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Assembly of Four Diverse Heterocyclic Libraries Enabled by Prins Cyclization, Au-Catalyzed Enyne Cycloisomerization, and Automated Amide Synthesis

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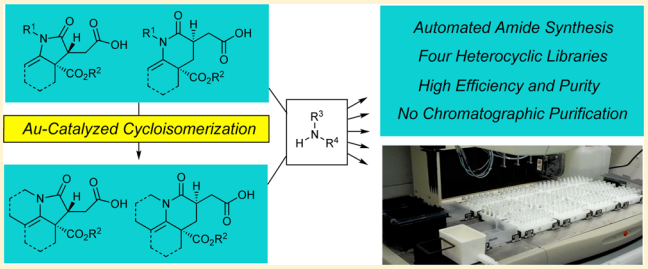
Supporting Information

ABSTRACT: We describe a unified synthetic strategy for efficient assembly of four new heterocyclic libraries. The synthesis began by creating a range of structurally diverse pyrrolidinones or piperidinones. Such compounds were obtained in a simple one-flask operation starting with readily available amines, ketoesters, and unsaturated anhydrides. The use of tetrahydropyran-containing ketoesters, which were rapidly assembled by our Prins cyclization protocol, enabled efficient fusion of pyran and piperidinone cores. A newly developed Au(I)-catalyzed cycloisomerization of alkyne-containing enamides further expanded heterocyclic diversity by providing rapid entry into a wide range of bicyclic and tricyclic dienamides. The final stage of the process entailed diversification of each of the initially produced carboxylic acids using a fully automated platform for amide synthesis, which delivered 1872 compounds in high diastereomeric and chemical purity.



INTRODUCTION

The amide-bond formation plays a central role in organic synthesis, chemical biology, and pharmaceutical research.[1] According to a recent survey, *N*-acylation of amines represents the most frequently employed reaction in drug discovery.[2] Thus, it is not surprising that amide synthesis has been extensively used for assembly of small-molecule libraries designed to deliver pharmacological probes and drugs.[3] While early work in this area has relied almost exclusively on solid-phase synthesis,[4] much of the recent effort has shifted to generating nonpeptide small-molecule libraries in solution.[5] The most attractive feature of solution-based methods is the high efficiency of monitoring and optimizing chemical reactions. Indeed, many innovative strategies have been developed to enable high-throughput organic synthesis in solution, including the use of soluble polymeric supports,[6] phase-separation tags,[7] scavenging agents,[8] or automated preparative LCMS methods.[9] Another attractive purification tactic is a liquid−liquid extraction, which takes advantage of the differences in aqueous solubility of reagents, reactants, and products under either basic or acidic conditions. This method is particularly well suited for amide-bond formation and can completely avoid chromatographic purification, use of scavenging agents or attachment of phase-separation tags. Boger and co-workers were the first to recognize the value of parallel solution-phase amide synthesis followed by a simple liquid−liquid extraction, and employed this strategy for preparation of several amide-containing libraries.[10,11] While small libraries were produced as individual compounds,[10] larger libraries were typically generated as compound mixtures presumably due to the manual nature of the assembly process.[11]

As the amide-bond formation continues to play a dominant role in organic, bioorganic, and medicinal chemistry, the automation of this important process could greatly improve its efficiency, enabling rapid access to large nonpeptide amide-containing libraries of individual, pure compounds. Herein, we report the development of a fully automated, chromatography-free protocol for parallel amide synthesis in solution, which was employed for the preparation of four representative heterocyclic libraries. The first stage of the assembly process entailed the synthesis of a range of structurally diverse pyrrolidinones or piperidinones. Such compounds were obtained in a one-flask operation starting with readily available amines, ketoesters, and unsaturated anhydrides. The use of tetrahydropyran-containing ketoesters, which were rapidly assembled by our Prins cyclization protocol, enabled efficient fusion of pyran and piperidinone cores. To further expand heterocyclic diversity, we developed Au(I)-catalyzed cycloisomerization of alkyne-containing enamides to afford a wide range of bicyclic and tricyclic dienamides. The final stage of the parallel assembly process entailed diversification of the initially produced heterocyclic

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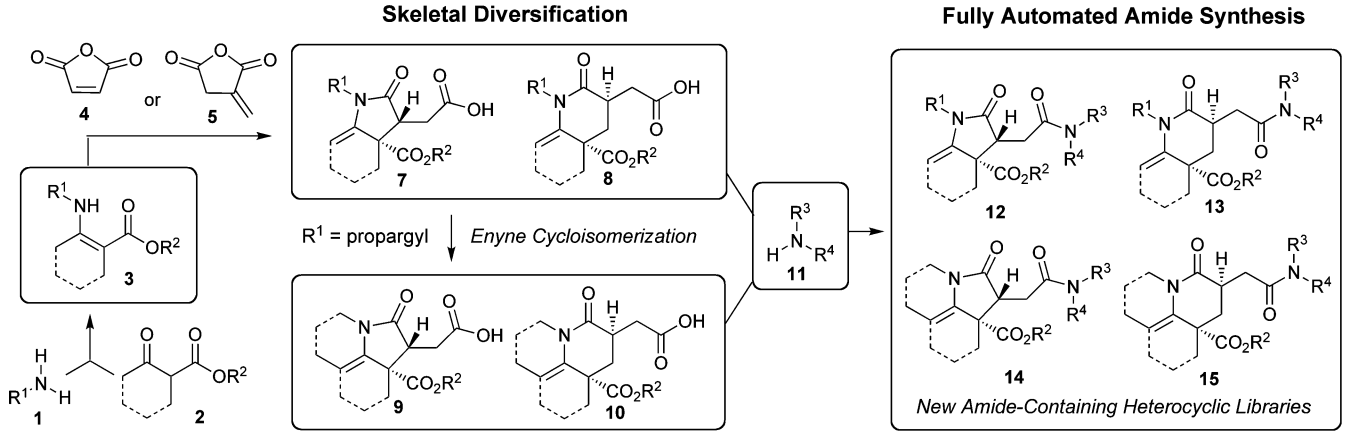

Figure 1. General Synthetic Strategy to Skeletally Diverse Heterocyclic Libraries. The assembly process is divided into two stages. First, a number of skeletally diverse lactams **7**-**10** are produced starting with readily available primary amines **1**, ketoesters **2** and unsaturated anhydrides **4** or **5**. Second, each of the lactams **7**-**10** is coupled to amines **11** in a fully automated fashion to deliver the resulting amide-containing heterocyclic libraries **12**-**15**.

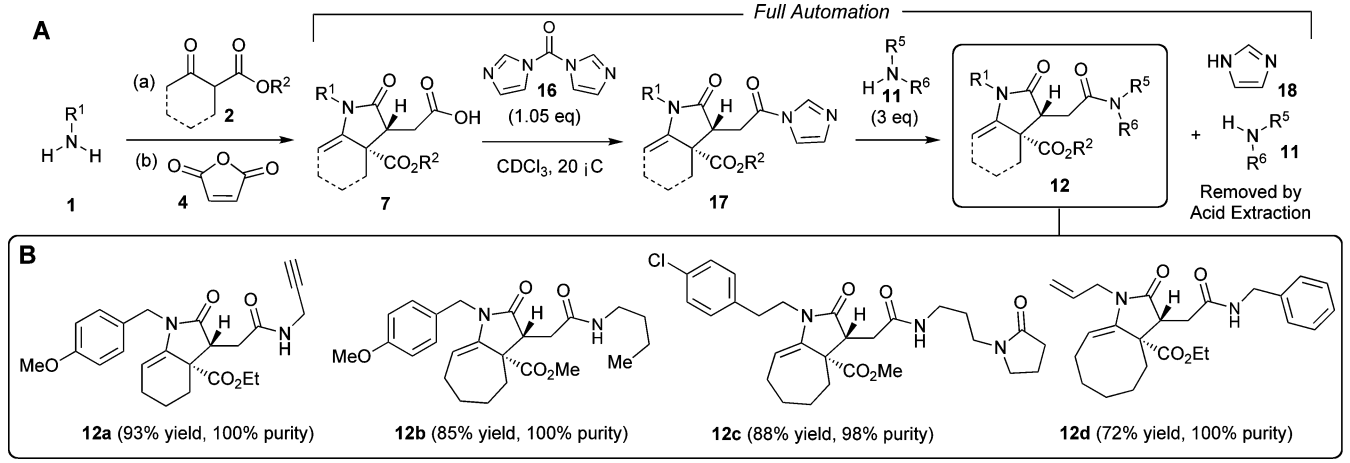

Figure 2. Development of an automation platform for solution-phase amide synthesis and liquid−liquid extraction. (A) Synthetic scheme used for the development of automated amide synthesis and extractive purification. Carboxylic acids **7** were manually prepared from primary amines **1**, ketoesters **2**, and anhydride **4** as previously described.[12] Automated amide synthesis entailed activation of each carboxylic acid **7** with 1,1′-carbonyldiimidazole (CDI, **16**), followed by treatment of the resulting acyl imidazole **17** with 3 equivalents of amines **11** for 48 h at 20 °C and washing the resulting chloroform solution with 1.2 M aqueous solution of HCl. (B) Structures and isolated yields of four representative amides, which were prepared by the above protocol following solvent evaporation. The purity of each compound was established by LCMS analysis and confirmed by ^{1}H NMR spectroscopy.

cores via a solution-phase amide synthesis, which was readily performed by a conventional liquid-handling robot. This automation platform delivered 1872 new heterocyclic compounds, which were obtained with high efficiency and excellent chemical purity without chromatographic purification.

RESULTS AND DISCUSSION

Library Design. Our previous work demonstrated that reactions of vinylogous carbamates with maleic anhydride delivered a library of functionalized pyrrolidinones, which yielded two noncompetitive inhibitors of facilitative glucose transport.[12a,b] While this library was produced using a short and efficient reaction sequence, chromatographic purification of all final compounds was required in order to ensure their high chemical purity prior to the biological evaluation.[12a,b] Building on this precedent, the objectives of our present study were 2-fold. First, we aimed to increase the size and skeletal diversity of newly designed heterocyclic libraries based on five- and six-membered lactams. Second, we set out to develop a fully automated protocol for solution-phase amide synthesis that could be efficiently employed for final-stage diversification of such libraries. Such an automation platform would deliver a large number of individual compounds in high purity without chromatographic purification.

Our general synthetic strategy is depicted in Figure 1. The assembly process begins with a condensation of primary amines **1** and ketoesters **2** to deliver the corresponding vinylogous carbamates **3**. Subsequent reaction of **3** with maleic anhydride **4** would afford pyrrolidinones **7**.[12] A similar transformation employing itaconic anhydride **5** is expected to give ring-expanded piperidinones **8**.[13] Structural diversity can be readily introduced into **7** and **8** by selecting a variety of amines **1** and ketoesters **2**. The use of alkyne-containing primary amines (R^1 = propargyl) could further expand skeletal diversity of lactams **7** and **8** via a transition-metal-catalyzed enyne cycloisomerization[14] to deliver tetrahydro-oxindolizines **9** and hexahydro-oxoquinolizines **10**. The final stage of the synthesis would rely on the development of an automated amide-bond forming protocol that would convert the initial set of core structures **7**−**10** to the final amide-containing libraries **12**−**15**, which would

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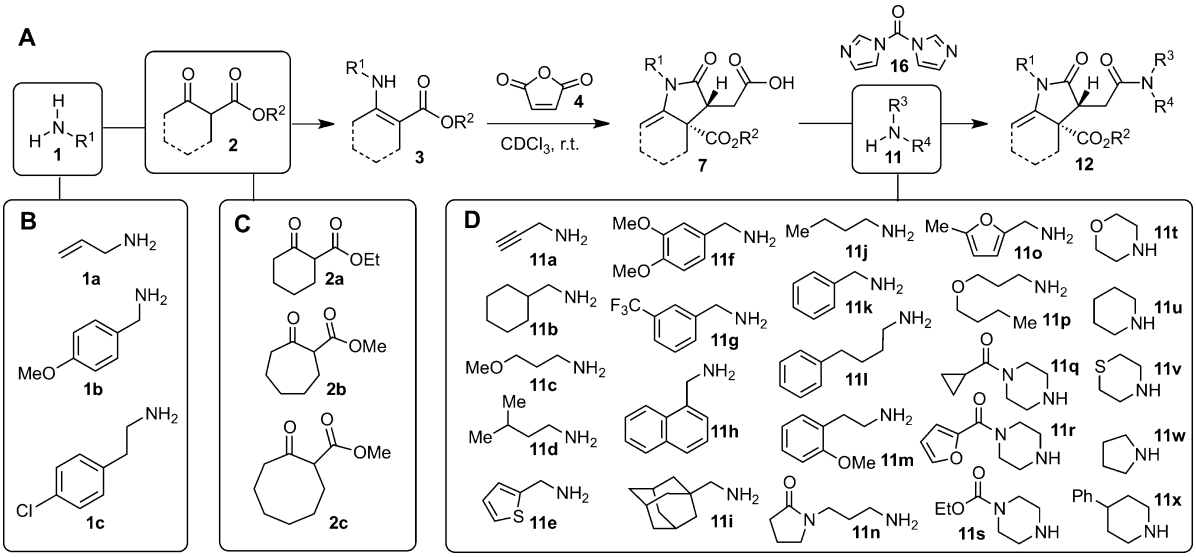

Figure 3. Synthesis of a 216-membered library of bicyclic pyrrolidinones. (A) Two-stage assembly process entailed preparation of nine carboxylic acids **7** starting with 3 amines **1** and 3 ketoesters **2**, followed by automated amide-bond synthesis using a set of 24 amines **11**. (B) Structures of 3 amines **1**. (C) Structures of 3 ketoesters **2**. (D) Structures of 24 amines **11**.

be produced on 10−20 mg scale and subjected to rigorous purity analysis. The use of cheminformatics methods would facilitate selection of the appropriate building blocks at each stage of the diversification process in order to produce all final compounds with favorable physicochemical properties *en route* to subsequent identification of new pharmacological probes.

Automation of the Solution-Phase Amide Synthesis. Our initial objective was to develop a general protocol for efficient, automated amide synthesis in solution that would employ readily available amide-coupling agents followed by a simple liquid−liquid extraction to purify final amide products (Figure 2). Such an automation platform was expected to possess excellent throughput capabilities by avoiding chromatographic purification using scavenging agents or attaching and detaching tags for phase separation. For purification, we intended to employ a single extraction step that would entail partitioning the reaction mixture between an organic phase and an acidic aqueous solution. This procedure would efficiently separate the amide-containing product, which would be collected in the organic phase, from an excess of starting amine, amide-coupling reagent and other coproducts, which would all partition into the acidic aqueous layer. In order to develop and validate this protocol, we prepared several pyrrolidinone-containing carboxylic acids **7** by reaction of amines **1** with ketoesters **2**, followed by cyclization with maleic anhydride **4** (Figure 2A). Evaluation of a number of existing amide-coupling protocols revealed that 1,1′-carbonyldiimidazole (CDI, **16**) served as the best reagent not only to promote efficient *N*-acylation but also to afford highest purity of the resulting amides following a single liquid−liquid extraction step. During the optimization studies, the efficiency of the initial acyl imidazole formation was conveniently monitored by ^{1}H NMR spectroscopy. This transformation proceeded to completion typically within 2−4 h at 20 °C in chloroform using a slight excess of CDI (1.05 equiv). The resulting acyl imidazole **17** was next treated with 3 equiv of either primary or secondary amines **11**. The excess of amine ensured complete conversion of acyl imidazole **17** to the corresponding amide **12**. The final reaction mixture was treated with a 1.2 M solution of hydrochloric acid. The two phases were thoroughly mixed and allowed to separate. Retrieval of the chloroform layer and evaporation produced several representative amide-containing products **12a−d** (Figure 2B) in high efficiency. High chemical purity of each of the products was established independently by LCMS analysis and 500 MHz ^{1}H NMR spectroscopy. We found that amide-bond formation and liquid−liquid extraction could be readily performed using a typical robotic liquid handler, followed by parallel evaporation. The use of this protocol can yield 1−100 mg of individual final products depending on the amount of carboxylic acid used for the amide-coupling step.

Synthesis of a Pyrrolidinone Library. Having developed an automated amide-coupling protocol, we next examined its first application to a larger set of pyrrolidinone-containing compounds. Our goal was to prepare a 216-membered library **12** on 20 mg scale starting from 3 primary amines **1**, 3 ketoesters **2**, and 24 amines **11** (Figure 3). We wanted to ensure that all reactions would produce final products **12** in high chemical purity without chromatographic purification of any of the final compounds. Selection of each of the building blocks shown in Figure 3B−D was guided by Accelrys Pipeline Pilot, which enabled virtual enumeration of the target library and estimation of various molecular properties *in silico*. Specifically, during the design process, we applied appropriate filters in order to select building blocks that would produce the target library **12** with molecular weight below 600 and calculated logarithmic value of *n*-octanol/water partition coefficient (cLogP) within a range of 1−5.[15] The distribution of both parameters for this library is shown in the Supporting Information (Figure S1).[16]

The synthesis began with condensations of three primary amines **1** (Figure 3B) with three ketoesters **2** (Figure 3C), followed by reactions of the resulting vinylogous carbamates **3** with maleic anhydride **4** to afford nine pyrrolidinone-containing carboxylic acids **7**. Each of the acids **7** was obtained as a single diastereomer approximately on a 500 mg scale in a single-flask operation starting with the corresponding amines **1** and ketoesters **2**. In order to ensure their high chemical purity, all pyrrolidinone-containing carboxylic acids **7** were purified by conventional chromatography. The second stage of the

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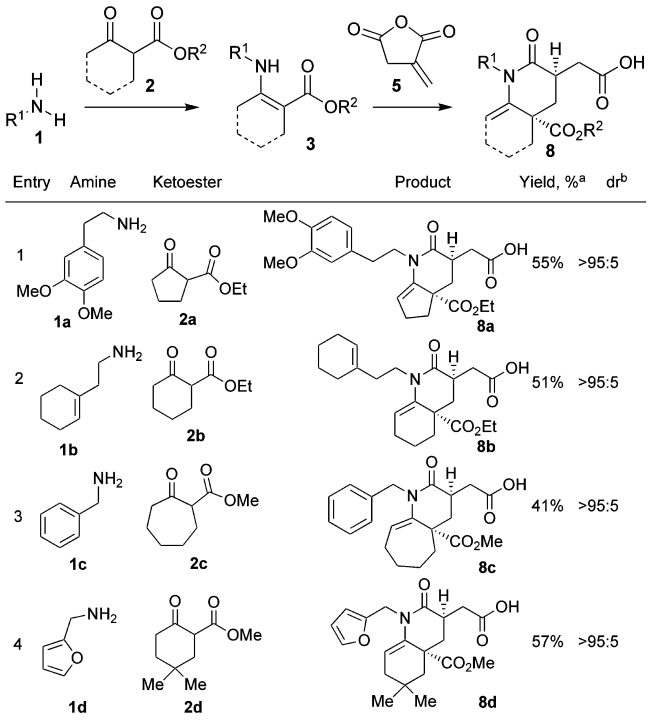
assembly process entailed a fully automated synthesis of the target library **12** using a set of 24 amines **11** (Figure 3D). To this end, each acid **7** was first treated with a slight excess of CDI (**16**) in chloroform at room temperature and divided into 24 equal batches. Upon completion of the acyl imidazole formation, each batch was treated for 48 h with a solution of amine **11** in chloroform at the same temperature, followed by addition of a 1.2 M aqueous solution of HCl. The organic and aqueous layers were thoroughly mixed and allowed to separate. The amides **12** were obtained by removal of the chloroform layer and parallel solvent evaporation. We determined the yields of all final compounds by automated weighing, which established that 216 *N*-acylations proceeded with high efficiency with an average isolated yield of 87.2 ± 7.2%. The high purity of each library member was established using LCMS.[16] In addition, we acquired 500 MHz ^{1}H NMR spectra of 18 randomly selected amides, which independently confirmed their high diastereomeric and chemical purities.[16]

Synthesis of a Piperidinone Library. The reactions of vinylogous carbamates with maleic anhydride provided efficient and fully diastereoselective entry into the 2-pyrrolidinone core **7** (Figure 3) via a tandem reaction sequence including conjugate addition and anhydride opening. We next examined the construction of ring-expanded 2-piperidinones **8** (Table 1)

Table 1. Synthesis of Bicyclic 2-Piperidinones



[a]Yields refer to those of isolated compounds following chromatographic purification. [b]Diastereomeric ratios (dr) were determined by ^{1}H NMR analysis of unpurified reaction mixtures.

via the corresponding reaction of vinylogous carbamates **3** with itaconic anhydride **5**. A representative reaction of amine **1a** with ketoester **2a** cleanly afforded enamine **3**, which was subsequently treated with anhydride **5** to give piperidinone **8a** with high efficiency and diastereoselectivity (Table 1, entry 1). The structure of **8a** was determined by X-ray crystallography.[16] Investigation of the scope of this transformation revealed that both six- and seven-membered ketoesters **2b** and **2c** efficiently afforded the corresponding pyrrolidinones **8b** and **8c** (Table 1, entries 2 and 3). The use of furan-containing primary amine **1d** was also tolerated (Table 1, entry 4). High diastereoselectivity was observed in all cases. Interestingly, the opposite stereochemical outcome was observed during the formation of six-membered lactams **8** compared to the corresponding cyclizations leading to five-membered 2-pyrrolidiones **7**.

The high level of diastereoselectivity of both reactions can be rationalized by examining conjugate addition and anhydride-opening steps (Figure 4). The two initial transition states **A** and **E** have one common feature: they both entail the approach of unsaturated anhydride, which facilitates subsequent lactam formation by placing the imine moiety in close spatial proximity to the carbonyl group of the anhydride for its subsequent opening. In the case of maleic anhydride, this process predicts the formation of intermediates **B** and **C** and explains the observed stereochemistry of the product **7**. For itaconic anhydride, similar logic predicts the intermediacy of anhydride **F** and *N*-acyliminium ion **G** *en route* to the observed six-membered lactam **8**.

Because a number of 2-piperidinones **8** were prepared with good efficiency and high diastereoselectivity (Table 1), we next employed this process for generating a 768-membered library **13** starting with 8 primary amines **1**, 4 ketoesters **2**, and 24 amines **11** (Figure 5). Analysis of the enumerated library *in silico* identified structures of 8 commercially available amines **1** (Figure 5B), 4 ketoesters **2** (Figure 5C), and the same set of 24 amines **11** (Figure 5D), which would deliver this chemical library with favorable molecular weight and a narrow cLogP distribution (Figure S2 in the Supporting Information). The synthesis began with parallel reactions of 8 amines **1** with each of the four ketoesters **2**. The resulting vinylogous carbamates **3** were not isolated but directly reacted with itaconic anhydride **5** to give 32 piperidinone-containing carboxylic acids **8**. Following this one-flask protocol, each of the acids **8** was obtained approximately on a 500 mg scale as a single diastereomer with good efficiency following conventional chromatographic purification in order to ensure their high purity. The final stage entailed CDI-promoted coupling of each of the 32 carboxylic acids **8** with 24 amines **11**. This operation was fully automated and conducted under the same conditions used for generating library of 2-pyrrolidinones **12**. This process delivered 768 amides **13**, which were prepared on a 15−20 mg scale. Parallel LCMS analysis of all library members established their high chemical purity, which was independently confirmed by obtaining 500 MHz ^{1}H NMR spectra of 64 randomly selected compounds.[16]

Synthesis of a Library of Fused Dihydropyrans and Piperidinones. Assembly of pyrrolidinones **12** and 2-piperidinones **13** thus far relied on the use of readily available carbocyclic ketoesters **2**, which limited the extent of their skeletal diversification. We next examined the ability of tetrahydropyran-containing ketoesters to participate in such lactam-forming reactions. This process would enable fusion of oxygen- and nitrogen-containing heterocyclic platforms, expanding both the skeletal and heteroatom diversity of the resulting libraries while maintaining their favorable physicochemical properties. Our previously developed Prins cyclization of *β*-hydroxy dioxinones enabled efficient assembly of a range of highly functionalized tetrahydropyranones.[17] Validated through several applications in the synthesis of complex polyketide natural products,[18] this method could afford a

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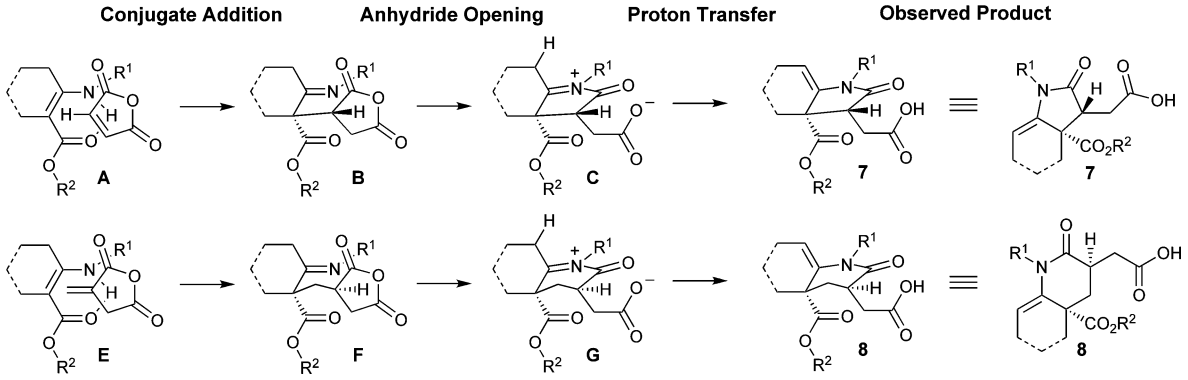

Figure 4. Proposed explanation of the diastereoselective formation of 2-pyrrolidinones **7** and 2-piperidinones **8**. In both cases, the tandem reaction sequence entails a conjugate addition of the enamine to unsaturated anhydride followed by a ring-opening and a proton transfer. Initial approach of each anhydride facilitates subsequent lactam formation by placing the reactive imine and carbonyl moieties in close spatial proximity, as shown in intermediates **B** and **F**.

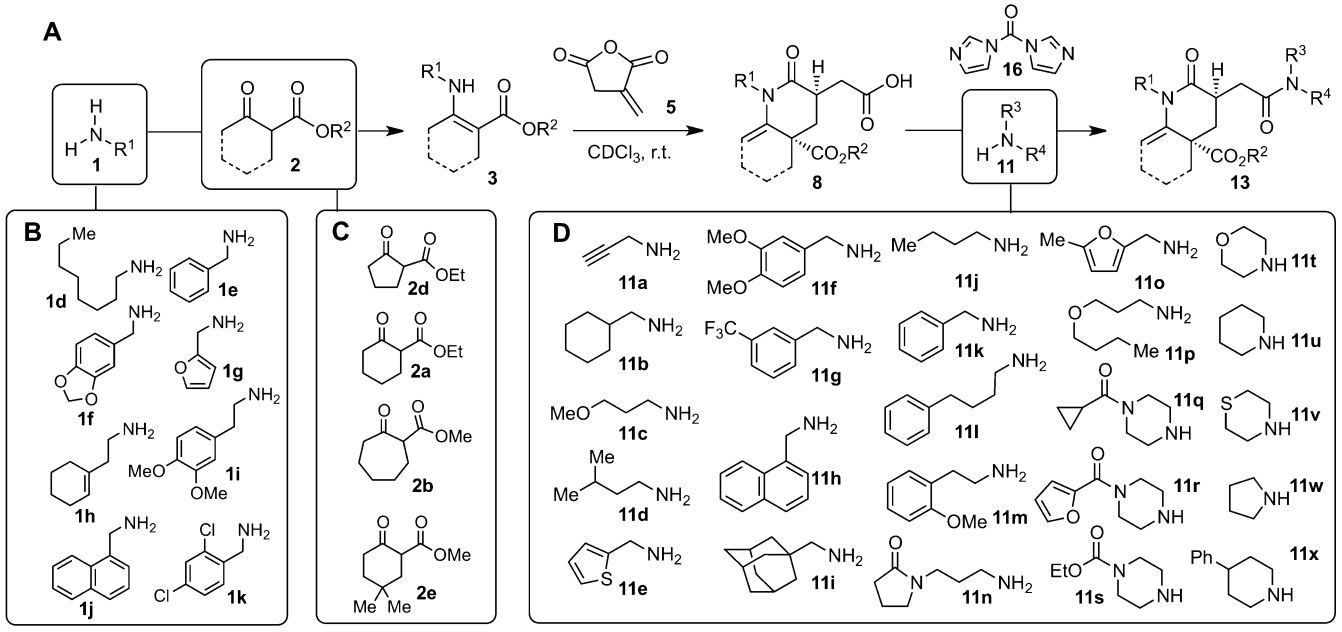

Figure 5. Synthesis of a 768-membered library of bicyclic piperidinones. (A) Two-stage assembly process entailed preparation of 32 carboxylic acids **8** starting with 8 amines **1** and 4 ketoesters **2**, followed by automated amide-bond synthesis using a set of 24 amines **11**. (B) Structures of 8 amines **1**. (C) Structures of 4 ketoesters **2**. (D) Structures of 24 amines **11**.

variety of 3-carbomethoxy-4-tetrahydropyranones **24** diversified at both the C(2) and the C(6) positions (Table 2).

The synthesis began with the Mukaiyama aldol reaction of silyl dienol ether **19** with aldehyde **20** to give *β*-hydroxy dioxinones **21**. The next step entailed the Lewis acid promoted Prins cyclization of dioxinones **21** with aldehydes **22**, which proceeded efficiently in all cases. Finally, treatment of dihydropyrans **23** with methanol at 150 °C afforded four requisite 3-carbomethoxy-4-tetrahydropyranones **24** with high diastereoselectivity. Erosion of diastereoselectivity in the final product was observed only in one case at the final methanolysis stage (Table 2, entry 3). However, the major diastereomer **24c** was readily obtained in good overall yield and high diastereomeric purity by chromatographic purification.

We next examined reactions of vinylogous carbamates **25** derived from tetrahydopyran-containing ketoesters **24** with unsaturated anhydrides **4** and **5**. While the reaction of maleic anhydride **4** with **25** proved low yielding, the corresponding condensation with itaconic anhydride successfully delivered the expected piperidinone-containing products **26**. The results of the initial scope study of this transformation are summarized in Table 3. The four ketoesters **24a–d** afforded the corresponding oxabicyclic piperidinones **26a–d** with high efficiency as single observed diastereomers. Excellent diastereoselectivity of this transformation, which affords products containing four stereogenic centers, is particularly noteworthy. Stereochemistry of the final products was determined by extensive NMR analysis and can be explained by considering a transition state model **E** (Figure 4) with the approach of itaconic anhydride **5** expected to occur opposite to the R^2 substituent, corresponding to a sterically more accessible face of the pyran moiety.

Having established efficient and fully diastereoselective access to dihydropyrans fused with piperidinones, we next examined the possibility of generating a large library of such heterocyclic compounds from four tetrahydropyran-containing ketoesters **24a–d** and the same two sets of amines **1** and **11**, which were used to prepare library **13**. This process would produce 768 compounds starting with 4 ketoesters **24**, 8 primary amines **1**,

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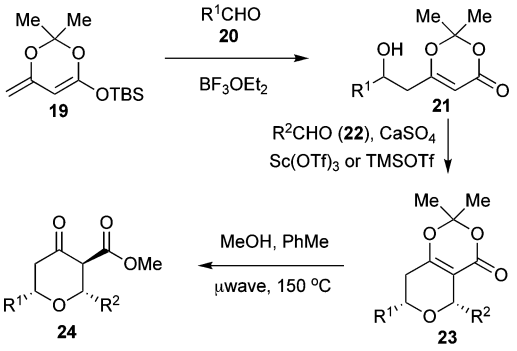
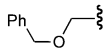
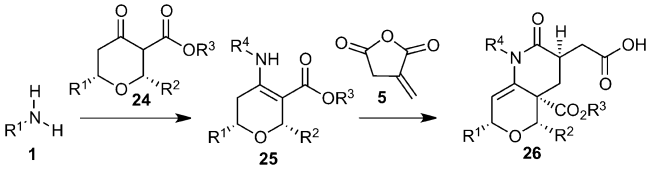
Table 2. Synthesis of Carbomethoxytetrahydropyranones

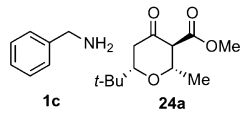
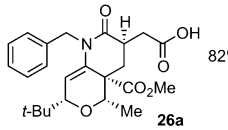
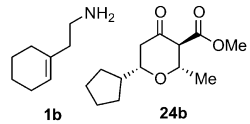
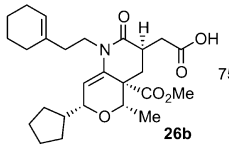
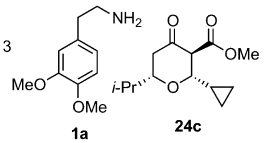
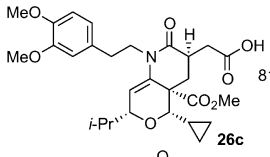
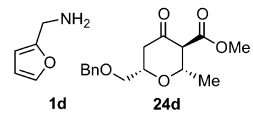
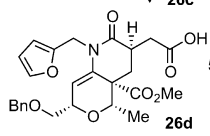


Entry	R^1	R^2	Ketoester	Yield,% (3 steps)[a]	dr[b]
1	*t*-Bu	Me	**24a**	60	>95:5
2		Me	**24b**	57	>95:5
3	*i*-Pr		**24c**	60	85:15[c]
4		Me	**24d**	53	>95:5

[a]Yields refer to those of isolated compounds following chromatographic purification. [b]Diastereomeric ratios (dr) were determined by ^{1}H NMR analysis of unpurified reaction mixtures. [c]Major diastereomer was obtained in diastereomerically pure form after chromatographic purification.

Table 3. Synthesis of Pyrrolidinones Fused to Dihydropyrans



Entry	Amine	Ketoester	Product	Yield, %[a]	dr[b]
1	 **1c**	**24a**	 **26a**	82%	>95:5
2	 **1b**	**24b**	 **26b**	75%	>95:5
3	 **1a**	**24c**	 **26c**	81%	>95:5
4	 **1d**	**24d**	 **26d**	54%	>95:5

[a]Yields refer to those of isolated compounds following chromatographic purification. [b]Diastereomeric ratios (dr) were determined by ^{1}H NMR analysis of unpurified reaction mixtures.

and 24 primary and secondary amines **11** (Figure 6). Analysis of the enumerated library *in silico* revealed that such compounds would display favorable molecular properties, including molecular weight and cLogP (Figure S3 in the Supporting Information).

The synthesis began with reactions of 8 amines **1** with each of the 4 ketoesters **24**, followed by treatment of the resulting vinylogous carbamates with itaconic anhydride **5**. This one-flask operation successfully delivered 32 expected carboxylic acids **26**, which were obtained with good efficiency and high purity following a single parallel chromatographic purification. Using the same automated liquid-handling platform employed for syntheses of libraries **12** and **13**, each of the acids **26** was activated using CDI (**16**) and coupled to 24 amines **11**, followed by liquid–liquid extraction and solvent evaporation. This process successfully delivered the target 768-membered library **27** on 15–20 mg scale in high efficiency and excellent purity, which was determined by LCMS.[16] The NMR analysis of 64 randomly selected compounds once again confirmed their high chemical and diastereomeric purity.[16]

Development of Au-Catalyzed Enynamide Cycloisomerization. The efficient access to a series of structurally diverse bicyclic lactams prompted us to further expand their skeletal diversity by examining the ability of such compounds to participate in enyne cycloisomerizations in the presence of an appropriate metal catalyst. Among transition metals that catalyze enyne cycloisomerizations, Au- and Pt-based complexes are particularly noteworthy for their ability to chemoselectively activate the alkyne moiety and provide access to various reaction topologies depending on the structure of the starting enyne.[14] Such reactions typically proceed under mild conditions, tolerate a wide variety of commonly used functional groups, and provide powerful methods for structural diversification in organic synthesis. Despite significant advances in Au- and Pt-catalyzed cycloisomerizations of 1,5-enynes, the vast majority of such reactions typically afford carbocyclic products.[14b] Only a few examples of Au-catalyzed syntheses of nitrogen heterocycles are known. Indeed, we reported a series of Au(I)-catalyzed double cyclizations that produced a number of oxygen and nitrogen heterocycles.[19] While such reactions efficiently proceeded under mild conditions, they were limited to the synthesis of several unique heterobicyclic products.[19] Recently, Schaus and co-workers described Au(III)-catalyzed cycloisomerizations of alkyne-tethered dihydropyrimidones.[20] While this new catalytic process yielded a number of pyridopyrimidones, such reactions were conducted at high temperatures presumably due to the requirement for the initial isomerization of a vinylogous imide. Furthermore, only internal alkynes participated in such cycloisomerizations.[20]

Prompted by the lack of general studies of transition-metal-catalyzed cycloisomerizations of enynes containing stable enamide fragments, we prepared several potential cyclization substrates **28a–c** by reactions of the corresponding primary propargyl amines **27a–c** with ketoester **2a**, followed by treatment of the resulting vinylogous carbamates with itaconic anhydride **5** (Table 4). Having examined several commonly employed transition metal complexes, we found that treatment of phenyl-substituted enyne **28a** with 5 mol % of PPh_3AuCl in the presence of a number of Ag-based additives produced cycloisomerization product **29a** (Table 1, entries 1–3). The reaction efficiency considerably decreased in the absence of PPh_3AuCl (Table 4, entry 4). Initially, the best results were obtained by combining PPh_3AuCl with $AgSbF_5$ in either dichloromethane or chloroform (Table 4, entries 1 and 5). The use of acetonitrile as a reaction solvent resulted in a further increase in efficiency and enabled nearly quantitative

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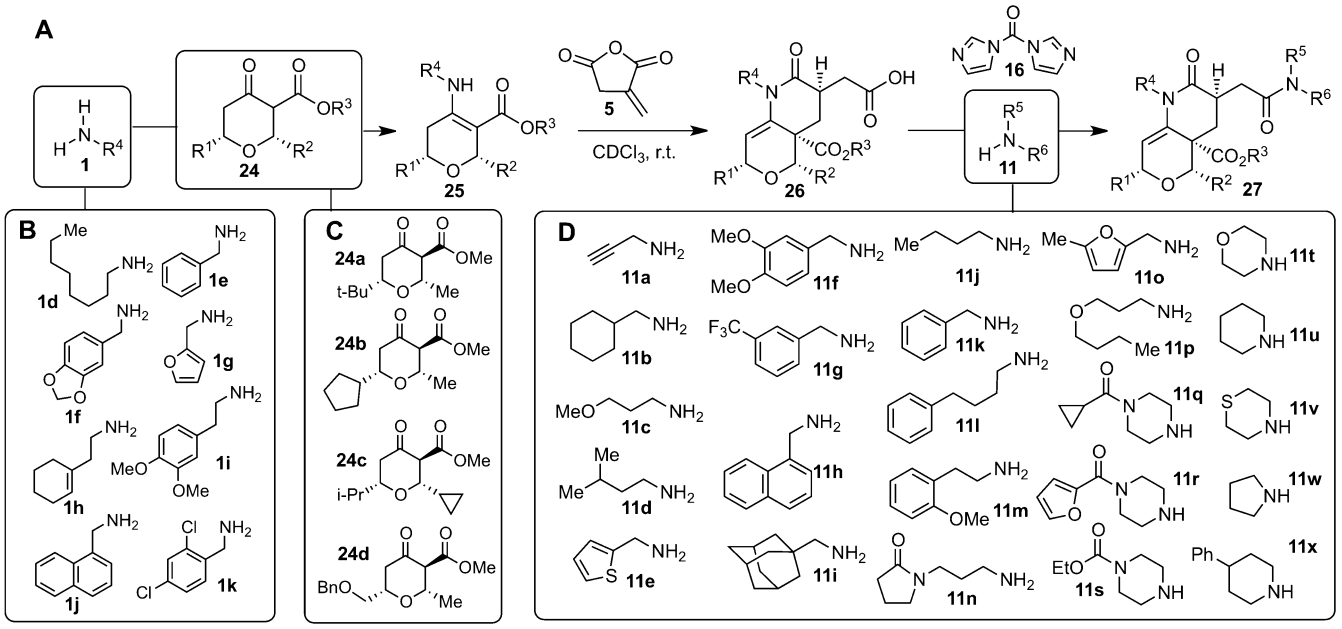
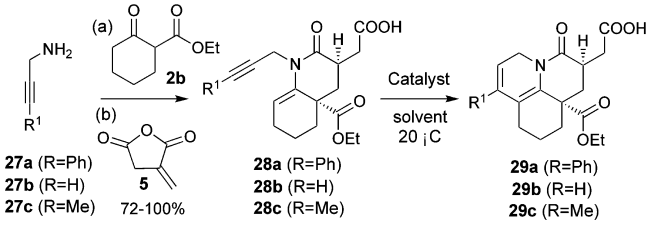
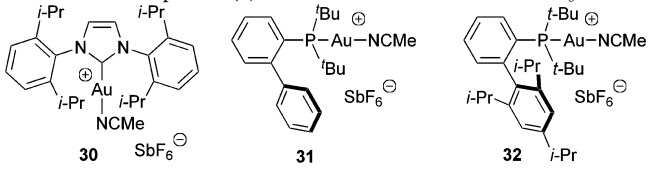


Figure 6. Synthesis of a 768-membered library of 2-piperidinones fused to dihydropyrans. (A) Assembly process entailed preparation of 32 carboxylic acids **26** starting with 8 amines **1** and 4 ketoesters **2**, followed by automated amide-bond synthesis using a set of 24 amines **11**. (B) Structures of 8 amines **1**. (C) Structures of 4 ketoesters **2**. (D) Structures of 24 amines **11**.

Table 4. Discovery and Optimization of Enyne Cycloisomerization



entry	R^1	enyne	catalyst(s), (mol %)	solvent	product	yield[a] (%)
1	Ph	**28a**	Ph_3PAuCl (5), $AgSbF_6$ (10)	CH_2Cl_2	**29a**	85
2	Ph	**28a**	Ph_3PAuCl(5),$AgBF_4$(10)	CH_2Cl_2	**29a**	75
3	Ph	**28a**	Ph_3PAuCl(5),AgOTf(10)	CH_2Cl_2	**29a**	60
4	Ph	**28a**	$AuSbF_6$ (10)	CH_2CL_2	**29a**	45
5	Ph	**28a**	Ph_3PAuCL(5),$AgSbF_6$(10)	$CHCl_3$	**29a**	85
6	Ph	**28a**	Ph_3PAuCl (5), $AgSbF_6$ (10)	CH_3CN	**29a**	95
7	H	**28b**	Ph_3PAuCl(5),$AgSbF_6$(10)	CH_3CN	**29b**	20
8	H	**28b**	$(p\text{-}CF_3Ph)_3PAuCl$ (5), $AgSbF_6$ (10)	CH_3CN	**29b**	30
9	H	**28b**	Cy_3PAuCl (5), $AgSbF_6$ (10)	CH_3CN	**29b**	95
10	H	**28b**	$t\text{-}Bu_3PAuCl$ (5), $AgSbF_6$ (10)	CH_3CN	**29b**	95
11	H	**28b**	$Ph(Me)_2PAuCl$ (5), $AgSbF_6$ (10)	CH_3CN	**29b**	87
12	H	**28b**	Et_3PAuCl (5), $AgSbF_6$ (10)	CH_3CN	**29b**	98
13	H	**28b**	complex **30** (3)	CH_3CN	**29b**	95
14	H	**28b**	complex **31** (3)	CH_3CN	**29b**	100
15	H	**28b**	complex **32** (3)	CH_3CN	**29b**	100
16	Ph	**28a**	complex **31** (3)	CH_3CN	**29a**	100
17	Me	**28c**	complex **31** (3)	CH_3CN	**29c**	100



[a]Yields were determined by 500 MHz ^{1}H NMR analysis of unpurified reaction mixtures using an internal standard. Each of the products **29** was subsequently isolated and fully characterized.

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conversion of **28a** to **29a** (Table 4, entry 6). However, this set of conditions did not give successful results when applied to enamide **28b** containing a terminal alkyne. Indeed, the conversion level dropped to 20% (Table 4, entry 7). We next examined the effect of the various phosphine ligands on the reaction outcome. While electron deficient phosphines did not provide much improvement (Table 4, entry 8), the use of sterically hindered or electron-rich phosphines substantially improved the efficiency of cycloisomerization of **28b** to **29b** (Table 4, entries 9−12). Interestingly, a similar trend was recently attributed to a more efficient protodemetalation step in the presence of bulky or electron rich phosphines when this step became turnover limiting.[21] Continuing to explore this trend, we evaluated a number of cationic gold complexes **30**, **31** and **32** containing bulky carbene or phosphine ligands (Table 4, entries 13−15). The best results were obtained using either **31** or **32**. In both cases, cycloisomerization of **28b** proceeded with quantitative efficiency. In addition, complex **31** proved superb at promoting cyclizations of **28a** and **28c** (Table 4, entries 16 and 17).

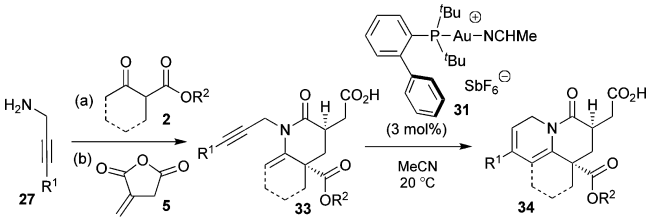
The high efficiency of this catalytic system, which operates at low catalyst loadings at room temperature to promote cyclizations of enamides containing both terminal and internal alkynes is highly noteworthy. Furthermore, this reaction tolerates a number of functional groups present in cycloisomerization substrates **28**, including unprotected carboxylic acids. The latter feature of the reaction is particularly important in maximizing synthetic efficiency of subsequent elaboration of of cycloisomerization products (vide infra) despite the known reactivity of carboxylic acids in a number of other Au-catalyzed reactions.[22]

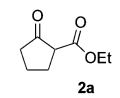
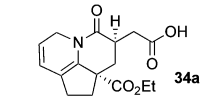
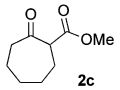
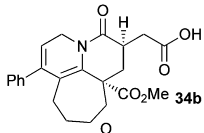
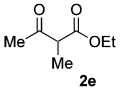
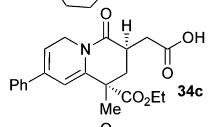
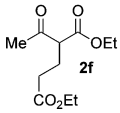
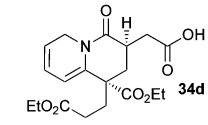
We next examined the utility of cationic gold-phosphine complex **31** in promoting cycloisomerizations of other structurally diverse alkyne-containing enamides **33**, which originated from propargyl amines **27**, ketoesters **2**, and itaconic anhydride **5** (Table 5). We found that enynes **33a** and **33b** successfully underwent cycloisomerizations to deliver the corresponding dienamides **34a** and **34b** in high yields (Table 5, entries 1 and 2). Such transformations further expanded the skeletal diversity of the tricyclic products that can be efficiently prepared by this approach. Furthermore, acyclic ketoesters **2e** or **2f** could be efficiently converted to the corresponding enynes **33c** and **33d**, which upon treatment with Au complex **31** afforded bicylic dienamides **34c** and **34d** (Table 5, entries 3 and 4).

While all enyne cycloisomerization products obtained thus far contained six-membered 2-piperidinones, we next examined the ability of this reaction to produce 1,3-dienamides incorporating five-membered lactams **36** (Table 6). The requisite alkyne-containing enamides **35** were prepared by the same one-pot procedure starting with propargyl amines **27**, ketoesters **2**, and maleic anhydride **4**. Subjections of enynes **35a** and **35b** to the general cycloisomerization protocol cleanly afforded the expected products **36a** and **36b** with quantitative efficiency (Table 6, entries 1 and 2). Similarly, cycloisomerizations of enynes **35c** and **35d**, which were derived from a seven-membered ketoester **2c**, successfully afforded dienamides **36c** and **36d** (Table 6, entries 3 and 4). The structure of tricylic lactam **36d** was confirmed by X-ray crystallography.[16]

Having established synthetic access to a variety of five- and six-membered lactams **34** and **36**, we next examined the preparation of a skeletally diverse chemical library using this

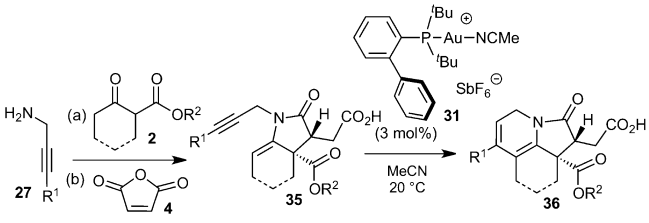
Table 5. Au-Catalyzed Cycloisomerizations of Enyne-Containing 2-Piperidinones

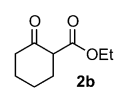
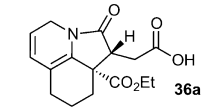
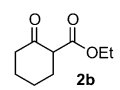
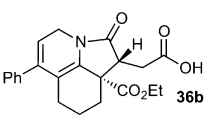
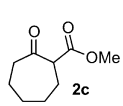
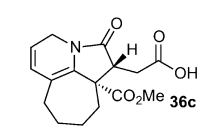
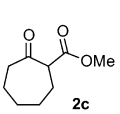
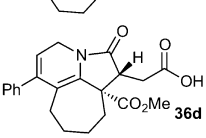


Entry	Ketoester	R^1	Enyne	Yield, %	Product	Yield, %[a]	dr[b]
1	 **2a**	H	**33a**	98	 **34a**	98	>95:5
2	 **2c**	Ph	**33b**	75	 **34b**	75	>95:5
3	 **2e**	Ph	**33c**	90	 **34c**	90	>95:5
4	 **2f**	H	**33d**	100	 **34d**	100	>95:5

[a]Yields were determined by 500 MHz ^{1}H NMR analysis of unpurified reaction mixtures using an internal standard. Each of the products **34** was subsequently isolated and fully characterized.

Table 6. Au-Catalyzed Cycloisomerizations of Enyne-Containing 2-Pyrrolidinones



Entry	Ketoester	R^1	Enyne	Yield, %	Product	Yield, %[a]	dr[b]
1	 **2b**	H	**35a**	100	 **36a**	100	>95:5
2	 **2b**	Ph	**35b**	100	 **36b**	100	>95:5
3	 **2c**	H	**35c**	72	 **36c**	72	>95:5
4	 **2c**	Ph	**35d**	77	 **36d**	77	>95:5

[a]Yields were determined by 500 MHz ^{1}H NMR analysis of unpurified reaction mixtures using an internal standard. Each of the products **36** was subsequently isolated and fully characterized.

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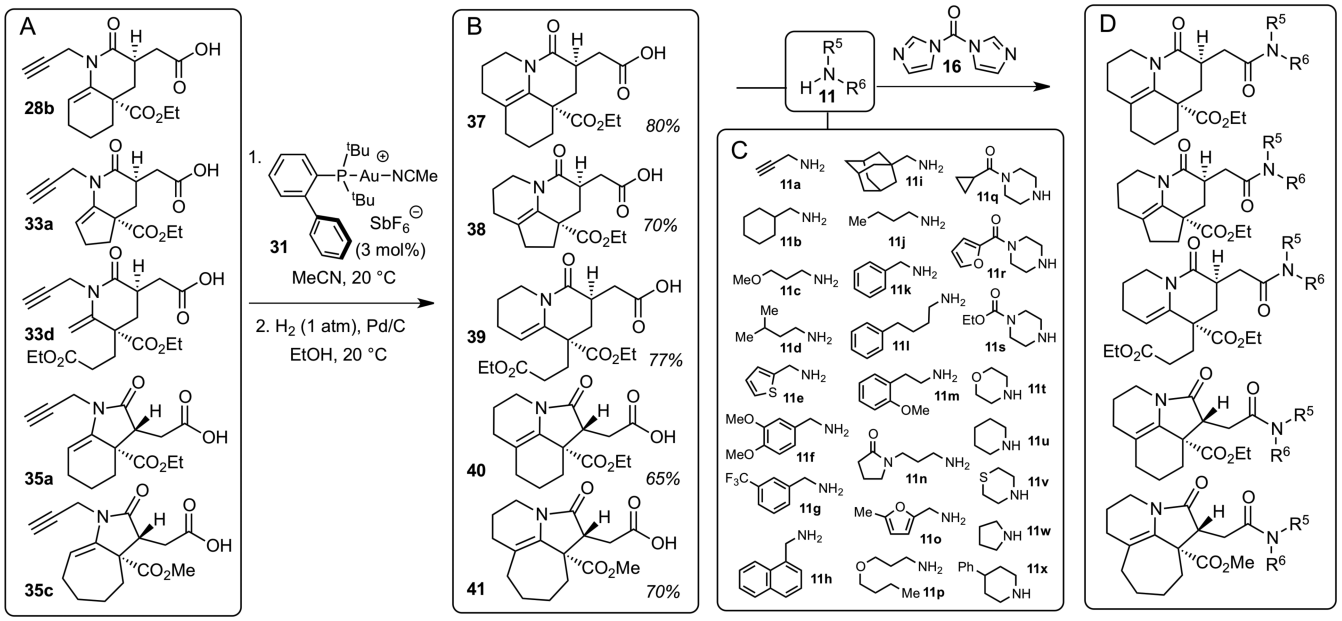

Figure 7. Synthesis of a 120-Membered Library of Tetrahydro-oxo-indolizines and Hexahydro-oxo-quinolizines. (A) Structures of five enamides employed for the Au-catalyzed cycloisomerization, followed by alkene hydrogenation. (B) Structures of tetrahydro-oxo-indolizines **37**, **38** and **39** and hexahydro-oxo-quinolizines **40** and **41**. (C) Structures of 24 amines **11** used for automated amide syntheis. (D) Final amide-containing library incorporating five skeletally diverse lactams.

newly uncovered enyne cycloisomerization and our previously developed automated amide synthesis protocol. Our initial studies established that chemical stability of the dienamide moiety found in **34** and **36** proved to be inadequate. Slow degradation of such compounds was observed upon their dissolution in either DMSO or MeOH. We found that this problem can be solved by partial hydrogenatation of the dienamide fragment. We next subjected five enynes shown in Figure 7A to Au-catalyzed cycloisomerization, followed by immediate heterogeneous hydrogenation (H_2, Pd/C, EtOH). This one-pot operation efficiently delivered the corresponding tricyclic lactams **37**–**41** (Figure 7B) as a result of chemoselective hydrogenation of disubstituted alkenes. The structure of **38** was established by X-ray crystallography.[16] Such partially hydrogenated lactams proved to be stable and were next diversified by coupling each of them with the same set of 24 amines **11** (Figure 7C), which were employed for synthesis of other libraries discussed above. This fully automated process delivered a 120-membered amide-containing library containing five heterotryclic cores (Figure 7D) with favorable distributions of molecular weight and cLogP (Figure S4 in the Supporting Information). The library was produced on a 15–20 mg scale with good efficiency and excellent chemical purity, which was established by LCMS analysis.[16] Diastereomeric purity of 10 randomly selected compounds was further confirmed by ^{1}H NMR.[16]

■ CONCLUSIONS

We have described a unified strategy for efficient synthesis of four new heterocyclic libraries. The first stage of the process entailed creation of a range of skeletally diverse pyrrolidinones or piperidinones in a single-flask operation starting with readily available amines, ketoesters and unsaturated anhydrides. In the course of this investigation, we employed our Lewis acid-promoted Prins cyclization protocol for efficient fusion of pyran and piperidinone cores and developed Au(I)-catalyzed cycloisomerization of alkyne-containing enamides to provide access into a wide range of bicyclic and tricyclic dienamides. Such catalytic processes substantially expanded heterocyclic diversity of the resulting libraries. For final diversification of each library, we developed a fully automated, chromatography-free protocol for parallel amide synthesis, which was applied to prepare 1870 heterocyclic products with favorable physicochemical properties. Because of the prominent role played by the amide-bond formation in high-throughput synthesis, chemical biology, and medicinal chemistry, the development of this automation platform represents an important and enabling synthetic advance that will facilitate access to a variety of new amide-containing libraries for subsequent biomedical applications. Results of the expansion of this automation platform to other commonly employed reactions, as well as the broad biological evaluation of the four new heterocyclic libraries will be reported in due course.[23]

■ EXPERIMENTAL PROCEDURES

General Procedure A: Synthesis of Pyrrolidinones and Piperidinones. A solution of ketoester (**2** or **24**, 5.0 mmol) in $CHCl_3$ (8.0 mL) was treated with primary amine (**1** or **27**, 5.0 mmol) and 4 Å molecular sieves. The reaction mixture was stirred at 70 °C. The completion of the reaction monitored by ^{1}H NMR spectroscopy, which typically required 12–18 h. The resulting mixture was treated with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to a 20 mL volume. The resulting solution was then treated with either maleic anhydride (**4**, 1.1 equiv) or itaconic anhydride (**5**, 1.1 equiv) and stirred overnight at room temperature. The removal of the solvent under reduced pressure followed by silica gel chromatographic purification afforded pyrrolidinones (**7** or **35**) or piperidinones (**8**, **26**, **28**, or **34**).

Pyrrolidinone-Containing Carboxylic Acid 7a (2-((3*SR*,3a*RS*)-1-Allyl-3a-(ethoxycarbonyl)-2-oxo-2,3,3a,4,5,6-hexahydro-1*H*-indol-3-yl)acetic Acid). Compound **7a** was prepared according to general procedure A from primary amine **1a**, ketoester **2a**, and maleic anhydride **4**: yield 661 mg, 43%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.18 (s, 1H), 4.94 (dddd, J = 17.5, 10.3, 6.1, 5.1 Hz, 1H), 4.46 (d, J = 17.2 Hz, 1H), 4.37 (d, J = 10.4 Hz, 1H), 4.26 (t, J = 3.8 Hz, 1H), 3.53–3.45

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(m, 1H), 3.40−3.28 (m, 2H), 3.15 (dd, J = 16.1, 6.1 Hz, 1H), 2.28 (dd, J = 8.5, 5.7 Hz, 1H), 2.10 (ddd, J = 17.5, 5.7, 1.0 Hz, 1H), 1.79 (dd, J = 9.5, 3.6 Hz, 1H), 1.53 (ddd, J = 17.5, 8.5, 1.0 Hz, 1H), 1.45−1.36 (m, 1H), 1.36−1.27 (m, 1H), 1.08−0.98 (m, 1H), 0.76−0.63 (m, 2H), 0.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 173.5, 171.4, 138.2, 131.4, 117.9, 102.2, 61.7, 52.2, 47.5, 43.1, 31.7, 30.6, 22.9, 19.7, 14.2; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{16}H_{22}NO_5$ 308.1498, found 308.1498.

Pyrrolidinone-Containing Carboxylic Acid 7b. Compound **7b** was prepared according to general procedure A from primary amine **1b**, ketoester **2a**, and maleic anhydride **4**: yield 1259 mg, 70%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27−7.22 (m, 1H), 6.88−6.83 (m, 1H), 5.06 (t, J = 3.7 Hz, 1H), 4.79 (d, J = 15.2 Hz, 1H), 4.48 (d, J = 15.1 Hz, 1H), 4.12 (dq, J = 10.8, 7.1 Hz, 1H), 4.03 (dq, J = 10.8, 7.1 Hz, 1H), 3.79 (s, 2H), 3.01 (dd, J = 8.4, 5.8 Hz, 1H), 2.80 (dd, J = 16.5, 8.5 Hz, 1H), 2.59 (dt, J = 12.2, 2.9 Hz, 1H), 2.47 (dd, J = 16.5, 5.9 Hz, 1H), 2.20−2.12 (m, 1H), 2.12−2.03 (m, 1H), 1.83 (ddd, J = 14.6, 6.6, 3.6 Hz, 1H), 1.58−1.40 (m, 2H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.8, 173.9, 171.3, 159.1, 138.2, 129.2, 127.9, 113.9, 102.2, 61.6, 55.4, 52.1, 47.5, 43.9, 31.6, 30.6, 22.8, 19.6, 14.2; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{21}H_{26}NO_6$ 388.1760, found 388.1753.

Pyrrolidinone-Containing Carboxylic Acid 7c. Compound **7c** was prepared according to general procedure A from primary amine **1c**, ketoester **2a**, and maleic anhydride **4**: yield 1319 mg, 50%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.21 (s, 1H), 7.24−7.18 (m, 2H), 7.17−7.10 (m, 2H), 5.02 (t, J = 3.7 Hz, 1H), 4.15−4.02 (m, 2H), 3.85 (ddd, J = 13.7, 10.6, 6.4 Hz, 1H), 3.38 (ddd, J = 13.8, 10.5, 5.1 Hz, 1H), 2.99 (dd, J = 8.4, 5.8 Hz, 1H), 2.90−2.81 (m, 2H), 2.77 (ddd, J = 13.6, 10.5, 6.4 Hz, 1H), 2.60−2.53 (m, 1H), 2.30 (dd, J = 17.4, 8.4 Hz, 1H), 2.20 (ddd, J = 17.8, 6.6, 4.0 Hz, 1H), 2.14−2.03 (m, 1H), 1.86−1.76 (m, 1H), 1.52−1.41 (m, 2H), 1.17 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.0, 173.0, 171.3, 164.1, 138.0, 136.9, 132.2, 130.0, 128.6, 101.1, 77.4, 61.4, 52.2, 47.2, 41.3, 32.0, 31.2, 30.5, 22.7, 19.5, 14.0; MS (ESI) calcd for $C_{21}H_{24}ClNO_5$ 405.13 (M$^+$), found 406.19 (M + H)$^+$.

Pyrrolidinone-Containing Carboxylic Acid 7d. Compound **7d** was prepared according to general procedure A from primary amine **1a**, ketoester **2b**, and maleic anhydride **4**: yield 1076 mg, 65%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.41−6.31 (m, 1H), 5.69 (ddt, J = 17.2, 10.3, 5.1 Hz, 1H), 5.25−5.12 (m, 3H), 4.20 (ddt, J = 16.3, 4.9, 1.8 Hz, 1H), 4.03 (ddt, J = 16.4, 5.0, 1.8 Hz, 1H), 3.69 (s, 3H), 3.06 (t, J = 6.9 Hz, 1H), 2.78 (dd, J = 17.0, 6.8 Hz, 1H), 2.53−2.44 (m, 1H), 2.37 (dd, J = 17.0, 7.0 Hz, 1H), 2.26−2.15 (m, 1H), 1.96−1.84 (m, 2H), 1.76−1.62 (m, 2H), 1.62−1.52 (m, 1H), 1.37−1.27 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.7, 173.3, 171.3, 142.7, 130.9, 130.2, 117.2, 105.9, 55.5, 52.3, 48.3, 42.9, 36.1, 32.1, 27.7, 27.4, 26.1; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{16}H_{22}NO_5$ 308.1498, found 308.1496.

Pyrrolidinone-Containing Carboxylic Acid 7e. Compound **7e** was prepared according to general procedure A from primary amine **1b**, ketoester **2b**, and maleic anhydride **4**: yield 1588 mg, 82%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21−7.14 (m, 2H), 6.89−6.81 (m, 2H), 5.20 (dd, J = 8.8, 4.4 Hz, 1H), 4.78 (d, J = 15.4 Hz, 1H), 4.55 (d, J = 15.4 Hz, 1H), 3.80 (d, J = 1.2 Hz, 3H), 3.66 (s, 3H), 3.04 (dd, J = 9.3, 4.8 Hz, 1H), 2.71 (ddd, J = 16.2, 9.3, 1.2 Hz, 1H), 2.56−2.41 (m, 2H), 2.22−2.09 (m, 1H), 1.95−1.79 (m, 2H), 1.79−1.64 (m, 2H), 1.62−1.52 (m, 1H), 1.34−1.21 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 173.8, 171.3, 158.9, 142.5, 128.4, 127.6, 114.0, 106.3, 55.4, 55.3, 52.3, 48.4, 43.8, 36.0, 32.0, 27.6, 27.4, 26.1; MS (ESI) calcd for $C_{21}H_{26}NO_6$ 388.1760 (M + H), found 388.1768.

Pyrrolidinone-Containing Carboxylic Acid 7f. Compound **7f** was prepared according to general procedure A from primary amine **1c**, ketoester **2b**, and maleic anhydride **4**: yield 1766 mg, 79%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.24 (m, 2H), 7.20−7.14 (m, 2H), 5.22 (dd, J = 8.9, 4.4 Hz, 1H), 3.79 (ddd, J = 13.8, 9.8, 6.4 Hz, 1H), 3.70 (s, 3H), 3.56 (ddd, J = 13.8, 9.8, 5.6 Hz, 1H), 3.01 (t, J = 6.9 Hz, 1H), 2.86 (ddd, J = 13.5, 9.8, 5.6 Hz, 1H), 2.82−2.72 (m, 2H), 2.49 (ddd, J = 13.6, 4.7, 2.6 Hz, 1H), 2.35 (dd, J = 17.2, 7.2 Hz, 1H), 2.31−2.22 (m, 1H), 2.01−1.89 (m, 2H), 1.80−1.64 (m, 2H), 1.61−1.53 (m, 1H), 1.37−1.26 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 173.1, 171.3, 142.7, 136.8, 132.5, 130.3, 128.7, 104.9, 55.5, 52.3, 48.2, 41.6, 36.1, 32.1, 31.7, 27.7, 27.4, 26.1; MS (ESI) calcd for $C_{21}H_{24}ClNO_5$ 405.13 (M$^+$), found 406.23 (M + H)$^+$.

Pyrrolidinone-Containing Carboxylic Acid 7g. Compound **7g** was prepared according to general procedure A from primary amine **1a**, ketoester **2c**, and maleic anhydride **4**: yield 838 mg, 65%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74−5.64 (m, 1H), 5.22−5.11 (m, 2H), 4.89−4.79 (m, 1H), 4.22−4.10 (m, 4H), 3.02 (t, J = 7.0 Hz, 1H), 2.87−2.77 (m, 1H), 2.62−2.51 (m, 1H), 2.40 (dd, J = 16.9, 7.3 Hz, 1H), 2.10−2.00 (m, 1H), 2.00−1.86 (m, 1H), 1.76−1.61 (m, 2H), 1.61−1.49 (m, 3H), 1.48−1.30 (m, 1H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 173.5, 171.4, 140.5, 130.7, 117.1, 104.0, 61.7, 53.9, 48.2, 42.8, 39.5, 32.8, 27.9, 26.1, 23.1, 22.7, 14.1; MS (ESI) calcd for $C_{18}H_{25}NO_5$ 335.17 (M$^+$), found 336.33 (M + H)$^+$.

Pyrrolidinone-Containing Carboxylic Acid 7h. Compound **7h** was prepared according to general procedure A from primary amine **1b**, ketoester **2c**, and maleic anhydride **4**: yield 1641 mg, 87%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (dd, J = 8.4, 1.5 Hz, 2H), 6.85−6.78 (m, 2H), 4.85−4.73 (m, 1H), 4.66 (s, 2H), 4.21−4.05 (m, 2H), 3.76 (s, 3H), 3.08 (t, J = 7.0 Hz, 1H), 2.89 (dd, J = 16.9, 6.5 Hz, 1H), 2.57 (dd, J = 12.9, 6.6 Hz, 1H), 2.49−2.40 (m, 1H), 2.01−1.84 (m, 2H), 1.73−1.62 (m, 1H), 1.61−1.42 (m, 3H), 1.35−1.23 (m, 1H), 1.23−1.15 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 173.8, 171.3, 158.9, 140.3, 128.2, 127.5, 114.0, 104.5, 61.6, 55.3, 53.9, 48.2, 43.6, 39.3, 32.8, 27.8, 25.8, 23.0, 22.6, 14.0; MS (ESI) calcd for $C_{23}H_{29}NO_6$ 415.20 (M$^+$), found 416.29 (M + H)$^+$.

Pyrrolidinone-Containing Carboxylic Acid 7i. Compound **7i** was prepared according to general procedure A from primary amine **1c**, ketoester **2c**, and maleic anhydride **4**: yield 1519 mg, 70%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.23 (m, 2H), 7.19−7.11 (m, 2H), 4.88 (dd, J = 10.6, 7.7 Hz, 1H), 4.23−4.14 (m, 2H), 3.79−3.66 (m, 2H), 2.94 (t, J = 7.0 Hz, 1H), 2.84 (t, J = 7.6 Hz, 2H), 2.77 (dd, J = 16.9, 6.7 Hz, 1H), 2.57 (dd, J = 13.1, 6.2 Hz, 1H), 2.37 (dd, J = 16.9, 7.2 Hz, 1H), 2.15−2.06 (m, 1H), 2.04−1.93 (m, 1H), 1.76−1.64 (m, 3H), 1.64−1.49 (m, 3H), 1.48−1.38 (m, 1H), 1.37−1.29 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 173.4, 171.4, 140.7, 136.7, 132.6, 130.3, 128.8, 103.0, 61.7, 54.0, 48.1, 41.6, 39.7, 32.8, 31.8, 27.9, 26.0, 23.1, 22.6, 14.1; MS (ESI) calcd for $C_{23}H_{28}ClNO_5$ 433.17 (M$^+$), found 434.24 (M + H)$^+$.

Piperidinone-Containing Carboxylic Acid 8a (2-((3*RS*,4a*SR*)-1-(3,4-Dimethoxyphenethyl)-4a-(ethoxycarbonyl)-2-oxo-2,3,4,4a,5,6-hexahydro-1*H*-cyclopenta[*b*]pyridin-3-yl)acetic Acid). Compound **8a** (1.59 g, 55%) was obtained according to general procedure A. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (m, 3H), 5.11 (t, J = 2.5 Hz, 1H), 4.15 (m, 2H), 3.95 (m, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.68 (m, 1H), 2.79 (m, 4H), 2.67 (m, 1H), 2.50 (m, 2H), 2.34 (m, 2H), 1.86 (dt, J = 12.8, 9.3 Hz, 1H), 1.69 (t, J = 12.8 Hz, 1H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 173.9, 169.7, 149.0, 147.7, 140.9, 131.5, 120.7, 112.2, 111.4, 106.8, 61.5, 56.0, 56.0, 54.4, 46.0, 36.9, 36.7, 36.4, 35.7, 32.3, 29.0, 14.2; MS (ESI) calcd for $C_{23}H_{29}NO_7$ 431.2 (M$^+$), found 414.3 (M − OH)$^+$, 432.3 (M + H)$^+$.

Piperidinone-Containing Carboxylic Acid 8b. Compound **8b** (1.12 g, 51%) was obtained according to general procedure A: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.42 (m, 1H), 5.32 (dd, J = 5.1, 2.8 Hz, 1H), 4.14 (m, 2H), 3.82 (m, 1H), 3.70 (m, 1H), 2.77 (dd, J = 16.2, 6.9 Hz, 1H), 2.67 (m, 1H), 2.52 (dd, J = 16.2, 4.9 Hz, 1H), 2.32 (dd, J = 13.0, 5.7 Hz, 1H), 2.25 (m, 3H), 2.14 (m, 1H), 2.05 (m, 1H), 1.95 (m, 5H), 1.68 (m, 1H), 1.58 (m, 3H), 1.50 (m, 4H), 1.37 (m, 1H), 1.27 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 173.9, 170.3, 135.8, 135.2, 122.7, 108.1, 61.7, 46.4, 43.2, 37.5, 36.8, 36.1, 34.9, 34.8, 28.6, 25.3, 24.5, 22.9, 22.4, 18.6, 14.3; MS (ESI) calcd for $C_{22}H_{31}NO_5$ 389.2 (M$^+$), found 372.3 (M − OH)$^+$, 390.3 (M + H)$^+$.

Piperidinone-Containing Carboxylic Acid 8c. Compound **8c** (814 mg, 37%) was obtained according to general procedure A: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.20 (m, 1H), 7.14 (d, J = 6.7 Hz, 2H), 5.42 (t, J = 7.0 Hz, 1H), 5.17 (d, J = 16.0 Hz, 1H), 4.75 (d, J = 16.1 Hz, 1H), 3.77 (s, 3H), 2.84 (m, 2H), 2.62 (m, 1H), 2.15 (dd, J = 13.2, 4.1 Hz, 1H), 2.05 (m, 2H), 1.93 (m, 2H), 1.69 (m, 3H),

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1.57 (m, 1H), 1.24 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 174.2, 171.1, 140.6, 137.3, 128.6, 126.8, 126.4, 116.1, 52.6, 51.6, 49.5, 39.5, 36.6, 35.6, 35.6, 26.3, 25.3, 24.8; MS (ESI) calcd for $C_{21}H_{25}NO_5$ 371.2 (M^+), found 354.2 ($M - OH$)$^+$, 372.2 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8d. Compound **8b** (582 mg, 57%) was obtained according to general procedure A: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, J = 1.7, 0.8 Hz, 1H), 6.32 (dd, J = 3.2, 1.9 Hz, 1H), 6.26 (d, J = 3.2 Hz, 1H), 5.51 (t, J = 4.1 Hz, 1H), 5.28 (d, J = 15.8 Hz, 1H), 4.57 (d, J = 15.8 Hz, 1H), 3.65 (s, 3H), 2.77 (dd, J = 16.3, 7.5 Hz, 1H), 2.63 (m, 2H), 2.28 (dd, J = 12.9, 5.7 Hz, 1H), 2.22 (d, J = 13.6 Hz, 1H), 2.00 (d, J = 4.1 Hz, 2H), 1.69 (t, J = 12.9 Hz, 1H), 1.43 (d, J = 13.6 Hz, 1H), 0.97 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 174.8, 170.6, 150.8, 141.7, 135.6, 110.7, 109.3, 108.3, 52.8, 47.2, 45.6, 42.6, 38.8, 38.7, 37.3, 36.0, 31.7, 28.7, 25.3; MS (ESI) calcd for $C_{20}H_{25}NO_6$ 375.2 (M^+), found 358.2 ($M - OH$)$^+$, 376.2 ($M + H$)$^+$, 398.2 ($M + Na$)$^+$.

Piperidinone-Containing Carboxylic Acid 8e. Compound **8e** was prepared according to general procedure A from primary amine **1d**, ketoester **2d**, and itaconic anhydride **5**: yield 1144 mg, 63%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.04 (s, 1H), 4.13 (m, 2H), 3.79 (m, 1H), 3.42 (m, 1H), 2.77 (m, 2H), 2.61 (m, 1H), 2.50 (dd, J = 12.6, 5.2 Hz, 1H), 2.43 (dd, J = 16.1, 9.3 Hz, 1H), 2.31 (dd, J = 12.7, 7.4 Hz, 2H), 1.82 (dt, J = 12.8, 9.2 Hz, 1H), 1.64 (t, J = 12.7 Hz, 1H), 1.53 (m, 2H), 1.21 (m, 15H), 0.83 (t, J = 6.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 174.0, 169.9, 140.9, 107.1, 61.5, 54.3, 44.2, 36.9, 36.9, 36.4, 35.9, 31.9, 29.4, 29.3, 29.0, 27.1, 26.5, 22.7, 14.2, 14.2, 14.2; MS (ESI) calcd for $C_{21}H_{33}NO_5$ 379.2 (M^+), found 362.3 ($M - OH$)$^+$, 380.3 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8f. Compound **8f** was prepared according to general procedure A from primary amine **1e**, ketoester **2d**, and itaconic anhydride **5**: yield 626 mg, 55%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (m, 5H), 5.00 (m, 2H), 4.84 (m, 1H), 4.14 (m, 2H), 2.91 (m, 2H), 2.81 (m, 1H), 2.56 (dd, J = 12.9, 5.8 Hz, 1H), 2.36 (m, 2H), 2.26 (m, 1H), 1.85 (m, 2H), 1.19 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.3, 174.1, 170.2, 141.2, 136.7, 128.4, 127.0, 126.9, 108.2, 61.5, 54.4, 54.4, 47.9, 36.9, 36.5, 36.4, 35.5, 29.0, 14.2, 14.1; MS (ESI) calcd for $C_{20}H_{23}NO_5$ 357.2 (M^+), found 340.2 ($M - OH$)$^+$, 358.2 ($M + H$)$^+$, 380.2 ($M + Na$)$^+$.

Piperidinone-Containing Carboxylic Acid 8g. Compound **8g** was prepared according to general procedure A from primary amine **1f**, ketoester **2d**, and itaconic anhydride **5**: yield 855 mg, 55%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (m, 3H), 5.91 (s, 2H), 5.06 (dd, J = 3.2, 1.8 Hz, 1H), 4.81 (m, 2H), 4.14 (m, 2H), 2.92 (dq, J = 12.8, 5.6 Hz, 1H), 2.81 (dd, J = 5.6, 1.6 Hz, 2H), 2.55 (dd, J = 12.7, 5.6 Hz, 1H), 2.33 (m, 3H), 1.83 (m, 2H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.5, 174.0, 170.4, 147.9, 146.7, 141.2, 130.6, 120.5, 108.4, 108.3, 107.8, 101.1, 61.6, 54.5, 47.7, 37.0, 36.6, 36.6, 35.8, 29.1, 14.2; MS (ESI) calcd for $C_{21}H_{23}NO_7$ 401.1 (M^+), found 402.2 ($M + H$)$^+$, 424.2 ($M + Na$)$^+$.

Piperidinone-Containing Carboxylic Acid 8h. Compound **8h** was prepared according to general procedure A from primary amine **1g**, ketoester **2d**, and itaconic anhydride **5**: yield 705 mg, 42%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (dd, J = 1.8, 0.9 Hz, 1H), 6.28 (m, 1H), 5.27 (t, J = 2.5 Hz, 1H), 4.92 (m, 1H), 4.81 (m, 1H), 4.12 (m, 2H), 2.90 (m, 1H), 2.81 (m, 1H), 2.70 (m, 1H), 2.54 (dd, J = 12.7, 5.6 Hz, 1H), 2.46 (m, 1H), 2.34 (m, 2H), 1.86 (dt, J = 13.2, 9.2 Hz, 1H), 1.71 (t, J = 12.8 Hz, 1H), 1.18 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.0, 173.9, 170.3, 150.2, 141.9, 140.9, 110.6, 108.4, 108.3, 61.6, 54.5, 41.2, 37.0, 36.9, 36.5, 35.9, 29.2, 14.2; MS (ESI) calcd for $C_{18}H_{21}NO_6$ 347.1 (M^+), found 330.2 ($M - OH$)$^+$, 348.2 ($M + H$)$^+$, 370.2 ($M + Na$)$^+$.

Piperidinone-Containing Carboxylic Acid 8i. Compound **8i** was prepared according to general procedure A from primary amine **1h**, ketoester **2d**, and itaconic anhydride **5**: yield 571 mg, 47%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.41 (t, J = 3.4 Hz, 1H), 5.10 (t, J = 2.4 Hz, 1H), 4.14 (m, 2H), 3.82 (m, 1H), 3.59 (m, 1H), 2.80 (m, 2H), 2.60 (m, 1H), 2.52 (dd, J = 12.3, 5.4 Hz, 1H), 2.46 (m, 1H), 2.34 (m, 2H), 2.19 (m, 1H), 2.11 (m, 1H), 1.95 (m, 4H), 1.85 (dt, J = 12.6, 9.3 Hz, 1H), 1.65 (m, 1H), 1.59 (m, 2H), 1.52 (m, 2H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.5, 173.9, 169.9, 140.8, 135.0, 122.9, 107.1, 61.5, 54.3, 43.2, 37.1, 37.0, 36.4, 35.9, 34.6, 29.0, 28.5, 25.3, 23.0, 22.4, 14.2; MS (ESI) calcd for $C_{21}H_{29}NO_5$ 375.2 (M^+), found 358.3 ($M - OH$)$^+$, 376.3 ($M + H$)$^+$, 398.3 ($M + Na$)$^+$.

Piperidinone-Containing Carboxylic Acid 8j. Compound **8j** was prepared according to general procedure A from primary amine **1j**, ketoester **2d**, and itaconic anhydride **5**: yield 1277 mg, 49%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (m, 2H), 7.87 (m, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.53 (ddd, J = 8.4, 6.8, 1.7 Hz, 1H), 7.49 (td, J = 8.6, 6.9, 1.5 Hz, 1H), 7.35 (d, J = 7.0 Hz, 1H), 5.48 (d, J = 16.4 Hz, 1H), 5.36 (d, J = 16.1 Hz, 1H), 4.87 (dd, J = 3.2, 1.6 Hz, 1H), 4.23 (m, 2H), 4.14 (m, 1H), 3.01 (m, 2H), 2.83 (dd, J = 16.8, 3.9 Hz, 1H), 2.63 (dd, J = 12.7, 5.4 Hz, 1H), 2.36 (m, 2H), 2.22 (m, 1H), 1.95 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.3, 174.2, 170.3, 141.3, 133.7, 130.8, 130.8, 128.9, 127.4, 126.1, 125.6, 125.5, 122.9, 122.5, 108.6, 61.5, 54.5, 45.9, 37.0, 36.6, 36.2, 35.5, 28.9, 14.2; MS (ESI) calcd for $C_{24}H_{25}NO_5$ 407.2 (M^+), found 390.2 ($M - OH$)$^+$, 408.3 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8k. Compound **8k** was prepared according to general procedure A from primary amine **1k**, ketoester **2d**, and itaconic anhydride **5**: yield 568 mg, 35%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 1.9 Hz, 1H), 7.16 (m, 2H), 5.01 (d, J = 16.9 Hz, 1H), 4.86 (d, J = 16.9 Hz, 2H), 4.20 (m, 2H), 2.98 (dd, J = 17.4, 5.3 Hz, 1H), 2.91 (m, 1H), 2.76 (dd, J = 17.0, 4.4 Hz, 1H), 2.56 (dd, J = 12.7, 5.5 Hz, 1H), 2.37 (m, 2H), 2.26 (m, 1H), 1.91 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.6, 174.1, 170.2, 141.0, 133.3, 133.2, 132.4, 129.2, 128.4, 127.4, 108.3, 61.7, 54.5, 45.4, 37.1, 36.5, 36.0, 35.4, 29.0, 14.3; MS (ESI) calcd for $C_{20}H_{21}Cl_2NO_5$ 425.1 (M^+), found 408.2 ($M - OH$)$^+$, 426.2 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8l. Compound **8l** was prepared according to general procedure A from primary amine **1d**, ketoester **2a**, and itaconic anhydride **5**: yield 1018 mg, 88%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.25 (dd, J = 5.2, 2.8 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.64 (t, J = 8.0 Hz, 2H), 2.76 (dd, J = 16.3, 6.1 Hz, 1H), 2.66 (dq, J = 11.9, 5.8 Hz, 3H), 2.52 (dd, J = 16.3, 5.6 Hz, 1H), 2.30 (dd, J = 12.9, 5.7 Hz, 1H), 2.22 (m, 2H), 2.12 (m, 1H), 1.65 (m, 1H), 1.55 (t, J = 13.0 Hz, 1H), 1.46 (m, 2H), 1.34 (m, 1H), 1.24 (m, 12H), 1.18 (t, J = 7.1 Hz, 3H), 0.82 (t, J = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 173.9, 169.9, 135.9, 107.8, 61.5, 46.3, 44.0, 37.2, 36.6, 36.1, 34.9, 31.8, 29.3, 29.3, 27.1, 26.7, 24.4, 22.6, 18.5, 14.2, 14.1; MS (ESI) calcd for $C_{22}H_{35}NO_5$ 393.3 (M^+), found 376.3 ($M - OH$)$^+$, 394.3 ($M + H$)$^+$, 416.3 ($M + Na$)$^+$.

Piperidinone-Containing Carboxylic Acid 8m. Compound **8m** was prepared according to general procedure A from primary amine **1e**, ketoester **2a**, and itaconic anhydride **5**: yield 858 mg, 79%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (m, 2H), 7.21 (m, 3H), 5.39 (d, J = 16.0 Hz, 1H), 5.21 (dd, J = 5.2, 2.8 Hz, 1H), 4.55 (d, J = 16.0 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.47 (s, 1H), 2.81 (m, 3H), 2.40 (m, 1H), 2.27 (dt, J = 12.9, 3.4 Hz, 1H), 2.15 (m, 1H), 2.04 (m, 1H), 1.81 (t, J = 12.8 Hz, 1H), 1.66 (m, 1H), 1.52 (td, J = 13.6, 13.2, 2.8 Hz, 1H), 1.37 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 174.2, 170.4, 137.4, 136.9, 128.6, 128.5, 126.7, 126.2, 109.1, 61.6, 48.9, 46.6, 36.5, 36.4, 36.3, 34.8, 24.2, 18.5, 14.3; MS (ESI) calcd for $C_{21}H_{25}NO_5$ 371.2 (M^+), found 354.2 ($M - OH$)$^+$, 372.2 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8n. Compound **8n** was prepared according to general procedure A from primary amine **1f**, ketoester **2a**, and itaconic anhydride **5**: yield 1014 mg, 83%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69 (m, 3H), 5.89 (s, 2H), 5.22 (m, 2H), 4.47 (d, J = 15.8 Hz, 1H), 4.16 (m, 2H), 2.78 (m, 3H), 2.36 (dd, J = 12.9, 5.5 Hz, 1H), 2.25 (dt, J = 13.1, 3.3 Hz, 1H), 2.14 (m, 1H), 2.05 (m, 1H), 1.79 (t, J = 13.0 Hz, 1H), 1.64 (dd, J = 14.0, 5.2 Hz, 1H), 1.50 (td, J = 13.6, 13.1, 2.8 Hz, 1H), 1.36 (m, 1H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.7, 174.2, 170.3, 147.9, 146.4, 136.8, 131.3, 119.4, 109.0, 108.3, 107.1, 100.9, 61.6, 48.5, 46.6, 36.5, 36.4, 36.3, 34.8, 24.3, 18.5, 14.3; MS (ESI) calcd for $C_{22}H_{25}NO_7$ 415.2 (M^+), found 398.2 ($M - OH$)$^+$, 416.3 ($M + H$)$^+$, 438.2 ($M + Na$)$^+$.

Piperidinone-Containing Carboxylic Acid 8o. Compound **8o** was prepared according to general procedure A from primary amine **1g**, ketoester **2a**, and itaconic anhydride **5**: yield 583 mg, 55%; ^{1}H

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NMR (500 MHz, $CDCl_3$) δ 7.31 (m, 1H), 6.27 (m, 2H), 5.51 (dd, J = 5.2, 2.8 Hz, 1H), 5.24 (d, J = 15.8 Hz, 1H), 4.54 (d, J = 15.8 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 2.82 (dd, J = 16.1, 5.8 Hz, 1H), 2.75 (dq, J = 12.9, 5.6 Hz, 1H), 2.65 (dd, J = 16.1, 5.3 Hz, 1H), 2.37 (dd, J = 13.0, 5.7 Hz, 1H), 2.25 (m, 2H), 2.13 (m, 1H), 1.66 (m, 2H), 1.50 (td, J = 13.6, 13.1, 2.6 Hz, 1H), 1.38 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.2, 174.0, 170.2, 150.9, 141.6, 136.7, 110.6, 109.0, 108.0, 61.7, 46.6, 42.2, 37.0, 36.7, 36.2, 34.9, 24.4, 18.6, 14.3; MS (ESI) calcd for $C_{19}H_{23}NO_6$ 361.2 (M^+), found 344.2 ($M - OH$)$^+$, 362.2 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8p. Compound **8p** was prepared according to general procedure A from primary amine **1i**, ketoester **2a**, and itaconic anhydride **5**: yield 914 mg, 58%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (m, 3H), 5.33 (dd, J = 5.2, 2.8 Hz, 1H), 4.12 (q, J = 7.0 Hz, 2H), 3.86 (m, 2H), 3.84 (s, 4H), 3.81 (s, 3H), 2.85 (m, 1H), 2.76 (dd, J = 16.0, 5.7 Hz, 1H), 2.69 (m, 2H), 2.62 (dd, J = 16.1, 5.6 Hz, 1H), 2.32 (dd, J = 13.0, 5.6 Hz, 1H), 2.25 (m, 2H), 2.14 (m, 1H), 1.67 (m, 1H), 1.61 (t, J = 12.8 Hz, 1H), 1.48 (td, J = 13.4, 12.9, 2.6 Hz, 1H), 1.38 (m, 1H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 173.9, 169.8, 148.9, 147.5, 135.9, 131.7, 120.5, 112.1, 111.3, 107.6, 61.5, 55.9, 55.9, 46.4, 45.6, 36.8, 36.4, 36.1, 34.8, 32.4, 24.4, 18.5, 14.2; MS (ESI) calcd for $C_{24}H_{31}NO_7$ 445.2 (M^+), found 428.3 ($M - OH$)$^+$, 446.3 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8q. Compound **8q** was prepared according to general procedure A from primary amine **1j**, ketoester **2a**, and itaconic anhydride **5**: 1040 mg, 84%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.2 Hz, 1H), 7.88 (m, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.51 (m, 3H), 7.33 (d, J = 7.1 Hz, 1H), 5.90 (d, J = 16.7 Hz, 1H), 5.07 (dd, J = 5.1, 2.9 Hz, 1H), 5.02 (d, J = 16.7 Hz, 1H), 4.25 (m, 2H), 3.03 (dd, J = 16.6, 5.1 Hz, 1H), 2.85 (m, 2H), 2.47 (dd, J = 12.9, 5.4 Hz, 1H), 2.31 (dt, J = 13.3, 3.3 Hz, 1H), 2.03 (m, 3H), 1.66 (m, 1H), 1.58 (td, J = 13.5, 2.8 Hz, 1H), 1.40 (m, 1H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.1, 174.2, 170.1, 137.0, 133.6, 131.3, 130.3, 128.8, 127.1, 125.9, 125.7, 125.5, 122.4, 122.4, 109.1, 61.6, 47.4, 46.7, 36.3, 36.2, 36.1, 34.7, 24.1, 18.5, 14.3; MS (ESI) calcd for $C_{25}H_{27}NO_5$ 421.2 (M^+), found 404.3 ($M - OH$)$^+$, 422.3 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8r. Compound **8r** was prepared according to general procedure A from primary amine **1k**, ketoester **2a**, and itaconic anhydride **5**: yield 861 mg, 67%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (s, 1H), 7.13 (m, 2H), 5.26 (d, J = 17.1 Hz, 1H), 4.91 (dd, J = 5.1, 2.8 Hz, 1H), 4.56 (d, J = 17.1 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.00 (dd, J = 16.9, 5.1 Hz, 1H), 2.69 (m, 2H), 2.35 (dd, J = 12.9, 5.6 Hz, 1H), 2.25 (dt, J = 13.2, 3.2 Hz, 1H), 2.11 (m, 1H), 2.00 (m, 1H), 1.90 (t, J = 12.9 Hz, 1H), 1.64 (m, 1H), 1.51 (td, J = 13.7, 2.8 Hz, 1H), 1.34 (m, 1H), 1.24 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.3, 174.2, 170.3, 136.7, 133.0, 133.0, 132.7, 129.1, 128.3, 127.4, 109.0, 61.8, 46.8, 46.8, 36.2, 36.1, 35.8, 34.8, 24.2, 18.5, 14.4; MS (ESI) calcd for $C_{21}H_{23}Cl_2NO_5$ 439.1 (M^+), found 422.2 ($M - OH$)$^+$, 440.2 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8s. Compound **8s** was prepared according to general procedure A from primary amine **1d**, ketoester **2b**, and itaconic anhydride **5**: yield 443 mg, 38%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.54 (t, J = 7.1 Hz, 1H), 3.76 (s, 4H), 3.60 (m, 1H), 2.80 (dd, J = 16.1, 7.5 Hz, 1H), 2.70 (m, 1H), 2.40 (dd, J = 16.1, 5.1 Hz, 1H), 2.23 (m, 1H), 2.05 (m, 3H), 1.79 (m, 1H), 1.70 (m, 4H), 1.56 (m, 2H), 1.40 (m, 1H), 1.26 (m, 11H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 174.1, 171.3, 140.3, 115.1, 52.7, 51.6, 51.6, 45.5, 40.0, 37.0, 36.6, 35.6, 31.9, 29.4, 29.4, 27.1, 26.9, 26.5, 25.5, 25.0, 22.8, 14.2; MS (ESI) calcd for $C_{22}H_{35}NO_5$ 393.3 (M^+), found 376.3 ($M - OH$)$^+$, 394.4 ($M + H$)$^+$, 416.4 ($M + Na$)$^+$.

Piperidinone-Containing Carboxylic Acid 8t. Compound **8t** was prepared according to general procedure A from primary amine **1f**, ketoester **2b**, and itaconic anhydride **5**: yield 595 mg, 33%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (d, J = 7.9 Hz, 1H), 6.64 (d, J = 1.7 Hz, 1H), 6.62 (dd, J = 8.0, 1.8 Hz, 1H), 5.92 (d, J = 1.7 Hz, 2H), 5.46 (t, J = 7.0 Hz, 1H), 5.04 (d, J = 15.8 Hz, 1H), 4.69 (d, J = 15.8 Hz, 1H), 3.77 (s, 3H), 2.88–2.76 (m, 2H), 2.63–2.56 (m, 1H), 2.19–2.07 (m, 2H), 2.07–2.00 (m, 1H), 2.00–1.92 (m, 1H), 1.88 (t, J = 13.2 Hz, 1H), 1.78–1.54 (m, 4H), 1.33–1.23 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 174.2, 171.3, 148.0, 146.5, 140.6, 131.2, 119.6, 116.2, 108.4, 107.1, 101.0, 52.7, 51.6, 49.4, 39.6, 36.7, 35.9, 35.6, 26.3, 25.3, 24.9; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{22}H_{26}NO_7$ 416.1709, found 416.1714.

Piperidinone-Containing Carboxylic Acid 8u. Compound **8u** was prepared according to general procedure A from primary amine **1g**, ketoester **2b**, and itaconic anhydride **5**: yield 452 mg, 28%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, J = 1.7, 0.9 Hz, 1H), 6.28 (dd, J = 3.1, 1.8 Hz, 1H), 6.18 (d, J = 3.2 Hz, 1H), 5.68 (t, J = 7.1 Hz, 1H), 5.08 (d, J = 15.9 Hz, 1H), 4.69 (d, J = 15.9 Hz, 1H), 3.74 (s, 3H), 2.86 (dd, J = 16.7, 6.0 Hz, 1H), 2.76 (dt, J = 6.8, 4.4 Hz, 1H), 2.48 (dd, J = 16.7, 6.4 Hz, 1H), 2.17 (m, 1H), 2.11 (dd, J = 13.2, 4.4 Hz, 1H), 2.00 (m, 2H), 1.78 (m, 2H), 1.64 (m, 2H), 1.27 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.6, 174.1, 171.0, 150.8, 141.5, 140.5, 116.3, 110.5, 108.1, 52.6, 51.8, 42.9, 39.5, 36.6, 35.6, 35.6, 26.4, 25.3, 24.9; MS (ESI) calcd for $C_{19}H_{23}NO_6$ 361.2 (M^+), found 344.2 ($M - OH$)$^+$, 362.2 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8v. Compound **8v** was prepared according to general procedure A from primary amine **1h**, ketoester **2b**, and itaconic anhydride **5**: yield 438 mg, 38%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.54 (t, J = 7.2 Hz, 3H), 5.39 (m, 3H), 3.98 (m, 3H), 3.74 (s, 9H), 3.60 (m, 3H), 2.80 (dd, J = 16.3, 6.9 Hz, 3H), 2.68 (m, 3H), 2.37 (dd, J = 16.3, 5.7 Hz, 3H), 2.19 (m, 9H), 2.03 (m, 9H), 1.95 (m, 13H), 1.79 (m, 3H), 1.68 (m, 13H), 1.57 (m, 6H), 1.50 (m, 6H), 1.36 (m, 2H), 1.23 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 174.1, 171.1, 140.2, 135.0, 123.0, 114.9, 52.6, 51.6, 43.3, 39.7, 37.0, 36.2, 35.5, 34.8, 28.4, 26.8, 25.6, 25.3, 25.0, 22.9, 22.4; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{22}H_{32}NO_5$ 390.2280, found 390.2280.

Piperidinone-Containing Carboxylic Acid 8w. Compound **8w** was prepared according to general procedure A from primary amine **1i**, ketoester **2b**, and itaconic anhydride **5**: yield 1090 mg, 42%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (m, 3H), 5.64 (t, J = 7.2 Hz, 1H), 4.06 (m, 1H), 3.88 (s, 3H), 3.85 (s, 4H), 3.76 (s, 3H), 2.85 (dt, J = 9.4, 5.6 Hz, 2H), 2.78 (dd, J = 16.4, 7.1 Hz, 1H), 2.72 (dt, J = 12.6, 6.0 Hz, 1H), 2.40 (dd, J = 15.9, 4.8 Hz, 1H), 2.26 (m, 1H), 2.05 (m, 3H), 1.80 (m, 1H), 1.67 (m, 3H), 1.60 (t, J = 13.3 Hz, 1H), 1.39 (m, 1H), 1.24 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 174.0, 170.8, 148.8, 147.5, 140.4, 131.3, 120.6, 114.6, 112.0, 111.2, 77.4, 77.2, 76.9, 55.9, 52.5, 51.5, 46.1, 39.4, 36.7, 35.6, 35.5, 32.4, 26.6, 25.5, 24.9; MS (ESI) calcd for $C_{24}H_{31}NO_7$ 445.2 (M^+), found 428.2 ($M - OH$)$^+$, 446.2 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8x. Compound **8x** was prepared according to general procedure A from primary amine **1j**, ketoester **2b**, and itaconic anhydride **5**: yield 791 mg, 32%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.3 Hz, 1H), 7.88 (m, 1H), 7.74 (d, J = 8.3 Hz, 1H), 7.52 (m, 2H), 7.43 (t, J = 7.7 Hz, 1H), 7.20 (d, J = 7.1 Hz, 1H), 5.56 (d, J = 16.4 Hz, 1H), 5.36 (t, J = 7.0 Hz, 1H), 5.27 (d, J = 16.6 Hz, 1H), 3.81 (s, 3H), 2.89 (m, 2H), 2.71 (m, 1H), 2.20 (dd, J = 13.2, 4.2 Hz, 1H), 2.03 (m, 3H), 1.89 (m, 1H), 1.69 (m, 3H), 1.57 (m, 1H), 1.24 (m, 1H); MS (ESI) calcd for $C_{25}H_{27}NO_5$ 421.2 (M^+), found 404.3 ($M - OH$)$^+$, 422.3 ($M + H$)$^+$.

Piperidinone-Containing Carboxylic Acid 8y. Compound **8y** was prepared according to general procedure A from primary amine **1k**, ketoester **2b**, and itaconic anhydride **5**: yield 1118 mg, 46%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 2.1 Hz, 1H), 7.19 (dd, J = 8.4, 2.1 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 5.18 (t, J = 6.9 Hz, 1H), 4.98 (d, J = 17.2 Hz, 1H), 4.86 (d, J = 17.0 Hz, 1H), 3.79 (s, 3H), 2.77 (m, 3H), 2.11 (m, 3H), 1.98 (m, 2H), 1.80 (m, 2H), 1.63 (m, 2H), 1.34 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.0, 174.2, 170.8, 140.8, 133.1, 133.0, 129.2, 128.3, 127.5, 115.4, 52.8, 51.7, 47.9, 39.2, 36.9, 35.6, 35.3, 26.1, 25.3, 24.9; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{21}H_{24}Cl_2NO_5$ 440.1032, found 440.1037.

Piperidinone-Containing Carboxylic Acid 8z. Compound **8z** was prepared according to general procedure A from primary amine **1d**, ketoester **2e**, and itaconic anhydride **5**: yield 479 mg, 41%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.19 (t, J = 4.1 Hz, 1H), 3.66 (m, 2H), 3.61 (s, 3H), 2.70 (m, 1H), 2.53 (m, 2H), 2.19 (m, 2H), 1.97 (d, J = 4.1 Hz, 2H), 1.59 (m, 2H), 1.47 (m, 1H), 1.38 (d, J = 13.7 Hz, 1H),

1.23 (m, 11H), 0.92 (s, 3H), 0.82 (t, J = 6.7 Hz, 3H), 0.79 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 175.1, 169.8, 134.9, 107.4, 52.4, 47.2, 45.3, 44.5, 38.7, 38.4, 37.1, 35.9, 31.8, 31.6, 29.3, 29.3, 28.5, 27.2, 26.7, 25.3, 22.6, 14.1, 14.1; MS (ESI) calcd for $C_{23}H_{37}NO_5$ 407.3 (M^+), found 390.3 $(M - OH)^+$, 408.3 $(M + H)^+$.

Piperidinone-Containing Carboxylic Acid 8aa. Compound **8aa** was prepared according to general procedure A from primary amine **1e**, ketoester **2e**, and itaconic anhydride **5**: yield 474 mg, 76%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (m, 2H), 7.22 (m, 3H), 5.50 (d, J = 16.1 Hz, 1H), 5.14 (t, J = 4.1 Hz, 1H), 4.49 (d, J = 16.0 Hz, 1H), 3.67 (s, 3H), 2.90 (m, 1H), 2.74 (dd, J = 17.0, 5.2 Hz, 1H), 2.63 (dt, J = 18.5, 5.4 Hz, 1H), 2.29 (dd, J = 12.8, 5.8 Hz, 1H), 2.22 (d, J = 13.5 Hz, 1H), 1.88 (m, 3H), 1.46 (d, J = 13.6 Hz, 1H), 0.94 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.5, 175.4, 170.3, 137.5, 137.5, 136.0, 128.6, 126.8, 126.3, 108.8, 52.6, 49.5, 47.2, 45.6, 38.6, 38.3, 36.5, 36.1, 31.7, 28.6, 25.4; MS (ESI) calcd for $C_{22}H_{27}NO_5$ 385.2 (M^+), found 368.2 $(M - OH)^+$, 386.3 $(M + H)^+$.

Piperidinone-Containing Carboxylic Acid 8ab. Compound **8ab** was prepared according to general procedure A from primary amine **1f**, ketoester **2e**, and itaconic anhydride **5**: yield 890 mg, 76%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (s, 1H), 6.74 (m, 2H), 6.69 (m, 1H), 5.92 (d, J = 1.8 Hz, 2H), 5.34 (d, J = 15.8 Hz, 1H), 5.19 (m, 1H), 4.45 (dd, J = 15.7, 3.4 Hz, 1H), 3.67 (s, 3H), 2.82 (m, 1H), 2.74 (m, 1H), 2.63 (dt, J = 13.1, 5.5 Hz, 1H), 2.28 (dd, J = 12.8, 5.8 Hz, 1H), 2.22 (d, J = 13.6 Hz, 1H), 1.91 (t, J = 3.0 Hz, 2H), 1.82 (td, J = 13.0, 3.0 Hz, 1H), 1.44 (d, J = 13.6 Hz, 1H), 0.94 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.0, 175.4, 170.4, 147.9, 146.4, 136.0, 131.4, 119.6, 108.8, 108.4, 107.2, 101.0, 66.0, 52.6, 49.2, 47.2, 45.6, 38.7, 38.3, 36.6, 36.1, 31.7, 28.6, 25.5, 15.3; MS (ESI) calcd for $C_{23}H_{27}NO_7$ 429.2 (M^+), found 412.2 $(M - OH)^+$, 430.2 $(M + H)^+$.

Piperidinone-Containing Carboxylic Acid 8ac. Compound **8ac** was prepared according to general procedure A from primary amine **1h**, ketoester **2e**, and itaconic anhydride **5**: yield 420 mg, 38%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.46 (m, 1H), 5.32 (m, 1H), 3.90 (m, 1H), 3.72 (m, 1H), 3.67 (s, 3H), 2.74 (dd, J = 15.7, 7.3 Hz, 1H), 2.53 (m, 2H), 2.31 (td, J = 12.3, 11.6, 5.6 Hz, 1H), 2.23 (m, 2H), 2.11 (m, 1H), 2.00 (m, 7H), 1.61 (m, 3H), 1.55 (m, 2H), 1.43 (d, J = 13.7 Hz, 1H), 1.21 (m, 1H), 0.97 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 175.1, 170.2, 135.2, 134.9, 122.6, 107.7, 52.6, 47.2, 45.3, 43.8, 38.8, 38.5, 37.4, 35.9, 34.8, 31.7, 28.6, 28.6, 25.4, 25.3, 22.9, 22.4; MS (ESI) calcd for $C_{23}H_{33}NO_5$ 403.2 (M^+), found 386.2 $(M - OH)^+$, 404.2 $(M + H)^+$.

Piperidinone-Containing Carboxylic Acid 8ad. Compound **8ad** was prepared according to general procedure A from primary amine **1i**, ketoester **2e**, and itaconic anhydride **5**: yield 570 mg, 46%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (m, 3H), 5.39 (dd, J = 5.0, 3.2 Hz, 1H), 3.96 (m, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.68 (s, 3H), 2.94 (m, 1H), 2.77 (m, 2H), 2.62 (m, 1H), 2.53 (dd, J = 16.0, 3.4 Hz, 1H), 2.26 (m, 2H), 2.06 (m, 2H), 1.63 (t, J = 13.0 Hz, 1H), 1.45 (d, J = 13.6 Hz, 1H), 1.00 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.7, 175.1, 169.8, 148.9, 147.5, 135.0, 131.8, 120.6, 112.1, 111.3, 107.4, 55.9, 55.9, 52.4, 47.1, 46.2, 45.3, 38.7, 38.2, 36.8, 35.9, 32.5, 31.6, 28.5, 25.3; MS (ESI) calcd for $C_{25}H_{33}NO_7$ 459.2 (M^+), found 442.3 $(M - OH)^+$, 460.3 $(M + H)^+$.

Piperidinone-Containing Carboxylic Acid 8ae. Compound **8ae** was prepared according to general procedure A from primary amine **1j**, ketoester **2e**, and itaconic anhydride **5**: yield 715 mg, 60%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.3 Hz, 1H), 7.88 (dd, J = 8.0, 1.5 Hz, 1H), 7.73 (d, J = 8.2 Hz, 1H), 7.53 (m, 2H), 7.43 (t, J = 7.7 Hz, 1H), 7.30 (d, J = 7.2 Hz, 1H), 5.99 (d, J = 16.7 Hz, 1H), 5.03 (dd, J = 5.1, 2.9 Hz, 1H), 4.93 (d, J = 16.7 Hz, 1H), 3.74 (s, 3H), 3.05 (m, 1H), 2.73 (m, 2H), 2.36 (dd, J = 12.8, 5.6 Hz, 1H), 2.27 (dd, J = 13.7, 1.9 Hz, 1H), 2.05 (m, 1H), 1.85 (m, 2H), 1.52 (d, J = 13.7 Hz, 1H), 0.95 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 175.6, 170.2, 136.3, 133.8, 131.6, 130.4, 128.9, 127.3, 126.1, 125.8, 125.6, 122.7, 122.6, 109.0, 77.4, 77.2, 76.9, 52.7, 48.3, 47.2, 45.7, 38.5, 38.3, 36.3, 36.2, 31.7, 28.6, 25.4; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{26}H_{30}NO_5$ 436.2124, found 436.2120.

Piperidinone-Containing Carboxylic Acid 8af. Compound **8af** was prepared according to general procedure A from primary amine **1k**, ketoester **2e**, and itaconic anhydride **5**: yield 944 mg, 77%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 1.9 Hz, 1H), 7.15 (m, 2H), 5.41 (d, J = 17.2 Hz, 1H), 4.89 (dd, J = 4.8, 3.2 Hz, 1H), 4.49 (d, J = 17.1 Hz, 1H), 3.71 (s, 3H), 3.09 (dd, J = 17.2, 4.9 Hz, 1H), 2.60 (m, 2H), 2.25 (m, 2H), 1.98 (t, J = 13.0 Hz, 1H), 1.89 (t, J = 4.1 Hz, 2H), 1.48 (d, J = 13.7 Hz, 1H), 0.94 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.3, 175.4, 170.1, 136.0, 133.2, 133.0, 132.7, 129.1, 128.3, 127.4, 108.5, 52.7, 47.6, 47.1, 45.6, 38.5, 37.9, 36.1, 35.7, 31.7, 28.6, 25.4; MS (ESI) calcd for $C_{22}H_{25}Cl_2NO_5$ 453.1 (M^+), found 436.2 $(M - OH)^+$, 454.2 $(M + H)^+$.

Carbomethoxytetrahydropyranone 24a ((2*RS*,6*RS*)-Methyl 6-*tert*-Butyl-2-methyl-4-oxotetrahydro-2*H*-pyran-3-carboxylate). Compound **24a** was prepared according to reported procedures:[17] ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.96 (dd, J = 10.4, 6.0 Hz, 1H), 3.77 (s, 3H), 3.31 (dd, J = 11.8, 2.3 Hz, 1H), 3.17 (dd, J = 10.4, 0.7 Hz, 1H), 2.45 (dd, J = 13.9, 2.3 Hz, 1H), 2.29 (ddd, J = 13.9, 11.9, 0.9 Hz, 1H), 1.32 (d, J = 6.0 Hz, 3H), 0.93 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.8, 168.9, 84.4, 75.0, 64.6, 52.2, 42.2, 34.4, 25.6, 20.9; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{20}O_4Na$ 251.1259, found 251.1267.

Carbomethoxytetrahydropyranone 24b. Compound **24b** was prepared according to reported procedures:[17] ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.97 (dq, J = 10.4, 6.0 Hz, 1H), 3.76 (s, 3H), 3.43 (ddd, J = 11.5, 7.9, 2.3 Hz, 1H), 3.19 (dd, J = 10.4, 0.8 Hz, 1H), 2.50 (dd, J = 14.2, 2.3 Hz, 1H), 2.27 (ddd, J = 14.2, 11.6, 0.9 Hz, 1H), 1.97 (q, J = 8.3 Hz, 1H), 1.87−1.81 (m, 1H), 1.69−1.51 (m, 6H), 1.45−1.40 (m, 1H), 1.32 (d, J = 6.0 Hz, 3H), 1.21−1.14 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.8, 168.8, 81.2, 75.0, 64.6, 52.3, 46.2, 45.5, 29.3, 28.6, 25.62, 25.43, 21.0; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{13}H_{20}O_4Na$ 263.1259, found 263.1266.

Carbomethoxytetrahydropyranone 24c. Compound **24c** was prepared according to reported procedures:[17] ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.39−3.33 (m, 2H), 3.33−3.27 (m, 1H), 2.46 (dd, J = 14.3, 2.3 Hz, 1H), 2.27−2.22 (m, 1H), 1.79 (dq, J = 13.4, 6.7 Hz, 1H), 0.99−0.93 (m, 1H), 0.90 (d, J = 6.8 Hz, 3H), 0.57−0.49 (m, 2H), 0.48−0.43 (m, 1H), 0.40−0.35 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.1, 168.8, 81.6, 81.4, 63.9, 52.2, 44.3, 33.4, 18.5, 18.1, 15.7, 2.9, 2.1; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{13}H_{20}O_4Na$ 263.1259, found 263.1258.

Carbomethoxytetrahydropyranone 24d. Compound **24d** was prepared according to reported procedures:[17] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.28 (m, 5H), 4.60 (q, J = 9.9 Hz, 2H), 4.04 (dq, J = 10.5, 6.0 Hz, 1H), 3.94−3.89 (m, 1H), 3.77 (s, 3H), 3.60−3.53 (m, 2H), 3.23 (dd, J = 10.5, 0.7 Hz, 1H), 2.53−2.41 (m, 2H), 1.36 (d, J = 6.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.1, 168.6, 137.8, 128.6, 127.95, 127.85, 76.1, 75.2, 73.6, 71.9, 64.3, 52.3, 43.4, 20.9; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{16}H_{20}O_5Na$ 315.1208, found 315.1211.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26a (2-((3*SR*,4a*RS*,5*RS*,7*RS*)-1-Benzyl-7-*tert*-butyl-4a-(methoxycarbonyl)-5-methyl-2-oxo-2,3,4,4a,5,7-hexahydro-1*H*-pyrano[4,3-*b*]pyridin-3-yl)acetic Acid). Compound **26a** (428 mg, 82%) was obtained according to general procedure A: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.28 (m, 1H), 7.25−7.20 (m, 1H), 5.43 (s, 1H), 5.27 (d, J = 15.5 Hz, 1H), 4.47 (d, J = 15.5 Hz, 1H), 3.84 (q, J = 6.4 Hz, 1H), 3.72 (s, 1H), 3.59 (s, 3H), 3.14−3.06 (m, 1H), 3.00 (dd, J = 17.0, 5.3 Hz, 1H), 2.78 (dd, J = 17.0, 5.2 Hz, 1H), 2.47 (dd, J = 12.6, 7.4 Hz, 1H), 1.79 (t, J = 12.6 Hz, 1H), 1.18 (d, J = 6.3 Hz, 3H), 0.73 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.4, 172.7, 170.9, 138.3, 137.4, 128.7, 127.2, 127.0, 111.6, 82.1, 74.6, 52.8, 51.4, 49.4, 37.5, 36.5, 34.7, 28.8, 25.5, 16.2; MS (ESI) calcd for $C_{24}H_{31}NO_6$ 429.2 (M^+), found 412.2 $(M - OH)^+$, 430.2 $(M + H)^+$, 452.2 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26b. Compound **26b** (366 mg, 74%) was obtained according to general procedure A: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.43 (s, 1H), 5.41−5.38 (m, 1H), 4.05 (d, J = 7.6 Hz, 1H), 3.98 (q, J = 6.6 Hz, 1H), 3.82−3.72 (m, 1H), 3.67 (s, 2H), 3.64−3.55 (m, 1H), 3.02−2.91 (m, 1H), 2.75 (dd, J = 16.8, 5.9 Hz, 1H), 2.71−2.63 (m, 1H), 2.38 (dd, J = 12.8, 7.2 Hz, 1H), 2.30−2.20 (m, 1H), 2.06−1.99 (m, 1H), 1.99−1.92 (m, 5H), 1.77−1.66 (m, 2H), 1.66−1.56 (m, 5H),

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1.56−1.47 (m, 4H), 1.44−1.34 (m, 1H), 1.34−1.24 (m, 1H), 1.19 (dd, J = 6.6, 2.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 172.6, 170.5, 170.5, 136.4, 135.0, 123.0, 111.0, 78.1, 74.5, 52.9, 51.3, 44.8, 43.4, 37.9, 37.9, 36.3, 34.9, 29.3, 28.7, 28.6, 28.5, 25.9, 25.8, 25.4, 23.0, 22.4, 16.6; MS (ESI) calcd for $C_{26}H_{37}NO_6$ 459.3 (M^+), found 460.4 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26c. Compound **26c** (609 mg, 81%) was obtained according to general procedure A: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77−6.68 (m, 3H), 5.27 (d, J = 1.9 Hz, 1H), 3.91 (dd, J = 6.2, 1.8 Hz, 1H), 3.89−3.82 (m, 1H), 3.81 (s, 3H), 3.81−3.76 (m, 4H), 3.78−3.72 (m, 1H), 3.62 (s, 3H), 3.30 (d, J = 8.0 Hz, 1H), 3.02−2.91 (m, 1H), 2.84−2.71 (m, 4H), 2.48 (dd, J = 12.8, 6.7 Hz, 1H), 1.85 (t, J = 12.1 Hz, 1H), 1.83−1.72 (m, 1H), 0.89 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H), 0.48 (d, J = 8.3 Hz, 2H), 0.45−0.36 (m, 1H), 0.18−0.11 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.6, 172.7, 170.3, 148.9, 147.5, 136.2, 131.5, 120.6, 111.9, 111.3, 108.9, 81.5, 78.7, 55.8, 55.8, 52.7, 51.6, 45.8, 37.1, 36.4, 33.2, 32.5, 29.8, 18.3, 18.0, 11.7, 3.5, 2.4; MS (ESI) calcd for $C_{28}H_{37}NO_8$ 515.3 (M^+), found 498.4 $(M - OH)^+$, 516.4 $(M + H)^+$, 538.4 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26d. Compound **26d** (293 mg, 54%) was obtained according to general procedure A: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 6.30 (dd, J = 3.3, 1.8 Hz, 1H), 6.23 (d, J = 3.2 Hz, 1H), 5.58 (d, J = 1.7 Hz, 1H), 4.91 (d, J = 15.7 Hz, 1H), 4.75 (d, J = 15.7 Hz, 1H), 4.59 (d, J = 12.1 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H), 4.48 (td, J = 6.0, 1.7 Hz, 1H), 4.07 (q, J = 6.5 Hz, 1H), 3.61 (s, 2H), 3.54 (dd, J = 9.9, 6.5 Hz, 1H), 3.40 (dd, J = 9.8, 5.6 Hz, 1H), 3.05−2.95 (m, 1H), 2.80 (dd, J = 16.9, 5.4 Hz, 1H), 2.72 (dd, J = 16.9, 6.2 Hz, 1H), 2.39 (dd, J = 12.8, 6.7 Hz, 1H), 1.71 (t, J = 12.1 Hz, 1H), 1.21 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 172.4, 170.3, 150.1, 141.8, 138.1, 136.6, 128.5, 128.5, 127.8, 127.8, 127.8, 110.6, 108.8, 108.7, 74.4, 73.5, 73.3, 72.7, 53.0, 51.2, 51.2, 41.0, 37.2, 36.4, 29.2, 16.8; MS (ESI) calcd for $C_{26}H_{29}NO_8$ 483.2 (M^+), found 484.3 $(M + H)^+$, 506.3 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26e. Compound **26e** was prepared according to general procedure A from primary amine **1d**, ketoester **24a**, and itaconic anhydride **5**: yield 454 mg, 93%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.46 (s, 1H), 3.88 (q, J = 6.4 Hz, 1H), 3.82 (s, 1H), 3.76−3.68 (m, 1H), 3.65 (s, 3H), 3.48−3.39 (m, 1H), 3.06−2.97 (m, 1H), 2.78 (dd, J = 16.9, 6.0 Hz, 1H), 2.67 (dd, J = 16.9, 5.2 Hz, 1H), 2.41 (dd, J = 12.7, 7.7 Hz, 1H), 1.60 (dd, J = 12.6, 10.7 Hz, 2H), 1.48−1.38 (m, 1H), 1.33−1.18 (m, 12H), 1.15 (d, J = 6.5 Hz, 3H), 0.91−0.81 (m, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 172.6, 170.4, 138.0, 110.0, 82.2, 74.6, 52.7, 51.4, 44.5, 37.8, 36.3, 34.7, 31.9, 29.3, 29.3, 28.6, 27.2, 26.8, 25.6, 22.7, 16.2, 14.2; MS (ESI) calcd for $C_{25}H_{41}NO_6$ 451.3 (M^+), found 434.4 $(M - OH)^+$, 452.4 $(M + H)^+$, 474.4 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26f. Compound **26f** was prepared according to general procedure A from primary amine **1f**, ketoester **24a**, and itaconic anhydride **5**: yield 431 mg, 77%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77−6.72 (m, 2H), 6.70 (dd, J = 7.8, 1.8 Hz, 1H), 5.94−5.90 (m, 2H), 5.49 (d, J = 1.6 Hz, 1H), 5.06 (d, J = 15.3 Hz, 1H), 4.48 (d, J = 15.3 Hz, 1H), 3.85 (q, J = 6.4 Hz, 1H), 3.74 (d, J = 1.5 Hz, 1H), 3.61 (s, 3H), 3.12−3.05 (m, 1H), 2.96 (dd, J = 17.0, 5.4 Hz, 1H), 2.75 (dd, J = 17.0, 5.3 Hz, 1H), 2.45 (dd, J = 12.6, 7.4 Hz, 1H), 1.76 (dd, J = 12.7, 11.1 Hz, 1H), 1.18 (d, J = 6.5 Hz, 3H), 0.78 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.0, 172.6, 170.9, 148.0, 146.7, 138.3, 131.2, 120.4, 111.5, 108.3, 107.9, 101.1, 82.1, 77.4, 77.4, 77.2, 76.9, 74.6, 52.8, 51.4, 49.0, 37.4, 36.5, 34.7, 28.7, 25.6, 16.2; MS (ESI) calcd for $C_{25}H_{31}NO_8$ 473.2 (M^+), found 474.2 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26g. Compound **26g** was prepared according to general procedure A from primary amine **1g**, ketoester **24a**, and itaconic anhydride **5**: yield 219 mg, 46%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, J = 1.7, 0.9 Hz, 1H), 6.30 (dd, J = 3.1, 1.8 Hz, 1H), 6.23 (d, J = 3.1 Hz, 1H), 5.69 (d, J = 1.5 Hz, 1H), 5.07 (d, J = 15.6 Hz, 1H), 4.47 (d, J = 15.6 Hz, 1H), 3.85 (q, J = 6.3 Hz, 1H), 3.79 (d, J = 1.6 Hz, 1H), 3.61 (s, 3H), 3.07−2.99 (m, 1H), 2.86 (dd, J = 17.0, 6.1 Hz, 1H), 2.70 (dd, J = 17.0, 4.6 Hz, 1H), 2.43 (dd, J = 12.7, 7.5 Hz, 1H), 1.66 (dd, J = 12.7, 10.9 Hz, 1H), 1.16 (d, J = 6.4 Hz, 3H), 0.83 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.0, 172.7, 170.4, 150.6, 141.7, 138.1, 111.1, 110.7, 108.6, 82.1, 74.5, 52.8, 51.3, 42.2, 37.4, 36.4, 34.7, 28.5, 25.5, 16.1; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{22}H_{30}NO_7$ 420.2022, found 420.2000.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26h. Compound **26h** was prepared according to general procedure A from primary amine **1h**, ketoester **24a**, and itaconic anhydride **5**: yield 363 mg, 71%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.54 (s, 1H), 5.47 (s, 1H), 3.90 (q, J = 6.5 Hz, 1H), 3.84 (s, 1H), 3.77 (ddd, J = 13.4, 11.3, 5.0 Hz, 1H), 3.68 (s, 3H), 3.62 (ddd, J = 13.5, 11.1, 5.5 Hz, 1H), 3.09−3.01 (m, 1H), 2.77−2.67 (m, 2H), 2.45 (dd, J = 12.7, 7.6 Hz, 1H), 2.31 (td, J = 12.3, 11.3, 5.4 Hz, 1H), 2.07−1.92 (m, 5H), 1.66−1.59 (m, 3H), 1.58−1.51 (m, 2H), 1.19 (d, J = 6.5 Hz, 3H), 0.91 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 172.5, 170.9, 137.9, 135.0, 123.1, 110.4, 82.2, 74.7, 52.8, 51.4, 44.0, 38.2, 36.3, 35.2, 34.8, 29.1, 28.6, 25.7, 25.4, 23.0, 22.4, 16.2; MS (ESI) calcd for $C_{25}H_{37}NO_6$ 447.3 (M^+), found 448.3 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26i. Compound **26i** was prepared according to general procedure A from primary amine **1i**, ketoester **24a**, and itaconic anhydride **5**: yield 460 mg, 80%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (d, J = 7.9 Hz, 1H), 6.76−6.71 (m, 2H), 5.42 (d, J = 1.5 Hz, 1H), 3.88 (q, J = 6.4 Hz, 2H), 3.86−3.80 (m, 7H), 3.80−3.72 (m, 1H), 3.62 (s, 3H), 3.07−3.00 (m, 1H), 2.90−2.81 (m, 2H), 2.79−2.72 (m, 1H), 2.69 (dd, J = 16.9, 4.9 Hz, 1H), 2.44 (dd, J = 12.7, 7.6 Hz, 1H), 1.63 (dd, J = 12.6, 10.5 Hz, 1H), 1.15 (d, J = 6.5 Hz, 3H), 0.85 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.9, 172.5, 170.4, 149.0, 147.6, 138.3, 131.7, 120.6, 111.9, 111.4, 110.3, 82.1, 74.5, 55.9, 55.9, 52.7, 51.4, 47.2, 37.6, 36.4, 34.6, 32.8, 28.5, 25.5, 16.1; MS (ESI) calcd for $C_{27}H_{37}NO_8$ 503.3 (M^+), found 486.4 $(M - OH)^+$, 504.4 $(M + H)^+$, 526.4 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26j. Compound **26j** was prepared according to general procedure A from primary amine **1j**, ketoester **24a**, and itaconic anhydride **5**: yield 395 mg, 72%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04−7.98 (m, 1H), 7.89−7.83 (m, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.56−7.51 (m, 1H), 7.48 (ddd, J = 8.0, 6.7, 1.2 Hz, 1H), 7.43 (dd, J = 8.2, 7.1 Hz, 1H), 7.36 (dd, J = 7.2, 1.3 Hz, 1H), 5.50 (d, J = 1.4 Hz, 1H), 5.46 (d, J = 16.0 Hz, 1H), 5.26 (d, J = 16.0 Hz, 1H), 3.82 (q, J = 6.4 Hz, 1H), 3.72 (d, J = 1.5 Hz, 1H), 3.28 (s, 3H), 3.21−3.13 (m, 2H), 2.85−2.78 (m, 1H), 2.49 (dd, J = 12.6, 7.2 Hz, 1H), 1.92 (dd, J = 12.7, 10.8 Hz, 1H), 1.18 (d, J = 6.4 Hz, 3H), 0.77 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.7, 172.7, 170.4, 138.1, 133.8, 131.5, 131.0, 128.8, 127.8, 126.3, 125.7, 125.4, 125.4, 123.2, 111.8, 82.0, 74.5, 52.4, 51.4, 47.0, 37.0, 36.5, 34.6, 28.4, 25.5, 16.1; MS (ESI) calcd for $C_{28}H_{33}NO_6$ 479.2 (M^+), found 480.4 $(M + H)^+$, 502.4 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26k. Compound **26k** was prepared according to general procedure A from primary amine **1k**, ketoester **24a**, and itaconic anhydride **5**: yield 468 mg, 82%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 2.0 Hz, 1H), 7.24−7.14 (m, 2H), 5.26 (d, J = 1.5 Hz, 1H), 5.23 (d, J = 16.8 Hz, 1H), 4.48 (d, J = 16.8 Hz, 1H), 3.83 (q, J = 6.4 Hz, 1H), 3.71 (d, J = 1.5 Hz, 1H), 3.68 (s, 3H), 3.22 (dd, J = 17.7, 5.2 Hz, 1H), 3.01 (ddt, J = 11.9, 7.3, 4.6 Hz, 1H), 2.69 (dd, J = 17.7, 4.2 Hz, 1H), 2.43 (dd, J = 12.6, 7.2 Hz, 1H), 1.91 (t, J = 12.1 Hz, 1H), 1.20 (d, J = 6.4 Hz, 3H), 0.75 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.1, 172.7, 170.4, 138.4, 133.3, 133.0, 132.8, 129.2, 129.1, 127.2, 111.2, 82.0, 74.6, 52.9, 51.4, 47.4, 36.3, 36.2, 34.7, 28.1, 25.5, 16.1; MS (ESI) calcd for $C_{24}H_{29}Cl_2NO_6$ 497.1 (M^+), found 480.3 $(M - OH)^+$, 498.3 $(M + H)^+$, 520.3 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26l. Compound **26l** was prepared according to general procedure A from primary amine **1d**, ketoester **24b**, and itaconic anhydride **5**: yield 357 mg, 76%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.37 (d, J = 1.7 Hz, 1H), 4.06 (dd, J = 7.5, 1.6 Hz, 1H), 3.97 (q, J = 6.5 Hz, 1H), 3.77 (ddd, J = 13.6, 10.2, 6.1 Hz, 1H), 3.67 (s, 3H), 3.50−3.40 (m, 1H), 3.00 (ddt, J = 11.1, 7.2, 5.7 Hz, 1H), 2.75 (dd, J = 16.8, 5.7 Hz, 1H), 2.69 (dd, J = 16.9, 6.1 Hz, 1H), 2.39 (dd, J = 12.7, 7.2 Hz,

1H), 2.02−1.92 (m, 1H), 1.78−1.34 (m, 12H), 1.33−1.21 (m, 12H), 1.19 (d, J = 6.5 Hz, 3H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 172.6, 170.5, 136.5, 111.1, 78.2, 74.6, 52.8, 51.3, 44.7, 44.0, 37.8, 36.3, 31.9, 29.4, 29.3, 29.1, 28.6, 28.4, 27.2, 26.7, 25.9, 25.8, 22.7, 16.5, 14.2; MS (ESI) calcd for $C_{26}H_{41}NO_6$ 463.3 (M^+), found 446.4 (M − OH)$^+$, 464.4 (M + H)$^+$, 486.4 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26m. Compound **26m** was prepared according to general procedure A from primary amine **1e**, ketoester **24b**, and itaconic anhydride **5**: yield 368 mg, 68%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.28 (m, 2H), 7.26−7.20 (m, 3H), 5.35 (d, J = 1.6 Hz, 1H), 5.15 (d, J = 15.5 Hz, 1H), 4.63 (d, J = 15.5 Hz, 1H), 4.00−3.93 (m, 2H), 3.59 (s, 3H), 3.10−3.03 (m, 1H), 2.90 (dd, J = 16.9, 5.3 Hz, 1H), 2.81 (dd, J = 17.0, 5.7 Hz, 1H), 2.43 (dd, J = 12.7, 6.9 Hz, 1H), 1.92−1.85 (m, 1H), 1.81 (dd, J = 12.7, 11.6 Hz, 1H), 1.69−1.60 (m, 1H), 1.55−1.37 (m, 5H), 1.32−1.23 (m, 1H), 1.20 (d, J = 6.6 Hz, 3H), 1.18−1.11 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 172.7, 170.9, 137.1, 136.7, 128.7, 127.3, 127.1, 112.2, 77.9, 74.5, 52.9, 51.3, 48.6, 44.5, 37.4, 36.4, 29.2, 28.6, 28.2, 25.9, 25.8, 16.6.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26n. Compound **26n** was prepared according to general procedure A from primary amine **1f**, ketoester **24b**, and itaconic anhydride **5**: yield 353 mg, 68%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77−6.66 (m, 3H), 5.93 (s, 2H), 5.39 (d, J = 1.6 Hz, 1H), 4.97 (d, J = 15.3 Hz, 1H), 4.61 (d, J = 15.4 Hz, 1H), 3.99 (dd, J = 7.3, 1.6 Hz, 1H), 3.96 (q, J = 6.8 Hz, 1H), 3.61 (s, 3H), 3.09−3.01 (m, 1H), 2.88 (dd, J = 17.0, 5.3 Hz, 1H), 2.79 (dd, J = 16.9, 5.8 Hz, 1H), 2.41 (dd, J = 12.6, 6.9 Hz, 1H), 1.96−1.87 (m, 1H), 1.79 (dd, J = 12.7, 11.6 Hz, 1H), 1.72−1.62 (m, 1H), 1.61−1.41 (m, 5H), 1.34−1.25 (m, 1H), 1.20 (d, J = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 172.7, 171.0, 148.0, 146.8, 136.7, 131.0, 120.5, 112.2, 108.3, 107.9, 101.1, 78.0, 74.5, 52.9, 51.3, 48.3, 44.5, 37.4, 36.4, 29.2, 28.6, 28.3, 25.9, 25.8, 16.6; MS (ESI) calcd for $C_{26}H_{31}NO_8$ 485.2 (M^+), found 486.2 (M + H)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26o. Compound **26o** was prepared according to general procedure A from primary amine **1g**, ketoester **24b**, and itaconic anhydride **5**: yield 283 mg, 60%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, J = 1.7, 0.9 Hz, 1H), 6.28 (dd, J = 3.2, 1.8 Hz, 1H), 6.21 (d, J = 3.2 Hz, 1H), 5.56 (d, J = 1.6 Hz, 1H), 4.98 (d, J = 15.6 Hz, 1H), 4.58 (d, J = 15.7 Hz, 1H), 4.03 (d, J = 7.3 Hz, 1H), 3.93 (q, J = 6.5 Hz, 1H), 3.59 (s, 2H), 3.03−2.95 (m, 1H), 2.80 (dd, J = 17.0, 6.2 Hz, 1H), 2.73 (dd, J = 17.1, 4.9 Hz, 1H), 2.39 (dd, J = 12.6, 7.1 Hz, 1H), 1.99−1.90 (m, 1H), 1.69 (dd, J = 12.7, 11.1 Hz, 3H), 1.58−1.41 (m, 4H), 1.38−1.20 (m, 2H), 1.16 (d, J = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.9, 172.6, 170.3, 150.3, 141.6, 136.7, 111.8, 110.6, 108.5, 78.0, 74.4, 52.8, 51.2, 44.4, 41.5, 37.2, 36.3, 28.8, 28.5, 28.1, 25.8, 25.8, 16.4; MS (ESI) calcd for $C_{23}H_{29}NO_7$ 431.2 (M^+), found 414.3 (M − OH)$^+$, 432.3 (M + H)$^+$, 454.3 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26p. Compound **26p** was prepared according to general procedure A from primary amine **1i**, ketoester **24b** and itaconic anhydride **5**: yield 457 mg, 73%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (d, J = 7.9 Hz, 1H), 6.76−6.72 (m, 2H), 5.35 (d, J = 1.6 Hz, 1H), 4.05 (d, J = 7.4 Hz, 1H), 3.98 (q, J = 6.5 Hz, 1H), 3.84 (d, J = 10.2 Hz, 7H), 3.73 (ddd, J = 13.5, 10.4, 5.0 Hz, 1H), 3.64 (s, 3H), 2.98 (dt, J = 12.0, 6.0 Hz, 1H), 2.88−2.81 (m, 1H), 2.80−2.70 (m, 2H), 2.40 (dd, J = 12.7, 7.1 Hz, 1H), 1.97−1.89 (m, 1H), 1.76−1.63 (m, 2H), 1.63−1.47 (m, 3H), 1.41−1.34 (m, 1H), 1.32−1.23 (m, 1H), 1.19 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.6, 172.6, 170.3, 149.0, 147.6, 136.7, 131.6, 120.6, 111.9, 111.3, 111.0, 78.0, 74.5, 55.9, 55.9, 52.8, 51.3, 46.3, 44.7, 37.5, 36.4, 32.6, 28.9, 28.6, 28.4, 25.8, 25.7, 16.5; MS (ESI) calcd for $C_{28}H_{37}NO_8$ 515.3 (M^+), found 516.4 (M + H)$^+$, 538.4 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26q. Compound **26q** was prepared according to general procedure A from primary amine **1j**, ketoester **24b**, and itaconic anhydride **5**: yield 379 mg, 63%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.4 Hz, 1H), 7.86 (dd, J = 8.1, 1.5 Hz, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.57−7.49 (m, 1H), 7.48 (ddd, J = 8.0, 6.7, 1.2 Hz, 1H), 7.42 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 7.1 Hz, 1H), 5.40 (d, J = 16.1 Hz, 1H), 5.36 (d, J = 1.4 Hz, 1H), 5.33 (d, J = 16.0 Hz, 1H), 4.01 (dd, J = 6.6, 1.5 Hz, 1H), 3.91 (q, J = 6.5 Hz, 1H), 3.29 (s, 3H), 3.12 (dt, J = 17.6, 4.0 Hz, 1H), 3.07 (d, J = 5.9 Hz, 1H), 2.85 (dd, J = 16.9, 4.3 Hz, 1H), 2.46 (dd, J = 12.6, 6.8 Hz, 1H), 1.98−1.86 (m, 2H), 1.67−1.58 (m, 1H), 1.53−1.38 (m, 5H), 1.31−1.22 (m, 1H), 1.19 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.4, 172.7, 170.4, 136.8, 133.8, 131.3, 131.1, 128.8, 127.8, 126.3, 125.7, 125.4, 125.2, 123.1, 112.6, 77.7, 74.5, 52.5, 51.3, 46.4, 44.3, 37.0, 36.5, 28.8, 28.2, 28.1, 25.9, 25.8, 16.4; MS (ESI) calcd for $C_{29}H_{33}NO_6$ 491.2 (M^+), found 492.4 (M + H)$^+$, 514.4 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26r. Compound **26r** was prepared according to general procedure A from primary amine **1k**, ketoester **24b**, and itaconic anhydride **5**: yield 360 mg, 56%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.33 (m, 1H), 7.16 (s, 2H), 5.16 (d, J = 16.8 Hz, 1H), 5.13 (d, J = 1.7 Hz, 1H), 4.60 (d, J = 16.7 Hz, 1H), 4.00−3.92 (m, 2H), 3.68 (s, 3H), 3.11 (dd, J = 17.5, 5.5 Hz, 1H), 3.01−2.91 (m, 1H), 2.72 (dd, J = 17.5, 4.4 Hz, 1H), 2.38 (dd, J = 12.7, 6.7 Hz, 1H), 1.93 (t, J = 12.3 Hz, 1H), 1.92−1.82 (m, 1H), 1.66−1.56 (m, 1H), 1.55−1.46 (m, 2H), 1.46−1.38 (m, 4H), 1.32−1.23 (m, 2H), 1.21 (d, J = 6.5 Hz, 3H), 1.19−1.13 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.6, 172.8, 170.3, 136.6, 133.3, 132.9, 132.8, 129.1, 129.1, 129.0, 127.3, 111.5, 77.6, 77.4, 74.4, 53.0, 51.3, 46.4, 44.4, 36.3, 36.2, 28.6, 28.3, 28.1, 25.9, 25.8, 16.6; MS (ESI) calcd for $C_{25}H_{29}Cl_2NO_6$ 509.1 (M^+), found 492.3 (M − OH)$^+$, 510.3 (M + H)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26s. Compound **26s** was prepared according to general procedure A from primary amine **1d**, ketoester **24c**, and itaconic anhydride **5**: yield 461 mg, 73%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.30 (d, J = 1.8 Hz, 1H), 3.93 (dd, J = 6.1, 1.7 Hz, 1H), 3.80−3.70 (m, 1H), 3.64 (s, 2H), 3.50−3.40 (m, 1H), 3.31 (d, J = 7.9 Hz, 1H), 3.02−2.92 (m, 1H), 2.73 (dd, J = 16.9, 5.2 Hz, 1H), 2.67 (dd, J = 16.9, 6.4 Hz, 1H), 2.48 (dd, J = 12.8, 6.8 Hz, 1H), 1.87−1.76 (m, 2H), 1.57−1.48 (m, 1H), 1.47−1.39 (m, 1H), 1.27−1.17 (m, 9H), 1.15 (t, J = 7.1 Hz, 1H), 0.90 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 6.7 Hz, 3H), 0.82 (t, J = 6.9 Hz, 3H), 0.52−0.45 (m, 2H), 0.44−0.36 (m, 1H), 0.18−0.11 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.6, 172.8, 170.3, 136.2, 108.9, 81.6, 78.8, 52.7, 51.6, 43.5, 37.4, 36.3, 33.2, 31.8, 29.9, 29.3, 29.2, 27.1, 26.5, 22.6, 18.3, 18.0, 14.1, 11.8, 3.4, 2.4; MS (ESI) calcd for $C_{26}H_{41}NO_6$ 463.3 (M^+), found 446.5 (M − OH)$^+$, 464.5 (M + H)$^+$, 486.4 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26t. Compound **26t** was prepared according to general procedure A from primary amine **1e**, ketoester **24c**, and itaconic anhydride **5**: yield 343 mg, 68%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.23 (m, 2H), 7.23−7.16 (m, 3H), 5.28 (d, J = 1.8 Hz, 1H), 5.15 (d, J = 15.7 Hz, 1H), 4.66 (d, J = 15.7 Hz, 1H), 3.83 (dd, J = 6.4, 1.8 Hz, 1H), 3.59 (s, 3H), 3.30 (d, J = 8.1 Hz, 1H), 3.09−2.99 (m, 1H), 2.92 (dd, J = 17.1, 6.1 Hz, 1H), 2.81 (dd, J = 17.1, 4.9 Hz, 1H), 2.50 (dd, J = 12.9, 6.4 Hz, 1H), 2.06 (t, J = 12.4 Hz, 1H), 1.75−1.65 (m, 1H), 0.88−0.83 (m, 1H), 0.81 (d, J = 6.7 Hz, 3H), 0.72 (d, J = 6.7 Hz, 3H), 0.57−0.50 (m, 1H), 0.50−0.44 (m, 1H), 0.44−0.37 (m, 1H), 0.22−0.13 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.2, 172.9, 170.6, 137.0, 136.0, 128.5, 127.1, 126.8, 109.9, 81.6, 78.6, 52.8, 51.6, 47.9, 36.8, 36.4, 33.2, 29.9, 18.1, 11.9, 3.9, 2.5; MS (ESI) calcd for $C_{25}H_{31}NO_6$ 441.2 (M^+), found 424.4 (M − OH)$^+$, 442.4 (M + H)$^+$, 464.4 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26u. Compound **26u** was prepared according to general procedure A from primary amine **1f**, ketoester **24c**, and itaconic anhydride **5**: yield 361 mg, 66%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74−6.64 (m, 3H), 5.89 (s, 2H), 5.32 (d, J = 1.9 Hz, 1H), 4.94 (d, J = 15.5 Hz, 1H), 4.67 (d, J = 15.5 Hz, 1H), 3.85 (dd, J = 6.4, 1.9 Hz, 1H), 3.61 (s, 3H), 3.31 (d, J = 8.2 Hz, 1H), 3.07−2.97 (m, 1H), 2.89 (dd, J = 17.1, 6.0 Hz, 1H), 2.79 (dd, J = 17.1, 4.9 Hz, 1H), 2.48 (dd, J = 12.9, 6.5 Hz, 1H), 2.02 (t, J = 12.4 Hz, 1H), 1.81−1.68 (m, 1H), 0.85 (d, J = 6.7 Hz, 3H), 0.77 (d, J = 6.7 Hz, 3H), 0.57−0.44 (m, 2H), 0.44−0.37 (m, 1H), 0.22−0.13 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.0, 172.9, 170.7, 147.9, 146.6, 136.0, 130.9, 120.2, 109.8, 108.2, 107.6, 101.0, 81.6, 78.7, 52.8, 51.6, 47.5, 36.8, 36.4, 33.2, 29.9, 18.3, 18.2,

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11.9, 3.9, 2.5; MS (ESI) calcd for $C_{26}H_{31}NO_8$ 485.2 (M^+), found 486.4 ($M + H)^+$, 508.3 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26v. Compound **26v** was prepared according to general procedure A from primary amine **1g**, ketoester **24c**, and itaconic anhydride **5**: yield 373 mg, 63%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29−7.28 (m, 1H), 6.28 (dd, J = 3.2, 1.8 Hz, 1H), 6.21 (d, J = 3.2 Hz, 1H), 5.52 (d, J = 1.7 Hz, 1H), 5.00 (d, J = 15.8 Hz, 1H), 4.64 (d, J = 15.8 Hz, 1H), 3.91 (dd, J = 6.0, 1.8 Hz, 1H), 3.61 (s, 3H), 3.30 (d, J = 8.0 Hz, 1H), 3.02 (dq, J = 11.9, 6.0 Hz, 1H), 2.77 (d, J = 5.7 Hz, 2H), 2.51 (dd, J = 12.9, 6.8 Hz, 1H), 1.90 (t, J = 12.2 Hz, 1H), 1.80 (h, J = 6.7 Hz, 1H), 0.89 (d, J = 6.8 Hz, 4H), 0.84 (d, J = 6.6 Hz, 4H), 0.50 (dq, J = 7.6, 4.7 Hz, 2H), 0.44−0.37 (m, 1H), 0.19−0.12 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 172.8, 170.4, 150.4, 141.6, 136.2, 110.6, 109.9, 108.3, 81.5, 78.8, 52.8, 51.6, 41.0, 37.0, 36.4, 33.2, 29.8, 18.1, 18.1, 11.7, 3.5, 2.5; MS (ESI) calcd for $C_{23}H_{29}NO_7$ 431.2 (M^+), found 432.4 ($M + H)^+$, 454.4 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26w. Compound **26w** was prepared according to general procedure A from primary amine **1h**, ketoester **24c**, and itaconic anhydride **5**: yield 520 mg, 77%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.39 (s, 1H), 5.33 (s, 1H), 3.91 (dd, J = 6.0, 1.8 Hz, 1H), 3.74 (ddd, J = 13.0, 10.6, 5.4 Hz, 1H), 3.64 (s, 3H), 3.30 (d, J = 8.0 Hz, 1H), 2.97−2.87 (m, 1H), 2.74 (dd, J = 16.8, 5.4 Hz, 1H), 2.64 (dd, J = 16.8, 6.3 Hz, 1H), 2.44 (dd, J = 12.9, 6.6 Hz, 1H), 2.23−2.13 (m, 1H), 2.06−1.97 (m, 1H), 1.95−1.88 (m, 4H), 1.87−1.78 (m, 2H), 1.59−1.52 (m, 2H), 1.52−1.45 (m, 2H), 0.91 (d, J = 6.7 Hz, 4H), 0.88 (d, J = 6.7 Hz, 4H), 0.51−0.46 (m, 2H), 0.44−0.37 (m, 1H), 0.20−0.12 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.5, 172.8, 170.2, 135.9, 134.9, 122.9, 108.5, 81.6, 78.7, 52.7, 51.6, 42.7, 37.2, 36.3, 34.7, 33.3, 29.9, 28.4, 25.2, 22.9, 22.3, 18.4, 18.1, 11.9, 3.7, 2.4; MS (ESI) calcd for $C_{26}H_{37}NO_6$ 459.3 (M^+), found 460.4 ($M + H)^+$, 482.4 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26x. Compound **26x** was prepared according to general procedure A from primary amine **1j**, ketoester **24c**, and itaconic anhydride **5**: yield 436 mg, 61%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 1H), 7.86 (dd, J = 8.0, 1.5 Hz, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.53 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.48 (ddd, J = 8.0, 6.8, 1.2 Hz, 1H), 7.45−7.38 (m, 1H), 7.32 (d, J = 7.0 Hz, 1H), 5.42 (d, J = 16.1 Hz, 1H), 5.36 (d, J = 16.0 Hz, 1H), 5.31 (d, J = 1.8 Hz, 1H), 3.86 (dd, J = 5.9, 1.8 Hz, 1H), 3.32 (s, 3H), 3.29 (d, J = 7.8 Hz, 1H), 3.23−3.13 (m, 1H), 3.04 (dd, J = 17.1, 5.9 Hz, 1H), 2.87 (dd, J = 17.2, 4.8 Hz, 1H), 2.60 (dd, J = 12.9, 6.8 Hz, 1H), 2.12 (t, J = 12.3 Hz, 1H), 1.77−1.66 (m, 1H), 0.95−0.86 (m, 1H), 0.82 (d, J = 6.8 Hz, 3H), 0.73 (d, J = 6.8 Hz, 3H), 0.55−0.45 (m, 2H), 0.47−0.38 (m, 1H), 0.18−0.11 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.3, 172.8, 170.6, 136.3, 133.8, 131.3, 131.1, 128.9, 127.8, 126.4, 125.8, 125.4, 125.0, 123.0, 110.9, 81.5, 78.8, 52.5, 51.7, 45.8, 37.0, 36.6, 33.1, 29.9, 18.2, 17.8, 11.7, 3.3, 2.5; MS (ESI) calcd for $C_{29}H_{33}NO_6$ 491.2 (M^+), found 492.4 ($M + H)^+$, 514.4 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26y. Compound **26y** was prepared according to general procedure A from primary amine **1k**, ketoester **24c**, and itaconic anhydride **5**: yield 450 mg, 60%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 2.0 Hz, 1H), 7.18 (dd, J = 8.4, 2.0 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 5.14−5.08 (m, 2H), 4.75 (d, J = 16.8 Hz, 1H), 3.82 (dd, J = 6.6, 1.9 Hz, 1H), 3.70 (s, 3H), 3.34 (d, J = 8.1 Hz, 1H), 3.04 (dd, J = 17.1, 5.6 Hz, 1H), 3.01−2.93 (m, 1H), 2.77 (dd, J = 17.1, 4.2 Hz, 1H), 2.47 (dd, J = 12.9, 6.0 Hz, 1H), 2.16 (t, J = 12.5 Hz, 1H), 1.79−1.69 (m, 1H), 0.96−0.87 (m, 1H), 0.85 (d, J = 6.7 Hz, 3H), 0.77 (d, J = 6.7 Hz, 3H), 0.61−0.49 (m, 2H), 0.49−0.41 (m, 1H), 0.27−0.18 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.6, 173.0, 170.5, 135.8, 133.4, 133.0, 132.7, 129.2, 128.8, 127.4, 109.5, 81.5, 78.5, 53.0, 51.7, 45.5, 36.3, 36.1, 33.3, 29.7, 18.4, 18.3, 12.0, 4.1, 2.5; MS (ESI) calcd for $C_{25}H_{29}Cl_2NO_6$ 509.1 (M^+), found 492.3 ($M - OH)^+$, 510.3 ($M + H)^+$, 532.3 ($M + Na)^+$.

Tetrahydropyran-fused Piperidinone-Containing Carboxylic Acid 26z. Compound **26z** was prepared according to general procedure A from primary amine **1d**, ketoester **24d**, and itaconic anhydride **5**: yield 351 mg, 65%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.23 (m, 5H), 5.34 (d, J = 1.8 Hz, 1H), 4.59 (d, J = 12.2 Hz, 1H), 4.54 (d, J = 12.2 Hz, 1H), 4.49 (td, J = 6.0, 1.7 Hz, 1H), 4.08 (q, J = 6.6 Hz, 1H), 3.85−3.75 (m, 1H), 3.67 (s, 3H), 3.54 (dd, J = 9.8, 6.4 Hz, 1H), 3.47−3.37 (m, 2H), 3.01−2.91 (m, 1H), 2.76 (dd, J = 16.8, 5.5 Hz, 1H), 2.64 (dd, J = 16.8, 6.2 Hz, 1H), 2.36 (dd, J = 12.7, 6.8 Hz, 1H), 1.64 (t, J = 12.1 Hz, 1H), 1.60−1.51 (m, 1H), 1.49−1.39 (m, 1H), 1.28−1.18 (m, 13H), 0.85 (t, J = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 172.4, 170.2, 137.9, 136.4, 128.5, 127.8, 127.8, 107.6, 74.4, 73.5, 73.3, 72.6, 52.9, 51.1, 43.6, 37.5, 36.2, 31.8, 29.3, 29.3, 29.2, 27.1, 26.5, 22.7, 16.8, 14.2; MS (ESI) calcd for $C_{29}H_{41}NO_7$ 515.3 (M^+), found 516.4 ($M + H)^+$, 538.4 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26aa. Compound **26aa** was prepared according to general procedure A from primary amine **1e**, ketoester **24d**, and itaconic anhydride **5**: yield 257 mg, 63%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.27 (m, 5H), 7.25−7.19 (m, 5H), 5.39 (s, 1H), 5.00 (d, J = 15.6 Hz, 1H), 4.82 (d, J = 15.6 Hz, 1H), 4.50 (d, J = 12.1 Hz, 1H), 4.45 (d, J = 12.1 Hz, 1H), 4.41 (td, J = 6.1, 1.8 Hz, 1H), 4.10 (q, J = 6.4 Hz, 1H), 3.58 (s, 3H), 3.48 (dd, J = 9.7, 6.3 Hz, 1H), 3.29 (dd, J = 9.8, 5.8 Hz, 1H), 3.09−2.99 (m, 1H), 2.85−2.78 (m, 2H), 2.40 (dd, J = 12.8, 6.5 Hz, 1H), 1.80 (t, J = 12.0 Hz, 1H), 1.20 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.4, 172.6, 170.6, 138.0, 136.8, 136.4, 128.6, 128.5, 128.5, 127.8, 127.8, 127.2, 127.1, 126.6, 108.5, 74.3, 73.5, 73.0, 72.7, 52.9, 51.3, 47.8, 37.0, 36.4, 29.4, 17.0; MS (ESI) calcd for $C_{28}H_{31}NO_7$ 493.2 (M^+), found 494.3 ($M + H)^+$, 516.3 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26ab. Compound **26ab** was prepared according to general procedure A from primary amine **1f**, ketoester **24d**, and itaconic anhydride **5**: yield 393 mg, 68%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.23 (m, 5H), 6.75−6.65 (m, 3H), 5.90 (d, J = 1.4 Hz, 1H), 5.90 (d, J = 1.4 Hz, 1H), 5.37 (d, J = 1.9 Hz, 1H), 4.86 (d, J = 15.6 Hz, 1H), 4.74 (d, J = 15.5 Hz, 1H), 4.51 (q, J = 12.1 Hz, 2H), 4.42 (td, J = 6.1, 1.8 Hz, 1H), 4.10 (q, J = 6.4 Hz, 1H), 3.62 (s, 3H), 3.49 (dd, J = 9.8, 6.4 Hz, 1H), 3.32 (dd, J = 9.8, 5.7 Hz, 1H), 3.05−2.95 (m, 1H), 2.81 (dd, J = 5.7, 2.1 Hz, 2H), 2.37 (dd, J = 12.7, 6.5 Hz, 1H), 1.80 (t, J = 12.3 Hz, 1H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 172.5, 170.6, 147.9, 146.7, 138.0, 136.4, 130.6, 128.5, 128.5, 127.8, 127.8, 127.8, 120.4, 108.5, 108.3, 107.8, 101.1, 74.3, 73.5, 73.1, 72.7, 53.0, 51.2, 47.5, 37.0, 36.4, 29.3, 17.0; MS (ESI) calcd for $C_{29}H_{31}NO_9$ 537.2 (M^+), found 538.3 ($M + H)^+$, 560.2 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26ac. Compound **26ac** was prepared according to general procedure A from primary amine **1h**, ketoester **24d**, and itaconic anhydride **5**: yield 555 mg, 70%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.31 (m, 4H), 7.31−7.27 (m, 1H), 5.45−5.41 (m, 1H), 5.40 (d, J = 1.9 Hz, 1H), 4.61 (d, J = 12.2 Hz, 1H), 4.56 (d, J = 12.2 Hz, 1H), 4.50 (td, J = 6.1, 1.7 Hz, 1H), 4.11 (q, J = 6.5 Hz, 1H), 3.82 (ddd, J = 13.5, 10.5, 5.2 Hz, 1H), 3.70 (s, 3H), 3.67−3.59 (m, 1H), 3.57 (dd, J = 9.7, 6.4 Hz, 1H), 3.43 (dd, J = 9.7, 5.8 Hz, 1H), 2.99−2.89 (m, 1H), 2.78 (dd, J = 16.7, 6.1 Hz, 1H), 2.63 (dd, J = 16.7, 5.8 Hz, 1H), 2.36 (dd, J = 12.7, 6.7 Hz, 1H), 2.28−2.17 (m, 1H), 2.10−2.00 (m, 1H), 1.99−1.92 (m, 4H), 1.64 (t, J = 11.5 Hz, 1H), 1.61−1.56 (m, 2H), 1.56−1.48 (m, 2H), 1.22 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 172.4, 170.3, 138.0, 136.2, 134.9, 128.6, 127.9, 127.9, 123.0, 107.6, 74.4, 73.5, 73.2, 72.7, 53.0, 51.2, 42.9, 37.6, 36.3, 34.7, 29.5, 28.6, 25.3, 23.0, 22.4, 17.0; MS (ESI) calcd for $C_{29}H_{37}NO_7$ 511.3 (M^+), found 512.3 ($M + H)^+$, 534.3 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26ad. Compound **26ad** was prepared according to general procedure A from primary amine **1i**, ketoester **24d**, and itaconic anhydride **5**: yield 339 mg, 53%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.28 (m, 4H), 7.28−7.23 (m, 1H), 6.77−6.68 (m, 3H), 5.37 (d, J = 1.9 Hz, 1H), 4.59 (d, J = 12.0 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H), 4.50 (td, J = 6.2, 1.9 Hz, 1H), 4.09 (q, J = 6.5 Hz, 1H), 3.97−3.87 (m, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.78−3.68 (m, 1H), 3.65 (s, 3H), 3.53 (dd, J = 9.7, 6.4 Hz, 1H), 3.38 (dd, J = 9.7, 5.9 Hz, 1H), 3.01−2.91 (m, 1H), 2.88−2.77 (m, 1H), 2.77−2.70 (m, 2H), 2.70−2.64 (m, 1H), 2.37 (dd, J = 12.7, 6.7 Hz, 1H), 1.68 (t, J = 12.1 Hz, 1H), 1.21 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 172.4, 170.1, 149.0, 147.6, 137.9, 136.5, 131.4, 128.5, 127.8, 127.8, 120.6, 112.0,

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111.3, 107.7, 74.4, 73.5, 73.2, 72.6, 55.9, 55.9, 52.9, 51.2, 45.7, 37.2, 36.3, 32.4, 29.2, 16.8; MS (ESI) calcd for $C_{31}H_{37}NO_9$ 567.2 (M^+), found 568.4 $(M + H)^+$, 590.4 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26ae. Compound **26ae** was prepared according to general procedure A from primary amine **1j**, ketoester **24d**, and itaconic anhydride **5**: yield 277 mg, 46%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 8.4 Hz, 1H), 7.86 (dd, J = 7.8, 1.8 Hz, 1H), 7.75 (d, J = 8.3 Hz, 1H), 7.56−7.45 (m, 2H), 7.42−7.35 (m, 1H), 7.27 (d, J = 7.1 Hz, 1H), 7.25−7.20 (m, 3H), 7.17−7.11 (m, 2H), 5.45 (d, J = 16.2 Hz, 1H), 5.34 (d, J = 1.8 Hz, 1H), 5.28 (d, J = 16.1 Hz, 1H), 4.45 (d, J = 12.0 Hz, 1H), 4.40 (d, J = 12.2 Hz, 1H), 4.37 (td, J = 5.5, 3.0 Hz, 1H), 4.04 (q, J = 6.4, 5.8 Hz, 1H), 3.45 (dd, J = 9.8, 6.4 Hz, 1H), 3.29 (s, 3H), 3.28−3.24 (m, 1H), 3.14−3.04 (m, 1H), 2.92 (dd, J = 17.0, 5.7 Hz, 1H), 2.84 (dd, J = 17.0, 5.2 Hz, 1H), 2.42 (dd, J = 12.8, 6.6 Hz, 1H), 1.91 (t, J = 12.3 Hz, 1H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 172.4, 170.3, 137.8, 136.4, 133.8, 131.0, 130.9, 128.8, 128.3, 127.8, 127.7, 127.7, 126.3, 125.7, 125.4, 124.8, 123.0, 108.8, 74.3, 73.3, 73.1, 72.5, 52.5, 51.2, 45.7, 36.7, 36.4, 29.1, 16.8; MS (ESI) calcd for $C_{32}H_{33}NO_7$ 543.2 (M^+), found 544.4 $(M + H)^+$, 566.4 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Carboxylic Acid 26af. Compound **26af** was prepared according to general procedure A from primary amine **1k**, ketoester **24d**, and itaconic anhydride **5**: yield 392 mg, 62%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 2.1 Hz, 1H), 7.34−7.26 (m, 3H), 7.23−7.20 (m, 2H), 7.16 (dd, J = 8.4, 2.1 Hz, 1H), 7.12 (d, J = 8.4 Hz, 1H), 5.15 (d, J = 1.9 Hz, 1H), 5.08 (d, J = 16.9 Hz, 1H), 4.74 (d, J = 16.9 Hz, 1H), 4.50 (d, J = 12.2 Hz, 1H), 4.45 (d, J = 12.1 Hz, 1H), 4.38 (td, J = 5.9, 1.9 Hz, 1H), 4.13 (q, J = 6.4 Hz, 1H), 3.72 (s, 3H), 3.47 (dd, J = 9.7, 6.4 Hz, 1H), 3.30 (dd, J = 9.7, 5.6 Hz, 1H), 3.03−2.89 (m, 2H), 2.76 (dd, J = 16.8, 4.0 Hz, 1H), 2.36 (dd, J = 12.7, 5.8 Hz, 1H), 1.94 (t, J = 12.3 Hz, 1H), 1.24 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.9, 172.7, 170.3, 137.9, 136.2, 133.4, 133.1, 132.4, 129.3, 128.7, 128.5, 127.8, 127.8, 127.8, 127.4, 108.0, 74.3, 73.5, 72.9, 72.6, 53.1, 51.2, 45.9, 36.4, 36.2, 29.2, 17.1; MS (ESI) calcd for $C_{28}H_{29}Cl_2NO_7$ 561.1 (M^+), found 562.4 $(M + H)^+$, 584.3 $(M + Na)^+$.

Enynamide 28a (2-((3*RS*,4a*SR*)-4a-(Ethoxycarbonyl)-2-oxo-1-(3-phenylprop-2-yn-1-yl)-1,2,3,4,4a,5,6,7-octahydroquinolin-3-yl)acetic Acid). Compound **28a** was prepared according to general procedure A from primary amine **27a**, ketoester **2a**, and itaconic anhydride **5** (3.16 g, 80%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35 (2H, m), 7.22−7.19 (3H, m), 5.59 (1H, dd, J = 4.5, 2.5 Hz), 5.02 (1H, d, J = 17.0 Hz), 4.27 (1H, d, J = 17.5 Hz), 4.09 (2H, 7.0 Hz), 2.83 (1H, dd, J = 16.0, 6.0 Hz), 2.71 (1H, m), 2.48 (1H, dd, J = 16.5, 5.5 Hz), 2.29−2.10 (3H, m), 1.65 (1H, br), 1.59 (1H, t, J = 13.0 Hz), 1.47 (1H, dt, J = 14.0, 2.5 Hz), 1.37 (1H, m), 1.15 (3H, t, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.6, 173.7, 169.9, 136.0, 131.8, 128.3, 128.2, 122.8, 109.3, 84.3, 83.4, 61.6, 46.4, 37.0, 36.7, 36.2, 35.2, 34.6, 24.3, 18.5, 14.1; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{23}H_{25}NO_5$ 396.1811, found 396.1818.

Enynamide 28b. Compound **28b** was prepared according to general procedure A from primary amine **27b**, ketoester **2a** and itaconic anhydride **5** (3.19 g, quant): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.47 (1H, dd, J = 5.0, 3.0 Hz), 4.80 (1H, dd, J = 17.0, 2.0 Hz), 4.10 (2H, q, J = 7.0 Hz), 4.05 (1H, dd, J = 17.5, 2.5 Hz), 2.81 (1H, dd, J = 16.5, 6.0 Hz), 2.69 (1H, m), 2.53 (1H, dd, J = 6.0 Hz), 2.33 (1H, dd, J = 13.0, 6.0 Hz), 2.27−2.09 (5H, m), 1.65 (1H, br), 1.59 (1H, t, J = 13.0 Hz), 1.47 (1H, dt, J = 14.0, 2.5 Hz), 1.39−1.29 (1H, m), 1.17(3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.1, 173.7, 169.6, 136.0, 108.8, 78.8, 71.7, 61.6, 46.4, 36.7, 36.6, 36.1, 34.6, 34.2, 24.2, 18.5, 14.1; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{17}H_{22}NO_5$ 320.1498, found 320.1497.

Enynamide 28c. Compound **28c** was prepared according to general procedure A from primary amine **27c**, ketoester **2a** and itaconic anhydride **5** (2.40 g, 72%): ^{1}H NMR (DMSO-d_6, 500 MHz) δ 5.40 (1H, dd, J = 4.5, 3.0 Hz), 4.66 (1H, dd, J = 17.0, 2.5 Hz), 4.11 (2H, q, J = 7.0 Hz), 4.03 (1H, dd, J = 17.0, 2.0 Hz), 2.65 (1H, dd, J = 16.5, 4.5 Hz), 2.50 (1H, m), 2.42 (1H, dd, J = 16.5, 7.0 Hz), 2.23−2.12 (4H, m), 1.17 (3H, s), 1.70 (1H, s, J = 13.0 Hz), 1.65 (1H, m), 1.51 (1H, dt, J = 13.5, 2.0 Hz), 1.26 (1H, m), 1.15 (3H, t, J = 7.0 Hz); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 173.4, 172.7, 168.3, 136.2, 106.5, 78.4, 75.2, 60.8, 45.9, 36.0, 35.8, 35.7, 33.9, 33.5, 23.7, 18.2, 13.9, 3.1; HRMS-EI m/z $[M]^+$ calcd for $C_{18}H_{23}NO_5$ 333.1576, found 333.1569

Enynamide 33a (2-((3*RS*,4a*SR*)-4a-(Ethoxycarbonyl)-2-oxo-1-(prop-2-yn-1-yl)-2,3,4,4a,5,6-hexahydro-1*H*-cyclopenta[*b*]-pyridin-3-yl)acetic Acid). Compound **33a** was prepared according to general procedure A from primary amine **27b**, ketoester **2d**, and itaconic anhydride **5** (1.71 g, 56%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.28 (1H, s), 4.60 (1H, dd, J = 17.5, 2.5 Hz), 4.36 (1H, dd, J = 17.5, 2.5 Hz), 4.18 (2H, m), 2.91−2.81 (2H, m), 2.70 (1H, dd, J = 6.0, 16.5 Hz), 2.59−2.50 (2H, m), 2.43−2.36 (2H, m), 2.21 (1H, t, J = 2.0 Hz), 1.91 (1H, m), 1.73 (1H, t, J = 12.5 Hz), 1.25 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.7, 173.7, 169.3, 140.3, 107.9, 77.9, 71.5, 61.5, 54.2, 36.8, 36.4, 36.3, 35.6, 33.4, 29.0, 14.1; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{16}H_{20}NO_5$ 306.1341, found 306.1339.

Enynamide 33b. Compound **33b** was prepared according to general procedure A from primary amine **27a**, ketoester **2b** and itaconic anhydride **5** (1.62 g, 41%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35 (2H, m), 7.22 (3H, m), 5.78 (1H, t, J = 7.0 Hz), 4.86 (1H, d, J = 17.5 Hz), 4.45 (1H, d, J = 17.5 Hz), 3.70 (3H, s), 2.83 (1H, dd, J = 16.5, 6.5 Hz), 2.71 (1H, m), 2.38 (1H, dd, J = 16.5, 6.0 Hz), 2.23 (1H, m), 2.10−1.98 (4H, m), 1.76−1.61 (5H, m), 1.42−1.34 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.9, 173.9, 170.7, 139.8, 131.8, 128.3, 128.2, 122.7, 116.3, 84.4, 83.4, 52.6, 51.6, 39.5, 36.5, 36.0, 35.7, 35.5, 26.3, 25.3, 24.9; HRMS-EI m/z $[M]^+$ calcd for $C_{23}H_{25}NO_5$ 395.1733, found 395.1734.

Enynamide 33c. Compound **33c** was prepared according to general procedure A from primary amine **27a**, ketoester **2e**, and itaconic anhydride **5** (1.85 g, 50%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34 (2H, m), 7.21 (3H, m), 4.95 (1H, d, J = 2.5 Hz), 4.87 (1H, d, J = 17.0 Hz), 4.62 (1H, d, J = 2.5 Hz), 4.53 (1H, d, J = 17.0 Hz), 4.07 (2H, q, J = 7.5 Hz), 2.98 (1H, m), 2.81 (1H, dd, J = 17.0, 5.5 Hz), 2.53 (1H, dd, J = 17.0, 6.5 Hz), 2.29 (1H, dd, J = 13.5, 6.0 Hz), 1.61 (1H, t, J = 13.0 Hz), 1.43 (3H, s), 1.14 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.3, 173.6, 170.3, 146.0, 131.8, 128.3, 128.1, 122.7, 96.2, 83.9, 83.4, 61.6, 46.5, 36.5, 36.4, 36.1, 35.4, 24.8, 14.0; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{21}H_{24}NO_5$ 370.1654, found 370.1652.

Enynamide 33d. Compound **33d** was prepared according to general procedure A from primary amine **27b**, ketoester **2f**, and itaconic anhydride **5** (1.47 g, 50%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.01 (1H, d, J = 2.0 Hz), 4.76 (1H, d, J = 2.0 Hz), 4.62 (1H, dd, J = 17.5, 1.5 Hz), 4.35 (1H, dd, J = 17.5, 1.5 Hz), 4.20 (2H, m), 4.14 (2H, q, J = 7.0 Hz), 3.14 (1H, m), 2.90 (1H, dd, J = 17.0, 5.5 Hz), 2.61 (1H, dd, J = 17.0, 6.5 Hz), 2.41−2.25 (5H, m), 2.18−2.12 (1H, m), 1.62 (1H, t, J = 13.0 Hz), 1.27 (3H, dt, J = 7.0, 1.0 Hz), 1.26 (3H, dt, J = 7.0, 1.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.7, 172.6, 170.4, 144.4, 97.6, 78.2, 72.0, 72.0, 61.8, 60.7, 49.7, 35.8, 35.7, 34.7, 33.0, 32.9, 29.5, 14.2, 14.0; HRMS-EI m/z $[M]^+$ calcd for $C_{19}H_{25}NO_7$ 379.1631, found 379.1623.

Enynamide 35a (2-((3*SR*,3a*RS*)-3a-(Ethoxycarbonyl)-2-oxo-1-(prop-2-yn-1-yl)-2,3,3a,4,5,6-hexahydro-1*H*-indol-3-yl)acetic Acid). Compound **35a** was prepared according to general procedure A from primary amine **27b**, ketoester **2a**, and maleic anhydride **4** (2.53 g, 83%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.19 (1H, t, J = 7.5 Hz), 4.23 (2H, dq, J = 17.5, 2.5 Hz), 4.13−4.03 (2H, m), 2.96 (1H, t, J = 7.0 Hz), 2.80 (1H, dd, J = 17.5, 6.5 Hz), 2.54 (1H, m), 2.29 (1H, dd, J = 17.5, 8.0 Hz), 2.22−2.07 (3H, m), 1.81 (1H, m), 1.55−1.42 (2H, m), 1.17 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.9, 172.5, 171.1, 137.3, 102.4, 76.8, 71.7, 61.5, 52.0, 47.3, 31.2, 30.3, 29.6, 22.7, 19.5, 14.0; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{16}H_{20}NO_5$ 306.1341, found 306.1339.

Enynamide 35b. Compound **35b** was prepared according to general procedure A from primary amine **27a**, ketoester **2a**, and maleic anhydride **4** (1.95 g, 51%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33 (2H, m), 7.25−7.19 (3H, m), 5.28 (1H, t, J = 3.5 Hz), 4.45 (2H, q, J = 11.5 Hz), 4.05 (2H, m), 2.98 (1H, t, J = 7.0 Hz), 2.79 (1H, dd, J = 17.0, 6.5 Hz), 2.53 (1H, m), 2.31 (1H, dd, J = 17.5, 7.5 Hz), 2.22−2.08 (2H, m), 1.80 (1H, m), 1.56−1.42 (2H, m), 1.13 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.5, 172.8, 171.1, 137.4, 131.8, 128.5,

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128.2, 122.5, 102.7, 83.4, 82.3, 61.5, 52.0, 47.4, 31.3, 30.6, 30.2, 22.8, 19.5, 14.0; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{22}H_{24}NO_5$ 382.1654, found 382.1647.

Enynamide 35c. Compound **35c** was prepared according to general procedure A from primary amine **27b**, ketoester **2b**, and maleic anhydride **4** (2.63 g, 86%):^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.40 (1H, dd, J = 9.0, 4.5 Hz), 4.40 (1H, d, J = 17.0 Hz), 4.20 (1H, d, J = 17.0 Hz), 3.71 (3H, s), 3.09 (1H, t, J = 6.5 Hz), 2.80 (1H, dd, J = 17.0, 6.5 Hz), 2.50 (1H, d, J = 11.5 Hz), 2.40−2.27 (2H, m), 2.21 (1H, s), 2.01−1.94 (2H, m), 1.78−1.60 (3H, m), 1.38 (1H, q, J = 12.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.9, 172.4, 171.1, 141.7, 106.2, 76.8, 71.6, 55.4, 52.3, 48.1, 35.6, 31.6, 30.0, 27.5, 27.2, 26.1; HRMS-EI m/z $[M - H]^+$ calcd for $C_{16}H_{18}NO_5$ 304.1185, found 304.1179.

Enynamide 35d. Compound **35d** was prepared according to general procedure A from primary amine **27a**, ketoester **2b**, and maleic anhydride **4** (1.95 g, 51%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34 (2H, m), 7.23 (3H, m), 5.42 (1H, dd, J = 8.5 4.0 Hz), 4.55 (1H, d, J = 17.5 Hz), 4.32 (1H, d, J = 17.5 Hz), 3.61 (3H, s), 3.02 (1H, t, J = 7.0 Hz), 2.66 (1H, dd, J = 17.0, 7.5 Hz), 2.41 (1H, d, J = 15.0 Hz), 2.34 (1H, dd, J = 17.0, 6.5 Hz), 2.24 (1H, m), 1.94−1.84 (2H, m), 1.67 (2H, m), 1.55 (1H, t, J = 13.5 Hz), 1.29 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.1, 172.8, 171.0, 141.6, 131.7, 128.4, 128.3, 122.4, 106.7, 83.4, 82.1, 55.4, 52.3, 48.2, 35.5, 31.6, 30.9, 27.4, 27.2, 26.1; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{22}H_{24}NO_5$ 382.1654, found 382.1653.

General Procedure B: Au-Catalyzed Enynamide Cycloisomerization. A solution of enyne-containing piperidinones (**28** or **33**, 5.00 mmol) or pyrrolidinones (**35**, 5.00 mmol) in CH_3CN (8.2 mL) was treated with JohnPhos-Au-NCMe·SbF_6 (**31**, 0.15 mmol, 3 mol %). The resulting solution was stirred overnight at room temperature under inert nitrogen atmosphere. Removal of solvent under reduced pressure afforded crude dienamides (**29**, **34**, or **36**), which were used for subsequent hydrogenation without purification.

Cycloisomerization product 29a (2-((2*RS*,10a*SR*)-10a-(Ethoxycarbonyl)-3-oxo-7-phenyl-1,2,3,5,8,9,10,10a-octahydropyrido[3,2,1-*ij*]quinolin-2-yl)acetic Acid). Compound **29a** was prepared according to general procedure B from enynamide **28a** (quantative yield by ^{1}H NMR using mesitylene as an internal standard): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34 (3H, m), 7.20 (2H, m), 5.66 (1H, dd, J = 6.0, 2.5 Hz), 5.22 (1H, dd, J = 17.5, 6.0 Hz), 4.24 (2H, m), 3.88 (1H, d, J = 17.5 Hz), 2.98 (1H, dd, J = 16.5, 6.5 Hz), 2.60 (1H, dd, J = 16.5, 6.0 Hz), 2.34 (1H, d, J = 13.0 Hz), 2.15 (1H, m), 1.89 (1H, dd, J = 18.0, 4.5 Hz), 1.70 (2H, m), 1.55−1.42 (2H, m), 1.30 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.6, 173.9, 169.3, 139.0, 138.7, 131.3, 128.4, 128.0, 127.3, 118.9, 116.8, 61.8, 46.5, 41.3, 37.3, 36.5, 36.1, 34.3, 27.0, 19.0, 14.2; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{23}H_{24}NO_5$ 395.1733, found 395.1724.

Cycloisomerization Product 29b. Compound **29b** was prepared according to general procedure B from enynamide **28b** (quantative yield by ^{1}H NMR using mesitylene as an internal standard): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.70 (2H, m), 5.03 (1H, dd, J = 18.0, 5.5 Hz), 4.20 (2H, m), 3.85 (1H, d, J = 18.0 Hz), 2.89 (1H, dd, J = 16.0, 6.0 Hz), 2.77 (1H, m), 2.54 (1H, dd, J = 16.5, 6.5 Hz), 2.39 (1H, dd, J = 13.0, 6.0 Hz), 2.30 (1H, m), 2.19 (2H, m), 1.70 (1H, m), 1.61 (1H, t, J = 13.0 Hz), 1.47 (2H, m), 1.26 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.9, 173.9, 169.1, 129.8, 125.5, 120.4, 115.1, 61.7, 45.7, 42.2, 37.0, 36.0, 35.9, 34.4, 27.3, 18.8, 14.2; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{17}H_{22}NO_5$ 320.1498, found 320.1506.

Cycloisomerization Product 29c. Compound **29c** was prepared according to general procedure B from enynamide **28c** (90% yield by ^{1}H NMR using mesitylene as an internal standard): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.49 (1H, m), 5.01 (1H, dd, J = 17.0, 6.0 Hz), 4.21 (2H, m), 3.70 (1H, dq, J = 17.5, 2.5 Hz), 2.89 (1H, dd, J = 16.5, 7.0 Hz), 2.78 (1H, m), 2.50 (1H, dd, J = 16.0, 5.0 Hz), 2.43 (1H, dd, J = 6.0, 13.0 Hz), 2.33−2.29 (2H, m), 2.23−2.16 (1H, m), 1.86−1.77 (1H, m), 1.77 (3H, m), 1.60 (1H, t, J = 12.5 Hz), 1.50−1.41 (2H, m), 1.27 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.8, 173.9, 169.4, 129.0, 117.8, 61.5, 46.0, 40.9, 37.7, 37.0, 35.6, 34.6, 29.7, 27.9, 21.6, 18.9, 14.2; HRMS-EI m/z $[M]^+$ calcd for $C_{18}H_{23}NO_5$ 333.1576, found 333.1569.

Cycloisomerization Product 34a (2-((2*RS*,9a*SR*)-9a-(Ethoxycarbonyl)-3-oxo-2,3,5,8,9,9a-hexahydro-1*H*-cyclopenta[*ij*]quinolizin-2-yl)acetic Acid). Compound **34a** (98% yield determined by ^{1}H NMR using mesitylene as an internal standard) was prepared according to the general procedure B: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.94 (1H, dt, J = 2.0, 10.0 Hz), 5.60 (1H, m), 4.85 (1H, dd, J = 19.5, 4.5), 4.16−4.28 (3H, m), 2.89 (2H, m), 2.60 (3H, m), 2.37 (2H, m), 1.89 (1H, dt, J = 18.5, 9.0 Hz), 1.67 (1H, t, J = 12.5 Hz), 1.28 (3H, t, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.3, 173.7, 168.5, 134.6, 121.2, 120.5, 116.0, 61.6, 53.0, 44.1, 36.6, 36.4, 36.3, 35.0, 29.8, 14.2; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{16}H_{20}NO_5$ 306.1341, found 306.1343.

Cycloisomerization Product 34b. Compound **34b** (75% yield determined by ^{1}H NMR using mesitylene as an internal standard) was prepared according to the general procedure B: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37−7.29 (3H, m), 7.18 (2H, m), 5.71 (1H, dd, J = 5.5, 4.5 Hz), 4.86 (1H, dd, J = 15.5, 5.5 Hz), 4.00 (1H, dd, J = 15.5, 4.0 Hz), 3.87 (3H, s), 2.97−2.86 (2H, m), 2.45 (1H, dd, J = 16.0, 6.0 Hz), 2.20 (3H, m), 2.02 (1H, m), 1.86−1.66 (5H, m), 1.35 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.0, 174.0, 171.1, 142.2, 139.1, 136.3, 128.2, 128.1, 127.3, 126.0, 117.2, 52.7, 51.9, 40.2, 40.0, 36.6, 35.7, 35.5, 29.5, 26.6, 25.6; HRMS-EI m/z $[M]^+$ calcd for $C_{23}H_{25}NO_5$ 395.1733, found 395.1736.

Cycloisomerization Product 34c. Compound **34c** (90% yield determined by ^{1}H NMR using mesitylene as an internal standard) was prepared according to the general procedure B: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.42−7.29 (5H, m), 5.88 (1H, m), 5.74 (1H, d, J = 1.5 Hz), 5.05 (1H, dd, J = 18.0, 5.5 Hz), 4.31−4.20 (3H, m), 3.09 (1H, m), 2.95 (1H, dd, J = 16.5, 6.0 Hz), 2.60 (1H, dd, J = 17.0, 6.5 Hz), 2.43 (1H, dd, J = 13.5, 6.0 Hz), 1.73 (1H, t, J = 13.0 Hz), 1.58 (3H, s), 1.29 (3H, t, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.3, 173.6, 169.7, 139.4, 138.5, 134.2, 128.6, 127.7, 125.5, 115.8, 106.7, 61.8, 45.9, 42.8, 36.6, 36.2, 36.2, 24.0, 14.1; HRMS-ESI m/z $[M]^+$ calcd for $C_{21}H_{23}NO_5$ 369.1576, found 369.1585.

Cycloisomerization Product 34d. Compound **34d** (quantitative yield determined by ^{1}H NMR using mesitylene as an internal standard) was prepared according to the general procedure B: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.95 (1H, m), 5.68 (1H, m), 5.48 (1H, d, J = 5.5 Hz), 4.55 (1H, dd, J = 17.5, 4.0 Hz), 4.40 (1H, d, J = 17.5 Hz), 4.22 (2H, m), 4.15 (2H, q, J = 7.0 Hz), 3.13 (1H, m), 2.90 (1H, dd, J = 17.0, 6.5 Hz), 2.54 (1H, dd, J = 16.5, 6.0 Hz), 2.39 (2H, t, J = 8.0 Hz), 2.31 (2H, m), 2.16−2.10 (1H, m), 1.58 (1H, t, J = 13.0 Hz), 1.30−1.25 (6H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.9, 172.7, 172.6, 170.5, 136.8, 122.2, 120.5, 107.3, 61.9, 60.8, 48.9, 41.6, 36.1, 35.8, 32.9, 32.8, 29.6, 14.2, 14.0; HRMS-EI m/z $[M - H]^+$ calcd for $C_{19}H_{24}NO_7$ 378.1553, found 378.1558.

Cycloisomerization Product 36a (2-((1*SR*,9a*RS*)-9a-(Ethoxycarbonyl)-2-oxo-2,4,7,8,9,9a-hexahydro-1*H*-pyrrolo[3,2,1-*ij*]quinolin-1-yl)acetic Acid). Compound **36a** (quantitative yield determined by ^{1}H NMR using mesitylene as an internal standard) was prepared according to the general procedure B: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.81 (1H, dq, J = 10.0, 1.5 Hz), 5.51 (1H, ddd, J = 9.5, 5.0, 2.0 Hz), 4.72 (1H, dd, J = 17.5, 5.0 Hz), 4.2 (2H, m), 4.1 (1H, d, J = 17.5), 3.01−2.93 (2H, m), 2.65 (1H, dt, J = 12.5, 3.0 Hz), 2.37 (1H, dd, J = 17.0, 8.0 Hz), 2.22 (1H, dd, J = 17.5, 6.5 Hz), 2.07 (1H, m), 1.92 (1H, m), 1.57 (1H, m), 1.46 (1H, td, J = 13.0, 2.5 Hz), 1.28 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.6, 173.0, 170.7, 133.5, 124.8, 117.9, 109.0, 61.5, 51.8, 47.3, 41.3, 31.3, 30.2, 24.3, 19.8, 13.9; HRMS-ESI m/z $[M - H]^+$ calcd for $C_{16}H_{18}NO_5$ 304.1185, found 304.1186.

Cycloisomerization Product 36b. Compound **36b** (quantitative yield determined by ^{1}H NMR using mesitylene as an internal standard) was prepared according to the general procedure B: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38−7.30 (3H, m), 7.21 (2H, m), 5.41 (1H, dd, J = 5.0, 2.5 Hz), 4.83 (1H, dd, J = 17.5, 5.5 Hz), 4.84 (3H, m), 3.08 (1H, t, J = 7.5 Hz), 2.96 (1H, dd, J = 17.0, 6.5 Hz), 2.65 (1H, d, J = 10.5 Hz), 2.43 (1H, dd, J = 17.5, 8.0 Hz), 2.09 (1H, dd, J = 16.5, 6.0 Hz), 1.89 (2H, m), 1.51 (2H, m), 1.32 (3H, 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.4, 173.1, 170.8, 138.9, 138.2, 134.1, 128.3, 128.0, 127.3, 116.8, 109.8, 61.8, 52.5, 47.4, 41.2, 31.5, 29.9, 23.9, 20.2,

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14.1; HRMS-ESI m/z $[M - H]^+$ calcd for $C_{22}H_{22}NO_5$ 380.1498, found 380.1494.

Cycloisomerization Product 36c. Compound **36c** (72% yield determined by ^1H NMR using mesitylene as an internal standard) was prepared according to the general procedure B: ^1H NMR ($CDCl_3$, 500 MHz) δ 5.76 (1H, dt, J = 10.0, 2.0 Hz), 5.46 (1H, m), 4.56 (1H, dd, J = 18.0, 4.5 Hz), 4.22 (1H, dq, J = 18.0 2.5 Hz), 3.76 (3H, s), 3.05 (1H, t, J = 6.5 Hz), 2.80 (1H, dd, J = 17.0, 7.0 Hz), 2.52 (1H, m), 2.40 (1H, dd, J = 17.5, 7.0 Hz), 2.21−2.10 (2H, m), 1.94 −1.91 (1H, m), 1.79−1.74 (1H, m), 1.60−1.70 (2H, m), 1.36−1.45 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.3, 173.1, 170.9, 136.2, 128.2, 116.7, 113.1, 55.8, 52.5, 47.5, 42.0, 35.7, 31.9, 31.9, 27.3, 26.9; HRMS-EI m/z $[M - H]^+$ calcd for $C_{16}H_{18}NO_5$ 304.1185, found 304.1187.

Cycloisomerization Product 36d. Compound **36d** (77% yield determined by ^1H NMR using mesitylene as an internal standard) was prepared according to the general procedure B: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34 (3H, m), 7.18 (2H, m), 5.40 (1H, dd, J = 5.0, 2.5 Hz), 4.71 (1H, dd, J = 17.5, 5.5 Hz), 4.24 (1H, d, J = 17.0 Hz), 3.79 (3H, s), 3.16 (1H, t, J = 6.5 Hz), 2.84 (1H, dd, J = 17.0, 7.0 Hz), 2.56 (1H, m), 2.43 (1H, 17.0, 7.0 Hz), 2.18 (1H, dd, J = 15.5, 6.5 Hz), 1.94−1.66 (5H, m), 1.40 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.5, 173.1, 171.0, 140.3, 139.8, 138.4, 128.2, 127.3, 115.6, 114.2, 56.3, 52.5, 47.8, 41.5, 35.3, 31.8, 28.2, 27.3, 26.7; HRMS-ESI m/z $[M - H]^+$ calcd for $C_{22}H_{22}NO_5$ 380.1498, found 380.1505.

General Procedure C: Diene Hydrogenations. To a round-bottom flask was added 10% Pd/C (0.30 mmol, 0.10 equiv) and the corresponding crude acid solution (prepared from general procedure B, 3.00 mmol, 1.00 equiv) in EtOH (30.0 mL). The mixture was stirred overnight at room temperature under H_2 atmosphere (1 atm). The mixture was filtered over Celite and concentrated under reduced pressure. The product was isolated after purification by Combi-flash column chromatography (DCM:(EtOAc + 1% HCOOH) = 95:5 to 30:70).

Tricyclic Carboxylic Acid 37 (2-((2*RS*,10a*SR*)-10a-(ethoxycarbonyl)-3-oxo-1,2,3,5,6,7,8,9,10,10a-decahydropyrido[3,2,1-*ij*]-quinolin-2-yl)acetic Acid). Compound **37** (771 mg, 80%) was prepared according to the general procedure C: ^1H NMR ($CDCl_3$, 500 MHz) δ 4.62 (1H, dt, J = 13.0, 3.5 Hz), 4.24−4.13 (2H, m), 2.97 (1H, dt, J = 12.0, 2.5 Hz), 2.82 (1H, dd, J = 16.0, 7.5), 2.36 (1H, dd, J = 13.0, 5.5 Hz), 2.27 (1H, m), 2.20−2.13 (1H, m), 2.09 (2H, m), 2.01−1.90 (2H, m), 1.80−1.71 (2H, m), 1.61 (1H, t, J = 13.0 Hz), 1.54−1.39 (2H, m), 1.26 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.1, 173.9, 169.4, 132.1, 130.1, 118.0, 116.2, 61.7, 46.1, 41.4, 37.5, 36.5, 35.9, 34.1, 25.2, 18.8, 18.1, 14.2; HRMS-ESI m/z $[M]^+$ calcd for $C_{17}H_{23}NO_5$ 321.1576, found 321.1584.

Tricyclic Carboxylic Acid 38. Compound **38** (645 mg, 70%) was prepared according to the general procedure C: ^1H NMR (CD_3CN, 500 MHz) δ 4.18−4.08 (2H, m), 3.85 (1H, m), 3.56 (1H, br), 3.31−3.26 (1H, m), 2.73−2.65 (2H, m), 2.57−2.52 (1H, m), 2.48−2.41 (2H, m), 2.29−2.22 (2H, m), 2.09 (2H, m), 1.97 (1H, quintet, J = 2.5 Hz), 1.88−1.78 (3H, m), 1.69 (1H, t, J = 12.5 Hz), 1.21 (3H, t, J = 7.0 Hz); ^{13}C NMR (CD_3CN, 125 MHz) δ 174.8, 174.0, 168.6, 133.5, 118.8, 61.3, 53.4, 40.1, 36.4, 35.6, 35.3, 35.2, 32.1, 22.4, 21.3, 13.4; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{16}H_{22}NO_5$ 308.1498, found 308.1503.

Tricyclic Carboxylic Acid 39. compound **39** (882 mg, 77%) was prepared according to the general procedure C: ^1H NMR ($CDCl_3$, 500 MHz) δ 5.19 (1H, t, J = 4.0 Hz), 4.23−4.13 (4H, m), 3.87 (1H, m), 3.65 (1H, m), 3.08 (1H, m), 2.85 (1H, dd, J = 16.0, 7.0 Hz), 2.56 (1H, dd, J = 16.0, 5.0 Hz), 2.38−2.24 (4H, m), 2.19 (2H, m), 2.14−2.08 (1H, m), 1.81 (2H, m), 1.59 (1H, t, J = 13.0 Hz), 1.28 (6H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.3, 173.0, 172.7, 170.1, 135.8, 109.1, 61.7, 60.8, 48.6, 41.1, 36.8, 35.5, 33.2, 32.3, 29.4, 22.6, 21.5, 14.2, 14.1; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{19}H_{28}NO_7$ 382.1866, found 382.1864.

Tricyclic Carboxylic Acid 40. Compound **40** (600 mg, 65%) was prepared according to the general procedure C: ^1H NMR ($CDCl_3$, 500 MHz) δ 4.22−4.11 (2H, m), 3.90 (1H, m), 3.31 (1H, dt, J = 10.5, 3.5 Hz), 2.96 (1H, t, J = 7.5 Hz), 2.84 (1H, dd, J = 17.0, 7.5 Hz), 2.61 (1H, t, J = 12.0, 2.5 Hz), 2.42 (1H, dd, J = 16.5, 6.5 Hz), 2.21−1.87 (6H, m), 1.71−1.80 (1H, m), 1.61−1.44 (2H, m), 1.26 (3H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.6, 172.5, 171.3, 131.4, 111.2, 61.4, 51.4, 48.0, 38.9, 32.0, 30.5, 26.8, 25.4, 20.9, 19.9, 14.1; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{16}H_{22}NO_5$ 308.1498, found 308.1507.

Tricyclic Carboxylic Acid 41. Compound **41** (645 mg, 70%) was prepared according to the general procedure C: ^1H NMR ($CDCl_3$, 500 MHz) δ 3.79 (1H, m), 3.73 (3H, s), 3.30 (1H, m), 2.98 (1H, dd, J = 9.0, 5.5 Hz), 2.68 (1H, dd, J = 16.5, 9.0 Hz), 2.50−2.42 (2H, m), 2.20−2.08 (3H, m), 2.00 (1H, m), 1.93−1.88 (2H, m), 1.78−1.69 (3H, m), 1.59 (1H, dt, J = 13.0, 3.5 Hz), 1.38 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.6, 172.4, 171.2, 134.2, 116.8, 55.4, 52.3, 48.2, 38.8, 35.5, 33.2, 32.4, 29.2, 27.3, 26.7, 20.5; HRMS-ESI m/z $[M]^+$ calcd for $C_{16}H_{21}NO_5$ 307.1420, found 307.1422.

General Procedure D: Automated Library Synthesis. A of solution of a carboxylic acid (**7**, **8**, **26**, or **36**, 1.25 mmol) in 25 mL of $CDCl_3$ was treated with CDI (**16**, 212.8 mg, 1.31 mmol, 1.05 equiv). The reaction was stirred at room temperature until NMR indicated complete conversion of the carboxylic acid to the corresponding acylimidazole, which typically took 2−4 h. Using a Perkin-Elmer Multiprobe II liquid handler, the resulting solution was distributed into 24 1-dram glass vials, delivering 0.95 mL of the above solution into each vial. For reactions involving the coupling with secondary amines, the glass vials were precharged with imidazole hydrochloride (9.9 mg, 0.095 mmol, 2 equiv). For each vial, a solution of one of the 24 amines **11** (2 M, 2.7 equiv) in 0.065 mL of chloroform was added. The resulting reaction mixtures were capped and agitated on an orbital shaker at room temperature for 48 h. The vials were then returned to the deck of the liquid handler and treated with 1.9 mL of 1.2 N HCl solution followed by eight cycles of rapid aspiration and dispensing to ensure thorough mixing. After complete phase separation, which can be accelerated by centrifugation for 10 min at 500 g (versus ∼2 h without centrifugation), the bottom layers were retrieved by the liquid hander and transferred to 24 empty barcoded, preweighed one-dram vials. The vials containing the product solutions were placed in a GeneVac centrifugal evaporator to remove solvent, and were weighed using an automated Mettler Toledo weigher to determine the yield of each final product. Each of the tips used for the above material transfer was then washed in another vial containing 0.5 mL of MeOH in order to dissolve the residual material present on the tip, which provided sufficient amount of material for purity analysis of each final compound using LC−MS equipped with an autosampler.

Pyrrolidinone-Containing Amide 12a ((3*SR*,3a*RS*)-Ethyl 1-(4-Methoxybenzyl)-2-oxo-3-(2-oxo-2-(prop-2-yn-1-ylamino)-ethyl)-2,3,3a,4,5,6-hexahydro-1*H*-indole-3a-carboxylate). Compound **12a** (18.85 mg, 93%) was prepared according to the general procedure D: 93% yield; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25−7.17 (m, 2H), 6.87−6.78 (m, 2H), 4.99 (t, J = 3.7 Hz, 1H), 4.77 (d, J = 15.2 Hz, 1H), 4.44 (d, J = 15.1 Hz, 1H), 4.12−3.95 (m, 3H), 3.78 (s, 3H), 2.99 (dd, J = 7.8, 5.6 Hz, 1H), 2.65 (dd, J = 15.1, 7.8 Hz, 1H), 2.56 (dt, J = 12.4, 3.1 Hz, 1H), 2.26−2.17 (m, 2H), 2.17−2.00 (m, 2H), 1.85−1.74 (m, 1H), 1.57−1.36 (m, 2H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 171.4, 170.6, 159.1, 138.2, 129.2, 128.1, 113.9, 102.0, 79.7, 71.5, 61.4, 55.4, 52.3, 48.5, 43.8, 33.4, 30.3, 29.4, 22.9, 19.5, 14.2; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{24}H_{29}N_2O_5$ 425.2076, found 425.2066.

Pyrrolidinone-Containing Amide 12b. Compound **12b** (18.02 mg, 85%) was prepared according to the general procedure D: ^1H NMR (500 MHz, $CDCl_3$) δ 7.20−7.11 (m, 2H), 6.87−6.81 (m, 2H), 6.76 (t, J = 5.7 Hz, 1H), 5.08 (dd, J = 8.6, 4.4 Hz, 1H), 4.73 (d, J = 15.4 Hz, 1H), 4.52 (d, J = 15.4 Hz, 1H), 3.78 (s, 3H), 3.62 (s, 3H), 3.33−3.17 (m, 2H), 3.07 (dd, J = 8.2, 4.8 Hz, 1H), 2.56 (dd, J = 15.0, 8.2 Hz, 1H), 2.50−2.43 (m, 1H), 2.20−2.07 (m, 2H), 1.92−1.82 (m, 1H), 1.82−1.70 (m, 1H), 1.70−1.61 (m, 1H), 1.61−1.45 (m, 3H), 1.41−1.21 (m, 3H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 171.5, 170.6, 158.9, 142.5, 128.5, 127.9, 113.9, 105.8, 55.7, 55.4, 52.1, 49.3, 43.8, 39.6, 35.2, 33.9, 31.7, 27.4, 27.2, 26.2, 20.2, 13.9; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{25}H_{35}N_2O_5$ 443.2546, found 443.2538.

Pyrrolidinone-Containing Amide 12c. Compound **12c** (19.75 mg, 88%) was prepared according to the general procedure D: ^1H

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NMR (500 MHz, $CDCl_3$) δ 7.30−7.22 (m, 3H), 7.19−7.14 (m, 2H), 7.08 (t, J = 6.2 Hz, 1H), 5.15 (dd, J = 8.7, 4.4 Hz, 1H), 3.76 (ddd, J = 13.6, 10.0, 6.3 Hz, 1H), 3.70 (s, 3H), 3.54 (ddd, J = 13.7, 9.9, 5.5 Hz, 1H), 3.48−3.29 (m, 4H), 3.27−3.15 (m, 2H), 3.14−3.08 (m, 1H), 2.85 (ddd, J = 13.5, 10.1, 5.6 Hz, 1H), 2.77 (ddd, J = 13.5, 10.0, 6.3 Hz, 1H), 2.53 (dd, J = 15.4, 7.3 Hz, 1H), 2.50−2.44 (m, 1H), 2.41 (t, J = 8.1 Hz, 2H), 2.30−2.18 (m, 1H), 2.12 (dd, J = 15.4, 6.2 Hz, 1H), 2.09−2.00 (m, 2H), 1.99−1.84 (m, 2H), 1.82−1.63 (m, 5H), 1.56 (ddd, J = 13.7, 12.2, 3.4 Hz, 1H), 1.38−1.25 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 173.7, 171.5, 170.5, 142.9, 137.2, 132.4, 130.3, 128.7, 103.9, 55.5, 52.3, 48.7, 47.5, 41.5, 39.8, 36.2, 35.5, 33.7, 31.7, 31.1, 27.5, 27.4, 26.6, 26.2, 18.1. MS(ESI) calcd for $C_{28}H_{36}ClN_3O_5$ 529.23 (M^+), found 530.18 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12d. Compound **12d** (22.01 mg, 72%) was prepared according to the general procedure D: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.20 (m, 6H), 5.71 (ddt, J = 17.3, 10.3, 5.1 Hz, 1H), 5.22−5.15 (m, 3H), 4.86 (t, J = 9.2 Hz, 1H), 4.48 (dd, J = 14.8, 5.9 Hz, 1H), 4.41 (dd, J = 14.8, 5.5 Hz, 2H), 4.19−4.10 (m, 3H), 3.04 (dd, J = 8.4, 4.6 Hz, 1H), 2.71 (dd, J = 15.3, 8.4 Hz, 1H), 2.61 (ddd, J = 14.4, 6.4, 2.2 Hz, 1H), 2.22 (dd, J = 15.3, 4.6 Hz, 1H), 2.07 (ddd, J = 9.1, 6.8, 3.5 Hz, 2H), 1.77−1.57 (m, 5H), 1.54−1.38 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 171.6, 170.6, 140.4, 138.4, 131.0, 128.7, 127.9, 127.4, 117.0, 104.1, 61.5, 54.7, 48.0, 43.9, 42.8, 34.7, 27.8, 26.5, 23.1, 22.6, 14.2; MS(ESI) calcd for $C_{25}H_{32}N_2O_4$ 424.24 (M^+), found 425.34 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12e. Compound **12e** was prepared according to the general procedure D from carboxylic acid **7b** and amine **11x**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (td, J = 7.5, 1.5 Hz, 2H), 7.29−7.18 (m, 5H), 6.89−6.82 (m, 2H), 4.98 (d, J = 3.8 Hz, 1H), 4.81 (dd, J = 15.2, 2.9 Hz, 2H), 4.47 (dd, J = 15.2, 7.9 Hz, 1H), 4.16−3.90 (m, 2H), 3.80 (s, 3H), 3.40 (dd, J = 8.6, 4.2 Hz, 1H), 3.22−3.10 (m, 1H), 3.01 (m, 1H), 2.81−2.59 (m, 2H), 2.33 (ddd, J = 17.0, 8.7, 2.4 Hz, 1H), 2.19−2.01 (m, 2H), 1.96−1.86 (m, 1H), 1.86−1.75 (m, 1H), 1.75−1.43 (m, 4H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 174.4, 172.1, 172.0, 168.6, 168.6, 158.9, 145.4, 145.3, 138.7, 129.2, 129.1, 128.7, 128.5, 126.9, 126.6, 113.9, 113.9, 101.2, 61.1, 61.1, 55.4, 52.5, 52.4, 47.9, 47.9, 46.3, 46.2, 43.7, 43.0, 43.0, 43.0, 43.0, 33.8, 33.7, 33.0, 33.0, 31.0, 30.2, 30.1, 22.9, 22.9, 19.8, 19.8, 14.3, 14.3. MS(ESI) calcd for $C_{32}H_{38}N_2O_5$ 530.28 (M^+), found 531.48 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12f. Compound **12f** was prepared according to the general procedure D from carboxylic acid **7e** and amine **11u**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20−7.14 (m, 2H), 6.83 (d, J = 8.6 Hz, 2H), 5.05 (dd, J = 8.9, 4.3 Hz, 1H), 4.73 (d, J = 15.6 Hz, 1H), 4.55 (d, J = 15.5 Hz, 1H), 3.78 (s, 3H), 3.63 (s, 3H), 3.62−3.57 (m, 1H), 3.57−3.50 (m, 1H), 3.45−3.33 (m, 2H), 2.91 (dd, J = 16.7, 4.6 Hz, 1H), 2.64−2.56 (m, 1H), 2.31 (dd, J = 16.7, 7.3 Hz, 1H), 2.15−2.05 (m, 1H), 1.92−1.79 (m, 2H), 1.70−1.51 (m, 7H), 1.30−1.18 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 172.0, 168.2, 158.7, 143.1, 128.4, 128.3, 128.1, 113.9, 113.8, 104.9, 55.7, 55.2, 51.9, 48.5, 46.5, 43.6, 43.2, 35.8, 30.3, 27.6, 27.4, 26.3, 26.1, 25.5, 24.6; MS(ESI) calcd for $C_{26}H_{34}N_2O_5$ 454.25 (M^+), found 455.41 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12g. Compound **12g** was prepared according to the general procedure D from carboxylic acid **7a** and amine **11d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.73 (t, J = 5.5 Hz, 1H), 5.81−5.69 (m, 1H), 5.27 (d, J = 17.2 Hz, 1H), 5.19 (dd, J = 10.3, 1.5 Hz, 1H), 5.02 (t, J = 3.7 Hz, 1H), 4.28 (dd, J = 15.9, 5.3 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 4.00−3.89 (m, 1H), 3.33−3.18 (m, 2H), 2.97 (dd, J = 7.6, 5.8 Hz, 1H), 2.63−2.52 (m, 2H), 2.27−2.06 (m, 3H), 1.89−1.79 (m, 1H), 1.69−1.58 (m, 1H), 1.57−1.36 (m, 4H), 1.23 (t, J = 7.1 Hz, 3H), 0.91 (d, J = 6.6 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 171.6, 170.7, 138.3, 131.6, 117.7, 101.7, 61.4, 52.4, 48.6, 43.0, 38.4, 38.2, 33.6, 30.2, 26.0, 22.9, 22.6, 22.6, 19.6, 14.3; MS(ESI) calcd for $C_{21}H_{32}N_2O_4$ 376.24 (M^+), found 377.39 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12h. Compound **12h** was prepared according to the general procedure D from carboxylic acid **7a** and amine **11e**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25−7.17 (m, 2H), 6.97 (dd, J = 3.4, 1.2 Hz, 1H), 6.93 (dd, J = 5.1, 3.4 Hz, 1H), 5.78−5.68 (m, 1H), 5.25 (d, J = 17.2 Hz, 1H), 5.17 (d, J = 10.3 Hz, 1H), 5.01 (t, J = 3.7 Hz, 1H), 4.67−4.53 (m, 2H), 4.26 (dd, J = 15.8, 5.3 Hz, 1H), 4.14−4.06 (m, 2H), 3.97−3.89 (m, 1H), 2.98 (dd, J = 7.6, 5.8 Hz, 1H), 2.63 (dd, J = 15.1, 7.7 Hz, 1H), 2.55 (dt, J = 12.5, 3.0 Hz, 1H), 2.24−2.15 (m, 1H), 2.15−2.05 (m, 1H), 1.87−1.78 (m, 1H), 1.58−1.39 (m, 2H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 171.5, 170.5, 141.1, 138.2, 131.6, 126.9, 126.0, 125.1, 117.7, 101.8, 61.5, 52.4, 48.4, 43.0, 38.5, 33.5, 30.3, 22.9, 19.6, 14.2; MS(ESI) calcd for $C_{21}H_{26}N_2O_4S$ 402.16 (M^+), found 403.33 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12i. Compound **12i** was prepared according to the general procedure D from carboxylic acid **7h** and amine **11f**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15−7.08 (m, 3H), 6.90−6.77 (m, 5H), 4.80 (dd, J = 10.1, 8.2 Hz, 1H), 4.67 (d, J = 15.5 Hz, 1H), 4.59 (d, J = 15.5 Hz, 1H), 4.39 (d, J = 5.6 Hz, 2H), 4.15−4.01 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.77 (s, 3H), 3.08 (dd, J = 8.4, 4.6 Hz, 1H), 2.72 (dd, J = 15.2, 8.4 Hz, 1H), 2.58 (ddd, J = 14.6, 6.7, 2.3 Hz, 1H), 2.22 (dd, J = 15.2, 4.6 Hz, 1H), 2.05−1.91 (m, 2H), 1.77−1.49 (m, 3H), 1.39−1.23 (m, 2H), 1.17 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 171.5, 170.5, 158.9, 149.2, 148.4, 140.2, 131.1, 128.3, 127.7, 120.1, 114.0, 111.3, 111.2, 104.6, 61.5, 56.0, 56.0, 55.4, 54.6, 48.0, 43.7, 43.6, 37.5, 34.8, 27.8, 26.4, 23.1, 22.5, 14.2; MS(ESI) calcd for $C_{32}H_{40}N_2O_7$ 564.28 (M^+), found 565.4 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12j. Compound **12j** was prepared according to the general procedure D from carboxylic acid **7h** and amine **11g**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (t, J = 5.9 Hz, 1H), 7.57−7.48 (m, 3H), 7.47−7.41 (m, 1H), 7.16−7.10 (m, 2H), 6.86−6.79 (m, 2H), 4.83 (dd, J = 10.3, 8.1 Hz, 1H), 4.69 (d, J = 15.4 Hz, 1H), 4.60 (d, J = 15.5 Hz, 1H), 4.54 (dd, J = 15.2, 6.0 Hz, 1H), 4.46 (dd, J = 15.2, 5.8 Hz, 1H), 4.17−4.02 (m, 2H), 3.78 (s, 3H), 3.04 (dd, J = 8.8, 4.1 Hz, 1H), 2.77 (dd, J = 15.2, 8.8 Hz, 1H), 2.58 (ddd, J = 14.7, 6.3, 2.9 Hz, 1H), 2.25 (dd, J = 15.2, 4.1 Hz, 1H), 2.08−1.93 (m, 2H), 1.76−1.49 (m, 5H), 1.43−1.23 (m, 1H), 1.17 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 171.4, 171.0, 159.0, 140.0, 139.7, 131.2 (q, 4JC−F = 1.3 Hz), 129.2, 128.3, 127.6, 131.0 (q, $^2J_{C-F}$ = 32.2 Hz), 124.4 (q, $^3J_{C-F}$ = 3.8 Hz), 124.2 (q, $^3J_{C-F}$ = 3.8 Hz), 124.2 (q, $^1J_{C-F}$ = 273.4 Hz), 114.0, 105.0, 61.5, 55.4, 54.8, 47.9, 43.6, 43.3, 37.1, 34.7, 27.7, 26.5, 23.1, 22.5, 14.2; MS(ESI) calcd for $C_{31}H_{35}F_3N_2O_5$ 572.25 (M^+), found 573.37 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12k. Compound **12k** was prepared according to the general procedure D from carboxylic acid **7i** and amine **11r**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (dd, J = 1.8, 0.9 Hz, 1H), 7.29−7.23 (m, 2H), 7.22−7.15 (m, 2H), 7.07 (dd, J = 3.5, 0.9 Hz, 1H), 6.51 (dd, J = 3.5, 1.8 Hz, 1H), 4.86 (dd, J = 10.7, 7.5 Hz, 1H), 4.23−4.07 (m, 2H), 3.94−3.63 (m, 7H), 3.61−3.48 (m, 2H), 3.48−3.41 (m, 1H), 3.18 (dd, J = 8.3, 4.7 Hz, 1H), 2.92−2.79 (m, 2H), 2.75−2.63 (m, 2H), 2.34 (dd, J = 16.6, 8.4 Hz, 1H), 2.15−2.07 (m, 1H), 2.05−1.94 (m, 1H), 1.81−1.72 (m, 1H), 1.72−1.50 (m, 4H), 1.50−1.39 (m, 1H), 1.40−1.30 (m, 1H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 172.2, 169.2, 159.3, 147.7, 144.1, 141.4, 136.8, 132.5, 130.6, 128.7, 117.3, 111.6, 102.2, 61.3, 54.2, 48.7, 45.5, 42.1, 41.3, 39.5, 31.9, 31.8, 28.4, 25.9, 23.2, 23.0, 14.3; MS(ESI) calcd for $C_{32}H_{38}ClN_3O_6$ 595.24 (M^+), found 596.34 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12l. Compound **12l** was prepared according to the general procedure D from carboxylic acid **7i** and amine **11o**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.23 (m, 2H), 7.19−7.13 (m, 2H), 6.87 (t, J = 5.5 Hz, 1H), 6.11 (d, J = 3.1 Hz, 1H), 5.90 (dd, J = 3.1, 1.3 Hz, 1H), 4.86 (dd, J = 10.0, 8.3 Hz, 1H), 4.43 (dd, J = 15.4, 5.8 Hz, 1H), 4.36−4.28 (m, 1H), 4.20−4.07 (m, 2H), 3.76 (dt, J = 13.9, 8.0 Hz, 1H), 3.66 (dt, J = 14.1, 7.1 Hz, 1H), 2.96 (dd, J = 8.0, 5.2 Hz, 1H), 2.83 (t, J = 7.7 Hz, 2H), 2.64−2.53 (m, 2H), 2.27 (s, 3H), 2.18−2.03 (m, 3H), 1.71−1.58 (m, 5H), 1.48−1.37 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 171.6, 170.3, 151.9, 149.5, 140.7, 136.9, 132.6, 130.4, 128.8, 108.3, 106.4, 103.0, 61.5, 54.7, 47.9, 41.5, 37.8, 37.0, 34.6, 31.8, 27.9, 26.5, 23.1, 22.6, 14.2, 13.7; MS(ESI) calcd for $C_{29}H_{35}ClN_2O_5$ 526.22 (M^+), found 527.33 (M + H)$^+$.

Pyrrolidinone-Containing Amide 12m. Compound **12m** was prepared according to the general procedure D from carboxylic acid **7g** and amine **11m**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25−7.18 (m, 1H), 7.14 (dd, J = 7.4, 1.8 Hz, 1H), 6.92−6.82 (m, 3H), 6.72 (t, J = 5.5 Hz,

1H), 5.72 (ddt, J = 17.2, 10.2, 5.0 Hz, 1H), 5.22−5.14 (m, 2H), 4.84 (dd, J = 10.0, 8.4 Hz, 1H), 4.21−3.99 (m, 3H), 3.83 (s, 4H), 3.60−3.38 (m, 2H), 3.00 (dd, J = 7.4, 5.7 Hz, 1H), 2.92−2.76 (m, 3H), 2.70−2.53 (m, 2H), 2.16−1.97 (m, 3H), 1.74−1.53 (m, 5H), 1.52−1.37 (m, 2H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 171.7, 170.4, 157.6, 140.6, 131.0, 130.8, 127.9, 127.5, 120.7, 116.9, 110.5, 103.7, 61.4, 55.4, 54.6, 48.0, 42.7, 40.0, 34.7, 30.3, 27.9, 26.4, 23.1, 22.6, 14.2; MS(ESI) calcd for $C_{27}H_{36}N_2O_5$ 468.26 (M^+), found 469.38 $(M + H)^+$.

Pyrrolidinone-Containing Amide 12n. Compound **12n** was prepared according to the general procedure D from carboxylic acid **7f** and amine **11b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.23 (m, 3H), 7.22−7.13 (m, 2H), 6.82 (t, J = 5.9 Hz, 1H), 5.18 (dd, J = 8.6, 4.4 Hz, 1H), 3.85−3.71 (m, 1H), 3.68 (s, 3H), 3.60−3.49 (m, 1H), 3.21−3.10 (m, 1H), 3.09−3.01 (m, 1H), 2.98−2.92 (m, 1H), 2.91−2.82 (m, 1H), 2.81−2.74 (m, 1H), 2.54−2.45 (m, 2H), 2.33−2.19 (m, 1H), 2.14 (dd, J = 15.0, 4.8 Hz, 1H), 2.03−1.84 (m, 2H), 1.84−1.60 (m, 11H), 1.56 (ddd, J = 14.1, 12.3, 3.5 Hz, 1H), 1.51−1.41 (m, 1H), 1.40−1.28 (m, 1H), 1.28−1.09 (m, 4H), 1.00−0.86 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 171.4, 170.6, 142.6, 137.0, 132.5, 130.3, 128.8, 104.5, 55.9, 52.2, 49.1, 46.2, 41.6, 38.0, 35.2, 33.8, 31.7, 31.0, 27.4, 27.2, 26.6, 26.2, 26.0; MS(ESI) calcd for $C_{28}H_{37}ClN_2O_4$ 500.24 (M^+), found 501.14 $(M + H)^+$.

Pyrrolidinone-Containing Amide 12o. Compound **12o** was prepared according to the general procedure D from carboxylic acid **7d** and amine **11i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97−6.88 (m, 1H), 5.70 (ddt, J = 17.3, 10.3, 5.1 Hz, 1H), 5.21 (ddd, J = 17.3, 1.6 Hz, 1H), 5.16 (ddd, J = 10.3, 1.5 Hz, 1H), 5.12 (dd, J = 8.6, 4.4 Hz, 1H), 4.19 (ddt, J = 16.4, 5.1, 1.8 Hz, 1H), 4.04 (ddt, J = 16.2, 5.2, 1.7 Hz, 1H), 3.67 (s, 3H), 3.02−2.95 (m, 2H), 2.88 (dd, J = 13.4, 6.0 Hz, 1H), 2.54 (dd, J = 15.0, 8.4 Hz, 1H), 2.51−2.45 (m, 1H), 2.25−2.12 (m, 2H), 1.99−1.92 (m, 4H), 1.92−1.83 (m, 1H), 1.82−1.64 (m, 6H), 1.64 (s, 0H), 1.50−1.45 (m, 7H), 1.37−1.24 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 171.4, 170.8, 142.6, 131.2, 117.1, 105.4, 55.7, 52.2, 51.5, 49.3, 42.9, 40.3, 37.1, 35.2, 33.8, 33.8, 28.4, 27.4, 27.2, 26.1; MS(ESI) calcd for $C_{27}H_{38}N_2O_4$ 454.28 (M^+), found 455.36 $(M + H)^+$.

Pyrrolidinone-Containing Amide 12p. Compound **12p** was prepared according to the general procedure D from carboxylic acid **7d** and amine **11q**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.69 (ddt, J = 17.2, 10.3, 5.0 Hz, 1H), 5.20 (ddd, J = 17.3, 1.6 Hz, 1H), 5.17−5.09 (m, 2H), 4.20−4.13 (m, 1H), 4.09−4.00 (m, 1H), 3.78−3.59 (m, 9H), 3.58−3.37 (m, 1H), 3.29 (dd, J = 7.0, 5.0 Hz, 1H), 2.83 (dd, J = 16.5, 5.1 Hz, 1H), 2.55 (dd, J = 11.3, 5.0 Hz, 1H), 2.30 (dd, J = 16.5, 6.9 Hz, 1H), 2.24−2.14 (m, 1H), 1.96−1.84 (m, 3H), 1.75−1.65 (m, 3H), 1.65−1.54 (m, 2H), 1.35−1.24 (m, 1H), 1.01−0.95 (m, 2H), 0.81−0.73 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 172.4, 172.2, 171.9, 171.1, 169.0, 142.9, 131.2, 116.7, 105.6, 104.8, 55.6, 52.0, 48.5, 48.2, 45.2, 42.7, 41.9, 41.7, 36.1, 30.1, 27.6, 27.4, 26.1, 11.0, 7.6; MS(ESI) calcd for $C_{24}H_{33}N_3O_5$ 443.24 (M^+), found 444.35 $(M + H)^+$.

Pyrrolidinone-Containing Amide 12q. Compound **12q** was prepared according to the general procedure D from carboxylic acid **7c** and amine **11v**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.22 (m, 3H), 7.17 (dq, J = 9.1, 4.0, 3.3 Hz, 3H), 5.01 (t, J = 3.7 Hz, 1H), 4.13−4.05 (m, 2H), 3.94−3.82 (m, 2H), 3.72 (q, J = 4.0 Hz, 2H), 3.42 (ddd, J = 13.8, 10.4, 4.9 Hz, 1H), 3.28 (dd, J = 8.6, 4.4 Hz, 1H), 2.93−2.72 (m, 3H), 2.66−2.53 (m, 7H), 2.28−2.08 (m, 3H), 1.88−1.80 (m, 1H), 1.60−1.43 (m, 2H), 1.34−1.22 (m, 1H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 172.2, 168.8, 138.6, 137.2, 132.4, 130.2, 128.8, 100.6, 61.2, 52.7, 48.4, 47.7, 45.0, 41.4, 32.2, 31.0, 30.2, 27.7, 27.5, 23.0, 19.9, 14.4; MS(ESI) calcd for $C_{25}H_{31}ClN_2O_4S$ 490.17 (M^+), found 491.28 $(M + H)^+$.

Pyrrolidinone-Containing Amide 12r. Compound **12r** was prepared according to the general procedure D from carboxylic acid **7c** and amine **11l**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.23 (m, 5H), 7.22−7.13 (m, 7H), 6.77 (t, J = 5.7 Hz, 1H), 5.05 (t, J = 3.7 Hz, 1H), 4.17−4.06 (m, 2H), 3.88 (ddd, J = 13.8, 10.7, 6.3 Hz, 1H), 3.44 (ddd, J = 13.8, 10.6, 5.2 Hz, 1H), 3.35−3.19 (m, 3H), 2.98−2.76 (m, 3H), 2.68−2.51 (m, 5H), 2.31−2.20 (m, 1H), 2.21−2.08 (m, 2H), 1.87 (ddt, J = 13.6, 6.5, 3.3 Hz, 1H), 1.74−1.63 (m, 2H), 1.62−1.50 (m, 3H), 1.46 (ddd, J = 15.4, 10.1, 2.9 Hz, 1H), 1.35−1.25 (m, 1H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 171.5, 170.8, 142.3, 138.2, 137.1, 132.5, 130.2, 128.8, 128.5, 128.4, 125.9, 101.0, 61.5, 52.6, 48.5, 41.5, 39.7, 35.6, 33.5, 32.2, 30.2, 29.2, 28.8, 23.0, 19.7, 14.3; MS(ESI) calcd for $C_{31}H_{37}ClN_2O_4$ 536.24 (M^+), found 537.47 $(M + H)^+$.

Piperidinone-Containing Amide 13a ((3*RS*,4a*SR*)-Ethyl 1-Benzyl-3-(2-(4-(furan-2-carbonyl)piperazin-1-yl)-2-oxoethyl)-2-oxo-2,3,4,4a,5,6-hexahydro-1*H*-cyclopenta[*b*]pyridine-4a-carboxylate). Compound **13a** was prepared according to the general procedure D from carboxylic acid **8f** and amine **11r**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (dd, J = 1.7, 0.8 Hz, 1H), 7.29 (d, J = 4.3 Hz, 4H), 7.24−7.18 (m, 1H), 7.04 (dd, J = 3.5, 0.9 Hz, 1H), 6.49 (dd, J = 3.5, 1.8 Hz, 1H), 5.00 (dd, J = 3.2, 1.8 Hz, 1H), 4.95 (d, J = 15.5 Hz, 1H), 4.89 (d, J = 15.5 Hz, 1H), 4.19−4.05 (m, 2H), 3.81 (s, 4H), 3.74−3.63 (m, 2H), 3.57 (t, J = 5.2 Hz, 2H), 2.99−2.90 (m, 2H), 2.79−2.73 (m, 1H), 2.54 (dd, J = 12.7, 5.1 Hz, 1H), 2.44−2.35 (m, 1H), 2.32 (dd, J = 12.7, 7.0 Hz, 1H), 2.25 (ddd, J = 15.4, 8.6, 3.2 Hz, 1H), 2.05−1.98 (m, 1H), 1.91−1.81 (m, 1H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 170.7, 169.6, 159.3, 147.7, 144.1, 141.5, 137.2, 128.5, 127.1, 127.0, 127.0, 119.4, 117.2, 111.6, 107.8, 61.4, 54.5, 47.8, 45.5, 43.8, 41.8, 37.0, 36.8, 35.9, 35.1, 29.1, 14.3; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{29}H_{34}N_3O_6$ 520.2448, found 520.2452.

Piperidinone-Containing Amide 13b. Compound **13b** was prepared according to the general procedure D from carboxylic acid **8f** and amine **11m**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32−7.27 (m, 2H), 7.25−7.19 (m, 3H), 7.18 (dd, J = 6.8, 1.4 Hz, 1H), 7.11 (dd, J = 7.4, 1.8 Hz, 1H), 6.90−6.82 (m, 2H), 6.08 (t, J = 5.6 Hz, 1H), 4.98 (dd, J = 3.2, 1.7 Hz, 1H), 4.92−4.86 (m, 2H), 4.19−4.07 (m, 2H), 3.82 (s, 3H), 3.53−3.37 (m, 2H), 2.92−2.85 (m, 1H), 2.78 (t, J = 6.9 Hz, 2H), 2.68 (dd, J = 14.7, 5.6 Hz, 1H), 2.59−2.48 (m, 2H), 2.42−2.29 (m, 2H), 2.24 (ddd, J = 14.9, 8.6, 3.2 Hz, 1H), 1.90−1.82 (m, 2H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 170.9, 170.7, 157.6, 141.5, 136.9, 130.7, 128.5, 127.9, 127.5, 127.1, 127.0, 120.7, 110.5, 107.8, 61.4, 55.4, 54.6, 47.8, 39.8, 38.5, 37.5, 37.0, 35.7, 30.4, 29.0, 14.3; MS(ESI) calcd for $C_{29}H_{34}N_2O_5$ 490.25 (M^+), found 491.28 $(M + H)^+$, 513.24 $(M + Na)^+$.

Piperidinone-Containing Amide 13c. Compound **13c** was prepared according to the general procedure D from carboxylic acid **8g** and amine **11e**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (dd, J = 4.8, 1.5 Hz, 1H), 6.95−6.89 (m, 2H), 6.76−6.69 (m, 3H), 5.91 (s, 2H), 5.03 (t, J = 2.3 Hz, 1H), 4.83 (d, J = 15.4 Hz, 1H), 4.70 (d, J = 15.3 Hz, 1H), 4.57 (d, J = 5.5 Hz, 2H), 4.19−4.07 (m, 2H), 3.47 (s, 1H), 2.91 (dq, J = 13.1, 5.4 Hz, 1H), 2.81 (dd, J = 14.6, 5.0 Hz, 1H), 2.56 (ddd, J = 14.4, 7.8, 5.5 Hz, 2H), 2.46−2.31 (m, 2H), 2.27 (ddd, J = 15.3, 8.7, 3.3 Hz, 1H), 1.93−1.81 (m, 2H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 170.9, 170.8, 147.9, 146.7, 141.2, 141.1, 130.7, 127.0, 126.0, 125.2, 120.4, 108.2, 107.7, 101.1, 61.5, 54.6, 47.5, 38.4, 38.2, 37.6, 37.0, 35.7, 29.1, 14.2; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{26}H_{29}N_2O_6S$ 497.1746, found 497.1740.

Piperidinone-Containing Amide 13d. Compound **13d** was prepared according to the general procedure D from carboxylic acid **8g** and amine **11k**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.26 (m, 2H), 7.24 (td, J = 6.5, 1.7 Hz, 3H), 6.76−6.69 (m, 3H), 5.89 (s, 2H), 5.03 (dd, J = 3.2, 1.8 Hz, 1H), 4.81 (d, J = 15.3 Hz, 1H), 4.69 (d, J = 15.3 Hz, 1H), 4.40 (d, J = 5.6 Hz, 2H), 4.18−4.08 (m, 2H), 3.46 (s, 1H), 2.95−2.88 (m, 1H), 2.83 (dd, J = 14.7, 5.0 Hz, 1H), 2.57 (ddd, J = 14.7, 5.5, 2.6 Hz, 2H), 2.45−2.36 (m, 1H), 2.33 (dd, J = 12.7, 7.0 Hz, 1H), 2.27 (ddd, J = 15.3, 8.7, 3.2 Hz, 1H), 1.92−1.82 (m, 2H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 171.2, 170.9, 147.9, 146.7, 141.2, 138.4, 130.6, 128.8, 127.8, 127.5, 120.4, 108.3, 108.2, 107.7, 101.1, 61.5, 54.5, 47.6, 43.7, 38.2, 37.6, 37.0, 35.7, 29.1, 14.2; MS(ESI) calcd for $C_{28}H_{30}N_2O_6$ 490.21 (M^+), found 491.22 $(M + H)^+$, 513.21 $(M + Na)^+$.

Piperidinone-Containing Amide 13e. Compound **13e** was prepared according to the general procedure D from carboxylic acid **8h** and amine **11a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, J = 0.9 Hz, 1H), 6.37 (s, 1H), 6.32−6.29 (m, 1H), 6.28−6.25 (m, 1H), 5.23 (t, J = 2.4 Hz, 1H), 4.94 (d, J = 15.5 Hz, 1H), 4.78 (d, J = 15.7 Hz, 1H),

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4.17−4.08 (m, 2H), 4.05−3.97 (m, 1H), 3.96−3.87 (m, 1H), 3.48 (s, 1H), 2.90−2.82 (m, 1H), 2.75−2.68 (m, 1H), 2.58−2.51 (m, 2H), 2.49−2.40 (m, 1H), 2.38−2.28 (m, 2H), 2.21−2.17 (m, 1H), 1.91−1.82 (m, 1H), 1.77 (dd, J = 13.5, 12.5 Hz, 1H), 1.21−1.15 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 170.8, 170.4, 150.4, 141.9, 141.1, 110.5, 108.2, 108.0, 79.8, 71.5, 61.5, 54.6, 41.2, 38.3, 37.6, 36.9, 35.8, 29.2, 29.1, 14.2; MS(ESI) calcd for $C_{21}H_{24}N_2O_5$ 384.17 (M^+), found 407.16 (M + Na)$^+$.

Piperidinone-Containing Amide 13f. Compound **13f** was prepared according to the general procedure D from carboxylic acid **8h** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32−7.27 (m, 1H), 6.73 (s, 1H), 6.28 (dd, J = 3.1, 1.8 Hz, 1H), 6.25 (dd, J = 3.3, 1.0 Hz, 1H), 5.16 (dd, J = 3.2, 1.8 Hz, 1H), 4.87 (d, J = 15.6 Hz, 1H), 4.82 (d, J = 15.6 Hz, 1H), 4.15−4.05 (m, 2H), 3.46 (s, 1H), 3.36 (t, J = 7.1 Hz, 2H), 3.31 (t, J = 6.4 Hz, 2H), 3.21−3.07 (m, 2H), 2.90−2.81 (m, 1H), 2.66−2.55 (m, 2H), 2.49 (dd, J = 12.8, 5.7 Hz, 1H), 2.46−2.35 (m, 5H), 2.34−2.24 (m, 2H), 2.09−1.96 (m, 2H), 1.88−1.73 (m, 2H), 1.69−1.59 (m, 2H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 174.2, 171.1, 170.2, 150.7, 141.7, 141.3, 110.5, 107.9, 107.3, 61.4, 54.6, 47.5, 41.1, 39.9, 38.5, 37.2, 37.0, 36.0, 35.9, 31.1, 29.1, 26.7, 18.1, 14.2; MS(ESI) calcd for $C_{25}H_{33}N_3O_6$ 471.24 (M^+), found 472.25 (M + H)$^+$, 494.24 (M + Na)$^+$.

Piperidinone-Containing Amide 13g. Compound **13g** was prepared according to the general procedure D from carboxylic acid **8i** and amine **11f**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85−6.74 (m, 3H), 5.42−5.37 (m, 1H), 5.06 (t, J = 2.4 Hz, 1H), 4.40 (dd, J = 14.4, 6.0 Hz, 1H), 4.27 (dd, J = 14.6, 5.4 Hz, 1H), 4.19−4.09 (m, 2H), 3.91−3.81 (m, 7H), 3.77 (ddd, J = 13.2, 10.6, 5.8 Hz, 1H), 3.47 (ddd, J = 13.2, 10.7, 5.3 Hz, 1H), 2.85−2.77 (m, 1H), 2.69 (dd, J = 14.6, 4.8 Hz, 1H), 2.61−2.41 (m, 3H), 2.38−2.27 (m, 2H), 2.09 (m, 2H), 2.00−1.89 (m, 4H), 1.85 (dt, J = 13.0, 9.4 Hz, 1H), 1.74 (t, J = 13.0 Hz, 1H), 1.64−1.56 (m, 2H), 1.56−1.48 (m, 2H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 171.1, 170.1, 149.2, 148.4, 141.0, 135.0, 131.2, 122.8, 120.1, 111.2, 111.1, 106.8, 61.5, 56.0, 56.0, 54.4, 43.5, 43.1, 38.7, 37.6, 37.0, 35.9, 34.5, 29.1, 28.6, 25.4, 23.0, 22.4, 14.3; MS(ESI) calcd for $C_{30}H_{40}N_2O_6$ 524.29 (M^+), found 525.29 (M + H)$^+$.

Piperidinone-Containing Amide 13h. Compound **13h** was prepared according to the general procedure D from carboxylic acid **8i** and amine **11s**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.43 (dd, J = 3.3, 1.8 Hz, 1H), 5.07 (t, J = 2.3 Hz, 1H), 4.21−4.08 (m, 4H), 3.88 (ddd, J = 13.3, 10.7, 5.6 Hz, 1H), 3.66−3.31 (m, 9H), 2.85−2.70 (m, 3H), 2.55−2.41 (m, 2H), 2.39−2.26 (m, 3H), 2.25−2.08 (m, 2H), 2.05−1.92 (m, 4H), 1.91−1.77 (m, 2H), 1.66−1.56 (m, 2H), 1.56−1.48 (m, 2H), 1.32−1.18 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 169.7, 169.4, 155.3, 141.1, 135.1, 122.5, 106.0, 61.6, 61.2, 54.2, 45.1, 43.5, 43.0, 41.3, 37.5, 36.9, 36.5, 35.8, 35.2, 34.4, 28.9, 28.4, 25.2, 22.9, 22.3, 14.6, 14.2; MS(ESI) calcd for $C_{28}H_{41}N_3O_6$ 515.30 (M^+), found 516.32 (M + H)$^+$, 538.3 (M + Na)$^+$.

Piperidinone-Containing Amide 13i. Compound **13i** was prepared according to the general procedure D from carboxylic acid **8a** and amine **11l**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (m, 2H), 7.14 (m, 3H), 6.79 (m, 3H), 6.03 (s, 1H), 5.09 (t, J = 2.5 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 4.01 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.64 (m, 1H), 3.23 (m, 2H), 2.79 (m, 3H), 2.66 (m, 1H), 2.60 (t, J = 7.6 Hz, 2H), 2.55 (dd, J = 13.0, 5.8 Hz, 1H), 2.48 (dd, J = 14.5, 5.3 Hz, 2H), 2.35 (m, 2H), 1.87 (m, 1H), 1.78 (t, J = 13.0 Hz, 1H), 1.60 (m, 2H), 1.50 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 171.0, 170.2, 149.1, 147.8, 142.2, 141.1, 131.7, 128.5, 128.4, 125.9, 120.8, 112.3, 111.5, 106.6, 61.5, 56.1, 56.1, 54.5, 45.9, 39.4, 38.5, 37.6, 36.9, 35.8, 35.6, 32.5, 29.4, 29.0, 28.7, 14.3; MS(ESI) calcd for $C_{33}H_{42}N_2O_6$ 562.30 (M^+), found 563.37 (M + H)$^+$.

Piperidinone-Containing Amide 13j. Compound **13j** was prepared according to the general procedure D from carboxylic acid **8a** and amine **11w**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (m, 3H), 5.09 (t, J = 2.2 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 4.00 (m, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.71 (m, 1H), 3.42 (m, 4H), 2.82 (m, 4H), 2.61 (dd, J = 15.9, 2.9 Hz, 1H), 2.49 (m, 2H), 2.35 (m, 2H), 1.90 (m, 6H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 170.5, 169.2, 149.0, 147.6, 141.5, 132.1, 120.7, 112.3, 111.4, 105.8, 61.3, 56.0, 56.0, 54.5, 46.6, 45.9, 45.7, 37.0, 36.6, 36.5, 36.0, 32.4, 29.1, 26.2, 24.5, 14.3; MS(ESI) calcd for $C_{27}H_{36}N_2O_6$ 484.26 (M^+), found 485.32 (M + H)$^+$, 507.31 (M + Na)$^+$.

Piperidinone-Containing Amide 13k. Compound **13k** was prepared according to the general procedure D from carboxylic acid **8j** and amine : ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03−7.94 (m, 1H), 7.92−7.77 (m, 4H), 7.71 (d, J = 8.1 Hz, 1H), 7.59−7.32 (m, 7H), 7.25−7.20 (m, 1H), 6.29 (t, J = 5.1 Hz, 1H), 5.10 (d, J = 16.5 Hz, 1H), 5.03 (dd, J = 14.4, 6.5 Hz, 1H), 4.75 (d, J = 16.4 Hz, 1H), 4.72−4.65 (m, 2H), 4.18 (dq, J = 11.0, 7.2 Hz, 1H), 4.10 (dq, J = 10.8, 7.1 Hz, 1H), 3.02−2.89 (m, 2H), 2.65 (dd, J = 13.0, 5.5 Hz, 1H), 2.51 (dd, J = 14.0, 4.6 Hz, 1H), 2.39−2.28 (m, 2H), 2.25−2.16 (m, 1H), 2.01 (t, J = 13.0 Hz, 1H), 1.96−1.85 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 170.7, 170.5, 140.9, 134.1, 134.0, 133.8, 131.5, 130.9, 130.9, 129.0, 128.8, 128.6, 127.5, 127.0, 126.7, 126.1, 126.1, 125.7, 125.6, 125.6, 123.9, 122.8, 122.6, 108.3, 61.5, 54.5, 45.1, 41.6, 38.3, 38.0, 37.1, 35.5, 29.0, 14.3; MS(ESI) calcd for $C_{35}H_{34}N_2O_4$ 546.25 (M^+), found 547.28 (M + H)$^+$.

Piperidinone-Containing Amide 13l. Compound **13l** was prepared according to the general procedure D from carboxylic acid **8j** and amine **11w**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.3 Hz, 1H), 7.90−7.84 (m, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.55−7.39 (m, 4H), 5.45 (d, J = 16.4 Hz, 1H), 5.38 (d, J = 16.4 Hz, 1H), 4.84 (dd, J = 3.4, 1.7 Hz, 1H), 4.23−4.15 (m, 1H), 4.14−4.05 (m, 1H), 3.57−3.48 (m, 1H), 3.47−3.38 (m, 3H), 3.03−2.93 (m, 2H), 2.69−2.60 (m, 1H), 2.57 (dd, J = 12.7, 5.4 Hz, 1H), 2.40−2.30 (m, 2H), 2.28−2.15 (m, 2H), 1.99−1.88 (m, 3H), 1.88−1.78 (m, 2H), 1.26−1.19 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 171.2, 169.2, 141.8, 133.8, 131.4, 131.0, 128.9, 127.3, 126.0, 125.8, 125.5, 123.5, 122.7, 107.8, 61.3, 54.6, 46.6, 46.0, 45.7, 37.2, 36.8, 36.5, 36.0, 29.1, 26.2, 24.5, 14.3; MS(ESI) calcd for $C_{28}H_{32}N_2O_4$ 460.24 (M^+), found 461.26 (M + H)$^+$, 483.25 (M + Na)$^+$.

Piperidinone-Containing Amide 13m. Compound **13m** was prepared according to the general procedure D from carboxylic acid **8k** and amine **11a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.33 (m, 1H), 7.23−7.16 (m, 2H), 6.16 (t, J = 5.4 Hz, 1H), 4.99−4.90 (m, 2H), 4.85 (dd, J = 3.2, 1.7 Hz, 1H), 4.27−4.12 (m, 2H), 4.07−3.94 (m, 2H), 2.95−2.87 (m, 1H), 2.82 (dd, J = 15.1, 5.0 Hz, 1H), 2.60−2.50 (m, 2H), 2.42−2.32 (m, 2H), 2.29−2.21 (m, 1H), 2.20 (t, J = 2.5 Hz, 1H), 1.98 (t, J = 13.0 Hz, 1H), 1.94−1.85 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 170.8, 170.6, 141.1, 133.3, 133.3, 132.4, 129.2, 128.5, 127.4, 108.1, 79.6, 71.7, 61.6, 54.6, 45.3, 37.8, 37.4, 37.1, 35.6, 29.3, 29.0, 14.4; MS(ESI) calcd for $C_{23}H_{24}Cl_2N_2O_4$ 462.11 (M^+), found 533.39 (M + H)$^+$, 555.38 (M + Na)$^+$.

Piperidinone-Containing Amide 13n. Compound **13n** was prepared according to the general procedure D from carboxylic acid **8k** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, J = 2.1 Hz, 1H), 7.27−7.23 (m, 1H), 7.17 (dd, J = 8.4, 2.1 Hz, 1H), 6.74 (t, J = 6.2 Hz, 1H), 4.96−4.88 (m, 2H), 4.79 (dd, J = 3.2, 1.7 Hz, 1H), 4.24−4.11 (m, 2H), 3.38−3.26 (m, 4H), 3.21−3.11 (m, 2H), 2.92−2.85 (m, 1H), 2.78 (dd, J = 15.4, 5.6 Hz, 1H), 2.58−2.47 (m, 2H), 2.41−2.30 (m, 4H), 2.25−2.17 (m, 1H), 2.06−1.95 (m, 3H), 1.91−1.82 (m, 1H), 1.67−1.59 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 174.2, 170.9, 170.8, 141.4, 133.2, 133.1, 132.8, 129.0, 128.8, 127.4, 107.3, 61.5, 54.6, 47.5, 45.2, 39.8, 37.9, 37.1, 37.0, 35.8, 35.8, 31.0, 29.0, 26.6, 18.1, 14.4; MS(ESI) calcd for $C_{27}H_{33}Cl_2N_3O_5$ 549.18 (M^+), found 550.18 (M + H)$^+$.

Piperidinone-Containing Amide 13o. Compound **13o** was prepared according to the general procedure D from carboxylic acid **8l** and amine **11a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69 (t, J = 5.4 Hz, 1H), 5.25 (dd, J = 5.3, 2.8 Hz, 1H), 4.16 (dd, J = 7.0, 2.0 Hz, 1H), 4.14 (dd, J = 7.1, 1.9 Hz, 1H), 4.05−3.94 (m, 2H), 3.71 (ddd, J = 13.6, 10.5, 5.2 Hz, 1H), 3.64 (ddd, J = 13.7, 10.7, 5.7 Hz, 1H), 2.68−2.59 (m, 2H), 2.56−2.49 (m, 1H), 2.34 (dd, J = 13.1, 5.4 Hz, 1H), 2.31−2.21 (m, 2H), 2.17 (t, J = 2.6 Hz, 1H), 2.16−2.09 (m, 1H), 1.72−1.58 (m, 3H), 1.55−1.45 (m, 2H), 1.43−1.35 (m, 1H), 1.34−1.20 (m, 13H), 0.87 (t, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 171.0, 170.0, 136.2, 107.3, 79.8, 71.4, 61.6, 46.6, 44.2, 38.8, 37.3, 36.7, 35.0, 32.0, 29.5, 29.4, 29.2, 27.3, 27.0, 24.5, 22.8, 18.7, 14.4, 14.2; MS(ESI) calcd for $C_{25}H_{38}N_2O_4$ 430.28 (M^+), found 431.29 (M + H)$^+$.

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Piperidinone-Containing Amide 13p. Compound **13p** was prepared according to the general procedure D from carboxylic acid **8l** and amine **11o**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.46 (t, J = 5.7 Hz, 1H), 6.04 (d, J = 3.0 Hz, 1H), 5.85 (dd, J = 3.1, 1.3 Hz, 1H), 5.22 (dd, J = 5.3, 2.8 Hz, 1H), 4.35 (dd, J = 15.5, 5.6 Hz, 1H), 4.29 (dd, J = 15.4, 5.4 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.71−3.58 (m, 2H), 2.70−2.60 (m, 2H), 2.56−2.49 (m, 1H), 2.39−2.32 (m, 1H), 2.31−2.20 (m, 5H), 2.18−2.09 (m, 1H), 1.73−1.64 (m, 2H), 1.62−1.54 (m, 1H), 1.54−1.34 (m, 3H), 1.33−1.18 (m, 13H), 0.87 (t, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 170.9, 169.9, 151.8, 149.7, 136.3, 108.1, 107.1, 106.3, 61.5, 46.6, 44.1, 38.7, 37.4, 36.7, 36.5, 35.0, 32.0, 29.5, 27.3, 26.8, 24.5, 22.8, 18.7, 14.3, 14.2, 13.7; MS(ESI) calcd for $C_{28}H_{42}N_2O_5$ 486.31 (M^+), found 487.32 (M + H)$^+$, 509.3 (M + Na)$^+$.

Piperidinone-Containing Amide 13q. Compound **13q** was prepared according to the general procedure D from carboxylic acid **8m** and amine **11c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, J = 8.2, 6.9 Hz, 2H), 7.23−7.17 (m, 3H), 6.38 (t, J = 5.7 Hz, 1H), 5.39 (d, J = 16.0 Hz, 1H), 5.13 (dd, J = 5.2, 2.8 Hz, 1H), 4.54 (d, J = 16.1 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.44−3.29 (m, 3H), 3.28 (s, 3H), 3.27−3.20 (m, 1H), 2.79−2.68 (m, 2H), 2.59−2.51 (m, 1H), 2.42 (dd, J = 13.1, 5.3 Hz, 1H), 2.29−2.22 (m, 1H), 2.17−2.08 (m, 1H), 2.06−1.95 (m, 1H), 1.91 (t, J = 13.0 Hz, 1H), 1.76−1.67 (m, 2H), 1.68−1.60 (m, 1H), 1.52 (td, J = 13.6, 2.7 Hz, 1H), 1.40−1.30 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 170.9, 170.7, 137.7, 137.2, 128.6, 126.8, 126.2, 108.5, 71.4, 61.5, 58.8, 48.8, 46.8, 38.6, 37.8, 37.6, 36.6, 34.9, 29.3, 24.4, 18.7, 14.4; MS(ESI) calcd for $C_{25}H_{34}N_2O_5$ 442.25 (M^+), found 443.27 (M + H)$^+$, 465.23 (M + Na)$^+$.

Piperidinone-Containing Amide 13r. Compound **13r** was prepared according to the general procedure D from carboxylic acid **8m** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, J = 8.2, 6.9 Hz, 2H), 7.23−7.17 (m, 3H), 6.38 (t, J = 5.7 Hz, 1H), 5.39 (d, J = 16.0 Hz, 1H), 5.13 (dd, J = 5.2, 2.8 Hz, 1H), 4.54 (d, J = 16.1 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.44−3.29 (m, 3H), 3.28 (s, 3H), 3.27−3.20 (m, 1H), 2.79−2.68 (m, 2H), 2.59−2.51 (m, 1H), 2.42 (dd, J = 13.1, 5.3 Hz, 1H), 2.29−2.22 (m, 1H), 2.17−2.08 (m, 1H), 2.06−1.95 (m, 1H), 1.91 (t, J = 13.0 Hz, 1H), 1.76−1.67 (m, 2H), 1.68−1.60 (m, 1H), 1.52 (td, J = 13.6, 2.7 Hz, 1H), 1.40−1.30 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 170.9, 170.7, 137.7, 137.2, 128.6, 126.8, 126.2, 108.5, 71.4, 61.5, 58.8, 48.8, 46.8, 38.6, 37.8, 37.6, 36.6, 34.9, 29.3, 24.4, 18.7, 14.4; MS(ESI) calcd for $C_{28}H_{37}N_3O_5$ 495.27 (M^+), found 496.28 (M + H)$^+$.

Piperidinone-Containing Amide 13s. Compound **13s** was prepared according to the general procedure D from carboxylic acid **8n** and amine **11i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (d, J = 7.9 Hz, 1H), 6.70 (d, J = 1.6 Hz, 1H), 6.67 (dd, J = 7.9, 1.7 Hz, 1H), 6.23 (t, J = 6.3 Hz, 1H), 5.92 (s, 2H), 5.23−5.13 (m, 2H), 4.57 (d, J = 15.8 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.00 (dd, J = 13.4, 6.8 Hz, 1H), 2.87−2.67 (m, 3H), 2.56 (dd, J = 13.8, 4.5 Hz, 1H), 2.41 (dd, J = 13.2, 5.4 Hz, 1H), 2.30−2.22 (m, 1H), 2.15 (dt, J = 18.3, 5.4 Hz, 1H), 2.09−1.98 (m, 1H), 1.97−1.84 (m, 4H), 1.74−1.55 (m, 8H), 1.55−1.46 (m, 1H), 1.45−1.41 (m, 6H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 171.2, 170.9, 148.0, 146.5, 137.0, 131.5, 119.6, 108.7, 108.4, 107.3, 101.0, 61.6, 51.1, 48.3, 46.8, 40.3, 38.8, 37.8, 37.1, 36.6, 34.9, 33.7, 28.4, 24.4, 18.7, 14.4; MS(ESI) calcd for $C_{33}H_{42}N_2O_6$ 562.30 (M^+), found 563.31 (M + H)$^+$.

Piperidinone-Containing Amide 13t. Compound **13t** was prepared according to the general procedure D from carboxylic acid **8n** and amine **11w**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (d, J = 1.6 Hz, 1H), 6.80−6.70 (m, 2H), 5.95−5.87 (m, 2H), 5.31 (d, J = 15.9 Hz, 1H), 5.17 (dd, J = 5.2, 2.7 Hz, 1H), 4.42 (d, J = 15.8 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.51 (dt, J = 13.0, 6.8 Hz, 1H), 3.41 (p, J = 6.9, 6.3 Hz, 3H), 2.90 (dd, J = 16.5, 6.2 Hz, 1H), 2.73 (dtd, J = 12.4, 5.9, 3.3 Hz, 1H), 2.62 (dd, J = 16.4, 3.3 Hz, 1H), 2.36 (dd, J = 12.8, 5.8 Hz, 1H), 2.28−2.18 (m, 1H), 2.18−1.97 (m, 3H), 1.97−1.89 (m, 2H), 1.87−1.78 (m, 2H), 1.67−1.58 (m, 1H), 1.52 (td, J = 13.6, 2.7 Hz, 1H), 1.42−1.30 (m, 1H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 171.1, 169.1, 148.0, 146.3, 137.6, 132.2, 119.5, 108.3, 108.2, 107.5, 100.9, 61.5, 48.9, 46.8, 46.6, 45.8, 36.7, 36.6, 36.4, 35.1, 26.2, 24.5, 24.5, 18.8, 14.4; MS(ESI) calcd for $C_{26}H_{32}N_2O_6$ 468.23 (M^+), found 469.23 (M + H)$^+$, 491.22 (M + Na)$^+$.

Piperidinone-Containing Amide 13u. Compound **13u** was prepared according to the general procedure D from carboxylic acid **8o** and amine **11g**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52−7.45 (m, 2H), 7.42−7.37 (m, 2H), 7.27 (dd, J = 1.8, 0.8 Hz, 1H), 6.74 (d, J = 6.0 Hz, 1H), 6.27 (dd, J = 3.2, 1.8 Hz, 1H), 6.22 (d, J = 3.1 Hz, 1H), 5.50 (dd, J = 5.2, 2.8 Hz, 1H), 5.22 (d, J = 15.8 Hz, 1H), 4.51 (d, J = 15.9 Hz, 1H), 4.43 (dd, J = 15.3, 6.3 Hz, 1H), 4.34 (dd, J = 15.3, 5.8 Hz, 1H), 4.15 (qd, J = 7.1, 1.8 Hz, 2H), 2.81−2.69 (m, 2H), 2.59−2.52 (m, 1H), 2.40 (dd, J = 13.1, 5.4 Hz, 1H), 2.30−2.20 (m, 2H), 2.12 (dddd, J = 18.0, 11.1, 6.4, 2.9 Hz, 1H), 1.78−1.64 (m, 2H), 1.50 (td, J = 13.6, 13.2, 2.6 Hz, 1H), 1.44−1.31 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 171.3, 170.5, 151.2, 141.6, 139.8, 136.9, 131.0, 131.0, 129.1, 124.3 (q, 3JC−F = 3.6 Hz), 124.2 (q, 3JC−F = 3.5 Hz), 124.2 (q, 1JC−F = 272.8 Hz), 110.6, 108.8, 107.9, 61.6, 46.8, 43.0, 42.1, 38.7, 37.6, 36.6, 34.8, 24.5, 18.6, 14.3; MS(ESI) calcd for $C_{27}H_{29}F_3N_2O_5$ 518.20 (M^+), found 519.21 (M + H)$^+$, 541.21 (M + Na)$^+$.

Piperidinone-Containing Amide 13v. Compound **13v** was prepared according to the general procedure D from carboxylic acid **8o** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, J = 1.9 Hz, 1H), 6.71 (t, J = 6.0 Hz, 1H), 6.30 (dd, J = 3.2, 1.8 Hz, 1H), 6.25 (d, J = 3.1 Hz, 1H), 5.41 (dd, J = 5.1, 2.7 Hz, 1H), 5.24 (d, J = 15.9 Hz, 1H), 4.51 (d, J = 15.9 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.36 (t, J = 7.1 Hz, 2H), 3.30 (t, J = 6.5 Hz, 2H), 3.22−3.06 (m, 2H), 2.78−2.70 (m, 1H), 2.60 (d, J = 5.3 Hz, 2H), 2.41−2.32 (m, 3H), 2.28−2.18 (m, 2H), 2.14−1.97 (m, 3H), 1.79−1.71 (m, 1H), 1.69−1.60 (m, 3H), 1.50 (td, J = 13.6, 2.6 Hz, 1H), 1.42−1.31 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.8, 174.3, 171.0, 170.2, 151.4, 141.4, 137.2, 110.6, 108.1, 107.7, 61.5, 47.4, 46.7, 42.2, 39.9, 38.6, 37.1, 36.7, 36.1, 34.9, 31.1, 26.8, 24.5, 18.7, 18.1, 14.3; MS(ESI) calcd for $C_{26}H_{35}N_3O_6$ 485.25 (M^+), found 486.26 (M + H)$^+$, 508.24 (M + Na)$^+$.

Piperidinone-Containing Amide 13w. Compound **13w** was prepared according to the general procedure D from carboxylic acid **8p** and amine **11r**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51−7.46 (m, 1H), 7.04 (d, J = 3.4 Hz, 1H), 6.82−6.78 (m, 3H), 6.49 (dt, J = 3.3, 1.4 Hz, 1H), 5.35 (dd, J = 5.2, 2.7 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.95−3.87 (m, 2H), 3.87−3.83 (m, 7H), 3.83−3.76 (m, 2H), 3.75−3.67 (m, 1H), 3.67−3.60 (m, 1H), 3.58−3.52 (m, 2H), 3.51−3.42 (m, 1H), 2.96−2.86 (m, 1H), 2.85−2.68 (m, 4H), 2.37 (dd, J = 12.8, 5.4 Hz, 1H), 2.33−2.22 (m, 2H), 2.22−2.15 (m, 1H), 1.82 (t, J = 12.6 Hz, 1H), 1.73−1.65 (m, 1H), 1.54 (td, J = 13.5, 13.0, 2.6 Hz, 1H), 1.47−1.39 (m, 1H), 1.30−1.21 (m, 4H), 1.19 (t, J = 7.0 Hz, 3H), 0.90−0.81 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 169.9, 169.5, 159.3, 149.0, 147.6, 144.1, 136.5, 132.2, 120.7, 117.2, 112.2, 111.6, 111.4, 106.8, 66.0, 61.5, 56.0, 56.0, 46.6, 45.6, 41.8, 36.8, 36.6, 35.3, 35.2, 32.6, 31.7, 24.6, 22.8, 18.8, 15.4, 14.4, 14.2; MS(ESI) calcd for $C_{33}H_{41}N_3O_8$ 607.29 (M^+), found 608.35 (M + H)$^+$, 630.31 (M + Na)$^+$.

Piperidinone-Containing Amide 13x. Compound **13x** was prepared according to the general procedure D from carboxylic acid **8p** and amine **11q**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (d, J = 3.2 Hz, 4H), 5.35 (dd, J = 5.3, 2.7 Hz, 1H), 4.16 (q, J = 7.0 Hz, 2H), 3.95−3.88 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.75−3.55 (m, 6H), 3.53−3.41 (m, 2H), 2.96−2.86 (m, 1H), 2.85−2.66 (m, 4H), 2.40−2.22 (m, 2H), 2.22−2.12 (m, 1H), 1.81 (t, J = 12.6 Hz, 1H), 1.70 (dq, J = 13.5, 5.3, 4.5 Hz, 2H), 1.54 (td, J = 13.5, 12.9, 2.6 Hz, 1H), 1.46−1.38 (m, 1H), 1.23 (t, J = 7.1 Hz, 3H), 1.03−0.96 (m, 2H), 0.83−0.75 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 172.4, 170.0, 169.5, 149.0, 147.6, 136.5, 132.1, 120.7, 112.2, 111.3, 106.9, 61.5, 56.0, 56.0, 46.6, 45.6, 45.3, 41.6, 36.8, 36.6, 35.3, 35.2, 32.6, 24.6, 18.8, 14.4, 11.1, 7.8; MS(ESI) calcd for $C_{32}H_{43}N_3O_7$ 581.31 (M^+), found 582.37 (M + H)$^+$, 604.34 (M + Na)$^+$.

Piperidinone-Containing Amide 13y. Compound **13y** was prepared according to the general procedure D from carboxylic acid **8q** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.2 Hz, 1H), 7.87 (dd, J = 8.0, 1.5 Hz, 1H), 7.73 (d, J = 7.7 Hz, 1H), 7.56−7.40 (m, 4H), 5.85 (d, J = 16.6 Hz, 1H), 5.04 (dd, J = 5.1, 2.8 Hz, 1H),

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4.97 (d, J = 16.6 Hz, 1H), 4.27−4.14 (m, 2H), 3.64 (ddt, J = 9.2, 6.9, 4.7 Hz, 6H), 3.47 (dd, J = 6.1, 3.6 Hz, 2H), 2.97 (dd, J = 16.2, 6.4 Hz, 1H), 2.87−2.80 (m, 1H), 2.75 (dd, J = 16.2, 3.2 Hz, 1H), 2.47 (dd, J = 12.8, 5.7 Hz, 1H), 2.29 (dt, J = 13.3, 3.3 Hz, 1H), 2.16 (t, J = 12.8 Hz, 1H), 2.06 (dt, J = 18.1, 5.5 Hz, 1H), 2.02−1.93 (m, 1H), 1.69−1.54 (m, 2H), 1.44−1.34 (m, 1H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 170.7, 169.4, 137.7, 133.8, 132.0, 130.5, 128.9, 127.1, 126.0, 125.5, 123.0, 122.7, 108.8, 67.0, 66.6, 61.6, 47.8, 46.9, 45.9, 42.0, 36.9, 36.8, 35.1, 34.8, 24.4, 18.8, 14.5; MS(ESI) calcd for $C_{29}H_{34}N_2O_5$ 490.25 (M^+), found 491.28 $(M + H)^+$, 513.27 $(M + Na)^+$.

Piperidinone-Containing Amide 13z. Compound **13z** was prepared according to the general procedure D from carboxylic acid **8q** and amine **11p**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02−7.95 (m, 1H), 7.91−7.85 (m, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.58−7.47 (m, 2H), 7.42 (dd, J = 8.2, 7.1 Hz, 1H), 7.23 (dd, J = 7.1, 1.4 Hz, 1H), 6.38 (t, J = 5.5 Hz, 1H), 5.86 (d, J = 16.7 Hz, 1H), 5.01 (dd, J = 5.1, 2.8 Hz, 1H), 4.96 (d, J = 16.7 Hz, 1H), 4.26−4.19 (m, 2H), 3.45−3.36 (m, 3H), 3.31 (t, J = 6.6 Hz, 2H), 3.29−3.21 (m, 1H), 2.85−2.77 (m, 2H), 2.58−2.45 (m, 2H), 2.30 (dd, J = 13.2, 3.5 Hz, 1H), 2.11−2.01 (m, 2H), 2.01−1.92 (m, 1H), 1.78−1.62 (m, 4H), 1.58 (td, J = 13.6, 2.8 Hz, 1H), 1.53−1.45 (m, 2H), 1.42−1.33 (m, 1H), 1.30 (t, J = 7.1 Hz, 4H), 0.87 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 170.8, 170.6, 137.4, 133.8, 131.7, 130.5, 129.0, 127.2, 126.1, 125.8, 125.7, 122.6, 122.5, 108.8, 71.0, 69.5, 61.6, 47.5, 47.0, 38.4, 38.1, 37.7, 36.6, 34.9, 31.9, 29.4, 24.3, 19.5, 18.7, 14.5, 14.0; MS(ESI) calcd for $C_{29}H_{34}N_2O_5$ 490.25 (M^+), found 491.28 $(M + H)^+$, 513.27 $(M + Na)^+$.

Piperidinone-Containing Amide 13aa. Compound **13aa** was prepared according to the general procedure D from carboxylic acid **8r** and amine **11c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 1.7 Hz, 1H), 7.23−7.17 (m, 2H), 6.20 (t, J = 5.9 Hz, 1H), 5.26 (d, J = 17.2 Hz, 1H), 4.91 (dd, J = 5.2, 2.8 Hz, 1H), 4.61 (d, J = 17.2 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 3.46−3.37 (m, 2H), 3.37−3.23 (m, 6H), 2.82 (dd, J = 15.0, 5.4 Hz, 1H), 2.74−2.67 (m, 1H), 2.47 (dd, J = 15.0, 4.3 Hz, 1H), 2.39 (dd, J = 13.1, 5.7 Hz, 1H), 2.27 (dd, J = 13.0, 3.3 Hz, 1H), 2.13 (dt, J = 17.8, 5.6 Hz, 1H), 2.08−1.97 (m, 2H), 1.77−1.63 (m, 2H), 1.54 (td, J = 13.7, 2.8 Hz, 1H), 1.35 (m, 1H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 170.8, 170.7, 137.1, 133.3, 133.0, 132.8, 129.1, 128.6, 127.5, 108.4, 71.6, 61.6, 58.9, 46.9, 46.7, 38.0, 37.8, 37.2, 36.4, 34.9, 29.3, 24.3, 18.7, 14.4; MS(ESI) calcd for $C_{25}H_{32}Cl_2N_2O_5$ 510.17 (M^+), found 511.19 $(M + H)^+$, 533.18 $(M + Na)^+$.

Piperidinone-Containing Amide 13ab. Compound **13ab** was prepared according to the general procedure D from carboxylic acid **8r** and amine **11q**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 2.1 Hz, 1H), 7.20 (dd, J = 8.3, 2.2 Hz, 1H), 5.32 (d, J = 17.2 Hz, 1H), 4.95 (dd, J = 5.3, 2.7 Hz, 1H), 4.54 (d, J = 17.2 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 3.76−3.56 (m, 6H), 3.56−3.42 (m, 2H), 3.08 (dd, J = 16.5, 5.7 Hz, 1H), 2.77−2.68 (m, 1H), 2.61 (dd, J = 16.6, 3.2 Hz, 1H), 2.34 (dd, J = 12.8, 5.7 Hz, 1H), 2.30−2.22 (m, 1H), 2.20−2.10 (m, 2H), 2.07−1.97 (m, 1H), 1.76−1.62 (m, 2H), 1.55 (td, J = 13.6, 2.8 Hz, 1H), 1.44−1.33 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H), 1.04−0.96 (m, 2H), 0.84−0.75 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 172.5, 170.8, 169.4, 137.3, 133.6, 132.9, 132.7, 129.0, 127.5, 108.4, 61.6, 47.2, 46.9, 45.2, 41.9, 41.6, 36.6, 35.0, 34.6, 24.4, 18.7, 14.5, 11.2, 7.8; MS(ESI) calcd for $C_{29}H_{35}Cl_2N_3O_5$ 575.20 (M^+), found 576.22 $(M + H)^+$, 598.18 $(M + Na)^+$.

Piperidinone-Containing Amide 13ac. Compound **13ac** was prepared according to the general procedure D from carboxylic acid **8s** and amine **11b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (t, J = 6.0 Hz, 1H), 5.49 (t, J = 7.2 Hz, 1H), 3.75 (s, 3H), 3.60 (ddd, J = 14.2, 10.0, 5.4 Hz, 1H), 3.06 (dt, J = 13.2, 6.6 Hz, 1H), 2.99 (dt, J = 13.1, 6.3 Hz, 1H), 2.65−2.58 (m, 1H), 2.50 (d, J = 5.4 Hz, 2H), 2.27−2.17 (m, 1H), 2.13 (dd, J = 13.5, 4.2 Hz, 1H), 2.08−1.95 (m, 1H), 1.77−1.60 (m, 10H), 1.60−1.49 (m, 1H), 1.49−1.34 (m, 1H), 1.34−1.08 (m, 18H), 0.95−0.83 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 171.0, 169.2, 141.1, 113.5, 52.5, 51.7, 46.6, 45.1, 42.9, 40.1, 37.0, 35.8, 34.3, 31.9, 29.5, 29.4, 27.2, 26.9, 26.6, 26.5, 25.7, 25.5, 25.2, 24.7, 22.8, 14.2; MS(ESI) calcd for $C_{29}H_{48}N_2O_4$ 488.36 (M^+), found 489.38 $(M + H)^+$.

Piperidinone-Containing Amide 13ad. Compound **13ad** was prepared according to the general procedure D from carboxylic acid **8s** and amine **11u**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.47 (t, J = 7.1 Hz, 1H), 3.84−3.68 (m, 4H), 3.65−3.53 (m, 1H), 3.47−3.38 (m, 2H), 3.38−3.29 (m, 1H), 2.99 (dd, J = 16.3, 3.8 Hz, 1H), 2.82−2.73 (m, 1H), 2.33 (dd, J = 16.4, 8.3 Hz, 1H), 2.26−2.14 (m, 2H), 2.08−1.99 (m, 2H), 1.81−1.44 (m, 14H), 1.45−1.33 (m, 1H), 1.33−1.18 (m, 10H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 171.0, 169.2, 141.1, 113.5, 52.5, 51.7, 46.6, 45.1, 42.9, 40.1, 37.0, 35.8, 34.3, 31.9, 29.5, 29.4, 27.2, 26.9, 26.6, 26.5, 25.7, 25.5, 25.2, 24.7, 22.8, 14.2; MS(ESI) calcd for $C_{27}H_{44}N_2O_4$ 460.33 (M^+), found 461.35 $(M + H)^+$, 483.32 $(M + Na)^+$.

Piperidinone-Containing Amide 13ae. Compound **13ae** was prepared according to the general procedure D from carboxylic acid **8c** and amine **11d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dd, J = 8.2, 6.9 Hz, 2H), 7.24−7.19 (m, 1H), 7.15−7.10 (m, 2H), 6.32 (d, J = 5.9 Hz, 1H), 5.40 (t, J = 7.1 Hz, 1H), 5.14 (d, J = 16.1 Hz, 1H), 4.79 (d, J = 16.1 Hz, 1H), 3.78 (s, 3H), 3.27−3.14 (m, 2H), 2.81−2.74 (m, 1H), 2.56 (d, J = 5.4 Hz, 2H), 2.21 (dd, J = 13.5, 4.4 Hz, 1H), 2.12−2.02 (m, 2H), 1.96−1.85 (m, 2H), 1.77−1.62 (m, 3H), 1.62−1.52 (m, 2H), 1.33 (q, J = 7.3 Hz, 2H), 1.25−1.15 (m, 1H), 0.95−0.84 (m, 7H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 171.7, 171.1, 140.9, 137.4, 128.7, 126.9, 126.3, 115.9, 52.7, 51.8, 49.4, 39.7, 38.5, 37.9, 37.8, 36.8, 36.8, 26.6, 26.0, 25.5, 24.9, 22.6, 22.6; MS(ESI) calcd for $C_{26}H_{36}N_2O_4$ 440.27 (M^+), found 441.27 $(M + H)^+$, 463.24 $(M + Na)^+$.

Piperidinone-Containing Amide 13af. Compound **13af** was prepared according to the general procedure D from carboxylic acid **8c** and amine **11l**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32−7.22 (m, 5H), 7.22−7.08 (m, 5H), 6.36 (s, 1H), 5.38 (t, J = 7.1 Hz, 1H), 5.08 (d, J = 16.1 Hz, 1H), 4.78 (d, J = 16.1 Hz, 1H), 3.76 (s, 3H), 3.25−3.16 (m, 2H), 2.77 (ddd, J = 10.8, 8.8, 4.9 Hz, 1H), 2.66−2.49 (m, 4H), 2.20 (dd, J = 13.5, 4.3 Hz, 1H), 2.12−1.98 (m, 2H), 1.95−1.84 (m, 2H), 1.78−1.52 (m, 8H), 1.51−1.43 (m, 2H), 1.26−1.14 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 171.7, 171.1, 142.3, 140.9, 137.4, 128.7, 128.5, 128.4, 126.9, 126.3, 125.9, 115.9, 52.7, 51.7, 49.4, 39.7, 39.4, 37.8, 36.8, 36.8, 35.6, 29.3, 28.8, 26.6, 25.5, 24.9; MS(ESI) calcd for $C_{31}H_{38}N_2O_4$ 502.28 (M^+), found 503.28 $(M + H)^+$, 505.3 $(M + Na)^+$.

Piperidinone-Containing Amide 13ag. Compound **13ag** was prepared according to the general procedure D from carboxylic acid **8u** and amine **11j**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, J = 1.8, 0.9 Hz, 1H), 6.33 (s, 1H), 6.30 (dd, J = 3.2, 1.8 Hz, 1H), 6.19 (d, J = 3.2 Hz, 1H), 5.67 (t, J = 7.1 Hz, 1H), 5.11 (d, J = 15.9 Hz, 1H), 4.69 (d, J = 15.9 Hz, 1H), 3.76 (s, 3H), 3.21−3.14 (m, 2H), 2.75−2.67 (m, 1H), 2.58−2.48 (m, 2H), 2.22−2.12 (m, 2H), 2.06−1.93 (m, 2H), 1.83−1.73 (m, 2H), 1.73−1.57 (m, 2H), 1.45−1.38 (m, 2H), 1.36−1.23 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 171.6, 171.1, 151.0, 141.6, 140.8, 116.1, 110.6, 108.0, 52.7, 51.8, 43.0, 39.6, 39.3, 37.7, 36.7, 36.6, 31.7, 26.6, 25.4, 24.9, 20.2, 13.9; MS(ESI) calcd for $C_{23}H_{32}N_2O_5$ 416.23 (M^+), found 417.27 $(M + H)^+$, 439.26 $(M + Na)^+$.

Piperidinone-Containing Amide 13ah. Compound **13ah** was prepared according to the general procedure D from carboxylic acid **8u** and amine **11o**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, J = 1.8, 0.9 Hz, 1H), 6.56 (s, 1H), 6.30 (dd, J = 3.2, 1.8 Hz, 1H), 6.19−6.16 (m, 1H), 6.05 (d, J = 3.1 Hz, 1H), 5.88−5.84 (m, 1H), 5.66 (t, J = 7.2 Hz, 1H), 5.06 (d, J = 16.0 Hz, 1H), 4.70 (d, J = 15.9 Hz, 1H), 4.34−4.29 (m, 2H), 3.76 (s, 3H), 2.78−2.71 (m, 1H), 2.60 (dd, J = 14.4, 6.1 Hz, 1H), 2.53 (dd, J = 14.4, 5.0 Hz, 1H), 2.27−2.21 (m, 3H), 2.21−2.12 (m, 2H), 2.06−1.92 (m, 2H), 1.83−1.72 (m, 2H), 1.72−1.57 (m, 3H), 1.31−1.22 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 171.5, 170.9, 151.8, 151.0, 149.7, 141.6, 140.8, 116.0, 110.6, 108.1, 108.0, 106.3, 52.7, 51.8, 43.0, 39.6, 37.5, 36.7, 36.7, 36.6, 26.6, 25.4, 25.0, 13.7; MS(ESI) calcd for $C_{25}H_{30}N_2O_6$ 454.21 (M^+), found 455.26 $(M + H)^+$, 477.24 $(M + Na)^+$.

Piperidinone-Containing Amide 13ai. Compound **13ai** was prepared according to the general procedure D from carboxylic acid **8v** and amine **11f**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85−6.72 (m, 4H),

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5.54−5.47 (m, 1H), 5.42−5.36 (m, 1H), 4.36 (dd, J = 14.6, 5.8 Hz, 1H), 4.31 (dd, J = 14.6, 5.6 Hz, 1H), 3.94−3.81 (m, 7H), 3.76 (s, 3H), 3.63−3.54 (m, 1H), 2.72−2.64 (m, 1H), 2.56 (dd, J = 14.2, 6.8 Hz, 1H), 2.45 (dd, J = 14.1, 4.2 Hz, 1H), 2.27−2.18 (m, 1H), 2.16−2.08 (m, 2H), 2.08−2.01 (m, 1H), 1.97 (s, 8H), 1.81 (dd, J = 11.2, 5.9 Hz, 1H), 1.75−1.62 (m, 3H), 1.62−1.56 (m, 2H), 1.56−1.48 (m, 2H), 1.40−1.30 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 171.3, 171.2, 149.2, 148.3, 140.6, 135.1, 131.3, 122.9, 120.0, 114.4, 111.1, 111.1, 56.0, 56.0, 52.6, 51.7, 43.5, 43.4, 39.9, 38.0, 37.1, 36.6, 34.9, 28.5, 27.0, 25.7, 25.4, 25.1, 23.0, 22.5; MS(ESI) calcd for $C_{31}H_{42}N_2O_6$ 538.30 (M^+), found 539.35 (M + H)$^+$.

Piperidinone-Containing Amide 13aj. Compound **13aj** was prepared according to the general procedure D from carboxylic acid **8v** and amine **11m**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (td, J = 7.8, 1.8 Hz, 1H), 7.11 (dd, J = 7.4, 1.8 Hz, 1H), 6.90−6.82 (m, 2H), 6.44 (s, 1H), 5.51 (dd, J = 8.2, 6.2 Hz, 1H), 5.42 (dd, J = 4.2, 2.4 Hz, 1H), 4.00−3.87 (m, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 3.60 (ddd, J = 14.2, 8.7, 5.9 Hz, 1H), 3.50−3.38 (m, 2H), 2.79 (t, J = 6.9 Hz, 2H), 2.67−2.59 (m, 1H), 2.56 (dd, J = 14.3, 6.3 Hz, 1H), 2.36−2.12 (m, 4H), 2.12−1.87 (m, 7H), 1.87−1.77 (m, 1H), 1.76−1.57 (m, 6H), 1.57−1.49 (m, 2H), 1.40−1.30 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 171.2, 171.2, 157.6, 140.7, 135.2, 130.7, 127.8, 127.5, 122.9, 120.7, 114.2, 110.4, 55.4, 52.6, 51.8, 43.4, 39.8, 39.7, 37.8, 37.1, 36.5, 35.0, 30.4, 28.5, 27.1, 25.7, 25.4, 25.1, 23.0, 22.5; MS(ESI) calcd for $C_{31}H_{42}N_2O_5$ 522.31 (M^+), found 523.37 (M + H)$^+$.

Piperidinone-Containing Amide 13ak. Compound **13ak** was prepared according to the general procedure D from carboxylic acid **8w** and amine **11x**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.27 (m, 2H), 7.25−7.12 (m, 3H), 6.83−6.74 (m, 3H), 5.59 (t, J = 7.1 Hz, 1H), 4.75 (d, J = 12.8 Hz, 1H), 4.11−3.96 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.81−3.74 (m, 3H), 3.16−2.95 (m, 2H), 2.92−2.79 (m, 3H), 2.77−2.57 (m, 2H), 2.45−2.35 (m, 1H), 2.32−2.21 (m, 1H), 2.18 (dd, J = 13.0, 4.4 Hz, 1H), 2.12−1.99 (m, 2H), 1.91−1.83 (m, 3H), 1.82−1.75 (m, 1H), 1.75−1.54 (m, 6H), 1.46−1.38 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 171.2, 169.1, 149.0, 147.6, 145.3, 141.1, 131.9, 128.7, 126.8, 126.6, 120.8, 113.6, 112.2, 111.3, 56.0, 56.0, 52.6, 51.8, 46.5, 46.4, 46.2, 42.9, 42.8, 42.6, 42.5, 39.9, 36.9, 35.9, 34.2, 33.9, 33.1, 33.0, 32.7, 26.6, 25.5, 25.2; MS(ESI) calcd for $C_{35}H_{44}N_2O_6$ 588.32 (M^+), found 589.39 (M + H)$^+$.

Piperidinone-Containing Amide 13al. Compound **13al** was prepared according to the general procedure D from carboxylic acid **8w** and amine **11v**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82−6.73 (m, 3H), 5.58 (t, J = 7.1 Hz, 1H), 4.10−4.02 (m, 1H), 4.01−3.93 (m, 1H), 3.86 (d, J = 10.6 Hz, 7H), 3.78 (s, 4H), 3.74−3.64 (m, 2H), 2.91 (dd, J = 16.3, 4.0 Hz, 1H), 2.88−2.83 (m, 2H), 2.82−2.76 (m, 1H), 2.69−2.53 (m, 4H), 2.32 (dd, J = 16.3, 7.7 Hz, 1H), 2.25 (q, J = 7.9, 7.3 Hz, 1H), 2.12 (dd, J = 13.0, 4.4 Hz, 1H), 2.09−1.97 (m, 2H), 1.82−1.75 (m, 1H), 1.75−1.60 (m, 4H), 1.45−1.37 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 171.0, 169.3, 149.0, 147.7, 141.0, 131.9, 120.8, 113.8, 112.2, 111.3, 56.1, 56.0, 52.6, 51.8, 48.2, 46.3, 44.5, 39.9, 36.9, 35.8, 34.2, 32.7, 27.9, 27.5, 26.6, 25.6, 25.2; MS(ESI) calcd for $C_{28}H_{38}N_2O_6S$ 530.25 (M^+), found 531.31 (M + H)$^+$.

Piperidinone-Containing Amide 13am. Compound **13am** was prepared according to the general procedure D from carboxylic acid **8x** and amine **11x**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 8.2 Hz, 1H), 7.87 (dd, J = 8.0, 1.6 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.56−7.47 (m, 2H), 7.44 (t, J = 7.7 Hz, 1H), 7.36−7.26 (m, 3H), 7.24−7.13 (m, 3H), 5.58 (dd, J = 17.2, 6.7 Hz, 1H), 5.32 (t, J = 6.9 Hz, 1H), 5.26 (dd, J = 16.5, 8.5 Hz, 1H), 4.81 (d, J = 12.1 Hz, 1H), 4.06−3.99 (m, 1H), 3.83 (s, 3H), 3.16−3.06 (m, 1H), 3.05−2.93 (m, 2H), 2.77−2.58 (m, 3H), 2.34−2.27 (m, 1H), 2.14 (t, J = 13.1 Hz, 1H), 2.10−2.00 (m, 2H), 1.95−1.84 (m, 3H), 1.83−1.54 (m, 6H), 1.33−1.23 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 171.3, 145.3, 141.4, 133.8, 132.0, 130.7, 128.9, 128.7, 127.2, 126.9, 126.6, 126.0, 125.9, 125.6, 123.6, 122.8, 115.3, 52.6, 51.9, 48.7, 46.2, 42.9, 42.7, 42.5, 40.0, 36.6, 36.1, 34.1, 33.8, 33.1, 26.1, 25.0; MS(ESI) calcd for $C_{36}H_{40}N_2O_4$ 564.30 (M^+), found 565.3 (M + H)$^+$.

Piperidinone-Containing Amide 13an. Compound **13an** was prepared according to the general procedure D from carboxylic acid **8x** and amine **11o**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (dd, J = 8.3, 1.3 Hz, 1H), 7.90−7.85 (m, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.56−7.47 (m, 2H), 7.41 (dd, J = 8.3, 7.1 Hz, 1H), 7.14 (dd, J = 7.1, 1.3 Hz, 1H), 6.53 (s, 1H), 6.03 (d, J = 3.0 Hz, 1H), 5.85−5.82 (m, 1H), 5.45 (d, J = 16.4 Hz, 1H), 5.35−5.27 (m, 2H), 4.41−4.28 (m, 2H), 3.81 (s, 3H), 2.94−2.83 (m, 1H), 2.63 (d, J = 5.4 Hz, 2H), 2.30−2.23 (m, 1H), 2.22 (s, 3H), 2.10−1.98 (m, 3H), 1.91−1.83 (m, 1H), 1.78−1.62 (m, 3H), 1.62−1.52 (m, 1H), 1.26−1.15 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 171.4, 170.9, 151.8, 149.6, 141.1, 133.9, 131.5, 130.6, 129.0, 127.4, 126.1, 125.7, 123.2, 122.7, 116.0, 108.1, 106.3, 52.7, 51.8, 48.4, 39.6, 37.6, 36.9, 36.8, 36.8, 26.5, 25.4, 25.0, 13.7; MS(ESI) calcd for $C_{31}H_{34}N_2O_5$ 514.25 (M^+), found 515.25 (M + H)$^+$, 527.23 (M + Na)$^+$.

Piperidinone-Containing Amide 13ao. Compound **13ao** was prepared according to the general procedure D from carboxylic acid **8y** and amine **11d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, J = 2.1 Hz, 1H), 7.19 (dd, J = 8.3, 2.2 Hz, 1H), 6.99 (d, J = 8.3 Hz, 1H), 6.05 (s, 1H), 5.16 (t, J = 7.0 Hz, 1H), 4.91 (s, 2H), 3.80 (s, 3H), 3.26−3.14 (m, 2H), 2.81−2.72 (m, 1H), 2.59 (dd, J = 14.6, 4.8 Hz, 1H), 2.52 (dd, J = 14.6, 5.7 Hz, 1H), 2.21 (dd, J = 13.4, 4.6 Hz, 1H), 2.14−1.99 (m, 3H), 1.97−1.87 (m, 1H), 1.82−1.72 (m, 2H), 1.72−1.52 (m, 3H), 1.37−1.23 (m, 3H), 0.89 (d, J = 3.4 Hz, 3H), 0.87 (d, J = 3.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 171.5, 170.8, 141.0, 133.1, 133.0, 133.0, 129.3, 128.3, 127.5, 115.2, 52.8, 51.8, 47.8, 39.5, 38.5, 38.0, 37.4, 37.0, 36.6, 26.4, 26.0, 25.4, 25.0, 22.6, 22.6; MS(ESI) calcd for $C_{26}H_{34}Cl_2N_2O_4$ 508.19 (M^+), found 509.23 (M + H)$^+$, 531.22 (M + Na)$^+$.

Piperidinone-Containing Amide 13ap. Compound **13ap** was prepared according to the general procedure D from carboxylic acid **8y** and amine **11i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, J = 2.1 Hz, 1H), 7.18 (dd, J = 8.4, 2.2 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 6.28 (s, 1H), 5.17 (t, J = 7.0 Hz, 1H), 5.01 (d, J = 17.1 Hz, 1H), 4.82 (d, J = 17.2 Hz, 1H), 3.80 (s, 3H), 2.94−2.84 (m, 2H), 2.82−2.72 (m, 1H), 2.64 (dd, J = 14.1, 4.5 Hz, 1H), 2.56 (dd, J = 14.4, 5.9 Hz, 1H), 2.22 (dd, J = 13.5, 4.5 Hz, 1H), 2.15−1.98 (m, 3H), 1.98−1.86 (m, 4H), 1.83−1.64 (m, 6H), 1.64−1.54 (m, 4H), 1.45−1.39 (m, 6H), 1.32−1.24 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 171.6, 171.1, 141.1, 133.1, 133.0, 132.9, 129.3, 128.3, 127.5, 115.2, 52.8, 51.8, 51.1, 47.8, 40.3, 39.5, 37.5, 37.1, 37.0, 36.7, 33.7, 28.3, 26.6, 25.5, 25.0; MS(ESI) calcd for $C_{32}H_{40}Cl_2N_2O_4$ 586.24 (M^+), found 587.28 (M + H)$^+$.

Piperidinone-Containing Amide 13aq. Compound **13aq** was prepared according to the general procedure D from carboxylic acid **8z** and amine **11v**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.20 (t, J = 4.1 Hz, 1H), 3.98−3.89 (m, 1H), 3.79−3.66 (m, 5H), 3.65 (s, 3H), 2.78−2.64 (m, 2H), 2.62−2.48 (m, 5H), 2.25 (dd, J = 12.6, 5.9 Hz, 1H), 2.19 (d, J = 13.6 Hz, 1H), 2.00 (d, J = 4.1 Hz, 2H), 1.80 (t, J = 12.7 Hz, 1H), 1.69−1.61 (m, 1H), 1.59−1.51 (m, 1H), 1.43 (d, J = 13.5 Hz, 1H), 1.35−1.21 (m, 10H), 0.95 (s, 3H), 0.87 (t, J = 6.9 Hz, 3H), 0.84 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.8, 169.8, 169.2, 135.6, 106.4, 52.4, 48.3, 47.5, 45.5, 44.5, 44.5, 38.9, 38.7, 36.5, 35.4, 32.0, 31.9, 29.5, 29.5, 28.7, 27.9, 27.5, 27.4, 26.9, 25.5, 22.8, 14.2; MS(ESI) calcd for $C_{27}H_{44}N_2O_4S$ 492.30 (M^+), found 493.42 (M + H)$^+$, 515.4 (M + Na)$^+$.

Piperidinone-Containing Amide 13ar. Comound **13ar** was prepared according to the general procedure D from carboxylic acid **8z** and amine **11l**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.23 (m, 3H), 7.21−7.13 (m, 3H), 6.29 (s, 1H), 5.16 (t, J = 4.1 Hz, 1H), 3.72−3.65 (m, 2H), 3.64 (s, 3H), 3.28−3.14 (m, 2H), 2.67−2.57 (m, 3H), 2.54−2.39 (m, 2H), 2.26 (dd, J = 12.9, 5.7 Hz, 1H), 2.19 (d, J = 13.7 Hz, 1H), 2.00−1.95 (m, 2H), 1.72 (t, J = 13.1 Hz, 1H), 1.68−1.56 (m, 3H), 1.55−1.45 (m, 2H), 1.42 (d, J = 13.6 Hz, 1H), 1.35−1.22 (m, 10H), 0.95 (s, 3H), 0.88 (t, J = 6.7 Hz, 3H), 0.83 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 171.1, 170.0, 142.3, 135.3, 128.5, 128.4, 125.9, 106.9, 52.5, 47.3, 45.5, 44.5, 39.4, 38.8, 38.4, 37.4, 35.6, 32.0, 31.8, 29.5, 29.5, 29.4, 28.7, 28.6, 27.4, 26.9, 25.4, 22.8, 14.2; MS(ESI) calcd for $C_{33}H_{50}N_2O_4$ 538.38 (M^+), found 539.49 (M + H)$^+$.

Piperidinone-Containing Amide 13as. Compound **13as** was prepared according to the general procedure D from carboxylic acid **8aa** and amine **11f**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.27 (m, 2H), 7.23−7.16 (m, 3H), 6.79−6.72 (m, 3H), 6.38 (s, 1H), 5.41 (d, J

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= 16.1 Hz, 1H), 5.09 (t, J = 4.1 Hz, 1H), 4.50 (d, J = 16.1 Hz, 1H), 4.42−4.34 (m, 1H), 4.25 (dd, J = 14.4, 5.3 Hz, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 3.66 (s, 3H), 2.77 (dd, J = 14.4, 5.0 Hz, 1H), 2.65 (dt, J = 18.4, 5.3 Hz, 1H), 2.50 (dd, J = 14.4, 4.9 Hz, 1H), 2.34 (dd, J = 12.9, 5.8 Hz, 1H), 2.26−2.19 (m, 1H), 2.03 (t, J = 13.2 Hz, 1H), 1.90−1.85 (m, 2H), 1.47 (d, J = 13.7 Hz, 1H), 0.93 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 170.8, 170.5, 149.2, 148.4, 137.7, 136.2, 131.1, 128.6, 126.8, 126.3, 120.1, 111.2, 111.2, 108.3, 56.0, 55.9, 52.6, 49.2, 47.2, 45.7, 43.4, 38.7, 38.6, 38.5, 37.4, 31.8, 28.6, 25.4; MS(ESI) calcd for $C_{31}H_{38}N_2O_6$ 534.27 (M^+), found 535.34 (M + H)$^+$, 557.33 (M + Na)$^+$.

Piperidinone-Containing Amide 13at. Compound **13at** was prepared according to the general procedure D from carboxylic acid **8aa** and amine **11g**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51−7.44 (m, 2H), 7.42−7.34 (m, 2H), 7.31−7.26 (m, 2H), 7.22−7.17 (m, 3H), 6.77 (t, J = 6.1 Hz, 1H), 5.39 (d, J = 16.1 Hz, 1H), 5.12 (t, J = 4.1 Hz, 1H), 4.56−4.44 (m, 2H), 4.31 (dd, J = 15.2, 5.6 Hz, 1H), 3.66 (s, 3H), 2.79 (dd, J = 14.4, 4.8 Hz, 1H), 2.69−2.60 (m, 1H), 2.54 (dd, J = 14.4, 5.2 Hz, 1H), 2.35 (dd, J = 13.0, 5.8 Hz, 1H), 2.23 (d, J = 13.6 Hz, 2H), 1.99 (t, J = 13.2 Hz, 1H), 1.91−1.86 (m, 2H), 1.48 (d, J = 13.7 Hz, 1H), 0.94 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 171.2, 170.6, 139.7, 137.6, 136.2, 131.1, 131.0 (q, $^2J_{C-F}$ = 31.5 Hz), 129.2, 128.6, 126.9, 126.3, 124.2 (q, $^1J_{C-F}$ = 272.2 Hz), 124.4 (q, $^3J_{C-F}$ = 3.8 Hz), 124.2 (q, $^3J_{C-F}$ = 3.8 Hz), 108.6, 52.6, 49.3, 47.2, 45.7, 43.0, 38.7, 38.6, 38.5, 37.5, 31.8, 28.6, 25.4; MS(ESI) calcd for $C_{30}H_{33}F_3N_2O_4$ 542.24 (M^+), found 543.32 (M + H)$^+$, 565.3 (M + Na)$^+$.

Piperidinone-Containing Amide 13au. Compound **13au** was prepared according to the general procedure D from carboxylic acid **8ab** and amine **11c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77−6.72 (m, 2H), 6.71−6.65 (m, 1H), 6.36 (s, 1H), 5.94−5.89 (m, 2H), 5.36 (d, J = 15.8 Hz, 1H), 5.12 (t, J = 4.1 Hz, 1H), 4.42 (d, J = 15.8 Hz, 1H), 3.66 (s, 3H), 3.44−3.38 (m, 2H), 3.38−3.32 (m, 1H), 3.29 (s, 3H), 3.27−3.17 (m, 1H), 2.74 (dd, J = 14.5, 5.3 Hz, 1H), 2.63−2.54 (m, 1H), 2.49 (dd, J = 14.6, 4.7 Hz, 1H), 2.30 (dd, J = 13.0, 5.8 Hz, 1H), 2.20 (d, J = 13.6 Hz, 1H), 1.95 (t, J = 13.1 Hz, 1H), 1.90−1.86 (m, 2H), 1.77−1.68 (m, 2H), 1.45 (d, J = 13.6 Hz, 1H), 0.92 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.61, 170.76, 170.59, 148.00, 146.40, 136.34, 131.84, 119.49, 108.35, 108.17, 107.29, 101.01, 71.45, 58.84, 52.55, 49.13, 47.23, 45.65, 38.72, 38.43, 38.35, 37.86, 37.29, 31.85, 29.31, 28.63, 25.44; MS(ESI) calcd for $C_{27}H_{36}N_2O_7$ 500.25 (M^+), found 501.33 (M + H)$^+$, 523.31 (M + Na)$^+$.

Piperidinone-Containing Amide 13av. Compound **13av** was prepared according to the general procedure D from carboxylic acid **8ab** and amine **11i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77−6.70 (m, 2H), 6.70−6.65 (m, 1H), 5.94−5.90 (m, 2H), 5.27 (d, J = 15.7 Hz, 1H), 5.17 (t, J = 4.1 Hz, 1H), 4.52 (d, J = 15.7 Hz, 1H), 3.65 (s, 3H), 3.03 (dd, J = 13.4, 6.8 Hz, 1H), 2.96−2.84 (m, 1H), 2.80 (dd, J = 13.4, 5.5 Hz, 1H), 2.63−2.50 (m, 2H), 2.34 (dd, J = 13.0, 5.6 Hz, 1H), 2.21 (d, J = 13.6 Hz, 1H), 1.97−1.91 (m, 3H), 1.89 (d, J = 4.0 Hz, 2H), 1.68 (d, J = 12.4 Hz, 4H), 1.65−1.55 (m, 4H), 1.49−1.39 (m, 7H), 0.93 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 171.4, 171.0, 148.0, 146.5, 136.1, 131.4, 119.7, 108.3, 107.4, 101.0, 52.5, 51.3, 49.0, 47.1, 45.6, 40.3, 40.2, 39.7, 38.7, 38.4, 37.4, 37.0, 36.5, 33.8, 31.8, 28.6, 28.3, 28.0, 25.4; MS(ESI) calcd for $C_{34}H_{44}N_2O_6$ 576.32 (M^+), found 577.39 (M + H)$^+$.

Piperidinone-Containing Amide 13aw. Compound **13aw** was prepared according to the general procedure D from carboxylic acid **8d** and amine **11r**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (dd, J = 1.6, 0.8 Hz, 1H), 7.32 (dd, J = 1.7, 0.9 Hz, 1H), 7.04 (dd, J = 3.5, 0.9 Hz, 1H), 6.49 (dd, J = 3.5, 1.8 Hz, 1H), 6.34−6.28 (m, 2H), 5.38 (t, J = 4.1 Hz, 1H), 5.29 (d, J = 15.9 Hz, 1H), 4.56 (d, J = 15.9 Hz, 1H), 3.79 (s, 4H), 3.64 (s, 4H), 3.54 (t, J = 5.0 Hz, 2H), 2.83 (dd, J = 16.4, 6.7 Hz, 1H), 2.75 (dd, J = 16.4, 3.6 Hz, 1H), 2.67−2.59 (m, 1H), 2.30 (dd, J = 12.7, 5.9 Hz, 1H), 2.20 (d, J = 13.6 Hz, 1H), 2.00−1.95 (m, 2H), 1.91 (t, J = 12.8 Hz, 1H), 1.44 (d, J = 13.7 Hz, 1H), 0.94 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.7, 170.1, 169.4, 159.3, 151.4, 147.8, 144.1, 141.4, 136.2, 117.2, 111.6, 110.7, 108.0, 107.7, 52.6, 47.4, 45.7, 42.8, 38.8, 38.8, 36.6, 35.0, 31.8, 28.7, 25.4; MS(ESI) calcd for $C_{29}H_{35}N_3O_7$ 537.25 (M^+), found 538.33 (M + H)$^+$, 560.31 (M + Na)$^+$.

Piperidinone-Containing Amide 13ax. Compound **13ax** was prepared according to the general procedure D from carboxylic acid **8d** and amine **11o**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, J = 1.8, 0.9 Hz, 1H), 6.38−6.27 (m, 2H), 6.25 (dd, J = 3.2, 1.0 Hz, 1H), 6.03 (d, J = 3.0 Hz, 1H), 5.85 (dd, J = 2.7, 1.4 Hz, 1H), 5.40 (t, J = 4.1 Hz, 1H), 5.27 (d, J = 15.9 Hz, 1H), 4.53 (d, J = 15.9 Hz, 1H), 4.36 (dd, J = 15.4, 5.9 Hz, 1H), 4.17 (dd, J = 15.4, 5.1 Hz, 1H), 3.64 (s, 3H), 2.71 (dd, J = 14.4, 5.1 Hz, 1H), 2.62−2.53 (m, 1H), 2.50 (dd, J = 14.3, 4.9 Hz, 1H), 2.29 (dd, J = 13.0, 5.9 Hz, 1H), 2.24 (s, 3H), 2.20 (d, J = 13.6 Hz, 1H), 1.97 (d, J = 4.0 Hz, 2H), 1.80 (t, J = 13.1 Hz, 1H), 1.44 (d, J = 13.7 Hz, 1H), 0.95 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 170.6, 170.2, 151.8, 151.3, 149.6, 141.6, 136.0, 110.6, 108.2, 108.2, 107.9, 106.3, 52.6, 47.2, 45.6, 42.5, 38.8, 38.4, 38.4, 37.3, 36.7, 31.8, 28.7, 25.3, 13.7; MS(ESI) calcd for $C_{26}H_{32}N_2O_6$ 468.23 (M^+), found 469.31 (M + H)$^+$, 491.28 (M + Na)$^+$.

Piperidinone-Containing Amide 13ay. Compound **13ay** was prepared according to the general procedure D from carboxylic acid **8ac** and amine **11h**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, J = 6.8, 2.4 Hz, 1H), 7.87−7.81 (m, 1H), 7.77 (t, J = 4.8 Hz, 1H), 7.53−7.45 (m, 2H), 7.41−7.36 (m, 2H), 6.48 (t, J = 5.2 Hz, 1H), 5.34 (t, J = 3.5 Hz, 1H), 5.06 (dd, J = 14.5, 6.8 Hz, 1H), 4.94 (t, J = 4.0 Hz, 1H), 4.60 (dd, J = 14.5, 4.6 Hz, 1H), 3.59 (s, 3H), 3.42 (t, J = 8.3 Hz, 2H), 2.80 (dd, J = 13.9, 4.6 Hz, 1H), 2.51−2.38 (m, 2H), 2.25 (dd, J = 12.9, 5.7 Hz, 1H), 2.18 (d, J = 13.4 Hz, 1H), 2.05−1.91 (m, 6H), 1.90−1.84 (m, 2H), 1.77−1.64 (m, 2H), 1.62−1.50 (m, 4H), 1.38 (d, J = 13.6 Hz, 1H), 0.97 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 170.5, 169.5, 135.3, 134.9, 134.0, 134.0, 131.5, 128.8, 128.6, 126.9, 126.6, 125.9, 125.5, 123.9, 122.4, 106.8, 52.4, 47.2, 45.4, 43.3, 41.5, 38.8, 38.5, 38.1, 37.5, 34.4, 31.9, 28.6, 28.6, 25.4, 25.4, 23.0, 22.5; MS(ESI) calcd for $C_{34}H_{42}N_2O_4$ 542.31 (M^+), found 543.38 (M + H)$^+$.

Piperidinone-Containing Amide 13az. Compound **13az** was prepared according to the general procedure D from carboxylic acid **8ac** and amine **11k**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.27 (m, 2H), 7.26−7.20 (m, 3H), 6.62 (t, J = 5.6 Hz, 1H), 5.44 (m, 1H), 5.21 (t, J = 4.1 Hz, 1H), 4.45 (dd, J = 14.6, 6.9 Hz, 1H), 4.32 (dd, J = 15.0, 5.5 Hz, 1H), 3.81−3.66 (m, 2H), 3.64 (s, 3H), 2.71 (dd, J = 13.7, 4.3 Hz, 1H), 2.57−2.45 (m, 2H), 2.28 (dd, J = 12.8, 5.6 Hz, 1H), 2.24−2.18 (m, 2H), 2.04−1.92 (m, 7H), 1.75 (t, J = 13.0 Hz, 1H), 1.65−1.51 (m, 4H), 1.45 (d, J = 13.7 Hz, 1H), 0.97 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 171.0, 169.8, 138.6, 135.4, 135.3, 128.7, 127.8, 127.4, 122.5, 106.9, 52.5, 47.3, 45.5, 43.6, 43.5, 38.9, 38.7, 38.4, 37.4, 34.8, 31.8, 28.7, 28.6, 25.5, 25.4, 23.1, 22.5; MS(ESI) calcd for $C_{30}H_{40}N_2O_4$ 492.30 (M^+), found 493.35 (M + H)$^+$, 515.34 (M + Na)$^+$.

Piperidinone-Containing Amide 13ba. Compound **13ba** was prepared according to the general procedure D from carboxylic acid **8ad** and amine **11c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84−6.78 (m, 3H), 5.27 (t, J = 4.1 Hz, 1H), 3.93 (t, J = 8.4 Hz, 2H), 3.88 (s, 3H), 3.85 (s, 3H), 3.65 (s, 3H), 3.42 (t, J = 5.9 Hz, 2H), 3.35−3.27 (m, 5H), 2.98−2.88 (m, 1H), 2.81−2.71 (m, 1H), 2.66−2.59 (m, 1H), 2.59−2.47 (m, 4H), 2.27 (dd, J = 12.6, 5.3 Hz, 1H), 2.24−2.18 (m, 1H), 2.05−1.99 (m, 2H), 1.82−1.69 (m, 3H), 1.46 (d, J = 13.6 Hz, 1H), 0.97 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 170.8, 170.0, 149.0, 147.7, 135.4, 132.1, 120.7, 112.2, 111.4, 106.8, 71.4, 58.9, 56.1, 56.0, 52.5, 47.3, 46.1, 45.5, 38.9, 38.5, 38.4, 37.8, 37.1, 32.7, 31.8, 29.4, 28.7, 25.4; MS(ESI) calcd for $C_{29}H_{42}N_2O_7$ 530.30 (M^+), found 531.36 (M + H)$^+$, 553.35 (M + Na)$^+$.

Piperidinone-Containing Amide 13bb. Compound **13bb** was prepared according to the general procedure D from carboxylic acid **8ad** and amine **11i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84−6.76 (m, 3H), 6.24 (s, 1H), 5.29 (t, J = 4.0 Hz, 1H), 4.07−3.97 (m, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.65 (s, 3H), 2.97−2.83 (m, 3H), 2.81−2.71 (m, 2H), 2.58−2.45 (m, 2H), 2.29 (dd, J = 12.9, 5.6 Hz, 1H), 2.23 (dd, J = 13.6, 1.7 Hz, 1H), 2.05−1.99 (m, 2H), 1.96−1.91 (m, 3H), 1.80 (t, J = 13.0 Hz, 1H), 1.73−1.55 (m, 8H), 1.50−1.40 (m, 7H), 0.97 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 171.1, 170.1, 149.0, 147.7, 135.3, 132.0, 120.6, 112.1, 111.4, 107.1, 56.0, 56.0, 52.5, 51.1, 47.3, 45.9, 45.6, 40.3, 39.7, 38.9, 38.6, 38.3, 37.5, 37.0, 36.5, 33.7,

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32.6, 31.8, 28.7, 28.3, 28.0, 25.5; MS(ESI) calcd for $C_{36}H_{50}N_2O_6$ 606.37 (M^+), found 607.42 $(M + H)^+$.

Piperidinone-Containing Amide 13bc. Compound **13bc** was prepared according to the general procedure D from carboxylic acid **8ae** and amine **11b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 8.2 Hz, 1H), 7.93−7.87 (m, 1H), 7.77 (d, J = 8.2 Hz, 1H), 7.54 (m, 2H), 7.42 (t, J = 7.7 Hz, 1H), 7.13 (d, J = 7.0 Hz, 1H), 5.94 (d, J = 16.7 Hz, 1H), 5.10 (t, J = 4.1 Hz, 1H), 4.97 (d, J = 16.7 Hz, 1H), 3.73 (s, 3H), 3.27 (s, 1H), 3.21 (dt, J = 13.2, 6.5 Hz, 1H), 2.99 (m, 1H), 2.74−2.66 (m, 1H), 2.63 (dd, J = 14.9, 7.0 Hz, 1H), 2.49 (dd, J = 13.2, 5.8 Hz, 1H), 2.28 (dd, J = 13.6, 1.8 Hz, 1H), 2.05 (t, J = 13.2 Hz, 1H), 1.91−1.77 (m, 2H), 1.71−1.57 (m, 6H), 1.51 (d, J = 13.8 Hz, 2H), 1.21−1.06 (m, 3H), 0.94 (s, 3H), 0.91−0.84 (m, 2H), 0.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 172.1, 171.7, 135.9, 133.8, 131.0, 130.3, 129.1, 127.6, 126.4, 126.0, 125.7, 122.5, 122.2, 52.8, 48.5, 46.8, 45.6, 38.6, 38.5, 37.5, 37.0, 31.7, 30.9, 30.9, 30.4, 28.7, 26.4, 25.8, 25.8, 25.4, 25.3; MS(ESI) calcd for $C_{33}H_{42}N_2O_4$ 530.31 (M^+), found 531.4 $(M + H)^+$.

Piperidinone-Containing Amide 13bd. Compound **13bd** was prepared according to the general procedure D from carboxylic acid **8ae** and amine **11p**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.73 (d, J = 8.2 Hz, 1H), 7.58−7.47 (m, 2H), 7.42 (t, J = 7.6 Hz, 1H), 7.24 (d, J = 7.1 Hz, 1H), 6.38 (s, 1H), 5.97 (d, J = 16.7 Hz, 1H), 4.97 (dd, J = 5.1, 3.0 Hz, 1H), 4.89 (d, J = 16.7 Hz, 1H), 3.71 (s, 3H), 3.46−3.36 (m, 3H), 3.30 (t, J = 6.6 Hz, 2H), 3.27−3.17 (m, 1H), 2.83 (dd, J = 14.6, 5.4 Hz, 1H), 2.72−2.62 (m, 1H), 2.49 (dd, J = 14.6, 4.6 Hz, 1H), 2.39 (dd, J = 13.0, 5.8 Hz, 1H), 2.25 (dd, J = 13.7, 1.8 Hz, 1H), 2.14 (t, J = 13.2 Hz, 1H), 1.89−1.74 (m, 2H), 1.74−1.65 (m, 2H), 1.56−1.44 (m, 3H), 1.35−1.23 (m, 2H), 0.92 (s, 3H), 0.87 (t, J = 7.4 Hz, 3H), 0.83 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.7, 170.7, 170.4, 136.6, 133.8, 131.9, 130.5, 128.9, 127.2, 126.1, 125.8, 125.7, 122.8, 122.6, 108.5, 71.0, 69.5, 52.6, 48.2, 47.3, 45.8, 38.6, 38.5, 38.2, 38.1, 37.5, 31.9, 31.9, 29.3, 28.7, 25.4, 19.5, 14.0; MS(ESI) calcd for $C_{33}H_{44}N_2O_5$ 548.33 (M^+), found 549.41 $(M + H)^+$, 571.39 $(M + Na)^+$.

Piperidinone-Containing Amide 13be. Compound **13be** was prepared according to the general procedure D from carboxylic acid **8af** and amine **11e**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, J = 2.0 Hz, 1H), 7.26−7.21 (m, 1H), 7.21−7.14 (m, 2H), 6.94−6.88 (m, 2H), 6.31 (s, 1H), 5.31 (d, J = 17.2 Hz, 1H), 4.88 (t, J = 4.0 Hz, 1H), 4.63−4.44 (m, 3H), 3.71 (s, 3H), 2.88 (dd, J = 15.1, 5.0 Hz, 1H), 2.64−2.54 (m, 1H), 2.44 (dd, J = 15.1, 4.4 Hz, 1H), 2.30 (dd, J = 12.9, 5.8 Hz, 1H), 2.23 (d, J = 13.7 Hz, 1H), 2.14 (t, J = 13.1 Hz, 1H), 1.91−1.86 (m, 2H), 1.50 (d, J = 13.6 Hz, 1H), 0.94 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 170.6, 170.5, 141.0, 136.1, 133.3, 133.1, 132.8, 129.1, 128.6, 127.5, 127.0, 126.0, 125.2, 108.2, 52.7, 47.3, 47.2, 45.7, 38.6, 38.4, 38.2, 37.6, 37.1, 31.8, 28.7, 25.5; MS(ESI) calcd for $C_{27}H_{30}Cl_2N_2O_4S$ 548.13 (M^+), found 549.2 $(M + H)^+$.

Piperidinone-Containing Amide 13bf. Compound **13bf** was prepared according to the general procedure D from carboxylic acid **8af** and amine **11j**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, J = 1.8 Hz, 1H), 7.23−7.16 (m, 2H), 5.87 (s, 1H), 5.37 (d, J = 17.2 Hz, 1H), 4.87 (t, J = 4.1 Hz, 1H), 4.52 (d, J = 17.2 Hz, 1H), 3.71 (s, 3H), 3.28−3.17 (m, 1H), 3.16−3.05 (m, 1H), 2.85 (dd, J = 14.9, 5.0 Hz, 1H), 2.56 (dt, J = 15.0, 5.1 Hz, 1H), 2.40 (dd, J = 15.0, 4.3 Hz, 1H), 2.29 (dd, J = 12.9, 5.8 Hz, 1H), 2.22 (d, J = 13.7 Hz, 1H), 2.14 (t, J = 13.1 Hz, 1H), 1.90−1.85 (m, 2H), 1.49 (d, J = 13.7 Hz, 1H), 1.45−1.35 (m, 2H), 1.34−1.23 (m, 2H), 0.93 (s, 3H), 0.88 (t, J = 7.3 Hz, 3H), 0.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 170.7, 170.7, 136.2, 133.3, 133.0, 132.8, 129.1, 128.5, 127.4, 108.2, 52.7, 47.5, 47.2, 45.7, 39.5, 38.6, 38.3, 37.7, 37.2, 31.8, 31.7, 28.7, 25.4, 20.2, 13.9; MS(ESI) calcd for $C_{26}H_{34}Cl_2N_2O_4$ 508.19 (M^+), found 509.23 $(M + H)^+$, 531.23 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27a ((3*SR*,4a*RS*,5*RS*,7*RS*)-Methyl 7-*tert*-Butyl-5-methyl-1-octyl-2-oxo-3-(2-oxo-2-(prop-2-yn-1-ylamino)ethyl)-2,3,4,4a,5,7-hexahydro-1*H*-pyrano[4,3-*b*]pyridine-4a-carboxylate). Compound **27a** was prepared according to the general procedure D from carboxylic acid **26e** and amine **11a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.48 (d, J = 1.8 Hz, 1H), 4.02 (ddd, J = 17.7, 5.2, 2.6 Hz, 1H), 3.96 (ddd, J = 17.5, 4.9, 2.6 Hz, 1H), 3.90 (q, J = 6.4 Hz, 1H), 3.83 (d, J = 1.6 Hz, 1H), 3.82−3.75 (m, 1H), 3.67 (s, 3H), 3.50−3.43 (m, 1H), 3.10−3.02 (m, 1H), 2.68−2.60 (m, 1H), 2.56 (dd, J = 14.8, 5.9 Hz, 1H), 2.46 (dd, J = 12.9, 7.6 Hz, 1H), 2.20 (t, J = 2.6 Hz, 1H), 1.69−1.58 (m, 2H), 1.50−1.41 (m, 1H), 1.34−1.20 (m, 12H), 1.17 (d, J = 6.5 Hz, 3H), 0.89 (d, J = 15.2 Hz, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 170.8, 170.7, 138.1, 110.0, 82.1, 74.7, 71.5, 52.7, 51.5, 44.5, 40.0, 37.5, 34.8, 31.9, 29.4, 29.4, 29.3, 29.1, 27.3, 27.0, 25.7, 22.8, 16.3, 14.2; MS(ESI) calcd for $C_{28}H_{44}N_2O_5$ 488.33 (M^+), found 489.42 $(M + H)^+$, 511.41 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27b. Compound **27b** was prepared according to the general procedure D from carboxylic acid **26e** and amine **11e**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (dd, J = 5.0, 1.4 Hz, 1H), 6.97−6.90 (m, 3H), 5.47 (s, 1H), 4.62−4.51 (m, 2H), 3.90 (q, J = 6.4 Hz, 1H), 3.83 (d, J = 1.5 Hz, 1H), 3.75 (ddd, J = 13.5, 10.1, 6.0 Hz, 1H), 3.67 (s, 3H), 3.42 (ddd, J = 14.2, 10.0, 4.9 Hz, 1H), 3.10−3.02 (m, 1H), 2.62−2.56 (m, 2H), 2.48 (dd, J = 12.9, 7.6 Hz, 1H), 1.67 (dd, J = 12.9, 10.9 Hz, 1H), 1.63−1.54 (m, 1H), 1.48−1.38 (m, 1H), 1.34−1.21 (m, 13H), 1.18 (d, J = 6.5 Hz, 3H), 0.89 (d, J = 17.9 Hz, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 170.9, 170.8, 138.0, 127.0, 126.2, 125.2, 110.1, 82.1, 74.8, 52.7, 51.5, 44.4, 39.8, 38.5, 37.5, 34.8, 34.8, 31.9, 29.4, 29.4, 29.1, 27.3, 26.9, 25.7, 22.8, 16.3, 14.2; MS(ESI) calcd for $C_{30}H_{46}N_2O_5S$ 546.31 (M^+), found 547.43 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27c. Compound **27c** was prepared according to the general procedure D from carboxylic acid **26a** and amine **11c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, J = 7.5 Hz, 2H), 7.24−7.17 (m, 3H), 6.35 (s, 1H), 5.39 (d, J = 1.6 Hz, 1H), 5.20 (d, J = 15.4 Hz, 1H), 4.54 (d, J = 15.5 Hz, 1H), 3.84 (q, J = 6.4 Hz, 1H), 3.71 (d, J = 1.5 Hz, 1H), 3.57 (s, 3H), 3.43 (t, J = 5.8 Hz, 2H), 3.40−3.24 (m, 5H), 3.14−3.06 (m, 1H), 2.66 (dd, J = 14.7, 4.9 Hz, 1H), 2.59 (dd, J = 14.9, 6.5 Hz, 1H), 2.50 (dd, J = 12.8, 7.4 Hz, 1H), 1.84−1.70 (m, 3H), 1.18 (d, J = 6.5 Hz, 3H), 0.74 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 171.1, 170.7, 138.4, 137.5, 128.7, 127.2, 127.0, 110.8, 82.0, 74.7, 71.5, 58.9, 52.7, 51.4, 48.9, 40.1, 37.9, 37.8, 34.7, 29.3, 29.1, 25.6, 16.4; MS(ESI) calcd for $C_{28}H_{40}N_2O_6$ 500.29 (M^+), found 501.33 $(M + H)^+$, 523.32 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27d. Compound **27d** was prepared according to the general procedure D from carboxylic acid **26a** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32−7.18 (m, 6H), 5.42 (d, J = 1.4 Hz, 1H), 5.17 (d, J = 15.6 Hz, 1H), 4.57 (d, J = 15.5 Hz, 1H), 3.85 (q, J = 6.4 Hz, 1H), 3.72 (d, J = 1.5 Hz, 1H), 3.70−3.52 (m, 8H), 3.46 (t, J = 4.7 Hz, 2H), 3.14−3.06 (m, 1H), 2.85 (dd, J = 16.0, 3.5 Hz, 1H), 2.76 (dd, J = 16.0, 7.5 Hz, 1H), 2.48 (dd, J = 12.6, 7.3 Hz, 1H), 1.84 (dd, J = 12.6, 10.9 Hz, 1H), 1.17 (d, J = 6.4 Hz, 3H), 0.76 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 171.2, 169.2, 138.6, 137.7, 128.5, 127.2, 127.0, 110.6, 82.1, 74.7, 67.0, 66.7, 52.6, 51.5, 48.9, 46.0, 42.0, 37.2, 36.5, 34.7, 29.1, 25.6, 16.4; MS(ESI) calcd for $C_{28}H_{38}N_2O_6$ 498.27 (M^+), found 499.31 $(M + H)^+$, 521.31 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27e. Compound **27e** was prepared according to the general procedure D from carboxylic acid **26f** and amine **11j**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (d, J = 7.8 Hz, 1H), 6.71 (d, J = 1.7 Hz, 1H), 6.67 (dd, J = 7.9, 1.8 Hz, 1H), 6.00 (s, 1H), 5.92 (s, 2H), 5.45 (d, J = 1.5 Hz, 1H), 5.01 (d, J = 15.3 Hz, 1H), 4.53 (d, J = 15.3 Hz, 1H), 3.84 (q, J = 6.4 Hz, 1H), 3.72 (d, J = 1.5 Hz, 1H), 3.59 (s, 3H), 3.28−3.12 (m, 2H), 3.12−3.02 (m, 1H), 2.61 (dd, J = 5.6, 3.1 Hz, 2H), 2.48 (dd, J = 12.8, 7.4 Hz, 1H), 1.79 (dd, J = 12.9, 11.1 Hz, 1H), 1.49−1.39 (m, 2H), 1.37−1.26 (m, 2H), 1.18 (d, J = 6.5 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H), 0.78 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 171.2, 170.6, 148.0, 146.7, 138.4, 131.4, 120.4, 110.8, 108.3, 107.9, 101.1, 82.0, 74.7, 52.7, 51.4, 48.5, 40.0, 39.4, 37.9, 34.7, 31.8, 29.0, 25.6, 20.2, 16.3, 13.9; MS(ESI) calcd for $C_{29}H_{40}N_2O_7$ 528.28 (M^+), found 529.37 $(M + H)^+$, 551.37 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27f. Compound **27f** was prepared according to the general procedure D from carboxylic acid **26f** and amine **11u**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (s, 1H), 6.73 (s, 2H), 5.91 (d, J = 1.6 Hz, 1H), 5.91 (d,

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J = 1.4 Hz, 1H), 5.44 (d, J = 1.5 Hz, 1H), 5.02 (d, J = 15.4 Hz, 1H), 4.54 (d, J = 15.4 Hz, 1H), 3.85 (q, J = 6.5 Hz, 1H), 3.75−3.72 (m, 2H), 3.59 (s, 3H), 3.58−3.52 (m, 1H), 3.52−3.44 (m, 1H), 3.44−3.33 (m, 2H), 3.12−3.03 (m, 1H), 2.87 (dd, J = 15.9, 3.2 Hz, 1H), 2.77−2.67 (m, 1H), 2.47 (dd, J = 12.6, 7.3 Hz, 1H), 1.80 (dd, J = 12.8, 10.7 Hz, 1H), 1.66−1.58 (m, 2H), 1.58−1.47 (m, 4H), 1.17 (d, J = 6.4 Hz, 3H), 0.80 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 171.5, 168.6, 147.9, 146.5, 138.7, 131.8, 120.5, 110.3, 108.2, 108.1, 101.0, 82.1, 74.8, 52.6, 51.5, 48.5, 46.6, 42.8, 37.3, 36.9, 34.7, 29.1, 26.5, 25.7, 25.6, 24.7, 16.4; MS(ESI) calcd for $C_{30}H_{40}N_2O_7$ 540.28 (M^+), found 541.37 $(M + H)^+$, 563.35 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27g. Compound **27g** was prepared according to the general procedure D from carboxylic acid **26g** and amine **11s**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.30 (m, 1H), 6.33−6.29 (m, 2H), 5.67 (s, 1H), 5.03 (d, J = 15.7 Hz, 1H), 4.57 (d, J = 15.7 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.87 (q, J = 6.4 Hz, 1H), 3.80 (d, J = 1.6 Hz, 1H), 3.60 (s, 3H), 3.59−3.49 (m, 1H), 3.49−3.37 (m, 6H), 3.13−3.05 (m, 1H), 2.84 (dd, J = 16.0, 3.5 Hz, 1H), 2.67 (dd, J = 15.9, 7.8 Hz, 1H), 2.48 (dd, J = 12.6, 7.4 Hz, 1H), 1.70 (t, J = 11.6 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H), 1.17 (d, J = 7.0 Hz, 3H), 0.86 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 170.9, 169.2, 155.5, 150.9, 141.6, 138.5, 110.7, 110.6, 108.4, 82.1, 74.7, 61.8, 52.8, 51.5, 45.3, 43.6, 42.0, 41.5, 37.2, 36.8, 34.8, 29.1, 25.6, 16.3, 14.8; MS(ESI) calcd for $C_{29}H_{41}N_3O_8$ 559.29 (M^+), found 560.44 $(M + H)^+$, 582.43 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27h. Compound **27h** was prepared according to the general procedure D from carboxylic acid **26g** and amine **11w**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (s, 1H), 6.31 (d, J = 1.4 Hz, 2H), 5.64 (d, J = 1.7 Hz, 1H), 5.04 (d, J = 15.7 Hz, 1H), 4.58 (d, J = 15.7 Hz, 1H), 3.86 (q, J = 6.4 Hz, 1H), 3.79 (s, 1H), 3.60 (s, 3H), 3.43 (t, J = 6.9 Hz, 2H), 3.37 (t, J = 6.8 Hz, 2H), 3.10 (dtd, J = 10.9, 7.7, 3.5 Hz, 1H), 2.76 (dd, J = 16.2, 3.5 Hz, 1H), 2.60 (dd, J = 16.2, 7.9 Hz, 1H), 2.52 (dd, J = 12.6, 7.3 Hz, 1H), 1.97−1.87 (m, 2H), 1.83 (q, J = 6.8 Hz, 2H), 1.72 (dd, J = 12.7, 10.7 Hz, 1H), 1.18 (d, J = 6.4 Hz, 3H), 0.86 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 171.2, 169.0, 151.1, 141.5, 138.6, 110.7, 110.2, 108.3, 82.1, 74.8, 52.7, 51.5, 46.6, 45.8, 42.0, 38.2, 37.0, 34.8, 29.2, 26.2, 25.7, 24.5, 16.4; MS(ESI) calcd for $C_{26}H_{36}N_2O_6$ 472.26 (M^+), found 473.4 $(M + H)^+$, 495.38 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27i. Compound **27i** was prepared according to the general procedure D from carboxylic acid **26h** and amine **11c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.37 (t, J = 5.7 Hz, 1H), 5.48 (d, J = 1.5 Hz, 1H), 5.47−5.43 (m, 1H), 3.89 (q, J = 6.5 Hz, 1H), 3.83 (d, J = 1.5 Hz, 1H), 3.79 (ddd, J = 13.4, 11.2, 5.0 Hz, 1H), 3.66 (s, 3H), 3.57 (ddd, J = 13.4, 11.0, 5.3 Hz, 1H), 3.43 (t, J = 5.9 Hz, 2H), 3.32 (s, 2H), 3.29 (q, J = 6.4, 5.5 Hz, 2H), 3.07−2.97 (m, 1H), 2.58 (dd, J = 14.7, 5.1 Hz, 1H), 2.53−2.39 (m, 2H), 2.36−2.24 (m, 1H), 2.08−1.91 (m, 5H), 1.80−1.68 (m, 3H), 1.66−1.57 (m, 3H), 1.57−1.49 (m, 2H), 1.17 (d, J = 6.5 Hz, 3H), 0.90 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 170.7, 170.6, 138.3, 135.1, 122.9, 109.5, 82.1, 74.7, 71.5, 58.9, 52.7, 51.5, 43.7, 40.4, 37.8, 37.7, 35.3, 34.8, 29.4, 29.4, 29.0, 28.6, 25.7, 25.7, 25.4, 23.0, 22.4, 16.4; MS(ESI) calcd for $C_{29}H_{46}N_2O_6$ 518.34 (M^+), found 519.43 $(M + H)^+$, 541.43 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27j. Compound **27j** was prepared according to the general procedure D from carboxylic acid **26h** and amine **11m**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (td, J = 7.8, 1.7 Hz, 1H), 7.11 (dd, J = 7.4, 1.8 Hz, 1H), 6.93−6.81 (m, 2H), 6.07 (t, J = 5.6 Hz, 1H), 5.50−5.44 (m, 2H), 3.89 (q, J = 6.5 Hz, 1H), 3.87−3.79 (m, 4H), 3.81−3.72 (m, 1H), 3.66 (s, 3H), 3.56 (ddd, J = 13.4, 11.0, 5.4 Hz, 1H), 3.50−3.36 (m, 2H), 3.05−2.95 (m, 1H), 2.79 (t, J = 6.9 Hz, 2H), 2.54 (dd, J = 14.6, 5.0 Hz, 1H), 2.50−2.40 (m, 2H), 2.35−2.22 (m, 1H), 2.07−1.93 (m, 5H), 1.67−1.58 (m, 3H), 1.58−1.50 (m, 2H), 1.17 (d, J = 6.4 Hz, 3H), 0.90 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 170.6, 170.6, 157.6, 138.3, 135.1, 130.7, 127.9, 127.5, 122.9, 120.8, 110.5, 109.5, 82.1, 74.7, 55.4, 52.7, 51.5, 43.8, 40.3, 39.8, 37.7, 35.3, 34.8, 30.4, 28.8, 28.6, 25.7, 25.4, 23.0, 22.5, 16.4; MS(ESI) calcd for $C_{34}H_{48}N_2O_6$ 580.35 (M^+), found 581.45 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27k. Compound **27k** was prepared according to the general procedure D from carboxylic acid **26i** and amine **11i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (d, J = 7.9 Hz, 1H), 6.78−6.72 (m, 2H), 6.12 (t, J = 6.4 Hz, 1H), 5.38 (d, J = 1.5 Hz, 1H), 3.94−3.87 (m, 2H), 3.86 (s, 3H), 3.85 (s, 1H), 3.82 (d, J = 1.4 Hz, 1H), 3.78−3.70 (m, 1H), 3.65 (s, 3H), 3.10−3.02 (m, 1H), 2.96−2.88 (m, 2H), 2.88−2.83 (m, 1H), 2.83−2.76 (m, 1H), 2.64 (dd, J = 14.7, 5.3 Hz, 1H), 2.56−2.47 (m, 2H), 1.98−1.92 (m, 4H), 1.73−1.64 (m, 5H), 1.64−1.56 (m, 5H), 1.49−1.44 (m, 7H), 1.17 (d, J = 6.5 Hz, 3H), 0.87 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 171.0, 170.7, 149.2, 147.8, 138.6, 131.8, 120.7, 112.1, 111.5, 110.3, 82.1, 74.7, 56.0, 56.0, 52.7, 51.7, 51.1, 47.1, 40.6, 40.4, 40.3, 39.7, 37.9, 37.1, 37.0, 36.5, 34.7, 33.7, 33.0, 29.1, 28.4, 28.4, 28.0, 25.6, 16.3; MS(ESI) calcd for $C_{38}H_{54}N_2O_7$ 650.39 (M^+), found 651.54 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27l. Compound **27l** was prepared according to the general procedure D from carboxylic acid **26i** and amine **11s**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81−6.75 (m, 3H), 5.46 (d, J = 1.5 Hz, 1H), 4.15 (q, J = 7.0 Hz, 2H), 3.94−3.89 (m, 1H), 3.88−3.82 (m, 8H), 3.77−3.69 (m, 1H), 3.65 (s, 3H), 3.59−3.53 (m, 2H), 3.51−3.40 (m, 7H), 3.10−3.03 (m, 1H), 2.91−2.75 (m, 3H), 2.69 (dd, J = 16.1, 7.8 Hz, 1H), 2.48 (dd, J = 12.6, 7.5 Hz, 1H), 1.72−1.61 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H), 1.18 (d, J = 6.5 Hz, 3H), 0.89 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 170.9, 169.1, 155.5, 149.1, 147.7, 138.7, 132.0, 120.7, 112.2, 111.5, 109.8, 82.2, 74.7, 61.8, 56.0, 56.0, 52.7, 51.7, 46.8, 45.3, 43.6, 41.5, 37.2, 37.1, 34.8, 32.9, 29.1, 25.7, 16.4, 14.8; MS(ESI) calcd for $C_{34}H_{49}N_3O_9$ 643.35 (M^+), found 644.51 $(M + H)^+$, 666.47 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27m. Compound **27m** was prepared according to the general procedure D from carboxylic acid **26j** and amine **11l**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06−8.00 (m, 1H), 7.88 (dd, J = 8.0, 1.5 Hz, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.57−7.48 (m, 2H), 7.41 (dd, J = 8.2, 7.1 Hz, 1H), 7.31−7.25 (m, 3H), 7.24−7.14 (m, 4H), 6.08−6.02 (m, 1H), 5.46−5.39 (m, 2H), 5.28 (d, J = 16.0 Hz, 1H), 3.82 (q, J = 6.4 Hz, 1H), 3.71 (d, J = 1.4 Hz, 1H), 3.34−3.28 (m, 1H), 3.26 (s, 3H), 3.25−3.13 (m, 2H), 2.73 (dd, J = 14.7, 6.0 Hz, 1H), 2.67−2.58 (m, 4H), 2.52 (dd, J = 12.9, 7.4 Hz, 1H), 1.92 (dd, J = 12.9, 11.2 Hz, 1H), 1.68−1.60 (m, 3H), 1.56−1.48 (m, 2H), 1.18 (d, J = 6.5 Hz, 3H), 0.78 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 171.0, 170.7, 142.3, 138.1, 133.9, 131.6, 131.2, 128.9, 128.5, 128.5, 128.4, 127.9, 126.5, 125.9, 125.9, 125.8, 125.3, 125.2, 123.3, 111.3, 82.0, 74.7, 52.4, 51.4, 46.5, 39.9, 39.5, 38.0, 35.6, 34.7, 29.3, 29.1, 28.8, 25.6; MS(ESI) calcd for $C_{38}H_{46}N_2O_5$ 610.34 (M^+), found 611.48 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27n. Compound **27n** was prepared according to the general procedure D from carboxylic acid **26j** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 8.3 Hz, 1H), 7.85 (dd, J = 8.1, 1.4 Hz, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.54−7.49 (m, 1H), 7.49−7.45 (m, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 7.2 Hz, 1H), 6.77 (t, J = 6.0 Hz, 1H), 5.45−5.40 (m, 2H), 5.26 (d, J = 16.0 Hz, 1H), 3.79 (q, J = 6.4 Hz, 1H), 3.69 (d, J = 1.5 Hz, 1H), 3.35−3.27 (m, 4H), 3.25 (s, 3H), 3.22−3.13 (m, 3H), 2.74 (dd, J = 15.0, 6.4 Hz, 1H), 2.67 (dd, J = 15.0, 4.8 Hz, 1H), 2.48 (dd, J = 12.7, 7.5 Hz, 1H), 2.38 (t, J = 8.1 Hz, 2H), 2.03−1.95 (m, 2H), 1.86 (dd, J = 12.8, 11.0 Hz, 1H), 1.69−1.61 (m, 2H), 1.16 (d, J = 6.5 Hz, 3H), 0.75 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.8, 172.7, 170.9, 170.8, 138.3, 133.9, 131.8, 131.2, 128.8, 127.7, 126.3, 125.7, 125.4, 125.4, 123.4, 110.9, 82.1, 74.7, 52.4, 51.4, 47.4, 46.5, 39.8, 39.8, 37.6, 36.0, 34.7, 31.1, 28.9, 26.7, 25.6, 18.0, 16.3; MS(ESI) calcd for $C_{35}H_{45}N_3O_6$ 603.33 (M^+), found 604.47 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27o. Compound **27o** was prepared according to the general procedure D from carboxylic acid **26k** and amine **11d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, J = 2.0 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.20 (dd, J = 8.4, 2.1 Hz, 1H), 5.71 (t, J = 5.7 Hz, 1H), 5.25 (d, J = 1.4 Hz, 1H), 5.19 (d, J = 16.7 Hz, 1H), 4.57 (d, J = 16.7 Hz, 1H), 3.84 (q, J = 6.5 Hz, 1H), 3.70 (d, J = 1.5 Hz, 1H), 3.67 (s, 3H), 3.29−3.13 (m, 3H), 3.05−2.96 (m, 1H), 2.78 (dd, J = 15.1, 5.7 Hz, 1H), 2.51 (dd, J = 15.1, 4.5 Hz, 1H), 2.44 (dd, J = 12.7, 7.1 Hz, 1H), 1.98 (t,

J = 12.1 Hz, 1H), 1.63−1.53 (m, 1H), 1.38−1.30 (m, 2H), 1.21 (d, J = 6.5 Hz, 3H), 0.92−0.86 (m, 8H), 0.78 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 171.2, 170.3, 138.3, 133.3, 133.1, 133.0, 129.5, 129.2, 127.3, 110.5, 82.0, 74.8, 52.9, 51.5, 46.6, 38.9, 38.6, 38.0, 37.6, 34.7, 28.8, 26.0, 25.6, 22.6, 22.6, 22.6; MS(ESI) calcd for $C_{29}H_{40}Cl_2N_2O_5$ 566.23 (M^+), found 567.39 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27p. Compound **27p** was prepared according to the general procedure D from carboxylic acid **26k** and amine **11f**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 2.1 Hz, 1H), 7.26 (d, J = 1.2 Hz, 1H), 7.14 (dd, J = 8.4, 2.1 Hz, 1H), 6.80−6.74 (m, 3H), 6.00 (t, J = 5.7 Hz, 1H), 5.25 (d, J = 1.5 Hz, 1H), 5.20 (d, J = 16.8 Hz, 1H), 4.53 (d, J = 16.8 Hz, 1H), 4.36−4.31 (m, 2H), 3.84 (d, J = 7.2 Hz, 4H), 3.80 (s, 3H), 3.71 (d, J = 1.5 Hz, 1H), 3.67 (s, 3H), 3.08−2.99 (m, 1H), 2.84 (dd, J = 15.3, 5.6 Hz, 1H), 2.54 (dd, J = 15.3, 4.4 Hz, 1H), 2.45 (dd, J = 12.6, 7.1 Hz, 1H), 2.06 (t, J = 12.1 Hz, 1H), 1.21 (d, J = 6.4 Hz, 3H), 0.78 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 171.1, 170.3, 149.3, 148.5, 138.4, 133.3, 133.0, 132.9, 131.0, 129.5, 129.2, 127.3, 120.0, 111.2, 111.1, 110.5, 82.0, 74.8, 56.0, 56.0, 52.9, 51.5, 46.8, 43.4, 38.7, 37.5, 34.7, 28.9, 25.6, 16.3; MS(ESI) calcd for $C_{33}H_{40}Cl_2N_2O_7$ 646.22 (M^+), found 647.38 $(M + H)^+$, 669.34 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27q. Compound **27q** was prepared according to the general procedure D from carboxylic acid **26l** and amine **11a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.54 (t, J = 5.6 Hz, 1H), 5.36 (d, J = 1.6 Hz, 1H), 4.08−3.93 (m, 4H), 3.79 (ddd, J = 13.6, 10.1, 5.9 Hz, 1H), 3.68 (s, 3H), 3.48 (ddd, J = 13.6, 10.1, 4.9 Hz, 1H), 3.02−2.92 (m, 1H), 2.63−2.52 (m, 2H), 2.40 (dd, J = 12.8, 7.1 Hz, 1H), 2.19 (t, J = 2.6 Hz, 1H), 2.03−1.92 (m, 1H), 1.81−1.35 (m, 11H), 1.35−1.22 (m, 10H), 1.20 (d, J = 6.5 Hz, 3H), 0.87 (t, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 170.7, 170.6, 136.4, 110.6, 79.8, 78.2, 74.6, 71.5, 52.8, 51.4, 44.9, 43.9, 39.7, 37.4, 31.9, 29.5, 29.4, 29.4, 29.3, 28.9, 28.6, 27.3, 26.8, 25.9, 25.8, 22.8, 16.7, 14.2; MS(ESI) calcd for $C_{29}H_{44}N_2O_5$ 500.33 (M^+), found 501.45 $(M + H)^+$, 524.44 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27r. Compound **27r** was prepared according to the general procedure D from carboxylic acid **26l** and amine **11j**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.12 (s, 1H), 5.34 (d, J = 1.6 Hz, 1H), 4.07−3.95 (m, 2H), 3.79 (ddd, J = 13.5, 10.1, 6.0 Hz, 1H), 3.68 (s, 3H), 3.46 (ddd, J = 14.2, 10.0, 4.9 Hz, 1H), 3.29−3.11 (m, 2H), 2.99−2.89 (m, 1H), 2.55 (d, J = 5.6 Hz, 2H), 2.40 (dd, J = 12.9, 7.1 Hz, 1H), 2.02−1.92 (m, 1H), 1.80−1.65 (m, 4H), 1.65−1.37 (m, 5H), 1.35−1.22 (m, 16H), 1.20 (d, J = 6.5 Hz, 3H), 0.94−0.83 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 170.8, 170.7, 136.5, 110.4, 78.2, 74.7, 52.8, 51.4, 44.9, 43.8, 39.9, 39.4, 37.7, 31.9, 31.8, 29.4, 29.4, 29.3, 28.9, 28.6, 27.3, 26.8, 25.8, 25.8, 22.8, 20.2, 16.7, 14.2, 13.9; MS(ESI) calcd for $C_{30}H_{50}N_2O_5$ 518.37 (M^+), found 519.48 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27s. Compound **27s** was prepared according to the general procedure D from carboxylic acid **26m** and amine **11j**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.14 (m, 5H), 6.08 (s, 1H), 5.30 (d, J = 1.7 Hz, 1H), 5.12 (d, J = 15.6 Hz, 1H), 4.69 (d, J = 15.6 Hz, 1H), 3.99 (q, J = 6.5 Hz, 1H), 3.93 (dd, J = 7.8, 1.7 Hz, 1H), 3.60 (s, 3H), 3.28−3.15 (m, 2H), 3.06−2.96 (m, 1H), 2.64 (dd, J = 5.5, 2.4 Hz, 2H), 2.43 (dd, J = 12.9, 6.7 Hz, 1H), 1.90−1.82 (m, 2H), 1.72−1.62 (m, 1H), 1.53−1.45 (m, 4H), 1.45−1.38 (m, 4H), 1.38−1.25 (m, 3H), 1.20 (d, J = 6.6 Hz, 3H), 0.90 (t, J = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 171.1, 170.8, 137.2, 136.4, 128.6, 127.2, 127.0, 111.2, 77.9, 74.5, 52.8, 51.4, 48.0, 44.8, 39.5, 39.5, 37.8, 31.8, 29.5, 28.9, 28.4, 25.8, 25.7, 20.2, 16.9, 13.9; MS(ESI) calcd for $C_{29}H_{40}N_2O_5$ 496.29 (M^+), found 497.33 $(M + H)^+$, 519.32 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27t. Compound **27t** was prepared according to the general procedure D from carboxylic acid **26m** and amine **11l**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.13 (m, 10H), 6.10 (t, J = 6.0 Hz, 1H), 5.29 (d, J = 1.6 Hz, 1H), 5.09 (d, J = 15.6 Hz, 1H), 4.68 (d, J = 15.6 Hz, 1H), 3.99 (q, J = 6.5 Hz, 1H), 3.93 (dd, J = 7.8, 1.8 Hz, 1H), 3.59 (s, 3H), 3.31−3.15 (m, 3H), 3.05−2.95 (m, 1H), 2.65−2.57 (m, 5H), 2.42 (dd, J = 12.9, 6.6 Hz, 1H), 1.90−1.81 (m, 2H), 1.71−1.58 (m, 2H), 1.55−1.40 (m, 6H), 1.35−1.23 (m, 1H), 1.19 (d, J = 6.5 Hz, 3H), 1.16−1.05 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 171.1, 170.8, 142.3, 137.2, 136.4, 128.6, 128.5, 128.4, 127.2, 127.0, 125.9, 111.2, 77.9, 74.5, 52.8, 51.4, 48.0, 44.8, 39.5, 39.5, 37.7, 35.6, 29.6, 29.3, 28.9, 28.8, 28.4, 25.8, 25.7, 16.9; MS(ESI) calcd for $C_{35}H_{44}N_2O_5$ 572.33 (M^+), found 573.37 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27u. Compound **27u** was prepared according to the general procedure D from carboxylic acid **26n** and amine **11g**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 6.9 Hz, 2H), 7.46 (d, J = 7.5 Hz, 1H), 7.44−7.39 (m, 1H), 6.75−6.69 (m, 2H), 6.66 (dd, J = 7.9, 1.7 Hz, 1H), 6.62 (t, J = 6.0 Hz, 1H), 5.93−5.89 (m, 2H), 5.34 (d, J = 1.6 Hz, 1H), 4.92 (d, J = 15.5 Hz, 1H), 4.63 (d, J = 15.4 Hz, 1H), 4.50 (dd, J = 15.2, 5.8 Hz, 1H), 4.45 (dd, J = 15.2, 6.0 Hz, 1H), 4.00 (q, J = 6.6 Hz, 1H), 3.95 (dd, J = 7.9, 1.6 Hz, 1H), 3.62 (s, 3H), 3.08−3.00 (m, 1H), 2.70 (dd, J = 15.0, 5.5 Hz, 1H), 2.65 (dd, J = 15.0, 5.7 Hz, 1H), 2.42 (dd, J = 12.8, 6.7 Hz, 1H), 1.94−1.82 (m, 2H), 1.74−1.64 (m, 1H), 1.59−1.41 (m, 5H), 1.37−1.28 (m, 1H), 1.23−1.12 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 171.1, 171.0, 148.0, 146.7, 139.7, 136.3, 131.2, 131.2, 131.0, 131.0 (q, $^2J_{C-F}$ = 31.8 Hz), 129.2, 124.4 (q, $^3J_{C-F}$ = 3.8 Hz), 124.3 (q, $^3J_{C-F}$ = 3.8 Hz), 124.2 (q, $^1J_{C-F}$ = 272.7 Hz), 120.3, 111.3, 108.3, 107.7, 101.1, 78.0, 74.5, 52.9, 51.3, 47.7, 44.8, 43.1, 39.4, 37.6, 29.7, 28.9, 28.5, 25.8, 25.8, 16.8; MS(ESI) calcd for $C_{34}H_{37}F_3N_2O_7$ 642.26 (M^+), found 643.32 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27v. Compound **27v** was prepared according to the general procedure D from carboxylic acid **26n** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (d, J = 1.5 Hz, 1H), 6.76−6.70 (m, 2H), 5.91 (s, 2H), 5.34 (d, J = 1.6 Hz, 1H), 4.95 (d, J = 15.4 Hz, 1H), 4.65 (d, J = 15.5 Hz, 1H), 4.01−3.93 (m, 2H), 3.70−3.63 (m, 4H), 3.62 (s, 5H), 3.46 (t, J = 4.9 Hz, 2H), 3.04−2.97 (m, 1H), 2.85−2.76 (m, 2H), 2.38 (dd, J = 12.5, 6.7 Hz, 1H), 1.95−1.86 (m, 2H), 1.74−1.64 (m, 1H), 1.60−1.41 (m, 5H), 1.33 (dq, J = 12.5, 7.9, 7.4 Hz, 1H), 1.22−1.13 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.1, 169.1, 147.9, 146.6, 136.8, 131.5, 120.4, 110.8, 108.2, 108.0, 101.0, 78.2, 74.6, 67.0, 66.7, 52.7, 51.4, 47.9, 45.9, 44.7, 42.1, 37.0, 35.9, 29.4, 28.9, 28.4, 25.8, 25.8, 16.8; MS(ESI) calcd for $C_{30}H_{38}N_2O_8$ 554.26 (M^+), found 555.37 $(M + H)^+$, 577.33 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27w. Compound **27w** was prepared according to the general procedure D from carboxylic acid **26o** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (dd, J = 1.8, 0.9 Hz, 1H), 6.74 (t, J = 6.3 Hz, 1H), 6.31 (dd, J = 3.2, 1.8 Hz, 1H), 6.26 (d, J = 3.2 Hz, 1H), 5.53 (d, J = 1.5 Hz, 1H), 5.00 (d, J = 15.8 Hz, 1H), 4.63 (d, J = 15.7 Hz, 1H), 3.99 (dd, J = 8.0, 1.6 Hz, 1H), 3.95 (q, J = 6.5 Hz, 1H), 3.61 (s, 3H), 3.37 (t, J = 7.0 Hz, 2H), 3.31 (td, J = 6.5, 2.6 Hz, 2H), 3.21−3.08 (m, 2H), 3.06−2.99 (m, 1H), 2.64 (dd, J = 15.0, 5.0 Hz, 1H), 2.55 (dd, J = 14.9, 6.6 Hz, 1H), 2.42−2.35 (m, 3H), 2.08−1.99 (m, 2H), 1.99−1.90 (m, 1H), 1.77−1.61 (m, 6H), 1.61−1.45 (m, 3H), 1.41−1.32 (m, 1H), 1.29−1.21 (m, 1H), 1.18 (d, J = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 172.8, 170.8, 170.7, 150.8, 141.6, 136.8, 111.1, 110.7, 108.4, 78.2, 74.6, 52.8, 51.3, 47.5, 44.8, 41.4, 39.8, 39.5, 37.3, 36.0, 31.1, 29.2, 28.9, 28.4, 26.7, 25.8, 25.8, 18.1, 16.7; MS(ESI) calcd for $C_{30}H_{41}N_3O_7$ 555.29 (M^+), found 556.48 $(M + H)^+$, 578.46 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27x. Compound **27x** was prepared according to the general procedure D from carboxylic acid **26o** and amine **11s**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (dd, J = 1.7, 0.9 Hz, 1H), 6.31 (dd, J = 3.2, 1.8 Hz, 1H), 6.28 (d, J = 3.2 Hz, 1H), 5.55 (d, J = 1.5 Hz, 1H), 4.96 (d, J = 15.7 Hz, 1H), 4.69 (d, J = 15.7 Hz, 1H), 4.15 (q, J = 7.1 Hz, 3H), 4.00 (dd, J = 7.9, 1.5 Hz, 1H), 3.96 (q, J = 6.5 Hz, 1H), 3.64−3.57 (m, 4H), 3.56−3.37 (m, 6H), 3.07−2.99 (m, 1H), 2.84 (dd, J = 16.1, 3.5 Hz, 1H), 2.70 (dd, J = 16.2, 7.5 Hz, 1H), 2.42 (dd, J = 12.6, 6.9 Hz, 1H), 2.01−1.91 (m, 1H), 1.81−1.62 (m, 4H), 1.62−1.45 (m, 4H), 1.43−1.33 (m, 1H), 1.30−1.22 (m, 4H), 1.19 (d, J = 6.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 170.7, 169.2, 155.5, 150.8, 141.6, 136.9, 111.2, 110.7, 108.4, 78.3, 74.6, 61.8, 52.8, 51.4, 45.3, 44.7, 43.7, 41.5, 41.4, 37.0, 36.3, 29.4, 28.9, 28.4, 25.9, 25.8, 16.7, 14.8; MS(ESI) calcd for

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$C_{30}H_{41}N_3O_8$ 571.29 (M^+), found 572.48 (M + H)$^+$, 594.46 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27y. Compound **27y** was prepared according to the general procedure D from carboxylic acid **26b** and amine **11i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.25 (s, 1H), 5.45 (d, J = 3.3 Hz, 1H), 5.37 (d, J = 1.6 Hz, 1H), 4.07−3.97 (m, 2H), 3.89 (ddd, J = 13.4, 11.0, 5.3 Hz, 1H), 3.68 (s, 3H), 3.56 (ddd, J = 13.5, 10.8, 5.2 Hz, 1H), 3.04−2.79 (m, 3H), 2.60 (d, J = 5.7 Hz, 2H), 2.40 (dd, J = 12.9, 6.7 Hz, 1H), 2.25 (ddd, J = 15.2, 10.7, 5.1 Hz, 1H), 2.11−1.88 (m, 10H), 1.80−1.67 (m, 7H), 1.67−1.57 (m, 7H), 1.57−1.48 (m, 2H), 1.47−1.37 (m, 5H), 1.33−1.23 (m, 1H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 171.1, 170.6, 136.2, 135.1, 122.9, 110.2, 78.1, 74.5, 52.8, 51.4, 51.1, 45.1, 42.9, 40.3, 39.8, 37.8, 37.1, 36.5, 34.9, 33.7, 32.3, 29.5, 29.0, 28.7, 28.6, 28.4, 28.0, 25.8, 25.8, 25.4, 23.0, 22.4, 16.8; MS(ESI) calcd for $C_{37}H_{54}N_2O_5$ 606.40 (M^+), found 607.55 (M + H)$^+$, 609.57 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27z. Compound **27z** was prepared according to the general procedure D from carboxylic acid **26b** and amine **11p**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.42 (t, J = 5.5 Hz, 1H), 5.45 (t, J = 3.4 Hz, 1H), 5.37 (d, J = 1.6 Hz, 1H), 4.08−3.95 (m, 2H), 3.81 (ddd, J = 13.4, 11.0, 5.2 Hz, 1H), 3.68 (s, 3H), 3.59 (ddd, J = 13.3, 10.9, 5.3 Hz, 1H), 3.47 (t, J = 5.8 Hz, 2H), 3.40 (t, J = 6.6 Hz, 3H), 3.35−3.26 (m, 2H), 2.97−2.87 (m, 1H), 2.59 (dd, J = 14.8, 5.1 Hz, 1H), 2.47 (dd, J = 14.8, 6.4 Hz, 1H), 2.38 (dd, J = 12.8, 6.9 Hz, 1H), 2.30−2.22 (m, 1H), 2.09−2.01 (m, 1H), 2.01−1.93 (m, 5H), 1.80−1.69 (m, 5H), 1.69−1.58 (m, 5H), 1.58−1.48 (m, 6H), 1.46−1.24 (m, 5H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 170.7, 170.5, 136.5, 135.2, 122.9, 109.9, 78.2, 74.6, 71.0, 69.7, 52.8, 51.4, 45.0, 43.0, 39.7, 38.1, 37.5, 35.0, 31.9, 29.4, 29.4, 29.0, 28.7, 28.6, 25.8, 25.8, 25.4, 23.0, 22.5, 19.5, 16.8, 14.1; MS(ESI) calcd for $C_{33}H_{52}N_2O_6$ 572.38 (M^+), found 573.53 (M + H)$^+$, 595.53 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27aa. Compound **27aa** was prepared according to the general procedure D from carboxylic acid **26p** and amine **11c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83−6.73 (m, 3H), 6.32 (q, J = 5.9 Hz, 1H), 5.34 (d, J = 1.6 Hz, 1H), 4.05−3.98 (m, 2H), 3.94 (ddd, J = 13.5, 10.5, 6.2 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.78−3.68 (m, 1H), 3.66 (s, 3H), 3.44 (t, J = 5.9 Hz, 2H), 3.37−3.27 (m, 6H), 3.01−2.91 (m, 1H), 2.91−2.81 (m, 1H), 2.81−2.72 (m, 1H), 2.61 (dd, J = 14.9, 5.1 Hz, 1H), 2.54 (dd, J = 14.8, 6.5 Hz, 1H), 2.41 (dd, J = 12.8, 7.0 Hz, 1H), 1.99−1.87 (m, 1H), 1.80−1.64 (m, 6H), 1.64−1.56 (m, 2H), 1.56−1.48 (m, 2H), 1.44−1.36 (m, 1H), 1.32−1.22 (m, 1H), 1.21 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 170.7, 170.6, 149.1, 147.7, 136.8, 131.8, 120.7, 112.2, 111.5, 110.4, 78.2, 74.6, 71.6, 58.9, 56.0, 56.0, 52.8, 51.5, 46.0, 45.0, 39.7, 38.0, 37.5, 32.8, 29.4, 29.3, 29.0, 28.7, 25.8, 25.7, 16.8; MS(ESI) calcd for $C_{32}H_{46}N_2O_8$ 586.33 (M^+), found 587.48 (M + H)$^+$, 609.47 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ab. Compound **27ab** was prepared according to the general procedure D from carboxylic acid **26p** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83−6.74 (m, 3H), 5.37 (d, J = 1.6 Hz, 1H), 4.06−3.90 (m, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.79−3.69 (m, 1H), 3.66 (d, J = 5.8 Hz, 6H), 3.63−3.51 (m, 3H), 3.45 (t, J = 4.9 Hz, 2H), 3.03−2.93 (m, 1H), 2.91−2.73 (m, 3H), 2.70 (dd, J = 16.2, 7.5 Hz, 1H), 2.41 (dd, J = 12.6, 6.9 Hz, 1H), 2.01−1.89 (m, 1H), 1.80−1.73 (m, 2H), 1.72−1.65 (m, 1H), 1.65−1.49 (m, 4H), 1.49−1.36 (m, 1H), 1.34−1.23 (m, 1H), 1.21 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 170.7, 169.2, 149.1, 147.7, 136.9, 131.9, 120.7, 112.2, 111.4, 110.2, 78.3, 74.7, 67.0, 66.7, 56.0, 56.0, 52.8, 51.5, 45.9, 45.0, 42.1, 36.9, 36.3, 32.7, 29.4, 29.0, 28.7, 25.8, 25.8, 16.8; MS(ESI) calcd for $C_{32}H_{44}N_2O_8$ 584.31 (M^+), found 585.47 (M + H)$^+$, 607.45 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ac. Compound **27ac** was prepared according to the general procedure D from carboxylic acid **26q** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06−8.00 (m, 1H), 7.85 (dd, J = 8.0, 1.5 Hz, 1H), 7.75 (dd, J = 7.7, 1.8 Hz, 1H), 7.52 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.47 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H), 7.42 (d, J = 7.2 Hz, 1H), 7.40−7.37 (m, 1H), 5.41 (d, J = 16.0 Hz, 1H), 5.37−5.30 (m, 2H), 3.95 (dd, J = 7.4, 1.5 Hz, 1H), 3.91 (q, J = 6.5 Hz, 1H), 3.67 (dd, J = 5.4, 3.0 Hz, 4H), 3.64−3.57 (m, 2H), 3.48 (t, J = 4.8 Hz, 2H), 3.25 (s, 3H), 3.13−3.06 (m, 1H), 2.91 (dd, J = 16.2, 6.9 Hz, 1H), 2.81 (dd, J = 16.2, 3.4 Hz, 1H), 2.42 (dd, J = 12.5, 6.8 Hz, 1H), 2.00 (dd, J = 12.5, 11.4 Hz, 1H), 1.95−1.86 (m, 1H), 1.70−1.61 (m, 1H), 1.52−1.38 (m, 5H), 1.35−1.25 (m, 1H), 1.21−1.15 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 171.0, 169.2, 136.9, 133.9, 131.8, 131.3, 128.8, 127.7, 126.3, 125.7, 125.5, 125.5, 123.3, 111.7, 78.1, 74.6, 67.0, 66.7, 52.4, 51.4, 46.0, 45.9, 44.6, 42.1, 37.0, 35.9, 29.3, 28.6, 28.3, 25.9, 25.8, 16.6; MS(ESI) calcd for $C_{33}H_{40}N_2O_6$ 560.29 (M^+), found 561.44 (M + H)$^+$, 583.44 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ad. Compound **27ad** was prepared according to the general procedure D from carboxylic acid **26q** and amine **11w**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 8.3 Hz, 1H), 7.85 (dd, J = 8.2, 1.4 Hz, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.52 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.49−7.45 (m, 1H), 7.44−7.37 (m, 2H), 5.43 (d, J = 16.1 Hz, 1H), 5.36−5.30 (m, 2H), 3.96−3.88 (m, 2H), 3.51−3.44 (m, 2H), 3.44−3.38 (m, 2H), 3.27 (s, 3H), 3.09 (dtd, J = 10.5, 6.6, 3.2 Hz, 1H), 2.88 (dd, J = 16.3, 6.9 Hz, 1H), 2.74 (dd, J = 16.3, 3.4 Hz, 1H), 2.42 (dd, J = 12.6, 6.8 Hz, 1H), 2.06 (t, J = 12.1 Hz, 1H), 1.97−1.79 (m, 5H), 1.70−1.62 (m, 1H), 1.51−1.36 (m, 5H), 1.35−1.26 (m, 1H), 1.18 (d, J = 6.5 Hz, 3H), 1.16−1.08 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.3, 169.0, 136.8, 133.8, 131.8, 131.3, 128.8, 127.6, 126.3, 125.6, 125.5, 125.5, 123.3, 111.3, 78.1, 74.6, 52.4, 51.4, 46.6, 45.8, 45.8, 44.7, 37.4, 37.0, 29.4, 28.8, 28.4, 26.2, 25.8, 25.8, 24.5, 16.8; MS(ESI) calcd for $C_{33}H_{40}N_2O_5$ 544.29 (M^+), found 545.44 (M + H)$^+$, 567.43 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ae. Compound **27ae** was prepared according to the general procedure D from carboxylic acid **26r** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 2.1 Hz, 1H), 7.19 (dd, J = 8.5, 2.1 Hz, 1H), 5.19−5.12 (m, 2H), 4.65 (d, J = 16.8 Hz, 1H), 3.98 (q, J = 6.5 Hz, 1H), 3.93 (dd, J = 7.8, 1.7 Hz, 1H), 3.69 (s, 3H), 3.66 (s, 3H), 3.62−3.53 (m, 1H), 3.48−3.41 (m, 2H), 3.02−2.90 (m, 2H), 2.66 (dd, J = 16.2, 2.9 Hz, 1H), 2.32 (dd, J = 12.5, 6.2 Hz, 1H), 2.10 (t, J = 12.0 Hz, 1H), 1.94−1.85 (m, 1H), 1.71−1.61 (m, 1H), 1.55−1.40 (m, 6H), 1.33 (dt, J = 13.1, 7.4 Hz, 1H), 1.26−1.14 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 171.2, 169.0, 136.7, 133.2, 133.1, 133.0, 129.6, 129.0, 127.3, 110.7, 78.0, 74.5, 67.0, 66.6, 52.9, 51.4, 46.1, 45.8, 44.7, 42.0, 36.8, 35.1, 29.1, 28.8, 28.4, 25.9, 25.8, 16.9; MS(ESI) calcd for $C_{29}H_{36}Cl_2N_2O_6$ 578.20 (M^+), found 579.36 (M + H)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27af. Compound **27af** was prepared according to the general procedure D from carboxylic acid **26r** and amine **11v**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J = 8.5 Hz, 1H), 7.36 (d, J = 2.1 Hz, 1H), 7.18 (dd, J = 8.4, 2.1 Hz, 1H), 5.18−5.11 (m, 2H), 4.64 (d, J = 16.8 Hz, 1H), 3.98 (q, J = 6.5 Hz, 2H), 3.93 (dd, J = 7.7, 1.6 Hz, 1H), 3.92−3.78 (m, 1H), 3.75−3.66 (m, 5H), 3.02−2.90 (m, 2H), 2.69−2.55 (m, 5H), 2.31 (dd, J = 12.4, 6.3 Hz, 1H), 2.09 (t, J = 12.0 Hz, 1H), 1.95−1.85 (m, 1H), 1.71−1.62 (m, 1H), 1.56−1.40 (m, 6H), 1.37−1.27 (m, 1H), 1.27−1.14 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 171.2, 168.7, 136.7, 133.2, 133.1, 132.9, 129.6, 129.0, 127.3, 110.7, 78.0, 74.5, 52.9, 51.4, 48.2, 46.1, 44.7, 44.4, 36.9, 35.3, 29.1, 28.8, 28.3, 27.9, 27.5, 25.9, 25.8, 16.8; MS(ESI) calcd for $C_{29}H_{36}Cl_2N_2O_5S$ 594.17 (M^+), found 595.33 (M + H)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ag. Compound **27ag** was prepared according to the general procedure D from carboxylic acid **26s** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.34 (d, J = 1.8 Hz, 1H), 3.95 (dd, J = 6.6, 1.8 Hz, 1H), 3.82 (ddd, J = 13.8, 10.0, 6.3 Hz, 1H), 3.69 (s, 3H), 3.68−3.63 (m, 4H), 3.61−3.55 (m, 2H), 3.53−3.44 (m, 3H), 3.32 (d, J = 8.4 Hz, 1H), 3.05−2.98 (m, 1H), 2.86 (dd, J = 16.1, 3.5 Hz, 1H), 2.59 (dd, J = 16.1, 7.9 Hz, 1H), 2.52 (dd, J = 12.8, 6.6 Hz, 1H), 1.96−1.83 (m, 2H), 1.62−1.53 (m, 1H), 1.53−1.45 (m, 1H), 1.33−1.21 (m, 11H), 0.98 (d, J = 6.7 Hz, 3H), 0.93 (d, J = 6.8 Hz, 4H), 0.86 (t, J = 6.7 Hz, 3H), 0.58−0.48 (m, 2H), 0.47−0.41 (m, 1H), 0.22−0.16 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 170.7, 169.4, 136.3, 108.0, 82.2,

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79.0, 67.0, 66.7, 52.7, 51.8, 46.0, 43.3, 42.1, 36.9, 36.2, 33.5, 31.9, 30.5, 29.4, 29.4, 27.3, 26.7, 22.8, 18.6, 18.5, 14.2, 12.1, 4.0, 2.7; MS(ESI) calcd for $C_{30}H_{48}N_2O_6$ 532.35 (M^+), found 533.53 $(M + H)^+$, 555.5 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ah. Compound **27ah** was prepared according to the general procedure D from carboxylic acid **26s** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (s, 1H), 5.31 (d, J = 1.9 Hz, 1H), 3.93 (dd, J = 6.6, 1.9 Hz, 1H), 3.79 (ddd, J = 13.6, 10.0, 6.0 Hz, 1H), 3.68 (s, 3H), 3.56−3.45 (m, 1H), 3.38 (t, J = 7.0 Hz, 2H), 3.35−3.28 (m, 3H), 3.23−3.12 (m, 2H), 3.04−2.95 (m, 1H), 2.64 (dd, J = 15.1, 5.4 Hz, 1H), 2.54−2.43 (m, 2H), 2.39 (t, J = 8.1 Hz, 2H), 2.10−1.99 (m, 2H), 1.92−1.81 (m, 2H), 1.67 (td, J = 6.4, 2.5 Hz, 2H), 1.61−1.52 (m, 1H), 1.52−1.43 (m, 1H), 1.35−1.18 (m, 10H), 0.97 (d, J = 6.7 Hz, 3H), 0.92 (d, J = 6.6 Hz, 4H), 0.89−0.84 (m, 3H), 0.57−0.47 (m, 2H), 0.47−0.40 (m, 1H), 0.23−0.15 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 173.1, 171.0, 170.7, 136.2, 107.9, 82.0, 78.9, 52.8, 51.7, 47.5, 43.4, 39.8, 39.6, 37.1, 36.0, 33.5, 31.9, 31.1, 30.4, 29.4, 29.4, 27.2, 26.7, 26.7, 22.8, 18.6, 18.5, 18.1, 14.2, 12.2, 4.0, 2.6; MS(ESI) calcd for $C_{33}H_{53}N_3O_6$ 587.39 (M^+), found 588.57 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ai. Compound **27ai** was prepared according to the general procedure D from carboxylic acid **26t** and amine **11b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, J = 7.5 Hz, 2H), 7.25−7.17 (m, 3H), 6.14 (d, J = 6.8 Hz, 1H), 5.28 (d, J = 1.9 Hz, 1H), 5.10 (d, J = 15.7 Hz, 1H), 4.80 (d, J = 15.7 Hz, 1H), 3.80 (dd, J = 7.2, 1.9 Hz, 1H), 3.62 (s, 3H), 3.32 (d, J = 8.5 Hz, 1H), 3.07 (t, J = 6.4 Hz, 2H), 3.02−2.95 (m, 1H), 2.69−2.60 (m, 2H), 2.49 (dd, J = 13.2, 6.1 Hz, 1H), 2.11 (t, J = 12.7 Hz, 1H), 1.77−1.60 (m, 6H), 1.47−1.37 (m, 1H), 1.27−1.09 (m, 3H), 0.95−0.81 (m, 6H), 0.74 (d, J = 6.7 Hz, 3H), 0.60−0.53 (m, 1H), 0.51−0.40 (m, 2H), 0.25−0.19 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.3, 170.8, 137.1, 135.6, 128.7, 127.2, 126.9, 109.1, 81.9, 78.5, 52.8, 51.7, 47.4, 45.9, 39.4, 38.0, 37.7, 33.5, 30.9, 30.6, 26.5, 26.0, 18.6, 18.5, 12.3, 4.6, 2.6; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{32}H_{45}N_2O_5$ 537.3328, found 537.3327.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27aj. Compound **27aj** was prepared according to the general procedure D from carboxylic acid **26t** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, J = 8.6, 6.7 Hz, 2H), 7.23−7.18 (m, 3H), 6.85 (d, J = 6.3 Hz, 1H), 5.25 (d, J = 1.9 Hz, 1H), 5.12 (d, J = 15.8 Hz, 1H), 4.75 (d, J = 15.8 Hz, 1H), 3.79 (dd, J = 7.2, 1.9 Hz, 1H), 3.62 (s, 3H), 3.38−3.27 (m, 5H), 3.24−3.12 (m, 2H), 3.08−3.01 (m, 1H), 2.70 (dd, J = 15.1, 5.2 Hz, 1H), 2.60 (dd, J = 15.1, 6.4 Hz, 1H), 2.44 (dd, J = 13.0, 6.2 Hz, 1H), 2.41−2.36 (m, 2H), 2.08 (t, J = 12.6 Hz, 1H), 2.06−1.99 (m, 2H), 1.68 (dp, J = 18.8, 6.5 Hz, 3H), 0.90−0.81 (m, 4H), 0.73 (d, J = 6.7 Hz, 3H), 0.59−0.52 (m, 1H), 0.50−0.38 (m, 2H), 0.23−0.17 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 173.1, 171.1, 170.9, 137.3, 135.7, 128.6, 127.0, 126.9, 108.6, 82.0, 78.6, 52.8, 51.7, 47.5, 47.4, 39.8, 39.2, 37.2, 36.0, 33.5, 31.1, 30.5, 26.7, 18.6, 18.5, 18.1, 12.3, 4.6, 2.6; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{32}H_{44}N_3O_6$ 566.3230, found 566.3225.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ak. Compound **27ak** was prepared according to the general procedure D from carboxylic acid **26u** and amine **11e**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (dd, J = 5.0, 1.3 Hz, 1H), 6.97−6.90 (m, 2H), 6.73 (d, J = 7.9 Hz, 1H), 6.70 (d, J = 1.6 Hz, 1H), 6.67 (dd, J = 7.9, 1.7 Hz, 1H), 5.92 (s, 2H), 5.33 (d, J = 1.9 Hz, 1H), 4.87 (d, J = 15.6 Hz, 1H), 4.75 (d, J = 15.6 Hz, 1H), 4.63−4.54 (m, 2H), 3.82 (dd, J = 7.2, 1.9 Hz, 1H), 3.64 (s, 3H), 3.33 (d, J = 8.5 Hz, 1H), 3.04−2.97 (m, 1H), 2.71 (dd, J = 14.9, 5.5 Hz, 1H), 2.65 (dd, J = 14.9, 5.5 Hz, 1H), 2.48 (dd, J = 13.1, 6.2 Hz, 1H), 2.09 (t, J = 12.7 Hz, 1H), 1.81−1.73 (m, 1H), 0.91 (d, J = 6.6 Hz, 3H), 0.89−0.83 (m, 2H), 0.60−0.53 (m, 1H), 0.53−0.47 (m, 1H), 0.47−0.39 (m, 1H), 0.25−0.18 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 171.3, 170.7, 148.0, 146.7, 141.2, 135.6, 130.8, 127.0, 126.1, 125.1, 120.2, 109.2, 108.3, 107.6, 101.1, 81.8, 78.6, 52.9, 51.6, 47.1, 38.9, 38.4, 37.5, 33.5, 30.5, 18.6, 18.6, 12.3, 4.5, 2.7; MS(ESI) calcd for $C_{31}H_{36}N_2O_7S$ 580.22 (M^+), found 581.4 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27al. Compound **27al** was prepared according to the general procedure D from carboxylic acid **26u** and amine **11l**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29−7.23 (m, 3H), 7.19−7.13 (m, 3H), 6.73 (d, J = 7.9 Hz, 1H), 6.70 (d, J = 1.6 Hz, 1H), 6.66 (dd, J = 8.0, 1.7 Hz, 1H), 5.91 (s, 2H), 5.32 (d, J = 2.0 Hz, 1H), 4.91 (d, J = 15.6 Hz, 1H), 4.73 (d, J = 15.5 Hz, 1H), 3.82 (dd, J = 7.1, 1.9 Hz, 1H), 3.63 (s, 3H), 3.32 (d, J = 8.5 Hz, 1H), 3.27−3.21 (m, 2H), 3.02−2.94 (m, 1H), 2.68−2.57 (m, 4H), 2.48 (dd, J = 13.1, 6.3 Hz, 1H), 2.07 (t, J = 12.7 Hz, 1H), 1.80−1.72 (m, 1H), 1.68−1.59 (m, 2H), 1.56−1.48 (m, 2H), 0.90 (d, J = 6.7 Hz, 3H), 0.89−0.82 (m, 1H), 0.79 (d, J = 6.7 Hz, 3H), 0.59−0.52 (m, 1H), 0.51−0.40 (m, 2H), 0.24−0.17 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 171.4, 170.8, 148.0, 146.7, 142.3, 135.7, 130.9, 128.5, 128.4, 125.9, 120.2, 108.3, 107.6, 101.1, 81.9, 78.6, 52.9, 51.7, 47.2, 39.6, 39.1, 37.6, 35.6, 33.5, 30.5, 29.3, 28.8, 18.6, 18.6, 12.3, 4.5, 2.6; MS(ESI) calcd for $C_{36}H_{44}N_2O_7$ 616.31 (M^+), found 617.49 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27am. Compound **27am** was prepared according to the general procedure D from carboxylic acid **26v** and amine **11d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, J = 2.3 Hz, 1H), 6.31 (dd, J = 3.2, 1.9 Hz, 1H), 6.25 (d, J = 3.2 Hz, 1H), 5.99 (s, 1H), 5.56 (d, J = 1.8 Hz, 1H), 5.07 (d, J = 15.8 Hz, 1H), 4.66 (d, J = 15.7 Hz, 1H), 3.89 (dd, J = 6.7, 1.8 Hz, 1H), 3.64 (s, 3H), 3.32 (d, J = 8.2 Hz, 1H), 3.24−3.13 (m, 2H), 3.03−2.95 (m, 1H), 2.58 (d, J = 5.3 Hz, 1H), 2.52 (dd, J = 13.1, 6.6 Hz, 1H), 1.95 (dd, J = 13.1, 11.8 Hz, 1H), 1.87−1.78 (m, 1H), 1.62−1.53 (m, 1H), 1.36−1.29 (m, 2H), 0.94 (d, J = 6.7 Hz, 3H), 0.92−0.85 (m, 11H), 0.57−0.46 (m, 2H), 0.46−0.39 (m, 1H), 0.22−0.16 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 171.1, 170.7, 150.7, 141.8, 136.2, 110.7, 109.4, 108.3, 81.8, 78.8, 52.9, 51.7, 41.0, 39.5, 38.6, 38.0, 37.7, 33.4, 30.3, 26.0, 22.6, 22.6, 22.6, 18.5, 18.4, 12.1, 4.0, 2.6; MS(ESI) calcd for $C_{28}H_{40}N_2O_6$ 500.29 (M^+), found 501.45 $(M + H)^+$, 523.44 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27an. Compound **27an** was prepared according to the general procedure D from carboxylic acid **26v** and amine **11q**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, J = 1.6, 0.9 Hz, 1H), 6.31 (dd, J = 3.1, 1.8 Hz, 1H), 6.27 (d, J = 3.2 Hz, 1H), 5.52 (d, J = 1.8 Hz, 1H), 5.02 (d, J = 15.8 Hz, 1H), 4.73 (d, J = 15.8 Hz, 1H), 3.90 (dd, J = 6.7, 1.8 Hz, 1H), 3.74−3.65 (m, 6H), 3.64 (s, 3H), 3.60 (s, 2H), 3.47 (s, 1H), 3.31 (d, J = 8.3 Hz, 1H), 3.12−3.03 (m, 1H), 2.89 (dd, J = 16.2, 3.7 Hz, 1H), 2.69 (s, 1H), 2.52 (dd, J = 12.8, 6.5 Hz, 1H), 1.98 (t, J = 11.6 Hz, 1H), 1.83 (h, J = 6.7 Hz, 1H), 1.70 (s, 1H), 1.00 (dt, J = 6.3, 3.2 Hz, 2H), 0.94 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H), 0.79 (dt, J = 8.0, 3.5 Hz, 2H), 0.56−0.46 (m, 2H), 0.45−0.39 (m, 1H), 0.21−0.14 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 170.8, 150.8, 141.6, 136.3, 110.7, 108.2, 81.9, 52.8, 51.8, 45.3, 42.0, 41.7, 40.9, 37.0, 36.0, 33.4, 30.5, 18.5, 18.5, 12.1, 11.2, 7.8, 4.0, 2.6; MS(ESI) calcd for $C_{31}H_{41}N_3O_7$ 567.29 (M^+), found 568.48 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ao. Compound **27ao** was prepared according to the general procedure D from carboxylic acid **26w** and amine **11e**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (dd, J = 5.0, 1.3 Hz, 1H), 6.96−6.88 (m, 2H), 6.61 (t, J = 5.8 Hz, 1H), 5.43 (t, J = 3.3 Hz, 1H), 5.36 (d, J = 1.9 Hz, 1H), 4.63 (dd, J = 15.2, 5.9 Hz, 1H), 4.51 (dd, J = 15.3, 5.3 Hz, 1H), 3.92 (dd, J = 7.0, 1.9 Hz, 1H), 3.78 (ddd, J = 13.5, 10.7, 5.4 Hz, 1H), 3.69 (s, 3H), 3.67−3.58 (m, 1H), 3.34 (d, J = 8.4 Hz, 1H), 2.95−2.86 (m, 1H), 2.62 (dd, J = 14.7, 5.6 Hz, 1H), 2.56 (dd, J = 14.7, 5.6 Hz, 1H), 2.47 (dd, J = 13.0, 6.3 Hz, 1H), 2.23−2.13 (m, 1H), 2.09−2.00 (m, 1H), 2.00−1.90 (m, 5H), 1.87 (dt, J = 13.5, 6.8 Hz, 1H), 1.61 (dq, J = 6.4, 4.1, 3.7 Hz, 2H), 1.57−1.49 (m, 2H), 0.99 (d, J = 6.7 Hz, 3H), 0.96−0.86 (m, 4H), 0.60−0.49 (m, 2H), 0.46 (dq, J = 10.2, 4.8 Hz, 1H), 0.26−0.18 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 170.7, 170.6, 141.4, 135.7, 135.0, 126.9, 125.9, 125.0, 123.0, 108.0, 81.9, 78.7, 52.9, 51.7, 42.5, 39.4, 38.3, 37.5, 34.9, 33.7, 30.5, 28.6, 25.4, 23.0, 22.4, 18.8, 18.7, 12.3, 4.4, 2.7; MS(ESI) calcd for $C_{31}H_{42}N_2O_5S$ 554.28 (M^+), found 555.44 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ap. Compound **27ap** was prepared according to the general procedure D from carboxylic acid **26w** and amine **11o**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.36 (t, J = 5.3 Hz, 1H), 6.06 (d, J = 3.0 Hz, 1H), 5.86 (d, J = 2.6 Hz, 1H), 5.47−5.41 (m, 1H), 5.35 (d, J = 1.9 Hz, 1H), 4.36

(dd, J = 15.4, 5.5 Hz, 1H), 4.29 (dd, J = 15.4, 5.1 Hz, 1H), 3.93 (dd, J = 6.9, 1.8 Hz, 1H), 3.79 (ddd, J = 13.5, 10.7, 5.3 Hz, 1H), 3.69 (s, 3H), 3.67−3.59 (m, 1H), 3.33 (d, J = 8.4 Hz, 1H), 2.96−2.88 (m, 1H), 2.62 (dd, J = 14.8, 5.4 Hz, 1H), 2.54 (dd, J = 14.7, 5.9 Hz, 1H), 2.47 (dd, J = 13.0, 6.4 Hz, 1H), 2.24 (s, 3H), 2.22−2.15 (m, 1H), 2.10−2.02 (m, 1H), 2.01−1.89 (m, 5H), 1.86 (dt, J = 13.5, 6.8 Hz, 1H), 1.65−1.57 (m, 2H), 1.57−1.49 (m, 2H), 0.98 (d, J = 6.7 Hz, 3H), 0.95−0.86 (m, 4H), 0.58−0.48 (m, 2H), 0.48−0.42 (m, 1H), 0.24−0.18 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 170.6, 170.6, 151.9, 149.7, 135.9, 135.1, 123.0, 108.2, 108.0, 106.3, 81.9, 78.7, 52.8, 51.8, 42.6, 39.5, 37.5, 36.8, 34.9, 33.6, 30.4, 28.6, 25.4, 23.0, 22.4, 18.7, 18.6, 13.7, 12.3, 4.2, 2.6; MS(ESI) calcd for $C_{32}H_{44}N_2O_6$ 552.32 (M^+), found 553.49 ($M + H)^+$, 575.47 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27aq. Compound **27aq** was prepared according to the general procedure D from carboxylic acid **26c** and amine **11d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82−6.74 (m, 3H), 6.02 (s, 1H), 5.31 (d, J = 1.8 Hz, 1H), 3.98−3.90 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.79 (ddd, J = 13.6, 9.8, 5.6 Hz, 1H), 3.68 (s, 3H), 3.33 (d, J = 8.3 Hz, 1H), 3.29−3.18 (m, 2H), 2.98−2.90 (m, 1H), 2.87−2.74 (m, 2H), 2.56 (dd, J = 9.4, 5.7 Hz, 1H), 2.50 (dd, J = 12.9, 6.5 Hz, 1H), 1.93 (dd, J = 13.1, 11.6 Hz, 1H), 1.86−1.78 (m, 1H), 1.63−1.54 (m, 1H), 1.37 (q, J = 7.3 Hz, 2H), 0.96 (d, J = 6.7 Hz, 3H), 0.94−0.85 (m, 11H), 0.58−0.48 (m, 2H), 0.48−0.41 (m, 1H), 0.24−0.17 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 170.9, 170.6, 149.1, 147.8, 136.2, 131.7, 120.7, 112.2, 111.5, 108.4, 81.9, 78.8, 56.0, 56.0, 52.9, 51.9, 45.6, 39.6, 38.6, 38.0, 37.6, 33.5, 32.7, 30.4, 26.0, 22.6, 22.6, 22.6, 18.6, 18.5, 12.2, 4.1, 2.6; MS(ESI) calcd for $C_{33}H_{48}N_2O_7$ 584.35 (M^+), found 585.51 ($M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ar. compound **27ar** was prepared according to the general procedure D from carboxylic acid **26c** and amine **11i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 6.82−6.72 (m, 3H), 6.15 (t, J = 6.4 Hz, 1H), 5.31 (d, J = 1.9 Hz, 1H), 4.00 (ddd, J = 13.7, 9.7, 7.0 Hz, 1H), 3.92 (dd, J = 7.1, 1.9 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.76 (ddd, J = 13.9, 9.5, 5.5 Hz, 1H), 3.68 (s, 3H), 3.34 (d, J = 8.4 Hz, 1H), 2.98 (dd, J = 13.6, 6.4 Hz, 1H), 2.92 (dd, J = 11.8, 6.1 Hz, 1H), 2.89−2.75 (m, 3H), 2.62 (dd, J = 5.6, 2.0 Hz, 2H), 2.49 (dd, J = 13.1, 6.4 Hz, 1H), 2.06−1.89 (m, 5H), 1.86−1.78 (m, 1H), 1.74−1.55 (m, 10H), 1.45 (d, J = 2.9 Hz, 6H), 0.96 (d, J = 6.6 Hz, 3H), 0.92−0.84 (m, 5H), 0.58−0.48 (m, 2H), 0.48−0.42 (m, 1H), 0.25−0.19 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 170.9, 170.8, 149.1, 147.8, 136.0, 131.7, 120.7, 112.2, 111.5, 108.2, 81.8, 78.7, 56.0, 56.0, 52.9, 51.8, 51.3, 51.0, 45.5, 40.4, 40.3, 39.7, 39.6, 37.7, 37.1, 37.0, 36.5, 33.8, 33.6, 32.6, 32.3, 30.4, 28.4, 28.3, 28.0, 18.7, 18.6, 12.3, 4.3, 2.7; MS(ESI) calcd for $C_{39}H_{54}N_2O_7$ 662.39 (M^+), found 663.55 ($M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27as. Compound **27as** was prepared according to the general procedure D from carboxylic acid **26x** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 8.3 Hz, 1H), 7.86 (d, J = 7.9 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.53 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.48 (ddd, J = 7.9, 6.8, 1.2 Hz, 1H), 7.44−7.35 (m, 2H), 5.47 (d, J = 16.0 Hz, 1H), 5.32 (d, J = 16.3 Hz, 1H), 5.29 (d, J = 1.8 Hz, 1H), 3.86−3.79 (m, 1H), 3.71−3.63 (m, 5H), 3.63−3.55 (m, 2H), 3.54−3.43 (m, 2H), 3.32 (s, 3H), 3.27 (d, J = 8.2 Hz, 1H), 3.20−3.12 (m, 1H), 2.86 (d, J = 5.2 Hz, 2H), 2.54 (dd, J = 12.7, 6.5 Hz, 1H), 2.19 (t, J = 12.2 Hz, 1H), 1.78−1.68 (m, 1H), 0.99−0.87 (m, 1H), 0.85 (d, J = 6.7 Hz, 3H), 0.71 (d, J = 6.7 Hz, 3H), 0.55−0.44 (m, 2H), 0.44−0.36 (m, 1H), 0.19−0.10 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.2, 169.3, 136.3, 133.9, 131.7, 131.2, 128.9, 127.7, 126.3, 125.7, 125.5, 125.2, 123.2, 109.8, 78.8, 67.0, 66.7, 52.4, 51.8, 46.0, 45.3, 42.1, 37.1, 35.7, 33.4, 30.4, 18.4, 18.2, 12.0, 3.9, 2.6; MS(ESI) calcd for $C_{33}H_{40}N_2O_6$ 560.29 (M^+), found 561.46 ($M + H)^+$, 583.44 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27at. Compound **27at** was prepared according to the general procedure D from carboxylic acid **26x** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 7.7 Hz, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.53 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.48 (ddd, J = 8.1, 6.8, 1.2 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.28 (dd, J = 7.2, 1.3 Hz, 1H), 6.82 (t, J = 6.3 Hz, 1H), 5.42 (d, J = 16.2 Hz, 1H), 5.35 (d, J = 16.2 Hz, 1H), 5.23 (d, J = 1.8 Hz, 1H), 3.80 (dd, J = 6.5, 1.8 Hz, 1H), 3.38 (s, 3H), 3.36−3.24 (m, 5H), 3.23−3.09 (m, 3H), 2.70 (d, J = 5.6 Hz, 2H), 2.52 (dd, J = 13.0, 6.5 Hz, 1H), 2.37 (t, J = 8.1 Hz, 2H), 2.14 (t, J = 12.4 Hz, 1H), 2.04−1.93 (m, 2H), 1.83 (s, 1H), 1.76−1.60 (m, 3H), 0.99−0.86 (m, 1H), 0.83 (d, J = 6.7 Hz, 3H), 0.68 (d, J = 6.7 Hz, 3H), 0.61−0.43 (m, 2H), 0.44−0.36 (m, 1H), 0.21−0.12 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 173.0, 171.1, 170.9, 136.1, 133.8, 131.5, 131.1, 128.9, 127.7, 126.3, 125.7, 125.5, 124.7, 123.1, 109.5, 81.9, 78.7, 52.5, 51.7, 47.4, 45.3, 39.8, 39.3, 37.4, 36.0, 33.4, 31.1, 30.4, 26.7, 18.4, 18.3, 18.0, 12.1, 4.1, 2.6; MS(ESI) calcd for $C_{36}H_{45}N_3O_6$ 615.33 (M^+), found 616.51 ($M + H)^+$, 638.49 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27au. Compound **27au** was prepared according to the general procedure D from carboxylic acid **26y** and amine **11c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (t, J = 1.2 Hz, 1H), 7.21 (d, J = 1.2 Hz, 2H), 6.21 (t, J = 5.6 Hz, 1H), 5.10 (d, J = 2.0 Hz, 1H), 5.05 (d, J = 16.8 Hz, 1H), 4.88 (d, J = 16.8 Hz, 1H), 3.78 (dd, J = 7.4, 2.0 Hz, 1H), 3.71 (s, 3H), 3.44 (t, J = 5.8 Hz, 2H), 3.38−3.27 (m, 5H), 2.99−2.89 (m, 1H), 2.70 (dd, J = 15.2, 5.8 Hz, 1H), 2.59 (dd, J = 15.2, 4.8 Hz, 1H), 2.43 (dd, J = 13.0, 6.0 Hz, 1H), 2.24 (t, J = 12.8 Hz, 1H), 1.83−1.67 (m, 4H), 0.90 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.7 Hz, 3H), 0.59 (td, J = 8.8, 4.1 Hz, 1H), 0.55−0.41 (m, 2H), 0.30−0.21 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 171.2, 170.5, 135.4, 133.3, 133.1, 132.8, 129.2, 129.0, 127.5, 108.3, 81.8, 78.5, 71.7, 58.9, 53.0, 51.7, 44.9, 38.4, 38.1, 37.3, 33.6, 30.4, 29.3, 18.7, 18.7, 12.4, 4.8, 2.6; MS(ESI) calcd for $C_{29}H_{38}Cl_2N_2O_6$ 580.21 (M^+), found 581.39 ($M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27av. Compound **27av** was prepared according to the general procedure D from carboxylic acid **26y** and amine **11p**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, J = 1.7 Hz, 1H), 7.24−7.18 (m, 2H), 6.28 (t, J = 5.4 Hz, 1H), 5.09 (d, J = 2.0 Hz, 1H), 5.06 (d, J = 16.8 Hz, 1H), 4.87 (d, J = 16.8 Hz, 1H), 3.78 (dd, J = 7.4, 2.0 Hz, 1H), 3.71 (s, 3H), 3.48 (t, J = 5.8 Hz, 2H), 3.39 (t, J = 6.6 Hz, 2H), 3.36−3.30 (m, 2H), 2.99−2.89 (m, 1H), 2.70 (dd, J = 15.2, 5.8 Hz, 1H), 2.58 (dd, J = 15.2, 4.6 Hz, 1H), 2.42 (dd, J = 13.0, 5.9 Hz, 1H), 2.24 (t, J = 12.7 Hz, 1H), 1.80−1.69 (m, 3H), 1.59−1.49 (m, 2H), 1.40−1.31 (m, 2H), 0.96−0.86 (m, 8H), 0.77 (d, J = 6.7 Hz, 3H), 0.59 (dtd, J = 10.1, 5.6, 4.8, 2.8 Hz, 1H), 0.54−0.41 (m, 2H), 0.29−0.22 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 171.2, 170.4, 133.3, 133.1, 132.8, 129.2, 129.1, 127.5, 108.3, 81.8, 78.5, 71.1, 69.9, 53.0, 51.7, 44.9, 38.4, 38.3, 37.2, 33.6, 31.9, 30.3, 29.3, 19.5, 18.7, 18.7, 14.1, 12.4, 4.8, 2.6; MS(ESI) calcd for $C_{32}H_{44}Cl_2N_2O_6$ 622.26 (M^+), found 623.44 ($M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27aw. Compound **27aw** was prepared according to the general procedure D from carboxylic acid **26z** and amine **11a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.32 (m, 4H), 7.32−7.28 (m, 1H), 6.46 (t, J = 5.4 Hz, 1H), 5.35 (d, J = 1.7 Hz, 1H), 4.61 (d, J = 12.2 Hz, 1H), 4.56 (d, J = 12.3 Hz, 1H), 4.50 (td, J = 6.0, 1.8 Hz, 1H), 4.11 (q, J = 6.5 Hz, 1H), 4.03 (ddd, J = 17.6, 5.4, 2.5 Hz, 1H), 3.95 (ddd, J = 17.4, 5.0, 2.5 Hz, 1H), 3.85−3.75 (m, 2H), 3.70 (s, 3H), 3.56 (dd, J = 9.8, 6.4 Hz, 1H), 3.52−3.45 (m, 1H), 3.43 (dd, J = 9.7, 5.7 Hz, 1H), 2.93 (m, 1H), 2.59 (dd, J = 15.0, 5.6 Hz, 1H), 2.54 (dd, J = 15.0, 5.7 Hz, 1H), 2.37 (dd, J = 12.8, 6.7 Hz, 1H), 2.19 (t, J = 2.6 Hz, 1H), 1.71 (t, J = 12.3 Hz, 1H), 1.65−1.53 (m, 1H), 1.53−1.42 (m, 1H), 1.36−1.23 (m, 10H), 1.22 (d, J = 6.6 Hz, 3H), 0.91−0.84 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 170.7, 170.5, 138.1, 136.4, 128.6, 127.9, 127.9, 107.3, 79.8, 74.5, 73.6, 73.3, 72.8, 71.5, 52.9, 51.3, 43.6, 39.3, 37.3, 31.9, 29.5, 29.5, 29.4, 29.3, 27.3, 26.7, 22.8, 17.0, 14.2; MS(ESI) calcd for $C_{32}H_{44}N_2O_6$ 552.32 (M^+), found 553.5 ($M + H)^+$, 575.48 ($M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ax. Compound **27ax** was prepared according to the general procedure D from carboxylic acid **26z** and amine **11f**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.30 (m, 4H), 7.30−7.27 (m, 1H), 6.84−6.75 (m, 3H), 6.33 (t, J = 5.7 Hz, 1H), 5.32 (d, J = 1.8 Hz, 1H), 4.60 (d, J = 12.2 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H), 4.50 (td, J = 5.9, 1.7 Hz, 1H), 4.32 (dd, J = 14.1, 5.4 Hz, 2H), 4.11 (q, J = 6.6 Hz, 1H), 3.96 (d, J = 12.6 Hz, 2H), 3.89−3.85 (m, 3H), 3.85−3.82 (m, 3H), 3.68 (s, 3H),

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3.56 (dd, J = 9.8, 6.4 Hz, 1H), 3.43 (dd, J = 9.9, 5.6 Hz, 1H), 2.95 (m, 1H), 2.60 (dd, J = 14.8, 5.5 Hz, 1H), 2.53 (dd, J = 14.8, 5.9 Hz, 1H), 2.37 (dd, J = 12.8, 6.6 Hz, 1H), 1.72 (t, J = 12.2 Hz, 1H), 1.61−1.50 (m, 1H), 1.49−1.40 (m, 1H), 1.33−1.22 (m, 10H), 1.21 (d, J = 6.6 Hz, 3H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.1, 172.6, 170.7, 170.5, 149.2, 148.5, 138.1, 136.5, 131.2, 128.6, 127.9, 127.9, 127.0, 120.1, 119.8, 111.3, 111.3, 111.2, 110.9, 110.5, 109.1, 107.0, 74.5, 73.6, 73.3, 72.9, 56.3, 56.1, 56.1, 56.1, 56.1, 56.0, 56.0, 56.0, 56.0, 52.9, 44.6, 43.5, 43.5, 39.5, 37.4, 31.9, 29.6, 29.5, 29.4, 29.4, 27.3, 26.7, 22.8, 17.0, 14.2; MS(ESI) calcd for $C_{38}H_{52}N_2O_8$ 664.37 (M^+), found 665.55 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ay. Compound **27ay** was prepared according to the general procedure D from carboxylic acid **26aa** and amine **11h**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.1 Hz, 1H), 7.87 (dd, J = 7.7, 1.7 Hz, 1H), 7.80 (dd, J = 6.3, 3.3 Hz, 1H), 7.56−7.45 (m, 2H), 7.43−7.36 (m, 2H), 7.34−7.26 (m, 4H), 7.26−7.15 (m, 6H), 6.20 (t, J = 5.6 Hz, 1H), 5.27 (d, J = 1.9 Hz, 1H), 4.91−4.78 (m, 3H), 4.74 (d, J = 15.8 Hz, 1H), 4.49 (d, J = 12.1 Hz, 1H), 4.43 (d, J = 12.1 Hz, 1H), 4.40 (td, J = 5.6, 2.8 Hz, 1H), 4.13 (q, J = 6.5 Hz, 1H), 3.59 (s, 3H), 3.47 (dd, J = 9.8, 6.4 Hz, 1H), 3.31 (dd, J = 9.8, 5.7 Hz, 1H), 3.04−2.96 (m, 1H), 2.70−2.58 (m, 2H), 2.38 (dd, J = 12.8, 6.3 Hz, 1H), 1.87 (t, J = 12.4 Hz, 1H), 1.18 (d, J = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 170.8, 170.4, 138.1, 136.8, 136.2, 134.0, 133.7, 131.5, 128.9, 128.7, 128.6, 128.5, 127.8, 127.8, 127.2, 127.0, 126.8, 126.8, 126.1, 125.5, 123.7, 107.7, 74.2, 73.5, 72.9, 72.9, 52.9, 51.4, 47.4, 41.8, 39.0, 37.5, 29.6, 17.2; MS(ESI) calcd for $C_{39}H_{40}N_2O_6$ 632.29 (M^+), found 633.45 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27az. Compound **27az** was prepared according to the general procedure D from carboxylic acid **26aa** and amine **11u**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.27 (m, 5H), 7.26−7.19 (m, 5H), 5.29 (d, J = 1.8 Hz, 1H), 4.98 (d, J = 15.7 Hz, 1H), 4.87 (d, J = 15.7 Hz, 1H), 4.51 (d, J = 12.2 Hz, 1H), 4.45 (d, J = 12.1 Hz, 1H), 4.41 (td, J = 6.6, 1.5 Hz, 1H), 4.12 (q, J = 6.6 Hz, 1H), 3.64−3.56 (m, 4H), 3.48 (dd, J = 9.9, 6.6 Hz, 1H), 3.45−3.32 (m, 1H), 3.30 (dd, J = 9.8, 5.7 Hz, 1H), 3.01−2.93 (m, 1H), 2.87 (dd, J = 16.2, 3.4 Hz, 1H), 2.76 (dd, J = 16.2, 7.5 Hz, 1H), 2.37 (dd, J = 12.7, 6.2 Hz, 1H), 1.94 (t, J = 12.2 Hz, 1H), 1.68−1.59 (m, 3H), 1.59−1.47 (m, 5H), 1.20 (d, J = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 171.2, 168.6, 138.2, 137.2, 136.7, 128.6, 128.5, 127.8, 127.8, 127.2, 127.0, 107.1, 74.4, 73.5, 73.0, 52.8, 51.4, 47.5, 46.6, 42.9, 37.0, 35.9, 29.8, 26.5, 25.7, 24.7, 17.2; MS(ESI) calcd for $C_{33}H_{40}N_2O_6$ 560.29 (M^+), found 561.46 $(M + H)^+$, 583.44 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27ba. Compound **27ba** was prepared according to the general procedure D from carboxylic acid **26ab** and amine **11a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.31 (m, 2H), 7.31−7.26 (m, 2H), 7.25 (d, J = 1.4 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 1.5 Hz, 1H), 6.67 (dd, J = 7.9, 1.8 Hz, 1H), 6.28 (t, J = 5.0 Hz, 1H), 5.92 (s, 2H), 5.34 (d, J = 1.8 Hz, 1H), 4.88 (d, J = 15.5 Hz, 1H), 4.75 (d, J = 15.6 Hz, 1H), 4.53 (d, J = 12.1 Hz, 1H), 4.48 (d, J = 12.1 Hz, 1H), 4.41 (td, J = 6.1, 1.8 Hz, 1H), 4.12 (q, J = 6.5 Hz, 1H), 4.00 (dd, J = 5.3, 2.6 Hz, 2H), 3.64 (s, 3H), 3.49 (dd, J = 9.8, 6.3 Hz, 1H), 3.33 (dd, J = 9.8, 5.7 Hz, 1H), 2.97 (m, 1H), 2.66 (dd, J = 14.9, 5.6 Hz, 1H), 2.60 (dd, J = 15.0, 5.4 Hz, 1H), 2.37 (dd, J = 12.9, 6.4 Hz, 1H), 2.20 (t, J = 2.5 Hz, 1H), 1.84 (t, J = 12.4 Hz, 1H), 1.64 (s, 1H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 171.0, 170.5, 148.0, 146.7, 138.1, 136.3, 130.7, 128.5, 127.9, 127.8, 120.3, 108.4, 108.0, 107.7, 101.1, 79.7, 74.3, 73.5, 72.9, 72.8, 71.6, 53.0, 51.4, 47.4, 38.8, 37.4, 29.6, 29.3, 17.1; MS(ESI) calcd for $C_{32}H_{34}N_2O_8$ 574.23 (M^+), found 575.35 $(M + H)^+$, 597.34 $(M + Na)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bb. Compound **27bb** was prepared according to the general procedure D from carboxylic acid **26ab** and amine **11w**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.24 (m, 5H), 6.79 (d, J = 1.1 Hz, 1H), 6.72 (t, J = 1.1 Hz, 2H), 5.90 (d, J = 1.2 Hz, 2H), 5.30 (d, J = 1.7 Hz, 1H), 4.86 (d, J = 15.6 Hz, 1H), 4.79 (d, J = 15.6 Hz, 1H), 4.54 (d, J = 12.0 Hz, 1H), 4.47 (d, J = 12.3 Hz, 1H), 4.42 (td, J = 6.6, 6.2, 1.7 Hz, 1H), 4.12 (q, J = 6.4, 6.0 Hz, 1H), 3.64 (s, 3H), 3.54−3.48 (m, 2H), 3.43 (m, 4H), 3.33 (dd, J = 9.8, 5.7 Hz, 1H), 2.99−2.91 (m, 1H), 2.82 (dd, J = 16.4, 6.6 Hz, 1H), 2.68 (dd, J = 16.5, 3.5 Hz, 1H), 2.33 (dd, J = 12.6, 6.2 Hz, 1H), 2.02 (t, J = 12.3 Hz, 1H), 1.93 (m, 2H), 1.87−1.80 (m, 2H), 1.21 (d, J = 6.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.3, 168.9, 147.9, 146.5, 138.2, 136.8, 131.2, 128.5, 127.8, 127.8, 120.3, 108.2, 107.9, 107.0, 101.0, 74.4, 73.5, 73.1, 73.0, 52.8, 51.4, 47.3, 46.6, 45.8, 36.9, 36.7, 29.6, 26.2, 24.5, 17.2; MS(ESI) calcd for $C_{33}H_{38}N_2O_8$ 590.26 (M^+), found 591.38 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bc. Compound **27bc** was prepared according to the general procedure D from carboxylic acid **26d** and amine **11d**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.26 (m, 5H), 6.30 (dd, J = 3.2, 1.9 Hz, 1H), 6.24 (d, J = 3.2 Hz, 1H), 5.91 (t, J = 5.4 Hz, 1H), 5.56 (d, J = 1.8 Hz, 1H), 4.95 (d, J = 15.8 Hz, 1H), 4.72 (d, J = 15.8 Hz, 1H), 4.58 (d, J = 12.1 Hz, 1H), 4.53 (d, J = 12.1 Hz, 1H), 4.46 (td, J = 6.0, 1.8 Hz, 1H), 4.09 (q, J = 6.5 Hz, 1H), 3.62 (s, 3H), 3.54 (dd, J = 9.7, 6.4 Hz, 1H), 3.40 (dd, J = 9.8, 5.7 Hz, 1H), 3.20−3.14 (m, 2H), 2.94 (m, 1H), 2.55 (dd, J = 5.6, 2.0 Hz, 2H), 2.38 (dd, J = 12.9, 6.6 Hz, 1H), 1.75 (dd, J = 12.9, 11.6 Hz, 1H), 1.61−1.51 (m, 1H), 1.43−1.34 (m, 1H), 1.34−1.27 (m, 2H), 1.19 (d, J = 6.5 Hz, 3H), 0.89 (d, J = 1.2 Hz, 3H), 0.87 (d, J = 1.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 170.8, 170.6, 150.4, 141.8, 138.2, 136.6, 128.5, 127.8, 127.8, 110.6, 108.5, 108.3, 74.4, 73.6, 73.2, 72.8, 53.0, 51.4, 41.0, 39.2, 38.5, 38.0, 37.6, 29.4, 26.0, 22.6, 22.6, 17.0; MS(ESI) calcd for $C_{31}H_{40}N_2O_7$ 552.28 (M^+), found 553.46 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bd. Compound **27bd** was prepared according to the general procedure D from carboxylic acid **26d** and amine **11x**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.27 (m, 6H), 7.25−7.17 (m, 4H), 6.32−6.27 (m, 2H), 5.53 (d, J = 1.8 Hz, 1H), 4.95−4.79 (m, 2H), 4.76−4.70 (m, 1H), 4.60 (d, J = 12.2 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H), 4.51−4.47 (m, 1H), 4.10 (dd, J = 6.6, 4.7 Hz, 1H), 4.00−3.92 (m, 1H), 3.62 (d, J = 2.6 Hz, 3H), 3.60−3.53 (m, 1H), 3.42 (dd, J = 9.8, 5.5 Hz, 1H), 3.14−3.05 (m, 1H), 3.04−2.96 (m, 1H), 2.90 (ddd, J = 17.2, 14.2, 3.4 Hz, 1H), 2.80−2.67 (m, 2H), 2.66−2.57 (m, 1H), 2.46−2.37 (m, 1H), 1.86 (q, J = 12.1, 11.6 Hz, 3H), 1.69−1.56 (m, 3H), 1.28−1.18 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 170.9, 168.8, 168.7, 150.6, 145.3, 141.6, 138.2, 137.0, 128.9, 128.7, 128.6, 128.5, 128.5, 127.9, 127.8, 127.8, 127.8, 127.2, 126.9, 126.8, 126.8, 126.6, 110.6, 108.4, 108.3, 107.7, 107.6, 74.5, 73.5, 73.4, 73.3, 73.0, 52.9, 51.4, 51.4, 46.2, 44.7, 42.9, 42.6, 42.6, 40.9, 40.8, 40.7, 37.0, 36.9, 36.1, 36.1, 33.9, 33.8, 33.0, 33.0, 30.0, 29.6, 17.0, 17.0; MS(ESI) calcd for $C_{37}H_{42}N_2O_7$ 626.30 (M^+), found 627.47 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27be. Compound **27be** was prepared according to the general procedure D from carboxylic acid **26ac** and amine **11g**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56−7.48 (m, 2H), 7.48−7.38 (m, 2H), 7.38−7.31 (m, 4H), 7.31−7.27 (m, 1H), 6.73 (q, J = 6.5, 6.0 Hz, 1H), 5.44−5.40 (m, 1H), 5.37 (d, J = 1.7 Hz, 1H), 4.60 (d, J = 12.1 Hz, 1H), 4.55 (d, J = 12.1 Hz, 1H), 4.53−4.46 (m, 2H), 4.40 (dd, J = 15.2, 5.7 Hz, 1H), 4.14 (q, J = 6.3 Hz, 1H), 3.80 (ddd, J = 13.1, 10.8, 5.3 Hz, 1H), 3.69 (s, 3H), 3.61−3.51 (m, 2H), 3.44 (dd, J = 9.7, 5.8 Hz, 1H), 2.96−2.86 (m, 1H), 2.62 (dd, J = 14.7, 5.8 Hz, 1H), 2.55 (dd, J = 15.0, 5.5 Hz, 1H), 2.36 (dd, J = 12.7, 6.4 Hz, 1H), 2.23−2.13 (m, 1H), 2.08−1.99 (m, 1H), 1.99−1.91 (m, 4H), 1.70 (t, J = 12.4 Hz, 1H), 1.64−1.56 (m, 2H), 1.56−1.48 (m, 2H), 1.21 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 171.1, 170.5, 139.7, 138.1, 136.0, 134.9, 131.2, 129.2, 128.6, 127.9, 127.9, 124.4 (q, $^3J_{C-F}$ = 3.6 Hz), 124.3 (q, $^3J_{C-F}$ = 3.5 Hz), 124.2 (q, $^1J_{C-F}$ = 273.3 Hz), 123.0, 107.0, 74.3, 73.6, 73.0, 72.9, 53.0, 51.3, 43.1, 42.6, 39.5, 37.4, 34.7, 29.8, 28.6, 25.4, 23.0, 22.4, 17.1; MS(ESI) calcd for $C_{37}H_{43}F_3N_2O_6$ 668.31 (M^+), found 669.42 $(M + H)^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bf. Compound **27bf** was prepared according to the general procedure D from carboxylic acid **26ac** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.32 (m, 4H), 7.31−7.27 (m, 1H), 5.50−5.40 (m, 1H), 5.37 (d, J = 1.8 Hz, 1H), 4.61 (d, J = 12.1 Hz, 1H), 4.55 (d, J = 12.1 Hz, 1H), 4.52 (td, J = 6.1, 1.6 Hz, 1H), 4.12 (q, J = 6.5 Hz, 1H), 3.86 (ddd, J = 13.5, 11.0, 5.4 Hz, 1H), 3.70 (s, 3H), 3.68−3.62 (m, 4H), 3.62−3.49 (m, 4H), 3.47−3.39 (m, 3H), 2.96−2.88 (m, 1H),

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2.83 (dd, J = 16.2, 3.4 Hz, 1H), 2.62 (dd, J = 16.2, 7.7 Hz, 1H), 2.37 (dd, J = 12.6, 6.5 Hz, 1H), 2.28−2.18 (m, 1H), 2.12−2.02 (m, 1H), 1.99−1.91 (m, 4H), 1.75 (t, J = 12.0 Hz, 1H), 1.63−1.56 (m, 2H), 1.56−1.49 (m, 2H), 1.23 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 170.3, 169.3, 138.1, 136.7, 135.1, 128.5, 127.9, 127.8, 122.8, 106.4, 74.5, 73.5, 73.3, 73.0, 67.0, 66.6, 52.9, 51.4, 45.9, 42.6, 42.1, 36.8, 35.9, 34.7, 29.6, 28.6, 25.4, 23.0, 22.5, 17.1; MS(ESI) calcd for $C_{33}H_{44}N_2O_7$ 580.31 (M^+), found 581.45 (M + H)$^+$, 603.42 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bg. Compound **27bg** was prepared according to the general procedure D from carboxylic acid **26ad** and amine **11g**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58−7.37 (m, 4H), 7.36−7.30 (m, 4H), 7.30−7.27 (m, 1H), 6.78−6.69 (m, 3H), 6.56 (t, J = 6.0 Hz, 1H), 5.37 (d, J = 1.8 Hz, 1H), 4.60 (d, J = 12.1 Hz, 1H), 4.55 (d, J = 12.3 Hz, 1H), 4.53−4.49 (m, 1H), 4.46 (dd, J = 18.7, 5.8 Hz, 1H), 4.14 (q, J = 6.5 Hz, 1H), 3.94 (ddd, J = 13.5, 10.4, 6.2 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.76−3.69 (m, 1H), 3.69 (s, 3H), 3.55 (dd, J = 9.7, 6.3 Hz, 1H), 3.41 (dd, J = 9.7, 6.0 Hz, 1H), 2.96 (m, 1H), 2.85−2.77 (m, 1H), 2.77−2.69 (m, 1H), 2.65−2.56 (m, 2H), 2.38 (dd, J = 12.8, 6.5 Hz, 1H), 1.75 (t, J = 12.3 Hz, 1H), 1.21 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.6, 171.0, 170.6, 149.1, 147.8, 139.7, 138.1, 136.3, 131.5, 131.2, 131.1, 131.1 ($^2J_{C-F}$ = 32.4 Hz), 129.2, 128.6, 127.9, 127.9, 124.4 ($^3J_{C-F}$ = 3.8 Hz), 124.3 ($^3J_{C-F}$ = 3.8 Hz), 124.2 ($^1J_{C-F}$ = 272.9 Hz), 120.7, 74.4, 73.6, 73.1, 72.9, 56.1, 56.0, 53.0, 51.4, 45.4, 43.1, 39.4, 37.4, 32.6, 29.7, 17.1; MS(ESI) calcd for $C_{39}H_{43}F_3N_2O_8$ 724.30 (M^+), found 725.46 (M + H)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bh. Compound **27bh** was prepared according to the general procedure D from carboxylic acid **26ad** and amine **11q**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.30 (m, 4H), 7.29 (s, 1H), 6.77 (d, J = 10.7 Hz, 3H), 5.37 (d, J = 1.8 Hz, 1H), 4.61 (d, J = 12.1 Hz, 1H), 4.58−4.49 (m, 2H), 4.11 (q, J = 6.6 Hz, 1H), 3.98 (ddd, J = 13.3, 10.6, 6.2 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.78−3.71 (m, 1H), 3.71−3.60 (m, 8H), 3.56 (dd, J = 9.7, 6.6 Hz, 1H), 3.41 (dd, J = 9.7, 5.9 Hz, 1H), 3.01−2.91 (m, 1H), 2.89−2.81 (m, 2H), 2.81−2.71 (m, 3H), 2.38 (dd, J = 12.6, 6.6 Hz, 1H), 1.84−1.76 (m, 1H), 1.72 (s, 1H), 1.23 (d, J = 6.6 Hz, 3H), 1.01 (dq, J = 6.6, 3.9 Hz, 3H), 0.83−0.76 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 170.5, 149.1, 147.7, 138.1, 136.9, 131.8, 128.6, 127.9, 120.7, 112.2, 111.4, 74.6, 73.5, 73.3, 72.9, 56.0, 56.0, 52.9, 51.4, 45.5, 45.3, 41.9, 41.7, 36.8, 36.0, 32.6, 29.5, 17.0, 11.2, 7.8; MS(ESI) calcd for $C_{39}H_{49}N_3O_9$ 703.35 (M^+), found 704.5 (M + H)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bi. Compound **27bi** was prepared according to the general procedure D from carboxylic acid **26ae** and amine **11i**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.87 (dd, J = 7.9, 1.7 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.58−7.46 (m, 2H), 7.39 (t, J = 7.6 Hz, 1H), 7.24 (dd, J = 6.4, 2.7 Hz, 3H), 7.14 (dd, J = 6.6, 3.0 Hz, 2H), 6.10 (s, 1H), 5.53 (d, J = 16.2 Hz, 1H), 5.30−5.20 (m, 2H), 4.45 (d, J = 12.1 Hz, 1H), 4.39 (d, J = 12.2 Hz, 1H), 4.36 (td, J = 6.4, 6.0, 2.3 Hz, 1H), 4.11 (q, J = 6.5 Hz, 1H), 3.44 (dd, J = 9.8, 6.5 Hz, 1H), 3.35 (s, 3H), 3.27 (dd, J = 9.8, 5.5 Hz, 1H), 3.07−3.00 (m, 1H), 2.92 (d, J = 6.2 Hz, 2H), 2.75 (dd, J = 14.6, 5.8 Hz, 1H), 2.70−2.62 (m, 3H), 2.43 (dd, J = 12.9, 6.3 Hz, 1H), 2.06−2.01 (m, 2H), 2.01−1.90 (m, 2H), 1.75−1.56 (m, 8H), 1.51−1.39 (m, 3H), 1.20 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.7, 171.0, 170.9, 138.0, 136.2, 133.9, 131.2, 131.0, 128.9, 128.5, 127.8, 127.8, 127.8, 126.4, 125.8, 125.5, 124.6, 123.0, 108.2, 74.2, 73.5, 72.9, 72.8, 52.7, 51.4, 51.3, 51.1, 45.4, 40.4, 40.3, 39.8, 39.2, 37.9, 37.1, 37.1, 36.5, 33.7, 32.3, 29.7, 28.4, 28.3, 28.0, 17.1; MS(ESI) calcd for $C_{43}H_{50}N_2O_6$ 690.37 (M^+), found 691.53 (M + H)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bj. Compound **27bj** was prepared according to the general procedure D from carboxylic acid **26ae** and amine **11n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 7.3 Hz, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.53 (ddd, J = 8.5, 6.8, 1.6 Hz, 1H), 7.49 (ddd, J = 8.1, 6.9, 1.3 Hz, 1H), 7.40 (t, J = 7.7 Hz, 1H), 7.28 (d, J = 7.1 Hz, 1H), 7.25−7.18 (m, 3H), 7.16−7.10 (m, 2H), 6.80 (t, J = 6.3 Hz, 1H), 5.43 (d, J = 16.4 Hz, 1H), 5.32 (d, J = 16.5 Hz, 1H), 5.23 (d, J = 1.8 Hz, 1H), 4.45 (d, J = 12.1 Hz, 1H), 4.40−4.34 (m, 2H), 4.09 (q, J = 6.5 Hz, 1H), 3.44 (dd, J = 9.8, 6.7 Hz, 1H), 3.39 (s, 3H), 3.35−3.24 (m, 5H), 3.18 (q, J = 6.2 Hz, 2H), 3.10−3.03 (m, 1H), 2.70 (t, J = 5.7 Hz, 1H), 2.37 (dd, J = 9.5, 7.0 Hz, 3H), 2.03−1.93 (m, 3H), 1.65 (tt, J = 6.4 Hz, J = 6.4 Hz, 2H), 1.21 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 172.8, 170.9, 170.8, 138.1, 136.6, 133.9, 131.2, 131.1, 128.9, 128.4, 127.8, 127.7, 127.7, 126.4, 125.8, 125.6, 124.6, 123.1, 107.7, 74.3, 73.4, 73.0, 72.9, 52.7, 51.4, 47.5, 45.6, 39.8, 38.9, 37.3, 37.2, 36.0, 31.1, 29.6, 26.7, 18.0, 17.1; MS(ESI) calcd for $C_{39}H_{45}N_3O_7$ 667.33 (M^+), found 668.51 (M + H)$^+$, 690.45 (M + Na)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bk. Compound **27bk** was prepared according to the general procedure D from carboxylic acid **26af** and amine **11o**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.27 (m, 4H), 7.25−7.21 (m, 2H), 7.19−7.13 (m, 2H), 6.06 (d, J = 3.0 Hz, 1H), 6.02 (t, J = 5.3 Hz, 1H), 5.88−5.84 (m, 1H), 5.10 (d, J = 1.9 Hz, 1H), 5.01 (d, J = 16.9 Hz, 1H), 4.79 (d, J = 16.9 Hz, 1H), 4.51 (d, J = 12.3 Hz, 1H), 4.45 (d, J = 12.1 Hz, 1H), 4.38 (td, J = 6.2, 1.9 Hz, 1H), 4.33 (d, J = 5.2 Hz, 2H), 4.16 (q, J = 6.6 Hz, 1H), 3.72 (s, 3H), 3.48 (dd, J = 9.8, 6.4 Hz, 1H), 3.31 (dd, J = 9.8, 5.6 Hz, 1H), 2.96−2.86 (m, 1H), 2.77 (dd, J = 15.2, 5.8 Hz, 1H), 2.58 (dd, J = 15.3, 4.6 Hz, 1H), 2.34 (dd, J = 12.9, 6.1 Hz, 1H), 2.24 (s, 3H), 2.02 (t, J = 12.6 Hz, 1H), 1.23 (d, J = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 170.9, 170.2, 152.0, 149.4, 138.1, 136.1, 133.4, 133.1, 132.5, 129.2, 128.8, 128.5, 128.5, 127.8, 127.8, 127.5, 108.4, 107.2, 106.4, 74.2, 73.5, 72.8, 72.8, 53.1, 51.4, 45.5, 38.0, 37.2, 36.8, 29.5, 17.3, 13.7; MS(ESI) calcd for $C_{34}H_{36}Cl_2N_2O_7$ 654.19 (M^+), found 655.37 (M + H)$^+$.

Tetrahydropyran-Fused Piperidinone-Containing Amide 27bl. Compound **27bl** was prepared according to the general procedure D from carboxylic acid **26af** and amine **11p**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.27 (m, 4H), 7.25−7.14 (m, 4H), 6.27 (t, J = 5.5 Hz, 1H), 5.08 (d, J = 1.9 Hz, 1H), 5.04 (d, J = 17.0 Hz, 1H), 4.79 (d, J = 17.0 Hz, 1H), 4.51 (d, J = 12.2 Hz, 1H), 4.45 (d, J = 12.0 Hz, 1H), 4.38 (td, J = 5.8, 1.9 Hz, 1H), 4.16 (q, J = 6.5 Hz, 1H), 3.72 (s, 3H), 3.51−3.43 (m, 3H), 3.39 (t, J = 6.6 Hz, 2H), 3.35−3.26 (m, 2H), 2.93−2.83 (m, 1H), 2.73 (dd, J = 15.3, 5.8 Hz, 1H), 2.54 (dd, J = 15.3, 4.4 Hz, 1H), 2.32 (dd, J = 12.8, 6.0 Hz, 1H), 2.04 (t, J = 12.5 Hz, 1H), 1.73 (tt, J = 6.0 Hz, 2H), 1.58−1.49 (m, 2H), 1.40−1.30 (m, 2H), 1.23 (d, J = 6.5 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 170.9, 170.3, 138.1, 136.2, 133.3, 133.1, 132.6, 129.2, 128.9, 128.5, 127.8, 127.8, 127.5, 107.0, 74.2, 73.5, 72.9, 72.8, 71.1, 70.0, 53.1, 51.4, 45.6, 38.5, 38.0, 37.2, 31.9, 29.6, 29.2, 19.5, 17.3, 14.1; MS(ESI) calcd for $C_{35}H_{44}Cl_2N_2O_7$ 674.25 (M^+), found 675.41 (M + H)$^+$.

Tricyclic Amide 42 ((6*RS*,7a*SR*)-Ethyl 6-(2-((3,4-Dimethoxybenzyl)amino)-2-oxoethyl)-5-oxo-2,3,5,6,7,7a,8,9-octahydro-1*H*-cyclopenta[*ij*]quinolizine-7a-carboxylate). Compound **42** was prepared according to the general procedure D from carboxylic acid **38** and amine **11f**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (s, 1H), 6.77 (s, 2H), 6.58 (t, J = 5.9 Hz, 1H), 4.40 (dd, J = 14.6, 6.2 Hz, 1H), 4.25 (dd, J = 14.6, 5.4 Hz, 1H), 4.18−4.07 (m, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.79 (ddd, J = 13.1, 6.9, 4.0 Hz, 1H), 3.36 (ddd, J = 12.7, 8.6, 3.7 Hz, 1H), 2.84−2.74 (m, 1H), 2.65 (dd, J = 14.5, 4.9 Hz, 1H), 2.58−2.41 (m, 2H), 2.27 (dd, J = 12.9, 6.9 Hz, 1H), 2.20 (dd, J = 15.3, 8.7 Hz, 1H), 2.15−2.06 (m, 1H), 2.03 (dt, J = 17.2, 5.6 Hz, 1H), 1.86−1.65 (m, 3H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 171.2, 168.7, 149.2, 148.4, 133.9, 131.4, 120.0, 118.5, 111.2, 111.2, 61.3, 56.0, 56.0, 53.6, 43.3, 40.3, 38.4, 37.7, 36.0, 35.9, 32.6, 23.0, 21.7, 14.3; MS(ESI) calcd for $C_{25}H_{32}N_2O_6$ 456.23 (M^+), found 457.11 (M + H)$^+$.

Tricyclic Amide 43. Compound **43** was prepared according to the general procedure D from carboxylic acid **38** and amine **11p**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.49 (s, 1H), 4.20−4.08 (m, 2H), 3.94 (ddd, J = 13.0, 6.2, 4.3 Hz, 1H), 3.44 (t, J = 6.0 Hz, 2H), 3.41−3.21 (m, 5H), 2.75 (dt, J = 12.9, 5.5 Hz, 1H), 2.61−2.41 (m, 3H), 2.27 (dd, J = 12.9, 6.9 Hz, 1H), 2.19 (dd, J = 15.3, 8.7 Hz, 1H), 2.15−1.99 (m, 2H), 1.90−1.75 (m, 3H), 1.75−1.64 (m, 3H), 1.53 (tt, J = 8.1, 6.4 Hz, 2H), 1.39−1.29 (m, 2H), 1.22 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 171.2, 168.7, 134.1, 118.2, 71.0,

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69.4, 61.3, 53.6, 40.3, 38.3, 37.8, 37.5, 36.0, 35.8, 32.6, 31.9, 29.5, 23.0, 21.8, 19.5, 14.3, 14.0; MS(ESI) calcd for $C_{23}H_{36}N_2O_5$ 420.26 (M^+), found 421.52 $(M + H)^+$.

Tricyclic Amide 44. Compound **44** was prepared according to the general procedure D from carboxylic acid **37** and amine **11h**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05−7.98 (m, 1H), 7.86−7.80 (m, 1H), 7.77 (dd, J = 5.8, 3.7 Hz, 1H), 7.48 (m, 2H), 7.41−7.35 (m, 2H), 6.66−6.58 (m, 1H), 5.08 (dd, J = 14.6, 6.9 Hz, 1H), 4.61 (dd, J = 14.6, 4.5 Hz, 1H), 4.33−4.24 (m, 1H), 4.16−4.03 (m, 2H), 2.84−2.71 (m, 2H), 2.64−2.54 (m, 1H), 2.50 (dd, J = 14.1, 5.4 Hz, 1H), 2.35 (dd, J = 13.0, 5.6 Hz, 1H), 2.23−2.15 (m, 1H), 2.01−1.91 (m, 3H), 1.75−1.58 (m, 3H), 1.46−1.29 (m, 2H), 1.18 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 170.8, 168.6, 134.2, 133.9, 131.4, 129.3, 128.7, 128.5, 126.6, 126.5, 125.9, 125.5, 123.9, 116.3, 61.4, 46.1, 41.5, 40.6, 38.6, 37.3, 36.5, 34.7, 29.8, 28.1, 21.5, 19.1, 14.3; MS(ESI) calcd for $C_{28}H_{32}N_2O_4$ 460.24 (M^+), found 461.30 $(M + H)^+$.

Tricyclic Amide 45. Compound **45** was prepared according to the general procedure D from carboxylic acid **37** and amine **11j**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.45 (s, 1H), 4.63−4.49 (m, 1H), 4.22−4.00 (m, 2H), 3.30−3.08 (m, 2H), 3.00−2.83 (m, 1H), 2.63−2.53 (m, 2H), 2.53−2.45 (m, 1H), 2.34 (dd, J = 13.1, 5.5 Hz, 1H), 2.20 (ddd, J = 12.3, 3.9, 2.3 Hz, 1H), 2.16−2.05 (m, 1H), 2.05−1.97 (m, 2H), 1.97−1.83 (m, 2H), 1.73−1.61 (m, 2H), 1.52−1.35 (m, 4H), 1.35−1.25 (m, 2H), 1.21 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 171.2, 169.0, 129.7, 116.3, 61.4, 46.2, 40.8, 39.2, 38.9, 37.3, 36.8, 34.7, 31.8, 29.8, 28.1, 21.9, 20.2, 19.1, 14.3, 13.8; MS(ESI) calcd for $C_{21}H_{32}N_2O_4$ 376.24 (M^+), found 377.47 $(M + H)^+$.

Tricyclic Amide 46. Compound **46** was prepared according to the general procedure D from carboxylic acid **40** and amine **11c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (t, J = 5.7 Hz, 1H), 4.18−4.03 (m, 2H), 3.83 (dt, J = 12.6, 4.7 Hz, 1H), 3.44 (t, J = 6.0 Hz, 2H), 3.36−3.27 (m, 5H), 3.27−3.18 (m, 1H), 2.90 (t, J = 6.8 Hz, 1H), 2.62 (dd, J = 15.2, 7.1 Hz, 1H), 2.54 (dt, J = 12.6, 3.2 Hz, 1H), 2.18−1.64 (m, 8H), 1.60−1.47 (m, 1H), 1.41 (ddd, J = 13.7, 12.4, 3.0 Hz, 1H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 172.1, 171.1, 132.0, 110.4, 71.4, 61.4, 59.0, 51.8, 49.5, 39.1, 37.9, 34.0, 30.7, 29.6, 27.3, 25.9, 21.4, 20.3, 14.5; MS(ESI) calcd for $C_{20}H_{30}N_2O_5$ 378.22 (M^+), found 379.10 $(M + H)^+$.

Tricyclic Amide 47. Compound **47** was prepared according to the general procedure D from carboxylic acid **40** and amine **11m**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21−7.16 (m, 1H), 7.14 (dd, J = 7.4, 1.7 Hz, 1H), 6.90−6.81 (m, 2H), 6.75 (t, J = 5.6 Hz, 1H), 4.16−4.01 (m, 2H), 3.88−3.75 (m, 4H), 3.55−3.39 (m, 2H), 3.28−3.18 (m, 1H), 2.91−2.77 (m, 3H), 2.61 (dd, J = 15.2, 7.1 Hz, 1H), 2.54 (dt, J = 12.7, 3.2 Hz, 1H), 2.17−1.78 (m, 6H), 1.77−1.65 (m, 1H), 1.60−1.45 (m, 1H), 1.40 (ddd, J = 13.8, 12.5, 3.0 Hz, 1H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 171.8, 170.8, 157.7, 131.7, 130.7, 127.8, 127.5, 120.6, 110.4, 110.1, 61.1, 55.3, 51.6, 49.2, 39.8, 38.8, 33.6, 30.4, 30.4, 27.0, 25.6, 21.2, 20.0, 14.2; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{25}H_{33}N_2O_5$ 441.2389, found 441.2384.

Tricyclic Amide 48. Compound 48 was prepared according to the general procedure D from carboxylic acid **41** and amine **11t**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77−3.69 (m, 1H), 3.69−3.60 (m, 7H), 3.60−3.52 (m, 1H), 3.50−3.43 (m, 1H), 3.43−3.37 (m, 1H), 3.28−3.18 (m, 2H), 2.79 (dd, J = 16.6, 5.0 Hz, 1H), 2.59−2.50 (m, 1H), 2.22 (dd, J = 16.6, 7.3 Hz, 1H), 2.16−2.03 (m, 3H), 1.98−1.90 (m, 1H), 1.89−1.80 (m, 2H), 1.75−1.63 (m, 2H), 1.64−1.54 (m, 2H), 1.34 (dddd, J = 13.2, 10.5, 8.0, 2.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 172.1, 169.2, 135.0, 114.8, 67.0, 66.6, 55.7, 52.1, 48.7, 46.0, 42.4, 38.7, 36.0, 33.5, 30.1, 29.6, 27.6, 26.9, 20.9; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{20}H_{29}N_2O_5$ 377.2076, found 377.2086.

Tricyclic Amide 49. Compound **49** was prepared according to the general procedure D from carboxylic acid **41** and amine **11k**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (t, J = 5.8 Hz, 1H), 7.36−7.29 (m, 3H), 7.29−7.23 (m, 1H), 4.50 (dd, J = 14.9, 5.9 Hz, 1H), 4.42 (dd, J = 14.9, 5.5 Hz, 1H), 3.76 (dt, J = 12.8, 4.8 Hz, 1H), 3.65 (s, 3H), 3.25−3.14 (m, 1H), 2.98 (dd, J = 8.5, 4.8 Hz, 1H), 2.56 (dd, J = 15.1, 8.5 Hz, 1H), 2.47 (dt, J = 13.8, 4.0 Hz, 1H), 2.21 (dd, J = 15.1, 4.8 Hz, 1H), 2.17−2.03 (m, 3H), 2.02−1.94 (m, 1H), 1.90−1.81 (m, 2H), 1.80−1.65 (m, 1H), 1.56 (ddd, J = 13.8, 12.2, 4.0 Hz, 1H), 1.44−1.32 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 171.8, 170.7, 138.6, 134.5, 128.7, 127.8, 127.3, 115.5, 55.6, 52.2, 49.2, 43.8, 38.6, 35.2, 33.9, 33.3, 29.5, 27.2, 26.9, 20.8; MS(ESI) calcd for $C_{23}H_{28}N_2O_4$ 396.20 (M^+), found 397.13 $(M + H)^+$.

Tricyclic Amide 50. Compound **50** was prepared according to the general procedure D from carboxylic acid **39** and amine **11a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.68 (t, J = 5.3 Hz, 1H), 5.11 (t, J = 4.0 Hz, 1H), 4.21−4.08 (m, 4H), 4.05 (ddd, J = 17.5, 5.6, 2.6 Hz, 1H), 3.95 (ddd, J = 17.5, 5.1, 2.5 Hz, 1H), 3.72 (dd, J = 6.9, 4.3 Hz, 2H), 3.05−2.92 (m, 1H), 2.63−2.51 (m, 2H), 2.36−2.28 (m, 2H), 2.28−2.17 (m, 2H), 2.17−2.11 (m, 2H), 2.11−2.01 (m, 1H), 1.82−1.71 (m, 2H), 1.60 (t, J = 13.1 Hz, 1H), 1.24 (t, J = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 172.9, 171.0, 170.2, 136.2, 108.7, 79.9, 71.3, 61.7, 60.8, 48.8, 41.1, 38.0, 36.7, 33.1, 32.8, 29.6, 29.2, 22.8, 21.8, 14.3, 14.2; MS(ESI) calcd for $C_{22}H_{30}N_2O_6$ 418.21 (M^+), found 419.36 $(M + H)^+$.

Tricyclic Amide 51. Compound **51** was prepared according to the general procedure D from carboxylic acid **39** and amine **11w**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.04 (t, J = 4.0 Hz, 1H), 4.21−4.04 (m, 4H), 3.90 (ddd, J = 12.7, 6.3, 4.2 Hz, 1H), 3.53 (ddd, J = 12.3, 7.4, 4.4 Hz, 1H), 3.42 (m, 4H), 3.03 (m, 1H), 2.73 (dd, J = 16.4, 4.2 Hz, 1H), 2.57 (dd, J = 16.3, 6.8 Hz, 1H), 2.34 (ddd, J = 8.9, 6.1, 2.1 Hz, 2H), 2.28−2.17 (m, 2H), 2.17−2.00 (m, 3H), 1.97−1.86 (m, 2H), 1.86−1.70 (m, 4H), 1.28−1.17 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 173.1, 170.2, 169.4, 136.7, 107.4, 61.5, 60.7, 48.8, 46.6, 45.7, 40.9, 36.2, 35.8, 33.3, 32.3, 29.7, 26.2, 24.5, 22.9, 21.7, 14.3, 14.2; MS (ESI) calcd for $C_{23}H_{34}N_2O_6$ 434.24 (M^+), found 435.5 $(M + H)^+$.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures as well as analytical characterization data. This information is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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