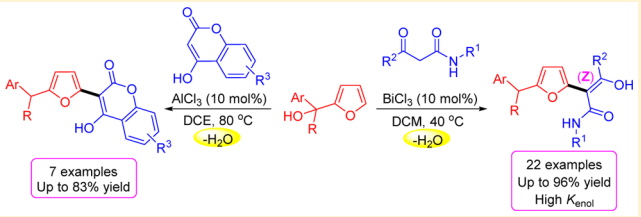
Supporting Information

ABSTRACT: Lewis acid catalyzed directly dehydrative carbon−carbon bond formation reaction of 2-furylcarbinols with β-keto amides provides a straightforward method for regioselective synthesis of (*Z*)-furyl enols. Moreover, this Lewis acid catalyzed cross-coupling reaction can be extended to an interesting heterocyclic version featuring a functionalized 3-furyl-4-hydroxycoumarin synthesis.



Furans constitute an important class of compounds that exist in nature as well as numerous pharmaceuticals and materials[1] (Figure 1). Therefore, the derivatization of furans,[2]

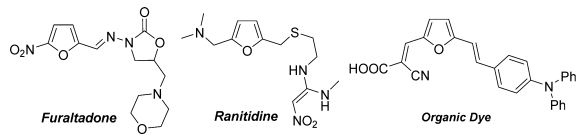


Figure 1. Bioactive compounds and synthetic dye with furan core.

especially the development of carbon−carbon bond-forming reactions of these compounds, has gained great attention. Pioneering studies have demonstrated that electrophilic,[3] nucleophilic,[4] and transition-metal-catalyzed[5] reactions could lead to construction of carbon−carbon bond with furans and their derivatives. However, the direct nucleophilic substitution reactions on these heterocyclics have been largely uninvestigated because the reactions usually limited to the specific combination of the substrates having strong electron-withdrawing groups and highly reactive carbanions.[6] Recently, some appealing methods for installing functional groups on furan through direct nucleophilic substitution reactions have been developed; for example, Kita[7] has developed regioselective nucleophilic substitution reactions of furans via the Pummerer-type reaction. Wang and co-workers[8] have established an efficient method for introducing nucleophiles on furan via the in situ formation of benzyl-type carbocations. However, these methods still suffer from limitations in substrate scope and multistep processes to reactants. Accordingly, development of straightforward, milder, and environmentally benign methods for the preparation of functional furans from easily available substrates is highly desirable.

However, furans are also valuable synthons for the preparation of complex carbo- and heterocycles[9] due to the low resonance energy of the furan ring.[10] Among furan derivatives, 2-furylcarbinols are readily available molecules that have served as useful building blocks in organic synthesis.[11] In principle, the presence of Lewis acid or Brönsted acid will lead to the formation of furfuryl cations, which have served as well-known reactive intermediates.[12] For example, in the 1970s, Piancatelli et al. reported an interesting acid-catalyzed cascade rearrangement of certain 2-furylcarbinols for the synthesis of 4-hydroxycyclopentenone derivatives through key intermediates furfuryl cations. Recently, several elegant works have been disclosed on the basis of the Piancatelli rearrangement, such as intramolecular reactions with oxygen-, carbon-, or nitrogen-containing nucleophiles[13] (Scheme 1, A). In addition, the furfuryl cations are important precursors to furan ring-fused cycloheptenes following [4 + 3] cycloaddition reactions with 1,3-dienes[14] (Scheme 1, B). In a more recent study, Gao reported a novel method to generate highly functionalized 1,2,3-triazoles from highly polarized olefin in a furfuryl cation by a [3 + 2] cycloaddition with alkyl azide[15] (Scheme 1, C). Herein, we disclose our observation of a Lewis acid catalyzed coupling reaction of 2-furylcarbinols with β-keto amides via furfuryl cation intermediates, which affords stable furyl enols with high selectivity (Scheme 1, D).

Initially, we examined the reaction of furan-2-yldiphenylmethanol (**1a**) with 1.0 equiv of 3-oxo-*N*-phenylbutanamide (**2a**) in DCE at 80 °C in the presence of 10% $ZnCl_2$, affording a solid product **3a** in 39% yield (Table 1, entry 1). We identified the solid state of **3a** that contains an enol unit with a furyl group attached to the C═C bond, showing an exclusive *Z* selectivity from X-ray diffraction analysis (Figure S1). It should be mentioned that small amount of ketone form was observed and the K_{enol} value of **3a** was up to 23.6 in $CDCl_3$ at 23 °C by ^1H NMR.

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Scheme 1. Applications of Furfuryl Cations in Organic Synthesis and Our Observations

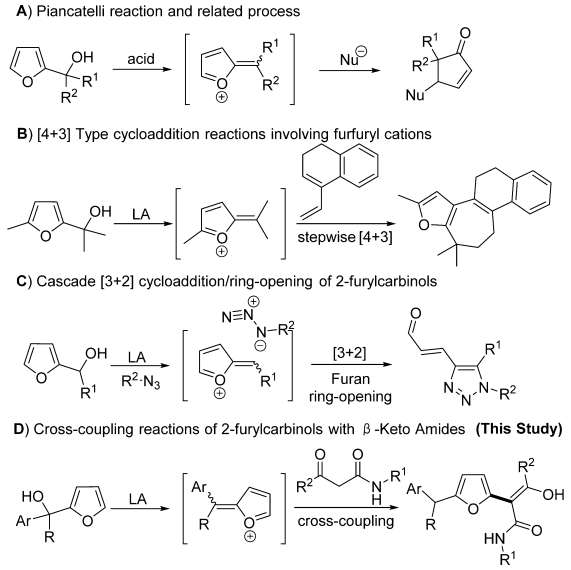
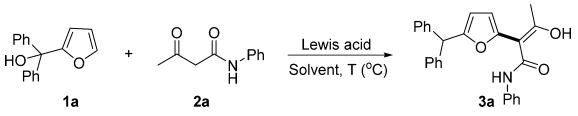


Table 1. Optimization of the Reaction Conditions[a]



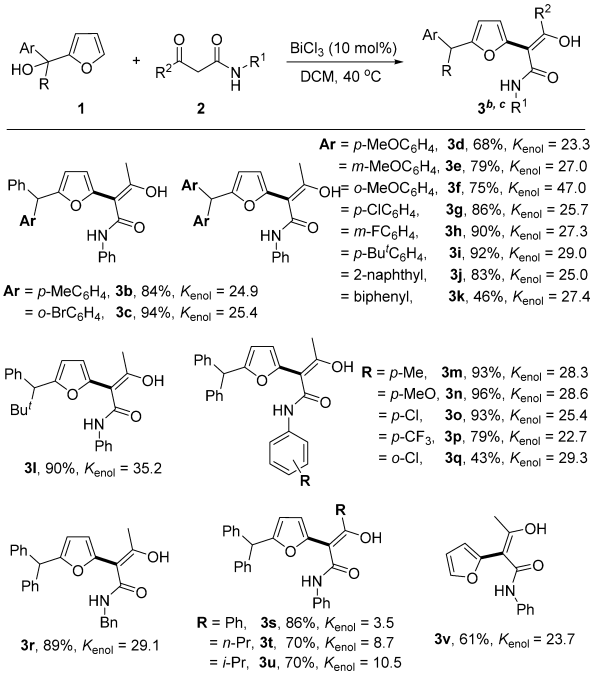
entry	catalyst (10 mol %)	solvent	T (°C)	3a[b] (%)
1	$ZnCl_2$	DCE	80	39
2	$FeCl_3$	DCE	80	70
3	$AlCl_3$	DCE	80	72
4	$BF_3{\cdot}Et_2O$	DCE	80	45
5	$BiCl_3$	DCE	80	85
6	$CeCl_3{\cdot}7H_2O$	DCE	80	75
7	$CoCl_2$	DCE	80	41
8	$BiCl_3$	CH_3CN	80	67
9	$BiCl_3$	toluene	80	84
10	$BiCl_3$	THF	80	0
11	$BiCl_3$	DMF	80	0
12	$BiCl_3$	DCE	40	88
13	$BiCl_3$	DCE	0	60
14	**$BiCl_3$**	**DCM**	**40**	**92**

[a]Unless otherwise stated, the reaction was carried out using **1a** (0.5 mmol), **2a** (0.55 mmol), and 10% of catalyst in 3 mL of solvent in open air. [b]Isolated yields.

Encouraged by this result, we optimized the reaction conditions to improve the product yield. Other Lewis acids, e.g., $FeCl_3$, $AlCl_3$, $BF_3{\cdot}Et_2O$, $BiCl_3$, $CeCl_3{\cdot}7H_2O$, and $CoCl_2$, were examined as catalysts; all of them could promote the reaction (Table 1, entries 2−7). The best result was obtained when $BiCl_3$ was employed, and **3a** could be obtained in 85% yield (Table 1, entry 5). The following examination of the solvent effects indicated that DCE was the most suitable solvent. Slightly lower yields were observed when solvents such as CH_3CN and toluene were used (Table 1, entries 8 and 9). Nevertheless, the solvent THF or DMF turned out to be totally disfavored (Table 1, entries 10 and 11). Moreover, the temperature effects were tested, and the yield could be improved to 88% when the temperature decreased to 40 °C (Table 1, entry 12). Finally, a better result was achieved when the solvent was further switched to DCM at 40 °C (Table 1, entry 14). Thus, the best conditions are to carry out the reaction in DCM at 40 °C using 10% of $BiCl_3$.

With the optimized reaction conditions in hand, we first evaluated the reaction of various 2-furylcarbinols **1** with 3-oxo-*N*-phenylbutanamide (**2a**). As shown in Table 2, the non-

Table 2. Reaction Scope for the Formation of Furyl Enols 3[a]



[a]The reaction was carried out using **1a** (0.5 mmol) and various **2** (0.55 mmol) in the presence of 10% of $BiCl_3$ in 3 mL of DCM under an air atmosphere at 40 °C. [b]Isolated yields. [c]Measured in $CDCl_3$ at 23 °C by ^1H NMR.

symmetric diaryl-2-furylcarbinol afforded the corresponding furyl enol derivatives **3b,c** in good to excellent yields. In the case of the symmetric diaryl-2-furylcarbinol, the reaction proceeded smoothly to give the expected compounds **3d−k** in moderate to excellent yields. Obviously, the nature of substituents on the aromatic ring has a demonstrable effect on this reaction. Diaryl-2-furylcarbinols with strongly electron-donating groups on both of the aromatic rings (Ar = R = *p*-$MeOC_6H_4$, *m*-$MeOC_6H_4$, *o*-$MeOC_6H_4$) were converted into the corresponding products in more moderate yields (see **3d−f**), whereas substrates with weak electron-donating groups or electron-withdrawing groups (Ar = R = *p*-$Bu^tC_6H_4$, *p*-ClC_6H_4, *m*-FC_6H_4) gave the products in excellent yields (see **3g−i**). The position of substituents on the aromatic ring has little effect on the reaction (see **3d−f**). Moreover, a di-2-naphthyl or dibiphenyl group in 2-furylcarbinol **1** could also be tolerated, and the products were afforded in 83% and 46% yields (see **3j,k**). When 2-furylcarbinol bearing Ph and Bu^t groups was employed, the desired **3l** could be obtained in 90% yield. Unfortunately, when we proceeded to examine the substrate with Ar = *p*-$MeOC_6H_4$, R = H, no desired product was detected. Furthermore, we examined the reaction of diphenyl-2-furylmethanol **1a** with various *β*-keto amides **2** as shown in Table 2. The electronic effect of the aromatic substituents on nitrogen of *β*-keto amides was investigated. It was found that electron-donating aryl groups (*p*-MeC_6H_4, *p*-$MeOC_6H_4$) and

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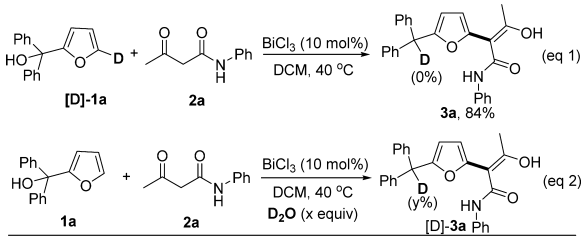
weak electron-withdrawing groups (p-ClC_6H_4) afforded the corresponding products **3m**−**o** in excellent yields. Strongly electron-withdrawing aryl groups (p-$CF_3C_6H_4$) gave good yields of product (see **3p**). The aryl group (o-ClC_6H_4) produced the **3q** in 43% yield, indicating that the position of substituents largely affects this reaction. The substituent on the nitrogen of β-keto amides could also be benzyl, and the corresponding **3r** was obtained in 89% yield. When groups such as Ph, n-Pr, or i-Pr on carbonyl carbon of β-keto amides were tested, the reaction proceeded smoothly to give **3s**−**u** in 86%, 70%, and 70% yields, respectively. Notably, we studied the cross-coupling type reaction of 2,5-dimethoxy-2,5-dihydrofuran with 3-oxo-N-phenylbutanamide **2a** in the presence of 10% $ZnCl_2$ in elevated temperature (80 °C). The monosubstituted furyl enol **3v** could be obtained in 61% yield. Finally, the reactions of other coupling partners ethyl acetoacetate or acetylacetone only led to complex mixtures.

In addition, K_{enol} values for product **3** were listed in Table 2 which were measured in low dielectric solvents $CDCl_3$ at 23 °C. The dependence of K_{enol} on the nature of groups Ar, R is negligible (see **3a**−**l**). In addition, the higher steric hindrance of groups Ar, R gave even higher K_{enol} values (see **3f**, **3l**). The groups of R^1 attaching to the nitrogen of the products exhibited little effect on the K_{enol} (see **3m**−**r**). On the basis of the substituents of R^2, K_{enol} values in $CDCl_3$ showed the great substituent effects. As for **3s**, R^2 = Ph (aromatic substituent), the value decreased dramatically probably due to the conjugated effect of the carbonyl group with a delocalized π bond. Compared with a methyl group, K_{enol} values dropped to 8.7 or 10.5 with R^2 = n-Pr or i-Pr, which might be caused by steric hindrance.

To elucidate the mechanism, the deuterium-labeling experiments were further performed. The substrate [**D**]-**1a** was employed under the standard conditions (Scheme 2, eq 1);

Scheme 2. Control Experiment

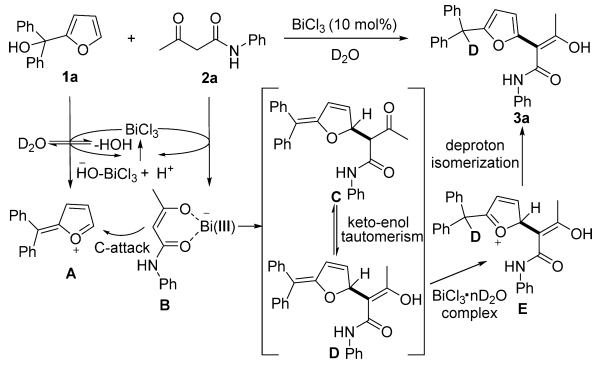


entry	D_2O (x equiv)	yield of **3a** (%)	deuterium rate (y%)
1	5	94	50
2	10	85	64
3	20	89	71

however, no deuterium labels were observed in any carbons of **3a**. Experiments using different excesses of D_2O (5, 10, and 20 equiv) as the additive gave [**D**]-**3a** with different deuterium incorporations ranging from 50 to 71% (Scheme 2, eq 2).

On the basis of the above observation, we proposed a plausible mechanism for this reaction (Scheme 3). Initially, oxocarbenium ion **A** was generated via a dearomatization process of 2-furylcarbinol **1a** in the presence of $BiCl_3$. Meanwhile, the β-keto amide **2a** was activated usually through coordination to the Bi(III) center in a bidentate fashion by both of the carbonyl groups.[16] Then, the α-carbon of oxocarbenium intermediate **A** was selectively attacked by an activated β-keto amides **B** to afford keto−enol tautomerism species **C** or **D**. In contrast, position 6 of intermediate **A** avoided attack by a nucleophile probably due to its steric

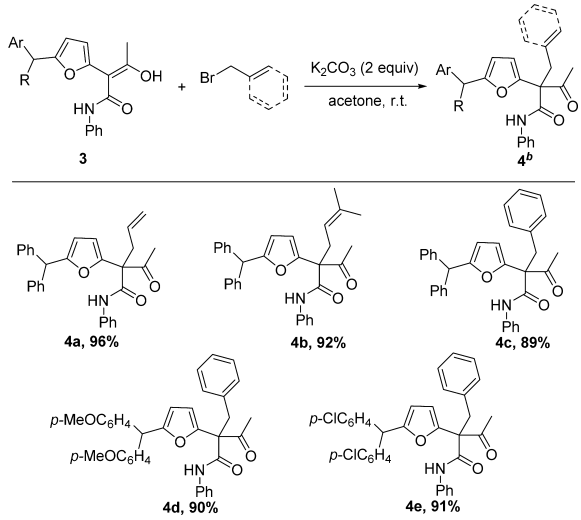
Scheme 3. Proposed Mechanism



crowding originating from diaryl substituents.[17] Next, the double bond of intermediate **D** might be activated by Brönsted acid or Lewis acid assisted Brönsted acid to give oxocarbenium ion **E**. It should be mentioned that the acid species would be generated either by hydrolysis or hydration of the bismuth trichloride salt, and this step was proved by addition of the additive D_2O through a hydrogen−deuterium exchange reaction. Finally, the oxocarbenium intermediate **E** could undergo deprotonation and rearomatization to produce product **3a**.

The furyl enol **3** could serve as a useful building block for further transformation. As a demonstration of this synthetic utility, **3** could be allylated with different allylic bromides or benzyl bromide under mild conditions to form the functionalized furans with a quaternary carbon center in excellent yields (Table 3).

Table 3. Chemical Derivatization of 3[a]



[a]The reaction was carried out using **3** (0.3 mmol), various allylic bromides, or benzyl bromide **2** (0.6 mmol) in the presence of 1.5 equiv of K_2CO_3 in 2 mL of acetone under an air atmosphere at room temperature. [b]Isolated yields.

After establishment of the feasibility of Lewis acid catalyzed cross-dehydrative coupling reactions, we became interested in exploring such a cross-dehydrative coupling reaction involving 2-furylcarbinols with 4-hydroxycoumarins for the coumarin nucleus is a key core structure that widely occurs in natural products and biological molecules[18] and is also widely used in materials chemistry.[19]

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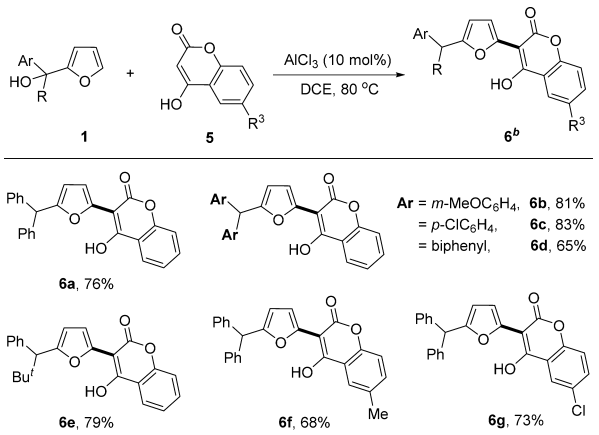
The 4-hydroxycoumarins participated in cross-coupling reactions with a variety of 2-furylcarbinols to afford products **6a−g** in high yields using $AlCl_3$ as catalyst in DCE at 80 °C (Table 4). The nature of the substituents on the aromatic ring has little effect on this reaction; for instance, diaryl-2-furylcarbinols (Ar = R = Ph, *p*-$MeOC_6H_4$, *p*-ClC_6H_4, biphenyl) were converted into the corresponding products (see **6a−d**) in 65−83% yields. With Ar = Ph, R = Bu^t, the reaction could proceed smoothly to produce **6e** in 79% yield. In addition, the −Cl- or −Me-substituted 4-hydroxycoumarins could react with **1a** to afford the products **6f,g** in 68% and 73% yields, respectively. The solid state of structure **6a** was further confirmed by single-crystal X-ray diffraction analysis (Figure S2).

Table 4. Reaction Scope for the Formation of 3-Furyl-4-hydroxycoumarins 6[a]



[a]The reaction was carried out using various **1** (0.5 mmol) and **5** (0.55 mmol) in the presence of 10% of $AlCl_3$ in 3 mL of DCE under an air atmosphere at 80 °C. [b]Isolated yields.

In summary, we have disclosed a new carbon−carbon bond-forming strategy to produce furyl enols from 2-furylcarbinols with *β*-keto amides or 4-hydroxycoumarins with well-defined regioselectivities. This reaction takes place efficiently under mild and environmentally benign conditions, providing a valuable alternative approach to modification furans. The resulted products could be allylated with different allylic bromides to give advanced functionalized furans. Mechanistic studies suggest that the step of rearomatization to furans occurs via a Brönsted acid or Lewis acid assisted Brönsted acid activation of double bond route.

EXPERIMENTAL SECTION

General Methods. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, using tetramethylsilane as the internal standard. Chemical shifts are expressed in ppm, and *J* values are given in hertz. Organic solvents used were dried by standard methods when necessary. THF and toluene were distilled from sodium benzophenone, and DCM, CH_3CN, DMF, and DMSO were distilled from CaH_2. Commercially obtained available reagents were used without further purification. Petroleum ether refers to the fraction with boiling point in the range 60−90 °C. All reactions were monitored by TLC with GF 254 silica gel coated plates. Flash column chromatography was carried out using 200−300 mesh silica gel.

Procedure for the Synthesis 3a−u. *(Z)-2-(5-Benzhydrylfuran-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3a**). Typical Procedure.* Furan-2-yldiphenylmethanol **1a** (125 mg, 0.5 mmol, 1.0 equiv), 3-oxo-*N*-phenylbutanamide **2a** (98 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) were dissolved in 3 mL of DCM in sequence. The mixture was then stirred at 40 °C for 2 h under ambient atmosphere. After completion of the reaction, the solvent was removed in vacuo, and the residue was purified with flash silica gel chromatography (petroleum ether/ethyl acetate 20:1 v/v) to afford **3a** (188 mg, 92%) as a white solid: mp 97−98 °C (petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) *δ* 15.04 (s, 1H), 7.28−7.34 (m, 5H), 7.19−7.27 (m, 8H), 7.09−7.13 (m, 2H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.25 (d, *J* = 2.8 Hz, 1H), 6.04 (d, *J* = 2.4 Hz, 1H), 5.49 (s, 1H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 20.6, 51.0, 96.0, 109.8, 112.3, 120.5, 124.4, 126.9, 128.5, 128.6, 128.7, 136.9, 141.3, 147.7, 157.2, 169.8, 177.3; TOF HRMS (ES^+) calcd for $C_{27}H_{24}NO_3$ $[M + H]^+$ 410.1756, found 410.1750.

Compounds **3b−u** were prepared similarly.

*(Z)-3-Hydroxy-N-phenyl-2-(5-(phenyl-p-tolylmethyl)furan-2-yl)-but-2-enamide (**3b**).* A mixture of **1b** (131 mg, 0.5 mmol, 1.0 equiv), **2a** (98 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3b** (178 mg, 84%) as a white solid: mp 135−136 °C (petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) *δ* 15.04 (s, 1H), 7.27−7.35 (m, 3H), 7.10−7.27 (m, 5H), 7.03−7.14 (m, 7H), 6.24 (s, 1H), 6.03 (s, 1H), 5.45 (s, 1H), 2.32 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 20.6, 21.0, 50.7, 96.1, 109.6, 112.2, 120.5, 124.4, 126.9, 128.4, 128.5, 128.6, 128.7, 129.3, 136.6, 136.9, 138.3, 141.5, 147.6, 157.4, 169.8, 177.2; TOF HRMS (ES^+) calcd for $C_{28}H_{26}NO_3$ $[M + H]^+$ 424.1913, found 424.1907.

*(Z)-2-(5-((2-Bromophenyl)phenylmethyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3c**).* A mixture of **1c** (165 mg, 0.5 mmol, 1.0 equiv), **2a** (98 mg, 0.5 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h o afford **3c** (230 mg, 94%) as a white solid: mp 42−44 °C (petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) *δ* 15.04 (s, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.30−7.36 (m, 3H), 7.24−7.29 (m, 3H), 7.16−7.23 (m, 5H), 7.05−7.14 (m, 3H), 6.28 (d, *J* = 2.4 Hz, 1H), 5.98 (d, *J* = 2.4 Hz, 1H), 5.95 (s, 1H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 20.6, 50.1, 95.9, 110.4, 112.5, 120.5, 124.5, 125.0, 127.1, 127.6, 128.6, 128.6, 128.8, 128.8, 130.1, 133.2, 136.8, 139.8, 140.6, 147.8, 156.2, 169.8, 177.4; TOF HRMS (ES^-) calcd for $C_{27}H_{21}BrNO_3$ $[M - H]^-$ 486.0705, found 486.0700.

*(Z)-2-(5-Bis(4-methoxyphenyl)methyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3d**).* A mixture of **1d** (155 mg, 0.5 mmol, 1.0 equiv), **2a** (98 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3d** (159 mg, 68%) as a white solid: mp 130−131 °C (petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) *δ* 15.03 (s, 1H), 7.34 (s, 1H), 7.20−7.26 (m, 2H), 7.03−7.16 (m, 7H), 6.80−6.89 (m, 4H), 6.24 (s, 1H), 6.02 (s, 1H), 5.40 (s, 1H), 3.77 (s, 6H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 20.6, 49.4, 55.2, 96.1, 109.4, 112.2, 114.0, 120.6, 124.4, 128.8, 129.5, 133.8, 136.9, 147.6, 157.9, 158.5, 169.9, 177.1; TOF HRMS (ES^+) calcd for $C_{29}H_{28}NO_5$ $[M + H]^+$ 470.1967, found 470.1967.

*(Z)-2-(5-(Bis(3-methoxyphenyl)methyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3e**).* A mixture of **1e** (155 mg, 0.5 mmol, 1.0 equiv), **2a** (98 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3e** (186 mg, 79%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) *δ* 15.06 (s, 1H), 7.34 (s, 1H), 7.19−7.25 (m, 4H), 7.11−7.16 (m, 2H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.75−6.85 (m, 6H), 6.25 (d, *J* = 3.2 Hz, 1H), 6.06 (d, *J* = 3.2 Hz, 1H), 5.43 (s, 1H), 3.71 (s, 6H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 20.5, 50.9, 55.0, 96.0, 109.8, 111.8, 112.2, 114.7, 120.5, 120.9, 124.3, 128.7, 129.6, 136.8, 142.6, 147.6, 156.9, 159.7, 169.8, 177.2; TOF HRMS (ES^+) calcd for $C_{29}H_{28}NO_5$ $[M + H]^+$ 470.1967, found 470.1969.

*(Z)-2-(5-(Bis(2-methoxyphenyl)methyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3f**).* A mixture of **1f** (155 mg, 0.5 mmol, 1.0 equiv), **2a** (98 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3f** (175 mg, 75%) as a white solid: mp 143−144 °C (petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) *δ* 15.00 (s, 1H),

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7.42 (s, 1H), 7.16−7.28 (m, 6H), 7.06 (t, J = 7.2 Hz, 1H), 6.96 (d, J = 7.2 Hz, 2H), 6.83−6.91 (m, 4H), 6.27 (s, 1H), 6.22 (d, J = 3.2 Hz, 1H), 5.89 (d, J = 2.0 Hz, 1H), 3.75 (s, 6H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 37.3, 55.7, 96.2, 109.1, 110.9, 112.3, 120.3, 120.4, 124.3, 127.9, 128.7, 129.0, 129.7, 137.0, 146.8, 157.0, 157.6, 169.9, 177.0; TOF HRMS (ES^+) calcd for $C_{29}H_{28}NO_5$ $[M + H]^+$ 470.1967, found 470.1961.

*(Z)-2-(5-(Bis(4-chlorophenyl)methyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3g**).* A mixture of **1g** (178 mg, 0.56 mmol, 1.0 equiv), **2a** (109 mg, 0.61 mmol, 1.1 equiv), and $BiCl_3$ (18 mg, 0.055 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3g** (230 mg, 86%) as a white solid: mp 47−49 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.06 (s, 1H), 7.26−7.33 (m, 6H), 7.22−7.25 (m, 1H), 7.05−7.16 (m, 7H), 6.28 (d, J = 2.8 Hz, 1H), 6.05 (d, J = 2.4 Hz, 1H), 5.43 (s, 1H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 49.7, 95.8, 110.0, 112.3, 120.4, 124.5, 128.8, 128.9, 129.8, 133.1, 136.7, 139.2, 148.2, 156.0, 169.6, 177.4; TOF HRMS (ES^+) calcd for $C_{27}H_{22}Cl_2NO_3$ $[M + H]^+$ 478.0977, found 478.0969.

*(Z)-2-(5-(Bis(3-fluorophenyl)methyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3h**).* A mixture of **1h** (143 mg, 0.5 mmol, 1.0 equiv), **2a** (98 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3h** (196 mg, 90%) as a yellow solid: mp 95−96 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.07 (m, 1H), 7.23−7.34 (m, 5H), 7.17−7.22 (m, 2H), 7.09 (t, J = 7.4 Hz, 1H), 6.95−7.05 (m, 4H), 6.88−6.95 (m, 2H), 6.32 (s, 1H), 6.09 (s, 1H), 5.49 (s, 1H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 50.3, 95.8, 110.2, 112.5, 114.2 (d, $^3J_{C-F}$ = 21.5 Hz), 115.6 (d, $^3J_{C-F}$ = 22.0 Hz), 120.5, 124.4 (d, $^2J_{C-F}$ = 32.1 Hz), 128.9, 130.2, 130.3, 136.8, 143.1 (d, $^4J_{C-F}$ = 7.0 Hz), 148.2, 155.8, 163.0 (d, $^1J_{C-F}$ = 245.8 Hz), 169.7, 177.6; TOF HRMS (ES^-) calcd for $C_{27}H_{20}F_2NO_3$ $[M - H]^-$ 444.1411, found 444.1403.

*(Z)-2-(5-(Bis(4-tert-butylphenyl)methyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3i**).* A mixture of **1i** (181 mg, 0.5 mmol, 1.0 equiv), **2a** (97 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3i** (241 mg, 92%) as a white solid: mp 64−66 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.03 (s, 1H), 7.30−7.38 (m, 5H), 7.20−7.28 (m, 4H), 7.12−7.18 (m, 4H), 7.04−7.09 (m, 1H), 6.25−6.29 (m, 1H), 6.04−6.09 (m, 1H), 5.42 (s, 1H), 1.98 (s, 3H), 1.29 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 31.3, 34.4, 50.2, 96.1, 109.6, 112.4, 120.6, 124.4, 125.4, 128.1, 128.8, 136.9, 138.5, 147.4, 149.6, 157.7, 169.9, 177.3; TOF HRMS (ES^+) calcd for $C_{35}H_{40}NO_3$ $[M + H]^+$ 522.3008, found 522.3006.

*(Z)-2-(5-(Di(naphthalen-2-yl)methyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3j**).* A mixture of **1j** (183 mg, 0.52 mmol, 1.0 equiv), **2a** (98 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3j** (220 mg, 83%) as a white solid: mp 148−149 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.09 (s, 1H), 7.76−7.84 (m, 4H), 7.68−7.74 (m, 2H), 7.66 (s, 2H), 7.38−7.50 (m, 6H), 7.28−7.34 (m, 1H), 6.85−6.99 (m, 5H), 6.28 (s, 1H), 6.12 (s, 1H), 5.82 (s, 1H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 51.2, 96.0, 110.1, 112.4, 120.2, 124.2, 126.0, 126.3, 126.9, 127.3, 127.6, 127.8, 128.4, 128.6, 132.5, 133.4, 136.7, 138.6, 147.9, 156.9, 169.7, 177.2; TOF HRMS (ES^+) calcd for $C_{35}H_{28}NO_3$ $[M + H]^+$ 510.2069, found 510.2072.

*(Z)-2-(5-(Di([1,1′-biphenyl]-4-yl)methyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3k**).* A mixture of **1k** (201 mg, 0.5 mmol, 1.0 equiv), **2a** (97 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3k** (129 mg, 46%) as a white solid: mp 180−181 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.10 (s, 1H), 7.52−7.59 (m, 8H), 7.42 (t, J = 7.6 Hz, 4H), 7.30−7.37 (m, 7H), 7.08−7.14 (m, 4H), 6.96−7.02 (m, 1H), 6.28 (d, J = 3.2 Hz, 1H), 6.13 (d, J = 2.8 Hz, 1H), 5.57 (s, 1H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 50.4, 96.0, 109.8, 112.3, 120.5, 124.4, 127.0, 127.3, 127.4, 128.7, 128.8, 129.0, 136.8, 139.9, 140.2, 140.5, 147.8, 156.9, 169.8, 177.3; TOF HRMS (ES^+) calcd for $C_{39}H_{32}NO_3$ $[M + H]^+$ 562.2382, found 562.2386.

*(Z)-2-(5-(2,2-Dimethyl-1-phenylpropyl)furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3l**).* A mixture of **1l** (115 mg, 0.5 mmol, 1.0 equiv), **2a** (98 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3l** (175 mg, 90%) as a white solid: mp 107−108 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.98 (s, 1H), 7.37−7.45 (m, 2H), 7.20−7.34 (m, 7H), 7.05−7.21 (m, 2H), 6.23−6.34 (m, 2H), 3.81 (s, 1H), 1.97 (s, 3H), 1.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 28.6, 35.0, 56.9, 96.2, 108.8, 112.6, 120.4, 124.5, 126.5, 127.9, 128.9, 129.8, 136.9, 139.9, 146.4, 157.5, 170.1, 177.4; TOF HRMS (ES^+) calcd for $C_{25}H_{28}NO_3$ $[M + H]^+$ 390.2069, found 390.2055.

*(Z)-2-(5-Benzhydrylfuran-2-yl)-3-hydroxy-N--tolylbut-2-enamide (**3m**).* A mixture of **1a** (125 mg, 0.5 mmol, 1.0 equiv), **2b** (105 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3m** (191 mg, 90%) as a white solid: mp 96−97 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.08 (s, 1H), 7.29−7.35 (m, 4H), 7.25−7.29 (m, 3H), 7.20−7.24 (m, 4H), 6.98−7.06 (m, 4H), 6.26 (d, J = 3.2 Hz, 1H), 6.03 (d, J = 2.4 Hz, 1H), 5.49 (s, 1H), 2.29 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 20.8, 51.1, 96.0, 109.8, 112.2, 120.6, 127.0, 128.6, 128.7, 129.3, 134.1, 134.3, 141.3, 147.8, 157.2, 169.8, 177.0; TOF HRMS (ES^+) calcd for $C_{28}H_{26}NO_3$ $[M + H]^+$ 424.1913, found 424.1907.

*(Z)-2-(5-Benzhydrylfuran-2-yl)-3-hydroxy-N-(4-methoxyphenyl)-but-2-enamide (**3n**).* A mixture of **1a** (125 mg, 0.5 mmol, 1.0 equiv), **2c** (114 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3n** (211 mg, 96%) as a white solid: mp 91−92 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.09 (s, 1H), 7.27−7.35 (m, 4H), 7.18−7.27 (m, 7H), 7.03 (d, J = 8.8 Hz, 2H), 6.77 (d, J = 8.8 Hz, 2H), 6.25 (d, J = 2.0 Hz, 1H), 6.03 (d, J = 2.0 Hz, 1H), 5.49 (s, 1H), 3.76 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 51.0, 55.4, 95.8, 109.7, 112.1, 113.9, 122.5, 126.9, 128.5, 128.6, 129.8, 141.3, 147.8, 156.6, 157.1, 169.7, 176.8; TOF HRMS (ES^+) calcd for $C_{28}H_{26}NO_4$ $[M + H]^+$ 440.1862, found 440.1859.

*(Z)-2-(5-Benzhydrylfuran-2-yl)-N-(4-chlorophenyl)-3-hydroxybut-2-enamide (**3o**).* A mixture of **1a** (125 mg, 0.5 mmol, 1.0 equiv), **2d** (116 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3o** (206 mg, 93%) as a white solid: mp 104−106 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.91 (s, 1H), 7.29−7.35 (m, 5H), 7.28 (s, 1H), 7.26 (s, 1H), 7.20−7.25 (m, 4H), 7.17 (d, J = 8.8 Hz, 2H), 7.00 (d, J = 8.8 Hz, 2H), 6.25 (d, J = 3.2 Hz, 1H), 6.05 (d, J = 3.0 Hz, H), 5.49 (s, 1H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 51.0, 96.0, 109.8, 112.3, 121.6, 127.0, 128.6, 128.7, 128.7, 129.4, 135.6, 141.2, 147.6, 157.2, 169.7, 177.5; TOF HRMS (ES^+) calcd for $C_{27}H_{23}ClNO_3$ $[M + H]^+$ 444.1366, found 444.1362.

*(Z)-2-(5-Benzhydrylfuran-2-yl)-3-hydroxy-N-(4-(trifluoromethyl)-phenyl)but-2-enamide (**3p**).* A mixture of **1a** (100 mg, 0.4 mmol, 1.0 equiv), **2e** (108 mg, 0.44 mmol, 1.1 equiv), and $BiCl_3$ (13 mg, 0.04 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3p** (150 mg, 79%) as a white solid: mp 143−144 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.85 (s, 1H), 7.41−7.54 (m, 3H), 7.20−7.34 (m, 10H), 7.10−7.19 (m, 2H), 6.27 (s, 1H), 6.07 (s, 1H), 5.51 (s, 1H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 51.0, 96.1, 109.9, 112.5, 119.9, 125.9, 126.0, 126.1, 127.1, 128.6, 128.7, 140.1, 141.2, 147.4, 157.3, 169.9, 178.0; TOF HRMS (ES^+) calcd for $C_{28}H_{23}F_3NO_3$ $[M + H]^+$ 478.1630, found 478.1624.

*(Z)-2-(5-Benzhydrylfuran-2-yl)-N-(2-chlorophenyl)-3-hydroxybut-2-enamide (**3q**).* A mixture of **1a** (63 mg, 0.25 mmol, 1.0 equiv), **2f** (58 mg, 0.275 mmol, 1.1 equiv), and $BiCl_3$ (8 mg, 0.025 mmol, 0.1 equiv) was stirred in 2 mL of DCM at 40 °C for 2 h to afford **3q** (48 mg, 43%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.72 (s, 1H), 8.28 (d, J = 4.0 Hz, 1H), 7.94 (s, 1H), 7.28−7.34 (m, 4H), 7.18−7.28 (m, 8H), 7.00−7.06 (m, 1H), 6.38 (d, J = 2.8 Hz, 1H), 6.03−6.06 (m, 1H), 5.48 (s, 1H), 1.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

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20.5, 51.1, 96.3, 109.8, 112.8, 121.7, 123.4, 124.7, 126.9, 127.6, 128.5, 128.7, 129.0, 134.1, 141.4, 147.0, 157.9, 169.9, 178.1; TOF HRMS (ES^+) calcd for $C_{27}H_{23}ClNO_3$ $[M + H]^+$ 444.1366, found 444.1364.

*(Z)-2-(5-Benzhydrylfuran-2-yl)-N-benzyl-3-hydroxybut-2-enamide (**3r**).* A mixture of **1a** (125 mg, 0.5 mmol, 1.0 equiv), **2g** (105 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3r** (189 mg, 89%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 15.15 (s, 1H), 7.27−7.32 (m, 2H), 7.20−7.26 (m, 7H), 7.10−7.17 (m, 6H), 6.17 (d, J = 3.2 Hz, 1H), 5.92−5.98 (m, 2H), 5.41 (s, 1H), 4.35 (d, J = 6.0 Hz, 2H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 42.9, 51.0, 95.5, 109.6, 111.8, 126.9, 127.2, 127.3, 128.5, 128.5, 128.6, 138.0, 141.4, 148.0, 156.8, 171.4, 176.0; TOF HRMS (ES^+) calcd for $C_{28}H_{26}NO_3$ $[M + H]^+$ 424.1913, found 424.1906.

*(Z)-2-(5-Benzhydrylfuran-2-yl)-3-hydroxy-N,3-diphenylacrylamide (**3s**).* A mixture of **1a** (125 mg, 0.5 mmol, 1.0 equiv), **2h** (132 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3s** (203 mg, 86%) as a white solid: mp 49−50 °C (petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 15.37 (s, 1H), 7.27−7.38 (m, 9H), 7.20−7.25 (m, 10H), 7.08−7.13 (m, 2H), 6.02 (d, J = 3.2 Hz, 1H), 5.96 (d, J = 2.4 Hz, 1H), 5.47 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.0, 95.6, 110.1, 113.4, 120.1, 120.6, 124.6, 126.9, 127.8, 128.3, 128.4, 128.5, 128.6, 128.6, 128.7, 128.8, 129.0, 130.1, 135.3, 136.9, 141.3, 147.7, 157.4, 170.5, 174.7; TOF HRMS (ES^+) calcd for $C_{32}H_{26}NO_3$ $[M + H]^+$ 472.1913, found 472.1906.

*(Z)-2-(5-Benzhydrylfuran-2-yl)-3-hydroxy-N-phenylhex-2-enamide (**3t**).* A mixture of **1a** (125 mg, 0.5 mmol, 1.0 equiv), **2i** (113 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3t** (153 mg, 70%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 15.06 (s, 1H), 7.28−7.34 (m, 4H), 7.21−7.26 (m, 9H), 7.13−7.17 (m, 2H), 7.06 (t, J = 7.2 Hz, 1H), 6.28 (d, J = 2.8 Hz, 1H), 6.05 (d, J = 3.2 Hz, 1H), 5.49 (s, 1H), 2.19 (t, J = 7.2 Hz, 2H), 1.51−1.63 (m, 2H), 0.84 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 20.2, 35.5, 51.0, 95.6, 109.7, 112.4, 120.5, 124.4, 126.9, 128.5, 128.6, 128.8, 136.9, 141.2, 147.6, 157.3, 170.1, 180.6; TOF HRMS (ES^-) calcd for $C_{29}H_{26}NO_3$ $[M-H]^-$ 436.1913, found 436.1911.

*(Z)-2-(5-Benzhydrylfuran-2-yl)-3-hydroxy-4-methyl-N-phenylpent-2-enamide (**3u**).* A mixture of **1a** (125 mg, 0.5 mmol, 1.0 equiv), **2j** (113 mg, 0.55 mmol, 1.1 equiv), and $BiCl_3$ (16 mg, 0.05 mmol, 0.1 equiv) was stirred in 3 mL of DCM at 40 °C for 2 h to afford **3u** (153 mg, 70%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 15.07 (s, 1H), 7.28−7.34 (m, 4H), 7.20−7.28 (m, 9H), 7.14−7.20 (m, 3H), 7.08 (t, J = 7.2 Hz, 1H), 6.30 (d, J = 2.8 Hz, 1H), 6.04 (d, J = 2.4 Hz, 1H), 5.49 (s, 1H), 2.54−2.64 (m, 1H) 1.07 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 31.9, 51.0, 93.8, 109.7, 112.3, 120.5, 124.4, 126.9, 128.6, 128.8, 136.9, 141.2, 147.5, 157.5, 170.3, 184.8; TOF HRMS (ES^-) calcd for $C_{29}H_{26}NO_3$ $[M - H]^-$ 436.1913, found 436.1911.

*(Z)-2-(Furan-2-yl)-3-hydroxy-N-phenylbut-2-enamide (**3v**).* A mixture of 2,5-dimethoxy-2,5-dihydrofuran **1n** (130 mg, 1.0 mmol, 1.0 equiv), **2a** (195 mg, 0.55 mmol, 1.1 equiv), and $ZnCl_2$ (14 mg, 0.1 mmol, 0.1 equiv) was stirred in 5 mL of DCE at 80 °C for 4 h to afford **3v** (148 mg, 61%) as a white solid: mp 72−74 °C (petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 15.04 (s, 1H), 7.55 (s, 1H), 7.36−7.42 (m, 2H), 7.30 (t, J = 8.0 Hz, 2H), 7.21 (s, 1H), 7.11 (t, J = 7.6 Hz, 1H), 6.49−6.53 (m, 1H), 6.38−6.42 (m, 1H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 95.6, 111.2, 111.9, 120.6, 124.6, 128.9, 136.8, 143.2, 148.1, 169.9, 177.7; TOF HRMS (ES^+) calcd for $C_{14}H_{14}NO_3$ $[M + H]^+$ 244.0974, found 244.0982.

Procedure for the Synthesis 4a−e. *2-Acetyl-2-(5-benzhydrylfuran-2-yl)-N-phenylpent-4-enamide (**4a**). Typical Procedure.* A solution of **3a** (123 mg, 0.3 mmol, 1.0 equiv), 3-bromoprop-1-ene (75 mg, 0.6 mmol, 2.0 equiv), and K_2CO_3 (62 mg, 0.45 mmol, 1.5 equiv) in 2 mL of acetone was stirred at room temperature. After being stirred overnight, the solvent was removed in vacuo, and the residue was purified with flash silica gel chromatography (petroleum ether/ethyl acetate 20:1 v/v) to afford **4a** (130 mg, 96%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.22−7.29 (m, 10H), 7.14−7.17 (m, 4H), 7.06−7.11 (m, 1H), 6.44 (d, J = 3.2 Hz, 1H), 6.00 (d, J = 2.4 Hz, 1H), 5.68−5.80 (m, 1H), 5.44 (s, 1H), 5.05−5.17 (m, 2H), 3.16 (dd, J_1 = 14.4 Hz, J_2 = 6.8 Hz, 1H), 2.97 (dd, J_1 = 14.4 Hz, J_2 = 7.6 Hz, 1H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.3, 38.0, 50.7, 65.2, 109.6, 110.6, 119.2, 120.1, 124.5, 126.9, 128.4, 128.5, 128.5, 128.5, 128.7, 128.8, 132.4, 137.1, 141.0, 141.1, 150.0, 157.5, 166.4, 203.8; TOF HRMS (EI) calcd for $C_{30}H_{27}NO_3$ (M^+) 449.1991, found 449.1993.

*2-Acetyl-2-(5-benzhydrylfuran-2-yl)-5-methyl-N-phenylhex-4-enamide (**4b**).* A mixture of **3a** (123 mg, 0.3 mmol, 1.0 equiv), 1-bromo-3-methylbut-2-ene (67 mg, 0.45 mmol, 1.5 equiv), and K_2CO_3 (62 mg, 0.45 mmol, 1.5 equiv) in 2 mL of acetone was stirred at room temperature overnight to afford **4b** (132 mg, 92%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.19−7.29 (m, 10H), 7.13−7.18 (m, 4H), 7.04−7.10 (m, 1H), 6.42 (d, J = 3.2 Hz, 1H), 5.98 (d, J = 2.4 Hz, 1H), 5.44 (s, 1H), 5.04 (t, J = 6.8 Hz, 1H), 3.10 (dd, J_1 = 14.8 Hz, J_2 = 6.4 Hz, 1H), 2.95 (dd, J_1 = 14.8 Hz, J_2 = 7.6 Hz, 1H), 2.12 (s, 3H), 1.64 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 25.9, 27.4, 32.5, 50.8, 65.1, 109.6, 110.4, 117.8, 120.0, 124.4, 126.8, 128.4, 128.5, 128.5, 128.6, 128.8, 136.1, 137.4, 141.2, 141.2, 150.5, 157.3, 166.7, 204.6; TOF HRMS (EI) calcd for $C_{32}H_{31}NO_3$ (M^+) 477.2304, found 477.2303.

*2-(5-Benzhydrylfuran-2-yl)-2-benzyl-3-oxo-N-phenylbutanamide (**4c**).* A mixture of **3a** (123 mg, 0.3 mmol, 1.0 equiv), (bromomethyl)-benzene (103 mg, 0.6 mmol, 2.0 equiv), and K_2CO_3 (62 mg, 0.45 mmol, 1.5 equiv) in 2 mL of acetone was stirred at room temperature overnight to afford **4c** (134 mg, 89%) as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.28−7.30 (m, 2H), 7.21−7.26 (m, 6H), 7.06−7.18 (m, 10H), 6.93 (d, J = 7.2 Hz, 2H), 6.45 (d, J = 3.2 Hz, 1H), 5.99 (d, J = 2.4 Hz, 1H), 5.42 (s, 1H), 3.73 (d, J = 14.0 Hz, 1H), 3.50 (d, J = 14.0 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.4, 39.9, 50.7, 66.7, 109.7, 111.1, 120.1, 124.6, 126.9, 126.9, 127.0, 128.2, 128.5, 128.5, 128.6, 128.7, 129.8, 135.6, 136.9, 141.0, 141.0, 149.8, 157.4, 166.4, 166.4, 203.4; TOF HRMS (ES^-) calcd for $C_{34}H_{28}NO_3$ $[M - H]^-$ 498.2069, found 498.2076.

*2-Benzyl-2-(5-(bis(4-methoxyphenyl)methyl)furan-2-yl)-3-oxo-N-phenylbutanamide (**4d**).* A mixture of **3d** (141 mg, 0.3 mmol, 1.0 equiv), (bromomethyl)benzene (103 mg, 0.6 mmol, 2.0 equiv), and K_2CO_3 (62 mg, 0.45 mmol, 1.5 equiv) in 2 mL of acetone was stirred at room temperature overnight to afford **4d** (151 mg, 90%) as a white solid: mp 113−115 °C (petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.21−7.27 (m, 2H), 7.10−7.18 (m, 5H), 7.01−7.09 (m, 5H), 6.92−6.98 (m, 2H), 6.75−6.85 (m, 4H), 6.44 (s, 1H), 5.96 (s, 1H), 5.32 (s, 1H), 3.75 (d, J = 4.8 Hz, 6H), 3.69−3.73 (m, 1H), 3.51 (d, J = 14.4 Hz, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.4, 39.9, 49.1, 55.2, 66.7, 109.4, 111.0, 113.7, 113.8, 120.1, 124.6, 127.0, 128.2, 128.7, 129.5, 129.8, 133.5, 135.7, 136.9, 149.6, 158.1, 158.3, 158.4, 166.5, 203.4; TOF HRMS (ES^+) calcd for $C_{36}H_{34}NO_5$ $[M + H]^+$ 560.2437, found 560.2435.

*2-Benzyl-2-(5-(bis(4-chlorophenyl)methyl)furan-2-yl)-3-oxo-N-phenylbutanamide (**4e**).* A mixture of **3g** (144 mg, 0.3 mmol, 1.0 equiv), (bromomethyl)benzene (103 mg, 0.6 mmol, 2.0 equiv), and K_2CO_3 (62 mg, 0.45 mmol, 1.5 equiv) in 2 mL of acetone was stirred at room temperature overnight to afford **4e** (155 mg, 91%) as a white solid: mp 149−151 °C (petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.20−7.30 (m, 6H), 7.09−7.20 (m, 6H), 7.00−7.09 (m, 4H), 6.94 (d, J = 7.2 Hz, 2H), 6.50 (d, J = 2.8 Hz, 1H), 5.98 (d, J = 2.4 Hz, 1H), 5.36 (s, 1H), 3.77 (d, J = 14 Hz, 1H), 3.50 (d, J = 14 Hz,1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5, 39.8, 49.4, 66.4, 110.0, 111.0, 120.1, 124.7, 127.2, 128.3, 128.7, 128.8, 128.9, 129.7, 129.8, 133.0, 133.0, 135.4, 136.9, 139.0, 139.1, 150.6, 156.2, 166.2, 203.9; TOF HRMS (ES^+) calcd for $C_{34}H_{28}Cl_2NO_3$ $[M + H]^+$ 568.1446, found 568.1442.

Procedure for the Synthesis of 6a−g. *3-(5-Benzhydrylfuran-2-yl)-4-hydroxy-2H-chromen-2-one (**6a**). Typical Procedure.* 4-Hydroxy-2*H*-chromen-2-one **5a** (73 mg, 0.45 mmol, 1.5 equiv) and $AlCl_3$ (4 mg, 0.03 mmol, 0.1 equiv) were dissolved in 1.5 mL of 1,2-dichloroethane at 80 °C. Then, furan-2-yldiphenylmethanol **1a** (75 mg, 0.3 mmol, 1.0 equiv) dissolved in 1.5 mL of 1,2-dichloroethane was slowly injected into the reaction system over 20 min by syringe.

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After being stirred for 2 h (monitored by TLC), the solvent was removed in vacuo, and the residue was purified with flash silica gel chromatography (petroleum ether/ethyl acetate 20:1 v/v) to afford **6a** (90 mg, 76%) as a white solid: mp 122−123 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.19−7.40 (m, 13H), 6.16 (d, J = 3.2 Hz, 1H), 5.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.8, 96.6, 110.8, 111.9, 115.4, 116.3, 123.5, 124.1, 127.2, 128.5, 128.7, 132.2, 140.8, 147.6, 151.7, 154.9, 158.0, 159.5; TOF HRMS (ES^-) calcd for $C_{26}H_{17}O_4$ $[M\text{-}H]^-$ 393.1127, found 393.1126.

*3-(5-(Bis(3-methoxyphenyl)methyl)furan-2-yl)-4-hydroxy-2H-chromen-2-one (**6b**).* 4-Hydroxy-2*H*-chromen-2-one **5a** (97 mg, 0.6 mmol, 1.5 equiv) and $AlCl_3$ (7 mg, 0.05 mmol, 0.1 equiv) were dissolved in 2 mL of 1,2-dichloroethane at 80 °C. Then **1e** (155 mg, 0.5 mmol, 1.0 equiv) dissolved in 2 mL of 1,2-dichloroethane was injected into the reaction system over 20 min and the mixture stirred for 2 h to afford **6b** (185 mg, 81%) as a white solid: mp 144−145 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.87 (d, J = 7.4 Hz, 1H), 7.46−7.57 (m, 1H), 7.20−7.35 (m, 5H), 6.70−6.88 (m, 6H), 6.20 (s, 1H), 5.48 (s, 1H), 3.77 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.7, 55.2, 96.6, 110.8, 110.9, 112.2, 114.6, 115.4, 116.3, 120.9, 123.5, 124.1, 129.7, 132.2, 142.1, 147.6, 151.7, 154.6, 158.0, 159.5, 159.8; TOF HRMS (ES^-) calcd for $C_{28}H_{21}O_6$ $[M\text{-}H]^-$ 453.1338, found 453.1339.

*3-(5-(Bis(4-chlorophenyl)methyl)furan-2-yl)-4-hydroxy-2H-chromen-2-one (**6c**).* 4-Hydroxy-2*H*-chromen-2-one **5a** (97 mg, 0.6 mmol, 1.5 equiv) and $AlCl_3$ (7 mg, 0.05 mmol, 0.1 equiv) were dissolved in 2 mL of 1,2-dichloroethane at 80 °C. Then **1g** (160 mg, 0.5 mmol, 1.0 equiv) dissolved in 2 mL of 1,2-dichloroethane was injected into the reaction system over 20 min and was stirred for 2 h to afford **6c** (193 mg, 83%) as a white solid: mp 179−180 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 7.8 Hz, 1H), 7.27−7.37 (m, 6H), 7.23−7.26 (m, 1H), 7.09−7.15 (m, 4H), 6.14 (d, J = 2.8 Hz, 1H), 5.50 (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.6, 96.5, 111.3, 112.0, 115.3, 116.3, 123.5, 124.2, 129.1, 129.8, 132.4, 133.4, 138.8, 148.2, 151.8, 153.8, 158.2, 159.4; TOF HRMS (ES^-) calcd for $C_{26}H_{15}Cl_2O_4$ $[M - H]^-$ 461.0347, found 461.0346.

*3-(5-(Di([1,1′-biphenyl]-4-yl)methyl)furan-2-yl)-4-hydroxy-2H-chromen-2-one (**6d**).* 4-Hydroxy-2*H*-chromen-2-one (97 mg, 0.6 mmol, 1.5 equiv) and $AlCl_3$ (7 mg, 0.05 mmol, 0.1 equiv) were dissolved in 2 mL of 1,2-dichloroethane at 80 °C. Then **1k** (201 mg, 0.5 mmol, 1.0 equiv) dissolved in 2 mL of 1,2-dichloroethane was injected into the reaction system over 20 min and was stirred for 2 h to afford **6d** (178 mg, 65%) as a white solid: mp 212−213 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.86 (d, J = 3.0 Hz, 1H), 7.55−7.65 (m, 8H), 7.38−7.46 (m, 4H), 7.20−7.37 (m, 10H), 6.25 (s, 1H), 5.62 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.2, 96.6, 111.0, 112.1, 115.4, 116.3, 123.5, 124.1, 127.0, 127.4, 127.5, 128.8, 129.0, 132.2, 139.8, 140.1, 140.5, 147.9, 151.8, 154.8, 158.1, 159.5; TOF HRMS (ES^-) calcd for $C_{38}H_{25}O_4$ $[M - H]^-$ 545.1753, found 545.1771.

*3-(5-(2,2-Dimethyl-1-phenylpropyl)furan-2-yl)-4-hydroxy-2H-chromen-2-one (**6e**).* 4-Hydroxy-2*H*-chromen-2-one (97 mg, 0.6 mmol, 1.5 equiv) and $AlCl_3$ (7 mg, 0.05 mmol, 0.1 equiv) were dissolved in 2 mL of 1,2-dichloroethane at 80 °C. Then **1l** (115 mg, 0.5 mmol, 1.0 equiv) dissolved in 2 mL of 1,2-dichloroethane was injected into the reaction system over 20 min and was stirred for 2 h to afford **6e** (178 mg, 79%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (s, 1H), 7.94 (d, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.20−7.40 (m, 8H), 6.45 (d, J = 3.6 Hz, 1H), 3.90 (s, 1H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.6, 35.4, 57.0, 96.7, 109.8, 112.1, 115.4, 116.2, 123.4, 124.1, 126.8, 128.1, 129.5, 132.1, 139.4, 146.5, 151.7, 155.1, 157.7, 159.5. TOF HRMS (ES^+) calcd for $C_{24}H_{23}O_4$ $[M + H]^+$ 375.1596, found 375.1609.

*3-(5-Benzhydrylfuran-2-yl)-7-chloro-4-hydroxy-2H-chromen-2-one (**6f**).* 7-Chloro-4-hydroxy-2*H*-chromen-2-one (71 mg, 0.36 mmol, 1.2 equiv) and $AlCl_3$ (4 mg, 0.03 mmol, 0.1 equiv) were dissolved in 1.5 mL of 1,2-dichloroethane at 80 °C. Then **1a** (75 mg, 0.3 mmol, 1.0 equiv) dissolved in 1.5 mL of 1,2-dichloroethane was injected into the reaction system over 20 min and was stirred for 2 h to afford **6f** (88 mg, 68%) as a white solid: mp 161−163 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.82 (d, J = 3.0 Hz, 1H), 7.45 (dd, J_1 = 8.8 Hz, J_2 = 3.0 Hz, 1H), 7.33−7.39 (m, 4H), 7.27−7.32 (m, 2H), 7.19−7.26 (m, 6H), 6.18 (d, J = 3.2 Hz, 1H), 5.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.9, 97.3, 110.9, 112.6, 116.6, 117.7, 123.0, 127.2, 128.5, 128.8, 129.7, 132.1, 140.7, 147.3, 150.1, 155.3, 156.6, 158.9; TOF HRMS (ES^-) calcd for $C_{26}H_{16}ClO_4$ $[M - H]^-$ 427.0737, found 427.0731.

*3-(5-Benzhydrylfuran-2-yl)-4-hydroxy-7-methyl-2H-chromen-2-one (**6g**).* 4-Hydroxy-7-methyl-2*H*-chromen-2-one (68 mg, 0.39 mmol, 1.3 equiv) and $AlCl_3$ (4 mg, 0.03 mmol, 0.1 equiv) were stirred in 2 mL of 1,2-dichloroethane at 80 °C. Then **1a** (75 mg, 0.3 mmol, 1.0 equiv) dissolved in 1.5 mL of 1,2-dichloroethane was injected into the reaction system over 20 min and was stirred for 2 h to afford **6g** (122 mg, 74%) as a white solid: mp 175−177 °C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.64 (s, 1H), 7.26−7.40 (m, 7H), 7.15−7.25 (m, 6H), 6.16 (s, 1H), 5,54 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 50.9, 96.5, 110.8, 111.8, 115.0, 116.0, 123.1, 127.2, 128.6, 128.8, 133.3, 133.8, 140.8, 147.8, 150.0, 154.8, 158.1, 159.6; TOF HRMS (ES^+) calcd for $C_{27}H_{21}O_4$ $[M + H]^+$ 409.1440, found 409.1435.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00734.

NMR (^{1}H, ^{13}C) spectra for **2a−2v**, **4a−4e**, and **6a−6g** (PDF)

X-ray crystallographic data for compound **3a** (CIF)

X-ray crystallographic data for compound **6a** (CIF)

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Notes

The authors declare no competing financial interest.

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