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Article

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Alkali-induced Ring-Opening of 2-Amidodihydrofuran and Manganese Catalyzed Aerobic Dehydrogenation Annulation: An Access to Functionalized Oxazole

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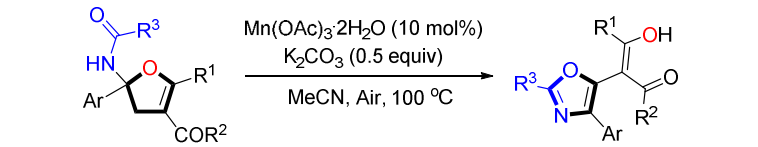


Abstract

A novel and efficient synthesis of functionalized oxazoles from 2-amidodihydrofurans has been achieved by alkali-induced intramolecular C–O bond cleavage and formation using air as a green oxidant. Moreover, these functionalized oxazoles could be readily transformed into the corresponding oxazole substituted pyrazoles and 2*H*-azirines.

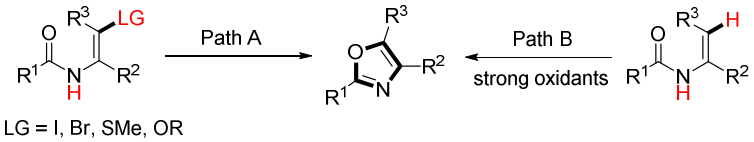
Introduction

The cleavage and construction of chemical bonds are basic elements in catalysis and organic synthesis, their realizations via an efficient, selective and highly atom economic manner are the long term goal for sustainable chemistry. C–O Bonds widely exist in oxygen-containing heterocycles and functional compounds such as alcohol and ether, their catalytic cleavages and transformations between different types for the advanced synthesis have attracted enormous interests in recent times.[1] Therefore, it is highly desirable and interesting if these C–O bond breakings and formations would catalytically occur in the diverse conversion of oxygen-containing heterocycle into another heterocyclic skeleton compound,[2] especially when such transformation simultaneously generates functional moiety for further transformations.

Oxazole skeleton is widely existed in natural products and pharmaceutical compounds,[3] extensive efforts have been devoted to the synthesis and functionalization of oxazoles.[4] In particular, the as-prepared or *in situ* generated enamides are active substrates or intermediates to yield oxazoles mainly *via* the following two pathways: first, intramolecular vinylation of

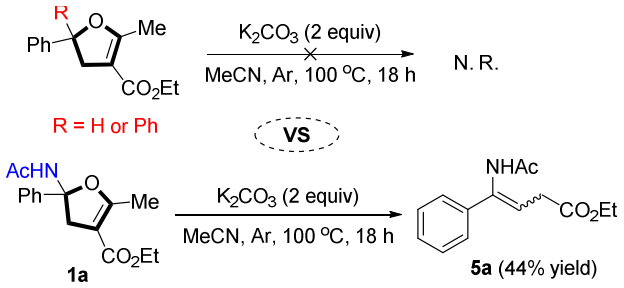
the amide as indicated in the path A of Scheme 1, and these specific enamides usually need a leaving group (LG) in the β-vinylic position;[5] second, direct cyclization of enamide with the neighbouring olefin through oxidative C−H functionalization,[6] nevertheless, such atom-economic transformation requires strong oxidants, such as $K_2S_2O_8$, $PhI(OAc)_2$, copper salts (Scheme 1, Path B). Compared with these two routes, the C–O bond formation of oxazole enabled by the catalytic aerobic oxidation represents a more challenging and greener way in view of the natural and environmentally benign character of air.[7] Herein, we develop a novel nonprecious metal-catalyzed procedure to synthesize the oxazole skeleton via the oxidative cyclization of enamide with the *in situ* generated allene moiety[8] using air as a green oxidant. In addition, the functional substituents could also be generated onto the oxazole ring due to the uniqueness of this procedure.

Scheme 1. Reported Synthesis of Oxazoles from Enamines.



Besides taking as a nucleophile for the annulation to yield oxazole, the amide group of 2-amidodihydrofuran is also herein proposed to be an assisting function to facilitate the ring opening of dihydrofuran *via* C−O bond cleavage in the presence of base,[9] which is then experimentally verified by replacing the amide with representative Ph or H, without any reaction observed as indicated in Scheme 2. However, the 2-aminodihydrofuran afforded the ring opening product **5a** with a mixture of *E* and *Z* isomer was obtained in total 44% yield with one isomer structurally confirmed by XRD (CCDC 1401603) under the same reaction condition, which showed that ring opening of **1a** indeed happened with the help of a base along with its catalyzed decarbonylation resulting in the loss of an acetyl moiety.

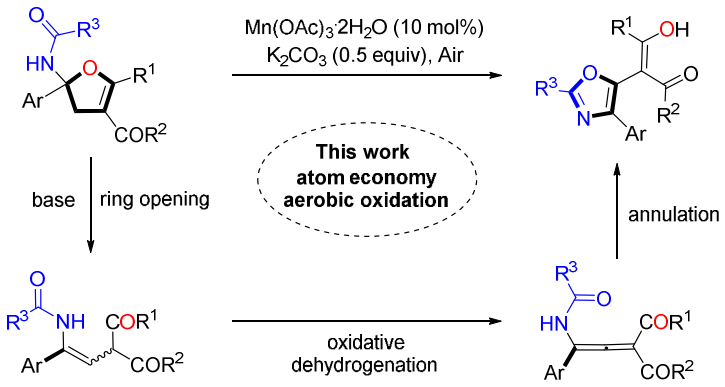
Scheme 2. Investigation on the Role of Amide Substitutent for the Ring-Opening of Dihydrofurans.



Taking such unique advantage, it is hypothesized as illustrated in Scheme 3 that the 2-amidodihydrofuran could go through C−O bond cleavage to generate γ-dicarbonyl enamide which thereafter undergoes an oxidative dehydrogenation process to

generate the allene intermediate,[8] eventually, from which the oxazoles bearing a 1,3-dicarbonyl moiety would be formed *via* an intramolecular nucleophilic annulation.

Scheme 3. Our Proposed Strategy for the Synthesis of Functionalized Oxazoles from 2-Amidodihydrofurans.

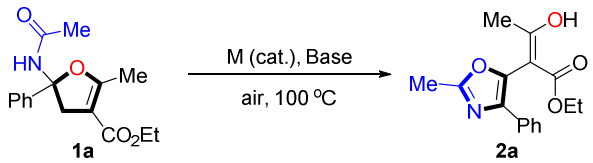


Results and Discussion

With the above assumption in mind, we started the investigation by the catalytic transformation of **1a** (Table 1). Considering that copper catalysts play a crucial role in the aerobic oxidation,[10] a series of copper salts were initially selected as the oxidation catalysts with the presence of Cs_2CO_3 to initiate the cyclic C−O cleavage under an air atmosphere. The expected oxazole **2a** was obtained in moderate yields (entries 1−6). Manganese catalyst, also a good single-electron oxidant,[11] can possibly facilitate the oxidization of the *in situ* generated 1,3-dicarbonyl anion species *via* C–O bond cleavage of **1a** to produce corresponding alkyl radical intermediate,[12] which would be easily trapped by O_2 to forward the oxidative dehydrogenation.[13] Within the screened manganese catalysts, $Mn(OAc)_3$ displayed higher efficiency (entries 7−9). Interestingly, the transformation of **1a** to **2a** could also proceed in the absence of metal catalyst but only giving 24% yield (entry 10), and no reaction occurred without base (entry 11), indicating the *in situ* generated 1,3-dicarbonyl anion intermediate could slowly react with O_2 without a metal catalyst although which could accelerate such process.[14] Present transformation was found to be very sensitive to solvent, it proceeded smoothly in DMF and DMSO (entries 12 and 13), however, only gave 10% yield of **2a** in toluene or DCE (entries 14 and 15). K_2CO_3 showed the best assisting activity among the screened bases (entries 16–18), giving **2a** in 73% yield. As mentioned in Scheme 2, **5a** was observed instead of **2a** when the reaction was conducted under an argon atmosphere, suggesting oxygen was expectedly involved in the oxidation step (entry 19). However, only 47% yield of **2a** was obtained in 1 atm oxygen owning to the **2a** will further oxidized in an excess of oxygen (entry 20). In addition, the yield dramatically decreased as the temperature declined, probably indicating one step among C–O cleavage, oxidative dehydrogenation and/or annulation is significantly temperature sensitive (entries 21 and 22).

To our delight, 78% yield of **2a** could be achieved even using 0.5 equiv. of K_2CO_3 (entries 23 and 24). However, only 45% yield of **2a** was obtained when using 0.25 equiv. of K_2CO_3, and the **1a** was still observed (entry 25).

Table 1. Reaction optimization[a]



1a **2a**

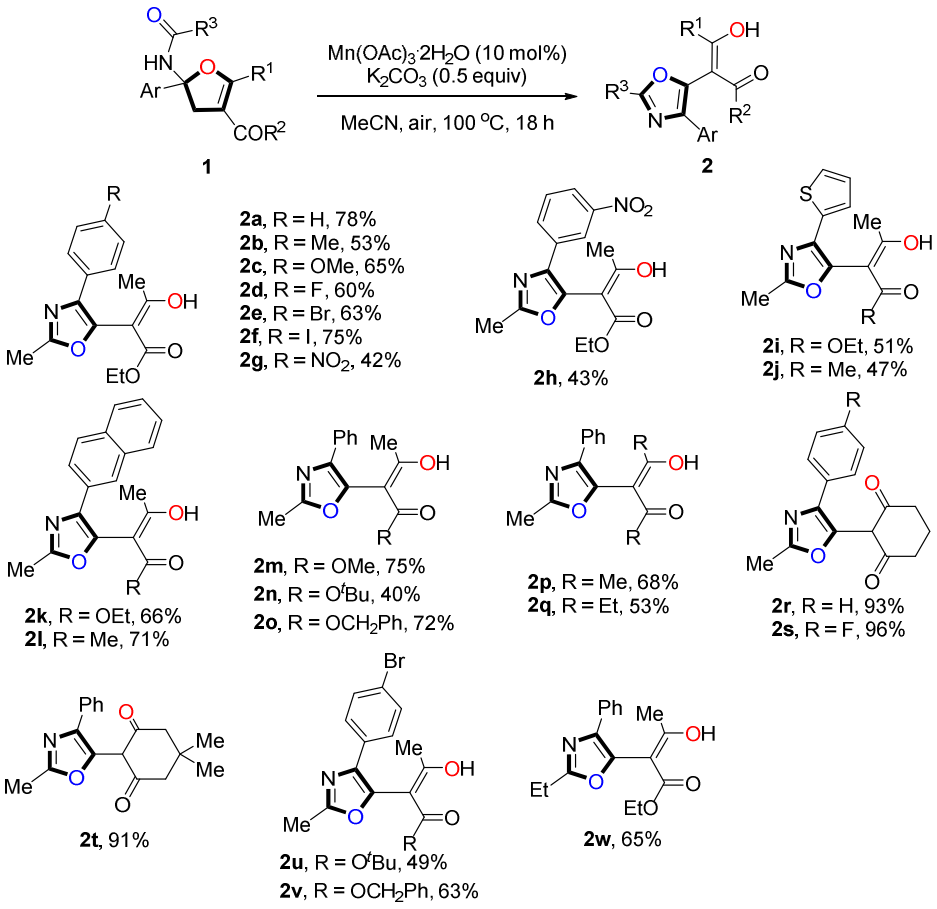
entry	catalyst (10 mol%)	base (equiv)	solvent	yield (%)
1	CuBr	Cs_2CO_3 (3)	MeCN	45
2	CuI	Cs_2CO_3 (3)	MeCN	54
3	$CuCl_2$	Cs_2CO_3 (3)	MeCN	51
4	CuF_2	Cs_2CO_3 (3)	MeCN	44
5	$Cu(TFA)_2$	Cs_2CO_3 (3)	MeCN	54
6	$Cu(OAc)_2$	Cs_2CO_3 (3)	MeCN	64
7	$MnCl_2.4H_2O$	Cs_2CO_3 (3)	MeCN	61
8	$Mn(OAc)_2.4H_2O$	Cs_2CO_3 (3)	MeCN	57
9	$Mn(OAc)_3.2H_2O$	Cs_2CO_3 (3)	MeCN	68
10		Cs_2CO_3 (3)	MeCN	24
11	$Mn(OAc)_3.2H_2O$		MeCN	0
12	$Mn(OAc)_3.2H_2O$	Cs_2CO_3 (3)	DMF	47
13	$Mn(OAc)_3.2H_2O$	Cs_2CO_3 (3)	DMSO	47
14	$Mn(OAc)_3.2H_2O$	Cs_2CO_3 (3)	DCE	10
15	$Mn(OAc)_3.2H_2O$	Cs_2CO_3 (3)	Toluene	10
16	$Mn(OAc)_3.2H_2O$	K_2CO_3 (3)	MeCN	73
17	$Mn(OAc)_3.2H_2O$	K_3PO_4 (3)	MeCN	57
18	$Mn(OAc)_3.2H_2O$	CsF (3)	MeCN	10
19[b]	$Mn(OAc)_3.2H_2O$	Cs_2CO_3 (3)	MeCN	N. D.
20[c]	$Mn(OAc)_3.2H_2O$	Cs_2CO_3 (3)	MeCN	47
21[d]	$Mn(OAc)_3.2H_2O$	Cs_2CO_3 (3)	MeCN	66
22[e]	$Mn(OAc)_3.2H_2O$	Cs_2CO_3 (3)	MeCN	35
23	$Mn(OAc)_3.2H_2O$	K_2CO_3 (1)	MeCN	76
24	$Mn(OAc)_3.2H_2O$	K_2CO_3 (0.5)	MeCN	78
25[f]	$Mn(OAc)_3.2H_2O$	K_2CO_3 (0.25)	MeCN	45

[a] All reactions were carried out on a 0.2 mmol scale in 2 mL of solvent in a 35 mL sealed tube (total volume 50 mL) in 100 °C for 18 h. [b] Under argon. [c] Under 1 atm O_2. [d] 90 °C. [e] 80 °C. [f] 36 h.

Having identified the optimized reaction conditions (Table 1, entry 23), we turned to examining the scope of this catalytic transformation (Scheme 4). 2-Acetamidedihydrofurans derived from various aromatic enamides (R^3 = Me, with different Ar) were initially investigated, substrates with electron-donating groups (R = Me or OMe) and electron-withdrawing groups (R = F, Br, I, or NO_2) were all suitable for this transformation, affording the desired oxazoles in 42% to 75% yields, respectively

(**2b**–**2h**). Besides, other representative aromatic substrates, such as thiophene and naphthalene groups, were also well tolerated (**2i**–**2l**). Subsequently, 2-acetamide-dihydrofurans derived from various 1,3-dicarbonyl compounds (different R^1, R^2) were examined, the unsymmetrical 1,3-dicarbonyl derived substrates gave the corresponding products in 40% to 75% yields, respectively (**2m**–**2o**, **2u** and **2v**). These 2-acetamidedihydrofurans derived from symmetrical 1,3-dicarbonyl compounds afforded desirable products in moderate to excellent yields (**2p**–**2t**), and the cyclic 2-amidodihydrofurans displayed higher activity in this transformation (**2r**–**2t**).

Scheme 4. Catalytic Tandem Synthesis of Functionalized Oxazoles from 2-Amidodihydrofurans.

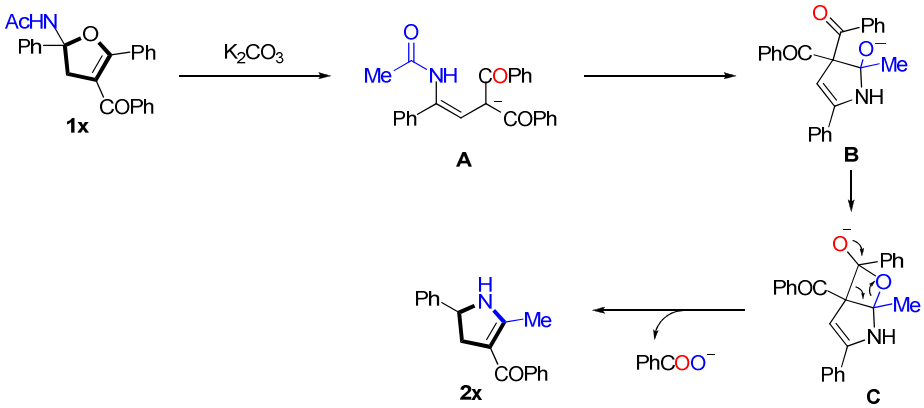


The structure of the representative oxazole **2u** is further confirmed by X-ray single crystal diffraction (XRD, CCDC 1401540). The C5–C12 bond length is 1.368 Å indicating its C=C character, and the hydrogen atom attached to O2 suggests the presence of alcoholic group. Moreover, it is worthy to note that a high chemical shift HNMR peak (13–18 ppm) belonging to product **2** (except for **2r**–**2t)** was observed which revealed the intramolecular O–H···O hydrogen bond between the hydroxyl and ketone group is stably present in the solution condition, this interesting observation is significantly different

with the reported structures of aryl substituted 1,3-dicarbonyl compounds which are keto- or keto-enol mixture in solution,[15] these functionalized oxazoles prepared by present method display exclusive enolic form in either liquid or solid condition.

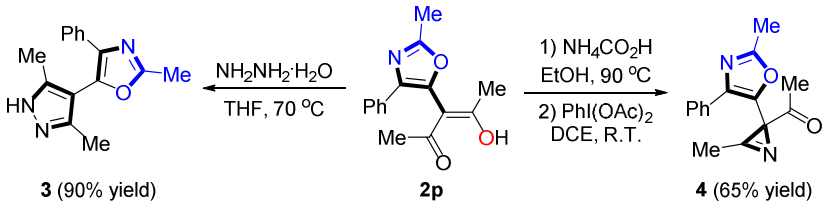
Moreover, the amide substituent of dihydrofuran could also be smoothly changed (**2w**). Surprisingly, dihydrofuran **1x** derived from 1,3-diphenylpropanedione ($R^1 = R^2$ = Ph, R^3 = Me, Ar = Ph) gave the pyrrole (**2x**) instead of oxazole in 86% yield via an another plausible process. It's worth noting that a little of pyrroles were detected in the transformation from dihydrofurans (**1p** and **1q**) to oxazoles (**2p** and **2q**) owing to losing the acetyl group. As shown in Scheme 5, the 2-amidodihydrofuran **1x** undergoes alkali-induced ring opening to form carbanion **A**. Then **A** experiences an intramolecular annulation to generate a five-membered ring **B**, followed by further intramolecular annulation to generate **C**. Eventually, the product **2x** would be generated from **C** via a ring-opening along with benzoate leaving. And the benzoic acid was detected by GC-MS.

Scheme 5. A Plausible Mechanism to Generate 2x.



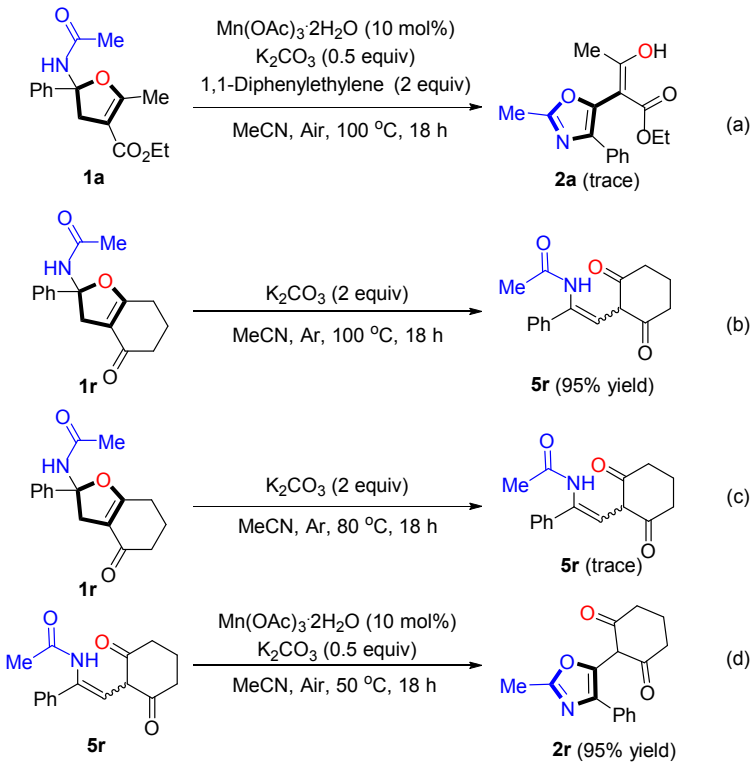
With the hydroxyl enone as a synthetic moiety, the above funtionalized oxazoles could be further transformed into other interesting oxazole substituted heterocyclic compounds as representatively shown in Scheme 6. The hydroxyl enone substituent of **2p** could react with hydrazine hydrate to obtain corresponding pyrazole **3** in 90% yield.[16] Besides, the oxazole substituted 2*H*-azirine **4** could be synthesized in 65% yield *via* a two-step reaction.[17]

Scheme 6. Further Transformations.



To understand the mechanism about this transformation, a series of control experiments were carried out (Scheme 7). Only trace amount of **2a** was detected in the presence of 1,1-diphenylethylene indicating present transformation appeared to undergo a radical process (Scheme 7a). Compared with the tranfomation from **2a** to **5a**, **1r** would transform into the corresponding enamide **5r** in 95% yield at 100 °C under argon without any side decarbonylation reaction observed possibly because the steric hinderance of the cyclohexone substitutent is much higher than previous actyl group (Scheme 7b). Note that the conversion of **1r** into **5r** was difficult to happen at 80 °C (Scheme 4c), but the resultant enamide **5r** could catalytically convert to the expected oxazole **2r** through oxidative cyclization in very high yield even at 50 °C (Scheme 4d). These results not only showed that the enamide generated from the ring opening of 2-amidodihydrofuran was the intermediate of such transformation, but also indicated that the C–O cleavage involved ring opening step need higher temperature than the aerobic dehydrogenation and the subsequent annulation.

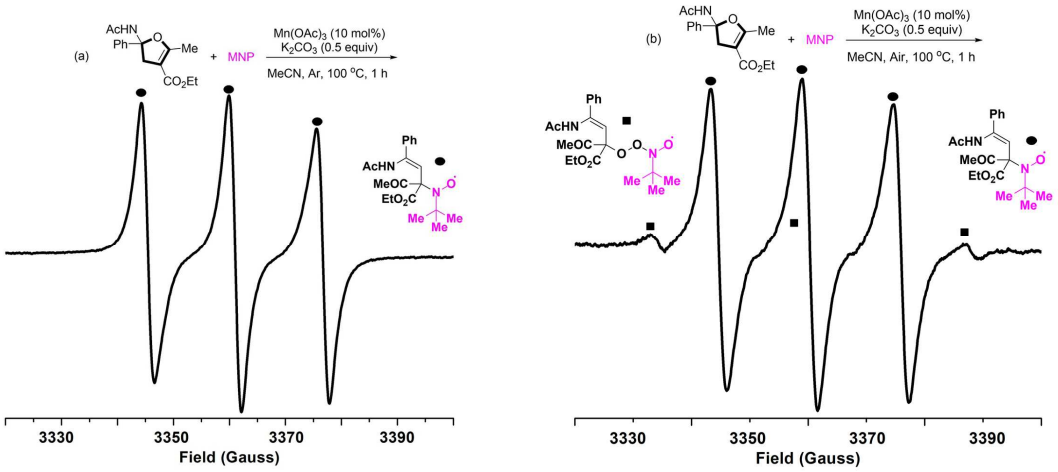
Scheme 7. Control Experiments.



In order to further understand the mechanism, Electron Paramagnetic Resonance (EPR) experiments were performed using 2-methyl-2-nitrosopropane (MNP) as a spin trapping reagent (Figure 1).[18] A mixture of **1a**, $Mn(OAc)_3$, K_2CO_3 and MNP was stirred under argon at 100 °C for one hour. Then the mixture was detected by EPR spectroscopy, and a strong signal with three Lorentzian lines (g = 2.0060, a (^{14}N) = 15.70 G) was clearly detected indicating the alkyl radical **B** possibly originated

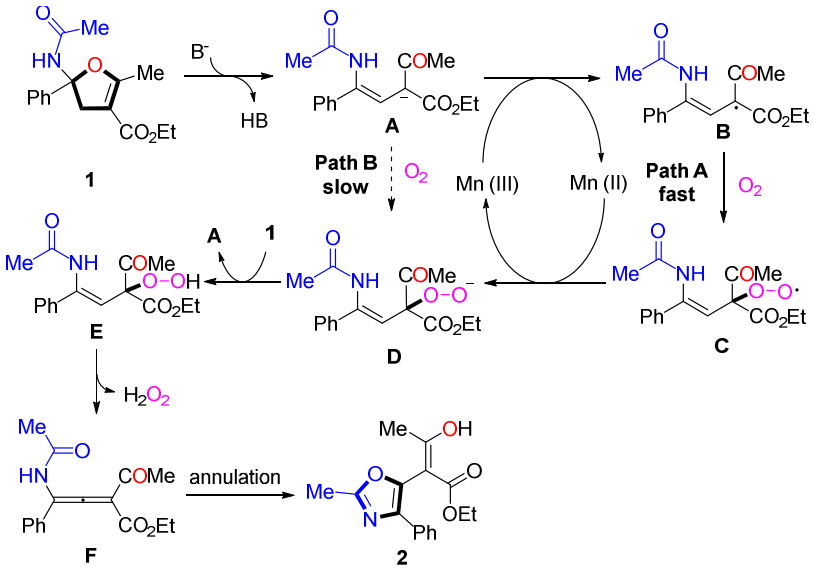
from the *in situ* generating γ-dicarbonyl enamide was trapped by MNP (Figure 1a). The above signal could also be detected when the reaction was conducted in air at 100 °C for one hour, more interestingly, another signal (g = 2.0055, a (^{14}N) = 27.03 G) derived from the trapping of peroxy radical **C** with MNP was also observed (Figure 1b). Notably, no signal was detected without manganese catalyst might indicate that carbanion **A** generated from the ring opening of **1a** would transform into corresponding alkyl radical **B** *via* single electron transfer process in the presence of manganese catalyst.[11]

Figure 1. EPR Studies of the Model Reaction under Ar and Air



Based on the above control experiments and EPR studies, a proposed mechanism is drawn in Scheme 8. Initially, the 2-amidodihydrofuran undergoes alkali-induced ring opening to form carbanion **A** which further converts to the alkyl radical **B** in the presence of Mn^{III} catalyst.[11] The radical **B** reacts with O_2 to produce a peroxy radical **C**,[12] both of them could be trapped with MNP and observed by EPR. The resultant Mn^{II} could be oxidized by **C** to regenerate Mn^{III} catalytic species with giving the peroxide anion intermediate **D** (Scheme 8, Path A).[19] As observed in previous catalyst optimization (Table 1, entry 10), **D** might be alternatively produced with much slower reaction rate from the reaction of **A** with O_2 (Scheme 8, Path B).[14] Then **D** captures a proton like a base from 2-amidodihydrofuran to form a peroxide **E** with the regeneration of **A**. Subsequently, **E** is transformed into an allene intermediate **F** possibly induced by heat or base,[13] and eventually converts to the oxazole **2** *via* an intramolecular annulation process.[20]

Scheme 8. A Plausiblem Mechanism.



Conclusions

In summary, we have developed a novel and efficient methodology to synthesize functionalized oxazoles from easily available 2-amidodihydrofurans. This highly atom-economic transformation employs inexpensive $Mn(OAc)_3$ as the catalyst and air as the oxidant. The control experiments and EPR studies reveal that present cascade catalytic transformation appears to involve γ-dicarbonyl enamide and allene intermediates through a series of base promoting ring-opening, manganese catalyzed aerobic oxidative dehydrogenation and annulation process. In addition, these functionalized oxazoles could be readily transformed into the corresponding oxazole substituted pyrazoles and 2*H*-azirines. Present cascade catalytic procedure would inspire new designs on the synthesis of heterocyclic skeletons *via* intramolecular C–O bond cleavage and formation.

Experimental Section

General Considerations. The ^1H and ^{13}C NMR spectra were recorded with 400 MHz spectrometers as solutions in $CDCl_3$ or MeOD. Chemical shifts are expressed in parts per million (ppm) and are referenced to $CHCl_3$ (δ = 7.26 ppm for ^1H and δ = 77.0 ppm for ^{13}C) or MeOD (δ = 3.34 ppm for ^1H and δ = 49.9 ppm for ^{13}C) as an internal standard.

General procedure to prepare 2-amidodihydrofurans 1.[9b] To a 50 mL Schlenk tube with a stir bar was added enamides (1 mmol), 1,3-dicarbonyl compounds (2 mmol), $Mn(OAc)_3{\cdot}2H_2O$ (804 mg, 3 mmol) and 10 mL of MeCN. The mixture was stirred under argon at 80 ºC for 6 h, cooled to room temperature, poured into brine and extracted with EtOAc. The combined extracts were dried over $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography (PE/EA = 2:1) to afford the desired 2-amidodihydrofurans **1**.

*Ethyl 5-acetamido-2-methyl-5-phenyl-4,5-dihydrofuran-3-carboxylate (**1a**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.31 (m, 5 H), 6.44 (bs, 1 H), 4.13 (q, *J* = 7.1 Hz, 2 H), 3.67 (d, *J* = 15.3 Hz, 1 H), 3.11 (d, *J* = 15.3 Hz, 1 H), 2.33 (s, 3 H), 1.99 (s, 3 H), 1.24 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 169.5, 165.7, 165.5, 142.9, 128.7, 128.4, 124.5, 101.6, 95.2, 59.5, 42.9, 24.0, 14.3, 13.9.

*Ethyl 5-acetamido-2-methyl-5-(p-tolyl)-4,5-dihydrofuran-3-carboxylate (**1b**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.0 Hz, 2 H), 7.18 (d, *J* = 8.0 Hz, 2 H), 6.48 (br, 1 H), 4.11 (q, *J* = 7.0 Hz, 2 H), 3.61 (t, *J* = 15.2 Hz, 1 H), 3.08 (d, *J* = 15.3 Hz, 1 H), 2.34 (s, 3 H), 2.31 (s, 3 H), 1.97 (s, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 169.6, 165.7, 165.6, 140.0, 138.3, 129.3, 124.4, 101.6, 95.3, 59.5, 42.8, 24.0, 21.0, 14.3, 13.88.

*Ethyl 5-acetamido-5-(4-methoxyphenyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (**1c**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.7 Hz, 2 H), 6.95–6.87 (m, 2 H), 6.20 (bs, 1 H), 4.13 (q, *J* = 7.1 Hz, 2 H), 3.81 (s, 3 H), 3.69 (d, *J* = 15.3 Hz, 1 H), 3.12 (dd, *J* = 15.3, 1.7 Hz, 1 H), 2.32 (s, 2 H), 2.01 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 169.5, 165.6, 159.5, 135.0, 125.9, 114.0, 101.7, 95.2, 59.5, 55.3, 42.7, 24.0, 14.3, 13.9.

*Ethyl 5-acetamido-5-(4-fluorophenyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (**1d**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 8.7, 5.2 Hz, 2 H), 7.03 (t, *J* = 8.5 Hz, 2 H), 6.66 (br, 1 H), 4.11 (q, *J* = 7.1 Hz, 2 H), 3.55 (d, *J* = 15.3 Hz, 1 H), 3.04 (d, *J* = 15.1 Hz, 1 H), 2.29 (s, 3H), 1.94 (s, 2 H), 1.23 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 169.7, 165.6, 165.4, 162.4 ($^1J_{CF}$ = 247.1 Hz), 138.61, 126.5 ($^3J_{CF}$ = 8.2 Hz), 115.4 ($^2J_{CF}$ = 22.0 Hz), 101.5, 94.8, 59.6, 43.4, 23.8, 14.3, 13.9.

*Ethyl 5-acetamido-5-(4-bromophenyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (**1e**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.3 Hz, 2 H), 7.31 (d, *J* = 8.3 Hz, 2 H), 6.38 (br, 1 H), 4.13 (q, *J* = 7.1 Hz, 2 H), 3.55 (d, *J* = 15.4 Hz, 1 H), 3.07 (d, *J* = 15.5 Hz, 1 H), 2.31 (s, 3 H), 1.99 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 169.4, 165.6, 165.3, 141.7, 131.8, 126.4, 122.5, 101.6, 94.8, 59.7, 43.5, 24.0, 14.4, 14.0.

*Ethyl 5-acetamido-5-(4-iodophenyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (**1f**)*[9a]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.4 Hz, 2 H), 7.18–7.16 (m, 2 H), 6.58 (s, 1 H), 4.12 (q, 7.1 Hz, 2 H), 3.51 (d, *J* = 15.4 Hz, 1 H), 3.04 (dd, *J* = 15.4, 1.7 Hz, 1 H), 2.30 (s, 3 H), 1.96 (s, 3 H), 1.24 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 169.6, 165.7, 165.3, 142.4, 137.7, 126.5, 101.4, 94.8, 94.1, 59.7, 43.5, 23.9, 14.3, 13.9.

*Ethyl 5-acetamido-2-methyl-5-(4-nitrophenyl)-4,5-dihydrofuran-3-carboxylate (**1g**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.7 Hz, 2 H), 7.59 (d, *J* = 8.8 Hz, 2 H), 6.89 (s, 1 H), 4.14 (q, *J* = 7.1 Hz, 2 H), 3.38 (d, *J* = 15.7 Hz, 1 H), 3.05 (dd, *J* = 15.7, 1.7 Hz, 1 H), 2.34 (s, 3 H), 1.99 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 169.7, 165.9,

165.1, 149.2, 147.4, 125.6, 123.9, 101.1, 94.2, 59.9, 44.5, 23.7, 14.3, 14.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{18}N_2NaO_6$ 357.1057, found 357.1060.

*Ethyl 5-acetamido-2-methyl-5-(3-nitrophenyl)-4,5-dihydrofuran-3-carboxylate (**1h**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (t, *J* = 1.7 Hz, 1 H), 8.17 (d, *J* = 8.1 Hz, 1 H), 7.81–7.76 (m, 1 H), 7.56 (t, *J* = 8.0 Hz, 1 H), 6.77 (bs, 1 H), 4.15 (q, *J* = 7.1 Hz, 2 H), 3.42 (d, *J* = 15.6 Hz, 1 H), 3.10 (dd, *J* = 15.7, 1.8 Hz, 1 H), 2.35 (s, 3 H), 2.01 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 169. 7, 165.9, 165.1, 148.4, 144.5, 130.9, 129.7, 123.1, 120.0, 101.3, 94.1, 60.0, 44.5, 23.8, 14.3, 14.1.

*Ethyl 5-acetamido-2-methyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-carboxylate (**1i**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 4.2 Hz, 1 H), 7.13 (d, *J* = 2.9 Hz, 1 H), 6.99 (dd, *J* = 5.1, 3.6 Hz, 1 H), 6.41 (bs, 1 H), 4.14 (q, *J* = 7.1 Hz, 2 H), 3.76 (d, *J* = 15.3 Hz, 1 H), 3.28 (dq, *J* = 15.4, 1.6 Hz, 1 H), 2.27 (s, 3 H), 2.04–1.96 (m, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 169.2, 165.4, 165.0, 146.5, 127.1, 125.7, 124.2, 102.2, 93.6, 59.7, 42.8, 24.0, 14.4, 13.8.

*N-(4-acetyl-5-methyl-2-(thiophen-2-yl)-2,3-dihydrofuran-2-yl)acetamide (**1j**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.25 (m, 1 H), 7.11 (d, *J* = 2.8 Hz, 1 H), 6.97 (dd, *J* = 5.0, 3.6 Hz, 1 H), 6.76 (bs, 1 H), 3.82 (d, *J* = 15.0 Hz, 1 H), 3.29 (dd, *J* = 15.1, 1.6 Hz, 1 H), 2.27 (s, 3 H), 2.16 (s, 3 H), 2.03–1.95 (m, 3 H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 194.3, 169.5, 164.6, 146.3, 127.1, 125.7, 124.2, 111.9, 93.6, 43.4, 29.4, 23.9, 14.7.

*Ethyl 5-acetamido-2-methyl-5-(naphthalen-2-yl)-4,5-dihydrofuran-3-carboxylate (**1k**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00–7.73 (m, 4 H), 7.51–7.49 (m, 3 H), 6.54 (s, 1 H), 4.12 (q, *J* = 7.1 Hz, 2 H), 3.72 (d, *J* = 15.3 Hz, 1 H), 3.18 (d, *J* = 15.5 Hz, 1 H), 2.39 (s, 3 H), 1.99 (s, 3 H), 1.24 (t, *J* = 7.1 Hz, 3 H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 169.6, 165.8, 165.5, 139.9, 133.0, 132.9, 128.9, 128.4, 127.6, 126.6 (two carbons overlap), 123.4, 122.4, 101.7, 95.3, 59.6, 42.9, 24.0, 14.3, 14.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{21}NNaO_4$ 362.1363, found 362.1369.

*N-(4-acetyl-5-methyl-2-(naphthalen-2-yl)-2,3-dihydrofuran-2-yl)acetamide (**1l**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91–7.83 (m, 4 H), 7.52–7.50 (m, 3 H), 6.50 (s, 1 H), 3.84 (d, *J* = 14.8 Hz, 1 H), 3.24 (d, *J* = 14.8 Hz, 1 H), 2.40 (s, 3 H), 2.18 (s, 3 H), 2.02 (s, 3 H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 194.2, 169.9, 165.5, 139.7, 132.9, 132.8, 128.8, 128.3, 127.5, 126.5 (two carbons overlap), 123.3, 122.3, 111.6, 95.3, 43.4, 29.3, 23.8, 14.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{19}NNaO_3$ 332.1257, found 332.1264.

*Methyl 5-acetamido-2-methyl-5-phenyl-4,5-dihydrofuran-3-carboxylate (**1m**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.29 (m, 5 H), 6.45 (bs, 1 H), 3.67 (d, *J* = 15.2 Hz, 1 H), 3.65 (s, 3 H), 3.09 (dd, *J* = 15.2, 1.5 Hz, 1 H), 2.32 (s, 3 H), 1.97 (s, 3 H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 169.6, 166.0, 165.9, 142.9, 128.7, 128.5, 124.4, 101.3, 95.3, 50.8, 42.8, 24.0, 13.9.

*Tert-butyl 5-acetamido-2-methyl-5-phenyl-4,5-dihydrofuran-3-carboxylate (**1n**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.29 (m, 5 H), 6.38 (bs, 1 H), 3.58 (d, *J* = 15.4 Hz, 1 H), 3.06 (dd, *J* = 15.4, 1.7 Hz, 1 H), 2.29 (s, 3 H), 1.98 (s, 3 H), 1.45 (s, 9 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 169.6, 165.0, 164.6, 142.9, 128.6, 128.2, 124.5, 102.8, 94.8, 79.7, 43.5, 28.3, 23.9, 13.9.

*Benzyl 5-acetamido-2-methyl-5-phenyl-4,5-dihydrofuran-3-carboxylate (**1o**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2 H), 7.36–7.23 (m, 7 H), 6.69 (s, 1 H), 5.11 (s, 2 H), 3.52 (d, *J* = 15.3 Hz, 1 H), 3.05 (dd, *J* = 15.4, 1.6 Hz, 1 H), 2.31 (s, 3 H), 1.92 (s, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 169.7, 166.4, 165.0, 141.6, 136.2, 131.7, 128.4, 128.0 (two carbons overlap), 126.3, 122.3, 101.1, 94.9, 65.5, 43.4, 23.8, 14.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{21}NNaO_4$ 374.1363, found 374.1365.

*N-(4-acetyl-5-methyl-2-phenyl-2,3-dihydrofuran-2-yl)acetamide (**1p**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.30 (m, 5 H), 6.56 (br, 1 H), 3.75 (d, *J* = 14.8 Hz, 1 H), 3.13 (d, *J* = 14.8 Hz, 1 H), 2.34 (s, 3 H), 2.16 (s, 3 H), 1.99 (s, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 194.2, 169.7, 165.3, 142.8, 128.8, 128.6, 124.4, 111.8, 95.2, 43.4, 29.4, 24.0, 14.8.

*N-(5-ethyl-2-phenyl-4-propionyl-2,3-dihydrofuran-2-yl)acetamide (**1q**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61–7.29 (m, 5 H), 6.39 (s, 1 H), 3.81 (d, *J* = 14.6 Hz, 1 H), 3.15 (dd, *J* = 14.9, 1.6 Hz, 1 H), 2.46–2.39 (m, 2 H), 2.37 (s, 3 H), 2.24 (q, *J* = 7.3 Hz, 2 H), 1.13 (t, *J* = 7.5 Hz, 3 H), 1.05 (t, *J* = 7.2 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 197.3, 173.2, 164.8, 143.0, 128.8, 128.5, 124.4, 110.7, 95.2, 43.1, 34.6, 29.9, 14.7, 9.1, 7.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{21}NNaO_3$ 310.1414, found 310.1417.

*N-(4-oxo-2-phenyl-2,3,4,5,6,7-hexahydrobenzofuran-2-yl)acetamide (**1r**)*[9b]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.33 (m, 5 H), 6.80 (bs, 1 H), 3.52 (d, *J* = 14.8 Hz, 1 H), 3.00 (d, *J* = 14.8 Hz, 1 H), 2.57–2.51 (m, 2 H), 2.42–2.24 (m, 2 H), 2.13–2.03 (m, 2 H), 1.98 (s, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 195.3, 175.4, 169.8, 142.4, 128.8, 128.6, 124.4, 112.4, 98.6, 39.6, 36.3, 23.9, 23.6, 21.6.

*N-(2-(4-fluorophenyl)-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran-2-yl)acetamide (**1s**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1 H), 7.40–7.28 (m, 2 H), 7.06–6.95 (m, 2 H), 3.37 (d, *J* = 15.1 Hz, 1 H), 2.85 (d, *J* = 15.1 Hz, 1 H), 2.54–2.51 (m, 2 H), 2.32–2.24 (m, 2 H), 2.10–2.01 (m, 2 H), 1.91 (s, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 195.5, 175.9, 170.3, 162.3 (d, $^1J_{CF}$ = 247.6 Hz), 138.1, 126.3 ($^3J_{CF}$ = 8.2 Hz), 115.4 ($^2J_{CF}$ = 21.8 Hz), 111.9, 98.2, 40.2, 36.2, 23.5 (two carbons overlap), 21.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{16}FNNaO_3$ 312.1006, found 312.1010.

*N-(6,6-dimethyl-4-oxo-2-phenyl-2,3,4,5,6,7-hexahydrobenzofuran-2-yl)acetamide (**1t**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.28 (m, 5 H), 6.55 (s, 1 H), 3.58 (d, *J* = 14.9 Hz, 1 H), 3.03 (d, *J* = 14.9 Hz, 1 H), 2.49–2.36 (m, 2 H), 2.28–2.16 (m, 2

H), 2.00 (s, 3 H), 1.18 (s, 3 H), 1.11 (s, 3 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 194.6, 174.1, 169.6, 142.6, 128.9, 128.8, 124.3, 111.1, 98.7, 50.8, 39.3, 37.4, 34.2, 28.9, 28.4, 24.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{21}NNaO_3$ 322.1414, found 322.1412.

*Tert-butyl 5-acetamido-5-(4-bromophenyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (**1u**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.4 Hz, 2 H), 7.30 (d, *J* = 8.6 Hz, 2 H), 6.61 (s, 1 H), 3.43 (d, *J* = 15.6 Hz, 1 H), 3.00 (dd, *J* = 15.4, 1.3 Hz, 1 H), 2.27 (s, 3 H), 1.96 (s, 3 H), 1.45 (s, 9 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 169.5, 164.8, 164.6, 141.8, 131.7, 126.4, 122.2, 102.8, 94.4, 80.0, 44.1, 28.3, 23.9, 14.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{22}BrNNaO_4$ 417.0546, found 417.0552.

*Benzyl 5-acetamido-5-(4-bromophenyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (**1v**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2 H), 7.36–7.23 (m, 7 H), 6.69 (s, 1 H), 5.11 (s, 2 H), 3.52 (d, *J* = 15.3 Hz, 1 H), 3.05 (dd, *J* = 15.4, 1.6 Hz, 1 H), 2.31 (s, 3 H), 1.92 (s, 3 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 169.7, 166.4, 165.0, 141.6, 136.2, 131.7, 128.4, 128.0 (two carbons overlap), 126.3, 122.3, 101.1, 94.9, 65.5, 43.4, 23.8, 14.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{20Br}NNaO_4$ 452.0468, found 452.0476.

*Ethyl 2-methyl-5-phenyl-5-propionamido-4,5-dihydrofuran-3-carboxylate (**1w**)*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.27 (m, 5 H), 6.61 (s, 1 H), 4.09 (q, *J* = 7.1 Hz, 2 H), 3.62 (d, *J* = 15.2 Hz, 1 H), 3.05 (d, *J* = 15.2 Hz, 1 H), 2.31 (s, 3 H), 2.18 (q, *J* = 7.4 Hz, 2 H), 1.21 (t, *J* = 7.1 Hz, 3 H), 1.08 (t, *J* = 7.4 Hz, 3 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 173.3, 165.7, 165.5, 143.0, 128.6, 128.3, 124.3, 101.4, 95.1, 59.5, 43.0, 29.7, 14.3, 13.9, 9.01. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{19}NNaO_5$ 340.1155, found 340.1159.

*N-(4-benzoyl-2,5-diphenyl-2,3-dihydrofuran-2-yl)acetamide (**1x**)*[9a]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.48 (m, 4 H), 7.44–7.34 (m, 3 H), 7.31 (d, *J* = 7.4 Hz, 2 H), 7.25–7.16 (m, 2 H), 7.10–7.07 (m, 4 H), 6.67 (bs, 1 H), 4.01 (d, *J* = 15.8 Hz, 1 H), 3.57 (d, *J* = 15.9 Hz, 1 H), 2.05 (s, 3 H)； $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 193.4, 169.7, 163.2, 143.1, 139.0, 131.2, 129.9, 129.7, 129.3, 129.0, 128.9, 128.7, 127.7, 127.6, 124.6, 111.7, 94.9, 45.5, 24.1.

General procedure to prepare oxazole 2 from 2-amidodihydrofurans 1. To a 35 mL tube (total volume 50 mL) with a stir bar was added 2-amidodihydrofuran (0.2 mmol), $Mn(OAc)_3{\cdot}2H_2O$ (0.02 mmol, 5.4 mg), K_2CO_3 (0.1 mmol, 14 mg) and 2 mL of MeCN. The mixture was stirred at 100 ºC for 18 h, cooled to room temperature, poured into brine and extracted with EtOAc. The combined extracts were dried over $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography (PE/EA = 6:1) to afford the desired oxazoles **2**.

*Ethyl 3-hydroxy-2-(2-methyl-4-phenyloxazol-5-yl)but-2-enoate (**2a**)*: 45 mg of **2a** was obtained from **1a** (57.8 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 78%; R_f= 0.20 (6:1 PE/EA); slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.49 (s, 1 H), 7.66–7.64 (m, 2 H), 7.39–7.32 (m, 2 H), 7.30–7.22 (m, 1 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 2.51 (s, 3 H), 1.88 (s, 3 H), 1.08 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 179.3, 171.8, 160.8, 139.7, 137.2, 132.0, 128.5, 127.5, 125.9, 93.0, 61.1, 19.9, 14.1, 14.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{18}NO_4$ 288.1230, found 288.1229.

*Ethyl 3-hydroxy-2-(2-methyl-4-(p-tolyl)oxazol-5-yl)but-2-enoate (**2b**)*: 32 mg of **2b** was obtained from **1b** (60.6 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 53%; R_f= 0.34 (6:1 PE/EA); yellow solid; m.p. 59 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.48 (s, 1 H), 7.54 (d, *J*=8.2 Hz, 2 H), 7.16 (d, *J*=8.0 Hz, 2 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 2.50 (s, 3 H), 2.34 (s, 3 H), 1.86 (s, 3 H), 1.10 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 179.2, 171.9, 160.7, 139.2, 137.2, 137.2, 129.2, 129.1, 125.8, 93.1, 61.1, 21.2, 19.8, 14.1, 14.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{20}NO_4$ 302.1387, found 302.1383.

*Ethyl 3-hydroxy-2-(4-(4-methoxyphenyl)-2-methyloxazol-5-yl)but-2-enoate (**2c**)*: 41 mg of **2c** was obtained from **1c** (63.8 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 65%; R_f= 0.22 (6:1 PE/EA); slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.47 (s, 1 H), 7.58 (d, *J* = 8.9 Hz, 2 H), 6.89 (d, *J* = 8.9 Hz, 2 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 3.81 (s, 3 H), 2.49 (s, 3 H), 1.86 (s, 3 H), 1.11 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 179.3, 171.9, 160.6, 159.0, 138.6, 137.0, 127.2, 124.6, 113.9, 93.0, 61.1, 55.2, 19.9, 14.1, 14.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{20}NO_5$ 318.1336, found 318.1320.

*Ethyl 2-(4-(4-fluorophenyl)-2-methyloxazol-5-yl)-3-hydroxybut-2-enoate (**2d**)*: 37 mg of **2d** was obtained from **1d** (61.4 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 60%; R_f= 0.37 (6:1 PE/EA); slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.49 (s, 1 H), 7.78–7.40 (m, 2 H), 7.15–6.88 (m, 2 H), 4.15 (q, *J* = 7.1 Hz, 2 H), 2.49 (s, 3 H), 1.87 (s, 3 H), 1.08 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 179.4, 171.7, 162.2 (d, $^1J_{CF}$ = 247.2 Hz), 160.8, 139.4 (d, $^5J_{CF}$ = 1.5 Hz), 136.4, 128.2 (d, $^4J_{CF}$ = 3.3 Hz), 127.7 (d, $^3J_{CF}$ = 8.0 Hz), 115.5 (d, $^2J_{CF}$ = 21.6 Hz), 92.8, 61.1, 19.9, 14.1, 14.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}FNO_4$ 306.1136, found 306.1126.

*Ethyl 2-(4-(4-bromophenyl)-2-methyloxazol-5-yl)-3-hydroxybut-2-enoate (**2e**)*: 46 mg of **2e** was obtained from **1e** (73.6 mg, 0.2 mmol). Purified by column chromatography (4:1 PE/EA), yield 63%; R_f= 0.29 (4:1 PE/EA); yellow solid; m.p. 73 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.49 (s, 1 H), 7.55–7.50 (m, 2 H), 7.48–7.43 (m, 2 H), 4.15 (q, *J* = 7.1 Hz, 2 H), 2.49 (s, 3 H), 1.87 (s, 3 H), 1.09 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 179.4, 171.5, 160.9, 140.0, 136.3, 131.6,

131.0, 127.5, 121.4, 92.7, 61.2, 19.9, 14.1, 14.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}BrNO_4$ 366.0335, found 366.0301.

*Ethyl 3-hydroxy-2-(4-(4-iodophenyl)-2-methyloxazol-5-yl)but-2-enoate (**2f**)*: 62 mg of **2f** was obtained from **1f** (83 mg, 0.2 mmol). Purified by column chromatography (4:1 PE/EA), yield 75%; R_f = 0.34 (4:1 PE/EA); white solid; m.p. 69 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.49 (s, 1 H), 7.68–7.66 (d, J = 8.6 Hz, 2 H), 7.50–7.32 (m, 2 H), 4.15 (q, J = 7.1 Hz, 2 H), 2.50 (s, 3 H), 1.87 (s, 3 H), 1.09 (t, J = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 179.4, 171.5, 160.9, 140.2, 137.6, 136.3, 131.5, 127.6, 93.0, 92.7, 61.2, 19.9, 14.1, 14.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}INO_4$ 414.0197, found 414.0193.

*Ethyl 3-hydroxy-2-(2-methyl-4-(4-nitrophenyl)oxazol-5-yl)but-2-enoate (**2g**)*: 28 mg of **2g** was obtained from **1g** (66.8 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 42%; R_f = 0.24 (6:1 PE/EA); yellow solid; m.p. 108 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.56 (s, 1 H), 8.32–8.16 (m, 2 H), 7.92–7.70 (m, 2 H), 2.53 (s, 3 H), 1.91 (s, 3 H), 1.07 (t, J = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 179.8, 171.2, 161.4, 146.7, 142.2, 138.5, 135.5, 126.4, 123.9, 92.5, 61.4, 20.0, 14.04, 13.98; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{17}N_2NaO_6$ 355.0901, found 355.0904.

*Ethyl 3-hydroxy-2-(2-methyl-4-(3-nitrophenyl)oxazol-5-yl)but-2-enoate (**2h**)*: 29 mg of **2h** was obtained from **1h** (66.8 mg, 0.2 mmol). Purified by column chromatography (4:1 PE/EA), yield 43%; R_f = 0.28 (4:1 PE/EA); slightly yellow solid; m.p. 113 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.56 (s, 1 H), 8.55 (t, J = 1.9 Hz, 1 H), 8.11 (ddd, J = 8.2, 2.2, 0.7 Hz, 1 H), 7.96–7.88 (m, 1 H), 7.52 (t, J = 8.0 Hz, 1 H), 7.26 (s, 1 H), 4.17 (q, J = 7.1 Hz, 2 H), 2.53 (s, 3 H), 1.90 (s, 3 H), 1.07 (t, J = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 179.9, 171.3, 161.3, 148.6, 141.2, 135.4, 133.9, 131.4, 129.4, 122.1, 120.9, 92.3, 61.3, 20.0, 14.04, 13.97; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{17}N_2O_6$ 333.1081, found 333.1097.

*Ethyl 3-hydroxy-2-(2-methyl-4-(thiophen-2-yl)oxazol-5-yl)but-2-enoate (**2i**)*: 30 mg of **2i** was obtained from **1i** (59 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 51%; R_f = 0.40 (6:1 PE/EA); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.60 (s, 1 H), 7.27–7.23 (m, 2 H), 7.03 (dd, J = 5.1, 3.6 Hz, 1 H), 4.18 (q, J = 7.1 Hz, 2 H), 2.50 (s, 3 H), 1.93 (s, 3 H), 1.14 (t, J = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 180.1, 171.7, 161.1, 138.7, 134.4, 133.7, 127.5, 125.0, 124.0, 92.0, 61.2, 19.8, 14.1, 14.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{16}NO_4S$ 294.0795, found 294.0807.

*4-Hydroxy-3-(2-methyl-4-(thiophen-2-yl)oxazol-5-yl)pent-3-en-2-one (**2j**)*: 25 mg of **2j** was obtained from **1j** (53 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 47%; R_f = 0.28 (6:1 PE/EA); yellow solid; m.p. 102 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 17.04 (s, 1 H), 7.29 (dd, J = 3.6, 1.1 Hz, 1 H), 7.28–7.26 (m, 1 H), 7.05 (dd, J = 5.1, 3.6 Hz, 1 H),

2.53 (s, 3 H), 1.99 (s, 6 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 194.1, 161.7, 139.9, 134.1, 133.8, 127.7, 125.4, 124.2, 102.0, 23.6, 14.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{14}NO_3S$ 264.0689, found 264.0686.

*Ethyl 3-hydroxy-2-(2-methyl-4-(naphthalen-2-yl)oxazol-5-yl)but-2-enoate (**2k**)*: 44 mg of **2k** was obtained from **1k** (67.8 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 66%; R_f= 0.32 (6:1 PE/EA); slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.56 (s, 1 H), 8.23 (s, 1 H), 7.90–7.83 (m, 1 H), 7.83–7.78 (m, 2 H), 7.72 (dd, *J* = 8.6, 1.7 Hz, 1 H), 7.51–7.42 (m, 2 H), 4.18 (q, *J* = 7.1 Hz, 2 H), 2.56 (s, 3 H), 1.90 (s, 3 H), 1.08 (t, *J* = 7.1 Hz, 3 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 179.4, 171.8, 160.9, 140.1, 137.2, 133.4, 132.6, 129.4, 128.3, 128.1, 127.6, 126.2, 126.0, 125.0, 123.6, 93.1, 61.2, 19.9, 14.1, 14.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}NO_4$ 338.1387, found 338.1392.

*4-Hydroxy-3-(2-methyl-4-(naphthalen-2-yl)oxazol-5-yl)pent-3-en-2-one (**2l**)*: 44 mg of **2l** was obtained from **1l** (61.8 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 71%; R_f= 0.28 (6:1 PE/EA); slightly yellow solid; m.p. 92 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 17.06 (s, 1 H), 8.26 (d, *J* = 0.8 Hz, 1 H), 7.89–7.85 (m, 1 H), 7.85–7.77 (m, 2 H), 7.73 (dd, *J* = 8.6, 1.7 Hz, 1 H), 7.52–7.43 (m, 2 H), 2.58 (s, 3 H), 2.00 (s, 6 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 193.8, 161.5, 141.4, 137.4, 133.5, 132.8, 128.8, 128.5, 128.3, 127.6, 126.4, 126.3, 125.1, 123.2, 103.3, 23.8, 14.1; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{17}NNaO_3$ 330.1101, found 330.1100.

*Methyl 3-hydroxy-2-(2-methyl-4-phenyloxazol-5-yl)but-2-enoate (**2m**)*: 41 mg of **2m** was obtained from **1m** (55 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 75%; R_f= 0.24 (6:1 PE/EA); slightly yellow solid; m.p. 72 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.38 (s, 1 H), 7.67–7.65 (m, 2 H), 7.37–7.33 (m, 2 H), 7.28–7.24 (m, 1 H), 3.70 (s, 3 H), 2.51 (s, 3 H), 1.85 (s, 3 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 179.4, 172.2, 160.9, 139.5, 137.2, 131.8, 128.6, 127.5, 125.8, 92.7, 52.1, 19.8, 14.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO_4$ 274.1074, found 274.1064.

*Tert-butyl 3-hydroxy-2-(2-methyl-4-phenyloxazol-5-yl)but-2-enoate (**2n**)*: 25 mg of **2n** was obtained from **1n** (63.4 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 40%; R_f= 0.44 (6:1 PE/EA); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.67 (s, 1 H), 7.66–7.64 (m, 2 H), 7.37–7.33 (m, 2 H), 7.27–7.25 (m, 1 H), 2.50 (s, 3 H), 1.90 (s, 3 H), 1.27 (s, 9 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 178.7, 171.3, 160.4, 140.3, 136.8, 132.3, 128.4, 127.3, 126.0, 94.1, 82.3, 27.9, 20.0, 14.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{22}NO_4$ 316.1543, found 316.1541.

*Benzyl 3-hydroxy-2-(2-methyl-4-phenyloxazol-5-yl)but-2-enoate (**2o**)*: 50 mg of **2o** was obtained from **1o** (70.2 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 72%; R_f= 0.28 (6:1 PE/EA); slightly yellow solid; m.p. 72 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.35 (s, 1 H), 7.69–7.59 (m, 2 H), 7.37–7.30 (m, 2 H), 7.30–7.20 (m, 4 H), 7.09–7.06 (m, 2 H), 5.15 (s, 2 H), 2.50 (s, 3 H), 1.89 (s, 3 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 179.8, 171.5, 160.9, 139.5, 137.4, 135.4,

131.8, 128.6, 128.4, 128.0, 127.6, 127.4, 126.0, 92.9, 66.4, 19.9, 14.1; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{19}NNaO_4$ 372.1206, found 372.1208.

*4-Hydroxy-3-(2-methyl-4-phenyloxazol-5-yl)pent-3-en-2-one (**2p**)*: 35 mg of **2p** was obtained from **1p** (51.8 mg, 0.2 mmol). Purified by column chromatography (4:1 PE/EA), yield 68%; R_f = 0.29 (4:1 PE/EA); brown solid; m.p. 46 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 16.98 (s, 1 H), 7.69–7.67 (m, 2 H), 7.41–7.33 (m, 2 H), 7.31–7.25 (m, 1 H), 2.53 (s, 3 H), 1.96 (s, 6 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 193.7, 161.3, 141.0, 137.4, 131.4, 128.8, 127.9, 125.7, 103.2, 23.7, 14.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO_3$ 258.1125, found 258.1128.

*5-Hydroxy-4-(2-methyl-4-phenyloxazol-5-yl)hept-4-en-3-one (**2q**)*: 30 mg of **2q** was obtained from **1q** (57.4 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 53%; R_f = 0.50 (6:1 PE/EA); slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 17.02 (s, 1 H), 7.71–7.69 (m, 2 H), 7.41–7.33 (m, 2 H), 7.30–7.26 (m, 1 H), 2.85 (q, J = 7.6 Hz, 2 H), 2.42–2.10 (m, 2 H), 1.94 (s, 3 H), 1.39 (t, J = 7.6 Hz, 3 H), 1.01 (t, J = 7.4 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 198.4, 192.1, 165.6, 140.7, 137.2, 131.5, 128.7, 127.8, 125.7, 102.6, 30.1, 23.2, 21.9, 11.3, 8.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{20}NO_3$ 286.1438, found 286.1440.

*2-(2-Methyl-4-phenyloxazol-5-yl)cyclohexane-1,3-dione (**2r**)*: 50 mg of **2r** was obtained from **1r** (54.2 mg, 0.2 mmol). Purified by column chromatography (19:1 DCM/MeOH), yield 93%; R_f = 0.21 (1:1 DCM/MeOH); slightly yellow solid; m.p. 196 ºC; ^{1}H NMR (400 MHz, MeOD) δ 7.56–7.54 (m, 2 H), 7.37–7.30 (m, 2 H), 7.26–7.22 (m, 1 H), 2.58 (t, J = 6.4 Hz, 4 H), 2.48 (s, 3 H), 2.14–2.04 (m, 2 H); ^{13}C{^{1}H}NMR (100 MHz, MeOD) δ 193.8, 162.5, 142.6, 137.5, 133.7, 129.2, 128.1, 127.1, 106.4, 35.6, 22.0, 13.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}NO_3$ 270.1125, found 270.1100.

*2-(4-(4-Fluorophenyl)-2-methyloxazol-5-yl)cyclohexane-1,3-dione (**2s**)*: 55 mg of **2s** was obtained from **1s** (57.8 mg, 0.2 mmol). Purified by column chromatography (19:1 DCM/MeOH), yield 96%; R_f = 0.17 (1:1 DCM/MeOH); slightly yellow solid; m.p. 212 ºC; ^{1}H NMR (400 MHz, MeOD) δ 7.62–7.55 (m, 2 H), 7.10–6.99 (m, 2 H), 2.53 (t, J = 6.4 Hz, 4 H), 2.46 (s, 3 H), 2.09–2.03 (m, 2 H); ^{13}C{^{1}H}NMR (100 MHz, MeOD) δ 192.5, 163.5 ($^1J_{CF}$ = 245.1 Hz), 162.9, 141.2, 137.3, 130.0 ($^4J_{CF}$ = 3.2 Hz), 129.1 (d, $^3J_{CF}$ = 8.0 Hz), 116.0 (d, $^2J_{CF}$ = 21.8 Hz), 106.7, 34.9, 21.8, 13.7; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNNaO_3$ 310.0850, found 310.0853.

*5,5-Dimethyl-2-(2-methyl-4-phenyloxazol-5-yl)cyclohexane-1,3-dione (**2t**)*: 54 mg of **2t** was obtained from **1t** (59.8 mg, 0.2 mmol). Purified by column chromatography (15:1 DCM/MeOH), yield 91%; R_f = 0.24 (15:1 DCM/MeOH); slightly yellow solid; m.p. 191 ºC; ^{1}H NMR (400 MHz, MeOD) δ 7.55–7.53 (m, 2 H), 7.35–7.29 (m, 2 H), 7.28–7.20 (m, 1 H), 2.48 (s, 3 H),

2.47 (s, 4 H), 1.16 (s, 6 H); $^{13}C\{^{1}H\}$NMR (100 MHz, MeOD) δ 190.0, 163.3, 139.8, 138.9, 133.2, 129.4, 128.6, 127.4, 106.3, 47.9, 32.9, 28.5, 13.7; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{19}NNaO_3$ 320.1257, found 320.1255.

*Tert-butyl 2-(4-(4-bromophenyl)-2-methyloxazol-5-yl)-3-hydroxybut-2-enoate (**2u**)*: 39 mg of **2u** was obtained from **1u** (79.2 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 49%; R_f= 0.28 (6:1 PE/EA); slightly yellow solid; m.p. 78 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.66 (s, 1 H), 7.55–7.51 (m, 2 H), 7.49–7.46 (m, 2 H), 2.49 (s, 3 H), 1.89 (s, 3 H), 1.28 (s, 9 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 178.9, 171.1, 160.6, 140.7, 135.9, 131.6, 131.3, 127.5, 121.2, 93.8, 82.5, 27.9, 20.0, 14.0; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{20}BrNO_4$ 416.0468, found 416.0465.

*Benzyl 2-(4-(4-bromophenyl)-2-methyloxazol-5-yl)-3-hydroxybut-2-enoate (**2v**)*: 54 mg of **2v** was obtained from **1v** (86 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 63%; R_f= 0.28 (6:1 PE/EA); slightly yellow solid; m.p. 96 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.37 (s, 1 H), 7.51–7.46 (m, 2 H), 7.44–7.38 (m, 2 H), 7.28–7.20 (m, 3 H), 7.09–7.03 (m, 2 H), 5.14 (s, 2 H), 2.49 (s, 3 H), 1.90 (s, 3 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 179.9, 171.2, 161.0, 139.8, 136.5, 135.3, 131.7, 130.8, 128.4, 128.1, 127.6, 127.5, 121.5, 92.7, 66.5, 20.0, 14.1; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{18}BrNNaO_4$ 450.0311, found 450.0333.

*Ethyl 2-(2-ethyl-4-phenyloxazol-5-yl)-3-hydroxybut-2-enoate (**2w**)*: 39 mg of **2w** was obtained from **1w** (60.6 mg, 0.2 mmol). Purified by column chromatography (6:1 PE/EA), yield 65%; R_f= 0.45 (6:1 PE/EA); slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.48 (s, 1 H), 7.67–7.65 (m, 2 H), 7.37–7.33 (m, 2 H), 7.27–7.23 (m, 1H), 4.15 (q, J = 7.1 Hz, 2 H), 2.84 (q, J = 7.6 Hz, 2 H), 1.87 (s, 3 H), 1.38 (t, J = 7.6 Hz, 3 H), 1.08 (t, J = 7.1 Hz, 3 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 179.1, 171.8, 165.1, 139.5, 136.9, 132.1, 128.5, 127.4, 126.0, 93.1, 61.0, 21.9, 19.9, 13.9, 11.3; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{19}NNaO_4$ 324.1206, found 324.1201.

*(2-Methyl-5-phenyl-1H-pyrrol-3-yl)(phenyl)methanone (**2x**)*: 45 mg of **2x** was obtained from **1x** (76.6 mg, 0.2 mmol). Purified by column chromatography (4:1 PE/EA), yield 86%; R_f= 0.36 (4:1 PE/EA); slightly yellow solid; m.p. 206 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1 H), 7.89–7.81 (m, 2 H), 7.56–7.52 (m, 1 H), 7.50–7.41 (m, 4 H), 7.37–7.33 (m, 2 H), 7.24–7.19 (m, 1 H), 6.68 (d, J = 2.8 Hz, 1 H), 2.62 (s, 3 H); $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ 192.5, 140.4, 137.5, 131.6, 131.3, 129.7, 129.02, 128.96, 128.1, 126.7, 123.8, 121.2, 109.2, 13.9; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{15}NO$ 284.1046, found 284.1051.

General procedure for further transformations.

*5-(3,5-Dimethyl-1H-pyrazol-4-yl)-2-methyl-4-phenyloxazole (**3**)*: To a 15 mL tube with a stir bar was added **2p** (51 mg, 0.2 mmol) and hydrazine hydrate (40 mg, 0.8 mmol) and THF (2 mL). Then the mixture was stirred at 70 ºC for 12 h, cooled to

room temperature, poured into brine and extracted with EtOAc. The combined extracts were dried over $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography to afford the corresponding pyrazole **3** (45 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1 H), 7.60–7.55 (m, 2 H), 7.30 (t, *J* = 7.4 Hz, 2 H), 7.25–7.21 (t, *J* = 7.3 Hz, 1 H), 2.54 (s, 3 H), 2.13 (s, 6 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 160.9, 144.3, 138.9, 136.1, 132.1, 128.4, 127.4, 126.1, 107.1, 14.1, 11.5; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{15}N_3O$ 276.1107, found 276.1106.

1-(3-Methyl-2-(2-methyl-4-phenyloxazol-5-yl)-2H-azirin-2-yl)ethanone (4): **2p** (51 mg, 0.2 mmol) and ammonium formate (50 mg, 0.8 mmol) and EtOH (4 mL) were introduced into a 15 mL tube with a stir bar, and the mixture was stirred at 90 ºC for 12 h. After the reaction was completed, it was cooled to room temperature, poured into brine and extracted with EtOAc. The combined extracts were dried over $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography to give the corresponding enamine. Then the enamine and DCE (2 mL) was added to a 15 mL tube with a stir bar. The mixture was cooled to 0 ºC, followed by the $PhI(OAc)_2$ (77 mg, 0.24 mmol). Then the mixture was stirred at room temperature for 6 h, poured into brine and extracted with EtOAc. The combined extracts were dried over $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography to provide the corresponding 2*H*-azirine **4** (33 mg, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.3 Hz, 2 H), 7.41 (t, *J* = 7.5 Hz, 2 H), 7.36–7.32 (m, 1 H), 2.50 (s, 3 H), 2.45 (s, 3 H), 2.10 (s, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 203.8, 161.1, 157.8, 143.0, 139.6, 131.0, 128.8, 128.5, 126.9, 39.4, 28.0, 14.1, 12.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{15}N_2O_2$ 255.1128, found 255.1125.

General procedure to prepare 5a from 1a: To a 50 mL Schlenk tube with a stir bar was added 2-amidodihydrofuran **1a** (58 mg, 0.2 mmol), K_2CO_3 (55 mg, 0.4 mmol) and 2 mL of MeCN. The mixture was stirred under argon at 100 ºC for 18 h. After the reaction was completed, it was cooled to room temperature, then poured into brine and extracted with EtOAc. The combined extracts were dried over $MgSO_4$, filtered, and evaporated. The residue was purified by column chromatography (PE/EA = 2:1) to afford the enamine **5a** (22 mg, 44% yield). **Major isomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.27 (m, 6 H), 5.94 (t, *J* = 7.1 Hz, 1 H), 4.17 (q, *J* = 7.1 Hz, 2 H), 3.18 (d, *J* = 7.1 Hz, 2 H), 2.13 (s, 3 H), 1.28 (t, *J* = 7.1 Hz, 3 H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 171.9, 168.3, 137.2, 136.4, 128.4, 128.3, 125.9, 116.0, 61.0, 34.0, 23.4, 14.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}NO_3$ 248.1281, found 248.1282. One isomer was confirmed by XRD, CCDC 1401603.

General procedure to prepare 5r from 1r: To a 100 mL Schlenk tube with a stir bar was added 2-amidodihydrofuran **1r** (271 mg, 1 mmol), K_2CO_3 (276 mg, 2 mmol) and 10 mL of MeCN. The mixture was stirred under argon at 100 ºC for 18 h, cooled to room temperature, poured into brine and extracted with EtOAc. The combined extracts were dried over $MgSO_4$,

filtered, and evaporated. The residue was purified by column chromatography (PE/EA) to afford the enamine **5r** (257 mg, 95% yield). *N-(2-(2,6-dioxocyclohexyl)-1-phenylvinyl)acetamide*: ^{1}H NMR (400 MHz, MeOD) δ 7.49 (d, *J* = 7.5 Hz, 2 H), 7.25 (t, *J* = 7.6 Hz, 2 H), 7.15 (t, *J* = 7.3 Hz, 1 H), 6.44 (s, 1 H), 2.44 (t, *J* = 6.3 Hz, 4 H), 2.01 (s, 3 H), 1.93 (t, *J* = 6.2 Hz, 2 H); ^{13}C{^{1}H}NMR (100 MHz, MeOD) δ 194.1, 170.7, 140.5, 133.1, 128.9, 127.5, 126.8, 117.0, 61.5, 36.8, 23.2, 22.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{18}NO_3$ 272.1281, found 272.1283.

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Supporting Information

Full ^{1}H and ^{13}C{^{1}H} NMR spectra of the new starting materials **1g, 1k, 1l, 1o, 1q, 1s, 1t, 1u, 1v** and **1w** and final products **2, 3, 4, 5** and X-ray crystallographic data for **2u** and **5a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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