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# Acid-Promoted Multicomponent Tandem Cyclization to Synthesize Fully Substituted Oxazoles via Robinson−Gabriel-Type Reaction

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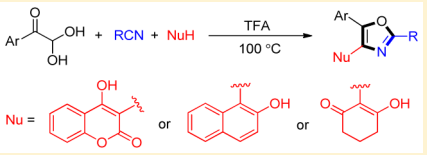
Supporting Information

**ABSTRACT:** An acid-promoted multicomponent reaction for the synthesis of diverse fully substituted oxazole derivatives from simple and readily available arylglyoxal monohydrates, nitriles, and various *C*-nucleophiles has been developed. This protocol features wide functional group diversity which is capable of installing 4-hydroxycoumarin, 2-naphthol, and 1,3-cyclohexanedione motifs to oxazoles. Mechanistic analysis indicates that a classical Robinson−Gabriel reaction served as the key step for this tandem transformation.




Oxazoles are privileged five-membered heterocyclic motifs which serve as useful building blocks in many natural products,[1] pharmaceutical drugs,[2] functional materials,[3] and ligand frameworks.[4] In particular, fully substituted oxazoles were also commonly found in numerous natural products and remarkably bioactive molecules, such as peptide alkaloid (−)-muscoride A,[5] antidiabetic agent AD-5061,[6] anti-inflammatory drugs aristoxazole,[7] oxaprozin,[8] and JTE-522[9] (Figure 1).

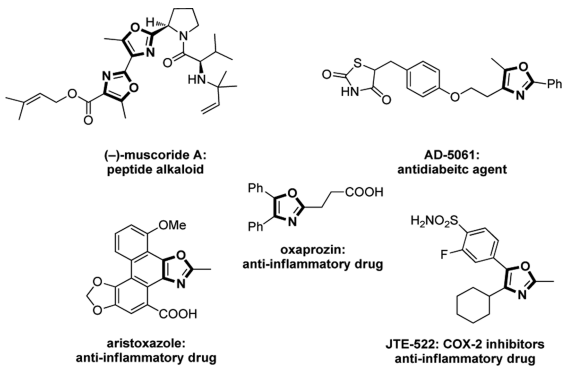
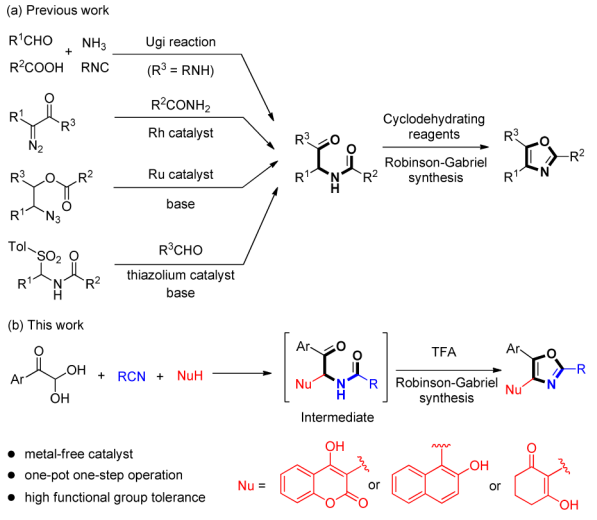



**Figure 1.** Examples of natural products and bioactive molecules containing fully substituted oxazole moiety.

Owing to their great importance, substantial attention has been paid toward the synthesis of fully substituted oxazole skeletons in the past decades.[10] Among them, the intramolecular cyclization of $\alpha$-acylamino ketones using Robinson−Gabriel synthesis is one of the most effective but challenging method due to the cumbersome preparation of the acyclic percursors.[11] To date, a variety of strategies have been concentrated on the synthesis of the acyclic precursors via Ugi reaction,[12] metal catalysis[13,14] or organic catalysis,[15] which could subsequently transform into oxazoles by the treatment of cyclodehydrating reagents (Scheme 1a). Despite these advances, the development of a straightforward method to access fully substituted oxazole derivatives without separating the precursors would be of great value. Herein, we report a novel acid-promoted multicomponent tandem cyclization reaction to synthesize diversified fully substituted oxazoles from readily available starting materials in one pot via Robinson−Gabriel-type synthesis (Scheme 1b). The successful employment of various *C*-nucleophiles including 4-hydroxycoumarin, 2-naphthol, and 1,3-cyclohexanedione greatly enhanced the functional group tolerance of this protocol.

**Scheme 1. Synthesis of Fully Substituted Oxazoles via Robinson−Gabriel Strategy**




We initially explored the reaction of phenylglyoxal monohydrate **1a** and 4-hydroxycoumarin **2** in acetonitrile at 80 °C in the presence of $PhCO_2H$, which afforded the desired

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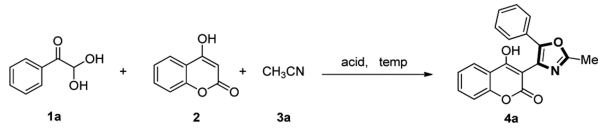
product **3a** in 45% yield (Table 1, entry 1). Encouraged by the preliminary result, various reaction conditions were investigated

**Table 1. Optimization of the Reaction Conditions**[ab]



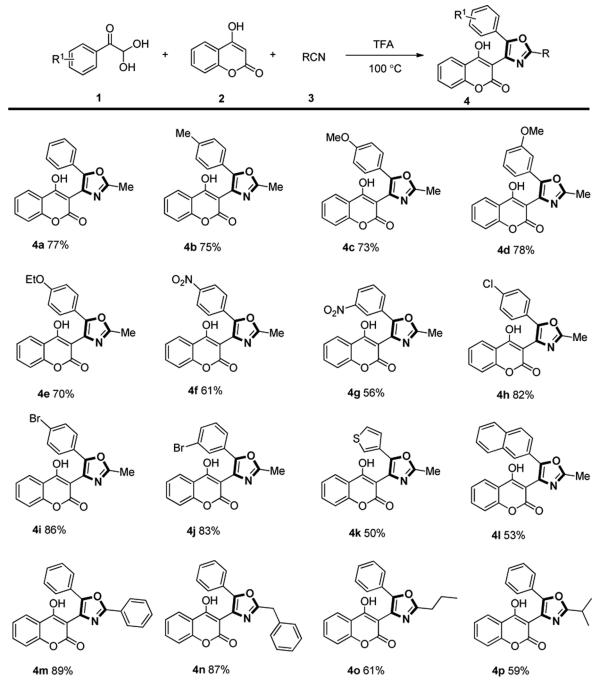

| entry | acid | amount of acid (equiv) | temp (°C) | yield[b] (%) |
|---|---|---|---|---|
| 1 | $PhCO_2H$ | 1.5 | 80 | 45 |
| 2 | $CF_3SO_3H$ | 1.5 | 80 | 5 |
| 3 | $CH_3SO_3H$ | 1.5 | 80 | 10 |
| 4 | $CH_3CO_2H$ | 1.5 | 80 | 40 |
| 5 | TFA | 1.5 | 80 | 65 |
| 6 | TsOH | 1.5 | 80 | 26 |
| 7 | HCl | 1.5 | 80 | 10 |
| 8 | $FeCl_3$ | 1.5 | 80 | 48 |
| 9 | $ZnCl_2$ | 1.5 | 80 | 50 |
| 10 | $AlCl_3$ | 1.5 | 80 | trace |
| 11 | TFA | | 80 | 0 |
| 12 | TFA | 0.5 | 80 | 35 |
| 13 | TFA | 1 | 80 | 70 |
| 14 | TFA | 2 | 80 | 63 |
| 15 | TFA | 1 | r.t. | 0 |
| 16 | TFA | 1 | 60 | 49 |
| 17 | **TFA** | **1** | **100** | **77** |
| 18 | TFA | 1 | 120 | 67 |

[a]Reaction conditions: **1a** (0.2 mmol, 1 equiv), **2** (0.2 mmol, 1 equiv), and acid (*x* mmol, *y* equiv) were heated in 2 mL of $CH_3CN$ in a sealed vessel under air for 4 h. [b]Isolated yields. TFA = trifluoroacetic acid.

and the results were summarized in Table 1. The results revealed that the nature of acid had a significant effect on the outcome of the reaction. Among various Brønsted acids, TFA gave the best result of 65% yield (Table 1, entries 1−7). The employment of Lewis acids was less effective, and only trace amount of the target product was formed when $AlCl_3$ was applied (Table 1, entries 8−10). After screening different amount of TFA, we found that 1 equiv of TFA was the most suitable acid (Table 1, entries 11−14). Gradually varying the reaction temperature from room temperature to 120 °C indicated that 100 °C was optimal for this reaction (Table 1, entries 15−18). Finally, the optimal conditions were determined as **1a** (1 equiv), **2** (1 equiv), and TFA (1 equiv) in $CH_3CN$ at 100 °C for 4 h.

With the optimized conditions in hand, the generality and scope of this reaction was subsequently investigated as shown in Scheme 2. Arylglyoxals bearing electron-neutral (4-H), electron-rich (4-Me, 4-OMe, 3-OMe, 4-OEt), electron-deficient (4-$NO_2$, 3-$NO_2$) substituents were smoothly converted to the corresponding products in moderate to good yields (56−78%; **4a**−**4g**). Pleasingly, halo-substituted (4-Cl, 4-Br, 3-Br) arylglyoxals were also found to furnish the desired products in excellent yields (82−86%; **4h**−**4j**), which provided possibilities for further functionalization. Heteroaryl (3-thienyl) and sterically hindered (2-naphthyl) substituents were suitable for this transformation, affording the corresponding products **4k** and **4l** in 50% and 53% yield, respectively. Moreover, benzonitrile and phenylacetonitrile reacted smoothly with phenylglyoxal monohydrate and 4-hydroxycoumarin to afford the target products **4m** and **4n** in 89% and 87% yields, respectively. This method was also found to be applicable to

**Scheme 2. Scope of Substrates to Form 4**[ab]




[a]Reaction conditions: **1** (0.5 mmol, 1 equiv), **2** (0.5 mmol, 1 equiv), and TFA (0.5 mmol, 1 equiv) were heated in 3 mL of RCN in a sealed vessel under air for 4 h. [b]Isolated yields.

aliphatic nitriles (butyronitrile and isobutyronitrile), which generated the corresponding products in moderate yields (59−61%; **4o**−**4p**). Furthermore, the structure of compound **4i** was unambiguously confirmed by X-ray crystallographic analysis (see Supporting Information).

In order to expand the molecular library of polyfunctional oxazole frameworks, our work was extended to the usage of other *C*-nucleophiles, such as 2-naphthols, to replace 4-hydroxycoumarin (Scheme 3). The results indicated that the electronic properties of the substituents on the arylglyoxals showed little influence on the efficiency of this reaction. In general, electron-neutral (4-H), electron-rich (4-Me, 4-OMe, 3,4-$OCH_2O$), electron-deficient (4-$NO_2$, 3-$NO_2$), and halogenated (4-Br, 3-Br, 2,4-$Cl_2$) groups were all compatible under the optimal reaction conditions in good to excellent yields (66−88%; **6a**−**6i**). 3-Thienyl and 1-naphthyl substituents were also tolerated in this reaction to give the desired products **6j** and **6k** in 63% and 78% yields, respectively. Moreover, 2-naphthols bearing electron-rich (4-OMe), electron-deficient (6-COOMe, 6-CN), and halogenated (6-Br, 7-Br) substituents were all well tolerated in the reaction and the desired products **6l**−**6p** were obtained in 48−89% yields.

In addition, the feasibility of this protocol was further expanded by utilizing 1,3-cyclohexanediones as the *C*-nucleophile. As shown in Scheme 4, for 1,3-cyclohexanediones with 5-alkyl or 5-aryl substituent, the reactions proceeded successfully under the optimized conditions to give the products in good yields (62−78%; **8a**−**8d**). However, the desired products were not obtained when acyclic 1,3-dicarbonyl compounds were tested as the *C*-nucleophile.

To gain some insight into the mechanism of this reaction, a series of control experiments were conducted as shown in Scheme 5. Initially, when phenylglyoxal **1a** and 4-hydroxycoumarin **2** were mixed under optimal conditions in the



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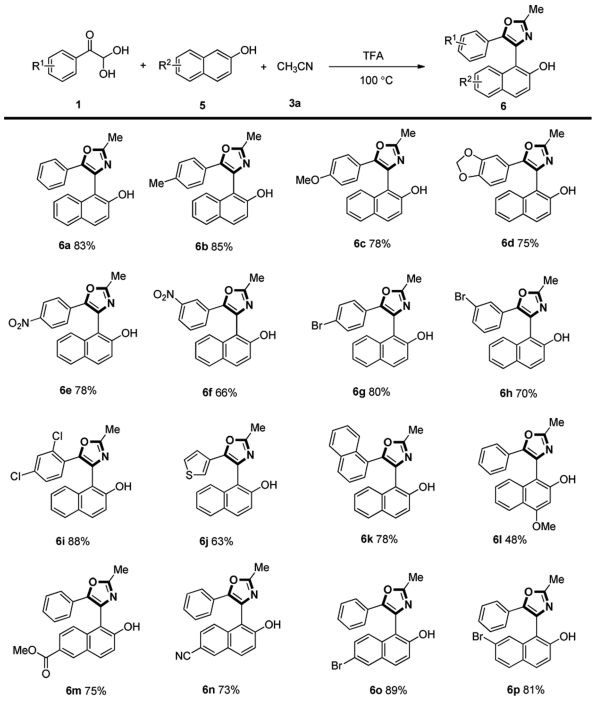
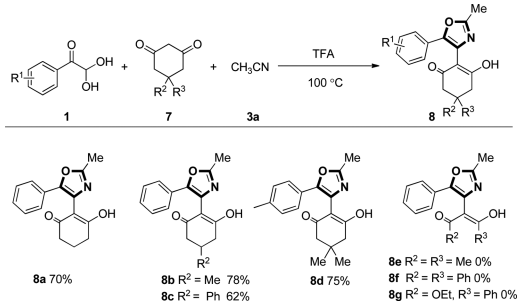
**Scheme 3. Scope of Substrates to Form 6**[ab]




[a]Reaction conditions: **1** (0.5 mmol, 1 equiv), **5** (0.5 mmol, 1 equiv), and TFA (0.5 mmol, 1 equiv) were heated in 3 mL of $CH_3CN$ in a sealed vessel under air for 5 h. [b]Isolated yields.

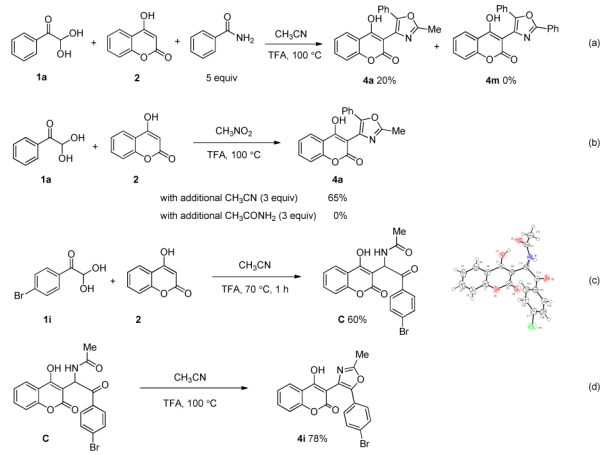
**Scheme 4. Synthesis of Oxazole Derivatives Using 1,3-Cyclohexanedione as the *C*-Nucleophile**[ab]




[a]Reaction conditions: **1** (0.5 mmol, 1 equiv), **7** (0.5 mmol, 1 equiv), and TFA (0.5 mmol, 1 equiv) were heated in 3 mL of $CH_3CN$ in a sealed vessel under air for 4 h. [b]Isolated yields.

presence of additional 5 equiv of benzamide, the product **4a** was obtained in 20% yield but the product **4m** was not observed (Scheme 5a). Additionally, when phenylglyoxal **1a** and 4-hydroxycoumarin **2** were subjected to $CH_3NO_2$ at 100 °C in the presence of TFA, the desired product **4a** was formed in 65% yield when 3 equiv of acetonitrile was added. On the contrary, no corresponding product was generated when 3 equiv of acetamide was added (Scheme 5b). These experiments clearly indicated that amides derived from nitriles did not participate in the formation of oxazoles. Moreover, the reaction of **1i** and 4-hydroxycoumarin **2** in $CH_3CN$ at 70 °C in the presence of TFA for 1 h could afford $\alpha$-acylamino ketone **C** in 60% yield, and the structure of compound **C** was determined by X-ray crystallographic analysis (Scheme 5c). Further subjecting **C** into the standard conditions gave the target product **4i** in

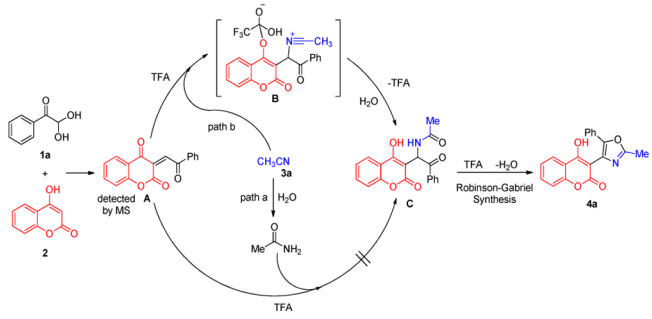
**Scheme 5. Control Experiments**




78% yield, which indicated that **C** was a possible intermediate for the reaction (Scheme 5d).

Based on the above results and previous reports,[16] a plausible mechanism for this multicomponent tandem cyclization reaction is proposed using **1a**, **2**, and **3a** as an example (Scheme 6). Initially, phenylglyoxal **1a** and 4-hydroxycoumarin

**Scheme 6. Proposed Mechanism**




**2** underwent dehydrative condensation to form intermediate **A**. Then, two pathways were proposed to achieve the subsequent transformations. In path a, acetonitrile was first hydrolyzed to acetamide, and the subsequent addition of acetamide to **A** afforded $\alpha$-acylamino ketone **C**. This path could be ruled out by aforementioned control experiments. In path b, acetonitrile attacked **A** in the presence of TFA to afford the intermediate **B** which was hydrolyzed to $\alpha$-acylamino ketone **C**. Finally, Robinson−Gabriel-type transformation of intermediate **C** would yield the product **4a**.

In conclusion, we have developed a facile and efficient multicomponent tandem cyclization reaction for the direct synthesis of highly functionalized oxazoles via a Robinson−Gabriel-type method. Acetonitrile served not only as a solvent but also as the substrate in the reaction. Efforts to prepare polyfunctional oxazoles by combining different *C*-nucleophiles including 4-hydroxycoumarin, 2-naphthols, and 1,3-cyclohexanediones were successful. This reaction represents a convenient methodology for the construction of diversely substituted heterocyclic scaffolds under mild conditions.

## EXPERIMENTAL SECTION

**General.** All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using precoated glass plates. Column chromatography was performed



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using silica gel (200−300 mesh). IR spectra were recorded on a PerkinElmer PE-983 infrared spectrometer as KBr pellets with absorption in $cm^{-1}$. $^1H$ spectra were recorded in $CDCl_3$ or DMSO-$d_6$ 600 MHz NMR spectrometers and resonances ($\delta$) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. $^{13}C$ spectra were recorded in $CDCl_3$ or DMSO-$d_6$ 150 MHz NMR spectrometers and resonances ($\delta$) are given in ppm. HRMS were obtained on a Bruker Apex-Ultra 7.0T FTMS equipped with an electrospray source (ESI-TOF analyzer). The X-ray crystal structure determination of **4i** and **C** were obtained on a Bruker SMART APEX CCD system. Melting points were determined using XT-4 apparatus and not corrected.

**General Procedure for Synthesis of 4, 6, 8 (4a as an Example).** A mixture of phenylglyoxal monohydrate **1a** (76 mg, 0.5 mmol), 4-hydroxycoumarin **2** (81 mg, 0.5 mmol), and $CF_3CO_2H$ (0.5 mmol) was heated at 100 °C in 3 mL of $CH_3CN$ in a sealed vessel for 4 h until almost completed conversion of the substrates monitored by TLC analysis. Then 50 mL water was added to the mixture, which was extracted with EtOAc three times (3 × 50 mL). The extract was dried over anhydrous $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 5/1) to afford the product **4a** as a yellow solid (123 mg, 77% yield).

**General Procedure for Synthesis of C.** A mixture of 1-(4-bromophenyl)-2,2-dihydroxyethanone **1i** (231 mg, 1 mmol), 4-hydroxycoumarin **2** (162 mg, 1 mmol), and $CF_3CO_2H$ (0.5 mmol) was heated at 70 °C in 3 mL of $CH_3CN$ in a sealed vessel for 1 h until almost completed conversion of the substrates monitored by TLC analysis. Then 50 mL water was added to the mixture, which was extracted with EtOAc three times (3 × 50 mL). The extract was dried over anhydrous $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 3/1) to afford the compound **C** as a white solid (250 mg, 60% yield).

**Analytical Data for Compounds 4, 6, 8, and C.** *4-Hydroxy-3-(2-methyl-5-phenyloxazol-4-yl)-2H-chromen-2-one (**4a**).* Yield: 77% (123 mg); Yellow solid; mp 205−207 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 8.00 (d, $J$ = 7.8 Hz, 1H), 7.56 (t, $J$ = 7.2 Hz, 1H), 7.46−7.42 (m, 2H), 7.39 (t, $J$ = 7.2 Hz, 2H), 7.37−7.34 (m, 1H), 7.34−7.29 (m, 2H), 2.59 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 164.3, 159.4, 158.9, 152.9, 147.4, 132.6, 129.1, 128.7, 127.7, 127.7, 127.2, 123.9, 123.8, 116.4, 115.7, 95.7, 13.9; IR (KBr): 3386, 2928, 1700, 1613, 1558, 1493, 1220, 964, 759, 693 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{19}H_{14}NO_4$: 320.0917; found: 320.0919.

*4-Hydroxy-3-(2-methyl-5-(p-tolyl)oxazol-4-yl)-2H-chromen-2-one (**4b**).* Yield: 75% (125 mg); White solid; mp 185−187 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 8.00 (d, $J$ = 7.2 Hz, 1H), 7.56 (t, $J$ = 7.2 Hz, 1H), 7.34−7.28 (m, 4H), 7.20 (d, $J$ = 7.8 Hz, 2H), 2.58 (s, 3H), 2.38 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 164.1, 159.1, 158.9, 152.8, 147.6, 138.7, 132.5, 128.5, 127.6, 126.6, 126.2, 123.8, 123.8, 116.4, 115.8, 95.9, 21.44, 13.9; IR (KBr): 3414, 3027, 2918, 1724, 1614, 1492, 1300, 1168, 964, 769 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{20}H_{16}NO_4$: 334.1074; found: 334.1077.

*4-Hydroxy-3-(5-(4-methoxyphenyl)-2-methyloxazol-4-yl)-2H-chromen-2-one (**4c**).* Yield: 73% (127 mg); Yellow solid; mp 162−163 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 7.99 (d, $J$ = 7.2 Hz, 1H), 7.55 (t, $J$ = 7.2 Hz, 1H), 7.36 (d, $J$ = 7.8 Hz, 2H), 7.33−7.27 (m, 2H), 6.92 (d, $J$ = 7.8 Hz, 2H), 3.83 (s, 3H), 2.57 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 164.1, 159.8, 159.0, 158.9, 152.8, 147.4, 132.4, 129.1, 126.0, 123.8, 123.8, 121.7, 116.4, 115.8, 113.2, 95.9, 55.2, 13.8; IR (KBr): 3430, 2928, 1719, 1704, 1610, 1510, 1253, 968, 757, 606 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{20}H_{16}NO_5$: 350.1023; found: 350.1028.

*4-Hydroxy-3-(5-(3-methoxyphenyl)-2-methyloxazol-4-yl)-2H-chromen-2-one (**4d**).* Yield: 78% (136 mg); White solid; mp 165−167 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 8.00 (d, $J$ = 7.8 Hz, 1H), 7.56 (t, $J$ = 7.8 Hz, 1H), 7.34−7.28 (m, 3H), 6.97−7.04 (m, 2H), 6.91 (d, $J$ = 7.8 Hz, 1H), 3.81 (s, 3H), 2.59 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 164.2, 159.4, 158.9, 152.9, 147.2, 132.6, 130.1, 128.7, 127.3, 123.9, 123.8, 120.5, 116.4, 115.7, 114.5, 113.0, 95.8, 55.2, 13.9; IR (KBr): 3429, 2837, 1729, 1602, 1494, 1419, 1292, 964, 758, 690 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{20}H_{16}NO_5$: 350.1023; found: 350.1025.

*3-(5-(4-Ethoxyphenyl)-2-methyloxazol-4-yl)-4-hydroxy-2H-chromen-2-one (**4e**).* Yield: 70% (127 mg); Yellow solid; mp 177−178 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 11.99 (s, 1H), 7.93 (d, $J$ = 7.8 Hz, 1H), 7.48 (t, $J$ = 7.8 Hz, 1H), 7.34 (d, $J$ = 9.0 Hz, 2H), 7.25−7.20 (m, 2H), 6.88 (d, $J$ = 9.0 Hz, 2H), 4.03−3.99 (m, 2H), 2.48 (s, 3H), 1.39 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 163.9, 159.0, 159.0, 158.7, 152.6, 147.4, 132.2, 128.7, 125.4, 123.6, 121.1, 116.0, 115.6, 113.6, 95.7, 63.2, 14.6, 13.5; IR (KBr): 3400, 2979, 2541, 1706, 1616, 1494, 1106, 967, 765, 677 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{21}H_{18}NO_5$: 364.1180; found: 364.1183.

*4-Hydroxy-3-(2-methyl-5-(4-nitrophenyl)oxazol-4-yl)-2H-chromen-2-one (**4f**).* Yield: 61% (110 mg); Yellow solid; mp 227−229 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 8.23 (d, $J$ = 9.0 Hz, 2H), 8.02 (d, $J$ = 7.8 Hz, 1H), 7.61 (t, $J$ = 7.8 Hz, 1H), 7.54 (d, $J$ = 8.4 Hz, 2H), 7.38−7.30 (m, 2H), 2.65 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 165.4, 160.7, 158.9, 152.9, 147.0, 144.8, 135.1, 133.2, 130.1, 128.5, 124.2, 124.0, 122.8, 116.5, 115.4, 95.0, 13.9; IR (KBr): 3394, 2924, 1701, 1613, 1519, 1348, 1108, 977, 758, 459 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{19}H_{13}N_2O_6$: 365.0768; found: 365.0769.

*4-Hydroxy-3-(2-methyl-5-(3-nitrophenyl)oxazol-4-yl)-2H-chromen-2-one (**4g**).* Yield: 56% (102 mg); Yellow solid; mp 227−229 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 8.31 (s, 1H), 8.21 (d, $J$ = 7.2 Hz, 1H), 8.04 (d, $J$ = 7.2 Hz, 1H), 7.67−7.63 (m, 1H), 7.61 (t, $J$ = 7.8 Hz, 1H), 7.56 (t, $J$ = 7.8 Hz, 1H), 7.37−7.31 (m, 2H), 2.66 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 165.3, 160.2, 159.1, 152.9, 147.5, 144.6, 134.1, 133.1, 130.8, 129.3, 128.4, 124.1, 124.0, 123.0, 122.7, 116.6, 115.6, 95.0, 13.9; IR (KBr): 3433, 3103, 1698, 1612, 1531, 1348, 979, 759, 711 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{19}H_{13}N_2O_6$: 365.0768; found: 365.0768.

*3-(5-(4-Chlorophenyl)-2-methyloxazol-4-yl)-4-hydroxy-2H-chromen-2-one (**4h**).* Yield: 82% (145 mg); Green solid; mp 183−185 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 8.01 (d, $J$ = 7.8 Hz, 1H), 7.58 (t, $J$ = 7.8 Hz, 1H), 7.39−7.34 (m, 4H), 7.34−7.30 (m, 2H), 2.60 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 164.6, 159.6, 158.9, 152.8, 146.2, 134.5, 132.7, 129.1, 127.9, 127.7, 127.6, 124.0, 123.9, 116.5, 115.7, 95.4, 13.9; IR (KBr): 3425, 2922,1707, 1608, 1491, 1423, 966, 770, 695, 470 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{19}H_{13}ClNO_4$: 354.0528; found: 354.0530.

*3-(5-(4-Bromophenyl)-2-methyloxazol-4-yl)-4-hydroxy-2H-chromen-2-one (**4i**).* Yield: 86% (171 mg); White solid; mp 189−191 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 7.99 (d, $J$ = 7.2 Hz, 1H), 7.56 (t, $J$ = 7.2 Hz, 1H), 7.50 (d, $J$ = 7.8 Hz, 2H), 7.33−7.28 (m, 2H), 7.26 (d, $J$ = 8.4 Hz, 2H), 2.58 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 164.6, 159.6, 158.8, 152.8, 146.2, 132.7, 130.8, 129.2, 128.0, 127.7, 123.9, 123.8, 122.8, 116.4, 115.6, 95.4, 13.8; IR (KBr): 3402, 2923, 1706, 1617, 1564, 1493, 1110, 966, 771 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{19}H_{13}BrNO_4$: 398.0023; found: 398.0024.

*3-(5-(3-Bromophenyl)-2-methyloxazol-4-yl)-4-hydroxy-2H-chromen-2-one (**4j**).* Yield: 83% (165 mg); White solid; mp 126−128 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 8.00 (d, $J$ = 7.8 Hz, 1H), 7.62 (s, 1H), 7.57 (t, $J$ = 7.8 Hz, 1H), 7.47 (d, $J$ = 7.2 Hz, 1H), 7.32 (t, $J$ = 7.8 Hz, 2H), 7.28−7.23 (m, 2H), 2.59 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 164.7, 159.7, 158.8, 152.9, 145.6, 132.8, 131.4, 131.0, 130.3, 129.0, 128.2, 126.9, 123.9, 123.9, 121.7, 116.4, 115.6, 95.3, 13.8; IR (KBr): 3429, 2923, 1708, 1615, 1555, 1493, 1418, 969, 754 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{19}H_{13}BrNO_4$: 398.0023; found: 398.0024.

*4-Hydroxy-3-(2-methyl-5-(thiophen-3-yl)oxazol-4-yl)-2H-chromen-2-one (**4k**).* Yield: 50% (81 mg); Yellow solid; mp 203−205 °C; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 8.00 (d, $J$ = 7.8 Hz, 1H), 7.56 (t, $J$ = 7.8 Hz, 1H), 7.47−7.42 (m, 1H), 7.35−7.28 (m, 3H), 7.19 (d, $J$ = 4.8 Hz, 1H), 2.57 (s, 3H); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 164.3, 159.2, 158.9, 152.9, 143.9, 132.6, 129.3, 127.3, 126.7, 124.7, 124.4, 123.9, 123.8, 116.4, 115.7, 95.7, 13.8; IR (KBr): 3391, 2679, 1702, 1614, 1566, 1290, 1272, 969, 760 $cm^{-1}$; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{17}H_{12}NO_4S$: 326.0482; found: 326.0487.

*4-Hydroxy-3-(2-methyl-5-(naphthalen-2-yl)oxazol-4-yl)-2H-chromen-2-one (**4l**).* Yield: 53% (98 mg); Yellow solid; mp 126−128 °C;



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$^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 8.03 (d, $J$ = 7.8 Hz, 1H), 7.96 (s, 1H), 7.87−7.79 (m, 3H), 7.58 (t, $J$ = 7.8 Hz, 1H), 7.48 (d, $J$ = 7.8 Hz, 3H), 7.36−7.30 (m, 2H), 2.64 (s, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 164.3, 159.6, 159.1, 152.9, 147.5, 133.1, 132.6, 132.6, 128.5, 127.7, 127.6, 127.2, 126.9, 126.6, 126.3, 125.5, 123.9, 123.9, 116.5, 115.8, 95.9, 14.0; IR (KBr): 3435, 2923, 1706, 1609, 1552, 1417, 1271, 971, 756 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{23}H_{16}NO_4$: 370.1074; found: 370.1074.

*3-(2,5-Diphenyloxazol-4-yl)-4-hydroxy-2H-chromen-2-one* (**4m**). Yield: 89% (170 mg); Yellow solid; mp 190−192 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 8.00 (t, $J$ = 8.4 Hz, 3H), 7.53 (t, $J$ = 7.8 Hz, 1H), 7.50−7.46 (m, 3H), 7.44 (d, $J$ = 7.8 Hz, 2H), 7.42−7.37 (m, 3H), 7.30 (t, $J$ = 7.8 Hz, 1H), 7.25 (d, $J$ = 8.4 Hz, 1H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 164.5, 159.3, 159.0, 152.8, 147.6, 132.7, 131.2, 128.9, 128.8, 128.6, 128.0, 127.8, 127.4, 126.4, 125.4, 123.9, 123.9, 116.3, 115.6, 95.9; IR (KBr): 3424, 2976, 1711, 1623, 1485, 1419, 1273, 976, 751 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{24}H_{16}NO_4$: 382.1074; found: 382.1071.

*3-(2-Benzyl-5-phenyloxazol-4-yl)-4-hydroxy-2H-chromen-2-one* (**4n**). Yield: 87% (172 mg); Yellow solid; mp 122−124 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.97 (d, $J$ = 7.2 Hz, 1H), 7.54 (t, $J$ = 7.2 Hz, 1H), 7.42−7.34 (m, 9H), 7.31−7.27 (m, 3H), 4.20 (s, 2H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 164.2, 161.0, 158.8, 152.7, 147.6, 134.2, 132.6, 128.9, 128.8, 128.7, 128.7, 127.7, 127.6, 127.4, 127.2, 123.9, 123.7, 116.4, 115.6, 95.6, 34.4; IR (KBr): 3424, 3031, 1724, 1612, 1556, 1494, 1418, 1170, 964, 763 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{25}H_{18}NO_4$: 396.1230; found: 396.1234.

*4-Hydroxy-3-(5-phenyl-2-propyloxazol-4-yl)-2H-chromen-2-one* (**4o**). Yield: 61% (106 mg); Yellow solid; mp 141−143 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 12.38 (s, 1H), 7.96 (d, $J$ = 7.8 Hz, 1H), 7.50 (t, $J$ = 7.8 Hz, 1H), 7.43 (d, $J$ = 7.2 Hz, 2H), 7.38 (t, $J$ = 7.2 Hz, 2H), 7.34 (d, $J$ = 7.2 Hz, 1H), 7.28−7.24 (m, 2H), 2.80 (t, $J$ = 7.2 Hz, 2H), 1.88−1.82 (m, 2H), 1.04 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 164.2, 162.7, 158.8, 152.6, 146.9, 132.4, 128.8, 128.4, 127.5, 127.4, 126.7, 123.7, 123.6, 116.1, 115.5, 95.6, 29.5, 19.9, 13.5; IR (KBr): 3412, 2970, 1724, 1614, 1555, 1418, 1325, 1183, 962, 764 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{21}H_{18}NO_4$: 348.1230; found: 348.1232.

*4-Hydroxy-3-(2-isopropyl-5-phenyloxazol-4-yl)-2H-chromen-2-one* (**4p**). Yield: 59% (102 mg); Yellow solid; mp 145−147 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 12.49 (s, 1H), 7.96 (d, $J$ = 7.2 Hz, 1H), 7.49 (t, $J$ = 7.2 Hz, 1H), 7.44 (d, $J$ = 7.2 Hz, 2H), 7.38 (t, $J$ = 7.2 Hz, 2H), 7.35−7.32 (m, 1H), 7.24 (t, $J$ = 7.8 Hz, 2H), 3.18−3.12 (m, 1H), 1.41 (d, $J$ = 7.2 Hz, 6H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 166.6, 164.1, 158.7, 152.5, 146.7, 132.3, 128.8, 128.3, 127.4, 127.4, 126.6, 123.6, 123.5, 116.0, 115.4, 95.5, 27.9, 19.8; IR (KBr): 3399, 2973, 1705, 1615, 1555, 1494, 1100, 961, 767, 697 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{21}H_{18}NO_4$: 348.1230; found: 348.1231.

*1-(2-Methyl-5-phenyloxazol-4-yl)naphthalen-2-ol* (**6a**). Yield: 83% (125 mg); White solid; mp 242−244 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.22 (s, 1H), 8.35 (d, $J$ = 8.4 Hz, 1H), 8.09 (d, $J$ = 7.8 Hz, 1H), 7.97 (d, $J$ = 7.8 Hz, 2H), 7.92 (d, $J$ = 9.0 Hz, 1H), 7.87 (d, $J$ = 9.0 Hz, 1H), 7.68 (d, $J$ = 7.8 Hz, 1H), 7.61−7.56 (m, 3H), 7.49−7.45 (m, 1H), 2.33 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.1, 150.2, 148.2, 130.4, 129.4, 129.0, 128.7, 127.2, 126.7, 126.3, 125.4, 124.9, 122.6, 122.4, 120.8, 116.7, 112.5, 23.0; IR (KBr): 3434, 2967, 1650, 1632, 1396, 1263, 1027, 802, 762, 683 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{20}H_{16}NO_2$: 302.1176; found: 302.1177.

*1-(2-Methyl-5-(p-tolyl)oxazol-4-yl)naphthalen-2-ol* (**6b**). Yield: 85% (134 mg); White solid; mp 295−297 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.13 (s, 1H), 8.30 (d, $J$ = 8.4 Hz, 1H), 8.05 (d, $J$ = 8.4 Hz, 1H), 7.87 (d, $J$ = 9.0 Hz, 1H), 7.82 (d, $J$ = 8.4 Hz, 3H), 7.63 (t, $J$ = 7.8 Hz, 1H), 7.54 (t, $J$ = 7.8 Hz, 1H), 7.36 (d, $J$ = 8.4 Hz, 2H), 2.37 (s, 3H), 2.28 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.1, 150.0, 148.5, 138.3, 130.4, 129.6, 128.9, 127.2, 126.6, 126.0, 125.4, 124.9, 122.5, 120.8, 116.0, 112.4, 23.0, 21.0;IR (KBr): 3302, 1659, 1525, 1492, 1395, 1263, 1102, 799 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{21}H_{18}NO_2$: 316.1332; found: 316.1334.

*1-(5-(4-Methoxyphenyl)-2-methyloxazol-4-yl)naphthalen-2-ol* (**6c**). Yield: 78% (129 mg); White solid; mp 248−250 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.09 (s, 1H), 8.29 (d, $J$ = 8.4 Hz, 1H), 8.04 (d, $J$ = 7.8 Hz, 1H), 7.89−7.83 (m, 3H), 7.83−7.80 (m, 1H), 7.63 (t, $J$ = 7.2 Hz, 1H), 7.53 (t, $J$ = 7.8 Hz, 1H), 7.12 (d, $J$ = 7.2 Hz, 2H), 3.83 (s, 3H), 2.27 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.1, 159.5, 149.8, 148.6, 130.4, 128.8, 127.1, 127.0, 126.5, 125.6, 124.7, 122.5, 121.9, 120.9, 115.1, 114.5, 112.4, 55.3, 23.0; IR (KBr): 3307, 2924, 1660, 1520, 1396, 1265, 1180, 1038, 798 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{21}H_{18}NO_3$: 332.1281; found: 332.1282.

*1-(5-(Benzo[d][1,3]dioxol-5-yl)-2-methyloxazol-4-yl)naphthalen-2-ol* (**6d**). Yield: 75% (129 mg); White solid; mp 253−255 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.13 (s, 1H), 8.30 (d, $J$ = 8.4 Hz, 1H), 8.04 (d, $J$ = 7.8 Hz, 1H), 7.85 (d, $J$ = 9.0 Hz, 1H), 7.79 (d, $J$ = 9.0 Hz, 1H), 7.63 (t, $J$ = 7.8 Hz, 1H), 7.53 (t, $J$ = 7.8 Hz, 1H), 7.46 (d, $J$ = 8.4 Hz, 1H), 7.44 (s, 1H), 7.11 (d, $J$ = 8.4 Hz, 1H), 6.12 (s, 2H), 2.29 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.2, 149.9, 148.3, 147.9, 147.7, 130.4, 128.9, 127.1, 126.6, 125.9, 124.9, 123.3, 122.5, 120.9, 120.0, 115.5, 112.4, 109.0, 105.6, 101.6, 23.1; IR (KBr): 3284, 2896, 1653, 1518, 1447, 1243, 1043, 799, 743 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{21}H_{16}NO_4$: 346.1074; found: 346.1073.

*1-(2-Methyl-5-(4-nitrophenyl)oxazol-4-yl)naphthalen-2-ol* (**6e**). Yield: 78% (135 mg); Yellow solid; mp >300 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.38 (s, 1H), 8.37 (d, $J$ = 8.4 Hz, 2H), 8.34 (d, $J$ = 7.8 Hz, 1H), 8.13 (d, $J$ = 8.4 Hz, 2H), 8.07 (d, $J$ = 7.8 Hz, 1H), 7.96 (d, $J$ = 8.4 Hz, 1H), 7.85 (d, $J$ = 9.0 Hz, 1H), 7.68 (t, $J$ = 7.2 Hz, 1H), 7.57 (t, $J$ = 7.2 Hz, 1H), 2.34 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.1, 151.2, 146.4, 145.8, 135.3, 130.5, 129.0, 127.9, 127.1, 125.8, 125.3, 124.4, 122.6, 120.5, 120.0, 112.5, 23.2; IR (KBr): 3275, 2924, 1660, 1593, 1511, 1341, 1027, 999, 804 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{20}H_{15}N_2O_4$: 347.1026; found: 347.1027.

*1-(2-Methyl-5-(3-nitrophenyl)oxazol-4-yl)naphthalen-2-ol* (**6f**). Yield: 66% (114 mg); Yellow solid; mp 241−243 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.38 (s, 1H), 8.63 (s, 1H), 8.35 (d, $J$ = 7.8 Hz, 1H), 8.27 (d, $J$ = 7.2 Hz, 1H), 8.22 (d, $J$ = 7.8 Hz, 1H), 8.04 (d, $J$ = 7.8 Hz, 1H), 7.90 (d, $J$ = 8.4 Hz, 1H), 7.84 (d, $J$ = 9.0 Hz, 1H), 7.80 (t, $J$ = 7.8 Hz, 1H), 7.66 (t, $J$ = 7.2 Hz, 1H), 7.55 (t, $J$ = 7.2 Hz, 1H), 2.36 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.1, 150.7, 148.1, 145.6, 131.0, 130.7, 130.7, 130.4, 128.9, 127.3, 127.1, 126.9, 125.1, 122.7, 122.5, 120.4, 119.3, 118.5, 112.4, 23.0; IR (KBr): 3242, 2926, 1656, 1530, 1349, 1263, 1005, 810, 739 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{20}H_{15}N_2O_4$: 347.1026; found: 347.1027.

*1-(5-(4-Bromophenyl)-2-methyloxazol-4-yl)naphthalen-2-ol* (**6g**). Yield: 80% (152 mg); White solid; mp 293−295 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.19 (s, 1H), 8.31 (d, $J$ = 8.4 Hz, 1H), 8.06 (d, $J$ = 8.4 Hz, 1H), 7.90 (d, $J$ = 9.0 Hz, 1H), 7.87−7.81 (m, 3H), 7.77−7.73 (m, 2H), 7.65 (t, $J$ = 7.8 Hz, 1H), 7.55 (t, $J$ = 7.8 Hz, 1H), 2.29 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.1, 150.4, 147.1, 132.0, 130.4, 128.9, 128.5, 127.2, 127.1, 126.8, 126.6, 125.0, 122.5, 121.8, 120.6, 117.3, 112.5, 23.1; IR (KBr): 3284, 1658, 1514, 1482, 1396, 1263, 1005, 799, 741 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{20}H_{15}BrNO_2$: 380.0281; found: 380.0280.

*1-(5-(3-Bromophenyl)-2-methyloxazol-4-yl)naphthalen-2-ol* (**6h**). Yield: 70% (133 mg); White solid; mp 252−255 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.25 (s, 1H), 8.31 (d, $J$ = 8.4 Hz, 1H), 8.08−8.04 (m, 2H), 7.91 (d, $J$ = 8.4 Hz, 2H), 7.84 (d, $J$ = 8.4 Hz, 1H), 7.67−7.61 (m, 2H), 7.56 (t, $J$ = 7.2 Hz, 1H), 7.51 (t, $J$ = 8.4 Hz, 1H), 2.29 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.1, 150.5, 146.4, 131.5, 131.3, 131.2, 130.4, 129.0, 127.6, 127.2, 126.9, 125.1, 124.2, 122.5, 122.3, 120.6, 117.8, 112.5, 23.0; IR (KBr): 3247, 2924, 1655, 1516, 1369, 1276, 1000, 800, 742 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{20}H_{15}BrNO_2$: 380.0281; found: 380.0281.

*1-(5-(2,4-Dichlorophenyl)-2-methyloxazol-4-yl)naphthalen-2-ol* (**6i**). Yield: 88% (163 mg); White solid; mp 226−228 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.03 (s, 1H), 8.35 (d, $J$ = 7.8 Hz, 1H), 8.07 (d, $J$ = 7.8 Hz, 1H), 7.92 (d, $J$ = 8.4 Hz, 1H), 7.86−7.81(m, 2H), 7.70−7.64 (m, 2H), 7.63−7.60 (m, 1H), 7.58−7.54 (m, 1H), 2.17 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 169.9, 151.1, 145.8, 134.9, 133.6, 132.8, 130.3, 129.8, 128.8, 127.7, 127.5, 127.1, 126.7, 126.6, 125.0, 122.8, 119.6, 119.1, 112.6, 22.9; IR (KBr): 3252, 1659, 1525, 1400, 1288, 1106, 1031, 808, 746 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{20}H_{14}Cl_2NO_2$: 370.0396; found: 370.0396.



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*1-(2-Methyl-5-(thiophen-3-yl)oxazol-4-yl)naphthalen-2-ol (**6j**).* Yield: 63% (97 mg); White solid; mp 259−260 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.11 (s, 1H), 8.29 (d, $J$ = 7.8 Hz, 1H), 8.04 (d, $J$ = 7.8 Hz, 1H), 8.00 (s, 1H), 7.86 (d, $J$ = 9.0 Hz, 1H), 7.82−7.79 (m, 1H), 7.77−7.75 (m, 1H), 7.65−7.60 (m, 2H), 7.53 (t, $J$ = 7.2 Hz, 1H), 2.30 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.2, 149.9, 146.3, 130.4, 130.0, 128.8, 127.6, 127.1, 126.6, 125.9, 125.0, 124.9, 123.0, 122.6, 120.6, 115.3, 112.4, 23.0; IR (KBr): 3268, 1652, 1536, 1386, 1276, 1004, 859, 800, 778 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{18}H_{14}NO_2S$: 308.0740; found: 308.0740.

*1-(2-Methyl-5-(naphthalen-1-yl)oxazol-4-yl)naphthalen-2-ol (**6k**).* Yield: 78% (137 mg); Yellow solid; mp 192−194 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.03 (s, 1H), 8.38 (d, $J$ = 8.4 Hz, 1H), 8.12−8.07 (m, 3H), 8.06 (d, $J$ = 7.2 Hz, 1H), 7.95−7.90 (m, 2H), 7.85 (d, $J$ = 7.2 Hz, 1H), 7.69 (t, $J$ = 7.8 Hz, 2H), 7.62−7.56 (m, 3H), 2.13 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.5, 151.1, 149.4, 133.5, 130.9, 130.4, 130.0, 128.8, 128.5, 128.4, 127.3, 127.0, 126.7, 126.4, 126.4, 126.1, 125.5, 124.9, 122.9, 120.3, 118.5, 112.7, 22.9; IR (KBr): 3253, 3044, 1656, 1508, 1388, 1276, 1186, 1010, 804, 740 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{24}H_{18}NO_2$: 352.1332; found: 352.1332.

*4-Methoxy-1-(2-methyl-5-phenyloxazol-4-yl)naphthalen-2-ol (**6l**).* Yield: 48% (80 mg); White solid; mp 287−289 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 9.96 (s, 1H), 8.32 (d, $J$ = 7.8 Hz, 1H), 8.25 (d, $J$ = 8.4 Hz, 1H), 7.97 (d, $J$ = 7.2 Hz, 2H), 7.71 (t, $J$ = 7.2 Hz, 1H), 7.59−7.52 (m, 3H), 7.43−7.39 (m, 1H), 6.91 (s, 1H), 4.00 (s, 3H), 2.22 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 169.3, 151.5, 146.5, 142.3, 129.8, 128.9, 128.3, 127.6, 125.2, 125.2, 123.6, 122.9, 122.8, 120.9, 119.4, 116.9, 95.8, 55.9, 23.0; IR (KBr): 3256, 1655, 1519, 1488, 1381, 1274, 1225, 1109, 841, 761 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{21}H_{18}NO_3$: 332.1281; found: 332.1281.

*Methyl 6-Hydroxy-5-(2-methyl-5-phenyloxazol-4-yl)-2-naphthoate (**6m**).* Yield: 75% (135 mg); White solid; mp 278−280 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.24 (s, 1H), 8.73 (s, 1H), 8.37 (d, $J$ = 8.4 Hz, 1H), 8.13 (d, $J$ = 7.2 Hz, 1H), 8.07 (d, $J$ = 9.0 Hz, 1H), 7.93 (d, $J$ = 7.2 Hz, 2H), 7.89 (d, $J$ = 8.4 Hz, 1H), 7.57−7.53 (m, 2H), 7.44 (t, $J$ = 6.6 Hz, 1H), 3.92 (s, 3H), 2.33 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.4, 166.3, 151.5, 148.7, 131.3, 129.6, 129.6, 129.1, 128.9, 127.6, 125.8, 125.5, 123.1, 120.8, 116.6, 113.5, 109.6, 52.3, 23.1; IR (KBr): 3248, 2951, 1722, 1656, 1435, 1287, 1254, 1115, 751 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{22}H_{18}NO_4$: 360.1230; found: 360.1231.

*6-Hydroxy-5-(2-methyl-5-phenyloxazol-4-yl)-2-naphthonitrile (**6n**).* Yield: 73% (119 mg); Yellow solid; mp >300 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.25 (s, 1H), 8.64 (s, 1H), 8.38 (d, $J$ = 8.4 Hz, 1H), 7.98−7.95 (m, 2H), 7.94−7.89 (m, 3H), 7.55 (t, $J$ = 7.2 Hz, 2H), 7.45 (t, $J$ = 7.2 Hz, 1H), 2.32 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.3, 151.5, 149.0, 134.9, 129.5, 129.1, 129.0, 128.9, 128.8, 127.3, 126.6, 125.6, 123.9, 120.8, 119.2, 116.5, 114.3, 107.2, 23.1; IR (KBr): 3236, 2224, 1654, 1519, 1488, 1388, 1264, 802, 765 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{21}H_{15}N_2O_2$: 327.1128; found: 327.1126.

*6-Bromo-1-(2-methyl-5-phenyloxazol-4-yl)naphthalen-2-ol (**6o**).* Yield: 89% (169 mg); White solid; mp >300 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.20 (s, 1H), 8.35 (s, 1H), 8.21 (d, $J$ = 9.0 Hz, 1H), 7.92 (d, $J$ = 7.8 Hz, 2H), 7.90−7.86 (m, 2H), 7.77 (d, $J$ = 9.0 Hz, 1H), 7.55 (t, $J$ = 7.2 Hz, 2H), 7.44 (t, $J$ = 7.2 Hz, 1H), 2.28 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.2, 150.3, 148.6, 131.9, 130.7, 129.5, 129.1, 129.1, 128.9, 125.7, 125.5, 125.4, 124.7, 120.9, 117.9, 116.5, 113.7, 23.1; IR (KBr): 3238, 1648, 1517, 1487, 1273, 1113, 994, 816, 764 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{20}H_{15}BrNO_2$: 380.0281; found: 380.0280.

*7-Bromo-1-(2-methyl-5-phenyloxazol-4-yl)naphthalen-2-ol (**6p**).* Yield: 81% (154 mg); White solid; mp 271−273 °C; $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$ 10.25 (s, 1H), 8.39 (s, 1H), 8.03 (d, $J$ = 8.4 Hz, 1H), 7.92 (d, $J$ = 7.8 Hz, 2H), 7.90−7.86 (m, 2H), 7.67 (d, $J$ = 9.0 Hz, 1H), 7.55 (t, $J$ = 7.8 Hz, 2H), 7.44 (t, $J$ = 7.2 Hz, 1H), 2.30 (s, 3H); $^{13}$C NMR (150 MHz, DMSO-$d_6$) $\delta$ 170.2, 150.7, 148.6, 131.1, 129.1, 129.1, 128.9, 128.9, 128.2, 127.8, 126.2, 125.5, 124.6, 120.1, 120.0, 116.3, 113.1, 22.9; IR (KBr): 3272, 1656, 1621, 1516, 1489, 1392, 1271, 829, 763 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{20}H_{15}BrNO_2$: 380.0281; found: 380.0281.

*3-Hydroxy-2-(2-methyl-5-phenyloxazol-4-yl)cyclohex-2-enone (**8a**).* Yield: 70% (94 mg); Yellow solid; mp 161−163 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.94 (s, 1H), 7.53 (d, $J$ = 7.8 Hz, 2H), 7.35 (t, $J$ = 7.2 Hz, 2H), 7.28−7.25 (m, 1H), 2.84 (t, $J$ = 6.0 Hz, 2H), 2.43 (t, $J$ = 6.0 Hz, 2H), 2.16−2.12 (m, 5H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 195.3, 168.9, 165.1, 145.4, 129.6, 128.0, 127.7, 125.2, 117.7, 115.7, 37.6, 23.3, 23.3, 22.2; IR (KBr): 3262, 2950, 1674, 1525, 1475, 1374, 1012, 768, 693 cm$^{-1}$; HRMS (ESI): $m/z$ [M + Na]$^+$ calcd for $C_{16}H_{15}NNaO_3$: 292.0944; found: 292.0948.

*3-Hydroxy-5-methyl-2-(2-methyl-5-phenyloxazol-4-yl)cyclohex-2-enone (**8b**).* Yield: 78% (110 mg); White solid; mp 158−160 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.78 (s, 1H), 7.53 (d, $J$ = 7.2 Hz, 2H), 7.37 (t, $J$ = 7.8 Hz, 2H), 7.28 (t, $J$ = 7.2 Hz, 1H), 2.99−2.94 (m, 1H), 2.60−2.51 (m, 2H), 2.47−2.42 (m, 1H), 2.27−2.23 (m, 1H), 2.19 (s, 3H), 1.18 (d, $J$ = 6.6 Hz, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 195.1, 168.6, 164.8, 145.6, 129.8, 128.1, 127.8, 125.4, 117.3, 115.7, 46.1, 31.4, 30.7, 23.5, 21.0; IR (KBr): 3469, 2959, 2927, 1739, 1660, 1426, 1378, 1215, 1142, 886 cm$^{-1}$; HRMS (ESI): $m/z$ [M + Na]$^+$ calcd for $C_{17}H_{17}NNaO_3$: 306.1100; found: 306.1104.

*5-Hydroxy-4-(2-methyl-5-phenyloxazol-4-yl)-1,6-dihydro-[1,1′-biphenyl]-3(2H)-one (**8c**).* Yield: 62% (107 mg); White solid; mp 95−97 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.86 (s, 1H), 7.56 (d, $J$ = 7.2 Hz, 2H), 7.40−7.33 (m, 4H), 7.30−7.24 (m, 4H), 3.56−3.48 (m, 1H), 3.15−3.10 (m, 1H), 3.06−3.00 (m, 1H), 2.76−2.65 (m, 2H), 2.18 (s, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 193.8, 168.9, 164.2, 146.1, 141.9, 129.6, 128.8, 128.1, 127.9, 127.2, 126.7, 125.3, 117.7, 115.7, 45.0, 41.0, 31.1, 23.4; IR (KBr): 3440, 3012, 1680, 1523, 1453, 1368, 1058, 764, 695 cm$^{-1}$; HRMS (ESI): $m/z$ [M + Na]$^+$ calcd for $C_{22}H_{19}NNaO_3$: 368.1257; found: 368.1258.

*3-Hydroxy-5,5-dimethyl-2-(2-methyl-5-(p-tolyl)oxazol-4-yl)-cyclohex-2-enone (**8d**).* Yield: 75% (117 mg); White solid; mp 157−159 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.82 (s, 1H), 7.43 (d, $J$ = 7.2 Hz, 2H), 7.17 (d, $J$ = 7.2 Hz, 2H), 2.74 (s, 2H), 2.34 (s, 5H), 2.17 (s, 3H), 1.14 (s, 6H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 194.4, 168.8, 163.8, 146.0, 137.3, 128.6, 126.7, 125.0, 116.5, 114.8, 51.8, 37.0, 35.0, 28.3, 23.1, 21.1; IR (KBr): 3448, 3264, 2963, 2251, 1679, 1545, 1367, 1057, 917, 822, 735 cm$^{-1}$; HRMS (ESI): $m/z$ [M+H]$^+$ calcd for $C_{19}H_{22}NO_3$: 312.1594; found: 312.1597.

*N-(2-(4-Bromophenyl)-1-(4-hydroxy-2-oxo-2H-chromen-3-yl)-2-oxoethyl)acetamide (**C**).* Yield: 60% (250 mg); White solid; mp 211−213 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 12.81 (s, 1H), 8.05−7.99 (m, 2H), 7.69 (d, $J$ = 8.4 Hz, 2H), 7.55 (t, $J$ = 7.2 Hz, 1H), 7.50 (d, $J$ = 8.4 Hz, 2H), 7.32 (t, $J$ = 7.8 Hz, 1H), 7.20 (d, $J$ = 8.4 Hz, 1H), 6.00 (d, $J$ = 6.0 Hz, 1H), 2.21 (s, 3H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 191.8, 173.6, 165.7, 161.7, 153.2, 133.0, 132.9, 132.0, 129.4, 128.8, 124.6, 124.2, 116.5, 116.4, 104.3, 51.8, 22.4; IR (KBr): 3293, 3061, 2885, 1694, 1589, 1526,1359,1071, 805, 756 cm$^{-1}$ ; HRMS (ESI): $m/z$ [M +H]$^+$ calcd for $C_{19}H_{15}BrNO_5$: 416.0128; found: 416.0130.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00763.

Copies of the $^1$H and $^{13}$C NMR spectra (PDF)
Crystallographic data of **4i** (CIF)
Crystallographic data of **C** (CIF)

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### Notes

The authors declare no competing financial interest.



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