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Cascade Cyclization of *o*-(2-Acyl-1-ethynyl)benzaldehydes with Amino Acid Derivatives: Synthesis of Indeno[2,1-*c*]pyran-3-ones and 1-Oxazolonylisobenzofurans via the Erlenmeyer−Plöchl Azlactone Reaction

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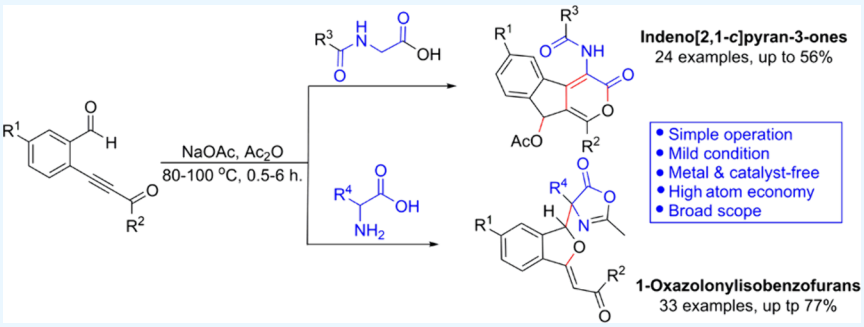

ABSTRACT: A highly regioselective divergent approach is reported for the synthesis of both indeno[2,1-*c*]pyran-3-one and 1-oxazolonylisobenzofuran derivatives using the Erlenmeyer−Plöchl azlactone (EPA) reaction. This approach involves the synthesis of *o*-(2-acyl-1-ethynyl)benzaldehydes, which reacted with various amino acids. Reaction with *N*-acylglycines resulted in the formation of indeno[2,1-*c*]pyran-3-ones, involving the sequential formation of two C−C bonds and two C−O bonds. Conversely, when the same conditions were applied to free amino acids, 1-oxazolonylisobenzofurans were obtained. This reaction involved the formation of a C−C bond between oxazolone and *o*-(2-acyl-1-ethynyl)benzaldehyde, followed by the formation of a C−O bond through a selective 5-*exo*-*dig* cyclization.

INTRODUCTION

In recent years, *o*-(2-acyl-1-ethynyl)benzaldehydes have been elaborated as a useful and versatile building block for constructing various structurally diverse organic frameworks including polycyclic products,[1] isoindolinone,[2] indenamine,[2a,3] isobenzofuran,[4] and indanone derivatives[5] frequently found as cores in many synthetically derived pharmaceuticals as well as natural products.[6] Indenopyrans, the 6/5/6-tricyclic-core-containing indenone derivatives fused with a pyran unit, are common in naturally occurring compounds with significant bioactivities as alcoholic fermentation activators and potential estrogen receptor binders while also displaying photoluminescence properties.[7] Nodulisporic acid (Figure 1A), isolated from an endophytic fungus, was used as an insecticidal agent since it exhibited both *in vitro* and *in vivo* antifeedant activity against fleas without toxicity to mammals.[8,9] Janthitrems E (Figure 1B) was isolated from cultures of *Penicillium janthinellum*.[10] Shearinine A (Figure 1C), an anti-insect, was isolated from the marine-derived fungus *Eupenicillium shearii* (NRRL 3324)[11] and *Penicillium janthinellum* Biourge[12] which was shown to induce apoptosis in human leukemia HL-60 cells. Isobenzofurans or phthalans are generally known as heterocyclic building blocks in a number of natural products with unique biological activities such as acremonide (Figure 1D), which was isolated from *Rhizophora apiculate* and showed antifungal activity against *C. albicans* and *C. neoformans*.[6a,13] In addition, (*Z*)-3-butylidenephthalide (Figure 1E), isolated from *Angelica glauca*, *Levisticum officinale*, and *Ligusticum porteri*, exhibits hypoglycemic activity,[14−17] while sinaspirolide (Figure 1F) is a dimeric phthalide natural product found in *Angelica sinensis* and contributes to the serotonergic activity.[18]

Various synthetic methodologies have been developed to construct indenopyrans and isobenzofurans from *o*-(2-acyl-1-ethynyl)benzaldehyde as a valuable synthon. Previously, Han

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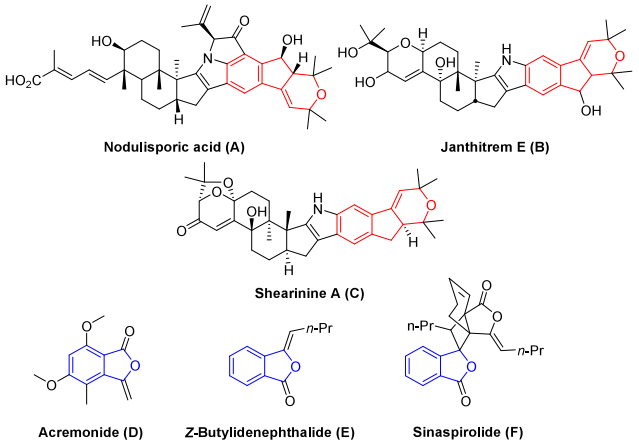
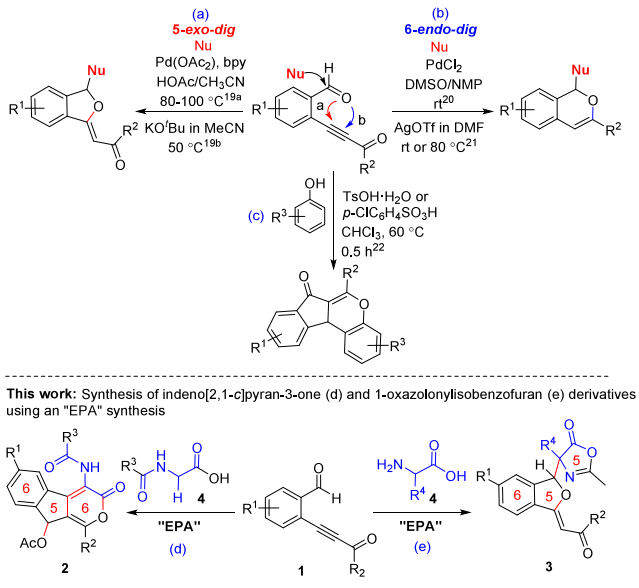


Figure 1. Selected bioactive compounds containing indenopyran and isobenzofuran skeletons.

reported an unexpected addition of acetic acid to *o*-(2-acyl-1-ethynyl)benzaldehydes catalyzed by palladium(II) acetate to provide dihydroisobenzofurans.[19a] Cao and You developed a KO^{t}Bu-mediated domino reaction of enynals with indoles to afford the corresponding indolyl-substituted isobenzofuran (Scheme 1a, Nu = indole).[19b] Other methods for the synthesis

Scheme 1. General Strategies for the Synthesis of (a) Isobenzofuran, (b) Isochroman, and (c) Indenopyran Using *o*-(2-Acyl-1-ethynyl)benzaldehydes and Our Strategy (d and e)



of isobenzofurans including iodocyclizations[19c] or intramolecular oxa-Michael reaction,[19d] oxo-cyclization/coupling,[19e] or intermolecular Heck coupling followed by intramolecular oxo-cyclization were previously reported through 5-*exo-dig* cyclization.[19f] However, another possibility for the reaction via 6-*endo-dig* cyclization was also reported. For instance, Li reported palladium-catalyzed domino reactions of *o*-(2-acyl-1-ethynyl)benzaldehydes with indoles to prepare 3-(1*H*-isochromen-1-yl)-1*H*-indole (Scheme 1b, Nu = indole).[20] Belmont and Michelet also reported hydroarylation/cycloisomerization reactions of *o*-(2-acyl-1-ethynyl)-benzaldehydes by silver catalysis to furnish the corresponding isochromene derivatives (Scheme 1b).[21] On the contrary, Cao and You reported the synthesis of tetracyclic indeno[2,1-*c*]chromen-7-one by acid-catalyzed domino reaction of *o*-(2-acyl-1-ethynyl)benzaldehydes with phenols (Scheme 1c).[22]

Despite the previous advances on the cyclization of *o*-(2-acyl-1-ethynyl)benzaldehydes, there is scope to develop novel cyclization pathways. To the best of our knowledge, there has been no report on the synthesis of indeno[2,1-*c*]pyran-3-ones and 1-oxazolonylisobenzofurans via the Erlenmeyer−Plöchl azlactone (EPA) reaction. In continuation of our efforts which have focused on the synthetic applications of azlactones,[23] herein, we describe the first examples of a divergent strategy utilizing *o*-(2-acyl-1-ethynyl)benzaldehydes **1** under the EPA reactions with different types of amino acids **4** including *N*-acylglycines (Scheme 1d) and free amino acids (Scheme 1e) to furnish the indeno[2,1-*c*]pyran-3-ones **2** and 1-oxazolonyliso-benzofurans **3**.

We envisaged that, under the EPA reaction, *o*-(2-acyl-1-ethynyl)benzaldehyde **1** could react with hippuric acid **4a** to afford the oxazolone, which further reacts with the aldehyde to form a reactive intermediate **5**. This intermediate could undergo a series of cascade cyclizations induced by the acetate anion, resulting in the formation of two C−C and two C−O bonds, ultimately constructing indeno[2,1-*c*]pyran-3-ones **2**. Additionally, using free amino acids instead of hippuric acid could lead to the formation of 1-oxazolonylisobenzofurans **3**. This process involves the initial formation of oxazolone, followed by a 1,2-addition at the aldehyde, and culminates in the formation of isobenzofuran via a 5-*exo-dig* cyclization.

RESULTS AND DISCUSSION

Initially, our investigation was carried out by using *o*-(2-acyl-1-ethynyl)benzaldehyde **1a**, hippuric acid **4a**, and NaOAc as a base in a 1:1.5:0.5 mol ratio at 50 °C with Ac_2O (5 equiv) as the solvent (Table 1). The reaction was performed for 1.5 h, and oxazolone **5a** was obtained in 29% yield via the Dakin−West-like reaction (entry 1).[24] Increasing the reaction temperature to 60 °C gave a higher yield (56%) of **5a** (entry 2). At 80 °C, the desired cascade cyclization product **2a** could be obtained in 32% yield (entry 3). Using other bases such as sodium trifluoroacetate under EPA reaction resulted in lower yield of the product **2a** (6% yield), and compound **5a** (19% yield) revealed the importance of NaOAc as a base in this reaction (entry 4).

The yield of product **2a** was improved by increasing the amount of base from 0.5 equiv to 1.1 equiv and the reaction temperature from 80 to 100 °C for 1 h (entry 5). In addition, using CH_3CN (2 M) as a cosolvent under standard conditions and decreasing the amount of Ac_2O from 5 equiv to 2.2 equiv at 100 °C for 1 h could furnish the desired product **2a** in 56% yield (entry 6). The reaction was performed with sodium bicarbonate and resulted in the product **2a** in 54% yield (entry 7). This result demonstrated the important role of acetic anhydride. When the reaction was performed without Ac_2O or using HOAc instead, compound **6a** was obtained in 9% and 27% yields, respectively (entries 8−9). This result suggested that Ac_2O played an important role in the reaction to promote the Dakin−West-like reaction[24] in the first step. Without Ac_2O, the intermediate **5a** could not be generated, while HOAc may attack the aldehyde followed by cyclization to form isobenzofuran **6a** via the 5-*exo-dig* cyclization. Based on our attempted optimization for the synthesis of indeno[2,1-*c*]pyran-3-one, **2a** was found to be NaOAc as a base (1.1

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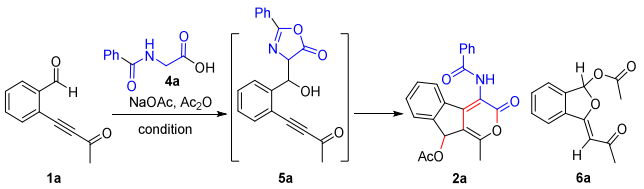
Table 1. Attempted Optimization of Reaction Conditions for the Synthesis of Indeno[2,1-*c*]pyran-3-one 2a



entry	NaOAc (equiv)	additive (equiv)	T (°C)	time (h)	yield 5a[a] (%)	yield 2a[a] (%)	yield 6a[a] (%)
1	0.5	Ac_2O (5)	50	1.5	29	-	-
2	0.5	Ac_2O (5)	60	1	56	-	-
3	0.5	Ac_2O (5)	80	1.5	-	32	-
4[b]	0.5	Ac_2O (5)	80	1.5	19	6	-
5	1.1	Ac_2O (5)	100	1	-	35	-
6[c]	1.1	Ac_2O (2.2)	100	1	-	56	-
7[c,d]	1.1	Ac_2O (2.2)	100	1	-	54	-
8[c,e]	1.1	-	100	1	-	-	9
9[c,f]	1.1	HOAc (2.2)	100	1	-	-	27

[a]Isolated yields. [b]Using sodium trifluoroacetate as a base instead of NaOAc. [c]Using CH_3CN (2 M) as a cosolvent. [d]Using sodium bicarbonate as a base instead of NaOAc. [e]RSM 58% yield. [f]RSM 40% yield.

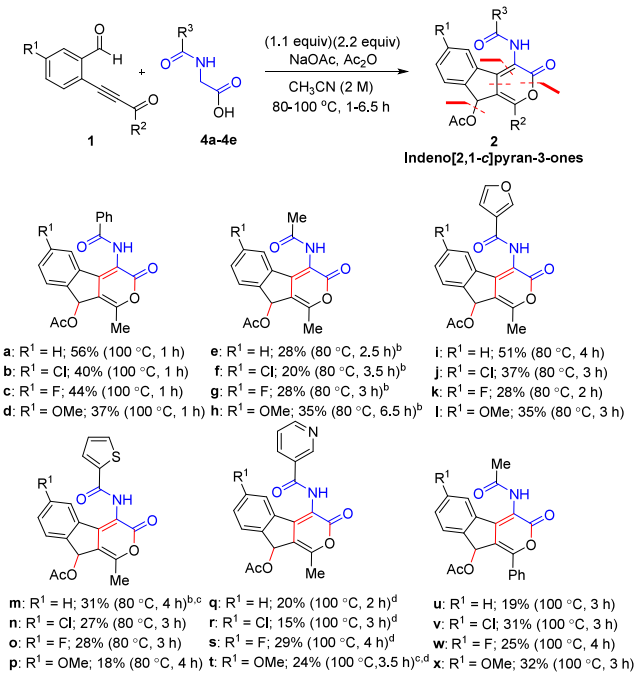
equiv) in CH_3CN as a cosolvent and Ac_2O (2.2 equiv) at 100 °C for 1 h.

With workable conditions in hand, we then explored the scope and generality of this EPA cascade cyclization for accessing a set of functionalized indeno[2,1-*c*]pyran-3-ones **2** as indicated in Scheme 2. The electronic effect of the substituent R^1 on the *o*-(2-acyl-1-ethynyl)benzaldehydes **1** was investigated; no influence on the yields of products **2** arising from the electronic effect was found. Methyl ketone delivered the product **2** in higher yields than a phenyl group. In addition, the certain acyl substituents R^3 of glycine derivatives **4a** (R^3 = phenyl) and **4c** (R^3 = furan) gave the desired products **2** in higher yields than the others, **4b** (R^3 = Me), **4d** (R^3 = thiophenyl), and **4e** (R^3 = nicotinyl).

We then extended the scope for this cascade cyclization reaction by using *N*-acetyl-DL-alanine **4f** instead of *N*-acetylglycine **4b**. Initially, *o*-(2-acyl-1-ethynyl)benzaldehyde **1c** and *N*-acetyl-DL-alanine **4f** were chosen as a model substrate as shown in Scheme 3. Surprisingly, using EPA reaction of compound **1c** with **4f** at 80 °C for 3 h, the reaction provided compound **3cj** in 51% yield (>99:1 *Z*/*E*). The configurations of product **3cj** could be established by the formation of an oxazolone intermediate from racemic **4f**. Subsequently, the 1,2-addition of the oxazolone ring to the aldehyde followed by oxynucleophilic cyclization via the 5-*exo*-*dig* cyclization yielded product **3cj**. The geometry of the *exo*-cyclic double olefin of **3cj** is the *Z*-configuration, as confirmed by comparisons of the NMR spectra of *Z* and *E*-**3ag** and X-ray crystallography analysis of *Z*-**3ag** and *E*-**3cg** (Figure 2).

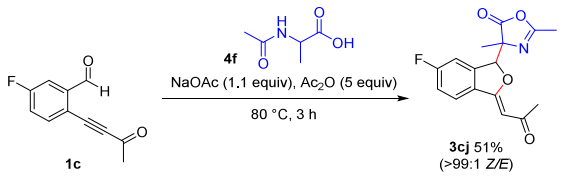
To extend the utility of this divergent synthesis using compound **1a** as a precursor to react with DL-phenylalanine **4g**

Scheme 2. Substrate Scope for the Synthesis of Indeno[2,1-*c*]pyran-3-ones 2[a]



[a]All reactions used NaOAc (1.1 equiv) and Ac_2O (2.2 equiv) in CH_3CN (2 M) and were heated at 80−100 °C. [b]Without CH_3CN. [c]Used Ac_2O (5 equiv). [d]Used CH_3CN (0.25 M) instead.

Scheme 3. Reaction of 1c with *N*-Acetyl-DL-alanine 4f



under EPA reaction, we then optimized the reaction conditions for the synthesis of 1-oxazolonylisobenzofurans **3** as shown in Table 2. Initially, the reaction was performed for 4 h, and the desired product **3ag** was obtained in 53% yield (>99:1 *Z*/*E*) (entry 1). Decreasing the reaction time to 1.5 h while lowering or increasing the reaction temperature to 50 and 100 °C, the yields of **3ag** were dramatically decreased to 22%, 30% and 43% yields, respectively (entries 2−4).

Other bases were screened such as sodium trifluoroacetate and Et_3N, but the yields of **3ag** did not improve as compared to that obtained when using NaOAc (entries 5−6). Using other solvents including THF, toluene, and CH_3CN led to the desired product **3ag** in 47%, 48%, and 54% yields, respectively (entries 7−9). To improve the product yield, using NEt_3 as a base and CH_3CN as a cosolvent resulted in 66% yield of a mixture of *Z*/*E*-**3ag** with the geometric ratio of 53:47 (entry 10). Further investigation with other anhydrides including TFAA and Tf_2O gave no 1-oxazolonylisobenzofuran formation (entries 11−12). The reactions performed without amino acid or using methyl ester also gave no formation of isobenzofuran (entries 13−14). The workable condition for the synthesis of 1-oxazolonylisobenzofuran was found to be NaOAc as a base (1.1 equiv) in neat Ac_2O (5 equiv) at 80 °C for 4 h.

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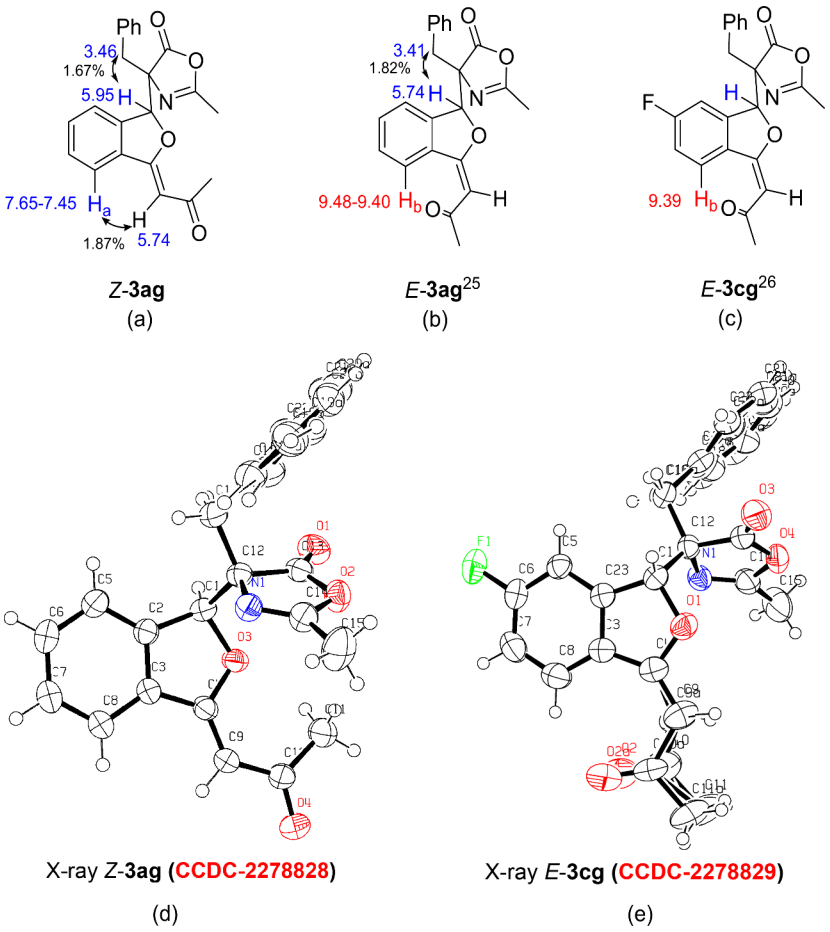
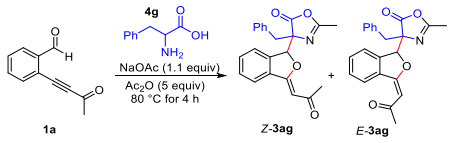


Figure 2. (a,b) NOE correlations of *Z*-**3ag** and *E*-**3ag**,[25] *(c) structure of E-**3cg**,[26] and (d,e) X-ray structures of Z-**3ag** and E-**3cg**.*

Table 2. Attempted Optimization of Reaction Conditions for the Synthesis of 1-Oxazolonylisobenzofurans 3ag



entry	conditions	yield (**3ag**)[a] (% *Z*/*E*)
1	none	53 (>99:1)
2	1.5 h instead of 4 h	22 (>99:1)
3	*T* = 50 °C instead of 80 °C	30 (60:40)
4	*T* = 100 °C instead of 80 °C	43 (>99:1)
5	sodium trifluoroacetate as base	12 (>99:1)[b]
6	Et_3N as base	53 (>99:1)
7	THF as solvent	47 (>99:1)
8	toluene as solvent	48 (>99:1)
9	CH_3CN as solvent	54 (>99:1)
10	Et_3N as base and CH_3CN as solvent	66 (53:47)
11	TFAA as an anhydride at 40 °C	NR
12	Tf_2O as an anhydride	NR
13	without amino acid **4g**	NR
14	L-Phenylalanine methyl ester hydrochloride instead of DL-phenylalanine	NR

[a]Isolated yields. [b]**1a** = 0.25 mmol. NR = no reaction.

A single-crystal X-ray crystallography analysis was performed on the major isomer of *Z*-**3ag** (Figure 2a, 2d). The result confirmed the C−C bond formation of the 1-oxazolonyliso-benzofuran framework and the C−O bond formation via the 5-*exo-dig* cyclization. The configuration of the *exo*-cyclic double bond was also determined to be *Z* with NOE correlation between the olefinic proton at δ_H 5.74 (s, 1H) and an aromatic proton of the benzofuran ring at δ_H 7.65−7.45 (m, H_a), thus confirming that the major product was *Z*-1-(isobenzofuran-1(3*H*)-ylidene)propan-2-one (*Z*-**3ag**). The minor product **3ag** was assigned to be *E*-1-(isobenzofuran-1(3*H*)-ylidene)propan-2-one.[25] In addition, the H_b aromatic proton appeared at a downfield chemical shift (δ_H 9.48−9.40 ppm) as a result of a through-space deshielding from the carbonyl of the acyl group, implying the *E*-isomer configuration (Figure 2b). The relative configurations of the two stereogenic centers at benzylic (C1) and α(C12)-carbons of a single diastereomer were also determined as (1*R**,12*R**)-*Z*-**3ag** and (1*S**,12*S**)-*E*-**3ag**, respectively. In the case of using NEt_3 as a base (entry 10), the reaction gave a 1:1 mixture of *Z*/*E*-**3ag** which was separated by column chromatography on silica gel.

Next, we sought to explore the scope of free amino acids **4** with a series of *o*-(2-acyl-1-ethynyl)benzaldehydes **1** to synthesize a set of 1-oxazolonylisobenzofurans **3** by decorating substituents R^1, R^2, and R^4 on the starting materials (Scheme 4). The *o*-(2-acyl-1-ethynyl)benzaldehydes **1** bear both EDG (R^1 = OMe) and EWG (R^1 = Cl, F) with free amino acids **4g**−**j** under the standard conditions. The reactions proceeded smoothly and gave moderate to good yields of the desired products.

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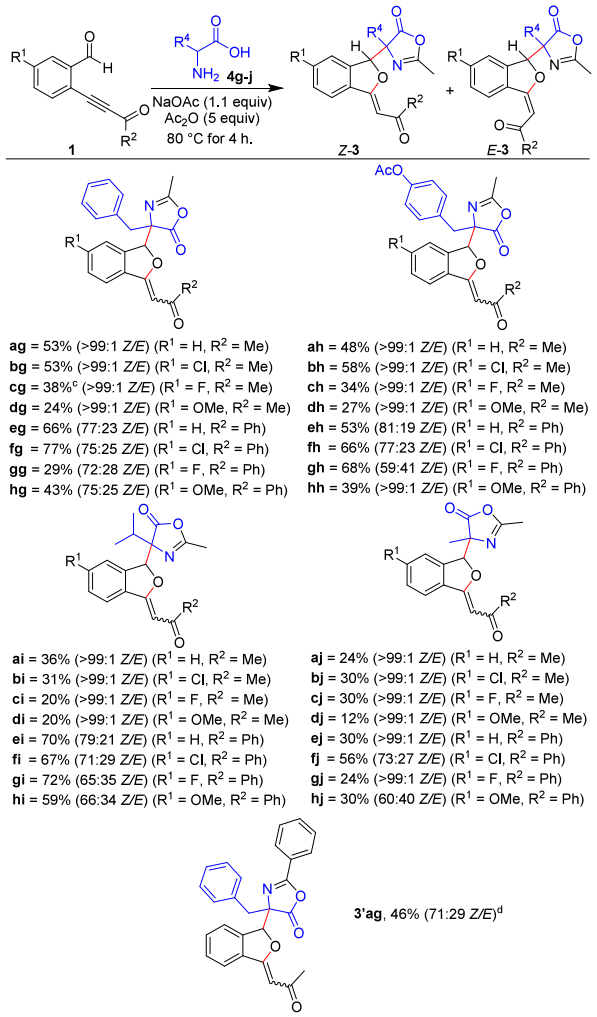
Scheme 4. Substrate Scope of 1-Oxazolonylisobenzofurans Derived from *o*-(2-Acyl-1-ethynyl)benzaldehydes[a,b]

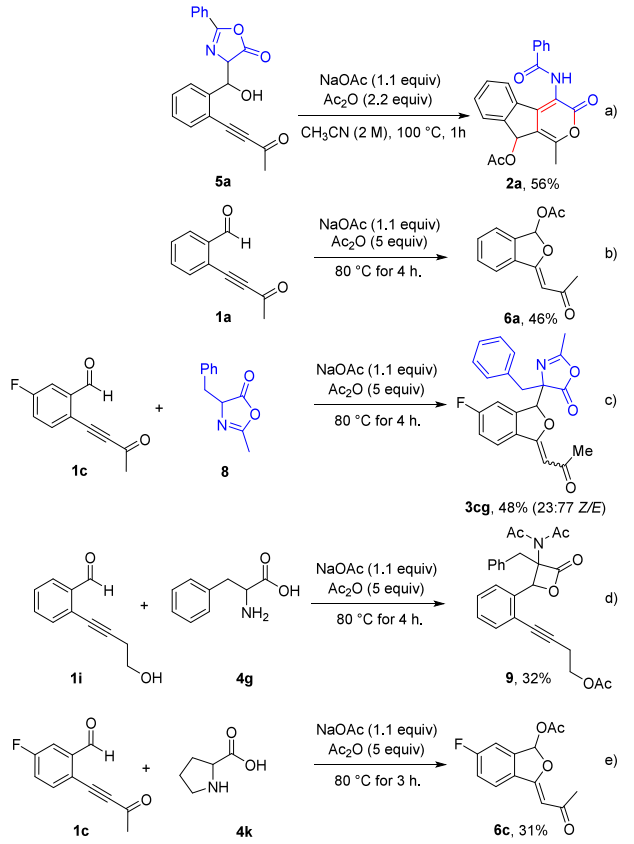


[a]Reaction conditions: **1** (0.5 mmol), **4** (0.75 mmol), NaOAc (0.55 mmol), and Ac_2O (2.5 mmol) and heated at 80 °C for 4 h. [b]Isolated yields and the geometric ratio (*Z*/*E*) values were determined by ^{1}H NMR. [c]Scale up to 7.31 mmol (**3cg**; 48% (96:4 *Z*/*E*)). [d]Bz_2O (1.05 mmol) was used as an anhydride instead of Ac_2O in CH_3CN (0.14 mL).

The reactions were highly stereoselective when arylbutynone derivatives (**1**, R^2 = Me) were used as starting materials. Using the diarylpropynone derivatives (**1**, R^2 = Ph), the reactions provided a mixture of *Z*- and *E*-isomers. The geometric ratio (*Z*/*E*) values were determined by ^{1}H NMR spectroscopy. Free racemic amino acids substituted with R^4 including phenylalanine (Phe, **4g**), tyrosine (Tyr, **4h**), valine (Val, **4i**), and alanine (Ala, **4j**) were screened. The results indicated that amino acids **4g**−**i** provided the corresponding products **3** in moderate to good yields, whereas **4j** gave the lower yields. Other amino acids including proline, serine, and cysteine were also screened, but the reactions did not proceed to furnish any desired products. In the case when benzoic anhydride was used instead of acetic anhydride in the presence of 1.1 equiv NaOAc and CH_3CN, the reaction provided compound **3′ag** in 46% yield (71:29 *Z*/*E*) (Scheme 4). The structures of these 1-oxazolonylisobensofuran derivatives **3** were characterized by their NMR spectroscopy and HRMS. In the case of *E*-**3cg**, its structure was unequivocally confirmed by carrying out single-crystal X-ray diffraction (Figure 2c and e).

In order to gain insight into both reaction mechanisms, some mechanistic studies were explored as shown in Scheme 5.

Scheme 5. Mechanistic Study



Using a proposed intermediate **5a** under the workable reaction conditions resulted in the formation of the corresponding product **2a** in 56% yield (Scheme 5a). In the case of no amino acid addition, compound **1a** could undergo the formation of compound **6a** in 46% yield under the EPA reaction (Scheme 5b).[19a] The result supported that the oxazolone was formed first from the alpha-amino acid via the Dakin−West-like reaction. This was further demonstrated when the oxazolone **8**[27] was reacted with compound **1c** which furnished **3cg** in 48% yield (23:77 *Z*/*E*) (Scheme 5c). Changing the conjugated ynone substrate to the alkynol **1i**,[28] the reaction proceeded to give the *β*-lactone **9** in 32% yield instead (Scheme 5d). Proline (**4k**) was also used as a representative of a secondary amine. The reaction proceeded to give the isobenzofuran **6c** in 31% yield without the incorporation of the proline moiety (Scheme 5e). These experiments revealed that the reaction required the internal alkyne containing the conjugated EWG for substrate **1**. This reaction condition was shown to be amenable to a relatively broad substrate scope of the amino acids containing the primary amino group and the free carboxylic acid.

Based on the results, a tentative cascade cyclization mechanism was proposed as shown in Scheme 6. Under EPA reaction between compound **1** and hippuric acid **4a**, the intermediate **5** was formed *in situ* through the Dakin−West-like reaction;[24] this intermediate was isolated from this reaction performed at 50−60 °C for 1.5 h (Table 1, entries

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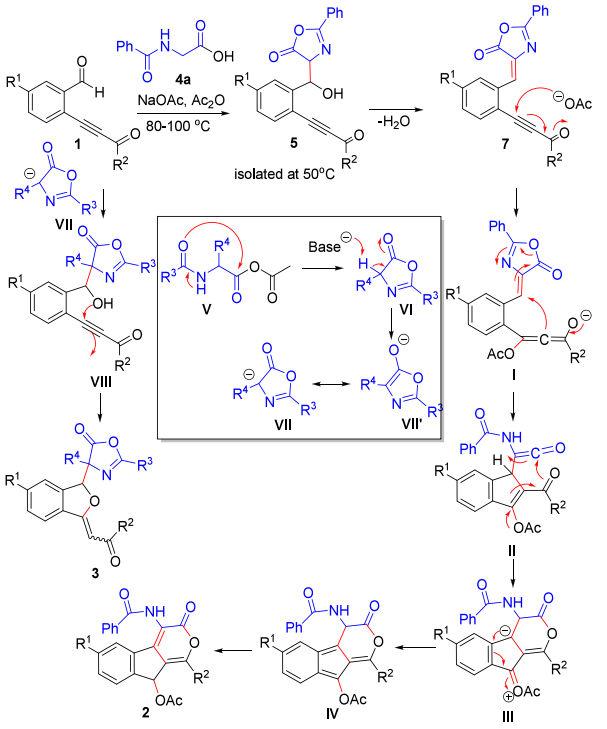
Scheme 6. Proposed Mechanism for the Formation of Indeno[2,1-*c*]pyran-3-one 2 and 1-Oxazolonylisobenzofuran 3



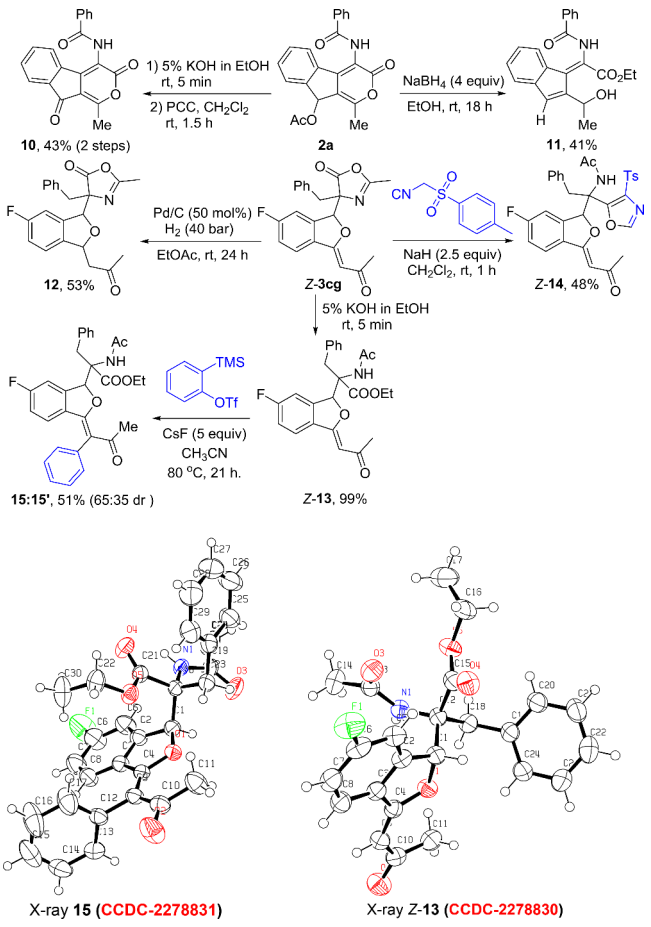
1−2). After dehydration, the intermediate **5** was converted to the corresponding ene-yne-one oxazolone **7**. Acetate undergoes 1,4-addition to compound **7**, generating the allene-enolate anion intermediate **I**.[2a] Intramolecular 1,4-addition of the intermediate **I** resulted in the C−C bond formation of the indene ring system with the concurrent ring opening of the oxazolone moiety to form the ketene intermediate **II**. Intramolecular cyclization and lactonization could lead to the intermediate **III**. Subsequent aromatization via intermediate **IV** would lead to the formation of compound **2**. Overall, the 6/5/6 skeleton of **2** was accomplished by the cascade cyclization to construct two C−C and two C−O bond formations in a single step.

According to our plausible mechanism of **3**, we hypothesized that under the EPA reaction amino acids **V** could result in the generation of the oxazolone intermediate **VI** *in situ* through the Dakin−West-like reaction.[24] The deprotonated oxazolone **VII**, with carbanionic character at the α-position, could react with the carbonyl carbon of the aldehyde to furnish the alcohol **VIII**. Subsequently oxa-Michael addition and then protonation of the intermediate **VIII** via 5-*exo-dig* cyclization would ultimately yield the corresponding 1-oxazolonylisobenzofuran **3**.

Indeno[2,1-*c*]pyran-3-ones **2** and 1-oxazolonylisobenzofurans **3** were further evaluated for their cytotoxicity against a panel of four human tumor cell lines: cholangiocarcinoma HuCCA-1, lung carcinoma A549, hepatoblastoma HepG2, and T-lymphoblast (acute lympho-blastic leukemia) MOLT-3. The results of the cytotoxicity assays indicated that compounds **2** and **3** had no cytotoxicity against these tumor cell lines.

Indeno[2,1-*c*]pyran-3-one **2a** and 1-oxazolonylisobenzofuran *Z*-**3cg** could undergo further transformations (Scheme 7). Saponification using 5% KOH in EtOH followed by PCC

Scheme 7. Transformation of Compounds 2a and *Z*-3cg



oxidation of **2a** led to the desired indeno[2,1-*c*]pyran **10** in 43% yield over two steps. Reduction of **2a** with $NaBH_4$ in EtOH furnished the corresponding indene **11** in 41% yield. The lactone underwent ring opening induced by the acetate leaving group, which performed ethanolysis followed by an E1cb-like reaction and reduction of ketone to yield indene **11**. The ^{1}H NMR spectrum showed very clearly the olefinic signal of indene as well as the substituted signals corresponding with the ^{13}C NMR spectrum (see the Supporting Information). Hydrogenation of *Z*-**3cg** was carried out using Pd/C as a catalyst which effectively reduced the *exo*-cyclic olefin to give compound **12** in 53% yield. Ethanolysis of *Z*-**3cg** by using 5% KOH in EtOH which also accompanied the ring opening of the oxazolone provided the compound *Z*-**13** in excellent yield (99%). The Van Leusen oxazole synthesis[29a] of *Z*-**3cg** involved the [3 + 2] cycloaddition of the carbonyl lactone to the oxazolone ring using toluenesulfonylmethyl isocyanide (TosMIC)[29] as a reagent, resulting in the formation of oxazole *Z*-**14** in 48% yield. Compound *Z*-**13** was further transformed to compound **15:15′** in 51% yield (65:35 dr) by reacting with benzyne[30] generated *in situ* via the 1,2-addition of the *exo*-cyclic double bond.

In conclusion, we have successfully developed a highly regioselective and divergent approach for synthesizing indeno[2,1-*c*]pyran-3-ones **2** and 1-oxazolonylisobenzofurans **3** from the common *o*-(2-acyl-1-ethynyl)benzaldehyde **1**. Using the Erlenmeyer−Plöchl azlactone (EPA) reaction, we have synthesized these compounds by employing various *N*-acylglycines and free amino acids. Our developed method is

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operationally straightforward, conducted under mild conditions, and free from metal and catalyst requirements and demonstrates an atom-economic process with a relatively broad substrate scope. As a result, two distinct scaffolds could be selectively prepared.

EXPERIMENTAL SECTION

General Information. All reagents and solvents were purchased from commercial sources and used without further purification. All reactions were heated by an oil bath. ^{1}H NMR (300 and 400 MHz), ^{13}C{^{1}H} NMR (75 and 100 MHz), and ^{19}F{^{1}H} NMR spectra (376 MHz) were recorded on a Bruker Ultra shield model AV300 spectrometer and Bruker AVANCE 400 spectrometer, respectively. Chemical shifts were reported in parts per million on the scale relative to the internal standard (tetramethylsilane, TMS (0 ppm)) in $CDCl_3$ and solvent signals (2.50 ppm) in DMSO-d_6. The ^{13}C NMR chemical shifts were determined relative to the internal solvent signals (77.0 ppm) in $CDCl_3$ and (39.5 ppm) in DMSO-d_6. ^{19}F NMR chemical shifts were determined relative to C_6F_6 (δ −164.9 ppm) as the internal standard. Coupling constants (J) were given in hertz (Hz). Infrared spectra were measured using a PerkinElmer FT-IR spectrometer, in cm^{-1}. High resolution mass spectra (HRMS) were obtained using time-of-flight (TOF) via the electrospray ionization (ESI). Single-crystal was determined with an X-ray single-crystal diffractometer. All crystals were grown in CH_2Cl_2 and hexane (1:1; v/v) for 1 week at 25 °C. Melting points were measured on a Thermo Scientific digital melting point apparatus in open capillaries. The products were purified by column chromatography (silica gel 60, size 0.06−0.20 mm; 70−230 mesh ASTM). TLC-Aluminum sheets on silica gel 60 GF_{254} (thin layer chromatography on an aluminum sheet) were used for monitoring the reaction. Rotary evaporations were applied to remove organic solvent.

General Procedure for Preparation of *o*-(2-Acyl-1-ethynyl)benzaldehyde 1.[2a] The Schlenk flask charged with a stirring bar, a derivative of 2-bromobenzaldehyde (1.0 equiv), $PdCl_2(PPh_3)_2$ (3 mol %), and CuI (5 mol %) was evacuated and filled with Ar (g) three times, and then dry THF (0.27 M) was added under an argon atmosphere. To the above suspension was added alkynol (1.2 equiv) and Et_3N (0.25−0.53 M) sequentially. The resulting mixture was stirred at 60 °C overnight (18 h). The resulting mixture was cooled, and then the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: ethyl acetate in hexane) to give product **S1**.

Compound **S1** was dissolved with CH_2Cl_2 (0.2 M) at room temperature, and celite (0.25 g/mmol) and PCC (2.0 equiv) were added. The resulting mixture was stirred at room temperature (26 °C) for 2−3 h. After completion, the mixture was filtered through a short silica gel column using CH_2Cl_2 as the eluent, and then the solvent was removed to furnish compounds **1**.

*5-Chloro-2-(3-hydroxy-3-phenylprop-1-yn-1-yl)-benzaldehyde (**S1f**).* Following the general procedure, 2-bromo-5-chlorobenzaldehyde (1.76 g, 8.00 mmol, 1 equiv), 1-phenylprop-2-yn-1-ol (1.20 mL, 9.60 mmol, 1.2 equiv), $PdCl_2(PPh_3)_2$ (168.4 mg, 0.24 mmol, 3 mol %), CuI (75.0 mg, 0.39 mmol, 5 mol %), NEt_3 (15 mL, 0.53 M), and THF (30 mL, 0.27 M) were stirred at room temperature (26 °C) overnight. The crude product was purified by column chromatography using 15% EtOAc in hexane as eluent to furnish **S1f** (1.66 g, 77% yield) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.42 (s, 1H, C*H*═O), 7.87 (dd, J = 1.4, 1.4 Hz, 1H, Ar−H), 7.62−7.56 (m, 2H, Ar−H), 7.54−7.51 (m, 2H, Ar−H), 7.47−7.34 (m, 3H, Ar−H), 5.75 (d, J = 5.7 Hz, 1H, ArC*H*OH), 2.52 (d, J = 5.7 Hz, 1H, ArCHO*H*). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 190.0 (*C*O), 139.9, 137.2, 135.6, 134.7, 133.8, 128.9 (2C), 128.8, 127.4, 126.5 (2C), 124.0, 96.8 (*C* ≡ C), 81.2 (*C* ≡ C), 65.2 (Ar*C*HOH). IR (UATR) ν_{max} 3374 (OH), 3064, 3032, 2849, 2200 (C≡C), 1694 (CO), 1588, 1474 cm^{-1}. HRMS (ESI) calcd. for $C_{16}H_{11}ClNaO_2$ [M + Na]$^+$: 293.0340, found 293.0339.

*5-Chloro-2-(3-oxo-3-phenylprop-1-yn-1-yl)benzaldehyde (**1f**).* Following the general procedure, compound **S1f** (1.66 g, 6.15 mmol, 1 equiv), Celite (1.54 g, 0.25 g/mmol) and PCC (2.65 g, 12.3 mmol, 2 equiv) in CH_2Cl_2 (31 mL, 0.2 M) were stirred at room temperature (26 °C) for 2 h. The mixture was filtered through a short silica gel column to furnish compound **1f** (1.47 g, 89% yield) as a light-yellow solid. Mp 111.1−113.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.54 (s, 1H, C*H*═O), 8.26−8.20 (m, 2H, Ar−H), 7.99 (d, J = 2.1 Hz, 1H, Ar−H), 7.78 (d, J = 8.1 Hz, 1H, Ar−H), 7.73−7.63 (m, 2H, Ar−H), 7.60−7.52 (m, 2H, Ar−H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 188.9 (CH═O), 177.2 (*C*O), 138.2, 137.9, 136.5, 135.9, 134.6, 134.0, 129.6 (2C), 128.9 (2C), 128.5, 121.0, 92.9 (*C* ≡ C), 86.4 (*C* ≡ C). IR (UATR) ν_{max} 3065, 2871, 2194 (C≡C), 1793 (CO), 1696 (CO), 1642, 1596, 1579 cm^{-1}. HRMS (ESI) calcd. for $C_{16}H_9ClNaO_2$ [M + Na]$^+$: 291.0183, found 291.0181.

*5-Fluoro-2-(3-hydroxy-3-phenylprop-1-yn-1-yl)-benzaldehyde (**S1g**).* Following the general procedure, 2-bromo-5-fluorobenzaldehyde (1.63 g, 8.00 mmol, 1 equiv), 1-phenylprop-2-yn-1-ol (1.20 mL, 9.60 mmol, 1.2 equiv), $PdCl_2(PPh_3)_2$ (167.6 mg, 0.24 mmol, 3 mol %), CuI (75.2 mg, 0.40 mmol, 5 mol %), NEt_3 (15 mL, 0.53 M), and THF (30 mL, 0.27 M) were stirred at 60 °C overnight. The crude product was purified by column chromatography using 20% EtOAc in hexane as eluent to furnish compound **S1g** (1.69 g, 83% yield) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.40 (d, J = 3.0 Hz, 1H, C*H*═O), 7.60−7.50 (m, 4H, Ar−H), 7.44−7.30 (m, 3H, Ar−H), 7.28−7.18 (m, 1H, Ar−H), 5.71 (br s, 1H, ArC*H*OH), 3.18 (br d, J = 3.3 Hz, 1H, ArCHO*H*). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 190.3 (d, $^4J_{C-F}$ = 1.1 Hz, *C*H═O), 162.5 (d, $^1J_{C-F}$ = 251.6 Hz, *C*F), 140.0, 138.1 (d, $^3J_{C-F}$ = 6.8 Hz), 135.5 (d, $^3J_{C-F}$ = 7.7 Hz), 128.8 (2C), 128.7, 126.5 (2C), 121.9 (d, $^4J_{C-F}$ = 3.3 Hz), 121.3 (d, $^2J_{C-F}$ = 22.7 Hz), 113.8 (d, $^2J_{C-F}$ = 23.0 Hz), 95.7 (*C* ≡ C), 81.0 (*C* ≡ C), 65.0 (Ar*C*HOH). IR (UATR) ν_{max} 3376 (OH), 3067, 2852, 1694 (CO), 1603, 1487 cm^{-1}. HRMS (ESI) calcd. for $C_{16}H_{11}FNaO_2$ [M + Na]$^+$: 277.0635, found 277.0635.

*5-Fluoro-2-(3-oxo-3-phenylprop-1-yn-1-yl)benzaldehyde (**1g**).* Following the general procedure, compound **S1g** (1.69 g, 6.65 mmol, 1 equiv) and Celite (1.66 g, 0.25 g/mmol) and PCC (2.87 g, 13.3 mmol, 2 equiv) in CH_2Cl_2 (34 mL, 0.2 M) were stirred at room temperature (26 °C) for 2 h. The mixture was filtered through a short silica gel column to furnish compound **1f** (1.22 g, 73% yield) as a white solid. Mp 96.3−98.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.54 (d, J = 3.0 Hz, 1H, C*H*═O), 8.24−8.16 (m, 2H, Ar−H), 7.84 (dd, J_{H-H} = 7.9 Hz and J_{H-F} = 5.0 Hz, 1H, Ar−H), 7.71−7.63 (m, 2H, Ar−H), 7.54−7.50 (m, 2H, Ar−H), 7.39 (ddd, J = 10.4, 7.9, 2.7 Hz, 1H, Ar−H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 188.8 (d, $^4J_{C-F}$ = 1.6 Hz, CH═O), 177.2 (*C*O), 163.7 (d, $^1J_{C-F}$ = 255.0

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Hz, CF), 139.4 (d, $^3J_{C-F}$ = 7.1 Hz), 137.0 (d, $^3J_{C-F}$ = 8.1 Hz), 136.4, 134.5, 129.5 (2C), 128.8 (2C), 121.5 (d, $^2J_{C-F}$ = 22.7 Hz), 118.9 (d, $^4J_{C-F}$ = 3.6 Hz), 115.0 (d, $^2J_{C-F}$ = 23.1 Hz), 92.0 (d, $^5J_{C-F}$ = 1.7 Hz, *C* ≡ C), 86.5 (*C* ≡ C). IR (UATR) ν_{max} 3092, 2877, 2197 (C≡C), 1695 (CO), 1642, 1596, 1578 cm^{-1}. HRMS (ESI) calcd. for $C_{16}H_9FNaO_2$ $[M + Na]^+$: 275.0479, found 275.0475.

*2-(3-Hydroxy-3-phenylprop-1-yn-1-yl)-5-methoxybenzaldehyde (**S1h**).* Following the general procedure, using the 2-bromo-5-methoxybenzaldehyde (1.72 g, 8.00 mmol, 1 equiv), 1-phenylprop-2-yn-1-ol (1.20 mL, 9.60 mmol, 1.2 equiv), $PdCl_2(PPh_3)_2$ (169.0 mg, 0.24 mmol, 3 mol %), CuI (76.7 mg, 0.40 mmol, 5 mol %), NEt_3 (15 mL, 0.53 M), and THF (30 mL, 0.27 M) were stirred at 60 °C overnight. The crude product was purified by column chromatography using 20% EtOAc in hexane as eluent to furnish **S1h** (2.09 g, 99% yield) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.45 (s, 1H, C*H*═O), 7.63−7.57 (m, 2H, Ar−H), 7.50 (d, *J* = 8.7 Hz, 1H, Ar−H), 7.46−7.32 (m, 4H, Ar−H), 7.10 (dd, *J* = 8.7, 2.7 Hz, 1H, Ar−H), 5.74 (br d, *J* = 4.5 Hz, 1H, ArC*H*OH), 3.86 (s, 3H, Ar−OCH_3), 2.52 (br d, *J* = 5.7 Hz, 1H, ArCHO*H*). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 191.3 (*C*H═O), 160.0 (*CO*), 140.3, 137.6, 134.8, 128.8 (2C), 128.6, 126.6 (2C), 121.5, 118.5, 110.1, 94.3 (*C* ≡ C), 82.1 (*C* ≡ C), 65.2 (Ar*C*HOH), 55.6 (Ar−O*C*H_3). IR (UATR) ν_{max} 3396, 3032, 2843, 1688 (CO), 1601, 1561, 1492 cm^{-1}. HRMS (ESI) calcd. for $C_{17}H_{14}NaO_3$ $[M + Na]^+$: 289.0835, found 289.0831.

*2-(3-Hydroxy-3-phenylprop-1-yn-1-yl)-5-methoxybenzaldehyde (**1h**).* Following the general procedure, compound **S1h** (2.09 g, 7.92 mmol, 1 equiv) and Celite (1.98 g, 0.25 g/mmol), PCC (3.41 g, 15.8 mmol, 2 equiv), and CH_2Cl_2 (40 mL, 0.2 M) were stirred at room temperature (26 °C) for 2 h. The mixture was filtered through a short silica gel column to furnish compound **1h** (1.56 g, 75% yield) as a white solid. Mp 96.3−98.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.57 (s, 1H, C*H*═O), 8.25−8.18 (m, 2H, Ar−H), 7.75 (d, *J* = 8.4 Hz, 1H, Ar−H), 7.69−7.61 (m, 1H, Ar−H), 7.57−7.50 (m, 2H, Ar−H), 7.48 (d, *J* = 2.8 Hz, 1H, Ar−H), 7.20 (dd, *J* = 8.4, 2.8 Hz, 1H, Ar−H), 3.92 (s, 3H, Ar−OCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 190.1 (C*H*═O), 177.5 (*CO*), 161.7, 138.9, 136.7, 136.5, 134.3, 129.5 (2C), 128.7 (2C), 121.2, 115.0, 111.6, 91.8 (*C* ≡ C), 88.5 (*C* ≡ C), 55.8 (Ar−OCH_3). IR (UATR) ν_{max} 3082, 3064, 2851, 2184, 1699, 1638, 1596, 1579 cm^{-1}. HRMS (ESI) calcd. for $C_{17}H_{12}NaO_3$ $[M + Na]^+$: 287.0679, found 287.0676.

General Procedure for the Synthesis of Indeno[2,1-*c*]pyran-3-ones 2. To a suspension of *o*-(2-acyl-1-ethynyl)-benzaldehyde derivatives **1** (1 equiv), amino acid derivatives **4a−e** (1.5 equiv), NaOAc (1.1 equiv), and Ac_2O (2.2−5 equiv) in CH_3CN (0.25−2 M) or without CH_3CN in a sealed tube were added and stirred at 80−100 °C for 1−6.5 h. The reaction mixture was allowed to cool to room temperature and then quenched with sat. Na_2CO_3 (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). Combined organic layers were washed with sat. Na_2CO_3 until pH = 7, followed by water and brine, dried over anh. Na_2SO_4, and concentrated to give a brown oil. The crude product was purified by column chromatography on silica gel using 30−60% EtOAc in hexane or 10−70% EtOAc in CH_2Cl_2 to afford indeno[2,1-*c*]pyran-3-ones **2**.

*4-Benzamido-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]-pyran-9-yl Acetate (**2a**).* Following the general procedure, compound **1a** (172 mg, 1.00 mmol, 1 equiv), hippuric acid **4a** (269 mg, 1.50 mmol, 1.5 equiv), NaOAc (90.0 mg, 1.10 mmol, 1.1 equiv) and Ac_2O (0.21 mL, 2.20 mmol, 2.2 equiv) in CH_3CN (0.48 mL, 2 M) in a sealed tube were stirred at 100 °C for 1 h. The crude product was purified by column chromatography on silica gel using 40−50% EtOAc in hexane to furnish compound **2a** (209 mg, 56%) as a yellow-brown solid. Mp 214.8−215.9 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (br s, 1H, − N*H*), 7.98 (d, *J* = 7.5 Hz, 2H, Ar−H), 7.63−7.57 (m, 2H, Ar−H), 7.56−7.37 (m, 5H, Ar−H), 7.01 (s, 1H, − C*H*), 2.32 (s, 3H, CH_3), 2.17 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.0 (OCOCH_3), 166.0 (CONH), 162.6 (COO), 154.8, 146.1, 144.8, 135.8, 133.2, 132.5, 130.2, 128.9 (3C), 127.7 (2C), 127.6, 126.1, 117.4, 112.8, 71.6 (CH), 20.9 (OCOCH_3), 17.1 (CH_3). IR (UATR) ν_{max} 3292 (NH), 1739 (CO), 1699 (CO), 1668 (CO), 1613, 1601, 1512 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{17}NNaO_5$ $[M + Na]^+$: 398.0999, found 398.0994.

The structure of product **2a** was elucidated based on the comprehensive NMR spectroscopic techniques. The ^{1}H NMR spectrum showed key signals of indeno[2,1-*c*]pyran-3-one core structure at δ_H 8.20 (br s, 1H) for the secondary amide proton, at δ_H 7.01 (s, 1H) for the sp^3 oxymethine proton, at δ_H 2.32 (s, 3H) for the methyl group on the α-pyrone ring, and at δ_H 2.17 (s, 3H, OAc) for the indanyl acetate group. The ^{13}C NMR spectrum displayed five carbon characteristic peaks of the α-pyrone ring at δ_C 162.6, 154.8, 146.1, 117.4, and 112.8, with a methyl adjacent to the α-pyrone ring at δ_C 17.1, the carbonyl peak of *N*-acetyl amide at δ_C 166.0, the oxymethine carbon at δ_C 71.6, and the indanyl acetate at δ_C 171.0 and 20.9. The HMBC spectrum confirmed the correlations of the secondary amide proton (δ_H 8.20) to the sp^2 hybridized carbon (δ_C 146.1) at the α-position of the carbonyl of the α-pyrone ring; the oxymethine proton (δ_H 7.01) and the adjacent methyl protons (δ_H 2.32) to the sp^2 hybridized carbons (δ_C 154.8, 117.4); and the oxymethine proton (δ_H 7.01) and the acetyl protons (δ_H 2.17) to the carbonyl ester carbon (δ_C 171.0). Taken together, all spectroscopic data were consistent with and confirmed the framework of *N*-(6-methyl-2-oxo-2*H*-pyran-3-yl)benzamide fused with 1*H*-inden-1-yl acetate as also supported by the IR absorptions at υ_{max} 1739, 1699, and 1668 cm^{-1} (see the Supporting Information (SI), pages S23−24).

*4-Benzamido-6-chloro-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2b**).* Following the general procedure, compound **1b** (103 mg, 0.50 mmol, 1 equiv), hippuric acid **4a** (134 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.11 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in sealed tubes were stirred at 100 °C for 1 h. The crude product was purified by column chromatography on silica gel using 40% EtOAc in hexane to furnish compound **2b** (82.5 mg, 40%) as a yellow-brown solid. Mp 223.6−224.3 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (br s, 1H, − N*H*), 8.00−7.94 (m, 2H, Ar−H), 7.66−7.49 (m, 4H, Ar−H), 7.39 (dd, *J* = 8.6, 1.8 Hz, 1H, Ar−H), 7.30 (d, *J* = 8.6 Hz, 1H, Ar−H), 6.95 (s, 1H, − C*H*), 2.32 (s, 3H, CH_3), 2.19 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.9 (OCOCH_3), 165.8 (CONH), 162.3 (COO), 154.7, 146.2, 138.2, 134.5, 133.1, 132.8, 130.6, 129.0 (3C), 128.7, 127.7 (2C), 126.5, 117.2, 112.9, 71.2 (CH), 20.9 (OCOCH_3), 17.2 (CH_3). IR (UATR) ν_{max} 3328, 3070 (NH), 1740 (CO), 1701 (CO), 1674 (CO), 1600, 1504, 1477 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{16}ClNNaO_5$ $[M + Na]^+$: 432.0609, found 432.0604.

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*4-Benzamido-6-fluoro-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2c**).* Following the general procedure, compound **1c** (95.0 mg, 0.50 mmol, 1 equiv), hippuric acid **4a** (134 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.11 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 100 °C for 1 h. The crude product was purified by column chromatography on silica gel using 50% EtOAc in hexane to furnish compound **2c** (85.7 mg, 44%) as a brown solid. Mp 238.3−240.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (br s, 1H, − N*H*), 7.98 (d, J = 7.2 Hz, 2H, Ar−H), 7.65−7.59 (m, 1H, Ar−H), 7.56−7.50 (m, 2H, Ar−H), 7.39 (dd, J_{H-H} = 8.7 Hz and J_{H-F} = 5.0 Hz, 1H, Ar−H), 7.31 (dd, J_{H-F} = 8.6 Hz and J_{H-H} = 2.4 Hz, 1H, Ar−H), 7.12 (ddd, J_{H-H} = 8.7 Hz, J_{H-F} = 8.6 Hz and J_{H-H} = 2.4 Hz, 1H, Ar−H), 6.95 (s, 1H, − C*H*), 2.32 (s, 3H, CH_3), 2.19 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.9 (OCOCH$_3$), 166.0 (CONH), 164.9 (d, $^1J_{C-F}$ = 253.3 Hz, CF), 162.4 (COO), 154.6, 147.3 (d, $^3J_{C-F}$ = 9.1 Hz), 144.6, 133.1, 132.7, 132.1 (d, $^4J_{C-F}$ = 2.3 Hz), 129.6 (d, $^3J_{C-F}$ = 9.4 Hz), 128.9 (2C), 127.7 (2C), 117.9 (d, $^2J_{C-F}$ = 23.2 Hz), 117.4, 113.6 (d, $^2J_{C-F}$ = 23.4 Hz), 112.4, 71.3 (d, $^5J_{C-F}$ = 1.9 Hz, CH), 20.8 (OCOCH$_3$), 17.2 (CH$_3$). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 108.63. IR (UATR) ν_{max} 3328 (NH), 3077, 2925, 1740 (CO), 1674 (CO), 1662 (CO), 1607, 1505, 1478 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{17}FNO_5$ [M + H]$^+$: 394.1085, found 394.1086.

*4-Benzamido-6-methoxy-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2d**).* Following the general procedure, compound **1d** (102 mg, 0.50 mmol, 1 equiv), hippuric acid **4a** (134 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.11 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 100 °C for 1 h. The crude product was purified by column chromatography on silica gel using 40% EtOAc in hexane to furnish compound **2d** (75.8 mg, 37%) as a yellow solid. Mp 212.1−213.7 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (br s, 1H, − N*H*), 8.00−7.94 (m, 2H, Ar−H), 7.62−7.55 (m, 1H, Ar−H), 7.55−7.45 (m, 2H, Ar−H), 7.36 (d, J = 8.7 Hz, 1H, Ar−H), 7.09 (d, J = 2.5 Hz, 1H, Ar−H), 6.94 (dd, J = 8.7, 2.5 Hz, 1H, Ar−H), 6.93 (s, 1H, − C*H*), 3.83 (s, 3H, Ar−OCH_3), 2.20 (s, 3H, CH_3), 2.17 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 171.1 (OCOCH$_3$), 166.0 (CONH), 163.1, 162.7 (COO), 154.3, 147.2, 146.2, 133.4, 132.5, 129.0, 128.8 (2C), 128.5, 127.7 (2C), 117.7, 116.9, 111.0, 110.9, 71.5 (CH), 55.7 (Ar−OCH$_3$), 20.9 (OCOCH$_3$), 17.1 (CH$_3$). IR (UATR) ν_{max} 3325 (NH), 2942, 1739 (CO), 1700 (CO), 1674 (CO), 1605 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{19}NNaO_6$ [M + Na]$^+$: 428.1105, found 428.1103.

*4-Acetamido-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]-pyran-9-yl Acetate (**2e**).* Following the general procedure, compound **1a** (86.0 mg, 0.50 mmol, 1 equiv), *N*-acetylglycine **4b** (88.0 mg, 0.75 mmol, 1.5 equiv), and NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv) in Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) were stirred at 80 °C for 2.5 h. The crude product was purified by column chromatography on silica gel using 10−30% EtOAc in CH_2Cl_2 to furnish compound **2e** (44.6 mg, 28%) as a yellow solid. Mp 199.6−202.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65−7.56 (m, 2H, − N*H* and Ar−H), 7.53−7.44 (m, 3H, Ar−H), 6.96 (s, 1H, − C*H*), 2.31 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.16 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.0 (OCOCH$_3$), 169.1 (CONH), 162.6 (COO), 155.1, 146.8, 144.8, 135.7, 132.1, 130.2, 127.4, 126.1, 117.3, 112.4, 71.5 (CH), 23.7 (CH$_3$), 20.9 (OCOCH$_3$), 17.2 (CH$_3$). IR (UATR) ν_{max} 3331 (NH), 2996, 1718 (CO), 1694 (CO), 1677 (CO), 1614, 1508 cm^{-1}. HRMS (ESI) calcd. for $C_{17}H_{15}NNaO_5$ [M + Na]$^+$: 336.0842, found 336.0852.

*4-Acetamido-6-chloro-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2f**).* Following the general procedure, compound **1b** (103 mg, 0.50 mmol, 1 equiv), *N*-acetylglycine **4b** (88.0 mg, 0.75 mmol, 1.5 equiv), and NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv) in Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) were stirred at 80 °C for 3.5 h. The crude product was purified by column chromatography on silica gel using 10−50% EtOAc in CH_2Cl_2 to furnish compound **2f** (34.9 mg, 20%) as a pale brown solid. Mp 238.6−239.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (br s, 1H, − N*H*), 7.48−7.42 (m, 2H, Ar−H), 7.33 (d, J = 8.4 Hz, 1H, Ar−H), 6.91 (s, 1H, − C*H*), 2.31 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.18 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.9 (OCOCH$_3$), 168.9 (CONH), 162.3 (COO), 155.0, 146.2, 144.9, 138.3, 134.3, 130.6, 128.5, 126.5, 117.0, 112.6, 71.1 (CH), 23.9 (CH$_3$), 20.8 (OCOCH$_3$), 17.2 (CH$_3$). IR (UATR) ν_{max} 3333 (NH), 2923, 2853, 1721 (CO), 1694 (CO), 1616, 1600, 1513 cm^{-1}. HRMS (ESI) calcd. for $C_{17}H_{14}ClNNaO_5$ [M + Na]$^+$: 370.0453, found 370.0457.

*4-Acetamido-6-fluoro-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2g**).* Following the general procedure, compound **1c** (95.0 mg, 0.50 mmol, 1 equiv), *N*-acetylglycine **4b** (88.0 mg, 0.75 mmol, 1.5 equiv), and NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv) in Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) were stirred at 80 °C for 3 h. The crude product was purified by column chromatography on silica gel using 10−50% EtOAc in CH_2Cl_2 to furnish compound **2g** (46.5 mg, 28%) as a yellow-brown solid. Mp 246.4−247.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (br s, 1H, − N*H*), 7.41 (dd, J_{H-H} = 8.4 Hz and J_{H-F} = 5.2 Hz, 1H, Ar−H), 7.30 (dd, J_{H-F} = 8.4 Hz and J_{H-H} = 2.0 Hz, 1H, Ar−H), 7.18 (ddd, J_{H-H} = 8.4 Hz, J_{H-F} = 8.4 Hz and J_{H-H} = 2.0 Hz, 1H, Ar−H), 6.91 (s, 1H, − C*H*), 2.31 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.18 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.9 (OCOCH$_3$), 169.0 (CONH), 164.9 (d, $^1J_{C-F}$ = 253.2 Hz, CF), 162.4 (COO), 154.9, 147.3 (d, $^3J_{C-F}$ = 9.2 Hz), 145.3, 131.9 (d, $^4J_{C-F}$ = 1.7 Hz), 129.4 (d, $^3J_{C-F}$ = 9.4 Hz), 117.8 (d, $^2J_{C-F}$ = 23.0 Hz), 117.3, 113.6 (d, $^2J_{C-F}$ = 23.6 Hz), 112.0, 71.1 (CH), 23.8 (CH$_3$), 20.8 (OCOCH$_3$), 17.2 (CH$_3$). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 108.54. IR (UATR) ν_{max} 3337 (NH), 1721 (CO), 1694 (CO), 1682 (CO), 1608, 1511 cm^{-1}. HRMS (ESI) calcd. for $C_{17}H_{14}FNNaO_5$ [M + Na]$^+$: 354.0748, found 354.0744.

*4-Acetamido-6-methoxy-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2h**).* Following the general procedure, compound **1d** (101 mg, 0.50 mmol, 1 equiv), *N*-acetylglycine **4b** (88.0 mg, 0.75 mmol, 1.5 equiv), and NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv) in Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) were stirred at 80 °C for 6.5 h. The crude product was purified by column chromatography on silica gel using 10−50% EtOAc in CH_2Cl_2 to furnish compound **2h** (60.6 mg, 35%) as a brown solid. Mp 216.4−217.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (br s, 1H, − N*H*), 7.39 (d, J = 8.8 Hz, 1H, Ar−H), 7.07 (d, J = 2.1 Hz, 1H, Ar−H), 7.00 (dd, J = 8.8, 2.1 Hz, 1H, Ar−H), 6.89 (s, 1H, − C*H*), 3.86 (s, 3H, Ar−OCH_3), 2.29 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.16 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.0 (OCOCH$_3$), 169.2 (CONH), 163.1, 162.7

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(COO), 154.6, 147.2, 147.0, 128.8, 128.3, 117.5, 116.9, 110.8, 110.7, 71.4 (CH), 55.7 (Ar−OCH_3), 23.7 (CH_3), 20.9 ($OCOCH_3$), 17.1 (CH_3). IR (UATR) ν_{max} 3258 (NH), 2942, 2845, 1715 (CO), 1681 (CO), 1602, 1487 cm^{-1}. HRMS (ESI) calcd. for $C_{18}H_{17}NNaO_6$ $[M + Na]^+$: 366.0948, found 366.0948.

*4-(Furan-3-carboxamido)-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2i**).* Following the general procedure, compound **1a** (86.5 mg, 0.50 mmol, 1 equiv), (furan-3-carbonyl)glycine **4c** (127 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 80 °C for 4 h. The crude product was purified by column chromatography on silica gel using 45−50% EtOAc in hexane to furnish compound **2i** (92.8 mg, 51%) as a yellow solid. Mp 212.8−213.5 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 8.23 (br s, 1H, − N*H*), 8.11 (br s, 1H, Ar−H), 7.62−7.55 (m, 1H, Ar−H), 7.53−7.38 (m, 4H, Ar−H), 6.98 (s, 1H, − C*H*), 6.82 (br d, J = 1.2 Hz, 1H, Ar−H), 2.30 (s, 3H, CH_3), 2.16 (s, 3H, $OCOCH_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 171.0 ($OCOCH_3$), 162.9 (CONH), 161.2 (COO), 155.1, 147.3, 146.1, 144.8, 144.1, 135.7, 132.2, 130.3, 127.5, 126.1, 121.8, 117.5, 112.2, 108.7, 71.5 (CH), 20.9 ($OCOCH_3$), 17.2 (CH_3). IR (UATR) ν_{max} 3320 (NH), 3151, 1735 (CO), 1701 (CO), 1681 (CO), 1615, 1515, 1490 cm^{-1}. HRMS (ESI) calcd. for $C_{20}H_{15}NNaO_6$ $[M + Na]^+$: 388.0792, found 388.0793.

*6-Chloro-4-(furan-3-carboxamido)-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2j**).* Following the general procedure, compound **1b** (103 mg, 0.50 mmol, 1 equiv), (furan-3-carbonyl)glycine **4c** (127 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 80 °C for 3 h. The crude product was purified by column chromatography on silica gel using 40−50% EtOAc in hexane to furnish compound **2j** (74.7 mg, 37%) as a brown solid. Mp 241.7−243.0 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 8.45 (br, 1H, − N*H*), 8.14 (dd, J = 1.5, 0.9 Hz, 1H, Ar−H), 7.56−7.37 (m, 4H, Ar−H), 6.91 (s, 1H, − C*H*), 6.83 (dd, J = 2.1, 0.9 Hz, 1H, Ar−H), 2.30 (s, 3H, CH_3), 2.16 (s, 3H, $OCOCH_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 170.9 ($OCOCH_3$), 162.6 (CONH), 161.3 (COO), 155.4, 146.2, 146.1, 144.1, 142.9, 137.3, 136.3, 132.2, 127.5, 127.1, 121.5, 117.4, 112.9, 108.6, 71.0 (CH), 20.8 ($OCOCH_3$), 17.1 (CH_3). IR (UATR) ν_{max} 3315 (NH), 3147, 1740 (CO), 1701 (CO), 1678 (CO), 1612, 1600, 1515, 1489 cm^{-1}. HRMS (ESI) calcd. for $C_{20}H_{14}ClNNaO_6$ $[M + Na]^+$: 422.0402, found 422.0394.

*6-Fluoro-4-(furan-3-carboxamido)-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2k**).* Following the general procedure, compound **1c** (95.0 mg, 0.50 mmol, 1 equiv), (furan-3-carbonyl)glycine **4c** (127 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 80 °C for 2 h. The crude product was purified by column chromatography on silica gel using 50% EtOAc in hexane to furnish compound **2k** (53.9 mg, 28%) as a brown solid. Mp 245.8−247.5 °C. ^1H NMR (300 MHz, DMSO-d_6) δ 9.93 (br s, 1H, − N*H*), 8.44 (br s, 1H, Ar−H), 7.84 (dd, J = 1.6, 1.2 Hz, 1H, Ar−H), 7.71 (dd, J_{H-H} = 8.1 Hz and J_{H-F} = 5.0 Hz, 1H, Ar−H), 7.50−7.38 (m, 2H, Ar−H), 7.02 (d, J = 0.9 Hz, 1H, Ar−H), 6.99 (s, 1H, − C*H*), 2.30 (s, 3H, CH_3), 2.16 (s, 3H, $OCOCH_3$). $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6) δ 170.5 ($OCOCH_3$), 164.3 (d, $^1J_{C-F}$ = 250.1 Hz, CF), 161.1 (CONH), 160.8 (COO), 156.9, 148.0, 147.7 (d, $^3J_{C-F}$ = 9.4 Hz), 146.4, 144.4, 131.4 (d, $^4J_{C-F}$ = 2.0 Hz), 128.3 (d, $^3J_{C-F}$ = 9.7 Hz), 121.8, 118.0 (d, $^2J_{C-F}$ = 23.2 Hz), 116.1, 113.6 (d, $^2J_{C-F}$ = 23.5 Hz), 112.3, 109.2, 70.7 (d, $^5J_{C-F}$ = 1.4 Hz, CH), 20.6 ($OCOCH_3$), 17.0 (CH_3). $^{19}F\{^1H\}$ NMR (376 MHz, DMSO-d_6) − 108.13. IR (UATR) ν_{max} 3316 (NH), 3151, 1741 (CO), 1702 (CO), 1678 (CO), 1608 cm^{-1}. HRMS (ESI) calcd. for $C_{20}H_{14}FNNaO_6$ $[M + Na]^+$: 406.0697, found 406.0700.

*4-(Furan-3-carboxamido)-6-methoxy-1-methyl-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2l**).* Following the general procedure, compound **1d** (101 mg, 0.50 mmol, 1 equiv), (furan-3-carbonyl)glycine **4c** (127 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 80 °C for 3 h. The crude product was purified by column chromatography on silica gel using 50% EtOAc in hexane to furnish compound **2l** (69.0 mg, 35%) as a yellow solid. Mp 217.7−218.5 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 8.26 (br s, 1H, − N*H*), 8.09 (s, 1H, Ar−H), 7.46 (dd, J = 1.8, 1.4 Hz, 1H, Ar−H), 7.41 (d, J = 8.7 Hz, 1H, Ar−H), 7.07 (d, J = 2.4 Hz, 1H, Ar−H), 6.96 (dd, J = 8.7, 2.4 Hz, 1H, Ar−H), 6.91 (s, 1H, − C*H*), 6.81 (d, J = 1.4 Hz, 1H, Ar−H), 3.84 (s, 3H, Ar−OCH_3), 2.27 (s, 3H, CH_3), 2.17 (s, 3H, $OCOCH_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 171.0 ($OCOCH_3$), 163.2 (CONH), 163.1, 161.3 (COO), 154.7, 147.6, 147.3, 146.0, 144.0, 128.8, 128.3, 121.9, 117.8, 116.9, 110.9, 110.5, 108.7, 71.4 (CH), 55.7 (Ar−OCH_3), 20.9 ($OCOCH_3$), 17.1 (CH_3). IR (UATR) ν_{max} 3315 (NH), 3146, 2945, 1740 (CO), 1698 (CO), 1674 (CO), 1604, 1489 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{17}NNaO_7$ $[M + Na]^+$: 418.0897, found 418.0884.

*1-Methyl-3-oxo-4-(thiophene-2-carboxamido)-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2m**).* Following the general procedure, compound **1a** (86.5 mg, 0.50 mmol, 1 equiv), (thiophene-2-carbonyl)glycine **4e** (139 mg, 0.75 mmol, 1.5 equiv), and NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv) in Ac_2O (0.24 mL, 2.50 mmol, 5 equiv) were stirred at 80 °C for 4 h. The crude product was purified by column chromatography on silica gel using 30−50% EtOAc in hexane to furnish compound **2m** (59.3 mg, 31%) as a brown solid. Mp 230.0−230.9 °C. ^1H NMR (300 MHz, DMSO-d_6) δ 10.22 (br s, 1H, − N*H*), 8.09 (d, J = 3.3 Hz, 1H, Ar−H), 7.91 (dd, J = 4.8, 0.8 Hz, 1H, Ar−H), 7.74 (d, J = 7.2 Hz, 1H, Ar−H), 7.68−7.51 (m, 3H, Ar−H), 7.28 (dd, J = 4.8, 3.9 Hz, 1H, Ar−H), 7.02 (s, 1H, − C*H*), 2.32 (s, 3H, CH_3), 2.15 (s, 3H, $OCOCH_3$). $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6) δ 170.5 ($OCOCH_3$), 160.8 (CONH), 160.6 (COO), 157.0, 149.4, 144.9, 138.5, 134.9, 132.7, 132.3, 130.4, 129.8, 128.3, 126.4, 126.0, 116.0, 112.7, 71.1 (CH), 20.6 ($OCOCH_3$), 17.0 (CH_3). IR (UATR) ν_{max} 3318 (NH), 3106, 1734 (CO), 1698 (CO), 1671 (CO), 1612, 1489 cm^{-1}. HRMS (ESI) calcd. for $C_{20}H_{15}NNaO_5S$ $[M + Na]^+$: 404.0563, found 404.0555.

*6-Chloro-1-methyl-3-oxo-4-(thiophene-2-carboxamido)-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2n**).* Following the general procedure, compound **1b** (103 mg, 0.50 mmol, 1 equiv), (thiophene-2-carbonyl)glycine **4e** (136 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 80 °C for 3 h. The crude product was purified by precipitation with EtOAc and filtered off solid to furnish compound **2n** (110 mg, 27%) as a brown solid. Mp

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243.0−243.5 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.26 (br s, 1H, − N*H*), 8.10 (d, J = 3.1 Hz, 1H, Ar−H), 7.92 (dd, J = 5.0, 0.9 Hz, 1H, Ar−H), 7.74−7.63 (m, 3H, Ar−H), 7.28 (dd, J = 4.9, 3.8 Hz, 1H, Ar−H), 7.00 (s, 1H, − C*H*), 2.32 (s, 3H, CH_3), 2.16 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6) δ 170.6 (OCOCH$_3$), 160.7 (*C*ONH), 160.6 (*C*OO), 157.3, 148.1, 146.8, 138.4, 137.2, 133.7, 132.5, 130.7, 130.0, 128.4, 127.5, 126.6, 115.8, 113.0, 70.8 (*C*H), 20.7 (OCO*C*H$_3$), 17.1 (*C*H$_3$). IR (UATR) ν_{max} 3315 (NH), 3101, 1739 (CO), 1698 (CO), 1670 (CO), 1611, 1602, 1487 cm^{-1}. HRMS (ESI) calcd. for $C_{20}H_{14}ClNNaO_5S$ [M + Na]$^+$: 438.0173, found 438.0171.

*6-Fluoro-1-methyl-3-oxo-4-(thiophene-2-carboxamido)-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2o**).* Following the general procedure, compound **1c** (95.0 mg, 0.50 mmol, 1 equiv), (thiophene-2-carbonyl)glycine **4e** (139 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 80 °C for 3 h. The crude product was purified by column chromatography on silica gel using 30−40% EtOAc in hexane to furnish compound **2o** (55.5 mg, 28%) as a brown solid. Mp 244−246 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.22 (br s, 1H, − N*H*), 8.09 (d, J = 3.0 Hz, 1H, Ar−H), 7.91 (dd, J = 4.8, 0.9 Hz, 1H, Ar−H), 7.75 (dd, J_{H-H} = 8.1 Hz and J_{H-F} = 5.1 Hz, 1H, Ar−H), 7.51−7.40 (m, 2H, Ar−H), 7.28 (dd, J = 5.1, 3.8 Hz, 1H, Ar−H), 6.99 (s, 1H, − C*H*), 2.31 (s, 3H, CH_3), 2.16 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6) δ 170.5 (OCOCH$_3$), 164.4 (d, $^1J_{C-F}$ = 250.1 Hz, *C*F), 160.7 (*C*ONH), 160.68 (*C*OO), 157.0, 148.3, 147.7 (d, $^3J_{C-F}$ = 9.4 Hz), 138.4, 132.4, 131.3 (d, $^4J_{C-F}$ = 2.2 Hz), 129.9, 128.3, 128.2 (d, $^3J_{C-F}$ = 11.7 Hz), 118.1 (d, $^2J_{C-F}$ = 23.3 Hz), 116.1, 113.7 (d, $^2J_{C-F}$ = 23.6 Hz), 112.3 (d, $^4J_{C-F}$ = 1.5 Hz), 70.7 (d, $^5J_{C-F}$ = 1.6 Hz, *C*H), 20.6 (OCOCH$_3$), 17.0 (*C*H$_3$). ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6) − 107.99. IR (UATR) ν_{max} 3315 (NH), 3108, 3078, 1740 (CO), 1696 (CO), 1670 (CO), 1653, 1608, 1488 cm^{-1}. HRMS (ESI) calcd. for $C_{20}H_{14}FNNaO_5S$ [M + Na]$^+$: 422.0469, found 422.0467.

*6-Methoxy-1-methyl-3-oxo-4-(thiophene-2-carboxamido)-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2p**).* Following the general procedure, compound **1d** (101 mg, 0.50 mmol, 1 equiv), (thiophene-2-carbonyl)glycine **4e** (139 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 80 °C for 4 h. The crude product was purified by column chromatography on silica gel using 25−40% EtOAc in hexane to furnish compound **2p** (36.5 mg, 18%) as a yellow-orange solid. Mp 233.0−233.5 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.13 (br s, 1H, − N*H*), 8.08 (d, J = 3.3 Hz, 1H, Ar−H), 7.90 (dd, J = 5.1, 0.9 Hz, 1H, Ar−H), 7.65−7.58 (m, 1H, Ar−H), 7.27 (dd, J = 5.1, 3.8 Hz, 1H, Ar−H), 7.18−7.10 (m, 2H, Ar−H), 6.95 (s, 1H, − C*H*), 3.82 (s, 3H, Ar−OCH_3), 2.28 (s, 3H, CH_3), 2.16 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6) δ 170.6 (OCOCH$_3$), 162.9 (*C*ONH), 160.9, 160.6 (*C*OO), 156.4, 149.4, 147.4, 138.7, 132.2, 129.7, 128.2, 127.4, 127.3, 117.0, 116.3, 111.1, 110.7, 70.9 (*C*H), 55.8 (Ar−OCH$_3$), 20.6 (OCO*C*H$_3$), 16.9 (*C*H$_3$). IR (UATR) ν_{max} 3309 (NH), 1736 (CO), 1697 (CO), 1671 (CO), 1648, 1606, 1488 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{17}NNaO_6S$ [M + Na]$^+$: 434.0669, found 434.0670.

*1-Methyl-4-(nicotinamido)-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2q**).* Following the general procedure, compound **1a** (86.0 mg, 0.50 mmol, 1 equiv), nicotinoylglycine **4f** (135 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (2 mL, 0.25 M) in a sealed tube were stirred at 100 °C for 2 h. The crude product was purified by column chromatography on silica gel using 10−50% EtOAc in CH_2Cl_2 to furnish compound **2q** (38.2 mg, 20%) as a pale-yellow solid. Mp 213.4−214.9 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.43 (s, 1H, − N*H*), 9.21 (br s, 1H, Ar−H), 8.82 (dd, J = 4.8, 0.9 Hz, 1H, Ar−H), 8.39 (d, J = 7.8 Hz, 1H, Ar−H), 7.76 (d, J = 7.8 Hz, 1H, Ar−H), 7.67−7.49 (m, 4H, Ar−H), 7.02 (s, 1H, − C*H*), 2.32 (s, 3H, CH_3), 2.16 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6) δ 170.5 (OCOCH$_3$), 164.6 (*C*ONH), 160.7 (*C*OO), 157.0, 152.6, 149.3, 148.8, 144.9, 135.5, 134.8, 132.7, 130.5, 128.9, 126.4, 126.2, 123.7, 116.0, 112.8, 71.1 (*C*H), 20.6 (OCO*C*H$_3$), 17.0 (*C*H$_3$). IR (UATR) ν_{max} 3322 (NH), 3069, 2926, 1735 (CO), 1697 (CO), 1676 (CO), 1611, 1505 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{16}N_2NaO_5$ [M + Na]$^+$: 399.0951, found 399.0955.

*6-Chloro-1-methyl-4-(nicotinamido)-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2r**).* Following the general procedure, compound **1b** (103 mg, 0.50 mmol, 1 equiv), nicotinoylglycine **4f** (135 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (2 mL, 0.25 M) in a sealed tube were stirred at 100 °C for 3 h. The crude product was purified by column chromatography on silica gel using 10−50% EtOAc in CH_2Cl_2 to furnish compound **2r** (30.9 mg, 15%) as a brown solid. Mp 228.0−228.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.22 (d, J = 1.5 Hz, 1H, Ar−H), 8.81 (dd, J = 4.8, 1.5 Hz, 1H, Ar−H), 8.69 (s, 1H, − N*H*), 8.28 (dt, J = 8.1, 1.8 Hz, Ar−H), 7.55 (d, J = 8.1 Hz, 1H, Ar−H), 7.49−7.40 (m, 2H, Ar−H), 7.37 (d, J = 1.5 Hz, 1H, Ar−H), 6.92 (s, 1H, − C*H*), 2.32 (s, 3H, CH_3), 2.17 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.9 (OCOCH$_3$), 164.5 (*C*ONH), 162.2 (*C*OO), 155.7, 153.2, 148.7, 145.9, 143.1, 137.2, 136.3, 135.5, 132.3, 128.8, 127.34, 127.28, 123.7, 117.3, 112.9, 71.0 (*C*H), 20.8 (OCO*C*H$_3$), 17.2 (*C*H$_3$). IR (UATR) ν_{max} 3262 (NH), 3062, 2929, 1714 (CO), 1678 (CO), 1615, 1591, 1505, 1221, 1020 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{15}ClN_2NaO_5$ [M + Na]$^+$: 433.0562, found 433.0559.

*6-Fluoro-1-methyl-4-(nicotinamido)-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2s**).* Following the general procedure, compound **1c** (95.0 mg, 0.50 mmol, 1 equiv), nicotinoylglycine **4f** (135 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (2 mL, 0.25 M) in a sealed tube were stirred at 100 °C for 4 h. The crude product was purified by column chromatography on silica gel using 20−70% EtOAc in CH_2Cl_2 to furnish compound **2s** (58.1 mg, 29%) as a pale-yellow solid. Mp 234.8−236.3 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.42 (s, 1H, − N*H*), 9.20 (br s, 1H, Ar−H), 8.82 (dd, J = 4.8, 1.5 Hz, 1H, Ar−H), 8.38 (d, J = 7.8 Hz, 1H, Ar−H), 7.78 (dd, J_{H-H} = 8.4 Hz and J_{H-F} = 5.1 Hz, 1H, Ar−H), 7.62 (dd, J = 7.8, 4.8 Hz, 1H, Ar−H), 7.50−7.34 (m, 2H, Ar−H), 7.00 (s, 1H, − C*H*), 2.32 (s, 3H, CH_3), 2.16 (s, 3H, OCOCH_3). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6) δ 170.5 (OCOCH$_3$), 164.7 (*C*ONH), 164.4 (d, $^1J_{C-F}$ = 250.4 Hz, *C*F), 160.6 (*C*OO), 157.1, 152.7, 148.8, 148.2, 147.8 (d, $^3J_{C-F}$ = 9.3 Hz), 135.6, 131.3, 128.9, 128.5 (d, $^3J_{C-F}$ = 9.9 Hz), 123.7, 118.1 (d, $^2J_{C-F}$ = 23.3 Hz), 116.2, 113.7 (d, $^2J_{C-F}$ = 23.6 Hz), 112.5, 70.7 (*C*H), 20.6 (OCO*C*H$_3$), 17.0 (*C*H$_3$). ^{19}F{^{1}H} NMR (376 MHz, DMSO-d_6) δ − 107.99. IR (UATR) ν_{max}

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3319 (NH), 3082, 2940, 1742 (CO), 1699 (CO), 1678 (CO), 1669, 1606, 1589, 1505, 1224 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{15}FN_2NaO_5$ $[M + Na]^+$: 417.0857, found 417.0860.

*6-Methoxy-1-methyl-4-(nicotinamido)-3-oxo-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2t**).* Following the general procedure, compound **1d** (101 mg, 0.50 mmol, 1 equiv), nicotinoylglycine **4f** (135 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv) in CH_3CN (2 mL, 0.25 M) in a sealed tube were stirred at 100 °C for 3.5 h. The crude product was purified by column chromatography on silica gel using 20−70% EtOAc in CH_2Cl_2 to furnish compound **2t** (49.4 mg, 24%) as a yellow solid. Mp 222.0−223.5 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 10.34 (br s, 1H, − N*H*), 9.21 (br s, 1H, Ar−H), 8.82 (d, J = 4.0 Hz, 1H, Ar−H), 8.38 (d, J = 8.0 Hz, 1H, Ar−H), 7.66 (d, J = 8.4 Hz, 1H, Ar−H), 7.62 (dd, J = 8.0, 5.0 Hz, 1H, Ar−H), 7.15 (s, 1H, Ar−H), 7.13 (overlapped, 1H, Ar−H), 6.96 (s, 1H, − C*H*), 3.82 (s, 3H, Ar−OCH_3), 2.29 (s, 3H, CH_3), 2.16 (s, 3H, OCOCH_3). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 170.6 (OCOCH$_3$), 164.6 (CONH), 163.0, 160.8 (COO), 156.5, 152.6, 149.3, 148.8, 147.5, 135.6, 129.0, 127.6, 127.2, 123.7, 117.1, 116.4, 111.1, 110.8, 70.9 (CH), 55.8 (Ar−OCH$_3$), 20.7 (OCOCH$_3$), 17.0 (CH$_3$). IR (UATR) ν_{max} 3316 (NH), 1739 (CO), 1694 (CO), 1667 (CO), 1603, 1258, 1221 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{18}N_2NaO_6$ $[M + Na]^+$: 429.1057, found 429.1053.

*4-Acetamido-3-oxo-1-phenyl-3,9-dihydroindeno[2,1-c]-pyran-9-yl Acetate (**2u**).* Following the general procedure, compound **1e** (117 mg, 0.50 mmol, 1 equiv), *N*-acetylglycine **4b** (88.0 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 100 °C for 3 h. The crude product was purified by column chromatography on silica gel using 10% EtOAc in CH_2Cl_2 to furnish compound **2u** (36.4 mg, 19%) as a pale-brown solid. Mp 199.8−200.5 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.93 (br s, 1H, − N*H*), 7.75−7.65 (m, 2H, Ar−H), 7.64−7.55 (m, 1H, Ar−H), 7.55−7.42 (m, 6H, Ar−H), 7.30 (s, 1H, − C*H*), 2.34 (s, 3H, COCH_3), 1.79 (s, 3H, OCOCH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 170.9 (NCOCH$_3$), 169.2 (OCOCH$_3$), 162.0 (COO), 153.4, 147.4, 145.0, 135.4, 132.1, 130.9, 130.6, 130.1, 128.7 (2C), 127.4 (2C), 127.3, 125.9, 117.5, 113.4, 72.0 (CH), 23.8 (COCH$_3$), 20.4 (OCOCH$_3$). IR (UATR) ν_{max} 3264 (NH), 3060, 1699 (CO), 1599, 1496 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{17}NNaO_5$ $[M + Na]^+$: 398.0999, found 398.0990.

*4-Acetamido-6-chloro-3-oxo-1-phenyl-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2v**).* Following the general procedure, compound **1f** (134 mg, 0.50 mmol, 1 equiv), *N*-acetylglycine **4b** (88.0 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 100 °C for 3 h. The crude product was purified by column chromatography on silica gel using 5−20% EtOAc in CH_2Cl_2 to furnish compound **2v** (64.2 mg, 31%) as a pale-brown solid. Mp 227−229 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (br s, 1H, − N*H*), 7.72−7.65 (m, 2H, Ar−H), 7.59 (br s, 1H, Ar−H), 7.52−7.43 (m, 4H, Ar−H), 7.37 (d, J = 8.1 Hz, 1H, Ar−H), 7.26 (s, 1H, − C*H*), 2.35 (s, 3H, COCH_3), 1.81 (s, 3H, OCOCH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 170.9 (NCOCH$_3$), 169.0 (OCOCH$_3$), 161.8 160.6 (COO), 153.5, 146.5, 145.5, 138.3, 134.0, 130.8 (2C), 130.6, 128.8 (2C), 128.4, 127.4 (2C), 126.2, 117.2, 113.4, 71.6 (CH), 23.9 (COCH$_3$), 20.4 (OCOCH$_3$). IR (UATR) ν_{max} 3315 (NH), 2932, 1737 (CO), 1708 (CO), 1687 (CO), 1594, 1516, 1228 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{16}ClNNaO_5$ $[M + Na]^+$: 432.0609, found 432.0598.

*4-Acetamido-6-fluoro-3-oxo-1-phenyl-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2w**).* Following the general procedure, compound **1g** (126 mg, 0.50 mmol, 1 equiv), *N*-acetylglycine **4b** (88.0 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.10 mL, 1.10 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 100 °C for 4 h. The crude product was purified by column chromatography on silica gel using 10−20% EtOAc in CH_2Cl_2 to furnish compound **2w** (48.5 mg, 25%) as a pale-brown solid. Mp 221.0−222.8 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.89 (br s, 1H, − N*H*), 7.73−7.64 (m, 2H, Ar−H), 7.52−7.42 (m, 4H, Ar−H), 7.29 (dd, J = 8.3, 2.0 Hz, 1H, Ar−H), 7.25 (s, 1H, − C*H*), 7.19 (ddd, J = 8.7, 8.3, 2.0 Hz, 1H, Ar−H), 2.35 (s, 3H, COCH_3), 1.81 (s, 3H, OCOCH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 170.8 (NCOCH$_3$), 169.2 (OCOCH$_3$), 164.9 (d, $^1J_{C-F}$ = 252.8 Hz, CF), 161.9 (COO), 153.4, 147.5 (d, $^3J_{C-F}$ = 9.1 Hz), 146.0, 131.6, 130.8, 130.7, 129.3 (d, $^3J_{C-F}$ = 9.2 Hz), 128.8 (2C), 127.4 (2C), 117.8 (d, $^2J_{C-F}$ = 23.0 Hz), 117.4, 113.3 (d, $^2J_{C-F}$ = 23.5 Hz), 113.0, 71.7 (d, $^5J_{C-F}$ = 2.0 Hz, CH), 23.8 (COCH$_3$), 20.3 (OCOCH$_3$). $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ − 108.44. IR (UATR) ν_{max} 3275 (NH), 2926, 1706 (CO), 1607, 1589, 1368, 1219 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{16}FNNaO_5$ $[M + Na]^+$: 416.0905, found 416.0905.

*4-Acetamido-6-methoxy-3-oxo-1-phenyl-3,9-dihydroindeno[2,1-c]pyran-9-yl Acetate (**2x**).* Following the general procedure, compound **1h** (52.8 mg, 0.20 mmol, 1 equiv), *N*-acetylglycine **4b** (35.0 mg, 0.30 mmol, 1.5 equiv), NaOAc (18.0 mg, 0.22 mmol, 1.1 equiv), and Ac_2O (40 μL, 0.44 mmol, 2.2 equiv) in CH_3CN (0.24 mL, 2 M) in a sealed tube were stirred at 100 °C for 3 h. The crude product was purified by column chromatography on silica gel using 10% EtOAc in CH_2Cl_2 to furnish compound **2x** (25.9 mg, 32%) as a pale-yellow solid. Mp 199−200 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (br s, 1H, − N*H*), 7.72−7.63 (m, 2H, Ar−H), 7.50−7.40 (m, 4H, Ar−H), 7.22 (s, 1H, − C*H*), 7.06 (br s, 1H, Ar−H), 7.00 (dd, J = 8.7, 2.0 Hz, 1H, Ar−H), 3.84 (s, 3H, Ar−OCH_3), 2.33 (s, 3H, COCH_3), 1.79 (s, 3H, OCOCH_3). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 171.0 (NCOCH$_3$), 169.4 (OCOCH$_3$), 163.1, 162.2 (COO), 153.1, 147.8, 147.4, 130.9, 130.5, 128.63 (2C), 128.59, 127.9, 127.4 (2C), 117.7, 117.0, 111.5, 110.4, 71.9 (CH), 55.7 (Ar−OCH$_3$), 23.7 (COCH$_3$), 20.4 (OCOCH$_3$). IR (UATR) ν_{max} 3264 (NH), 2941, 1698 (CO), 1598, 1488, 1368, 1257, 1223 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{19}NNaO_6$ $[M + Na]^+$: 428.1105, found 428.1109.

General Procedure for the Synthesis of 1-Oxazolonylisobenzofurans *Z*/*E*-3. In a round-bottom flask with a magnetic bar, compounds **1** (1 equiv), amino acid derivatives **4g−j** (1.5 equiv), NaOAc (1.1 equiv), and Ac_2O (5 equiv) were stirred at 80 °C for 4 h. The reaction mixture was allowed to cool to room temperature (26 °C) and then quenched with sat. Na_2CO_3 (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). Combined organic layers were washed with sat. Na_2CO_3 until pH = 7, followed by water and brine, and dried over anh. Na_2SO_4 and concentrated to give a dark brown sticky gum. The crude product was purified by column chromatography on silica gel using 30−60% EtOAc in hexane or 0−50% EtOAc in CH_2Cl_2 to afford 1-oxazolonylisobenzofurans *Z*/*E*-**3**

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*(Z)-4-Benzyl-2-methyl-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (Z-**3ag**) and (E)-4-Benzyl-2-methyl-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (E-**3ag**).* Following the general procedure, using compound **1a** (86.7 mg, 0.51 mmol, 1 equiv), DL-phenylalanine **4g** (124 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.5 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 40% EtOAc in hexane to furnish compound *Z/E*-**3ag** (95.2 mg, 53% (>99:1 *Z/E*)).

***Z*-3ag**. (95.2 mg, 53% (75:25 dr) mixture of isomer) as a pale-yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65−7.45 (m, 4H, Ar−H, major), 7.38−7.11 (m, 5H, Ar−H, major), 5.95 (s, 1H, ArC*H*O, major), 5.94 (s, 1H, ArC*H*O, minor), 5.82 (s, 1H, =C*H*COCH$_3$, minor), 5.75 (s, 1H, =C*H*COCH$_3$, major), 3.46 (AB q, J = 13.8 Hz, 2H, CH_2Ph, major), 3.42 (AB q, J = 13.5 Hz, 2H, CH_2Ph, minor), 2.58 (s, 3H, =CHCOCH_3, minor), 2.50 (s, 3H, =CHCOCH_3, major), 1.96 (s, 3H, N=CCH_3, major), 1.78 (s, 3H, N=CCH_3, minor). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 197.12 (COCH$_3$, major), 197.07 (COCH$_3$, minor), 175.9 (COO, major), 164.72 (N=*C*CH$_3$, major), 164.67 (N=*C*CH$_3$, minor), 164.0 (=CO, major), 138.6 (major), 134.2 (major), 133.9 (minor), 132.9 (minor), 132.7 (major), 131.7 (minor), 131.6 (major), 130.3 (2C, major), 130.2 (2C, minor), 130.1 (major), 129.9 (minor), 128.4 (2C, major), 128.3 (2C, minor), 127.7 (major), 127.6 (minor), 122.4 (major), 122.3 (major), 122.1 (minor), 121.7 (minor), 99.3 (=*C*HCOCH$_3$, minor), 98.9 (=CHCOCH$_3$, major), 87.8 (Ar*C*HO, minor), 87.1 (Ar*C*HO, major), 76.72 (*C*, minor), 76.68 (*C*, major), 39.4 (CH$_2$Ph, minor), 39.0 (CH$_2$Ph, major), 31.1 (=CHCOCH$_3$, minor), 31.0 (=CHCOCH$_3$, major), 14.7 (N=C*C*H$_3$, major), 14.3 (N=C*C*H$_3$, minor). IR (UATR) ν_{max} 3034, 2925, 1823 (CO), 1684 (C=N), 1633, 1493, 1467, 1431, 1383, 1365 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{19}NNaO_4$ [M + Na]$^+$: 384.1206, found 384.1210.

*(Z)-4-Benzyl-4-(6-chloro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (Z-**3bg**) and (E)-4-Benzyl-4-(6-chloro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (E-**3bg**).* Following the general procedure, using compound **1b** (105 mg, 0.51 mmol, 1 equiv), DL-phenylalanine **4g** (124 mg, 0.75 mmol, 1.5 equiv), NaOAc (46.3 mg, 0.56 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 35% EtOAc in hexane to furnish compound *Z/E*-**3bg** (104 mg, 53% (>99:1 *Z/E*)).

***Z*-3bg**. (104 mg, 53% (65:35 dr) mixture of isomer) as a pale-brown solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55−7.10 (m, 8H, Ar−H, major), 5.91 (s, 1H, ArC*H*O, major), 5.87 (s, 1H, ArC*H*O, minor), 5.77 (s, 1H, =C*H*COCH$_3$, minor), 5.70 (s, 1H, =C*H*COCH$_3$, major), 3.43 (AB q, J = 13.4 Hz, 2H, CH_2Ph, major), 3.34 (s, 2H, CH_2Ph, minor), 2.56 (s, 3H, =CHCOCH_3, minor), 2.48 (s, 3H, =CHCOCH_3, major), 1.98 (s, 3H, N=CCH_3, major), 1.85 (s, 3H, N=CCH_3, minor). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 196.8 (COCH$_3$, major), 176.0 (COO, minor), 175.6 (COO, major), 164.3 (N=*C*CH$_3$, major), 136.5 (major), 163.4 (minor), 163.1 (minor), 140.3 (minor),140.2 (major), 137.9 (minor), 137.8 (major), 132.7 (minor), 132.6 (major), 132.50 (minor), 132.46 (major), 130.6 (major), 130.5 (minor), 130.3 (2C, major), 130.2 (2C, minor), 128.4 (2C, major), 128.3 (2C, minor), 127.8 (major), 127.7 (minor), 123.2 (major), 123.1 (minor), 122.9 (major), 122.4 (minor), 99.6 (=*C*HCOCH$_3$, minor), 99.3 (=CHCOCH$_3$, major), 87.1 (ArCHO, minor), 86.5 (ArCHO, major), 76.5 (*C*, major), 76.4 (*C*, minor), 39.0 (CH$_2$Ph, minor), 38.9 (CH$_2$Ph, major), 31.1 (=CHCOCH$_3$, minor), 31.0 (=CHCOCH$_3$, major), 14.7 (N=C*C*H$_3$, major), 14.4 (N=C*C*H$_3$, minor). IR (UATR) ν_{max} 3276, 3031, 2959, 2927, 2853, 1825 (CO), 1805 (CO), 1679 (C=N), 1626, 1605 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{18}ClNNaO_4$ [M + Na]$^+$: 418.0817, found 418.0819.

*(Z)-4-Benzyl-4-(6-fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (Z-**3cg**) and (E)-4-Benzyl-4-(6-fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (E-**3cg**).*[26] Following the general procedure, using compound **1c** (95.2 mg, 0.50 mmol, 1 equiv), DL-phenylalanine **4g** (124 mg, 0.75 mmol, 1.5 equiv), NaOAc (48.8 mg, 0.59 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 40% EtOAc in hexane to furnish compound *Z/E*-**3cg** (73.0 mg, 38% (>99:1 *Z/E*)).

*Gram Scale Synthesis of (Z)-4-Benzyl-4-(6-fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (Z-**3cg**) and (E)-4-Benzyl-4-(6-fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (E-**3cg**).* According to the general procedure, using compound **1c** (1.39 g, 7.31 mmol, 1 equiv), DL-phenylalanine **4g** (1.81 g, 11.0 mmol, 1.5 equiv), NaOAc (0.66 g, 8.05 mmol, 1.1 equiv), and Ac_2O (3.45 mL, 36.7 mmol, 5 equiv), the product *Z/E*-**3cg** was obtained (1.33 g, 48% (96:4 *Z/E*)).

***Z*-3cg**. (73.0 mg, 38% (58:42 dr) mixture of isomer) as a pale-yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (dd, J_{H-H} = 8.7 Hz and J_{H-F} = 4.8 Hz, 1H, Ar−H, major), 7.35−7.10 (m, 7H, Ar−H, major), 5.92 (s, 1H, ArC*H*O, minor), 5.88 (s, 1H, ArC*H*O, major), 5.75 (s, 1H, =C*H*COCH$_3$, major), 5.69 (s, 1H, =C*H*COCH$_3$, minor), 3.43 (AB q, J = 13.1 Hz, 2H, CH_2Ph, minor), 3.35 (s, 2H, CH_2Ph, major), 2.57 (s, 3H, =CHCOCH_3, major), 2.49 (s, 3H, =CHCOCH_3, minor), 1.98 (s, 3H, N=CCH_3, minor), 1.84 (s, 3H, N=CCH_3, major). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 196.9 (COCH$_3$, major), 176.0 (COO, major), 175.6 (COO, minor), 164.8 (d, $^1J_{C-F}$ = 246.8 Hz, CF, major), 164.7 (d, $^1J_{C-F}$ = 244.6 Hz, CF, minor), 164.3 (=CO, minor), 163.7 (=CO, major), 163.0 (N=*C*CH$_3$, major), 141.0 (d, $^3J_{C-F}$ = 9.5 Hz, major), 140.9 (d, $^3J_{C-F}$ = 10.7 Hz, minor), 132.6 (major), 132.5 (minor), 130.3 (2C, minor), 130.2 (2C, major), 129.9 (d, $^4J_{C-F}$ = 2.6 Hz, major), 128.4 (2C, minor), 128.3 (2C, major), 127.8 (minor), 127.7 (major), 124.1 (d, $^3J_{C-F}$ = 9.8 Hz, minor), 124.0 (d, $^3J_{C-F}$ = 9.6 Hz, major), 118.1 (d, $^2J_{C-F}$ = 23.7 Hz, minor), 117.9 (d, $^2J_{C-F}$ = 23.8 Hz, major), 110.0 (d, $^2J_{C-F}$ = 25.1 Hz, minor), 109.6 (d, $^2J_{C-F}$ = 25.0 Hz, major), 99.2 (d, $^6J_{C-F}$ = 1.5 Hz, =*C*HCOCH$_3$, major), 98.8 (d, $^6J_{C-F}$ = 1.5 Hz, =*C*HCOCH$_3$, minor), 87.1 (d, $^4J_{C-F}$ = 2.9 Hz, ArCHO major), 86.4 (d, $^4J_{C-F}$ = 2.9 Hz, ArCHO, minor), 76.5 (*C*, minor), 76.4 (*C*, major), 39.1 (CH$_2$Ph, major), 39.0 (CH$_2$Ph, minor), 31.1 (=CHCOCH$_3$, major), 31.0 (=CHCOCH$_3$, minor), 14.7 (N=C*C*H$_3$, minor), 14.4 (N=C*C*H$_3$, major). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 109.17 (minor), − 109.46 (major). IR (UATR) ν_{max} 3090, 3034, 2928, 1822 (CO), 1715 (CO), 1682 (C=N), 1635, 1619, 1599, 1526,

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1482, 1456, 1432 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{18}FNNaO_4$ $[M + Na]^+$: 402.1112, found 402.1108.

*(Z)-4-Benzyl-4-(6-methoxy-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (Z-**3dg**) and (E)-4-Benzyl-4-(6-methoxy-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (E-**3dg**).* Following the general procedure, using compound **1d** (104 mg, 0.51 mmol, 1 equiv), DL-phenylalanine **4g** (125 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.3 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 40% EtOAc in hexane to furnish compound *Z/E*-**3dg** (46.9 mg, 24% (>99:1 *Z/E*)).

*Z-**3dg**.* (46.9 mg, 24% (84:16 dr) mixture of isomer) as a brown sticky-gum. ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, J = 8.7 Hz, 1H, Ar−H, major), 7.31−7.12 (m, 5H, Ar−H, major), 7.03 (dd, J = 8.7, 2.1 Hz, 1H, Ar−H, major), 6.95 (d, J = 2.1 Hz, 1H, Ar−H, major), 6.83 (d, J = 2.1 Hz, Ar−H, minor), 5.88 (s, 1H, ArC*H*O, major), 5.85 (s, 1H, ArC*H*O, minor), 5.70 (s, 1H, =C*H*COCH$_3$, minor), 5.64 (s, 1H, =C*H*COCH$_3$, major), 3.87 (s, 3H, Ar−OC*H*$_3$, major), 3.85 (s, 3H, Ar−OC*H*$_3$, minor), 3.45 (AB q, J = 12.3 Hz, 2H, C*H*$_2$Ph, major), 3.39 (AB q, J = 13.2 Hz, 2H, C*H*$_2$Ph, minor), 2.55 (s, 3H, =CHCOC*H*$_3$, minor), 2.48 (s, 3H, =CHCOC*H*$_3$, major), 1.98 (s, 3H, N=CC*H*$_3$, major), 1.82 (s, 3H, N=CC*H*$_3$, minor). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 196.91 (*C*OCH$_3$, major), 196.88 (*C*OCH$_3$, minor), 176.3 (*C*OO, minor), 175.8 (*C*OO, major), 164.93 (=*C*O, major), 164.91 (=*C*O, minor), 164.1 (N=*C*CH$_3$, major), 162.82 (N=*C*CH$_3$, minor), 162.76 (minor), 162.66 (major), 140.9 (minor), 140.8 (major), 132.9 (minor), 132.7 (major), 130.3 (2C, major), 130.2 (2C, minor), 128.4 (2C, major), 128.3 (2C, minor), 127.7 (major), 127.6 (minor), 126.4 (major), 126.1 (minor), 123.6 (major), 123.4 (minor), 116.7 (minor), 116.5 (major), 107.5 (major), 106.4 (minor), 98.0 (=*C*HCOCH$_3$, minor), 97.7 (=CHCOCH$_3$, major), 87.3 (ArCHO, minor), 86.5 (ArCHO, major), 76.60 (*C*, minor), 76.56 (*C*, major), 55.81 (Ar−OCH$_3$, minor), 55.76 (Ar−OCH$_3$, major), 39.3 (*C*H$_2$Ph, minor), 39.0 (*C*H$_2$Ph, major), 30.9 (=CHCOCH$_3$, minor), 30.8 (=CHCOCH$_3$, major), 14.7 (N=C*C*H$_3$, major), 14.4 (N=C*C*H$_3$, minor). IR (UATR) ν_{max} 3100, 3020, 2929, 2840, 1822 (CO), 1680 (C=N), 1633, 1605, 1489, 1456, 1436, 1364 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{21}NNaO_5$ $[M + Na]^+$: 414.1312, found 414.1314.

*(Z)-4-Benzyl-2-methyl-4-(3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (Z-**3eg**) and (E)-4-Benzyl-2-methyl-4-(3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (E-**3eg**).* Following the general procedure, using compound **1e** (117 mg, 0.50 mmol, 1 equiv), DL-phenylalanine **4g** (124 mg, 0.75 mmol, 1.5 equiv), NaOAc (48.8 mg, 0.59 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 0−4% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3eg** (139.6 mg, 66% (77:23 *Z/E*)).

*Z-**3eg**.* (107.9 mg, 51%) as a pale-yellow sticky-gum. ^1H NMR (300 MHz, $CDCl_3$) δ 8.06−7.99 (m, 2H, Ar−H), 7.79−7.71 (m, 1H, Ar−H), 7.57−7.39 (m, 6H, Ar−H), 7.30−7.15 (m, 5H, Ar−H), 6.54 (s, 1H, =C*H*COPh), 5.90 (s, 1H, ArC*H*O), 3.40 (AB q, J = 13.4 Hz, 2H, C*H*$_2$Ph), 1.97 (s, 3H, N=CC*H*$_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 189.1 (*C*OPh), 175.6 (*C*OO), 165.8 (N=*C*CH$_3$), 164.3 (=*C*O), 139.9, 139.3, 134.6, 133.1, 131.8, 131.6, 130.5 (2C), 129.9, 128.29 (2C), 128.26 (2C), 128.0 (2C), 127.4, 122.3, 122.0, 93.0 (=CHCOPh), 86.6 (ArCHO), 76.3 (*C*), 39.3 (*C*H$_2$Ph), 14.7 (N=C*C*H$_3$). IR (UATR) ν_{max} 3059, 3032, 1822 (CO), 1716 (CO), 1660 (C=N), 1599, 1589, 1573, 1496, 1467 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{21}NNaO_4$ $[M + Na]^+$: 446.1363, found 446.1366.

*E-**3eg**.* (31.7 mg, 15%) as a pale-yellow sticky-gum. ^1H NMR (300 MHz, $CDCl_3$) δ 9.49−9.41 (m, 1H, Ar−H), 8.06−7.98 (m, 2H, Ar−H), 7.62−7.42 (m, 6H, Ar−H), 7.33−7.14 (m, 5H, Ar−H), 6.88 (s, 1H, =C*H*COPh), 5.82 (s, 1H, ArC*H*O), 3.44 (s, 2H, C*H*$_2$Ph), 1.95 (s, 3H, N=CC*H*$_3$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 189.3 (COPh), 176.1 (COO), 170.2 (N=*C*CH$_3$), 163.8 (=CO), 141.5, 139.9, 132.9, 132.3, 132.1, 132.0, 130.3 (2C), 129.9, 128.6, 128.4 (2C), 128.3 (2C), 127.9 (2C), 127.6, 121.7, 98.3 (=*C*HCOPh), 84.6 (ArCHO), 76.7 (*C*), 38.9 (*C*H$_2$Ph), 14.7 (N=C*C*H$_3$). IR (UATR) ν_{max} 3062, 3032, 2926, 2855, 1822 (CO), 1730 (CO), 1681 (C=N), 1650, 1588, 1567, 1496, 1466, 1383 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{21}NNaO_4$ $[M + Na]^+$: 446.1363, found 446.1357.

*(Z)-4-Benzyl-4-(6-chloro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (Z-**3fg**) and (E)-4-Benzyl-4-(6-chloro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (E-**3fg**).* Following the general procedure, using compound **1f** (136 mg, 0.50 mmol, 1 equiv), DL-phenylalanine **4g** (125 mg, 0.76 mmol, 1.5 equiv), NaOAc (46.7 mg, 0.57 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 0−2% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3fg** (176.3 mg, 77% (75:25 *Z/E*)).

*Z-**3fg**.* (132.8 mg, 58%) as a pale-yellow solid. Mp 189.2−190.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.04−7.98 (m, 2H, Ar−H), 7.67 (d, J = 8.4 Hz, 1H, Ar−H), 7.56−7.46 (m, 4H, Ar−H), 7.40 (br s, 1H, Ar−H), 7.31−7.23 (m, 3H, Ar−H), 7.23−7.16 (m, 2H, Ar−H), 6.49 (s, 1H, =C*H*COPh), 5.85 (s, 1H, ArC*H*O), 3.42 (AB q, J = 13.2 Hz, 2H (C*H*$_2$Ph), 2.00 (s, 3H, N=CC*H*$_3$). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.0 (COPh), 175.4 (COO), 164.54 (=CO), 164.52 (N=CCH$_3$), 140.9, 139.7, 137.8, 133.3, 132.9, 132.0, 130.5 (3C), 128.4 (2C), 128.3 (2C), 128.0 (2C), 127.6, 123.0, 122.8, 93.4 (=*C*HCOPh), 86.1 (ArCHO), 76.2 (*C*), 39.2 (*C*H$_2$Ph), 14.7 (N=C*C*H$_3$). IR (UATR) ν_{max} 3062, 3034, 2927, 1801 (CO), 1728 (CO), 1682 (C=N), 1665, 1606, 1576, 1495, 1469, 1455, 1432, 1383 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{20}ClNNaO_4$ $[M + Na]^+$: 480.0973, found 480.0966.

*E-**3fg**.* (43.5 mg, 19% (78:22 dr) mixture of isomer) as a brown solid. ^1H NMR (300 MHz, $CDCl_3$) δ 9.43 (d, J = 8.7 Hz, 1H, Ar−H, minor), 9.42 (d, J = 8.7 Hz, 1H, Ar−H, major), 8.06−7.97 (m, 2H, Ar−H, major), 7.58−7.43 (m, 4H, Ar−H, major), 7.37−7.33 (m, 1H, Ar−H, minor), 7.31−7.23 (m, 4H, Ar−H, major), 7.23−7.12 (m, 2H, Ar−H, major), 6.99 (s, 1H, =C*H*COPh, minor), 6.88 (s, 1H, =C*H*COPh, major), 5.77 (s, 1H, ArC*H*O, major), 5.75 (s, 1H, ArC*H*O, minor), 3.41 (s, 2H, C*H*$_2$Ph, major), 3.35 (AB q, J = 13.2 Hz, 2H, C*H*$_2$Ph, minor), 1.98 (s, 3H, N=CC*H*$_3$, major), 1.82 (s, 3H, N=CC*H*$_3$, minor). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ189.4 (COPh, minor), 189.3 (COPh, major), 176.4 (COO, minor), 175.9 (COO, major), 169.2 (=CO, minor), 169.1 (=CO, major), 164.1 (N=*C*CH$_3$, major), 163.1 (N=*C*CH$_3$, minor), 143.5 (minor), 143.2 (major), 139.8 (minor), 139.7 (major), 138.5 (minor), 138.3 (major), 132.9 (minor), 132.7 (major),

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132.2 (major), 130.9 (major), 130.7 (minor), 130.4 (2C, major), 130.3 (major), 130.2 (minor), 129.8 (major), 129.7 (minor), 128.5 (2C, major), 128.4 (2C, major), 128.3 (2C, minor), 128.0 (2C, major), 127.7 (major), 127.6 (minor), 122.1 (major), 121.4 (minor), 99.2 (=*C*HCOPh, minor), 98.6 (=*C*HCOPh, major), 84.8 (Ar*C*HO, minor), 84.2 (Ar*C*HO, major), 77.2 (*C*, minor), 76.5 (*C*, major), 39.2 (CH_2Ph, minor), 38.9 (CH_2Ph, major), 14.7 (N=C*C*H_3, major), 14.5 (N=C*C*H_3, minor). IR (UATR) ν_{max} 3063, 3033, 2928, 1823 (CO), 1682 (C=N), 1650, 1602, 1584, 1568, 1495, 1456, 1428, 1383 cm^{-1} HRMS (ESI) calcd. for $C_{27}H_{21}ClNO_4$ $[M + H]^+$: 458.1154, found 458.1156.

*(Z)-4-Benzyl-4-(6-fluoro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (Z-**3gg**) and (E)-4-Benzyl-4-(6-fluoro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (E-**3gg**).* Following the general procedure, using compound **1g** (126 mg, 0.50 mmol, 1 equiv), DL-phenylalanine **4g** (125 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.4 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 0−50% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3gg** (63.9 mg, 29% (72:28 *Z/E*)).

Z-3gg. (46.3 mg, 21%) as a pale-yellow sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04−7.98 (m, 2H, Ar−H), 7.72 (dd, J_{H-H} = 8.7 Hz and J_{H-F} = 4.8 Hz, 1H, Ar−H), 7.56−7.43 (m, 3H, Ar−H), 7.30−7.16 (m, 6H, Ar−H), 7.10 (dd, *J* = 7.8, 2.1 Hz, 1H, Ar−H), 6.48 (s, 1H, =C*H*COPh), 5.86 (s, 1H, ArC*H*O), 3.42 (AB q, *J* = 13.5 Hz, 2H, CH_2Ph), 2.00 (s, 3H, N=CCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.0 (*C*OPh), 175.4 (*C*OO), 164.7 (=*C*O), 164.6 (d, $^1J_{C-F}$ = 252.0 Hz, *C*F), 164.5 (N=*C*CH$_3$), 141.6 (d, $^3J_{C-F}$ = 9.4 Hz), 139.8, 132.9, 131.9, 130.7 (d, $^4J_{C-F}$ = 2.3 Hz), 130.5 (2C), 128.3 (4C), 128.0 (2C), 127.6. 123.9 (d, $^3J_{C-F}$ = 9.8 Hz), 117.9 (d, $^2J_{C-F}$ = 23.9 Hz), 109.9 (d, $^2J_{C-F}$ = 24.9 Hz), 92.9 (d, $^6J_{C-F}$ = 1.4 Hz, =*C*HCOPh), 86.0 (d, $^4J_{C-F}$ = 2.8 Hz, ArCHO), 76.1 (*C*), 39.3 (CH_2Ph), 14.8 (N=*C*CH$_3$). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 109.41. IR (UATR) ν_{max} 3063, 3034, 2929, 1824 (CO), 1720 (CO), 1678 (C=N), 1661, 1592, 1573, 1480, 1456, 1447 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{21}FNO_4$ $[M + H]^+$: 442.1449, found 442.1437.

E-3gg. (17.6 mg, 8% (65:35 dr) mixture of isomer) as a pale-yellow sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.53 (dd, J_{H-H} = 9.0 Hz and J_{H-F} = 5.4 Hz, 1H, Ar−H, major), 8.06−7.97 (m, 2H, Ar−H, major), 7.58−7.43 (m, 3H, Ar−H, major), 7.31−7.12 (m, 7H, Ar−H, major), 7.05 (dd, *J* = 7.8, 2.4 Hz, 1H, Ar−H, minor), 6.97 (s, 1H, =C*H*COPh, minor), 6.86 (s, 1H, =C*H*COPh, major), 5.78 (s, 1H, ArC*H*O, major), 5.76 (s, 1H, ArC*H*O, minor), 3.41 (s, 2H, CH_2Ph, major), 3.36 (AB q, *J* = 13.5 Hz, 2H, CH_2Ph, minor), 1.97 (s, 3H, N=CCH_3, major), 1.87 (s, 3H, N=CCH_3, minor). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.3 (*C*OPh, minor), 189.2 (*C*OPh, major), 176.5 (*C*OO, minor), 175.8 (*C*OO, major), 169.4 (=*C*O, minor), 169.3 (=*C*O, major), 164.7 (d, $^1J_{C-F}$ = 253.6 Hz, *C*F, major), 164.1 (N=*C*CH$_3$, major), 144.5 (d, $^3J_{C-F}$ = 9.4 Hz, minor), 144.2 (d, $^3J_{C-F}$ = 9.3 Hz, major), 139.9 (minor), 139.8 (major), 132.9 (minor), 132.7 (major), 132.1 (d, $^4J_{C-F}$ = 2.6 Hz, major), 131.03 (d, $^3J_{C-F}$ = 9.5 Hz, major), 130.96 (d, $^3J_{C-F}$ = 9.3 Hz, minor), 130.34 (2C, major), 130.28 (2C, minor), 128.6 (d, $^4J_{C-F}$ = 2.5 Hz, major), 128.44 (2C, major), 128.37 (2C, major), 128.30 (2C, minor), 128.0 (2C, minor), 127.9 (2C, major), 127.7 (major), 127.6 (minor), 117.4 (d, $^2J_{C-F}$ = 22.2 Hz, major), 117.3 (d, $^2J_{C-F}$ = 22.3 Hz, minor), 109.2 (d, $^2J_{C-F}$ = 25.0 Hz, major), 108.6 (d, $^2J_{C-F}$ = 24.7 Hz, minor), 98.4 (=*C*HCOPh, minor), 97.9 (=*C*HCOPh, major), 84.9 (d, $^4J_{C-F}$ = 3.0 Hz, ArCHO, minor), 84.2 (d, $^4J_{C-F}$ = 2.8 Hz, ArCHO, major), 77.2 (*C*, minor), 76.5 (*C*, major), 39.2 (CH_2Ph, minor), 38.9 (CH_2Ph, major), 14.7 (N=C*C*H_3, major), 14.4 (N=C*C*H_3, minor). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 107.94 (minor), − 108.27 (major). IR (UATR) ν_{max} 3063, 3034, 2929, 1824 (CO), 1720 (CO), 1678 (C=N), 1661, 1592, 1573, 1480 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{21}FNO_4$ $[M + H]^+$: 442.1449, found 422.1437.

*(Z)-4-Benzyl-4-(6-methoxy-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (Z-**3hg**) and (E)-4-Benzyl-4-(6-methoxy-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (E-**3hg**).* Following the general procedure, using compound **1h** (133 mg, 0.50 mmol, 1 equiv), DL-phenylalanine **4g** (125 mg, 0.75 mmol, 1.5 equiv), NaOAc (47.4 mg, 0.57 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 2−20% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3hg** (97.5 mg, 43% (75:25 *Z/E*)).

Z-3hg. (72.6 mg, 32%) as a pale brown solid. Mp 183.5−184.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.0, 1.7, 2H, Ar−H), 7.65 (d, *J* = 8.7 Hz, 1H, Ar−H), 7.55−7.42 (m, 3H, Ar−H), 7.31−7.17 (m, 5H, Ar−H), 7.03 (dd, *J* = 8.6, 2.3 Hz, 1H, Ar−H), 6.88 (d. *J* = 2.1 Hz, 1H, Ar−H), 6.42 (s, 1H, =C*H*COPh), 5.82 (s, 1H, ArC*H*O), 3.85 (s, 3H, Ar−OCH_3), 3.45 (AB q, *J* = 13.5 Hz, 2H, CH_2Ph), 2.00 (s, 3H, N=CCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.0 (*C*OPh), 175.5 (*C*OO), 166.1, 164.2 (=*C*O), 162.7 (N=*C*CH$_3$), 141.6, 140.2, 133.1, 131.6, 130.5 (2C), 128.3 (2C), 128.2 (2C), 127.9 (2C), 127.5, 127.0, 123.4, 116.6, 107.2, 91.7 (=*C*HCOPh), 86.1 (Ar*C*HO), 76.2 (*C*), 55.8 (Ar−O*C*H$_3$), 39.4 (CH_2Ph), 14.8 (N=CCH_3). IR (UATR) ν_{max} 3062, 3031, 2927, 2841, 1823 (CO), 1768 (CO), 1680 (C=N), 1656, 1599, 1586, 1571, 1488, 1455, 1382 cm^{-1}. HRMS (ESI) calcd. for $C_{28}H_{23}NNaO_5$ $[M + Na]^+$: 476.1468, found 476.1468.

E-3hg. (24.9 mg, 11% (50:50 dr) mixture of isomer) as a brown sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.47 (d, *J* = 9.0 Hz, 1H), 9.46 (d, *J* = 8.7 Hz, 1H, Ar−H), 8.02 (d, *J* = 8.4 Hz, 2H, Ar−H), 8.00 (d, *J* = 8.4 Hz, 2H, Ar−H), 7.56−7.41 (m, 6H, Ar−H), 7.31−7.12 (m, 10H, Ar−H), 7.06 (dd, *J* = 8.4, 2.3 Hz, 1H, Ar−H), 7.04 (dd, *J* = 8.4, 2.3 Hz, 1H, Ar−H), 6.96 (d, *J* = 1.8 Hz, 1H, Ar−H), 6.88 (s, 1H, =C*H*COPh), 6.79 (d, *J* = 2.1 Hz, 1H, Ar−H), 6.77 (s, 1H, =C*H*COPh), 5.74 (s, 2H, ArC*H*O), 3.88 (s, 3H, Ar−OCH_3), 3.86 (s, 3H, Ar−OCH_3), 3.43 (AB q, *J* = 13.8 Hz, 2H, CH_2Ph), 3.40 (AB q, *J* = 13.2 Hz, 2H, CH_2Ph), 1.97 (s, 3H, N=CCH_3), 1.78 (s, 3H, N=CCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.3 (*C*OPh), 189.2 (*C*OPh), 176.7 (*C*OO), 176.0 (*C*OO), 170.6 (=*C*O), 170.5 (=*C*O), 163.9 (N=*C*CH$_3$), 163.0 (N=*C*CH$_3$), 162.8, 162.7, 144.5, 144.2, 140.3, 140.2, 133.0, 132.9, 131.8, 131.7, 134.0, 130.34 (3C), 130.29 (2C), 128.3 (6C), 128.2 (2C), 127.9 (2C), 127.7 (2C), 127.6, 127.5, 125.0, 124.7, 115.6, 115.3, 107.3, 105.9, 97.1 (=*C*HCOPh), 96.5 (=*C*HCOPh), 85.0 (Ar*C*HO), 84.2 (Ar*C*HO), 76.9 (*C*), 76.5 (*C*), 55.74 (Ar−O*C*H$_3$), 55.70 (Ar−O*C*H$_3$), 39.4 (CH_2Ph), 38.9 (CH_2Ph), 14.7 (N=C*C*H_3), 14.4 (N=C*C*H_3). IR (UATR) ν_{max} 3061, 3033, 2932, 2839, 1821 (CO), 1725 (CO), 1680 (C=N), 1649, 1598, 1582, 1557,

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1484, 1437 cm^{-1}. HRMS (ESI) calcd. for $C_{28}H_{24}NO_5$ $[M + H]^+$: 454.1649, found 454.1646.

*(Z)-4-((2-Methyl-5-oxo-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (Z-**3ah**) and (E)-4-((2-Methyl-5-oxo-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (E-**3ah**).* Following the general procedure, using compound **1a** (86.7 mg, 0.50 mmol), L-tyrosine **4h** (137 mg, 0.76 mmol), NaOAc (46.8 mg, 0.59 mmol), and Ac_2O (0.24 mL, 2.50 mmol), the crude product was purified by column chromatography on silica gel using 50% EtOAc in hexane to furnish compound *Z/E*-**3ah** (101 mg, 48% (>99:1 *Z/E*)).

***Z*-3ah**. (101 mg, 48% (79:21 dr) mixture of isomer) as a brown sticky-gum. ^1H NMR (300 MHz, $CDCl_3$) δ 7.65−7.44 (m, 4H, Ar−H, major), 7.38−7.33 (m, 1H, Ar−H, minor), 7.21 (d, J = 8.4 Hz, 2H, Ar−H, major), 7.16 (d, J = 8.4 Hz, 2H, Ar−H, minor), 7.02 (d, J = 8.7 Hz, 2H, Ar−H, major), 7.00 (d, J = 8.1 Hz, 2H, Ar−H, minor), 5.933 (s, 1H, ArC*H*O, major), 5.925 (s, 1H, ArC*H*O, minor), 5.81 (s, 1H, =C*H*COCH$_3$, minor), 5.75 (s, 1H, =C*H*COCH$_3$, major), 3.45 (s, 2H, CH_2Ph, major), 3.40 (AB q, J = 13.2 Hz, 2H, CH_2Ph, minor), 2.57 (s, 3H, =CHCOCH_3, minor), 2.50 (s, 3H, =CHCOCH_3, major), 2.28 (s, 3H, OCOCH_3, major), 2.27 (s, 3H, OCOCH_3, minor), 1.98 (s, 3H, N=CCH_3, major), 1.80 (s, 3H, N=CCH_3, minor). ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ 197.0 (*C*OCH$_3$, major), 196.9 (*C*OCH$_3$, minor), 176.2 (OCOCH$_3$, minor), 175.9 (O*C*OCH$_3$, major), 169.2 (*C*OO, major), 164.57 (*C*OO, minor), 164.6 (=CO, major), 164.2 (N=*C*CH$_3$, major), 162.9 (N=*C*CH$_3$, minor), 150.20 (major), 150.16 (minor), 138.5 (major), 134.1 (major), 133.8 (minor), 131.7 (minor), 131.6 (major), 131.3 (2C, major), 131.2 (2C, minor), 130.5 (minor), 130.3 (major), 130.1 (major), 129.9 (minor), 122.4 (major), 122.3 (major), 122.1 (minor), 121.7 (minor), 121.5 (2C, major), 121.4 (2C, minor), 99.3 (=*C*HCOCH$_3$, minor), 98.9 (=*C*HCOCH$_3$, major), 87.7 (ArCHO, minor), 86.9 (ArCHO, major), 76.5 (*C*, major), 38.7 (*C*H$_2$Ph, minor), 38.4 (*C*H$_2$Ph, major), 31.1 (=CHCOCH_3, minor), 31.0 (=CHCOCH_3, major), 21.0 (OCOCH_3, major), 14.7 (N=*C*CH$_3$, major), 14.3 (N=*C*CH$_3$, minor). IR (UATR) ν_{max} 3055, 2927, 1820 (CO), 1757 (CO), 1681 (C=N), 1633, 1605, 1507 cm^{-1}. HRMS (ESI) calcd. for $C_{24}H_{22}NO_6$ $(M + H)^+$: 420.1442, found 420.1445.

*(Z)-4-((4-(6-Chloro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (Z-**3bh**) and (E)-4-((4-(6-Chloro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (E-**3bh**).* Following the general procedure, using compound **1b** (104 mg, 0.50 mmol, 1 equiv), L-tyrosine **4h** (135 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.8 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 50% EtOAc in hexane to furnish compound *Z/E*-**3bh** (131 mg, 58% (>99:1 *Z/E*)).

***Z*-3bh**. (131 mg, 58% (94:6 dr) mixture of isomer) as a brown solid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.55−7.37 (m, 3H, Ar−H, major), 7.21 (d, J = 8.4 Hz, 2H, Ar−H, major), 7.03 (d, J = 8.7 Hz, 2H, Ar−H, major), 5.89 (s, 1H, ArC*H*O, major), 5.86 (s, 1H, ArC*H*O, minor), 5.77 (s, 1H, =C*H*COCH$_3$, minor), 5.70 (s, 1H, =C*H*COCH$_3$, major), 3.42 (AB q, J = 13.5 Hz, 2H, CH_2Ph, major), 3.33 (s, 2H, CH_2Ph, minor), 2.55 (s, 3H, =CHCOCH_3, minor), 2.48 (s, 3H, =CHCOCH_3, major), 2.28 (s, 3H, OCOCH_3, major), 2.17 (s, 3H, OCOCH_3, minor), 2.00 (s, 3H, N=CCH_3, major), 1.87 (s, 3H, N=CCH_3, minor). ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ 196.7 (*C*OCH$_3$, major), 175.5 (OCOCH$_3$, major), 169.1 (*C*OO, major), 164.5 (=CO, major), 163.4 (N=*C*CH$_3$, major), 150.3 (major), 140.1 (major), 137.8 (major), 132.7 (major), 131.3 (2C, major), 131.2 (2C, minor), 130.6 (major), 130.5 (minor), 130.0 (major), 123.2 (major), 123.1 (minor), 122.8 (major), 122.4 (minor), 121.6 (2C, major), 121.5 (2C, minor), 99.6 (=*C*HCOCH$_3$, minor), 99.2 (=*C*HCOCH$_3$, major), 87.0 (ArCHO, minor), 86.3 (ArCHO, major), 76.4 (*C*, major), 38.3 (*C*H$_2$Ph, major), 31.1 (=CHCOCH_3, minor), 31.0 (=CHCOCH_3, major), 21.0 (OCOCH_3, major), 14.7 (N=*C*CH$_3$, major), 14.4 (N=*C*CH$_3$, minor). IR (UATR) ν_{max} 3072, 3049, 2932, 1823 (CO), 1759 (CO), 1684 (C=N), 1622, 1507, 1469, 1427, 1364 cm^{-1}. HRMS (ESI) calcd. for $C_{24}H_{21}ClNO_6$ $[M + H]^+$: 454.1052, found 454.1048.

*(Z)-4-((4-(6-Fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (Z-**3ch**) and (E)-4-((4-(6-Fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (E-**3ch**).* Following the general procedure, using compound **1c** (95.7 mg, 0.50 mmol, 1 equiv), L-tyrosine **4h** (137 mg, 0.75 mmol, 1.5 equiv), NaOAc (46.9 mg, 0.57 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 50% EtOAc in hexane to furnish compound *Z/E*-**3ch** (74.1 mg, 34% (>99:1 *Z/E*)).

***Z*-3ch**. (74.1 mg, 34% (88:12 dr) mixture of isomer) as a brown sticky-gum. ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (dd, J_{H-H} = 8.7 Hz and J_{H-F} = 4.7 Hz, 1H, Ar−H, major), 7.30−7.06 (m, 4H, Ar−H, major), 7.02 (d, J = 8.4 Hz, 2H, Ar−H, major), 5.90 (s, 1H, ArC*H*O, major), 5.87 (s, 1H, ArC*H*O, minor), 5.75 (s, 1H, =C*H*COCH$_3$, minor), 5.69 (s, 1H, =C*H*COCH$_3$, major), 3.42 (AB q, J = 13.5 Hz, 2H, CH_2Ph, major), 3.33 (s, 2H, CH_2Ph, minor), 2.55 (s, 3H, =CHCOCH_3, minor), 2.48 (s, 3H, =CHCOCH_3, major), 2.28 (s, 3H, OCOCH_3, major), 2.00 (s, 3H, N=CCH_3, major), 1.86 (s, 3H, N=CCH_3, minor). ^{13}C {^1H} NMR (75 MHz, $CDCl_3$) δ 196.7 (*C*OCH$_3$, major), 175.9 (OCOCH$_3$, minor), 175.5 (OCOCH$_3$, major), 169.1 (*C*OO, major), 164.7 (d, $^1J_{C-F}$ = 252.9 Hz, *C*F, minor), 164.6 (d, $^1J_{C-F}$ = 252.0 Hz, *C*F, major), 164.4 (=CO, major), 163.6 (N=*C*CH$_3$, major), 163.3 (N=*C*CH$_3$, minor), 150.21 (major), 150.16 (minor), 140.7 (d, $^3J_{C-F}$ = 9.2 Hz, major), 131.3 (2C, major), 131.2 (2C, minor), 130.1 (minor), 130.02 (2C, minor), 130.0 (2C, major), 124.1 (d, $^3J_{C-F}$ = 9.8 Hz, major), 123.9 (d, $^3J_{C-F}$ = 10.7 Hz, minor), 121.5 (2C, major), 121.4 (2C, minor), 118.0 (d, $^2J_{C-F}$ = 23.7 Hz, major), 117.9 (d, $^2J_{C-F}$ = 23.8 Hz, minor), 109.9 (d, $^2J_{C-F}$ = 25.1 Hz, major), 109.5 (d, $^2J_{C-F}$ = 24.9 Hz, minor), 99.0 (d, $^6J_{C-F}$ = 1.1 Hz, =*C*HCOCH$_3$, minor), 98.7 (d, $^6J_{C-F}$ = 1.4 Hz, =*C*HCOCH$_3$, major), 86.9 (d, $^4J_{C-F}$ = 2.9 Hz, ArCHO, minor), 86.2 (d, $^4J_{C-F}$ = 2.9 Hz, ArCHO, major), 76.3 (*C*, major), 76.2 (*C*, minor), 38.3 (*C*H$_2$Ph, major), 31.0 (*C*H$_2$Ph, minor), 30.9 (=CHCOCH$_3$, major), 21.0 (OCOCH_3, major), 14.6 (N=*C*CH$_3$, major), 14.4 (N=*C*CH$_3$, minor). ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ − 109.03 (minor), − 109.33 (major). IR (UATR) ν_{max} 3059, 2931, 1822 (CO), 1758 (CO), 1680 (C=N), 1637, 1616, 1597, 1506, 1481, 1432, 1366 cm^{-1}. HRMS (ESI) calcd. for $C_{24}H_{21}FNO_6$ $[M + H]^+$: 438.1347, found 438.1342.

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*(Z)-4-((4-(6-Methoxy-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (Z-**3dh**) and (E)-4-((4-(6-Methoxy-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (E-**3dh**).* Following the general procedure, using compound **1d** (101 mg, 0.50 mmol, 1 equiv), L-tyrosine **4h** (134 mg, 0.74 mmol, 1.5 equiv), NaOAc (49.9 mg, 0.61 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 50% EtOAc in hexane to furnish compound *Z/E*-**3dh** (60.5 mg, 27% (>99:1 *Z/E*)).

*Z-**3dh**.* (60.5 mg, 27%) as a brown sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, J = 8.4 Hz, 1H, Ar−H), 7.21 (d, J = 8.7 Hz, 2H, Ar−H), 7.06−6.97 (m, 3H, Ar−H), 6.93 (d, J = 2.1 Hz, 1H, Ar−H), 5.85 (s, 1H, ArC*H*O), 5.64 (s, 1H, =C*H*COCH$_3$), 3.87 (s, 3H, Ar−OCH_3), 3.45 (s, 2H, CH_2Ph), 2.47 (s, 3H, =CHCOCH_3), 2.28 (s, 3H, OCOCH_3), 2.00 (s, 3H, N=CCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 196.9 (*C*OCH$_3$), 175.7 (O*C*OCH$_3$), 169.2 (*C*OO), 164.9 (=*C*O), 164.2 (N=*C*CH$_3$), 162.7, 150.2, 140.7, 131.3 (2C), 130.3, 126.4, 123.6, 121.5 (2C), 116.5, 107.5, 97.6 (=CHCOCH$_3$), 86.4 (ArCHO), 76.4 (*C*), 55.8 (Ar−O*C*H$_3$), 38.4 (*C*H$_2$Ph), 30.8 (=CHCO*C*H$_3$), 21.0 (OCO*C*H$_3$), 14.7 (N=C*C*H$_3$). IR (UATR) ν_{max} 3058, 2939, 2837, 1821 (CO), 1757 (CO), 1679 (C=N), 1632, 1605, 1506, 1488, 1434, 1365 cm^{-1}. HRMS (ESI) calcd. for $C_{25}H_{24}NO_7$ [M + H]$^+$: 450.1547, found 450.1548.

*(Z)-4-((2-Methyl-5-oxo-4-(3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (Z-**3eh**) and (E)-4-((2-Methyl-5-oxo-4-(3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (E-**3eh**).* Following the general procedure, using compound **1e** (119 mg, 0.51 mmol, 1 equiv), L-tyrosine **4h** (136 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.4 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 0−10% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3eh** (127 mg, 53% (81:19 *Z/E*)).

*Z-**3eh**.* (103 mg, 43%) as a yellow sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07−7.99 (m, 2H, Ar−H), 7.79−7.71 (m, 1H, Ar−H), 7.60−7.36 (m, 6H, Ar−H), 7.22 (d, J = 8.7 Hz, 2H, Ar−H), 6.99 (d, J = 8.7 Hz, 2H, Ar−H), 6.53 (s, 1H, =C*H*COPh), 5.86 (s, 1H, ArC*H*O), 3.44 (s, 2H, CH_2Ph), 2.27 (s, 3H, OCOCH_3), 2.00 (s, 3H, N=CCH_3). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.2 (*C*OPh), 175.6 (O*C*OCH$_3$), 169.2 (*C*OO), 165.7 (=*C*O), 164.3 (N=*C*CH$_3$), 150.1, 140.0, 139.2, 134.6, 131.8, 131.6 (2C), 131.4, 130.1, 130.0, 128.3 (2C), 128.0 (2C), 122.3, 122.1, 121.4 (2C), 93.1 (=*C*HCOPh), 86.4 (ArCHO), 76.1 (*C*), 38.8 (*C*H$_2$Ph), 21.1 (OCO*C*H$_3$), 14.8 (N=C*C*H$_3$). IR (UATR) ν_{max} 3058, 2930, 1821 (CO), 1757 (CO), 1682 (C=N), 1662, 1600, 1589, 1573, 1508, 1467, 1433, 1370 cm^{-1}. HRMS (ESI) calcd. for $C_{29}H_{23}NNaO_6$ [M + Na]$^+$: 504.1418, found 504.1414.

*E-**3eh**.* (24.0 mg, 10% (83:17 dr) mixture of isomer) as a brown sticky-gum. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48−9.41 (m, 1H, Ar−H, major), 8.06−7.97 (m, 2H, Ar−H, major), 7.60−7.42 (m, 6H, Ar−H, major), 7.20 (d, J = 8.4 Hz, 2H, Ar−H, major), 7.17 (d, J = 8.4 Hz, 2H, Ar−H, major), 7.03−6.96 (m, 2H, Ar−H, major), 6.88 (s, 1H, =C*H*COPh, major), 5.79 (s, 1H, ArC*H*O, minor), 5.78 (s, 1H, ArC*H*O, major), 3.42 (s, 2H, CH_2Ph, major), 3.41 (AB q, J = 13.4 Hz, 2H, CH_2Ph, minor), 2.25 (s, 3H, OCOCH_3, major), 1.96 (s, 3H, N=CCH_3, major), 1.74 (s, 3H, N=CCH_3, minor). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 189.2 (COPh, minor), 189.1 (COPh, major), 176.5 (OCOCH$_3$, minor), 176.0 (OCOCH$_3$, major), 170.2 (COO, minor), 170.1 (COO, major), 169.1 (=CO, major), 163.9 (N=CCH$_3$, major), 162.8 (N=CCH$_3$, minor), 150.06 (major), 150.03 (minor), 141.4 (minor), 141.3 (major), 139.9 (minor), 139.8 (major), 132.19 (major), 132.15 (minor), 132.0 (major), 131.9 (major), 131.8 (minor), 131.3 (2C, major), 131.2 (2C, minor), 130.7 (minor), 130.5 (major), 129.8 (major), 129.6 (minor), 128.4 (major), 128.3 (2C, major), 127.8 (2C, major), 121.6 (major), 121.4 (2C, major), 121.3 (2C, minor), 120.7 (minor), 98.8 (=CHCOPh, minor), 98.2 (=CHCOPh, major), 85.2 (ArCHO, minor), 84.4 (ArCHO, major), 76.7 (C, minor), 76.4 (C, major), 38.7 (CH$_2$Ph, minor), 38.2 (CH$_2$Ph, major), 21.0 (OCOCH$_3$, major), 14.6 (N=CCH$_3$, major), 14.2 (N=CCH$_3$, minor). IR (UATR) ν_{max} 3060, 2930, 1820 (CO), 1759 (CO), 1682 (C=N), 1652, 1589, 1567, 1508, 1466, 1447, 1432, 1383, 1370 cm^{-1}. HRMS (ESI) calcd. for $C_{29}H_{23}NNaO_6$ [M + Na]$^+$: 504.1418, found 504.1412.

*(Z)-4-((4-(6-Chloro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (Z-**3fh**) and (E)-4-((4-(6-Chloro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (E-**3fh**).* Following the general procedure, using compound **1f** (135 mg, 0.50 mmol, 1 equiv), L-tyrosine **4h** (136 mg, 0.75 mmol, 1.5 equiv), NaOAc (44.3 mg, 0.54 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 0−20% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3fh** (171 mg, 66% (77:23 *Z/E*)).

*Z-**3fh**.* (132 mg, 51%) as a brown sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (m, 2H, Ar−H), 7.66 (d, J = 8.1 Hz, 1H, Ar−H), 7.57−7.42 (m, 4H, Ar−H), 7.37 (br s, 1H, Ar−H), 7.21 (d, J = 8.7 Hz, 2H, Ar−H), 7.00 (d, J = 8.4 Hz, 2H, Ar−H), 6.49 (s, 1H, =C*H*COPh), 5.81 (s, 1H, ArC*H*O), 3.40 (s, 2H, CH_2Ph), 2.26 (s, 3H, OCOCH_3), 2.02 (s, 3H, N=CCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 188.9 (*C*OPh), 175.3 (O*C*OCH$_3$), 169.2 (*C*OO), 164.6 (=*C*O), 164.4 (N=*C*CH$_3$), 150.1, 140.7, 139.6, 137.7, 133.1, 131.9, 131.5 (2C), 130.4 (2C), 128.3 (2C), 127.9 (2C), 123.0, 122.7, 121.4 (2C), 93.4 (=*C*HCOPh), 85.8 (ArCHO), 75.9 (*C*), 38.6 (*C*H$_2$Ph), 21.0 (OCO*C*H$_3$), 14.7 (N=C*C*H$_3$). IR (UATR) ν_{max} 3060, 2936, 1808 (CO), 1754 (CO), 1660 (C=N), 1600, 1587, 1574, 1507, 1464, 1447, 1424, 1370 cm^{-1}. HRMS (ESI) calcd. for $C_{29}H_{22}ClNNaO_6$ [M + Na]$^+$: 538.1028, found 538.1021.

*E-**3fh**.* (38.6 mg, 15% (81:19 dr) mixture of isomer) as a pale-yellow sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.43 (d, J = 8.7 Hz, 1H, Ar−H, minor), 9.42 (d, J = 8.7 Hz, 1H, Ar−H, major), 8.06−7.96 (m, 2H, Ar−H, major), 7.70−7.63 (m, 1H, Ar−H, minor), 7.59−7.42 (m, 5H, Ar−H, major), 7.36−7.32 (m, 1H, Ar−H, minor), 7.21 (d, J = 8.4 Hz, 2H, Ar−H, major), 7.16 (d, J = 8.7 Hz, 2H, Ar−H, minor), 7.05−6.98 (m, 2H, Ar−H, major), 6.88 (s, 1H, =C*H*COPh, major), 6.64 (s, 1H, =C*H*COPh, minor), 5.75 (s, 1H, ArC*H*O, major), 5.74 (s, 1H, ArC*H*O, minor), 3.41 (s, 2H, CH_2Ph, major), 3.37 (AB q, J = 13.5 Hz, 2H, CH_2Ph, minor), 2.28 (s, 3H, OCOCH_3, major), 2.00 (s, 3H, N=CCH_3, major), 1.83 (s, 3H, N=CCH_3, minor). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.33 (COPh, minor), 189.25 (COPh, major), 176.4

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($OCOCH_3$, minor), 175.8 ($OCOCH_3$, major), 169.2 (COO, major), 169.1 (COO, minor), 169.0 (=CO), major), 164.3 (N=CCH_3, major), 163.2 (N=CCH_3, minor), 150.24 (major), 150.19 (minor), 143.4 (minor), 143.1 (major), 139.8 (major), 139.7 (minor), 138.5 (minor), 138.3 (major), 132.2 (major), 131.4 (2C, major), 131.3 (2C, minor), 130.9 (major), 130.6 (minor), 130.5 (minor), 130.3 (2C, major), 130.2 (minor), 129.8 (major), 129.7 (minor), 128.5 (2C, major), 128.0 (2C, major), 122.0 (major), 121.5 (2C, major), 121.44 (2C, minor), 121.37 (2C, minor), 99.2 (=CHCOPh, minor), 98.6 (=CHCOPh, major), 84.7 (ArCHO, minor), 84.0 (ArCHO, major), 76.4 (C, major), 38.6 (CH_2Ph, minor), 38.3 (CH_2Ph, major), 21.1 ($OCOCH_3$, major), 20.9 ($OCOCH_3$, minor), 14.7 (N=CCH_3, major), 14.5 (N=CCH_3, minor). IR (UATR) ν_{max} 3061, 2927, 2853, 1753 (CO), 1656 (C=N), 1600, 1587, 1507, 1464, 1447, 1424, 1370 cm^{-1}. HRMS (ESI) calcd. for $C_{29}H_{22}ClNNaO_6$ $[M + Na]^+$: 538.1028, found 538.1023.

*(Z)-4-((4-(6-Fluoro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (Z-**3gh**) and (E)-4-((4-(6-Fluoro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (E-**3gh**).* Following the general procedure, using compound **1g** (127 mg, 0.50 mmol, 1 equiv), L-tyrosine **4h** (137 mg, 0.75 mmol, 1.5 equiv), NaOAc (49.1 mg, 0.60 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 2−50% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3gh** (171 mg, 68% (59:41 *Z/E*)).

***Z*-3gh**. (101 mg, 40%) as a yellow sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, J = 8.1 Hz, 2H, Ar−H), 7.72 (dd, J_{H-H} = 8.6 Hz and J_{H-F} = 4.7 Hz, 1H, Ar−H), 7.58−7.43 (m, 3H, Ar−H), 7.30−7.24 (m, 1H, Ar−H), 7.22 (d, J = 8.4 Hz, 2H, Ar−H), 7.08 (dd, J = 7.8, 1.8 Hz, 1H, Ar−H), 7.00 (d, J = 8.4 Hz, 2H, Ar−H), 6.48 (s, 1H, =C*H*COPh), 5.82 (s, 1H, ArC*H*O), 3.41 (AB q, J = 13.7 Hz, 2H, CH_2Ph), 2.28 (s, 3H, $OCOCH_3$), 2.03 (s, 3H, N=CCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.1 (COPh), 175.3 ($OCOCH_3$), 169.3 (COO), 164.7 (=CO), 164.6 (N=CCH_3), 164.2 (d, $^1J_{C-F}$ = 252.2 Hz, CF), 150.1, 141.5 (d, $^3J_{C-F}$ = 9.3 Hz), 139.8, 131.9, 131.6 (2C), 130.6 (d, $^4J_{C-F}$ = 2.3 Hz), 130.5, 128.3 (2C), 128.0 (2C), 123.9 (d, $^3J_{C-F}$ = 9.7 Hz), 121.5 (2C), 118.0 (d, $^2J_{C-F}$ = 23.8 Hz), 109.8 (d, $^2J_{C-F}$ = 25.0 Hz), 93.0 (d, $^6J_{C-F}$ = 1.8 Hz, =CHCOPh), 85.8 (d, $^4J_{C-F}$ = 2.7 Hz, ArCHO), 75.9 (C), 38.8 (CH_2Ph), 21.1 ($OCOCH_3$), 14.8 (N=CCH_3). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 109.31. IR (UATR) ν_{max} 3063, 2930, 1822 (CO), 1758 (CO), 1678 (C=N), 1662, 1592, 1575, 1507, 1481, 1436, 1370 cm^{-1}. HRMS (ESI) calcd. $C_{29}H_{22}FNNaO_6$ for $[M + Na]^+$: 522.1323, found 522.1308.

***E*-3gh**. (70.3 mg, 28%) as a pale-yellow sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.52 (dd, J_{H-H} = 8.9 Hz and J_{H-F} = 5.3 Hz, 1H, Ar−H), 8.04−7.97 (m, 2H, Ar−H), 7.58−7.44 (m, 3H, Ar−H), 7.31−7.25 (m, 1H, Ar−H), 7.21 (d, J = 8.7 Hz, 2H, Ar−H), 7.15 (dd, J = 8.0, 2.0 Hz, 1H, Ar−H), 7.02 (d, J = 8.4 Hz, 2H, Ar−H), 6.87 (s, 1H, =C*H*COPh), 5.77 (s, 1H, ArC*H*O), 3.41 (AB q, J = 13.8 Hz, 2H, CH_2Ph), 2.28 (s, 3H, $OCOCH_3$), 2.00 (s, 3H, N=CCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.3 (COPh), 175.7 ($OCOCH_3$), 169.3 (COO), 169.2 (=CO), 164.7 (d, $^1J_{C-F}$ = 253.4 Hz, CF), 164.3 (N=CCH_3), 150.2, 144.1 (d, $^3J_{C-F}$ = 9.5 Hz), 139.8, 132.1, 131.4 (2C), 131.1 (d, $^3J_{C-F}$ = 9.5 Hz), 130.3, 128.52 (d, $^4J_{C-F}$ = 2.2 Hz), 128.47 (2C), 127.9 (2C), 121.6 (2C), 117.4 (d, $^2J_{C-F}$ = 22.1 Hz), 109.2 (d, $^2J_{C-F}$ = 24.7 Hz), 98.0 (=CHCOPh), 84.1 (d, $^4J_{C-F}$ = 2.7 Hz, ArCHO), 76.3 (C), 38.4 (CH_2Ph), 21.1 ($OCOCH_3$), 14.8 (N=CCH_3). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 108.19. IR (UATR) ν_{max} 3063, 2927, 2851, 1822 (CO), 1760 (CO), 1682 (C=N), 1652, 1597, 1584, 1569, 1508, 1477, 1447, 1433, 1370 cm^{-1}. HRMS (ESI) calcd. $C_{29}H_{22}FNNaO_6$ for $[M + Na]^+$: 522.1323, found 522.1330.

*(Z)-4-((4-(6-Methoxy-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (Z-**3hh**) and (E)-4-((4-(6-methoxy-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyl-5-oxo-4,5-dihydrooxazol-4-yl)methyl)phenyl Acetate (E-**3hh**).* Following the general procedure, using compound **1h** (133 mg, 0.50 mmol, 1 equiv), L-tyrosine **4h** (136 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.3 mg, 0.59 mmol, 1.1 equiv) and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 2−30% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3hh** (99.6 mg, 39% (>99:1 *Z/E*)).

***Z*-3hh**. (99.6 mg, 39%) as an orange brown sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97−8.04 (m, 2H, Ar−H), 7.65 (d, J = 8.4 Hz, 1H, Ar−H), 7.55−7.42 (m, 3H, Ar−H), 7.25−7.20 (m, 2H, Ar−H), 7.07−6.85 (m, 4H, Ar−H), 6.42 (s, 1H, =C*H*COPh), 5.79 (s, 1H, ArC*H*O), 3.85 (s, 3H, Ar−OCH_3), 3.44 (s, 2H, CH_2Ph), 2.27 (s, 3H, $OCOCH_3$), 2.03 (s, 3H, N=CCH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.1 (COPh), 175.4 ($OCOCH_3$), 169.2 (COO), 166.1 (=CO), 164.4 (N=CCH_3), 162.7, 150.1, 141.5, 140.2, 131.6 (3C), 130.7, 128.3 (2C), 128.0 (2C), 126.9, 123.5, 121.4 (2C), 116.6, 107.2, 91.9 (=CHCOPh), 85.9 (ArCHO), 76.0 (C), 55.8 (Ar−OCH_3), 38.8 (CH_2Ph), 21.1 ($OCOCH_3$), 14.8 (N=CCH_3). IR (UATR) ν_{max} 3059, 2930, 2843, 1822 (CO), 1757 (CO), 1657 (C=N), 1599, 1585, 1569, 1506, 1487, 1436, 1369, 1290, 1216, 1194, 1167, 1113, 1011 cm^{-1}. HRMS (ESI) calcd. for $C_{30}H_{25}NNaO_7$ $[M + Na]^+$: 534.1523, found 534.1520.

*(Z)-4-Isopropyl-2-methyl-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (Z-**3ai**) and (E)-4-Isopropyl-2-methyl-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (E-**3ai**).* Following the general procedure, using compound **1a** (85.9 mg, 0.50 mmol, 1 equiv), L-valine **4i** (88.4 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.8 mg, 0.56 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by recrystallization with CH_2Cl_2 in hexane to furnish compound *Z/E*-**3ai** (56.4 mg, 36% (>99:1 *Z/E*)).

***Z*-3ai**. (56.4 mg, 36% (77:23 dr) mixture of isomer) as a brown solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63−7.30 (m, 4H, Ar−H, major), 6.05 (s, 1H, ArC*H*O, major), 6.04 (s, 1H, ArC*H*O, minor), 5.76 (s, 1H, =C*H*$COCH_3$, minor), 5.73 (s, 1H, =C*H*$COCH_3$, major), 2.62 (sept, J = 6.9 Hz, 1H, C*H*$(CH_3)_2$, major), 2.48 (s, 3H, =CHCOCH_3, major), 2.46 (s, 3H, =CHCOCH_3, minor), 2.20 (s, 3H, N=CCH_3, major), 2.09 (s, 3H, N=CCH_3, minor), 1.18 (d, J = 6.9 Hz, 3H, CH(C*H*$_3$)(CH_3), major), 1.13 (d, J = 6.9 Hz, 3H, CH(CH_3)(C*H*$_3$), major). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 197.3 ($COCH_3$, major), 196.9 ($COCH_3$, minor), 176.3 (COO, major), 165.0 (=CO, major), 164.6 (=CO, minor), 164.2 (N=CCH_3, major), 138.8 (major), 138.4 (minor), 134.1 (major), 131.6 (major), 129.9 (major), 129.8 (minor), 122.3 (major), 122.2 (minor), 121.9 (major), 121.6 (minor), 99.2 (=CHCOCH_3, minor), 98.9 (=CHCOCH_3, major), 86.8

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(ArCHO, minor), 85.4 (ArCHO, major), 78.3 (*C*, major), 31.7 ($CH(CH_3)_2$, minor), 31.4 ($CH(CH_3)_2$, major), 30.9 (=$CHCOCH_3$, major), 30.8 (=$CHCOCH_3$, minor), 17.1 ($CH(CH_3)(CH_3)$, minor), 16.8 ($CH(CH_3)(CH_3)$, major), 16.6 ($CH(CH_3)(CH_3)$, major), 16.4 ($CH(CH_3)(CH_3)$, minor), 15.0 (N=CCH_3, major), 14.7 (N=CCH_3, minor). IR (UATR) ν_{max} 3106, 3026, 2977, 2942, 2885, 1821 (CO), 1794 (CO), 1674 (C=N), 1633, 1605, 1464, 1434, 1416 cm^{-1}. HRMS (ESI) calcd. for $C_{18}H_{20}NO_4$ $[M + H]^+$: 314.1387, found 314.1388.

*(Z)-4-(6-Chloro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-4-isopropyl-2-methyloxazol-5(4H)-one (Z-**3bi**) and (E)-4-(6-Chloro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-4-isopropyl-2-methyloxazol-5(4H)-one (E-**3bi**).* Following the general procedure, using compound **1b** (103 mg, 0.50 mmol, 1 equiv), L-valine **4i** (89.3 mg, 0.76 mmol, 1.5 equiv), NaOAc (47.4 mg, 0.57 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by recrystallization with CH_2Cl_2 in hexane to furnish compound *Z/E*-**3bi** (53.9 mg, 31% (>99:1 *Z/E*)).

***Z*-3bi.** (53.9 mg, 31%) as a brown solid. Mp 187.0−189.0 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 8.4 Hz, 1H, Ar−H), 7.46 (dd, J = 8.4, 1.5 Hz, 1H, Ar−H), 7.34 (br s, 1H, Ar−H), 6.01 (s, 1H, ArCHO), 5.68 (s, 1H, =$CHCOCH_3$), 2.58 (sept, J = 6.9 Hz, 1H, $CH(CH_3)_2$), 2.46 (s, 3H, =$CHCOCH_3$), 2.21 (s, 3H, N=CCH_3), 1.18 (d, J = 6.9 Hz, 3H, $CH(CH_3)(CH_3)$), 1.12 (d, J = 6.9 Hz, 3H, $CH(CH_3)(CH_3)$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 196.9 ($COCH_3$), 176.0 (COO), 164.5 (=CO), 163.7 (N=CCH_3), 140.4, 137.9, 132.8, 130.5, 123.3, 122.5, 99.3 (=$CHCOCH_3$), 85.0 (ArCHO), 78.2 (*C*), 31.3 ($CH(CH_3)_2$), 30.9 (=$CHCOCH_3$), 16.8 ($CH(CH_3)(CH_3)$), 16.5 ($CH(CH_3)(CH_3)$), 14.9 (N=CCH_3). IR (UATR) ν_{max} 3365, 3293, 2974, 2880, 2359, 2341, 1818 (CO), 1707 (CO), 1680 (C=N), 1634, 1606, 1559, 1507, 1465, 1421 cm^{-1}. HRMS (ESI) calcd. for $C_{18}H_{19}ClNO_4$ $[M + H]^+$: 348.0997, found 348.998.

*(Z)-4-(6-Fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-4-isopropyl-2-methyloxazol-5(4H)-one (Z-**3ci**) and (E)-4-(6-Fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-4-isopropyl-2-methyloxazol-5(4H)-one (E-**3ci**).* Following the general procedure, using compound **1c** (95.3 mg, 0.50 mmol, 1 equiv), L-valine **4i** (88.3 mg, 0.75 mmol, 1.5 equiv), NaOAc (46.5 mg, 0.57 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by recrystallization with CH_2Cl_2 in hexane to furnish compound *Z/E*-**3ci** (33.1 mg, 20% (>99:1 *Z/E*)).

***Z*-3ci.** (33.1 mg, 20%) as a pale brown solid. Mp 183.6−185.6 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, J_{H-H} = 8.7 Hz and J_{H-F} = 4.8 Hz, 1H, Ar−H), 7.20 (td, J = 8.6, 2.1 Hz, 1H, Ar−H), 7.06 (dd, J = 8.0, 2.1 Hz, 1H, Ar−H), 6.02 (s, 1H, ArCHO), 5.66 (s, 1H, =$CHCOCH_3$), 2.59 (sept, J = 6.8 Hz, 1H, $CH(CH_3)_2$), 2.46 (s, 3H, =$CHCOCH_3$), 2.22 (s, 3H, N=CCH_3), 1.17 (d, J = 6.8 Hz, 3H, $CH(CH_3)(CH_3)$), 1.13 (d, J = 6.8 Hz, 3H, $CH(CH_3)(CH_3)$). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 197.0 ($COCH_3$), 176.0 (COO), 164.7 (d, $^1J_{C-F}$ = 251.9 Hz, CF), 164.5 (=CO), 163.9 (N=CCH_3), 141.0 (d, $^3J_{C-F}$ = 9.2), 130.1 (d, $^4J_{C-F}$ = 2.5 Hz), 124.1 (d, $^3J_{C-F}$ = 9.8 Hz), 117.9 (d, $^2J_{C-F}$ = 23.8 Hz), 109.6 (d, $^2J_{C-F}$ = 25.0), 98.7 (d, $^6J_{C-F}$ = 1.5 Hz, =$CHCOCH_3$), 84.8 (d, ^4J = 2.9 Hz, ArCHO), 78.1 (*C*), 31.3 ($CH(CH_3)_2$), 30.8 (=$CHCOCH_3$), 16.7 ($CH(CH_3)(CH_3)$), 16.5 ($CH(CH_3)(CH_3)$), 14.9 (N=CCH_3). $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ − 109.64. IR (UATR) ν_{max} 3076, 3049, 2974, 2942, 2880, 1820 (CO), 1798 (CO), 1680 (C=N), 1630, 1613, 1597, 1483, 1469, 1431, 1387 cm^{-1}. HRMS (ESI) calcd. for $C_{18}H_{19}FNO_4$ $[M + H]^+$: 332.1293, found 332.1294.

*(Z)-4-Isopropyl-4-(6-methoxy-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (Z-**3di**) and (E)-4-Isopropyl-4-(6-methoxy-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (E-**3di**).* Following the general procedure, using compound **1d** (103 mg, 0.51 mmol, 1 equiv) L-valine **4i** (88.7 mg, 0.75 mmol, 1.5 equiv), NaOAc (46.6 mg, 0.57 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by recrystallization with CH_2Cl_2 in hexane to furnish compound *Z/E*-**3di** (35.0 mg, 20% (>99:1 *Z/E*)).

***Z*-3di.** (35.0 mg, 20% (95:5 dr)) as a dark brown solid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, J = 8.7 Hz, 1H, Ar−H, major), 7.01 (dd, J = 8.7, 2.1 Hz, 1H, Ar−H, major), 6.84 (d, J = 2.1 Hz, 1H, Ar−H, major), 6.78 (d, J = 1.5 Hz, 1H, Ar−H, minor), 5.97 (s, 1H, ArCHO, major), 5.63 (s, 1H, =$CHCOCH_3$, minor), 5.61 (s, 1H, =$CHCOCH_3$, major), 3.86 (s, 3H, Ar−OCH_3, major), 2.62 (sept, J = 6.8 Hz, 1H, $CH(CH_3)_2$, major), 2.46 (s, 3H, =$CHCOCH_3$, major), 2.43 (s, 3H, =$CHCOCH_3$, minor), 2.22 (s, 3H, N=CCH_3, major), 2.12 (s, 3H, N=CCH_3, minor), 1.16 (d, J = 7.2 Hz, 3H, $CH(CH_3)(CH_3)$, major), 1.14 (d, J = 7.2 Hz, 3H, $CH(CH_3)(CH_3)$, major). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 197.0 ($COCH_3$, major), 176.1 (COO, major), 165.1 (=CO, major), 164.2 (N=CCH_3, major), 162.7 (major), 140.9 (major), 126.3 (major), 123.6 (major), 123.5 (minor), 116.3 (minor), 116.2 (major), 107.2 (major), 106.5 (minor), 97.8 (=$CHCOCH_3$, minor), 97.6 (=$CHCOCH_3$, major), 86.2 (ArCHO, minor), 84.8 (ArCHO, major), 78.2 (*C*, major), 55.8 (Ar−OCH_3, minor), 55.7 (Ar−OCH_3, major), 31.6 ($CH(CH_3)_2$, minor), 31.3 ($CH(CH_3)_2$, major), 30.7 (=$CHCOCH_3$, major), 17.1 ($CH(CH_3)(CH_3)$, minor), 16.7 ($CH(CH_3)(CH_3)$, major), 16.5 ($CH(CH_3)(CH_3)$, major), 16.4 ($CH(CH_3)(CH_3)$, minor), 14.9 (N=CCH_3, major), 14.7 (N=CCH_3, minor). IR (UATR) ν_{max} 3049, 3011, 2969, 2938, 2883, 2848, 1811 (CO), 1787 (CO), 1680 (C=N), 1626, 1607, 1488, 1468, 1432, 1414, 1386 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{22}NO_5$ $[M + H]^+$: 344.1492, found 344.1489.

*(Z)-4-Isopropyl-2-methyl-4-(3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (Z-**3ei**) and (E)-4-Isopropyl-2-methyl-4-(3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (E-**3ei**).* Following the general procedure, using compound **1e** (117 mg, 0.50 mmol, 1 equiv), L-valine **4i** (88.3 mg, 0.75 mmol, 1.5 equiv), NaOAc (46.2 mg, 0.56 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 2−20% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3ei** (130.7 mg, 70% (79:21 *Z/E*)).

***Z*-3ei.** (103.1 mg, 55% (83:17 dr) mixture of isomer) as a brown sticky-gum. ^1H NMR (300 MHz, $CDCl_3$) δ 8.03−7.94 (m, 2H, Ar−H, major), 7.76−7.70 (m, 1H, Ar−H, major), 7.56−7.40 (m, 5H, Ar−H, major), 7.40−7.31 (m, 1H, Ar−H, major), 6.58 (s, 1H, =$CHCOPh$, minor), 6.54 (s, 1H, =$CHCOPh$, major), 6.08 (s, 1H, ArCHO, minor), 6.03 (s, 1H, ArCHO, major), 2.67 (sept, J = 6.9 Hz, 1H, $CH(CH_3)_2$, major), 2.19 (s, 3H, N=CCH_3, major), 2.08 (s, 3H, N=CCH_3, minor), 1.14 (d, J = 6.6 Hz, 3H, $CH(CH_3)(CH_3)$, major), 1.11 (d, J = 6.9 Hz, 3H, $CH(CH_3)(CH_3)$, minor), 1.06

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(d, J = 6.9 Hz, 3H, CH(CH_3)(CH_3), major). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.0 (COPh, major), 188.6 (COPh, minor), 176.6 (COO, minor), 176.1 (COO, major), 166.2 (=CO, major), 166.0 (=CO, minor), 164.4 (N=CCH_3, major), 163.0 (N=CCH_3, minor), 140.0 (minor), 139.9 (major), 139.6 (major), 139.2 (minor), 134.7 (major), 134.5 (minor), 131.7 (major), 131.6 (major), 129.8 (major), 129.6 (minor), 128.2 (2C, major), 127.9 (2C, major), 127.8 (2C, minor), 122.0 (major), 121.9 (major), 121.8 (minor), 121.6 (minor), 92.8 (=CHCOPh, minor), 92.6 (=CHCOPh, major), 86.9 (ArCHO, minor), 85.1 (ArCHO, major), 79.0 (C, minor), 78.2 (C, major), 31.6 (CH(CH_3)$_2$, minor), 31.3 (CH(CH_3)$_2$, major), 17.1 (CH(CH_3)(CH_3), minor), 16.8 (CH(CH_3)-(CH_3), major), 16.7 (CH(CH_3)(CH_3), major), 16.6 (CH-(CH_3)(CH_3), minor), 15.0 (N=CCH_3, major), 14.6 (N=CCH_3, minor). IR (UATR) ν_{max} 3294, 3061, 2969, 2878, 1770 (CO), 1720 (CO), 1661 (C=N), 1619, 1560, 1590, 1573, 1528, 1467, 1448, 1374 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{21}NNaO_4$ [M + Na]$^+$: 398.1363, found 398.1368.

*E-**3ei**.* (27.6 mg, 15%) as a pale-yellow sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.48−9.40 (m, 1H, Ar−H), 8.05−7.97 (m, 2H, Ar−H), 7.60−7.41 (m, 5H, Ar−H), 7.41−7.32 (m, 1H, Ar−H), 6.85 (s, 1H, =CHCOPh), 5.91 (s, 1H, ArCHO), 2.65 (sept, J = 6.9 Hz, 1H, CH(CH_3)$_2$), 2.21 (s, 3H, N=CCH_3), 1.15 (d, J = 6.6 Hz, 3H, CH(CH_3)(CH_3)), 1.13 (d, J = 6.9 Hz, 3H, CH(CH_3)(CH_3)). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.3 (COPh), 176.5 (COO), 170.5 (=CO), 164.1 (N=CCH_3), 141.7, 140.0, 132.3, 132.1, 132.0, 129.8, 128.6, 128.4 (2C), 128.0 (2C), 121.1, 98.1 (=CHCOPh), 82.7 (ArCHO), 78.3 (C), 31.2 (CH(CH_3)$_2$), 16.9 (CH(CH_3)-(CH_3)), 16.7 (CH(CH_3)(CH_3)), 15.0 (N=CCH_3). IR (UATR) ν_{max} 3060, 2970, 2936, 2879, 1821 (CO), 1776 (CO), 1681 (C=N), 1661, 1600, 1590, 1568, 1467, 1384 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{21}NNaO_4$ [M + Na]$^+$: 398.1363, found 398.1364.

*(Z)-4-(6-Chloro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-4-isopropyl-2-methyloxazol-5(4H)-one (Z-**3fi**) and (E)-4-(6-Chloro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-4-isopropyl-2-methyloxazol-5(4H)-one (E-**3fi**).* Following the general procedure, using compound **1f** (134 mg, 0.50 mmol, 1 equiv), L-valine **4i** (89.4 mg, 0.76 mmol, 1.5 equiv), NaOAc (46.2 mg, 0.56 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 0−10% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3fi** (138 mg, 67% (71:29 *Z/E*)).

*Z-**3fi**.* (97.0 mg, 47%) as a yellow solid. Mp 177.5−178.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01−7.94 (m, 2H, Ar−H), 7.65 (d, J = 8.4 Hz, 1H, Ar−H), 7.56−7.41 (m, 4H, Ar−H), 7.35−7.31 (m, 1H, Ar−H), 6.50 (s, 1H, =CHCOPh), 5.99 (s, 1H, ArCHO), 2.62 (sept, J = 6.8 Hz, 1H, CH(CH_3)$_2$), 2.20 (s, 3H, N=CCH_3), 1.13 (d, J = 6.9 Hz, 3H, CH(CH_3)(CH_3)), 1.08 (d, J = 7.2 Hz, 3H, CH(CH_3)(CH_3)). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 188.7 (COPh), 175.9 (COO), 164.9 (=CO), 164.7 (N=CCH_3), 141.2, 139.6, 137.8, 133.3, 131.9, 130.3, 128.3 (2C), 127.9 (2C), 123.0, 122.5, 93.0 (=CHCOPh), 84.7 (ArCHO), 78.2 (C), 31.2 (CH(CH_3)$_2$), 16.7 (CH(CH_3)(CH_3)), 16.6 (CH(CH_3)-(CH_3)), 14.9 (N=CCH_3). IR (UATR) ν_{max} 3093, 2972, 2932, 1803 (CO), 1682 (C=N), 1663, 1602, 1576, 1466 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{20}ClNNaO_4$ [M + Na]$^+$: 432.0973, found 432.0983.

*E-**3fi**.* (41.0 mg, 20% (77:23 dr) mixture of isomer) as a brown sticky-gum. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (d, J = 8.0 Hz, 1H, Ar−H, minor), 9.40 (d, J = 8.0 Hz, 1H, Ar−H, major), 8.20−7.95 (m, 2H, Ar−H, major), 7.56−7.42 (m, 4H, Ar−H, major), 7.31 (br s, 1H, Ar−H, major), 7.23 (br s, 1H, Ar−H, minor), 6.85 (s, 1H, =CHCOPh, minor), 6.83 (s, 1H, =CHCOPh, major), 5.87 (s, 1H, ArCHO, major), 2.60 (sept, J = 8.0 Hz, 1H, CH(CH_3)$_2$, major), 2.21 (s, 3H, N=CCH_3, major), 2.07 (s, 3H, N=CCH_3, minor), 1.21 (d, J = 8.0 Hz, 3H, CH(CH_3)(CH_3), minor), 1.14 (d, J = 8.0 Hz, 3H, CH(CH_3)(CH_3), major), 1.12 (d, J = 8.0 Hz, 3H, CH(CH_3)-(CH_3), major), 1.04 (d, J = 8.0 Hz, 3H, CH(CH_3)(CH_3), minor). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 189.2 (COPh, major), 176.13 (COO, major), 176.10 (COO, minor), 169.3 (=CO, major), 169.1 (=CO, minor), 164.4 (N=CCH_3, major), 163.1 (minor), 143.41 (major), 143.35 (minor), 139.8 (minor), 139.7 (major), 138.3 (minor), 138.2 (major), 132.1 (major), 132.0 (minor), 130.8 (major), 130.7 (minor), 130.0 (major), 129.9 (minor), 129.7 (major), 129.6 (minor), 128.40 (2C, major), 128.37 (2C, major), 121.6 (major), 120.8 (minor), 98.8 (=CHCOPh, minor), 98.3 (=CHCOPh, major), 83.5 (ArCHO, minor), 82.3 (ArCHO, major), 78.6 (C, minor), 78.2 (C, major), 31.8 (CH(CH_3)$_2$, minor), 31.1 (CH(CH_3)$_2$, major), 17.0 (CH(CH_3)(CH_3), minor), 16.8 (CH(CH_3)(CH_3), major), 16.5 (CH(CH_3)(CH_3), major), 16.3 (CH(CH_3)(CH_3), minor), 14.9 (N=CCH_3, major), 14.6 (N=CCH_3, minor). IR (UATR) ν_{max} 3060, 2973, 2938, 2880, 1822 (CO), 1751 (CO), 1682 (C=N), 1652, 1600, 1584, 1568, 1459, 1431, 1385 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{20}ClNNaO_4$ [M + Na]$^+$: 432.0973, found 432.0977.

*(Z)-4-(6-Fluoro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-4-isopropyl-2-methyloxazol-5(4H)-one (Z-**3gi**) and (E)-4-(6-Fluoro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-4-isopropyl-2-methyloxazol-5(4H)-one (E-**3gi**).* Following the general procedure, using compound **1g** (131 mg, 0.52 mmol, 1 equiv), L-valine **4i** (90.3 mg, 0.77 mmol, 1.5 equiv), NaOAc (47.3 mg, 0.58 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 2−10% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3gi** (142 mg, 72% (65:35 *Z/E*)).

*Z-**3gi**.* (92.9 mg, 47% (83:17 dr) mixture of isomer) as a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03−7.91 (m, 2H, Ar−H, major), 7.71 (dd, J_{H-H} = 8.7 Hz and J_{H-F} = 4.8 Hz, 1H, Ar−H, major), 7.57−7.40 (m, 3H, Ar−H, major), 7.21 (td, J = 8.6, 2.1 Hz, 1H, Ar−H, major), 7.04 (dd, J = 8.0, 2.0 Hz, 1H, Ar−H, major), 6.51 (s, 1H, =CHCOPh, minor), 6.48 (s, 1H, =CHCOPh, major), 6.04 (s, 1H, ArCHO, minor), 5.99 (s, 1H, ArCHO, major), 2.64 (sept, J = 6.6 Hz, 1H, CH(CH_3)$_2$, major), 2.21 (s, 3H, N=CCH_3, major), 2.15 (s, 3H, N=CCH_3, minor), 1.12 (d, J = 6.9 Hz, 3H, CH(CH_3)-(CH_3), minor), 1.14 (d, J = 6.6 Hz, 3H, CH(CH_3)(CH_3), major), 1.06 (d, J = 6.9 Hz, 3H, CH(CH_3)(CH_3), major). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 188.8 (COPh, major), 188.4 (COPh, minor), 176.4 (COO, minor), 175.9 (COO, major), 165.1 (=CO, major), 164.9 (=CO, minor), 164.73 (d, $^1J_{C-F}$ = 252.2 Hz, CF, minor), 164.66 (d, $^1J_{C-F}$ = 251.9 Hz, CF, major), 164.65 (N=CCH_3, major), 163.3 (N=CCH_3, minor), 141.9 (d, $^3J_{C-F}$ = 9.3 Hz, major), 141.5 (d, $^3J_{C-F}$ = 9.5 Hz, minor), 139.9 (minor), 139.7 (major), 131.8 (major), 130.7 (d, $^4J_{C-F}$ = 2.2 Hz, major), 128.3 (2C, major), 127.9 (2C, major), 127.8 (2C, minor), 123.8 (d, $^3J_{C-F}$ = 9.6 Hz, major), 123.7 (d, $^3J_{C-F}$ = 9.5 Hz, minor), 117.7 (d, $^2J_{C-F}$ =

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23.7 Hz, major), 117.6 (d, $^{2}J_{C-F}$ = 23.7 Hz, minor), 109.5 (d, $^{2}J_{C-F}$ = 24.9 Hz, major), 109.3 (d, $^{2}J_{C-F}$ = 24.8 Hz, minor), 92.7 (d, $^{6}J_{C-F}$ = 1.5 Hz, =*C*HCOPh, minor), 92.5 (d, $^{6}J_{C-F}$ = 1.4 Hz, =*C*HCOPh, major), 86.3 (d, $^{4}J_{C-F}$ = 2.9 Hz, ArCHO, minor), 84.6 (d, $^{4}J_{C-F}$ = 2.9 Hz, ArCHO, major), 78.9 (*C*, minor), 78.1 (*C*, major), 31.5 (*C*H(CH$_3$)$_2$, minor), 31.3 (*C*H(CH$_3$)$_2$, major), 17.0 (CH(*C*H$_3$)(CH$_3$), minor), 16.7 (CH(*C*H$_3$)(CH$_3$), major), 16.63 (CH(CH$_3$)(*C*H$_3$), major), 16.58 (CH(CH$_3$)(*C*H$_3$), minor), 14.9 (N=C*C*H$_3$, major), 14.7 (N=C*C*H$_3$, minor). ^{19}F{^{1}H} NMR (376 MHz, CDCl$_3$) δ − 109.32 (minor), − 109.60 (major). IR (UATR) ν_{max} 3063, 2971, 2880, 1822 (CO), 1804 (CO), 1681 (C), 1661, 1592, 1575, 1481, 1447, 1383 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{20}FNNaO_4$ [M + Na]$^+$: 416.1269, found 416.1268.

*E-**3gi**.* (49.5 mg, 25% (82:18 dr) mixture of isomer) as a dark brown sticky-gum. ^{1}H NMR (300 MHz, CDCl$_3$) δ 9.51 (dd, J_{H-H} = 9.0 Hz and J_{H-F} = 5.4 Hz, 1H, Ar−H, major), 8.04−7.96 (m, 2H, Ar−H, major), 7.58−7.43 (m, 3H, Ar−H, major), 7.23 (td, *J* = 8.8, 2.3 Hz, 1H, Ar−H, major), 7.03 (dd, *J* = 8.1, 2.1 Hz, 1H, Ar−H, major), 6.95 (dd, *J* = 8.1, 1.8 Hz, 1H, Ar−H, minor), 6.84 (s, 1H, =C*H*COPh, minor), 6.82 (s, 1H, =C*H*COPh, major), 5.88 (s, 1H, ArC*H*O, major), 2.62 (sept, *J* = 6.9 Hz, 1H, C*H*(CH$_3$)$_2$, major), 2.22 (s, 3H, N=CC*H*$_3$, major), 2.06 (s, 3H, N=CC*H*$_3$, minor), 1.23 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)(CH$_3$), minor), 1.132 (d, *J* = 7.2 Hz, 3H, CH(C*H*$_3$)(CH$_3$), major), 1.128 (d, *J* = 6.6 Hz, 3H, CH(CH$_3$)(C*H*$_3$), major), 1.03 (d, *J* = 6.9 Hz, 3H, CH(CH$_3$)-(C*H*$_3$), minor). ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) δ 189.2 (*C*OPh, major), 176.2 (*C*OO, major), 169.5 (=*C*O, major), 169.3 (=*C*O, minor), 164.8 (d, $^{1}J_{C-F}$ = 253.1 Hz, *C*F, major), 164.4 (N=*C*CH$_3$, major), 144.44 (d, $^{3}J_{C-F}$ = 9.4 Hz, major), 144.40 (d, $^{3}J_{C-F}$ = 9.4 Hz, minor), 139.9 (minor), 139.8 (major), 132.0 (major), 131.02 (d, $^{3}J_{C-F}$ = 9.5 Hz, major), 130.97 (d, $^{3}J_{C-F}$ = 9.8 Hz, minor), 128.5 (d, $^{4}J_{C-F}$ = 2.3 Hz, major), 128.4 (2C, major), 127.9 (2C, major), 117.2 (d, $^{2}J_{C-F}$ = 22.2 Hz, major), 117.1 (d, $^{2}J_{C-F}$ = 22.4 Hz, minor), 108.7 (d, $^{2}J_{C-F}$ = 24.8 Hz, major), 108.0 (d, $^{2}J_{C-F}$ = 25.6 Hz, minor), 98.2 (d, $^{6}J_{C-F}$ = 1.9 Hz, =CHCOPh, minor), 97.7 (d, $^{6}J_{C-F}$ = 1.4 Hz, =CHCOPh, major), 83.6 (d, $^{4}J_{C-F}$ = 3.5 Hz, ArCHO, minor), 82.3 (d, $^{4}J_{C-F}$ = 2.8 Hz, ArCHO, major), 78.6 (*C*, minor), 78.2 (*C*, major), 31.8 (*C*H(CH$_3$)$_2$, minor), 31.2 (*C*H(CH$_3$)$_2$, major), 17.0 (CH(*C*H$_3$)(CH$_3$), minor), 16.8 (CH(*C*H$_3$)(CH$_3$), major), 16.6 (CH(CH$_3$)(*C*H$_3$), major), 16.3 (CH(CH$_3$)(*C*H$_3$), minor), 15.0 (N=C*C*H$_3$, major), 14.6 (N=C*C*H$_3$, minor). ^{19}F{^{1}H} NMR (376 MHz, CDCl$_3$) δ − 108.23 (minor), − 108.52 (major). IR (UATR) ν_{max} 2969, 2936, 2878, 1823 (CO), 1804 (CO), 1725 (CO), 1682 (C=N), 1661, 1600, 1593, 1575, 1530, 1480, 1384 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{20}FNNaO_4$ [M + Na]$^+$: 416.1269, found 416.1266.

*(Z)-4-Isopropyl-4-(6-methoxy-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (Z-**3hi**) and (E)-4-Isopropyl-4-(6-methoxy-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (E-**3hi**).* Following the general procedure, using compound **1h** (132. mg, 0.50 mmol, 1 equiv), L-valine **4i** (87.0 mg, 0.75 mmol, 1.5 equiv), NaOAc (46.1 mg, 0.56 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 2−20% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3hi** (119 mg, 59% (66:34 *Z/E*)).

*Z-**3hi**.* (78.9 mg, 39%) as a brown solid. Mp 120.0−122.0 °C. ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.03−7.94 (m, 2H, Ar−H), 7.64 (d, *J* = 8.7 Hz, 1H, Ar−H), 7.55−7.40 (m, 3H, Ar−H), 7.02 (dd, *J* = 8.6, 2.3 Hz, 1H, Ar−H), 6.83 (d, *J* = 1.8 Hz, 1H, Ar−H), 6.42 (s, 1H, =C*H*COPh), 5.96 (s, 1H, ArC*H*O), 3.86 (s, 3H, Ar−OC*H*$_3$), 2.69 (sept, *J* = 6.8 Hz, 1H, C*H*(CH$_3$)$_2$), 2.21 (s, 3H, N=CC*H*$_3$), 1.16 (d, *J* = 6.6 Hz, 3H, CH(C*H*$_3$)(CH$_3$)), 1.04 (d, *J* = 6.9 Hz, 3H, CH(CH$_3$)-(C*H*$_3$)). ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) δ 188.8 (*C*OPh), 176.0 (*C*OO), 166.5 (=*C*O), 164.4 (N=*C*CH$_3$), 162.7, 142.0, 140.2, 131.5, 128.2 (2C), 127.9 (2C), 127.0, 123.4, 116.3, 107.0, 91.5 (=CHCOPh), 84.6 (ArCHO), 78.2 (*C*), 55.8 (Ar−OCH$_3$), 31.3 (*C*H(CH$_3$)$_2$), 16.8 (2C, CH(*C*H$_3$)$_2$), 15.0 (N=C*C*H$_3$). IR (UATR) ν_{max} 3365, 2969, 2939, 2604, 1821 (CO), 1716 (CO), 1656 (C=N), 1618, 1599, 1586, 1569, 1517, 1486, 1436, 1375 cm^{-1}. HRMS (ESI) calcd. for $C_{24}H_{23}NNaO_5$ [M + Na]$^+$: 428.1468, found 428.1467.

*E-**3hi**.* (40.2 mg, 20% (67:23 dr) mixture of isomer) as a brown solid. ^{1}H NMR (300 MHz, CDCl$_3$) δ 9.45 (d, *J* = 9.0 Hz, 1H, Ar−H, major), 9.44 (d, *J* = 9.0 Hz, 1H, Ar−H, minor), 8.03−7.95 (m, 2H, Ar−H, major), 7.55−7.38 (m, 3H, Ar−H, major), 7.07−6.99 (m, 1H, Ar−H, major), 6.83 (d, *J* = 2.1 Hz, 1H, Ar−H, major), 6.76 (s, 1H, =C*H*COPh, minor), 6.74 (s, 1H, =C*H*COPh, major), 6.72 (d, *J* = 2.4 Hz, 1H, Ar−H, minor), 5.85 (s, 1H, ArC*H*O, minor), 5.84 (s, 1H, ArC*H*O, major), 3.873 (s, 3H, Ar−OC*H*$_3$, major), 3.868 (s, 3H, Ar−OC*H*$_3$, minor), 2.66 (sept, *J* = 6.9 Hz, 1H, C*H*(CH$_3$)$_2$, major), 2.65 (sept, *J* = 6.9 Hz, 1H, C*H*(CH$_3$)$_2$, minor), 2.60 (s, 3H, N=CC*H*$_3$, major), 2.03 (s, 3H, N=CC*H*$_3$, minor), 1.24 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)(CH$_3$), minor), 1.13 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)(CH$_3$), major), 1.12 (d, *J* = 6.8 Hz, 3H, CH(CH$_3$)(C*H*$_3$), major), 1.02 (d, *J* = 6.9 Hz, 3H, CH(CH$_3$)-(C*H*$_3$), minor). ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) δ 189.2 (*C*OPh, major), 176.5 (*C*OO, minor), 176.3 (*C*OO, major), 170.8 (=*C*O, major), 170.7 (=*C*O, minor), 164.1 (N=*C*CH$_3$, major), 163.0 (N=*C*CH$_3$, minor), 162.8 (major), 162.7 (minor), 144.5 (minor), 144.4 (major), 140.3 (major), 131.70 (major), 131.66 (minor), 130.5 (major), 130.4 (minor), 128.3 (2C, major), 127.8 (2C, major), 125.0 (major), 115.3 (minor), 115.0 (major), 106.9 (major), 105.6 (minor), 96.8 (=CHCOPh, minor), 96.3 (=CHCOPh, major), 83.6 (ArC*H*O, minor), 82.3 (ArC*H*O, major), 78.8 (*C*, minor), 78.3 (*C*, major), 55.73 (Ar−OCH$_3$, minor), 55.66 (Ar−OCH$_3$, major), 31.9 (*C*H(CH$_3$)$_2$, minor), 31.1 (*C*H-(CH$_3$)$_2$, major), 17.1 (CH(*C*H$_3$)(CH$_3$), minor), 16.8 (CH-(*C*H$_3$)(CH$_3$), major), 16.6 (CH(CH$_3$)(*C*H$_3$), major), 16.3 (CH(CH$_3$)(*C*H$_3$), minor), 15.0 (N=C*C*H$_3$, major), 14.6 (N=C*C*H$_3$, minor). IR (UATR) ν_{max} 3059, 2969, 2939, 1822 (CO), 1681 (C=N), 1647, 1582, 1557, 1485, 1448, 1387 cm^{-1}. HRMS (ESI) calcd. for $C_{24}H_{24}NO_5$ [M + H]$^+$: 406.1649, found 406.1644.

*(Z)-2,4-Dimethyl-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (Z-**3aj**) and (E)-2,4-Dimethyl-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (E-**3aj**).* Following the general procedure, using compound **1a** (87.3 mg, 0.51 mmol, 1 equiv), L-alanine **4j** (66.8 mg, 0.75 mmol, 1.5 equiv), NaOAc (46.3 mg, 0.56 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by recrystallization with CH_2Cl_2 in hexane to furnish compound *Z/E*-**3aj** (33.8 mg, 24% (>99:1 *Z/E*)).

*Z-**3aj**.* (33.8 mg, 24%) as a brown solid. Mp 163.0−164.2 °C. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.63−7.45 (m, 4H, Ar−H), 5.83 (s, 1H, ArC*H*O), 5.71 (s, 1H, =C*H*COCH$_3$), 2.45 (s, 3H, =CHCOC*H*$_3$), 2.15 (s, 3H, N=CC*H*$_3$), 1.73 (s, 3H,

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CH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 197.1 ($COCH_3$), 177.5 (*C*OO), 164.7 (=*C*O), 163.9 (N=*C*CH_3), 138.6, 134.1, 131.6, 130.0, 122.3, 122.2, 98.8 (=*C*HCOCH_3), 88.0 (Ar*C*HO), 71.7 (*C*), 30.9 (=CH*C*OCH_3), 19.0 (CH_3), 15.1 (N=*C*CH_3). IR (UATR) ν_{max} 3059, 2936, 1819 (CO), 1683 (C=N), 1630, 1467, 1430, 1363 cm^{-1}. HRMS (ESI) calcd. for $C_{16}H_{15}NNaO_4$ $[M + Na]^+$: 308.0893, found 308.0898.

*(Z)-4-(6-Chloro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (Z-**3bj**) and (E)-4-(6-Chloro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (E-**3bj**).* Following the general procedure, using compound **1b** (103 mg, 0.50 mmol, 1 equiv), L-alanine **4j** (66.6 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.2 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by recrystallization with CH_2Cl_2 in hexane to furnish compound *Z/E*-**3bj** (48.0 mg, 30% (>99:1 *Z/E*)).

***Z*-3bj.** (48.0 mg, 32% (97:3 dr) mixture of isomer) as a brown solid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.55−7.40 (m, 3H, Ar−H, major), 5.80 (s, 1H, Ar*C*HO, major), 5.72 (s, 1H, Ar*C*HO, minor), 5.69 (s, 1H, =*C*HCOCH$_3$, minor), 5.66 (s, 1H, =*C*HCOCH$_3$, major), 2.50 (s, 3H, =CHCOCH_3, minor), 2.43 (s, 3H, =CHCOCH_3, major), 2.16 (s, 3H, N=CCH_3, major), 2.05 (s, 3H, N=CCH_3, minor), 1.72 (s, 3H, CH_3, major), 1.59 (s, 3H, CH_3, minor). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 196.9 (*C*OCH_3, major), 177.2 (*C*OO, major), 164.3 (=*C*O, major), 163.5 (N=*C*CH_3, major), 140.1 (major), 137.9 (major), 132.7 (major), 131.8 (minor), 130.5 (major), 123.5 (minor), 123.2 (major), 122.8 (major), 122.2 (minor), 99.5 (=*C*HCOCH$_3$, minor), 99.2 (=*C*HCOCH$_3$, major), 87.7 (ArCHO, minor), 87.4 (ArCHO, major), 71.6 (*C*, major), 31.0 (=CHCO*C*H$_3$, minor), 30.9 (=CHCO*C*H$_3$, major), 19.0 (*C*H$_3$, major), 15.1 (N=C*C*H$_3$, major). IR (UATR) ν_{max} 3083, 3054, 2977, 2925, 1823 (CO), 1799 (CO), 1681 (C=N), 1625, 1608, 1469, 1445, 1425, 1383 cm^{-1}. HRMS (ESI) calcd. for $C_{16}H_{15}ClNO_4$ $[M + H]^+$: 320.0684, found 320.0683.

*(Z)-4-(6-Fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (Z-**3cj**) and (E)-4-(6-Fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (E-**3cj**).* Following the general procedure, compound **1c** (94.8 mg, 0.50 mmol, 1 equiv), L-alanine **4j** (66.3 mg, 0.74 mmol, 1.5 equiv), NaOAc (47.4 mg, 0.58 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by recrystallization with CH_2Cl_2 in hexane to furnish compound *Z/E*-**3cj** (45.5 mg, 30% (>99:1 *Z/E*)).

***Z*-3cj.** (45.5 mg, 30%) as a pale-yellow solid. Mp. 178.9−179.9 °C. ^1H NMR (300 MHz, $CDCl_3$) δ 7.57 (dd, J_{H-H} = 8.4 Hz and J_{H-F} = 4.8 Hz, 1H, Ar−H), 7.28−7.15 (m, 2H, Ar−H), 5.80 (s, 1H, Ar*C*HO), 5.65 (s, 1H, =*C*HCOCH$_3$), 2.43 (s, 3H, =CHCOCH_3), 2.16 (s, 3H, N=CCH_3), 1.72 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 196.9 (*C*OCH_3), 177.2 (*C*OO), 164.7 (d, $^1J_{C-F}$ = 252.1 Hz, *C*F), 164.2 (=*C*O), 163.7 (N=*C*CH_3), 140.8 (d, $^3J_{C-F}$ = 9.3 Hz), 130.1 (d, $^4J_{C-F}$ = 2.4 Hz), 124.1 (d, $^3J_{C-F}$ = 9.6 Hz), 118.0 (d, $^2J_{C-F}$ = 23.7 Hz), 110.0 (d, $^2J_{C-F}$ = 24.9 Hz), 98.7 (d, $^6J_{C-F}$ = 1.6 Hz, =*C*HCOCH$_3$), 87.4 (d, $^4J_{C-F}$ = 2.9 Hz, ArCHO), 71.6 (*C*O), 30.8 (=CHCO*C*H$_3$), 19.0 (*C*H$_3$), 15.1 (N=C*C*H$_3$). $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ − 109.49. IR (UATR) ν_{max} 3045, 2999, 2935, 1827 (CO), 1734 (CO), 1682 (C=N), 1617, 1598 cm^{-1}. HRMS (ESI) calcd. for $C_{16}H_{15}FNO_4$ $[M + H]^+$: 304.0980, found 304.0981.

*(Z)-4-(6-Methoxy-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (Z-**3dj**) and (E)-4-(6-Methoxy-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (E-**3dj**).* Following the general procedure, using compound **1d** (102 mg, 0.50 mmol, 1 equiv), L-alanine **4j** (67.3 mg, 0.76 mmol, 1.5 equiv), NaOAc (46.4 mg, 0.57 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by recrystallization with CH_2Cl_2 in hexane to furnish compound *Z/E*-**3dj** (19.4 mg, 12% (>99:1 *Z/E*)).

***Z*-3dj.** (19.4 mg, 12% (91:9 dr) mixture of isomer) as a white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 8.7 Hz, 1H, Ar−H, major), 7.03 (dd, J = 8.4, 2.1 Hz, 1H, Ar−H, major), 6.95 (d, J = 2.1 Hz, 1H, Ar−H, major), 6.86 (d, J = 1.8 Hz, 1H, Ar−H, minor), 5.76 (s, 1H, Ar*C*HO, major), 5.67 (s, 1H, Ar*C*HO, minor), 5.65 (s, 1H, =*C*HCOCH$_3$, minor), 5.60 (s, 1H, =*C*HCOCH$_3$, major), 3.88 (s, 3H, Ar−OCH_3, major), 3.87 (s, 3H, Ar−OCH_3, minor), 2.49 (s, 3H, =CHCOCH_3minor), 2.42 (s, 3H, =CHCOCH_3major), 2.16 (s, 3H, N=CCH_3, major), 2.13 (s, 3H, N=CCH_3, minor), 1.73 (s, 3H, CH_3, major), 1.62 (s, 3H, CH_3, minor). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 197.1 ($COCH_3$, major), 177.5 (*C*OO, major), 165.0 (=*C*O, major), 164.0 (N=*C*CH_3, major), 162.7 (major), 140.8 (major), 126.4 (major), 123.6 (major), 116.8 (minor), 116.4 (major), 107.5 (major), 106.7 (minor), 98.0 (=*C*HCOCH$_3$, minor), 97.7 (=*C*HCOCH$_3$, major), 87.6 (Ar*C*HO, minor), 87.5 (Ar*C*HO, major), 77.2 (*C*, minor), 71.7 (*C*, major), 55.8 (Ar−O*C*H$_3$, major), 30.9 (=CHCO*C*H$_3$, minor), 30.8 (=CHCO*C*H$_3$, major), 19.4 (*C*H$_3$, minor), 19.0 (*C*H$_3$, major), 15.15 (N=C*C*H$_3$, major), 15.05 (N=C*C*H$_3$, minor). IR (UATR) ν_{max} 3356, 2935, 2841, 1805 (CO), 1668 (C=N), 1604, 1488, 1443, 1369 cm^{-1}. HRMS (ESI) calcd. for $C_{17}H_{18}NO_5$ $[M + H]^+$: 316.1180, found 316.1177.

*(Z)-2,4-Dimethyl-4-(3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (Z-**3ej**) and (E)-2,4-Dimethyl-4-(3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4H)-one (E-**3ej**).* Following the general procedure, using compound **1e** (118 mg, 0.50 mmol, 1 equiv), L-alanine **4j** (67.1 mg, 0.75 mmol, 1.5 equiv), NaOAc (46.7 mg, 0.57 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 0−50% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3ej** (52.1 mg, 30% (>99:1 *Z/E*)).

***Z*-3ej.** (52.1 mg, 30% (90:10 dr) mixture of isomer) as a brown solid. ^1H NMR (300 MHz, $CDCl_3$) δ 8.02−7.92 (m, 2H, Ar−H, major), 7.76−7.66 (m, 1H, Ar−H, major), 7.56−7.34 (m, 6H, Ar−H, major), 6.59 (s, 1H, =*C*HCOPh, minor), 6.54 (s, 1H, =*C*HCOPh, major), 5.85 (s, 1H, Ar*C*HO, minor), 5.83 (s, 1H, Ar*C*HO, major), 2.12 (s, 3H, N=CCH_3, major), 2.05 (s, 3H, N=CCH_3, minor), 1.75 (s, 3H, CH_3, minor), 1.71 (s, 3H, CH_3, major). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 188.6 (*C*OPh, major), 177.2 (*C*OO, major), 165.9 (=*C*O, major), 164.4 (N=*C*CH_3, major), 139.8 (major), 139.3 (major), 134.7 (major), 131.8 (major), 131.7 (minor), 131.6 (minor), 131.5 (major), 129.8 (major), 129.7 (minor), 128.4 (2C, minor), 128.3 (2C, major), 127.8 (2C, major), 122.4 (major), 121.9 (major), 121.8 (minor), 121.6 (minor), 92.9 (=*C*HCOPh, minor), 92.5 (=*C*HCOPh, major), 88.5 (Ar*C*HO, minor), 87.8 (Ar*C*HO, major), 71.5 (*C*, major), 20.0 (*C*H$_3$, minor), 19.2 (*C*H$_3$, major), 15.1 (N=C*C*H$_3$, major), 14.8 (N=C*C*H$_3$, minor). IR (UATR) ν_{max} 3277, 3061, 2941, 2613, 1733 (CO), 1655 (C=N), 1587, 1566, 1467, 1375

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cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{18}NO_4$ $[M + H]^+$: 348.1230, found 348.1231.

*(Z)-4-(6-Chloro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (Z-**3fj**) and (E)-4-(6-Chloro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (E-**3fj**).* Following the general procedure, using compound **1f** (134 mg, 0.50 mmol, 1 equiv), L-alanine **4j** (66.2 mg, 0.74 mmol, 1.5 equiv), NaOAc (46.5 mg, 0.57 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by short-pad silica gel eluted with 5−15% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3fj** (106 mg, 56% (73:27 *Z/E*)).

*Z-**3fj**.* (77.2 mg, 41% (82:18 dr) mixture of isomer) as a brown sticky-gum. ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 8.4, 1.6 Hz, 2H, Ar−H, major), 7.66 (d, *J* = 8.4 Hz, 1H, Ar−H, major), 7.56−7.43 (m, 5H, Ar−H, major), 6.55 (s, 1H, =C*H*COPh, minor), 6.50 (s, 1H, =C*H*COPh, major), 5.80 (s, 1H, ArC*H*O, major), 2.13 (s, 3H, N=CCH_3, major), 1.71 (s, 3H, CH_3, minor), 1.70 (s, 3H, CH_3, major). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.4 (*C*OPh, major), 177.2 (*C*OO, minor), 176.9 (*C*OO, major), 164.7 (=*C*O, major), 164.6 (N=*C*CH$_3$, major), 164.58 (=*C*O, minor), 163.2 (N=*C*CH$_3$, minor), 140.8 (major), 140.6 (minor), 139.6 (minor), 139.5 (major), 137.9 (minor), 137.7 (major), 133.3 (major), 132.0 (major), 131.9 (minor), 130.34 (major), 130.32 (minor), 128.5 (minor), 128.3 (2C, major), 127.9 (minor), 127.8 (2C, major), 122.9 (major), 122.88 (major), 122.8 (minor), 122.3 (minor), 93.2 (=*C*HCOPh, minor), 92.8 (=*C*HCOPh, major), 87.8 (Ar*C*HO, minor), 87.2 (Ar*C*HO, major), 71.8 (*C*, minor), 71.4 (*C*, major), 19.8 (*C*H$_3$, minor), 19.1 (*C*H$_3$, major), 15.1 (N=C*C*H$_3$, major), 14.9 (N=C*C*H$_3$, minor). IR (UATR) ν_{max} 3061, 2937, 1822 (CO), 1730 (CO), 1655 (C=N), 1599, 1587, 1567, 1232 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{16}ClNNaO_4$ $[M + Na]^+$: 404.0660, found 404.0665.

*E-**3fj**.* (29.0 mg, 15%) as a brown sticky-gum. ^1H NMR (300 MHz, $CDCl_3$) δ 9.40 (d, *J* = 8.4 Hz, 1H, Ar−H), 8.04−7.94 (m, 2H, Ar−H), 7.59−7.42 (m, 5H, Ar−H), 6.81 (s, 1H, =C*H*COPh), 5.65 (s, 1H, ArC*H*O), 2.16 (s, 3H, N=CCH_3), 1.69 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 189.3 (*C*OPh), 177.5 (*C*OO), 169.1 (=*C*O), 164.1 (N=*C*CH$_3$), 143.2, 139.7, 138.4, 132.2, 130.9, 130.2, 129.7, 128.5 (2C), 127.9 (2C), 122.0, 98.3 (=*C*HCOPh), 85.0 (Ar*C*HO), 71.5 (*C*), 19.1 (*C*H$_3$), 15.1 (N=C*C*H$_3$). IR (UATR) ν_{max} 3063, 2928, 2853, 2200, 1824 (CO), 1743 (CO), 1663 (C=N), 1601, 1588, 1575, 1465, 1448, 1426, 1376 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{17}ClNO_4$ $[M + H]^+$: 382.0841, found 382.0843.

*(Z)-4-(6-Fluoro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (Z-**3gj**) and (E)-4-(6-Fluoro-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (E-**3gj**).* Following the general procedure, using compound **1g** (128 mg, 0.51 mmol, 1 equiv), L-alanine **4j** (69.6 mg, 0.78 mmol, 1.5 equiv), NaOAc (47.9 mg, 0.58 mmol, 5 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 2−50% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3gj** (44.4 mg, 24% (>99:1 *Z/E*)).

*Z-**3gj**.* (44.4 mg, 24%) as a brown solid. Mp 152.0−153.5 °C. ^1H NMR (300 MHz, $CDCl_3$) 8.04−7.92 (m, 2H, Ar−H), 7.72 (dd, *J* = 8.4, 4.8 Hz, 1H, Ar−H), 7.58−7.40 (m, 3H, Ar−H), 7.30−7.12 (m, 2H, Ar−H), 6.47 (s, 1H, =C*H*COPh), 5.80 (s, 1H, ArC*H*O), 2.14 (s, 3H, N=CCH_3), 1.70 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 188.4 (*C*OPh), 176.9 (*C*OO), 164.9 (=*C*O), 164.62 (d, $^1J_{C-F}$ = 252.0 Hz, *C*F), 164.59 (N=*C*CH$_3$), 141.6 (d, $^3J_{C-F}$ = 9.3 Hz), 139.6, 131.9, 130.7, 128.3 (2C), 127.8 (2C), 123.8 (d, $^3J_{C-F}$ = 9.8 Hz), 117.8 (d, $^2J_{C-F}$ = 23.7 Hz), 110.0 (d, $^2J_{C-F}$ = 24.8 Hz), 92.4 (d, $^6J_{C-F}$ = 1.4 Hz, =*C*HCOPh), 87.2 (d, $^4J_{C-F}$ = 2.9 Hz, Ar*C*HO), 71.4 (*C*), 19.2 (*C*H$_3$), 15.1 (N=C*C*H$_3$). $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ − 109.47. IR (UATR) ν_{max} 3064, 2959, 1820 (CO), 1802 (CO), 1682 (C=N), 1653, 1592, 1575, 1481, 1447, 1376 cm^{-1}. HRMS (ESI) calcd. for $C_{21}H_{17}FNO_4$ $[M + H]^+$: 366.1136, found 366.1128.

*(Z)-4-(6-Methoxy-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (Z-**3hj**) and (E)-4-(6-Methoxy-3-(2-oxo-2-phenylethylidene)-1,3-dihydroisobenzofuran-1-yl)-2,4-dimethyloxazol-5(4H)-one (E-**3hj**).* Following the general procedure, using compound **1h** (132 mg, 0.50 mmol, 1 equiv), L-alanine **4j** (67.0 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac_2O (0.24 mL, 2.50 mmol, 5 equiv), the crude product was purified by short-pad silica gel eluted with 5−15% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3hj** (56.0 mg, 30% (60:40 *Z/E*)), and minor product was decomposed in a further purification process.

*Z-**3hj**.* (33.9 mg, 18%) as a brown sticky-gum. ^1H NMR (300 MHz, $CDCl_3$) 7.97(dd, *J* = 8.8, 1.6 Hz, 2H, Ar−H), 7.64 (d, *J* = 8.4 Hz, 1H, Ar−H), 7.53−7.40 (m, 3H, Ar−H), 7.04 (dd, *J* = 8.4, 2.0 Hz, 1H, Ar−H), 6.94 (d, *J* = 2.0 Hz, 1H, Ar−H), 6.43 (s, 1H, =C*H*COPh), 5.77 (s, 1H, ArC*H*O), 3.88 (s, 3H, Ar−OCH_3), 2.14 (s, 3H, N=CCH_3), 1.71 (s, 3H, CH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 188.5 (*C*OPh), 177.0 (*C*OO), 166.3 (=*C*O), 164.4 (N=*C*CH$_3$), 162.7, 141.6, 140.0, 131.6, 128.2 (2C), 127.8 (2C), 127.0, 123.3, 116.5, 107.4, 91.2 (=*C*HCOPh), 87.3 (Ar*C*HO), 71.4 (*C*), 55.8 (Ar−O*C*H$_3$), 19.2 (*C*H$_3$), 15.1 (N=C*C*H$_3$). IR (UATR) ν_{max} 3060, 2939, 1807 (CO), 1739 (CO), 1546, 1487, 1229 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{19}NNaO_5$ $[M + Na]^+$: 400.1155, found 400.1153.

*(Z)-4-Benzyl-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-phenyloxazol-5(4H)-one (Z-**3′ag**) and (E)-4-Benzyl-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-phenyloxazol-5(4H)-one (E-**3′ag**).* Following the general procedure, using compound **1a** (86.7 mg, 0.50 mmol, 1 equiv), DL-phenylalanine **4g** (124 mg, 0.75 mmol, 1.5 equiv), Et_3N (0.08 mL, 0.55 mmol, 1.1 equiv), and Bz_2O (227 mg, 1.01 mmol, 2 equiv) in CH_3CN (0.24 mL), the crude product was purified by column chromatography on silica gel using 2−10% EtOAc in CH_2Cl_2 to furnish compound *Z/E*-**3′ag** (97.3 mg, 46% (71:29 *Z/E*)).

*Z-**3′ag**.* (69.2 mg, 33% (71:29 dr) mixture of isomer) as a brown sticky-gum. ^1H NMR (300 MHz, $CDCl_3$) δ 7.81−7.75 (m, 2H, Ar−H, major), 7.72−7.67 (m, 2H, Ar−H, minor), 7.62−7.12 (m, 12H, Ar−H, major), 6.02 (s, 1H, ArC*H*O, major), 6.01 (s, 1H, ArC*H*O, minor), 5.81 (s, 1H, =C*H*COCH$_3$, minor), 5.73 (s, 1H, =C*H*COCH$_3$, major), 3.60 (AB q, *J* = 13.5 Hz, 2H, CH_2Ph, major), 3.47 (AB q, *J* = 13.2 Hz, 2H, CH_2Ph, minor), 2.57 (s, 3H, =CHCOCH_3, minor), 2.51 (s, 3H, =CHCOCH_3, major). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 197.4 (*C*OCH$_3$, minor), 197.1 (*C*OCH$_3$, major), 175.9 (*C*OO, minor), 175.5 (*C*OO, major), 164.9 (=*C*O, minor), 164.7 (=*C*O, major), 162.4 (N=*C*Ph, major), 161.4 (N=*C*Ph, minor), 138.6 (major), 134.1 (major), 133.8 (minor), 133.2 (major), 132.91 (minor), 132.87 (major),

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131.7 (minor), 131.5 (major), 130.3 (2C, major), 130.2 (2C, minor), 129.9 (major), 129.8 (minor), 128.8 (2C, major), 128.6 (2C, minor), 128.3 (2C, major), 128.2 (2C, minor), 127.9 (2C, major), 127.8 (2C, minor), 127.6 (major), 127.5 (minor), 124.9 (major), 124.8 (minor), 122.5 (major), 122.1 (major), 121.9 (minor), 99.3 (=CHCOCH$_3$, minor), 98.9 (=*C*HCOCH$_3$, major), 88.0 (ArCHO, minor), 87.1 (ArCHO, major), 77.1 (*C*, minor), 76.9 (*C*, major), 39.8 (*C*H$_2$Ph, major), 39.3 (*C*H$_2$Ph, minor), 31.1 (=CHCO*C*H$_3$, minor), 31.0 (=CHCO*C*H$_3$, major). IR (UATR) ν_{max} 3063, 3034, 2922, 1817 (CO), 1633 (C=N), 1602, 1495, 1467 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{22}NO_4$ [M + H]$^+$: 424.1543, found 424.1538.

E-3′ag. (28.1 mg, 13% (85:15 dr) mixture of isomer) as a pale-yellow sticky-gum. ^{1}H NMR (300 MHz, CDCl$_3$) δ 9.32 (d, J = 7.8 Hz, 1H, Ar−H, major), 7.82−7.76 (m, 2H, Ar−H, major), 7.68−7.62 (m, 2H, Ar−H, minor), 7.59−7.52 (m, 1H, Ar−H, major), 7.52−7.46 (m, 1H, Ar−H, major), 7.46−7.39 (m, 4H, Ar−H, major), 7.39−7.30 (m, 1H, Ar−H, major), 7.25−7.14 (m, 4H, Ar−H, major), 6.31 (s, 1H, ArC*H*O, minor), 6.17 (s, 1H, ArC*H*O, major), 5.82 (s, 1H, =C*H*COCH$_3$, major), 3.55 (s, 2H, C*H*$_2$Ph, major), 3.43 (AB q, J = 13.2 Hz, 2H, C*H*$_2$Ph, minor), 2.32 (s, 3H, =CHCOC*H*$_3$, minor), 2.22 (s, 3H, =CHCOC*H*$_3$, major). ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) δ 196.5 (COCH$_3$, minor), 196.4 (*C*OCH$_3$, major), 176.4 (*C*OO, minor), 175.7 (*C*OO, major), 168.4 (=*C*O, minor), 168.2 (=*C*O, major), 162.3 (N=*C*Ph, major), 161.4 (N=*C*Ph, minor), 141.3 (minor), 141.1 (major), 133.2 (major), 133.0 (major), 132.8 (minor), 132.3 (major), 132.1 (minor), 131.9 (major), 130.4 (2C, major), 130.3 (2C, minor), 129.8 (major), 129.7 (minor), 129.0 (minor), 128.8 (2C, major), 128.6 (2C, minor), 128.3 (2C, major), 128.2 (major), 128.0 (2C, major), 127.9 (2C, minor), 127.5 (major), 125.2 (major), 124.9 (minor), 121.6 (major), 121.1 (minor), 102.0 (=*C*HCOCH$_3$, minor), 101.6 (=*C*HCOCH$_3$, major), 85.5 (ArCHO, minor), 84.4 (ArCHO, major), 77.2 (*C*, minor), 76.9 (*C*, major), 39.9 (*C*H$_2$Ph, major), 39.4 (*C*H$_2$Ph, minor), 32.0 (=CHCO*C*H$_3$, minor), 31.9 (=CHCO*C*H$_3$, major). IR (UATR) ν_{max} 3033, 2925, 1818 (CO), 1777 (CO), 1650 (C=N), 1608, 1591, 1578, 1496, 1467, 1452 cm^{-1}. HRMS (ESI) calcd. for $C_{27}H_{22}NO_4$ [M + H]$^+$: 424.1543, found 424.1536.

*Mechanistic Investigation. (4R)-4-(Hydroxy(2-(3-oxobut-1-yn-1-yl)phenyl)methyl)-2-phenyloxazol-5(4H)-one (**5a**).* To a suspension of compound **1a** (172 mg, 1.00 mmol, 1 equiv), hippuric acid **4a** (269 mg, 1.50 mmol, 1.5 equiv), NaOAc (41.0 mg, 0.50 mmol, 0.5 equiv) and Ac$_2$O (0.47 mL, 5.00 mmol, 5 equiv) were added in a sealed tube and stirred at 60 °C for 1 h. The reaction mixture was allowed to cool to room temperature and then quenched with sat. Na$_2$CO$_3$ (5 mL) and extracted with CH$_2$Cl$_2$ (3 × 10 mL). Combined organic layers were washed with sat. Na$_2$CO$_3$ until pH = 7, followed by water and brine, dried over anh. Na$_2$SO$_4$, and concentrated to give a yellow-brown solid. The crude product was purified by precipitation with cooled EtOH, filter off solid, and washed with cooled EtOH and hexane to afford desired product **5a** (186 mg, 56%) as a pale-yellow solid. Mp 168.8−170.1 °C. ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.77−8.69 (m, 1H, Ar−H), 8.16 (dd, J = 7.0, 1.5 Hz, 2H, Ar−H), 7.65−7.48 (m, 6H, Ar−H), 5.62 (br t, J = 7.2 Hz, 1H, ArC*H*OH), 5.10 (d, J = 7.2 Hz, 1H, − O*H*), 2.49 (overlapped, 4H, COC*H*$_3$ and C*H*N=). ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) δ 205.8 (COCH$_3$), 166.8 (*C*OO), 161.8 (N=*C*Ph), 149.9, 146.6, 137.8, 133.0, 132.8, 130.0, 129.0, 128.9 (2C), 128.15, 128.10 (2C), 125.7, 124.9, 74.7 (ArCHOH), 60.4 (CHN=), 32.8 (COCH$_3$). IR (UATR) ν_{max} 3326 (OH), 2926, 1781 (CO), 1711 (CO), 1656 (C=N) cm^{-1}. HRMS (ESI) calcd. for $C_{20}H_{15}NNaO_4$ [M + Na]$^+$: 356.0893, found 356.0900.

*(Z)-3-(2-Oxopropylidene)-1,3-dihydroisobenzofuran-1-yl Acetate (**6a**).* Following the general procedure, compound **1a** (87.0 mg, 0.50 mmol, 1 equiv), NaOAc (45.0 mg, 0.55 mmol, 1.1 equiv), and Ac$_2$O (0.24 mL, 2.50 mmol, 5 equiv) were stirred at 80 °C for 4 h. The crude product was purified by column chromatography on silica gel using 20−30% EtOAc in hexane to afford compound **6a** (53.8 mg, 46%) as a pale-yellow solid (^{1}H NMR data identical to that in the literature).[19a]

*4-(2-(3-(N-Acetylacetamido)-3-benzyl-4-oxooxetan-2-yl)-phenyl)but-3-yn-1-yl Acetate (**9**).* Following the general procedure, using compound **1i**[28] (121 mg, 0.69 mmol, 1 equiv), DL-phenylalanine **4g** (172 mg, 1.04 mmol, 1.5 equiv), NaOAc (63.9 mg, 0.78 mmol, 1.1 equiv), and Ac$_2$O (0.33 mL, 3.45 mmol, 5 equiv), the crude product was purified by column chromatography on silica gel using 2% EtOAc in CH$_2$Cl$_2$ to furnish compound **9** (95.9 mg, 32%) as a pale-yellow sticky-gum. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.53 (d, J = 6.0 Hz, 1H, Ar−H), 7.46 (d, J = 6.0 Hz, 1H, Ar−H), 7.42−7.24 (m, 2H, Ar−H), 7.22−7.15 (m, 3H, Ar−H), 7.04−6.96 (m, 2H, Ar−H), 6.66 (s, 1H, ArC*H*O), 4.36 (t, J = 6.0 Hz, 2H, OC*H*$_2$CH$_2$), 3.33 (d, J = 12.0 Hz, 1H, C*H*HPh), 2.30 (t, J = 7.5 Hz, 2H, (≡CC*H*$_2$), 2.69 (d, J = 12.0 Hz, 1H, CH*H*Ph), 2.07 (s, 3H, C*H*$_3$CO), 2.00 (s, 3H, C*H*$_3$CO), 1.99 (s, 3H C*H*$_3$COO). ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) δ 177.9 (*C*OO), 171.0 (CH$_3$*C*OO), 168.5 (*C*O), 162.1 (*C*O), 136.8, 133.3, 132.1, 130.2 (2C), 128.5, 128.3, 128.2, 128.1 (2C), 127.3, 123.7, 91.6 (*C* ≡), 79.7 (*C* ≡), 77.9 (*C*), 74.7 (ArCHO), 62.3 (OCH$_2$), 38.9 (*C*H$_2$Ph), 20.8 (*C*H$_3$), 20.7 (*C*H$_3$), 20.2 (≡C*C*H$_2$), 14.7 (OCOCH$_3$). IR (UATR) ν_{max} 3256, 3077, 3051, 2995, 2931, 1759 (CO), 1634, 1486, 1419, 1361 cm^{-1}. HRMS (ESI) calcd. for $C_{26}H_{26}NO_6$ [M + H]$^+$: 448.1755, found 448.1746.

*(Z)-6-Fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl Acetate (**6c**).* Following the general procedure, compound **1c** (95.1 mg, 0.50 mmol, 1 equiv), L-proline **4k** (86.4 mg, 0.75 mmol, 1.5 equiv), NaOAc (45.7 mg, 0.55 mmol, 1.1 equiv), and Ac$_2$O (0.24 mL, 2.50 mmol, 5 equiv) were stirred at 80 °C for 3 h. The crude product was purified by chromatography on silica gel using 15% EtOAc in hexane to furnish compound **6c** (38.4 mg, 31%) as a brown solid. Mp 130.0−131.0 °C. ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.59 (dd, J_{H-H} = 8.1 Hz and J_{H-F} = 4.5 Hz, 1H, Ar−H), 7.55 (s, 1H, Ar−H), 7.31−7.25 (m, 1H, Ar−H), 7.23 (s, 1H, ArC*H*O), 5.76 (s, 1H, =C*H*COCH$_3$), 2.49 (s, 3H, =CHCOC*H*$_3$), 2.20 (s, 3H, C*H*$_3$). ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) δ 197.1 (*C*OCH$_3$), 169.4 (*C*OO), 164.9 (d, $^1J_{C-F}$ = 252.6 Hz, *C*F), 161.4 (=*C*O), 140.4 (d, $^3J_{C-F}$ = 9.5 Hz), 129.3 (d, $^4J_{C-F}$ = 2.3 Hz), 123.6 (d, $^3J_{C-F}$ = 9.5 Hz), 118.9 (d, $^2J_{C-F}$ = 23.9 Hz), 110.8 (d, $^2J_{C-F}$ = 24.7 Hz), 100.4 (d, $^6J_{C-F}$ = 1.7 Hz, =*C*HCOCH$_3$), 98.2 (d, $^4J_{C-F}$ = 2.8 Hz, ArC*H*O), 31.0 (=CHCO*C*H$_3$), 20.9 (*C*H$_3$). ^{19}F{^{1}H} NMR (376 MHz, CDCl$_3$) δ − 109.14. IR (UATR) ν_{max} 3256, 3077, 3051, 2995, 2931, 1759 (CO), 1634, 1486, 1419, 1361 cm^{-1}. HRMS (ESI) calcd. for $C_{13}H_{11}FNaO_4$ [M + Na]$^+$: 273.0534, found 273.0539.

*Hydrolysis and Oxidation of Indeno[2,1-c]pyran-3-one **2a**. N-(1-Methyl-3,9-dioxo-3,9-dihydroindeno[2,1-c]pyran-4-yl)benzamide (**10**).* Compound **2a** (37.5 mg, 0.10 mmol, 1 equiv) was treated with 5% KOH in EtOH (0.18 mL) and

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stirred at room temperature (26 °C) for 5 min. The reaction mixture was quenched with 2 N HCl (0.20 mL) and extracted with CH_2Cl_2 (3 × 5 mL). Combined organic layers were washed with water and brine and dried over anh. Na_2SO_4 and concentrated to give an orange yellow solid which was further used in the next step without purification. The crude reaction was dissolved with CH_2Cl_2 (1.5 mL), and PCC was added (32.0 mg, 0.15 mmol, 1.5 equiv) and stirred at room temperature (26 °C) for 1.5 h. After completion, the mixture was filtered through a short silica gel column, eluent with CH_2Cl_2, and then the solvent was removed. The residue was purified by column chromatography on silica gel using 40% EtOAc in hexane to afford the compound **10** (14.2 mg, 43% (2 steps)) as a pale-yellow solid. Mp 278.6−280.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (br s, 1H, − N*H*), 8.10−7.80 (m, 3H, Ar−H), 7.80−7.40 (m, 6H, Ar−H), 2.74 (s, 3H, =CC*H*$_3$). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 187.9 (*C*O), 165.8 (=*C*O), 161.5 (*C*O), 161.1 (*C*OO), 141.4, 139.0, 138.7, 134.8, 132.9, 132.1, 129.0 (2C), 128.1, 127.8 (3C), 124.0, 113.6, 113.5, 16.6 (*C*H$_3$). IR (UATR) ν_{max} 3324, 3238, 1735 (CO), 1709 (CO), 1659 (CO), 1504, 1473 cm^{-1}. HRMS (ESI) calcd. for $C_{20}H_{13}NNaO_4$ [M + Na]$^+$: 354.0737, found 354.0735.

*Ethyl (E)-2-Benzamido-2-(2-(1-hydroxyethyl)-1H-inden-1-ylidene)acetate (**11**).* To a suspension of compound **2a** (38.0 mg, 0.10 mmol, 1 equiv) in EtOH (1.5 mL) $NaBH_4$ (15.0 mg, 0.40 mmol, 4 equiv) was added and stirred at room temperature (26 °C) for 18 h. The reaction mixture was quenched with water (1 mL) and extracted with EtOAc (3 × 5 mL). Combined organic layers were washed with water and brine, dried over anh. Na_2SO_4, and concentrated to give yellow oil. The residue was purified by PTLC using 30% EtOAc in hexane to afford the compound **11** (15.0 mg, 41%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.53 (br s, 1H, − N*H*), 8.00 (dd, *J* = 7.2, 1.6 Hz, 2H, Ar−H), 7.56−7.50 (m, 1H, Ar−H), 7.47−7.39 (m, 3H, Ar−H), 7.22−7.10 (m, 3H, Ar−H), 6.73 (s, 1H, ArC*H*=), 4.92−4.83 (m, 1H, CH$_3$C*H*OH), 4.64−4.49 (m, 2H, OC*H*$_2$CH$_3$), 2.74 (d, *J* = 8.0 Hz, 1H, − O*H*), 1.63 (d, *J* = 6.8 Hz, 3H, C*H*$_3$CHOH), 1.43 (t, *J* = 7.2 Hz, 3H, OCH$_2$C*H*$_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.9 (*C*O), 165.1 (*C*OO), 140.9, 140.2, 135.2, 132.5, 132.3, 130.4, 129.9, 128.7 (2C), 128.0 (2C), 127.1, 125.6, 123.7, 122.0, 121.5, 66.0 (*C*H$_3$CHOH), 62.4 (O*C*H$_2$CH$_3$), 21.5 (*C*H$_3$CHOH), 13.7 (OCH$_2$*C*H$_3$). IR (UATR) ν_{max} 3380 (OH), 3069, 2933, 1719 (CO), 1658 (CO), 1610, 1324, 1272 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{21}NNaO_4$ [M + Na]$^+$: 386.1363, found 386.1367.

*4-Benzyl-4-(6-fluoro-3-(2-oxopropyl)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4H)-one (**12**).* A suspension of compound *Z*-**3cg** (75.8 mg, 0.2 mmol, 1 equiv) and Pd/C (10.8 mg, 0.10 mmol, 50 mol %) in EtOAc (5 mL) was stirred at room temperature (25 °C) under H_2 atmosphere (40 bar). After being stirred for 24 h, the palladium catalyst was removed by filtration through Celite, and the filtrate was concentrated under reduced pressure to give the crude product, which was further purified by column chromatography on silica gel using 50% EtOAc in hexane to furnish compound **12** (40.4 mg, 53% (72:28 dr) mixture of isomer) as a pale-yellow viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.10 (m, 6H, Ar−H, major), 7.04 (t, *J* = 8.6 Hz, 1H, Ar−H, major), 6.95 (d, *J* = 8.4 Hz, 1H, Ar−H, major), 6.84 (d, *J* = 8.4 Hz, 1H, Ar−H, minor), 5.71−5.63 (m, 1H, ArC*H*CH$_2$, major), 5.51 (s, 1H, ArC*H*O, major), 5.48 (s, 1H, ArC*H*O, minor), 3.33 (AB q, *J* = 13.4 Hz, 2H, C*H*$_2$Ph, minor), 3.36 (AB q, *J* = 13.2 Hz, 2H, C*H*$_2$Ph, major), 3.14 (dd, *J* = 16.4, 8.0 Hz, 1H, ArCHC*H*H, major), 2.87 (dd, *J* = 16.4, 4.8 Hz, 1H, ArCHCH*H*, major), 2.32 (s, 3H, COC*H*$_3$, minor), 2.30 (s, 3H, COC*H*$_3$, major), 2.05 (s, 3H, N=CC*H*$_3$, major), 1.77 (s, 3H, N=CC*H*$_3$, minor). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.9 (*C*OCH$_3$, minor), 206.6 (*C*OCH$_3$, major), 177.7 (*C*OO, minor), 176.7 (*C*OO, major), 163.3 (N=*C*CH$_3$, major), 162.7 (d, $^1J_{C-F}$ = 244.6 Hz, *C*F, major), 162.6 (d, $^1J_{C-F}$ = 244.7 Hz, *C*F, minor), 161.6 (N=*C*CH$_3$, minor), 138.31 (d, $^3J_{C-F}$ = 8.4 Hz, major), 138.26 (d, $^3J_{C-F}$ = 8.2 Hz, minor), 137.58 (major), 137.56 (minor), 133.8 (minor), 133.4 (major), 130.3 (2C, major), 130.2 (2C, minor), 128.2 (2C, major), 128.1 (2C, minor), 127.4 (major), 127.3 (minor), 123.1 (d, $^3J_{C-F}$ = 8.9 Hz, major), 123.0 (d, $^3J_{C-F}$ = 7.9 Hz, minor), 116.4 (d, $^2J_{C-F}$ = 23.1 Hz, major), 116.1 (d, $^2J_{C-F}$ = 23.0 Hz, minor), 109.4 (d, $^2J_{C-F}$ = 24.2 Hz, major), 108.8 (d, $^2J_{C-F}$ = 24.0 Hz, minor), 85.5 (ArCHO, minor), 85.4 (ArCHO, major), 79.93 (ArCHCH$_2$, major), 79.88 (ArCHCH$_2$, minor), 77.8 (*C*, minor), 77.76 (*C*, major), 50.7 (ArCHCH$_2$CO, major), 50.6 (ArCHCH$_2$CO, minor), 39.6 (*C*H$_2$Ph, minor), 39.4 (*C*H$_2$Ph, major), 31.1 (COC*H*$_3$, minor), 30.8 (COC*H*$_3$, major), 14.8 (N=CC*H*$_3$, major), 14.4 (N=CC*H*$_3$, minor). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 117.10 (major), − 117.14 (minor). IR (UATR) ν_{max} 3368, 3031, 2924, 2875, 1713 (CO), 1615, 1519, 1489, 1431, 1402, 1364 cm^{-1}. HRMS (ESI) calcd. $C_{22}H_{20}FNNaO_4$ for [M + Na]$^+$: 404.1269, found 404.1272.

*Ethyl (Z)-2-Acetamido-2-(6-fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-3-phenylpropanoate (Z-**13**).* Compound *Z*-**3cg** (76.0 mg, 0.20 mmol) was treated with 5% KOH in EtOH (0.33 mL) and stirred at room temperature (25 °C) for 5 min. The reaction mixture was quenched with 2 N HCl (0.20 mL) and extracted with CH_2Cl_2 (3 × 5 mL). Combined organic layers were washed with water and brine, dried over anh. Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by precipitation with CH_2Cl_2 in EtOAc to afford the compound *Z*-**13** (84.3 mg, 99%) as a white solid. Mp 195.0−195.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (dd, J_{H-H} = 8.4 Hz and J_{H-F} = 4.8 Hz, 1H, Ar−H), 7.39 (dd, *J* = 8.4, 2.1 Hz, 1H, Ar−H), 7.32−7.24 (m, 3H, Ar−H), 7.19 (td, *J* = 8.4, 2.1 Hz, 1H, Ar−H), 7.13−7.03 (m, 2H, Ar−H), 6.67 (s, 1H, ArC*H*O), 6.54 (br s, 1H, − N*H*), 5.66 (s, 1H, =C*H*COCH$_3$), 4.03 (q, *J* = 7.2 Hz, 2H, OC*H*$_2$CH$_3$), 4.02 (d, *J* = 12.5 Hz, 1H, C*H*HPh), 3.42 (d, *J* = 12.5 Hz, 1H, CH*H*Ph), 2.43 (s, 3H, =CHCOC*H*$_3$), 1.97 (s, 3H, C*H*$_3$CONH), 0.99 (t, *J* = 7.2 Hz, 3H, OCH$_2$C*H*$_3$). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 197.0 (*C*O), 170.0 (*C*ONH), 168.9 (*C*OO), 164.6 (d, $^1J_{C-F}$ = 251.0 Hz, *C*F), 164.3 (=*C*O), 143.3 (d, $^3J_{C-F}$ = 9.6 Hz), 134.1, 130.1 (d, $^4J_{C-F}$ = 2.1 Hz), 129.7 (2C), 128.6 (2C), 127.6, 123.1 (d, $^3J_{C-F}$ = 9.5 Hz), 117.3 (d, $^2J_{C-F}$ = 23.9 Hz), 111.7 (d, $^2J_{C-F}$ = 25.1 Hz), 98.2 (=*C*HCOCH$_3$), 86.8 (d, $^4J_{C-F}$ = 2.9 Hz, ArCHO), 68.2 (*C*), 62.4 (OC*H*$_2$CH$_3$), 37.3 (*C*H$_2$Ph), 30.9 (=CHCOC*H*$_3$), 23.9 (NHCOC*H*$_3$), 13.6 (OCH$_2$*C*H$_3$). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 109.96. IR (UATR) ν_{max} 3282 (NH), 3034, 2930, 1727 (CO), 1683 (CO), 1632 (CO), 1615, 1482, 1371, 1264, 1257 cm^{-1}. HRMS (ESI) calcd. $C_{24}H_{24}FNNaO_5$ for [M + Na]$^+$: 448.1531, found 448.1522.

*(Z)-N-(1-(6-Fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-phenyl-1-(4-tosyloxazol-5-yl)ethyl)acetamide (Z-**14**).* A suspension of compound *Z*-**3cg** (75.9 mg, 0.20 mmol, 1 equiv) and TosMIC (78.2 mg, 0.40 mmol, 2 equiv) in CH_2Cl_2 (0.1 M) was added with NaH (22.1 mg, 0.50

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mmol, 2.5 equiv) and stirred at room temperature (26 °C) for 1 h. The reaction mixture was quenched with water (0.50 mL) and extracted with CH_2Cl_2 (3 × 5 mL). Combined organic layers were washed with water and brine and dried over anh. Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using 50% EtOAc in hexane to afford the compound *Z*-**14** (55.0 mg, 48%) as a white solid. Mp 224.0−225.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.20 (br s, 1H, − N*H*), 7.67 (s, 1H, OC*H*═N), 7.38 (dd, J_{H-H} = 8.6 Hz and J_{H-F} = 4.5 Hz, 1H, Ar−H), 7.31 (d, *J* = 8.4 Hz, 2H, Ar−H), 7.25−7.03 (m, 8H, Ar−H and ArC*H*O), 6.79−6.73 (m, 2H, Ar−H), 5.63 (s, 1H, ═C*H*COCH$_3$), 4.55 (AB q, *J* = 13.8 Hz, 1H, C*H*HPh), 3.78 (AB q, *J* = 13.8 Hz, 1H, CH*H*Ph), 2.61 (s, 3H, ═CHCOC*H*$_3$), 2.41 (s, 3H, C*H*$_3$), 2.27 (s, 3H, NHCOC*H*$_3$). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 197.0 (*C*O), 171.3 (*C*ONH), 164.8 (d, $^1J_{C-F}$ = 253.0 Hz, *C*F), 164.2, 150.1, 149.2 (OCH═N), 145.7, 142.4 (d, $^3J_{C-F}$ = 9.4 Hz), 140.0, 135.0, 134.9, 129.8 (2C), 129.4 (2C), 129.0 (d, $^4J_{C-F}$ = 2.1 Hz), 128.5 (2C), 128.2 (2C), 127.2, 123.6 (d, $^3J_{C-F}$ = 9.6 Hz), 117.8 (d, $^2J_{C-F}$ = 23.9 Hz), 110.4 (d, $^2J_{C-F}$ = 24.8 Hz), 98.5 (═*C*HCOCH$_3$), 86.9 (d, $^4J_{C-F}$ = 2.6 Hz, ArCHO), 66.3 (*C*), 38.7 (*C*H$_2$Ph), 31.1 (═CHCO*C*H$_3$), 24.3 (NHCO*C*H$_3$), 21.7 (*C*H$_3$). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 108.49. IR (UATR) ν_{max} 3305 (NH), 3066, 2959, 2872, 1680 (CO), 1638 (CO), 1618, 1597, 1521, 1481, 1456 cm^{-1}. HRMS (ESI) calcd. $C_{31}H_{27}FN_2NaO_6S$ for [M + Na]$^+$: 597.1466, found 597.1475.

*Ethyl (Z)-2-Acetamido-2-(6-fluoro-3-(2-oxo-1-phenylpropylidene)-1,3-dihydroisobenzofuran-1-yl)-3-phenylpropanoate (**15:15′**).* A suspension of compound *Z*-**13** (132 mg, 0.30 mmol, 1 equiv) and 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (0.07 mL, 0.30 mmol, 1 equiv) in CH_3CN (3 mL, 0.1 M) was added with CsF (228 mg, 1.5 mmol, 5 equiv) and stirred at 80 °C for 21 h. The resulting mixture was filtrated through short-pad silica gel, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using 15−80% EtOAc in hexane to furnish compounds **15:15′** (77.8 mg, 51% (65:35 dr))

15. (47.3 mg) as a white solid. Mp. 199.4−201.1 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.41 (m, 3H, Ar−H), 7.32−7.23 (m, 3H, Ar−H), 7.21−7.14 (m, 2H, Ar−H), 7.11−7.04 (m, 2H, Ar−H), 6.98 (dd, *J* = 8.0, 2.0 Hz, 1H, Ar−H), 6.81 (s, 1H, ArC*H*O), 6.72 (td, *J* = 8.8, 2.2 Hz, 1H, Ar−H), 6.51 (br s, 1H, − N*H*), 5.91 (dd, J_{H-H} = 8.9 Hz and J_{H-F} = 5.0 Hz, 1H, Ar−H), 4.29 (AB q, *J* = 13.8 Hz, 1H, C*H*HPh), 4.04 (dq, *J* = 10.8, 7.2 Hz, 1H, OC*H*HCH$_3$), 3.87 (dq, *J* = 10.8, 7.2 Hz, 1H, OCH*H*CH$_3$), 3.76 (AB q, *J* = 13.5 Hz, 1H, CH*H*Ph), 2.75 (s, 3H, ═CCOC*H*$_3$), 2.12 (s, 3H, NHCOC*H*$_3$), 1.13 (t, *J* = 7.1 Hz, 3H, OCH$_2$C*H*$_3$). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 197.3 (*C*O), 170.4 (*C*ONH), 169.9 (*C*OO), 163.6 (d, $^1J_{C-F}$ = 252.1 Hz, *C*F), 162.6, 143.4, 135.8, 135.0, 131.0 (2C), 129.8 (d, $^4J_{C-F}$ = 2.4 Hz), 129.7 (2C), 129.2 (2C), 128.5 (2C), 128.0, 127.8 (d, $^3J_{C-F}$ = 9.2 Hz), 127.3, 116.7 (d, $^2J_{C-F}$ = 22.9 Hz), 115.7 (d, $^6J_{C-F}$ = 1.6 Hz), 109.8 (d, $^2J_{C-F}$ = 23.6 Hz), 83.4 (d, $^4J_{C-F}$ = 2.9 Hz, ArCHO), 68.0 (*C*), 62.7 (O*C*H$_2$CH$_3$), 36.9 (*C*H$_2$Ph), 32.6 (═CCOCH$_3$), 24.5 (NHCOCH$_3$), 13.8 (OCH$_2$*C*H$_3$). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 110.72. IR (UATR) ν_{max} 3311 (NH), 3060, 3032, 2983, 1737 (CO), 1674 (CO), 1647 (CO), 1605, 1595, 1497, 1475, 1456, 1443, 1365 cm^{-1}. HRMS (ESI) calcd. $C_{30}H_{28}FNNaO_5$ for [M + Na]$^+$: 524.1844, found 524.1849.

15′. (30.5 mg) as a white solid. Mp. 200.0−201.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.41 (m, 3H, Ar−H), 7.35−7.24 (m, 4H, Ar−H), 7.16−7.06 (m, 4H, Ar−H), 6.76 (t, *J* = 8.4 Hz, 1H, Ar−H), 6.70 (s, 1H, ArC*H*O), 6.57 (br s, 1H, − N*H*), 5.91 (dd, J_{H-H} = 8.8 Hz and J_{H-F} = 4.8 Hz, 1H, Ar−H), 4.10−4.00 (m, 3H, OC*H*$_2$CH$_3$ and C*H*HPh), 3.46 (AB q, *J* = 12.6 Hz, 1H, CH*H*Ph), 2.52 (s, 3H, ═CCOC*H*$_3$), 2.01 (s, 3H, NHCOC*H*$_3$), 0.99 (t, *J* = 7.2 Hz, 3H, OCH$_2$C*H*$_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.2 (*C*O), 170.1 (*C*ONH), 169.1 (*C*OO), 163.7 (d, $^1J_{C-F}$ = 251.3 Hz, *C*F), 161.9, 144.3 (d, $^3J_{C-F}$ = 9.4 Hz), 135.8, 134.3, 131.0 (2C), 130.1 (d, $^4J_{C-F}$ = 2.4 Hz), 129.7 (2C), 129.2 (2C), 128.6 (2C), 128.0, 127.6 (d, $^3J_{C-F}$ = 10.0 Hz), 127.5, 116.4 (d, $^2J_{C-F}$ = 22.9 Hz), 115.6 (d, $^6J_{C-F}$ = 1.6 Hz), 110.9 (d, $^2J_{C-F}$ = 24.8 Hz), 85.2 (d, $^4J_{C-F}$ = 2.8 Hz, ArCHO), 68.5 (*C*), 62.4 (O*C*H$_2$CH$_3$), 37.0 (*C*H$_2$Ph), 32.3 (═CCOCH$_3$), 24.0 (NHCOCH$_3$), 13.6 (OCH$_2$*C*H$_3$). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 111.23. IR (UATR) ν_{max} 3319 (NH), 3059, 2983, 2930, 1733 (CO), 1670 (CO), 1591, 1542, 1497, 1474, 1457, 1444, 1367 cm^{-1}. HRMS (ESI) calcd. $C_{30}H_{28}FNNaO_5$ for [M + Na]$^+$: 524.1844, found 524.1842.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c03842.

Crystallographic data of molecular structure of compound *Z*-**3ag** (CIF)

Crystallographic data of molecular structure of compound *E*-**3cg** (CIF)

Crystallographic data of molecular structure of compound *Z*-**13** (CIF)

Crystallographic data of molecular structure of compound **15** (CIF)

Experimental details, characterization data, and ^{1}H and ^{13}C{^{1}H} NMR and HRMS data of all the compounds (PDF)

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Notes

The authors declare no competing financial interest.

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(25) Data of minor product *E*-**3ag** was collected by using Et_3N as a base under EPA conditions (Table 2, entry 10). (*E*)-4-Benzyl-2-methyl-4-(3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)oxazol-5(4*H*)-one (*E*-**3ag**) (81:19 dr (mixture of isomer)) as a brown sticky-gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.48−9.40 (m, 1H, Ar−H, major), 7.58−7.40 (m, 3H, Ar−H, major), 7.30−7.12 (m, 5H, Ar−H, major), 6.28 (s, 1H, =C*H*COCH$_3$, minor), 6.18 (s, 1H, =C*H*COCH$_3$, major), 5.75 (s, 1H, ArC*H*O, minor), 5.74 (s, 1H, ArC*H*O, major), 3.41 (s, 2H, CH_2Ph, major), 3.40 (AB q, J = 13.2 Hz, 2H, CH_2Ph, minor), 2.30 (s, 3H, =CHCOCH_3, minor), 2.27 (s, 3H, =CHCOCH_3, major), 1.96 (s, 3H, N=CCH_3, major), 1.72 (s, 3H, N=CCH_3, minor). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 196.3 (COCH$_3$, major), 176.0 (*C*OO, major), 168.1 (=*C*O, major), 163.7 (N=*C*CH$_3$, major), 141.1 (minor), 141.0 (major), 133.2 (minor), 132.9 (major), 132.2 (major), 132.0 (minor), 131.9 (major), 130.3 (2C, major), 130.2 (2C, minor), 129.8 (major), 129.6 (minor), 128.24 (2C, major), 128.19 (major), 128.06 (minor), 127.5 (major), 127.4 (minor), 121.5 (major), 120.6 (minor), 101.9 (=*C*HCOCH$_3$, minor), 101.3 (=*C*HCOCH$_3$, major), 85.1 (Ar*C*HO, minor), 84.3 (Ar*C*HO, major), 76.9 (*C*, minor), 76.5 (*C*, major), 39.5 (*C*H$_2$Ph, minor), 38.9 (*C*H$_2$Ph, major), 31.9 (=CHCO*C*H$_3$, major), 14.6 (N=C*C*H$_3$, major), 14.2 (N=CC*H*$_3$, minor). IR (UATR) ν_{max} 3034, 2928, 1820 (CO), 1681 (CO), 1608, 1509, 1577, 1496, 1466, 1456, 1432, 1384 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{19}NNaO_4$ [M + Na]$^+$: 384.1206, found 384.1206.

(26) Data of minor product *E*-**3cg** was collected from gram scale synthesis of **3cg**. (*E*)-4-Benzyl-4-(6-fluoro-3-(2-oxopropylidene)-1,3-dihydroisobenzofuran-1-yl)-2-methyloxazol-5(4*H*)-one (*E*-**3cg**) (57 mg, 78:22 dr (mixture of isomer)) as a pale-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.39 (dd, J_{H-H} = 8.9 Hz and J_{H-F} = 5.3 Hz, 1H, Ar−H, major), 7.31−7.14 (m, 6H, Ar−H, major), 7.11 (dd, J = 8.1, 2.1 Hz, 1H, Ar−H, major), 7.00 (dd, J = 8.0, 2.0 Hz, 1H, Ar−H, minor), 6.25 (s, 1H, =C*H*COCH$_3$, minor), 6.15 (s, 1H, =C*H*COCH$_3$, major), 5.70 (s, 1H, ArC*H*O, major), 3.39 (AB q, J = 13.2 Hz, 2H, CH_2Ph, major), 3.34 (AB q, J = 13.2 Hz, 2H, CH_2Ph, minor), 2.30 (s, 3H, =CHCOCH_3, minor), 2.27 (s, 3H, =CHCOCH_3, major), 1.98 (s, 3H, N=CCH_3, major), 1.79 (s, 3H, N=CCH_3, minor). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.6 (COCH$_3$, minor), 196.5 (COCH$_3$, major), 176.4 (COO, minor), 175.8 (COO, major), 167.3 (=CO, major), 164.6 (d, $^1J_{C-F}$ = 253.0 Hz, CF, major), 164.1 (N=CCH$_3$, major), 163.1 (N=CCH$_3$, minor), 144.0 (d, $^3J_{C-F}$ = 9.1 Hz, minor), 143.8 (d, $^3J_{C-F}$ = 9.3 Hz, major), 132.9 (minor), 132.7 (major), 130.7 (d, $^3J_{C-F}$ = 9.5 Hz, major), 130.6 (minor), 130.4 (2C, major), 130.3 (2C, minor), 128.5 (d, $^4J_{C-F}$ = 1.9 Hz, major), 128.4 (2C, major), 128.3 (2C, minor), 127.7 (major), 127.6 (minor), 117.4 (d, $^2J_{C-F}$ = 22.2 Hz, major), 117.2 (d, $^2J_{C-F}$ = 22.2 Hz, minor), 109.1 (d, $^2J_{C-F}$ = 24.8 Hz, major), 108.4 (d, $^2J_{C-F}$ = 24.6 Hz, minor), 101.6 (d, $^6J_{C-F}$ = 2.0 Hz, =*C*HCOCH$_3$, minor), 101.0 (d, $^6J_{C-F}$ = 1.2 Hz, =*C*HCOCH$_3$, major), 84.7 (d, $^4J_{C-F}$ = 3.4 Hz, ArCHO, minor), 83.9 (d, $^4J_{C-F}$ = 2.8 Hz, Ar*C*HO, major), 77.2 (*C*, minor), 76.4 (*C*, major), 39.3 (*C*H$_2$Ph, minor), 39.1 (CH$_2$Ph, major), 31.9 (=CHCO*C*H$_3$, major), 14.7 (N=C*C*H$_3$, major), 14.4 (N=CC*H*$_3$, minor). ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ − 108.21 (minor), − 108.54 (major). IR (UATR) ν_{max} 3034, 2929, 1824 (CO), 1678 (CO), 1615, 1583, 1496, 1478, 1456, 1432, 1385 cm^{-1}. HRMS (ESI) calcd. for $C_{22}H_{18}FNNaO_4$ [M + Na]$^+$: 402.1112, found 402.1116.

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