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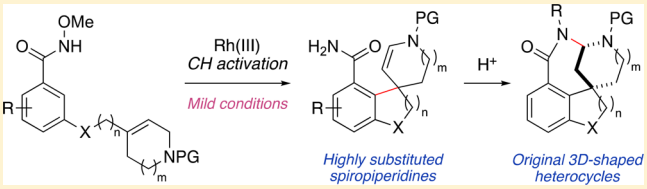
Rhodium(III)-Catalyzed Synthesis of Spiropiperidine Derivatives via C−H Activation

Augustin Peneau, Pascal Retailleau, Catherine Guillou,* and Laurent Chabaud*

Institut de Chimie des Substances Naturelles, CNRS UPR 2301, Univ Paris-Sud, Université Paris-Saclay, 1 av. de la Terrasse, 91198 Gif-sur-Yvette, France

Supporting Information

ABSTRACT: Spiropiperidine derivatives, an important class of bioactive molecules, were synthesized under mild conditions by rhodium(III)-catalyzed intramolecular ArC−H activation. This reaction provides a novel route to highly substituted tricyclic spiropiperidines in good to excellent yields. Under acidic conditions the resulting enamines reacted with pendant amides to afford spiropiperidines derivatives possessing an original tetracyclic structure.



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INTRODUCTION

Spirocycles are important scaffolds commonly embedded in various natural products or synthetic congeners with numerous biological properties.[1] Among them, spiropiperidines have attracted the attention of medicinal chemists and have shown interesting biological activity including human tryptase inhibitors **1**[2] and ghrelin receptor inhibitors such as Indane derivative[3] **2** and ibutamoren **3** (Figure 1).[4]

Owing to the well-defined tridimensional structure of these molecules and their ability to project functional groups in a specific direction, spiropiperidines have been considered by medicinal chemists as "privileged structures".[5] Accordingly, they are used to create focused chemical libraries and to explore the chemical space during structure−activity relationship studies.

Several strategies have been developed to access spiropiperidine derivatives including dialkylation reactions,[6a,b] intramolecular Fischer indole synthesis,[6c] Friedel−Crafts reaction,[6d] and Buchwald−Hartwig reaction of amides.[6e] Other general and straightforward approaches to synthesize aryl spiropiperidines **5** rely on cyclization of aryl halides **4** under radical conditions[7a] or through a Heck reaction (Scheme 1).[7b]

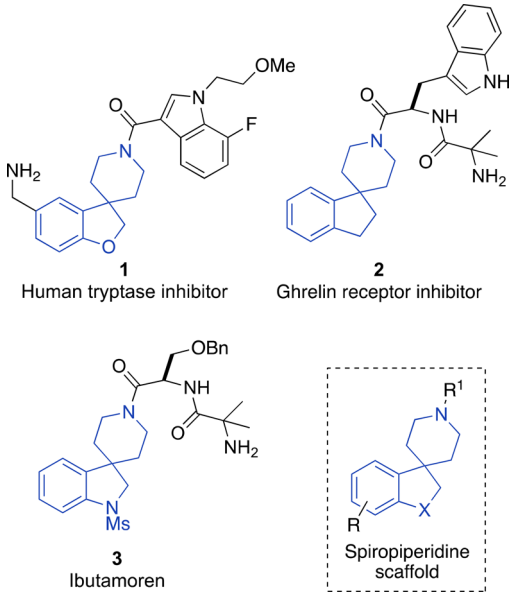
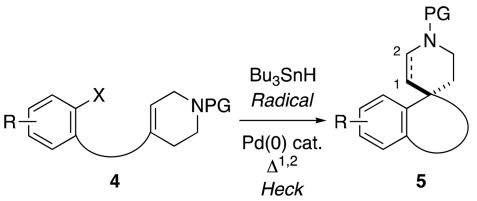


Figure 1. Some bioactive spiropiperidines developed by medicinal chemists.

Scheme 1. Spiropiperidines Synthesis from Aryl Halide by Radical Reaction or Pd(0)-Catalyzed Heck Reaction



However, these strategies require the preparation of aromatic rings bearing a halogen atom and are usually performed under harsh reaction conditions or in the presence of toxic reagents.

Recently, Rh(III)-catalyzed C−H bond activation reactions have attracted tremendous interest due to their high efficiency, functional-group tolerance, and selectivity. To date, Rh(III)-catalyzed C−H activation/intermolecular coupling reactions with different partners (alkenes, alkynes, diazo compounds, etc.) have been most widely studied to access a variety of heterocycles.[8] By contrast, the intramolecular variant has received much less attention, especially for substrates containing an olefin on the side chain.[9] Althought this

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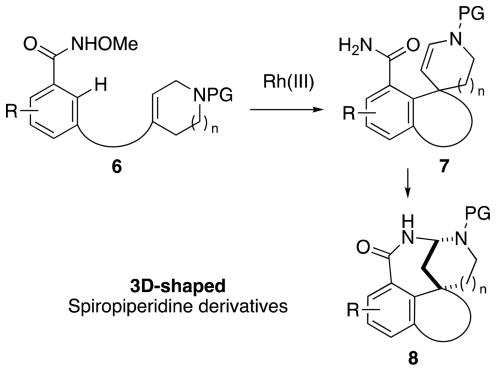
approach provides a useful method for the synthesis of spirocyclic compounds,[9d,e,10] the reaction has been limited to the synthesis of spirocarbocycles. Due to the occurrence of *N*-containing spiro heterocycles in bioactive compounds, we became interested in the Rh(III)-catalyzed C−H activation/spirocyclization of more sophisticated substrates **6** possessing an unsaturated *N*-heterocycle (Scheme 2). Albeit the reaction

Scheme 2. Rh(III)-Catalyzed Spiropiperidine 7 Synthesis and Tetracyclic Derivatives 8

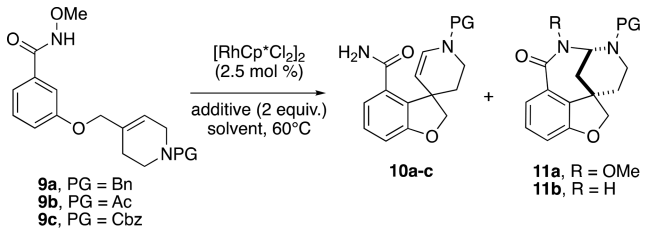


appeared challenging because of the potential catalyst inhibition by both coordinating groups, it would lead to *N*-containing spiro heterocycles **7**. We anticipated that further reaction of the primary amide with the resulting enamine would provide unprecedented heterocyclic compounds **8**.[11] Herein we describe the success of this approach.

RESULTS AND DISCUSSION

Our investigations initially focused on benzamide **9a** bearing a benzyl protecting group on the nitrogen atom (Table 1). The reaction was first conducted in the presence of $[RhCp^*Cl_2]_2$ (2.5 mol %) with 2 equiv of CsOAc in acetonitrile (C = 0.2 M)

Table 1. Optimization of the Rh(III)-Catalyzed Spirocyclization



entry	PG	solvent	additives	Cpd (%)[a]
1	Bn **9a**	CH_3CN	CsOAc	**11a**, 27[b]
2	Bn **9a**	1,2-DCE	CsOAc	**11a**, 53[c]
3	Bn **9a**	MeOH	CsOAc	**11a**, 53
4	Bn **9a**	*t*-AmOH	CsOAc	**11a**, 55[d]
5	Bn **9a**	*t*-AmOH	$Cu(OAc)_2$, $AgSbF_6$[e]	**11a**, 56
6	Ac **9b**	1,2-DCE	CsOAc	**10b**, 56
7	Ac **9b**	MeOH	CsOAc	**10b**, 71
8	Ac **9b**	*t*-AmOH	CsOAc	**10b**, 82
9	Cbz **9c**	*t*-AmOH	CsOAc	**10c**, 80

[a]Isolated yield. [b]16% of primary amide derived from **9a** and 15% of **9a** were isolated. [c]Recovery of 38% of starting material **9a**. [d]14% of primary amide derived from **9a** and 38% of **9a** were isolated. [e]2 equiv of $Cu(OAc)_2$ and 5 mol % of $AgSbF_6$ were used.

at 60 °C. Interestingly, under these conditions the tetracycle **11a** was directly formed and isolated in 27% yield,[12] as well as with recovered starting material (**9a**, 15%) and its corresponding primary amide (16%) (entry 1). No traces of enamine **10a** were observed. We noticed that the use of other solvents such as 1,2-DCE, MeOH, or *t*-AmOH slightly improved the isolated yield of **11a** (53% to 55%) (entries 2−4). However, the presence of the N-OMe still on amide **11a** indicates that the directing group does not efficiently reoxidize the catalyst. We thus performed the reaction in the presence of $Cu(OAc)_2$ (2 equiv) as an external oxidant, but no improvement of the yield was observed (entry 5). It is not clear at this stage why **11a** (R = OMe) could be formed in more than 50% yield even in the absence of an external oxidant in degassed solvents. It is possible that, with this particular substrate, the Rh(III)-catalyzed olefination occurs through a different mechanism than the one proposed by Xia et al., involving a Rh(III)/Rh(I) catalytic cycle.[13] Nevertheless, this observation led us to consider another parameter, especially the nature of the nitrogen protecting group.

We were delighted to see that an electron-withdrawing group (**9b**, PG = Ac) has a dramatic effect on the course of the reaction. Pleasingly, in the presence of $[RhCp^*Cl_2]_2$ (2.5 mol %) and CsOAc (2 equiv) in 1,2-DCE, the spirocycle **10b** resulting from the Heck-type reaction was obtained in 56% yield, without any trace of **11b** (R = H, PG = Ac) (entry 6). A rapid survey of solvents (entries 7−8) showed that *t*-AmOH gave the best yield (82%, entry 8). Interestingly, we also found that a CBz protecting group on the nitrogen atom (i.e., **9c**) was also tolerated and afforded the spirocyclic compound **10c** in 80% yield (entry 9), comparable to the *N*-acetyl **10b**.

Having established the optimal reaction conditions and the appropriate protecting group, we then examined the scope of the spirocyclization reaction (Table 2). We showed that the reaction is compatible with several substituted aryl moieties. For instance, substrates containing an electron-donating group on the aromatic ring such as a methoxy **9d** and dioxolane **9e** reacted well to provide **10d−10e** in excellent yields (83% and 70%, respectively). Additionally, *ortho* substitution by a methyl group (i.e., **9f**) led to sterically hindered amide **10f** in 64%. Electron-deficient *p*-fluoro **9g** and *p*-nitro **9h** substrates were also converted into cyclic enamines **10g−h** in 69% and 72% yields, respectively.

We next investigated the cyclization of substrates bearing different linkers. Amide **9i** reacted smoothly to produce the spirocyclic chromane **10i** in 76% yield, while the all-carbon tethered compound **9j** delivered the Indane substructure **10j** in 68% yield. Unfortunately, the mesylated aniline derivative **9k** did not cyclize under these reaction conditions.[14]

Interestingly, the regioisomeric *N*-acetyl piperidine **9l** led to the formation of the spiropiperidine **10l** in 72% yield. Furthermore, the related *N*-benzyl piperidine **9m** afforded the corresponding primary amide **10m** in 91% yield. This result contrasts with the cyclization of **9a** that gave N-OMe amide **11a** in modest yield (Table 1, entry 4). In the same manner, methylated analogue **10n** was obtained in excellent yield (82%) as a mixture of diastereomers (dr: 65/35). The cyclization can be extented to the pyrrolidine derivative **9o** bearing a Boc-protected nitrogen. In this case, the reaction afforded enamine **10o** that could not be isolated in pure form due to partial cyclization into tetracycle **11o** (see Table 3).

The formation of the tetracyclic spiropiperidines was then examined with enamines **10b−10j**, **10o** obtained by Rh(III)-

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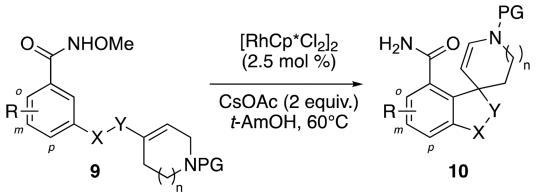
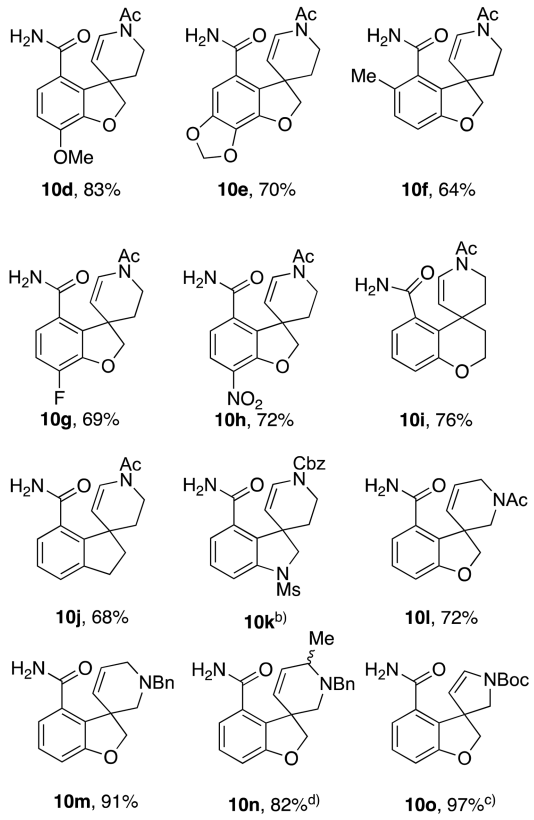
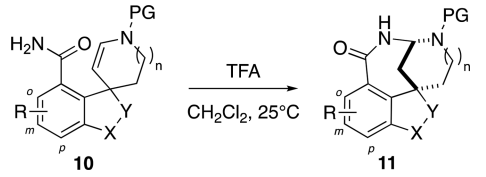
Table 2. Rh(III)-Catalyzed Synthesis Spiropiperidines 10[a]

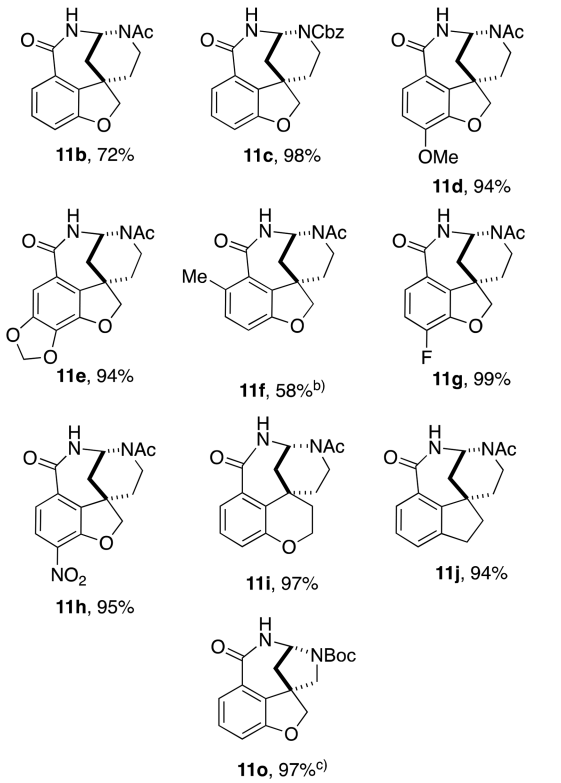




[a]Isolated yield. [b]No reaction. [c]Compound **10o** partially cyclizes during purification and was characterized as **11o** after treatment with TFA. [d]d.r. = 65/35.

Table 3. Synthesis of Spiropiperidine Derivatives 11[a]





[a]Isolated yield. [b]Yield brsm 99%. [c]Isolated yield over two steps.

catalyzed CH activation. After screening several conditions, we found that the spiropiperidine **10b** underwent smooth cyclization, with a catalytic amount of TFA (10 mol %), to give the tetracyclic derivative **11b** in 72% yield, as a single diastereomer (Table 3). Similarly, the CBz protected enamine **10c** efficiently afforded compound **11c** in 98% yield.

Substrates with electron-rich aromatic rings such as a methoxy (**10d**) or dioxolane (**10e**) also gave compounds **11d–11e** in nearly quantitative yield. We found that the reaction of *o*-methyl substituted amide **10f** with TFA did not reach completion even after a prolonged reaction time or at higher temperature (50 °C in 1,2 DCE). Consequently compound **11f** was isolated in 58% yield (brsm 99%). Other substrates **10g–h** bearing electron-withdrawing groups led to excellent isolated yields of polycyclic aminal **11g–h**. We also successfully transformed chromane and Indane derivatives **10i–j** into the corresponding aminals **11i–j** in excellent 97% and 94% yields. Finally, we found that the enamine of the unsaturated pyrrolidine **10o** is more reactive and partial cyclization to give **11o** was observed during its purification over silica gel. Interestingly, treatement of this mixture with 10 mol % of TFA led to isolation of **11o** in 97% yield over two steps, without deprotection of the Boc group.

To account for the formation of the spiropiperidine derivatives **10** and **11**, we postulate the proposed mechanism depicted in Figure 2.

Initial formation of reactive rhodium(III) species Cp*Rh(OAc)$_2$ from rhodium precatalyst [Cp*RhCl$_2$]$_2$ was achieved in the presence of CsOAc. The five-membered rhodacycle **A**, generated through a reversible C–H activation via a base-assisted concerted metalation/deprotonation (CMD) pathway,[15] underwent a *syn* olefin insertion to afford the seven-membered ring intermediate **B**. *β*-Elimination then occurred to provide **C**, which led to compound **10**, and regenerated the active catalysis. Cyclization of enamine **10** into tetracycle **11** was achieved under acidic conditions either in the reaction mixture (PG = Bn) or after subsequent treatment with TFA (PG = Ac, Cbz).

CONCLUSION

In summary, we have developed a rhodium(III)-catalyzed synthesis of spiropiperidines by means of an aryl CH activation/intramolecular Heck-type reaction. We found that the nature of the protecting group on the nitrogen atom has a critical influence on the reactivity. We showed that an electron-withdrawing group on the nitrogen (Ac, Cbz) was required to

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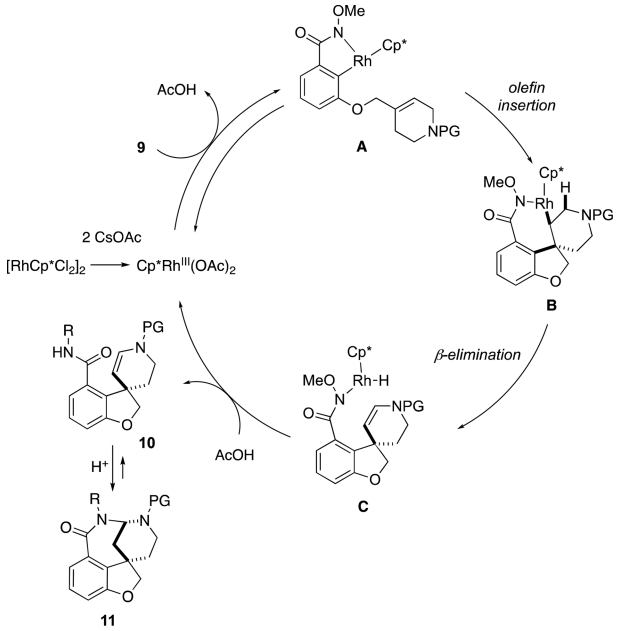

Figure 2. Mechanistic proposal.

provide complete selectivity for formation of the enamine. The conditions are mild, and the reaction is general with substrates having both electron-donating and electron-withdrawing groups on the aromatic ring. Different linkers and ring sizes of the *N*-heterocycles (six- and five-membered ring) are tolerated as well. Finally, the tricyclic spiro enamines prepared by this method were efficiently converted into tetracyclic *N*-heterocycles. Evaluation of the biological activities of these original structures is currently underway.

EXPERIMENTAL SECTION

Melting points were measured in capillary tubes and were uncorrected. Infrared spectra were recorded on an FT-IR spectrometer. Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on 300 and 500 MHz spectrometers (^{13}C, ^{31}P, ^{19}F - probe or Dual 13 C probe). Chemical shifts (δ) are reported in parts per million (ppm) with reference to $CDCl_3$ (^{1}H: 7.26; ^{13}C: 77.13). The following abbreviations are used for the proton spectra multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, quint: quintuplet, sept: septuplet, m: multiplet, br: broad. Coupling constants (J) are reported in hertz (Hz). The multiplicity of carbons was given using 2D spectra (HMQC and HMBC). The HRMS data were measured on a MALDI-TOF type of instrument for the high resolution mass spectra (HRMS). Thin-layer chromatography were performed on silica gel 60 F 254 on aluminum plates and visualized under a UVP Mineralight UVLS-28 lamp (254 nm). Flash chromatography was performed on silica gel 60 (230−400 mesh). All reagents were obtained from commercial suppliers and were used as received.

Procedure A: Alkylation. A solution of phenol (1 equiv), 4-(chloromethyl)pyridine hydrochloride (1.1 equiv), and K_2CO_3 (2.2 equiv) in acetonitrile or DMF (7 mL/mmol phenol) was heated at 60 °C overnight. Water was added, and the aqueous layers were extracted with EtOAc (×3). The organic layers were combined, washed with brine, and dried over Na_2SO_4. The solvent was removed under vacuum, and the crude mixture purified purified by flash column chromatography.

Procedure B: Pyridine Dearomatization. To a solution of pyridine derivative (1 equiv) in acetone (5 mL/mmol) was added benzyl bromide (1.2 equiv). The reaction was stirred under reflux overnight. After cooling, the main part of the acetone was evaporated under reduced pressure. Diisopropyl ether was added to the residue, and after 1 h of stirring the suspension was collected by filtration. The compounds obtained were pure enough and were used without further purification in the next step.

In a cooling mixture (−5 °C) of pyridinium (1 equiv) in methanol (5 mL/mmol) was added portionwise sodium borohydride (2 equiv). After the end of the addition, the reaction mixture was stirred for 2 h at room temperature. The main part of the solvent was removed under reduced pressure, and ethyl acetate was added. The organic layer was washed with aqueous saturated NH_4Cl, water, and brine and dried over $MgSO_4$. The solvent was evaporated under reduced pressure, and the crude product was purified by flash column chromatography.

Procedure C: Amide Synthesis. To a solution of ester (1 equiv) in ethanol (5.9 mL/mmol) was added a 3 M solution of NaOH (3.5 mL/mmol) at room temperature. The mixture was stirred for 2 h, and then HCl (2 N) was added at 0 °C until pH = 2−3. The aqueous layer was extracted with EtOAc, and the solvent was evaporated under vacuum. The crude mixture was used without purification.

Alternative Procedure. To a mixture of the ester in THF/MeOH/H_2O (v/v = 1/1/1, 8 mL/mmol) was added LiOH (8 equiv) at room temperature. Same treatment as above.

To a solution of carboxylic acid (1 equiv) in DMF (3 mL/mmol) were added successively EDCI (1.1 equiv) and HOBT (1.1 equiv), and the solution was stirred for 30 min at room temperature. The amine (1.1 equiv) was added, and then the mixture stirred for an additional 10 min. iPr$_2$NEt (2.3 equiv) was added at 0 °C, and then the mixture was stirred overnight at rt. The reaction mixture was diluted with brine, and the aqueous layer was extracted with EtOAc (×3). The organic layer was washed with water then dried over Na_2SO_4. The solvent was removed under vacuum. The crude mixture was purified through silica gel to afford the corresponding amide.

Procedure D: Cbz Protection. To a solution of *N*-benzyl amine (1 equiv) in CH_2Cl_2 (5 mL/mmol) was added $KHCO_3$ (1 equiv). Then a solution of $ClCO_2Bn$ (4.5 equiv) in CH_2Cl_2 (5 mL/mmol) was added dropwise at 0 °C. The solution was stirred overnight at room temperature. The mixture was cooled to room temperature and then poured into Na_2CO_3 (1 M). The aqueous layer was extracted with CH_2Cl_2 (×3), and the combined organic layers were washed with water and then brine and dried with Na_2SO_4, and the solvent was removed under vacuum. The crude mixture was purified through silica gel to afford the corresponding product.

Procedure E: Benzyl Deprotection. *N*-Benzyl amine (1 equiv) was dissolved in 1,2-dichloroethane (10 mL/mmol) and chilled to 4 °C before 1-chloroethyl chloroformate (ACE-Cl) (2 equiv) was added. The reaction mixture was stirred at 4 °C for 15 min and allowed to warm to rt before heating to reflux for 24 h. The solution was concentrated, and the residue was dissolved in dry MeOH (10 mL/mmol). The heated mixture was concentrated to give the title compound which was purified through silica gel.

Procedure F: Amine Acylation. To a solution of amine (1 equiv), triethylamine (4 equiv), and a catalytic amount of 4-dimethylaminopyridine in CH_2Cl_2 (14 mL/mmol amine) was added a solution of acetyl chloride (1.5 equiv) in CH_2Cl_2 (1.1 mL/mmol AcCl). The reaction stirred at room temperature for 1 h, and then the reaction was quenched with saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (×3), and the combined organic layers were washed with water and then brine and dried with Na_2SO_4, followed by solvent removal under vacuum. The crude mixture was purified through silica gel to afford the corresponding product.

Procedure G: Heck-Type Reaction. A seal tube was charged with a stir bar, amide (1 equiv), $[RhCp^*Cl_2]_2$ (0.025 equiv), and CsOAc (2 equiv). The tube was purged three times by vacuum and argon, and then *t*AmOH (0.2 M) was added. The vial was sealed and stirred at the indicated temperature for the indicated time. The reaction mixture was concentrated in vacuo. The crude residue was purified by column chromatography to afford the corresponding spirocycle.

Procedure H: Cyclization. To a solution of primary amide (1 equiv) in dichloromethane (5 mL/mmol) was added a catalytic amount of TFA. The solution was stirred at room temperature for 30 min, and then the solvent was removed under vacuo. The crude mixture was purified by column chromatography to afford the corresponding spirocycle.

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*Methyl 3-(Pyridin-4-ylmethoxy)benzoate (**S1**).* Prepared according to procedure A from methyl 3-hydroxybenzoate (1.53 g, 10 mmol), 4-(chloromethyl)pyridine hydrochloride (1.80 g, 11 mmol), and K_2CO_3 (2.68 g, 20 mmol) in acetonitrile (46 mL). The solvent was removed under vacuum, and the crude mixture was purified through silica gel (Hept. to Hept./EtOAc 6/4) to afford the corresponding compound as a white solid (m = 1.58 g, 71%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.61 (dd, J = 4.3, 1.9 Hz, 2H), 7.66 (td, J = 7.7, 1.5 Hz, 1H), 7.61 (dd, J = 2.7, 1.5 Hz, 1H), 7.38−7.31 (m, 3H), 7.15 (ddd, J = 8.2, 2.7, 1.1 Hz, 1H), 5.11 (s, 2H), 3.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.6 (Cq), 158.0 (Cq), 149.9 (CH), 145.7 (Cq), 131.6 (Cq), 129.6 (CH), 122.7 (CH), 121.4 (CH), 120.0 (CH), 114.9 (CH), 68.1 (CH_2), 52.2 (CH_3). IR υ (neat): 3085−2954, 1707, 1587, 1284 cm^{-1}. MS (ESI, m/z): 244.1 (100) [M + H]$^+$. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{14}NO_3^+$: 244.0974. Found: 244.0974. Mp = 48−50 °C.

*Methyl 3-((1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-benzoate (**S2**).* Prepared according to procedure B from methyl 3-(pyridin-4-ylmethoxy)benzoate (189 mg, 0.777 mmol) in acetone (3.9 mL) and benzyl bromide (0.115 mL, 0.97 mmol). The crude pyridinium was used without purification. Pyridinium (278 mg, 0.67 mmol) in methanol (3.9 mL) and sodium borohydride (55.8 mg, 1.48 mmol). The crude product was purified by flash column chromatography (Hept. to Hept./EtOAc 6/4) to afford the title compound (m = 244 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.63 (ddd, J = 7.7, 1.3, 1.1 Hz, 1H), 7.57 (dd, J = 2.6, 1.5 Hz, 1H), 7.39−7.23 (m, 6H), 7.10 (ddd, J = 8.1, 2.4, 0.9 Hz, 1H), 5.80 (m, 1H), 4.45 (s, 2H), 3.91 (s, 3H), 3.61 (s, 2H), 3.04 (m, 2H), 2.64 (t, J = 5.7 Hz, 2H), 2.26 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.9 (Cq), 158.8 (Cq), 138.1 (Cq), 132.1 (Cq), 131.3 (Cq), 129.3 (CH), 129.1 (CH), 128.2 (CH), 127.1 (CH), 123.4 (CH), 122.0 (CH), 120.0 (CH), 115.0 (CH), 71.4 (CH_2), 62.6 (CH_2), 52.4 (CH_2), 52.1 (CH_3), 49.4 (CH_2), 26.5 (CH_2). IR υ (neat): 3062−2754, 1719, 1444, 1274, 1012 cm^{-1}. MS (ESI, m/z): 338.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{24}NO_3^+$: 338.1756. Found: 338.1754.

*3-((1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-N-methoxy-benzamide (**9a**).* Prepared according to procedure C from methyl ester (128.9 mg, 0.382 mmol), NaOH 3 M (1.3 mL), EtOH (2.2 mL). The resulting crude carboxylic acid (0.382 mmol) was dissolved in DMF (1.2 mL) and reacted with EDCI (80.5 mg, 0.42 mmol), HOBt (56.7 mg, 0.42 mmol), $MeONH_2$.HCl (35.1 mg, 0.42 mmol), and iPr$_2$NEt (0.15 mL, 0.88 mmol). Purification over silica gel (Hept. to Hept./EtOAc 5/5 to 0/100) afforded the title compound as a yellow oil (m = 89.8 mg, 67% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.39 (brs, 1H), 7.35−7.23 (m, 8H), 7.03 (m, 1H), 5,75 (m, 1H), 4.40 (s, 2H), 3.85 (s, 3H), 3.59 (s, 2H), 3.01 (m, 2H), 2.62 (t, J = 5.7 Hz, 1H), 2.21 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 159.0 (Cq), 137.8 (Cq), 133.0 (Cq), 132.0 (Cq), 129.6 (CH), 129.2 (CH), 128.2 (CH), 127.1 (CH), 123.2 (CH), 119.0 (CH), 118.9 (CH), 71.4 (CH_2), 64.4 (CH_3), 62.6 (CH_2), 52.3 (CH_2), 49.4 (CH_2), 26.4 (CH_2). IR υ (neat): 3196, 3027−2805, 1646, 1579, 1234 cm^{-1}. MS (ESI, m/z): 353.2 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{25}N_2O_3^+$: 353.1865. Found: 353.1871.

*4-Benzyl-2-methoxy-3,4,5,6-tetrahydro-7H-3,6a-methanobenzo-furo[4,3-ef][1,3]diazonin-1(2H)-one (**11a**).* Prepared according to procedure D from amide (32 mg, 0.0908 mmol), $[RhCp^*Cl_2]_2$ (1.4 mg, 0.0023 mmol) and CsOAc (34.9 mg, 0.181 mmol) in tAmOH (0.45 mL) at 60 °C overnight. The crude mixture was purified over silica gel (Hept. to EtOAc) to afford a yellow oil (m = 17.5 mg, 55%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.97 (dd, J = 8.1, 1.1 Hz, 1H), 7.39−7.22 (m, 6H), 6.96 (dd, J = 7.9, 1.1 Hz, 1H), 5.05 (dd, J = 4.9, 2.4 Hz, 1H), 4.33 (d, J = 8.4 Hz, 1H), 4.21 (d, J = 14.0 Hz, 1H), 4.16 (d, J = 8.5 Hz, 1H), 3.70 (s, 3H), 3.69 (d, J = 14.0 Hz, 1H), 2.60 (ddd, J = 13.1, 4.1, 2.6 Hz, 1H), 2.43 (dd, J = 13.1, 4.8 Hz, 1H), 2.30 (ddd, J = 13.0, 11.3, 3.3 Hz, 1H), 2.14 (td, J = 13.1, 2.3 Hz, 1H), 1.88−1.69 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 165.3 (Cq), 158.7 (Cq), 138.9 (Cq), 131.0 (Cq), 128.6 (CH), 128.2 (CH), 127.0 (CH), 123.8 (CH), 113.3 (CH), 82.9 (CH_2), 77.7 (NCHN), 61.3 (CH_3), 59.3 (CH_2), 43.7 (Cq), 41.9 (CH_2), 36.1 (CH_2), 34.1 (CH_2). IR υ (neat): 3005−2837, 1638, 1587, cm^{-1}. MS (ESI, m/z): 351.2 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{23}N_2O_3^+$: 351.1703. Found: 351.1687. Mp = 154−156 °C.

*Methyl 3-((1,2,3,6-Tetrahydropyridin-4-yl)methoxy)benzoate (**S3**).* Prepared according to procedure E from N-benzyl amine (137.3 mg, 0.407 mmol), 1,2-dichloroethane (4.1 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.088 mL, 0.814 mmol), and then MeOH (4.1 mL). The mixture was concentrated to give the title compound which was purified through silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 95/5) to afford a beige solid (m = 99.6 mg, 99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.87 (brs, 1H), 7.59 (ddd, J = 7.4, 1.1, 1.1 Hz, 1H), 7.47 (dd, J = 2.7, 1.5 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 7.02 (ddd, J = 8.3, 2.8, 1.0 Hz, 1H), 5.79 (brs, 1H), 4.43 (s, 2H), 3.85 (s, 3H), 3.69 (brm, 2H), 3.31 (brm, 2H), 2.51 (brm, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.7 (Cq), 158.1 (Cq), 133.4 (Cq), 131.5 (Cq), 129.6 (CH), 122.6 (CH), 119.9 (CH), 116.7 (CH), 114.9 (CH), 70.1 (CH_2), 52.2 (CH_3), 41.2 (CH_2), 40.4 (CH_2), 22.2 (CH_2). IR υ (neat): 3042, 2965−2644, 1716, 1583, 1451, 1287 cm^{-1}. MS (ESI, m/z): 248.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{18}NO_3^+$: 248.1287. Found: 248.1288. Mp = 134−135 °C.

*Methyl 3-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-benzoate (**S4**).* Prepared according to procedure F from amine (183 mg, 0.740 mmol), triethylamine (0.41 mL, 2.9 mmol), 4-dimethyl-aminopyridine (cat.), CH_2Cl_2 (10.4 mL), and a solution of acetyl chloride (0.078 mL, 1.11 mmol) in CH_2Cl_2 (1.3 mL). The crude mixture was purified over silica gel (DCM to DCM/MeOH (9/1)) to afford a yellow oil (m = 201 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.64 (ddd, J = 7.8, 1.3, 1 Hz, 1H), 7.56 (dd, J = 2.7, 1.5 Hz, 1H), 7.34 (dd, J = 8.3, 7.7 Hz, 1H), 7.10 (ddd, J = 8.0, 2.8, 1.0 Hz, 1H), 5.83 (brs, 1H), 4.48 (s, 2H), 4,11 (brs, 1H), 4.00 (brs, 1H), 3.91 (s, 3H), 3.73 (brs, 1H), 3.57 (brs, 1H), 2.34−2.18 (brm, 2H), 2.12 (brs, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.3 (Cq), 166.8 (Cq), 158.5 (Cq), 131.8 (Cq), 131.5 (Cq), 129.4 (CH), 122.8 (CH), 122.3 (CH), 120.5 (CH), 120.0 (CH), 114.9 (CH), 71.2 (CH_2), 70.9 (CH_2), 52.2 (CH_3), 45.2 (CH_2), 43.0 (CH_2), 41.4 (CH_2), 37.9 (CH_2), 26.3 (CH_2), 25.3 (CH_2), 21.8 (CH_3), 21.4 (CH_3). IR υ (neat): 3022, 1719, 1642, 1278 cm^{-1}. MS (ESI, m/z): 312.2 (100) [M + Na$^+$]. HMRS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{16}H_{19}NO_4Na^+$: 312.1206. Found: 312.1210.

*3-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-N-methoxy-benzamide (**9b**).* Prepared according to procedure C from methyl ester (201 mg, 0.69 mmol), NaOH 3 M (2.15 mL), and EtOH (4.1 mL). The resulting crude carboxylic acid (0.41 mmol) was dissolved in DMF (1.2 mL) and reacted with EDCI (86.3 mg, 0.45 mmol), HOBt (60.8 mg, 0.45 mmol), $MeONH_2$·HCl (37.6 mg, 0.45 mmol), and iPr$_2$NEt (0.17 mL, 0.94 mmol). Purification over silica gel (DCM to DCM/MeOH 95/5 to 80/20) afforded the title compound as a white solid (m = 94.4 mg, 45% over two steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers) 9.04 (brs, 1H), 7.36−7.24 (m, 3 H), 7.05 (ddd, J = 7.9, 2.8, 1.4 Hz, 1H), 5.82 (m, 1H major rotamer), 5.79 (m, 1H minor rotamer), 4.46 (s, 2H), 4.10 (m, 1H major rotamer), 3.99 (m, 1H minor rotamer), 3.88 (s, 3H), 3.73 (t, J = 5.7 Hz, 1H minor rotamer), 3.57 (t, J = 5.7 Hz, 1H major rotamer), 2.27 (m, 1H major rotamer), 2.20 (m, 1H minor rotamer) 2.13 (s, 3H, major rotamer), 2.10 (s, 3H, minor rotamer). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.5 (Cq), 158.7 (Cq), 133.6 (Cq), 133.2 (Cq), 131.8 (Cq), 129.6 (CH), 122.5 (CH), 120.5 (CH), 119.3 (CH), 118.7 (CH), 113.1 (CH), 71.0 (CH_2), 70.9 (CH_2), 64.3 (CH_3), 45.2 (CH_2), 43.0 (CH_2), 41.5 (CH_2), 37.9 (CH_2), 26.2 (CH_2), 25.4 (CH_2), 21.8 (CH_3), 21.4 (CH_3). IR υ (neat): 3022, 2835, 1719, 1642, 1278 cm^{-1}. MS (ESI, m/z): 305.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{21}N_2O_4^+$: 305.1501 Found: 305.1505.

*1′-Acetyl-2′,3′-dihydro-1′H,2H-spiro[benzofuran-3,4′-pyridine]-4-carboxamide (**10b**).* Prepared according to procedure G from amide (56 mg, 0.184 mmol), $[RhCp^*Cl_2]_2$ (2.84 mg, 0.0046 mmol), and CsOAc (70.6 mg, 0.368 mmol) in t-AmOH (0.92 mL) at 60 °C overnight. The crude mixture was purified over silica gel (Hept. to EtOAc) to afford a white solid (m = 40.7 mg, 82%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers 60/40) 7.31 (d, J = 8.4 Hz, 1H, minor), 7.21 (t, J = 7.8 Hz, 1H, minor), 7.20 (t, J = 7.8 Hz, 1H,

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major), 7.05 (d, J = 7.9 Hz, 1H, minor), 7.03 (t, J = 7.9 Hz, 1H, major), 6.92 (t, J = 7.8 Hz, 1H, major), 6.91 (7.03 (t, J = 7.9 Hz, 1H, minor), 6.75 (d, J = 8.5 Hz, 1H major + 1H minor), 6.09 (brs, 1H minor), 5.98 (brs, 2H major + 1H minor), 5.01 (dd, J = 8.4, 1.8 Hz, 1H minor), 4.95 (dd, J = 8.3, 1.8 Hz, 1H major), 4.51 (ddd, J = 13.8, 4.3, 2.7 Hz, 1H major), 4.32 (d, J = 8.8 Hz, 1H major), 4.28 (d, J = 9.0 Hz, 1H minor), 4.22−4.14 (m, 1H major + 1H minor), 3.91 (ddd, J = 12.7, 4.0, 3.1 Hz, 1H minor), 3.35 (ddd, J = 13.4, 12.5, 2.8 Hz, 1H minor), 2.96 (ddd, J = 14.0, 13.4, 3.1 Hz, 1H minor), 2.75 (ddd, J = 13.8, 13.3, 4.3 Hz, 1H minor), 2.51 (ddt, J = 13.6, 4.5, 1.5 Hz, 1H major), 2.20 (s, 3H major), 2.18 (s, 3H minor), 2.04−1.91 (m, 1H major + 1H minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 170.2 (Cq), 169.6 (Cq), 168.4 (Cq), 168.3 (Cq), 160.9 (Cq), 160.7 (Cq), 133.2 (Cq), 132.7 (Cq), 131.2 (Cq), 130.7 (Cq), 129.1 (CH), 129.0 (CH), 127.2 (CH), 126.0 (CH), 120.0 (CH), 119.8 (CH), 112.5 (CH), 112.3 (CH), 109.4 (CH), 108.9 (CH), 81.8 (CH_2), 81.5 (CH_2), 45.4 (Cq), 45.2 (Cq), 41.9 (CH_2), 37.8 (CH_2), 32.0 (CH_2), 31.2 (CH_2), 21.9 (CH_3), 21.4 (CH_3). IR υ (neat): 3358, 3209, 2974−2875, 1659, 1634, 1396 cm^{-1}. MS (ESI, m/z): 273.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{17}N_2O_3^+$: 273.1240. Found: 273.1239. Mp = 196−199 °C.

*4-Acetyl-3,4,5,6-tetrahydro-7H-3,6a-methanobenzofuro[4,3-ef][1,3]diazonin-1(2H)-one (**11b**).* Prepared according to procedure H from amide (42.3 mg, 0.155 mmol), CH_2Cl_2 (0.77 mL), and TFA (87 μL, 0.0115 mmol). The crude mixture was purified over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 95/5) to afford a white solid (m = 30.4 mg, 72%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.91 (dd, J = 8.1, 0.8 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 7.02 (dd, J = 8.0, 0.9 Hz, 1H), 6.64 (d, J = 6.5 Hz, 1H), 6.22 (m, 1H), 4.33 (d, J = 8.5 Hz, 1H), 4.2 (d, J = 8.5 Hz, 1H), 3.63 (m, 1H), 3.13 (ddd, J = 14.3, 13.0, 2.8 Hz, 1H), 2.29−2.12 (m, 2H), 2.10 (s, 3H), 2.00 (m, 1H), 1.78 (dt, J = 13.1, 4.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.1 (Cq), 167.3 (Cq), 159.2 (Cq), 131.0 (Cq), 82.8 (CH_2), 57.2 (CH), 44.7 (Cq), 37.9 (CH_2), 35.7 (CH_2), 32.7 (CH_2), 21.8 (CH_3). IR υ (neat): 2983, 1643, 1402, 1214 cm^{-1}. MS (ESI, m/z): 273.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{17}N_2O_3^+$: 273.1240. Found: 273.1239. Mp = 208−210 °C.

*Benzyl 4-((3-(methoxycarbonyl)phenoxy)methyl)-3,6-dihydropyridine-1(2H)-carboxylate (**S5**).* Prepared according to procedure D from *N*-benzyl amine (200 mg, 0.593 mmol) in CH_2Cl_2 (2.9 mL), $KHCO_3$ (59.4 mg, 0.593 mmol), and $ClCO_2Bn$ (0.38 mL, 2.67 mmol) in CH_2Cl_2 (2.9 mL). The crude mixture was over silica gel (Hept. to Hept./EtOAc 7/3) to afford a colorless oil (m = 196 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.64 (td, J = 7.6, 1.3 Hz, 1H), 7.56 (dd, J = 2.7, 1.5 Hz, 1H), 7.40−7.29 (m, 6H), 7.10 (dd, J = 8.2, 2.6 Hz, 1H), 5.80 (d, J = 14.5 Hz, 1H), 5.16 (s, 2H), 4.46 (s, 2H), 4.03 (s, 2H), 3.91 (s, 3H), 3.64 (t, J = 5.6 Hz, 2H), 2.23 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.8 (Cq), 158.5 (Cq), 136.7 (Cq), 132.4 and 132.2 (Cq), 131.4 (2 × Cq), 129.4 (CH), 128.4 (CH), 128.0 (CH), 127.9 (CH), 122.2 (CH), 121.4 (CH), 120.0 (CH), 114.9 (CH), 71.1 (CH_2), 67.1 (CH_2), 52.2 (CH_3), 43.1 (CH_2), 40.4 and 40.1 (CH_2), 25.8 and 25.6 (CH_2). IR υ (neat): 3032−2950, 1699, 1430, 1275 cm^{-1}. MS (ESI, m/z): 382.2 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{24}NO_5^+$: 382.1654. Found: 382.1659.

*Benzyl 4-((3-(methoxycarbamoyl)phenoxy)methyl)-3,6-dihydropyridine-1(2H)-carboxylate (**9c**).* Prepared according to procedure C from methyl ester (196 mg, 0.514 mmol) in a mixture of THF/MeOH/H_2O (v/v = 1/1/1, 15.3 mL), LiOH (98.4 mg, 4.11 mmol) at room temperature. The crude mixture was used without purification. The carboxylic acid (0.514 mmol) was dissolved in DMF (1.54 mL) and reacted with EDCI (108.3 mg, 0.565 mmol), HOBt (76.3 mg, 0.565 mmol), $MeONH_2$·HCl (47.2 mg, 0.565 mmol), and iPr$_2$NEt (0.20 mL, 1.18 mmol). Purification over silica gel (Hept. to Hept./EtOAc 5/5) afforded the title compound as a colorless oil (m = 171.1 mg, 84% over two steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.46 (brs, 1H), 7.39−7.25 (m, 8H), 7.02 (m, 1H), 5.75 (brm, 1H), 5.13 (s, 2H), 4.42 (brs, 2H), 3.99 (brs, 2H), 3.85 (s, 3H), 3.6 (t, J = 5.7 Hz, 2H), 2.18 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) Due to rotamers some signals appears as pairs δ (ppm) 165.9 (Cq), 158.7 (Cq), 155.5 (Cq), 136.6 (Cq), 133.1 (Cq), 132.3 (Cq), 129.6 (CH), 128.4 (CH), 128.0 (CH), 127.8 (CH), 122.1 and 121.5 (CH), 119.2 (CH), 118.8 (CH), 113.1 (CH), 71.1 (CH_2), 67.1 (CH_2), 64.3 (CH_3), 43.1 (CH_2), 40.3 and 40.1 (CH_2), 25.7 and 25.5 (CH_2). IR υ (neat): 3212, 2935, 1697, 1665, 1428, 1232 cm^{-1}. MS (ESI, m/z): 397.2 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{25}N_2O_5^+$: 397.1763. Found: 397.1776.

*Benzyl 4-Carbamoyl-2′,3′-dihydro-1′H,2H-spiro[benzofuran-3,4′-pyridine]-1′-carboxylate (**10c**).* Prepared according to procedure G from amide (51.4 mg, 0.130 mmol), $[RhCp^*Cl_2]_2$ (2.0 mg, 0.0032 mmol), and CsOAc (49.5 mg, 0.259 mmol) in *t*AmOH (0.65 mL) at 60 °C overnight. The crude mixture was purified over silica gel (Hept. to Hept/EtOAc 5/5) to afford a white solid (m = 37.5 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers) 7.42−7.28 (m, 5H), 7.19 (t, J = 7.6 Hz, 1H), 7.08−6.95 (m, 2H), 6.90 (d, J = 7.8 Hz, 1H), 6.57 (brs, 1H), 6.16 (brs, 1H), 6.04 (brs, 1H), 5.98 (brs, 1H), 5.26−5.07 (m, 2H), 4.94 (d, J = 8.7 Hz, 1H), 4.84 (d, J = 8.2 Hz, 1H), 4.33−4.10 (m, 3H), 3.16 (m, 1H), 2.61 (m, 1H), 1.92 (dd, J = 13.1, 12.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 170.1 (Cq), 169.8 (Cq), 160.7 (Cq), 153.5 (Cq), 152.9 (Cq), 135.8 (Cq), 133.1 (Cq), 132.9 (Cq), 131.0 (Cq), 130.9 (Cq), 129.0 (CH), 128.5 (CH), 128.3 (CH), 128.1 (CH), 127.3 (CH), 126.5 (CH), 120.0 (CH), 112.4 (CH), 112.3 (CH), 108.0 (CH), 107.3 (CH), 81.9 (CH_2), 81.8 (CH_2), 67.8 (CH_2), 45.0 (Cq), 44.9 (Cq), 39.9 (CH_2), 39.6 (CH_2), 31.5 (CH_2), 31.2 (CH_2). IR υ (neat): 3335, 2932−2875, 1699, 1651, 1340 cm^{-1}. MS (ESI, m/z): 365.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{21}N_2O_4^+$: 365.1490. Found: 365.1490. Mp = 75−77 °C.

*Benzyl 1-Oxo-2,3,5,6-tetrahydro-7H-3,6a-methanobenzofuro-[4,3-ef][1,3]diazonine-4(1H)-carboxylate (**11c**).* Prepared according to procedure H from amide (70 mg, 0.192 mmol), CH_2Cl_2 (0.96 mL) and TFA (146 μL, 0.0192 mmol). The crude mixture was purified over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a colorless oil (m = 69 mg, 98%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers: 64/36): 8.21 (brs, 1H min.), 7.91 (d, J = 8.1 Hz, 1H), 7.62 (brs, 1H, maj.), 7.50−7.27 (m, 6H), 7.08 (d, J = 7.9 Hz, 1H), 5.93 (brm, 1H, maj.), 5.86 (brs, 1H, min.), 5.34−5.10 (m, 2H), 4.36 (d, J = 8.3 Hz, 1H), 4.22 (d, J = 8.5 Hz, 1H), 4.06 (brm, 1H), 2.84 (brm, 1H), 2.30−2.11 (brm, 2H), 1.98 (brm, 1H), 1.79 (ddd, J = 13.1, 12.6, 4.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) rotamers δ (ppm) 169.2 (Cq), 168.7 (Cq), 160.6 (Cq), 160.1 (Cq), 159.3 (Cq), 135.6 (Cq), 129.2 (CH), 128.6 (CH), 128.4 (CH), 128.1 (CH), 114.9 (CH), 114.8 (CH), 82.8 (CH_2), 68.4 (CH_2), 68.1 (CH_2), 60.6 (CH), 44.4 (Cq), 35.7 (CH_2), 34.9 (CH_2), 32.5 (CH_2). IR υ (neat): 3287, 3010−2872, 1695, 1645, 1586, 1398, 1293, 1211 cm^{-1}. MS (ESI, m/z): 365.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{21}N_2O_4^+$: 365.1496. Found: 365.1497.

*Methyl 4-Methoxy-3-(pyridin-4-ylmethoxy)benzoate (**S6**).* To a solution of methyl 3-hydroxy-4-methoxybenzoate (300 mg, 1.65 mmol) in DMF (11.5 mL) was added NaH 60% (144.8 mg, 3.62 mmol) at 0 °C. After the mixture stirred at 0 °C for 30 min, 4-(chloromethyl)pyridine hydrochloride (297 mg, 1.81 mmol) was added and the reaction was stirred overnight at room temperature. Saturated NH_4Cl was added, and the aqueous layer was extracted with EtOAc (×3). The combined organic layers were washed with water and then brine and dried over Na_2SO_4. The solvent was removed under vacuum, and the crude mixture was purified through silica gel (Hept. to Hept./EtOAc 5/5 to 3/7) to afford the corresponding compound as a white solid (m = 331.6 mg, 74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.62 (d, J = 5.6 Hz, 2H), 7.72 (dd, J = 8.6, 2.0 Hz, 1H), 7.54 (d, J = 2.1 Hz, 1H), 7.40 (dd, J = 5.2, 1.8 Hz, 2H), 6.93 (d, J = 8.5 Hz, 1H), 5.19 (s, 2H), 3.96 (s, 3H), 3.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.6 (Cq), 153.5 (Cq), 149.8 (CH), 147.1 (Cq), 146.0 (Cq), 124.5 (CH), 122.6 (Cq), 121.5 (CH), 114.4 (CH), 110.8 (CH), 69.1 (CH_2), 56.0 (CH_3), 52.0 (CH_3). IR υ (neat): 3061−2841, 1703, 1218 cm^{-1}. MS (ESI, m/z): 274.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{16}NO_4^+$: 274.1074. Found: 274.1066. Mp = 129−130 °C.

*Methyl 3-((1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-4-methoxybenzoate (**S7**).* Prepared according to procedure B from

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methyl 4-methoxy-3-(pyridin-4-ylmethoxy)benzoate (365.1 mg, 1.36 mmol) in acetone (6.80 mL) and benzyl bromide (0.20 mL, 1.67 mmol). The crude pyridinium was used without purification. The crude pyridinium was dissolved in methanol (6.8 mL), and sodium borohydride (113.4 mg, 2.99 mmol) was added. The crude product was purified by flash column chromatography (Hept. to Hept./EtOAc 5/5) to afford the title compound as a beige solid (m = 494 mg, 99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.67 (dd, J = 8.4, 2.0 Hz, 1H), 7.55 (d, J = 2.0 Hz, 1H), 7.41−7.26 (m, 5H), 6.88 (d, J = 8.5 Hz, 1H), 5.81 (m, 1H), 4.53 (s, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.64 (brs, 2H), 3.03 (brs, 2H), 2.64 (t, J = 5.7 Hz, 2H), 2.27 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.8 (Cq), 153.5 (Cq), 147.8 (Cq), 132.0 (Cq), 129.2 (CH), 128.2 (CH), 127.1 (CH), 123.7 (CH), 123.4 (CH), 122.5 (Cq), 114.3 (CH), 110.6 (CH), 72.3 (CH_2), 62.5 (CH_2), 55.9 (CH_3), 52.4 (CH_2), 51.9 (CH_3), 49.4 (CH_2), 26.4 (CH_2). IR υ (neat): 2940−2718, 1707, 1267, 1213, 1130 cm^{-1}. MS (ESI, m/z): 368.2 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{26}NO_4^+$: 368.1862. Found: 368.1847. Mp = 110−112 °C.

*Methyl 4-Methoxy-3-((1,2,3,6-tetrahydropyridin-4-yl)methoxy)-benzoate (**S8**).* Prepared according to procedure E from *N*-benzyl amine (453.7 mg, 1.235 mmol), 1,2-dichloroethane (12.3 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.27 mL, 2.47 mmol), and then MeOH (12.3 mL). The mixture was concentrated to give the title compound as a beige solid which was used without purification (m = 339.0 mg, 99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.90 (brs, 1H), 7.69 (dd, J = 8.4, 1.9 Hz, 1H), 7.51 (d, J = 2.1 Hz, 1H), 6.88 (d, J = 8.5 Hz, 1H), 5.87 (s, 1H), 4.53 (s, 2H), 3.90 (s, 3H), 3.87 (s, 3H), 3.73 (brs, 2H), 3.35 (brs, 2H), 2.59 (brs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.6 (Cq), 153.6 (Cq), 147.1 (Cq), 133.4 (Cq), 124.4 (CH), 122.6 (Cq), 116.9 (CH), 114.7 (CH), 110.8 (CH), 71.3 (CH_2), 55.9 (CH_3), 52.0 (CH_3), 41.2 (CH_2), 40.4 (CH_2), 22.1 (CH_2). IR υ (neat): 2937−2571, 1721, 1266, 1213 cm^{-1}. MS (ESI, m/z): 278.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{20}NO_4^+$: 278.1392. Found: 278.1390. Mp = 196−197 °C.

*Methyl 3-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-4-methoxybenzoate (**S9**).* Prepared according to procedure F from amine (339 mg, 1.23 mmol), triethylamine (0.79 mL, 5.85 mmol), 4-dimethylaminopyridine (cat.), CH_2Cl_2 (12.3 mL), and a solution of acetyl chloride (0.15 mL, 2.19 mmol) in CH_2Cl_2 (2.4 mL). The crude mixture was purified over silica gel (Hept./EtOAc 30/70 to 0/100) to afford a yellow solid (m = 297 mg, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers) 7.60 (dd, J = 8.5, 2.0 Hz, 1H), 7.46 (t, J = 1.8 Hz, 1H), 6.81 (d, J = 8.5 Hz, 1H), 5.77 (m, 1H major), 5.73 (m, 1H minor), 4.45 (s, 2H), 4,01 (brm, 1H major), 3.90 (brm, 1H minor), 3.83 (s, 3H), 3.79 (s, 3H), 3.64 (t, J = 5.8 Hz, 1H minor), 3.48 (t, J = 5.8 Hz, 1H major), 2.22 (brm, 1H, major), 2.15 (brm, 1H minor), 2.04 (s, 3H major), 2.01 (s, 3H minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.0 (Cq), 168.9 (Cq), 166.4 (Cq), 153.3 (Cq), 147.3 (Cq), 133.4 (Cq), 131.6 (Cq), 123.8 (CH), 122.5 (CH), 122.3 (Cq), 120.4 (CH), 114.2 (CH), 114.0 (CH), 110.5 (CH), 71.9 (CH_2), 71.5 (CH_2), 55.7 (CH_3), 51.7 (CH_3), 44.9 (CH_2), 42.7 (CH_2), 41.2 (CH_2), 37.6 (CH_2), 26.0 (CH_2), 25.2 (CH_2), 21.6 (CH_3), 21.2 (CH_3). IR υ (neat): 3022−2839, 1707, 1620, 1209 cm^{-1}. MS (ESI, m/z): 320.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{22}NO_5^+$: 320.1498. Found: 320.1486. Mp = 116−117 °C.

*3-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-N,4-dimethoxybenzamide (**9d**).* Prepared according to procedure C from methyl ester (297 mg, 0.93 mmol), LiOH (178.2 mg, 7.44 mmol), MeOH (3.7 mL), and H_2O (3.7 mL). The resulting crude carboxylic acid (0.93 mmol) was dissolved in DMF (2.8 mL) and reacted with EDCI (158.8 mg, 1.02 mmol), HOBt (156.7 mg, 1.02 mmol), $MeONH_2$·HCl (85.4 mg, 1.02 mmol), and iPr$_2$NEt (0.37 mL, 2.11 mmol). Purification over silica gel (DCM to DCM/MeOH 95/5) afforded the title compound as a white solid (m = 82.9 mg, 27% over 2 steps). ^{1}H NMR (300 MHz, DMSO) δ (ppm): (2 rotamers) 7.40−7.35 (m, 2H), 7.03 (d, J = 8.0 Hz, 1H), 5.82 (m, 1H), 4.48 (s, 2H), 3.99 (m, 2H minor), 3.94 (m, 2H major), 3.81 (s, 3H), 3.69 (s, 3H), 3.56 (t, J = 5.7 Hz, 2H minor), 3.52 (t, J = 5.8 Hz, 2H major), 2.21 (m, 2H major), 2.11 (m, 2H minor), 2.04 (s, 3H major), 2.00 (s, 3H minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 2 rotamers 168.5 (Cq), 168.4 (Cq), 151.9 (Cq), 147.3 (Cq), 132.7 (Cq), 132.3 (Cq), 124.2 (Cq), 121.9 (CH), 121.3 (CH), 120.6 (CH), 112.2 (CH), 111.3 (CH), 71.4 (CH_2), 71.2 (CH_2), 63.2 (CH_3), 55.7 (CH_3), 44.5 (CH_2), 42.3 (CH_2), 40.8 (CH_2), 37.2 (CH_2), 26.0 (CH_2), 25.2 (CH_2), 21.7 (CH_3), 21.3 (CH_3). IR υ (neat): 3172, 2966−2853, 1663, 1602, 1267 cm^{-1}. MS (ESI, m/z): 335.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{23}N_2O_5^+$: 335.1608 Found: 335.1607. Mp = 190−191 °C.

*1′-Acetyl-7-methoxy-2′,3′-dihydro-1′H,2H-spiro[benzofuran-3,4′-pyridine]-4-carboxamide (**10d**).* Prepared according to procedure G from amide (43 mg, 0.128 mmol), $[RhCp^*Cl_2]_2$ (1.99 mg, 0.0032 mmol), and CsOAc (49 mg, 0.256 mmol) in *t*-AmOH (0.64 mL) at 60 °C overnight. The crude mixture was purified over silica gel (Hept. to EtOAc) to afford a colorless oil (m = 32.2 mg, 83%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers 67/33) 7.28 (d, J = 8.5 Hz 1H, minor), 7.09 (d, J = 8.5 Hz 1H, minor), 7.06 (d, J = 8.9 Hz, 1H, major), 6.82−6.63 (m, 2H), 6.27−5.70 (m, 2H, NH_2), 4.97 (dd, J = 1.7, 8.3 Hz, 1H, minor), 4.89 (dd, J = 1.9, 8.4 Hz, 1H, major), 4.49 (m, 1H), 4.31 (dd, J = 8.9, 10.9 Hz, 1H), 4.19 (ddd, J = 1.50, 5.30, 8.9 Hz, 1H), 3.96−3.77 (m, 1H), 3.84 (s, 3H), 3.30 (dt, J = 2.9, 12.7 Hz, 1H, minor), 2.90 (dt, J = 3.1, 13.7 Hz, 1H, major), 2.71 (dt, J = 4.4, 13.6 Hz, 1H, minor), 2.50 (dt, J = 4.5, 13.6 Hz, 1H, major), 2.14 (s, 3H, major), 2.13 (s, 3H, minor), 1.98−1.84 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers): 169.7 (Cq), 169.2 (Cq), 168.5 (Cq), 146.9 (Cq), 132.6 (Cq), 127.0 (Cq), 125.9 (Cq), 125.0 (Cq), 124.5 (CH), 121.9 (CH), 121.6 (CH), 111.2 (CH), 111.1 (CH), 109.4 (CH), 109.0 (CH), 82.4 (CH_2), 82.1 (CH_2), 56.0 (CH_3), 46.2 (Cq), 45.9 (Cq), 42.9 (CH_2), 37.8 (CH_2), 31.7 (CH_2), 30.9 (CH_2), 21.9 (CH_3), 21.4 (CH_3). IR υ (neat): 3344, 3159−2915, 1615, 1388, 1279 cm^{-1}. MS (ESI, m/z): 303.3 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}N_2O_2^+$: 303.1345. Found: 303.1339.

*4-Acetyl-9-methoxy-3,4,5,6-tetrahydro-7H-3,6a-methanobenzofuro[4,3-ef][1,3]diazonin-1(2H)-one (**11d**).* Prepared according to procedure H from amide (31.6 mg, 0.104 mmol), CH_2Cl_2 (0.7 mL), and TFA (79 μL, 0.0104 mmol). The crude mixture was purified over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a yellow oil (m = 29.7 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers, 80/20) 8.09 (brs, 1H, minor), 7.87 (d, J = 8.8 Hz, 1H, major + minor), 6.86 (d, J = 8.9 Hz, 1H, major + minor), 6.83 (m, major), 6.60 (brs, 1H, NH), 6.16 (brm, 1H, major), 5.46 (brs, 1H, minor), 4.46 (m, minor), 4.33 (d, J = 8.5 Hz, 1H), 4.18 (d, J = 8.5 Hz, 1H), 3.88 (s, 3H major + minor), 3.57 (m, 1H, major), 3.09 (td, J = 2.3, 13.6 Hz, 1H, major), 2.55 (td, J = 2.7, 13.9 Hz, 1H, minor), 2.29−1.89 (m, 3H), 2.05 (s, 3H), 1.72 (dt, J = 4.8, 13.2 Hz, 1H, major), 1.64 (dt, J = 4.6, 13.3 Hz, 1H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): (2 rotamers) 170.3 (Cq), 167.6 (Cq), 148.4 (Cq), 146.6 (Cq), 132.1 (Cq), 126.6 (CH), 120.9 (Cq), 112.0 (CH), 83.4 (CH_2), 62.9 (CH), 57.1 (CH_2), 56.1 (CH_2), 45.4 (Cq), 38.1 (CH_2), 35.8 (CH_2), 35.2 (CH_2), 33.7 (CH_2), 32.9 (CH_2), 32.6 (CH_2), 21.7 (CH_3), 21.1 (CH_3). IR υ (neat): 3405, 3028−2794, 1713, 1604, 1436, 1283, 1235, 1106, 908 cm^{-1}. MS (ESI, m/z): 303.3 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}N_2O_4^+$: 303.1345. Found: 303.1342.

*Methyl 7-(Pyridin-4-ylmethoxy)benzo[d][1,3]dioxole-5-carboxylate (**S10**).* Prepared according to procedure A from methyl 7-hydroxybenzo[*d*][1,3]dioxole-5-carboxylate (368 mg, 1.87 mmol), 4-(chloromethyl)pyridine hydrochloride (338.4 mg, 2.06 mmol), and K_2CO_3 (570 mg, 4.13 mmol) in acetonitrile (9.4 mL). The solvent was removed under vacuum, and the crude mixture was purified through silica gel (Hept. to Hept./EtOAc 5/5) to afford the corresponding compound as a white solid (m = 420 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.62 (d, J = 5.0 Hz, 2H), 7.36 (d, J = 5.0 Hz, 2H), 7.35 (s, 1H), 7.23 (d, J = 1.4 Hz, 1H), 6.07 (s, 2H), 5.21 (s, 2H), 3.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.1 (Cq), 150.1 (CH), 149.0 (Cq), 145.4 (Cq), 141.8 (Cq), 139.8 (Cq), 124.5 (Cq), 121.5 (CH), 112.0 (CH), 104.5 (CH), 102.3 (CH_2), 69.6 (CH_2), 52.2 (CH_3). IR υ (neat): 2954, 1720, 1709, 1432, 1104 cm^{-1}. MS (ESI, m/z): 288.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{14}NO_5^+$: 288.0872. Found: 288.0862. Mp = 118−119 °C.

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*Methyl 7-((1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-benzo[d][1,3]dioxole-5-carboxylate (**S11**).* Prepared according to procedure B from methyl 7-(pyridin-4-ylmethoxy)benzo[*d*][1,3]-dioxole-5-carboxylate (425 mg, 1.48 mmol) in acetone (7.4 mL) and benzyl bromide (0.22 mL, 1.85 mmol). The crude pyridinium was used without purification. Pyridinium (1.48 mmol) in methanol (14.8 mL) and sodium borohydride (123.3 mg, 3.25 mmol). The crude product was purified by flash column chromatography (Hept. to Hept./EtOAc 8/2 to 5/5) to afford the title compound as a colorless oil (*m* = 483 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.37−7.27 (m, 6H), 7.19 (d, *J* = 1.5 Hz, 1H), 6.03 (s, 2H), 5.80 (s, 1H), 4.54 (s, 2H), 3.87 (s, 3H), 3.59 (s, 2H), 3.02 (brs, 2H), 2.62 (t, *J* = 5.7 Hz, 2H), 2.26 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.3 (Cq), 148.7 (Cq), 142.3 (Cq), 139.8 (Cq), 138.1 (Cq), 131.9 (Cq), 129.1 (CH), 128.2 (CH), 127.1 (CH), 124.2 (Cq), 124.0 (CH), 112.0 (CH), 103.8 (CH), 102.1 (CH_2), 72.8 (CH_2), 62.6 (CH_2), 52.4 (CH_2), 52.1 (CH_3), 49.4 (CH_2), 26.5 (CH_2). IR υ (neat): 3059−2760, 1708, 1442, 1270, 1015 cm^{-1}. MS (ESI, *m*/*z*): 382.1 (100) [M + H$^+$]. HMRS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{22}H_{24}NO_5^+$: 382.1654. Found: 382.1645.

*Methyl 7-((1,2,3,6-Tetrahydropyridin-4-yl)methoxy)benzo[d]-[1,3]dioxole-5-carboxylate (**S12**).* Prepared according to procedure E from *N*-benzyl amine (420.5 mg, 1.1 mmol), 1,2-dichloroethane (11 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.24 mL, 2.2 mmol), and then MeOH (11 mL). The mixture was concentrated to give the title compound which was purified through silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 95/5) to afford a beige solid (*m* = 310.4 mg, 96%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.93 (brs, 1H), 7.29 (d, *J* = 1.6 Hz, 1H), 7.21 (d, *J* = 1.4 Hz, 1H), 6.04 (s, 2H), 5.84 (m, 1H), 4.58 (s, 2H), 3.87 (s, 3H), 3.74 (m, 2H), 3.35 (m, 2H), 2.58 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.1 (Cq), 149.0 (Cq), 141.5 (Cq), 139.8 (Cq), 133.3 (Cq), 124.5 (Cq), 117.1 (CH), 112.4 (CH), 104.4 (CH), 102.3 (CH_2), 71.7 (CH_2), 52.2 (CH_3), 41.1 (CH_2), 40.4 (CH_2), 22.1 (CH_2). IR υ (neat): 2938, 2896−2657, 1703, 1435, 1260 cm^{-1}. MS (ESI, *m*/*z*): 292.1 (100) [M + H$^+$]. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{15}H_{18}NO_5^+$: 292.1185. Found: 292.1191. Mp = 210−211 °C.

*Methyl 7-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-benzo[d][1,3]dioxole-5-carboxylate (**S13**).* Prepared according to procedure F from amine (200 mg, 0.686 mmol), triethylamine (0.39 mL, 2.81 mmol), 4-dimethylaminopyridine (cat.), CH_2Cl_2 (6.8 mL), and a solution of acetyl chloride (0.073 mL, 1.03 mmol) in CH_2Cl_2 (1.1 mL). The crude mixture was purified over silica gel (DCM to DCM/MeOH 95/5) to afford a yellow oil (*m* = 204.8 mg, 89%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 2 rotamers 7.29 (s, 1H), 7.18 (s, 1H), 6.03 (s, 2H), 5.82 (brs, 1H, major), 5.78 (brs, 1H, minor), 4.54 (brs, 2H), 4.08 (brs, 2H, major), 3.97 (brs, 2H, minor), 3.85 (s, 3H), 3.71 (t, *J* = 6.0 Hz, 1H, minor), 3.54 (t, *J* = 5.8 Hz, 1H, major), 2.28 (brs, 2H, major), 2.21 (brs, 2H, minor), 2.11 (s, 3H, major), 2.08 (s, 3H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.2 (Cq), 169.1 (Cq), 166.1 (Cq), 148.8 (Cq), 141.8 (Cq), 139.7 (Cq), 133.4 (Cq), 131.5 (Cq), 124.2 (Cq), 123.2 (CH), 120.9 (CH), 112.0 (CH), 111.9 (CH), 104.0 (CH), 102.1 (CH_2), 72.5 (CH_2), 72.2 (CH_2), 52.0 (CH_3), 45.1 (CH_2), 42.9 (CH_2), 41.3 (CH_2), 37.7 (CH_2), 26.2 (CH_2), 25.3 (CH_2), 21.8 (CH_3), 21.3 (CH_3). IR υ (neat): 300−2839, 1710, 1626, 1429, 1325 cm^{-1}. MS (ESI, *m*/*z*): 334.1 (100) [M + H$^+$]. HMRS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{17}H_{20}NO_6^+$: 334.1291. Found: 334.1275. Mp = 100−101 °C.

*7-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-N-methoxy-benzo[d][1,3]dioxole-5-carboxamide (**9e**).* Prepared according to procedure C from methyl ester (202 mg, 0.606 mmol), LiOH (38.2 mg, 0.909 mmol), and MeOH (2.9 mL) H_2O (0.9 mL). The resulting crude carboxylic acid (0.606 mmol) was dissolved in DMF (1.8 mL) and reacted with EDCI (127.9 mg, 0.667 mmol), HOBt (90.1 mg, 0.667 mmol), $MeONH_2$·HCl (55.7 mg, 0.667 mmol), and *i*Pr_2NEt (0.24 mL, 1.39 mmol). Purification over silica gel (DCM to DCM/MeOH 95/5) afforded the title compound as a white foam (*m* = 149 mg, 70% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers 54/46) 10.4 (brs, 1H), 7.11 (s, 1H), 6.96 (d, *J* = 1.5 Hz, 1H), 5.97 (s, 3H), 5.75 (m, 1H), 4.50 (s, 2H), 4.03 (m, 2H major), 3.94 (m, 1H minor), 3.80 (s, 3H), 3.66 (t, *J* = 5.8 Hz, 1H minor), 3.52 (t, *J* = 5.7 Hz, 1H major), 2.24 (m, 1H major), 2.14 (m, 1H minor) 2.08 (s, 3H, major), 2.05 (s, 3H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 169.5 (Cq), 165.2 (Cq), 149.0 (Cq), 142.2 (Cq), 138.8 (Cq), 133.5 (Cq), 131.7 (Cq), 126.0 (Cq), 123.0 (CH), 121.0 (CH), 109.9 (CH), 102.1 (CH_2), 101.5 (CH), 72.6 (CH_2), 72.3 (CH_2), 64.3 (CH_3), 45.2 (CH_2), 43.0 (CH_2), 41.5 (CH_2), 37.9 (CH_2), 26.2 (CH_2), 25.4 (CH_2), 21.8 (CH_3), 21.4 (CH_3). IR υ (neat): 3175, 2932−2897, 1605, 1427, 1083 cm^{-1}. MS (ESI, *m*/*z*): 349.1 (100) [M + H$^+$]. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{17}H_{21}N_2O_6^+$: 349.1400 Found: 349.1396.

*1-Acetyl-2,3-dihydro-1H,7′H-spiro[pyridine-4,6′-[1,3]dioxolo[4,5-g]benzofuran]-5′-carboxamide (**10e**).* Prepared according to procedure G from amide (35.0 mg, 0.1 mmol), $[RhCp^*Cl_2]_2$ (1.5 mg, 0.0025 mmol), and CsOAc (38.6 mg, 0.2 mmol) in *t*-AmOH (0.5 mL) at 60 °C overnight. The crude mixture was purified over silica gel (Hept. to EtOAc) to afford a white solid (*m* = 22.1 mg, 70%). ^{1}H NMR (300 MHz, DMSO) δ (ppm): (2 rotamers) 7.56 (brs, 1H), 7.25 (brs, 1H), 7.12 (d, *J* = 8.3 Hz, 1H min.), 6.85 (d, *J* = 8.3 Hz, 1H maj.), 6.58 (s, 1H maj.), 6.55 (s, 1H, min.), 6.04 (s, 1H), 6.01 (s, 1H), 4.86 (dd, *J* = 8.5, 1.7 Hz, 1H, min.), 4.77 (dd, *J* = 8.2, 1.6 Hz, 1H, maj.), 4.46 (dd, *J* = 8.9, 7.9 Hz, 1H maj. + min.), 4.29 (ddd, *J* = 13.6, 3.4, 2.8 Hz, 1H, maj.), 4.09 (m, 1H, maj. + min.), 3.92 (ddd, *J* = 12.9, 3.9, 3.7 Hz, 1H, min.), 3.39 (ddd, *J* = 13.7, 13.4, 3.0 Hz, 1H, min.), 2.93 (ddd, *J* = 13.7, 13.4, 3.0 Hz, 1H, maj.), 2.55 (ddd, *J* = 13.7, 13.4, 3.2 Hz, 1H), 2.43 (ddd, *J* = 13.7, 13.4, 3.2 Hz, 1H), 2.12 (s, 3H, min.), 2.10 (s, 3H maj.), 1.81 (m, 1H, maj.), 1.77 (m, 1H, min.). ^{13}C NMR (75 MHz, DMSO) δ (ppm) (2 rotamers) 168.4 (Cq), 167.7 (Cq), 148.2 (Cq), 142.1 (Cq), 130.8 (Cq), 128.0 (Cq), 127.7 (CH), 127.5 (Cq), 127.3 (Cq), 124.7 (CH), 108.6 (CH), 108.0 (CH), 101.8 (CH_2), 100.9 (CH), 100.8 (CH), 82.0 (CH_2), 44.9 (Cq), 44.6 (Cq), 41.0 (CH_2), 37.3 (CH_2), 31.0 (CH_2), 30.6 (CH_2), 21.8 (CH_3), 21.2 (CH_3). IR υ (neat): 3356, 3176, 2970−2872, 1667, 1628, 1417 cm^{-1}. MS (ESI, *m*/*z*): 317.1 (100) [M + H$^+$]. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{16}H_{17}N_2O_5^+$: 317.1137. Found: 317.1136. Mp = 215−216 °C.

*5-Acetyl-4,5,6,7-tetrahydro-2H-2a,6-methano[1,3]dioxolo-[4′,5′:6,7]benzofuro[4,3-ef][1,3]diazonin-8(3H)-one (**11e**).* Prepared according to procedure H from amide (22.3 mg, 0.07 mmol), CH_2Cl_2 (0.35 mL), and TFA (53 μL, 0.007 mmol). The crude mixture was purified over silica gel (DCM to DCM/MeOH (95/5)) to afford a white solid (*m* = 20.9 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.44 (s, 1H), 6.59 (d, *J* = 6.8 Hz, 1H), 6.18 (m, 1H), 6.03 (dd, *J* = 10.6, 1.4 Hz, 2H), 4.38 (d, *J* = 8.4 Hz, 1H), 4.25 (d, *J* = 8.4 Hz, 1H), 3.63 (m, 1H), 3.12 (ddd, *J* = 14.1, 12.9, 2.9 Hz, 1H), 2.18 (m, 1H), 2.12 (m, 1H), 2.09 (s, 3H), 1.99 (m, 1H), 1.76 (dt, *J* = 13.3, 4.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.1 (Cq), 166.7 (Cq), 150.0 (Cq), 140.4 (Cq), 134.2 (Cq), 128.8 (Cq), 122.4 (Cq), 104.6 (CH), 102.4 (CH_2), 84.4 (CH_2), 56.9 (CH_3), 45.0 (Cq), 38.0 (CH_2), 35.8 (CH_2), 32.3 (CH_2), 21.8 (CH_3). IR υ (neat): 3224, 3086−2872, 1625, 1615, 1418, 1288 cm^{-1}. MS (ESI, *m*/*z*): 317.1 (100) [M + H$^+$]. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{16}H_{17}N_2O_5^+$: 317.1137. Found: 317.1134. Mp = 272−273 °C.

*Methyl 2-Methyl-5-(pyridin-4-ylmethoxy)benzoate (**S14**).* Prepared according to procedure A from methyl 5-hydroxy-2-methyl-benzoate (200 mg, 1.1 mmol), 4-(chloromethyl)pyridine hydrochloride (198 mg, 1.21 mmol), and K_2CO_3 (334 mg, 2.41 mmol) in DMF (7.7 mL). The solvent was removed under vacuum, and the crude mixture was purified through silica gel (Hept. to Hept./EtOAc 5/5) to afford the corresponding compound (*m* = 261.7 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.62 (m, 2H), 7.51 (d, *J* = 2.9 Hz, 1H), 7.37 (m, 2H), 7.16 (d, *J* = 8.5 Hz, 1H), 7.01 (dd, *J* = 8.4, 2.9 Hz, 1H), 5.10 (s, 2H), 3.89 (s, 3H), 2.52 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 167.5 (Cq), 155.8 (Cq), 149.8 (CH), 145.8 (Cq), 132.9 (Cq), 132.7 (CH), 130.2 (Cq), 121.3 (CH), 118.8 (CH), 116.1 (CH), 68.2 (CH_2), 51.8 (CH_3), 20.7 (CH_3). IR υ (neat): 3091−2836, 1720, 1286, 1213 cm^{-1}. MS (ESI, *m*/*z*): 258.1 (100) [M + H$^+$]. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{15}H_{16}NO_3^+$: 258.1125. Found: 258.1113. Mp = 40−42 °C.

*Methyl 5-((1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-2-methylbenzoate (**S15**).* Prepared according to procedure B from

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methyl 2-methyl-5-(pyridin-4-ylmethoxy)benzoate (218.5 mg, 0.849 mmol) in acetone (4.2 mL) and benzyl bromide (0.126 mL, 1.06 mmol). The crude pyridinium was used without purification. Pyridinium (0.849 mmol) in methanol (8.5 mL) and sodium borohydride (70.7 mg, 1.86 mmol). The crude product was purified by flash column chromatography (Hept. to Hept./EtOAc 5/5 to 0/100) to afford the title compound as a yellow oil (m = 146.2 mg, 49%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.47 (d, J = 2.8 Hz, 1H), 7.39−7.25 (m, 5H), 7.13 (d, J = 8.5 Hz, 1H), 6.96 (dd, J = 8.5, 3.1 Hz, 1H), 5.79 (brs, 1H), 4.41 (s, 2H), 3.88 (s, 3H), 3.61 (s, 2H), 3.04 (brs, 2H), 2.65 (t, J = 5.6 Hz, 2H), 2.52 (s, 3H), 2.25 (brs, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 167.8 (Cq), 156.5 (Cq), 137.9 (Cq), 132.5 (CH), 132.2 (Cq), 132.1 (Cq), 129.2 (CH), 128.2 (CH), 127.1 (CH), 123.1 (CH), 118.9 (CH), 116.1 (CH), 71.4 (CH_2), 62.5 (CH_2), 52.3 (CH_2), 51.8 (CH_3), 49.4 (CH_2), 26.4 (CH_2), 20.8 (CH_3). IR υ (neat): 2924, 1721, 1498, 1211 cm^{-1}. MS (ESI, m/z): 352.2 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{26}NO_3^+$: 352.1913. Found: 352.1913.

*Methyl 2-Methyl-5-((1,2,3,6-tetrahydropyridin-4-yl)methoxy)-benzoate (**S16**).* Prepared according to procedure E from *N*-benzyl amine (146.2 mg, 0.416 mmol), 1,2-dichloroethane (4.2 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.09 mL, 0.832 mmol), and then MeOH (4.2 mL). The mixture was concentrated to give the title compound which was purified through silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a beige solid (m = 93.1 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.46 (brs, 1H), 7.40 (d, J = 2.9 Hz, 1H), 7.12 (d, J = 8.5 Hz, 1H), 6.92 (dd, J = 8.4, 2.5 Hz, 1H), 5.81 (brs, 1H), 4.42 (s, 2H), 3.86 (s, 3H), 3.73 (brs, 2H), 3.34 (t, J = 6.0 Hz, 2H), 2.52 (m, 2H), 2.48 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 167.6 (Cq), 155.9 (Cq), 133.4 (Cq), 132.8 (Cq), 132.7 (CH), 130.2 (Cq), 118.8 (CH), 116.8 (CH), 116.1 (CH), 70.3 (CH_2), 51.8 (CH_3), 41.3 (CH_2), 40.5 (CH_2), 22.3 (CH_2), 20.7 (CH_3). IR υ (neat): 3423, 3043, 2959−2714, 1730; 1719, 1282 cm^{-1}. MS (ESI, m/z): 261.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{20}NO_3^+$: 262.1443. Found: 262.1448. Mp = 144−146 °C.

*Methyl 5-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-2-methylbenzoate (**S17**).* Prepared according to procedure F from amine (96.6 mg, 0.367 mmol), triethylamine (0.20 mL, 1.51 mmol), 4-dimethylaminopyridine (cat.), CH_2Cl_2 (3.8 mL), and a solution of acetyl chloride (0.04 mL, 0.55 mmol) in CH_2Cl_2 (0.63 mL). The crude mixture was purified over silica gel (Hept. to Hept./EtOAc 30/70) to afford a yellow oil (m = 80 mg, 72%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers): 7.44 (d, J = 2.8 Hz, 1H), 7.14 (d, J = 8.5 Hz, 1H), 6.95 (dd, J = 8.5, 2.7 Hz, 1H), 5.83 (brs, 1H, maj.), 5.78 (brs, 1H, min.), 4.43 (s, 2H), 4,10 (brm, 1H, maj.), 3.99 (brs, 1H, min.), 3.88 (s, 3H), 3.73 (t, J = 5.2 Hz, 1H, min.), 3.56 (t, J = 5.2 Hz, 1H, maj.), 2.51 (s, 3H), 2.27 (brm, 1H, maj.), 2.21 (brm, 1H, min.), 2.13 (brs, 3H, maj.), 2.10 (brs, 3H, min.). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.3 (Cq), 167.8 (Cq), 156.3 (Cq), 132.7 (CH), 132.5 (Cq), 130.2 (Cq), 122.6 (CH), 120.3 (CH), 118.9 (CH), 116.1 (CH), 71.2 (CH_2), 70.9 (CH_2), 51.9 (CH_3), 45.1 (CH_2), 43.0 (CH_2), 41.5 (CH_2), 37.9 (CH_2), 26.3 (CH_2), 25.5 (CH_2), 21.8 (CH_3), 21.4 (CH_3), 20.8 (CH_3). IR υ (neat): 3100−2850, 1720, 1636, 1434, 1281, 1239 cm^{-1}. MS (ESI, m/z): 304.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{22}NO_4^+$: 304.1549. Found: 304.1554.

*5-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-N-methoxy-2-methylbenzamide (**9f**).* Prepared according to procedure C from methyl ester (102.1 mg, 0.336 mmol), LiOH (64.5 mg, 2.69 mmol), MeOH (3.36 mL), and water (3.36 mL). The resulting crude carboxylic acid (0.336 mmol) was dissolved in DMF (1.0 mL) and reacted with EDCI (70.8 mg, 0.37 mmol), HOBt (50.0 mg, 0.37 mmol), $MeONH_2$·HCl (28.1 mg, 0.336 mmol), and iPr$_2$NEt (0.14 mL, 0.773 mmol). Purification over silica gel (DCM to DCM/MeOH 95/5) afforded the title compound as a colorless oil (m = 73.9 mg, 69% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers) 9.52 (brs, 1H), 7.06 (d, J = 8.3 Hz, 1H), 6.87−6.78 (m, 2H), 5.72 (m, 1H), 4.35 (s, 2H), 3.99 (m, 1H major), 3.93 (m, 1H minor), 3.82 (s, 3H), 3.33 (t, J = 5.9 Hz, 1H minor), 3.50 (t, J = 5.9 Hz, 1H major), 2.31 (s, 3H), 2.20 (m, 1H major), 2.12 (m, 1H minor), 2.04 (s, 3H, major), 2.02 (s, 3H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 169.4 (Cq), 167.1 (Cq), 156.1 (Cq), 133.6 (Cq), 131.7 (CH), 128.7 (Cq), 122.1 (CH), 120.3 (CH), 116.6 (CH), 113.6 (CH), 71.0 (CH_2), 64.1 (CH_3), 45.1 (CH_2), 42.9 (CH_2), 41.3 (CH_2), 37.8 (CH_2), 26.1 (CH_2), 25.3 (CH_2), 21.5 (CH_3), 21.1 (CH_3), 18.5 (CH_3). IR υ (neat): 3439, 3164, 2930, 1606, 1438, 1233 cm^{-1}. MS (ESI, m/z): 319.2 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{23}N_2O_4^+$: 319.1658 Found: 319.1669.

*1′-Acetyl-5-methyl-2′,3′-dihydro-1′H,2H-spiro[benzofuran-3,4′-pyridine]-4-carboxamide (**10f**).* Prepared according to procedure G from amide (36.9 mg, 0.116 mmol), $[RhCp^*Cl_2]_2$ (1.8 mg, 0.0029 mmol), and CsOAc (44.3 mg, 0.231 mmol) in *t*-AmOH (0.58 mL) at 60 °C overnight. The crude mixture was purified over silica gel (Hept. to EtOAc) to afford a white solid (m = 21.1 mg, 64%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers 60/40) 7.33 (d, J = 8.6 Hz, 1H min.), 7.01 (d, J = 8.3 Hz, 1H maj.), 6.81−6.70 (m, 2H, maj. + min.), 6.50 (brs, 1H min.), 5.98 (brs, 1H maj.), 5.78 (brs, 1H min.), 5.75 (brs, 1H maj.), 5.05 (d, J = 8.5 Hz, 1H min.), 4.99 (d, J = 8.5 Hz, 1H maj.), 4.48 (td, J = 13.9, 3.2 Hz, 1H maj.), 4.25 (t, J = 9.1 Hz, 2H maj.), 4.16 (t, J = 8.7 Hz, 2H min.), 3.88 (m, 1H min.), 3.35 (dt, J = 12.9, 2.2 Hz, 1H min.), 2.95 (dt, J = 13.7, 2.9 Hz, 1H maj.), 2.43 (dt, J = 13.5, 3.6 Hz, 1H), 2.30 (s, 3H major), 2.19 (s, 3H minor), 2.16 (s, 3H), 2.05−1.93 (m, 1H, maj.+ min.). ^{13}C NMR (75 MHz, DMSO) δ (ppm) (2 rotamers) 168.8 (Cq), 167.7 (Cq), 157.6 (Cq), 135.8 (Cq), 135.5 (Cq), 129.8 (CH), 128.8 (Cq), 127.7 (CH), 125.5 (CH), 124.6 (CH), 109.1 (CH), 108.5 (CH), 80.4 (CH_2), 44.7 (Cq), 44.5 (Cq), 40.9 (CH_2), 37.1 (CH_2), 31.3 (CH_2), 31.1 (CH_2), 21.7 (CH_3), 21.2 (CH_3), 17.8 (CH_3). IR υ (neat): 3367, 3175−2877, 1664, 1630, 1348, 969 cm^{-1}. MS (ESI, m/z): 309.1 (100) [M + Na$^+$]. HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{16}H_{18}N_2O_3Na^+$: 309.1215. Found: 309.1219. Mp = 234−235 °C.

*4-Acetyl-11-methyl-3,4,5,6-tetrahydro-7H-3,6a-methanobenzofuro[4,3-ef][1,3]diazonin-1(2H)-one (**11f**).* Prepared according to procedure H from amide (16.6 mg, 0.0579 mmol), CH_2Cl_2 (0.5 mL), and TFA (44 μL, 0.058 mmol). The crude mixture was purified over silica gel (DCM to DCM/MeOH (95/5)) to afford a white solid (m = 9.7 mg, 58%) with recovered starting material (m = 6.9 mg, 42%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.14 (d, J = 8.2 Hz, 1H), 6.89 (d, J = 8.2 Hz, 1H), 6.28 (brs 1H), 6.15 (m, 1H), 4.27 (d, J = 8.4 Hz, 1H), 4.16 (d, J = 8.4 Hz, 1H), 3.63 (m, 1H), 3.20 (ddd, J = 14.2, 12.9, 2.9 Hz, 1H), 2.63 (s, 3H), 2.21 (m, 1H), 2.11 (s, 3H), 2.09−2.00 (m, 2H), 1.77 (dt, J = 13.4, 4.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.0 (Cq), 169.8 (Cq), 157.4 (Cq), 135.9 (Cq), 133.7 (CH), 131.5 (Cq), 127.9 (Cq), 113.4 (CH), 83.1 (CH_2), 57.5 (CH), 45.2 (Cq), 38.1 (CH_2), 36.3 (CH_2), 32.9 (CH_2), 24.4 (CH_3), 21.8 (CH_3). IR υ (neat): 3286, 3194−2853, 1667, 1639 cm^{-1}. MS (ESI, m/z): 287.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}N_2O_3^+$: 287.1396. Found: 287.1384. Mp = 210−211 °C.

*Methyl 4-Fluoro-3-(pyridin-4-ylmethoxy)benzoate (**S18**).* Prepared according to procedure A from methyl 4-fluoro-3-hydroxybenzoate (166 mg, 0.976 mmol), 4-(chloromethyl)pyridine hydrochloride (176 mg, 1.07 mmol), and K_2CO_3 (297 mg, 2.15 mmol) in DMF (6.8 mL). The solvent was removed under vacuum, and the crude mixture was purified through silica gel (Hept. to Hept./EtOAc 5/5) to afford a white solid (m = 235.9 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.64 (d, J = 5.2 Hz, 2H), 7.72−7.65 (m, 1H), 7.68 (d, J = 7.3 Hz, 1H), 7.39 (d, J = 5.1 Hz, 2H), 7.17 (dd, J = 10.6, 8.7 Hz, 1H), 5.20 (s, 2H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 165.8 (Cq), 155.5 (Cq, d, J_{CF} = 255 Hz), 150.0 (CH), 146.0 (Cq, d, J_{CF} = 11.1 Hz) 145.0 (Cq), 126.6 (Cq, d, J_{CF} = 4.1 Hz), 124.0 (CH, d, J_{CF} = 7.7 Hz), 121.3 (CH), 116.4 (CH), 116.1 (CH), 69.2 (CH_2), 52.3 (CH_3). IR υ (neat): 3085−2956, 1719, 1294 cm^{-1}. MS (ESI, m/z): 262.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{12}FNO_3^+$: 262.0879. Found: 262.0891. Mp = 104−106 °C.

*Methyl 3-((1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-4-fluorobenzoate (**S19**).* Prepared according to procedure B from methyl 4-fluoro-3-(pyridin-4-ylmethoxy)benzoate (234 mg, 0.89 mmol) in acetone (4.45 mL) and benzyl bromide (0.13 mL, 1.12

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mmol). The crude pyridinium was used without purification. Pyridinium (327 mg, 0.75 mmol) in methanol (7.5 mL) and sodium borohydride (63 mg, 1.66 mmol). The crude product was purified by flash column chromatography (Hept. to Hept./EtOAc 7/3) to afford the title compound as a colorless oil (m = 217 mg, 68%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.66−7.57 (m, 2H), 7.35−7.19 (m, 5H), 7.07 (dd, J = 10.7, 8.7 Hz, 1H), 5.80 (brs, 1H), 4.49 (s, 2H), 3.86 (s, 3H), 3.57 (s, 2H), 3.00 (brm, 2H), 2.61 (t, J = 5.7 Hz, 2H), 2.24 (brm, 2H).^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 165.9 (Cq), 155.6 (Cq, d, J_{CF} = 254 Hz), 146.5 (Cq, d, J_{CF} = 11.0 Hz), 138.0 (Cq), 131.4 (Cq), 128.9 (CH), 128.0 (CH), 126.9 (CH), 126.2 (Cq, d, J_{CF} = 3.6 Hz), 123.0 (CH, d, J_{CF} = 8.1 Hz), 116.1 (CH, d, J_{CF} = 3.4 Hz), 115.8 (CH, d, J_{CF} = 19.1 Hz), 72.4 (CH_2), 62.4 (CH_2), 52.2 (CH_2), 52.0 (CH_3), 49.2 (CH_2), 26.3 (CH_2). IR υ (neat): 2800, 1719, 1511, 1290 cm^{-1}. MS (ESI, m/z): 356.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{23}FNO_3^+$: 356.1656. Found: 356.1648.

*Methyl 4-Fluoro-3-((1,2,3,6-tetrahydropyridin-4-yl)methoxy)-benzoate (**S20**).* Prepared according to procedure E from *N*-benzyl amine (217 mg, 0.61 mmol), 1,2-dichloroethane (6.1 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.13 mL, 1.22 mmol) then MeOH (6.1 mL). The mixture was concentrated to give the title compound which was used without purification (m = 168.5 mg, 99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.95 (brs, 1H), 7.67 (ddd, J = 6.2, 2.3, 2.0 Hz, 1H), 7.62 (dd, J = 8.1, 1.8 Hz, 1H), 7.12 (dd, J = 10.6, 8.4 Hz, 1H), 5.89 (brs, 1H), 4.56 (s, 2H), 3.90 (s, 3H), 3.76 (brm, 2H), 3.37 (brm, 2H), 2.60 (brm, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 165.9 (Cq), 155.8 (Cq, d, J_{CF} = 256 Hz), 146.1 (Cq, d, J_{CF} = 11.0 Hz), 132.9 (Cq), 126.0 (Cq), 123.9 (CH, d, J_{CF} = 8.5 Hz), 117.3 (CH), 116.5 (CH, d, J_{CF} = 3.2 Hz), 116.1 (CH), 71.4 (CH_2), 52.3 (CH_3), 41.1 (CH_2), 40.4 (CH_2), 22.1 (CH_2). IR υ (neat): 3408, 2947−2671, 1708, 1287 cm^{-1}. MS (ESI, m/z): 266.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{17}NO_3F^+$: 266.1192. Found: 266.1197. Mp = 180−182 °C.

*Methyl 3-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-4-fluorobenzoate (**S21**).* Prepared according to procedure F from amine (165 mg, 0.622 mmol), triethylamine (0.36 mL, 2.55 mmol), 4-dimethylaminopyridine (cat.), CH_2Cl_2 (6.2 mL), and a solution of acetyl chloride (0.066 mL, 0.933 mmol) in CH_2Cl_2 (1.0 mL). The crude mixture was purified over silica gel (DCM to DCM/MeOH 95/5) to afford a yellow oil (m = 147.7 mg, 77%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers) 7.66−7.58 (m, 2H), 7.10 (dd, J = 10.5, 9.0 Hz, 1H), 5.85 (brm, 1H, major), 5.81 (brm, 1H, minor), 4.52 (s, 2H), 4.09 (brs, 2H, major), 3.98 (brs, 2H, minor), 3.89 (s, 3H), 3.72 (t, J = 5.9 Hz, 2H, minor), 3.56 (t, J = 5.8 Hz, 2H, major), 2.29 (brm, 2H, major), 2.22 (brm, 2H, minor), 2.12 (s, 3H, major), 2.08 (s, 3H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.3 (Cq), 169.2 (Cq), 166.0 (Cq), 155.8 (Cq, d, J_{CF} = 255 Hz), 146.4 (Cq, d, J_{CF} = 11.5 Hz), 133.2 (Cq), 131.3 (Cq), 126.5 (Cq), 123.5 (CH, d, J_{CF} = 8.5 Hz), 123.4 (CH, d, J_{CF} = 8.5 Hz), 121.0 (CH), 116.5 (CH, d, J_{CF} = 3.5 Hz), 116.4 (CH, d, J_{CF} = 3.5 Hz), 116.2 (CH), 116.0 (CH), 72.4 (CH_2), 72.2 (CH_2), 52.2 (CH_3), 45.1 (CH_2), 42.9 (CH_2), 41.4 (CH_2), 37.8 (CH_2), 26.2 (CH_2), 25.4 (CH_2), 21.8 (CH_3), 21.4 (CH_3). IR υ (neat): 3072−2849, 1722, 1633, 1283 cm^{-1}. MS (ESI, m/z): 308.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}FNO_4^+$: 308.1298. Found: 308.1295. Mp = 110−111 °C (decomp.).

*3-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-4-fluoro-N-methoxybenzamide (**9g**).* Prepared according to procedure C from methyl ester (147 mg, 0.69 mmol), LiOH (30 mg, 0.717 mmol), and MeOH (2.4 mL) H_2O (0.76 mL). The resulting crude carboxylic acid (0.69 mmol) was dissolved in DMF (1.4 mL) and reacted with EDCI (100.8 mg, 0.526 mmol), HOBt (71.1 mg, 0.526 mmol), $MeONH_2$·HCl (44 mg, 0.526 mmol), and iPr$_2$NEt (0.19 mL, 1.1 mmol). Purification over silica gel (DCM to DCM/MeOH 95/5) afforded the title compound as a yellow oil (m = 95.8 mg, 62% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers) 10.1 (brs, 1H), 7.49 (dd, J = 7.9, 2.3 Hz, 1H), 7.33 (m, 1H), 7.07 (dd, J = 10.6, 8.4 Hz, 1H), 5.80 (s, 1H), 4.50 (s, 2H), 4.07 (m, 2H major), 3.98 (m, 2H minor), 3.84 (s, 3H), 3.69 (t, J = 5.7 Hz, 2H minor), 3.56 (t, J = 5.8 Hz, 2H major), 2.27 (m, 2H major), 2.18 (m, 2H minor) 2.11 (s, 3H, major), 2.08 (s, 3H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 169.6 (Cq), 169.5 (Cq), 165.1 (Cq), 154.9 (Cq, d, J_{CF} = 255 Hz), 146.6 (Cq, d, J_{CF} = 11.0 Hz), 133.2 (Cq), 131.5 (Cq), 128.7 (Cq), 128.3 (Cq), 123.1 (CH), 121.0 (CH), 120.4 (CH, d, J_{CF} = 7.5 Hz), 120.3 (CH, d, J_{CF} = 7.5 Hz), 116.2 (CH), 116.0 (CH), 114.7 (CH), 72.3 (CH_2), 72.0 (CH_2), 64.2 (CH_3), 45.2 (CH_2), 43.0 (CH_2), 41.4 (CH_2), 37.9 (CH_2), 26.2 (CH_2), 25.3 (CH_2), 21.8 (CH_3), 21.3 (CH_3). IR υ (neat): 3176, 2972−2936, 1605 cm^{-1}. MS (ESI, m/z): 323.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{20}FN_2O_4^+$: 323.1407 Found: 323.1418. Mp = 141−143 °C.

*1′-Acetyl-7-fluoro-2′,3′-dihydro-1′H,2H-spiro[benzofuran-3,4′-pyridine]-4-carboxamide (**10g**).* Prepared according to procedure G from amide (44.1 mg, 0.136 mmol), $[RhCp^*Cl_2]_2$ (2.1 mg, 0.0034 mmol), and CsOAc (52.5 mg, 0.274 mmol) in *t*-AmOH (0.68 mL) at 60 °C overnight. The crude mixture was purified over silica gel (Hept. to EtOAc) to afford a white solid (m = 27.1 mg, 69%). ^{1}H NMR (300 MHz, acetone d^6) δ (ppm): (2 rotamers) 7.29 (d, J = 8.4 Hz, 1H, min.), 7.13 (brs, 1H), 7.12−7.00 (m, 2H), 6.91 (d, J = 8.3 Hz, 1H maj.), 6.73 (brs, 1H), 4.97 (dd, J = 8.5, 1.9 Hz, 1H min.), 4.89 (dd, J = 8.3, 1.9 Hz, 1H maj.), 4.47 (dt, J = 13.9, 3.6 Hz, 1H, maj.), 4.26 (dd, J = 5.5, 1.3 Hz, 1H, maj.), 4.23 (dd, J = 5.5, 1.3 Hz, 1H, min.), 4.04 (dt, J = 12.2, 3.6 Hz, 1H, min.), 3.49 (dt, J = 13.1, 3.0 Hz, 1H, min.), 2.97 (dt, J = 13.7, 3.0 Hz, 1H, maj.), 2.76 (dt, J = 13.2, 4.2 Hz, 1H, min.), 2.64 (dt, J = 13.2, 4.2 Hz, 1H, maj.), 2.18 (s, 3H maj.), 2.17 (s, 3H min.), 1.98 (m, 1H, maj.), 1.93 (m, 1H, min.). ^{13}C NMR (75 MHz, DMSO) δ (ppm) (2 rotamers) 168.3 (Cq), 167.7 (Cq), 147.3 (Cq, d, J_{CF} = 245.0 Hz), 147.2 (Cq, d, J_{CF} = 245.0 Hz), 146.4 (Cq, d, J_{CF} = 11.1 Hz), 134.9 (Cq), 134.6 (Cq), 131.1 (Cq), 130.9 (Cq), 128.0 (CH), 125.0 (CH), 120.8 (CH, d, J_{CF} = 6.0 Hz), 120.6 (CH, d, J_{CF} = 6.0 Hz), 115.5 (CH), 115.2 (CH), 107.9 (CH), 107.4 (CH), 81.8 (CH_2), 45.6 (Cq), 45.3 (Cq), 40.9 (CH_2), 37.1 (CH_2), 31.0 (CH_2), 30.7 (CH_2), 21.8 (CH_3), 21.2 (CH_3). IR υ (neat): 3370, 3212, 2931−2881, 1660, 1638, 1621 cm^{-1}. MS (ESI, m/z): 291.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{16}N_2O_3F^+$: 291.1145. Found: 291.1141. Mp = 203−204 °C.

*4-Acetyl-9-fluoro-3,4,5,6-tetrahydro-7H-3,6a-methanobenzofuro[4,3-ef][1,3]diazonin-1(2H)-one (**11g**).* Prepared according to procedure H from amide (27.1 mg, 0.093 mmol), CH_2Cl_2 (0.47 mL), and TFA (71 μL, 0.0093 mmol). The crude mixture was purified over silica gel (DCM to DCM/MeOH (95/5)) to afford a white solid (m = 27 mg, 99%). ^{1}H NMR (300 MHz, DMSO) δ (ppm) (2 rotamers): 8.68 (d, J = 6.1 Hz, 1H maj.), 8.35 (d, J = 6.7 Hz, 1H min.), 7.73 (dd, J = 8.9, 4.5 Hz, 1H, maj. + min.), 7.26 (dd, J = 10.4, 8.9 Hz, 1H, maj. + min.), 6.04 (brm, 1H, min.), 5.47 (brm, 1H, maj.), 4.50 (d, J = 8.6 Hz, 1H, maj. + min.), 4.31 (d, J = 8.2 Hz, 1H, maj. + min.), 4.27 (m, 1H, maj.), 3.70 (m, 1H min.), 2.85 (m, 1H min.), 2.36−2.19 (m, 1H), 2.22 (s, 3H maj.), 2.17−2.05 (m, 2H), 2.04 (s, 3H min.), 1.93−1.60 (m, 2H, maj. + min.). ^{13}C NMR (75 MHz, DMSO) δ (ppm) 168.0 (Cq), 165.2 (Cq), 149.0 (Cq, d, J_{CF} = 249.0 Hz), 144.6 (Cq, d, J_{CF} = 13.9 Hz), 136.2 (Cq, d, J_{CF} = 13.9 Hz), 125.0 (CH), 124.8 (CH, d, J_{CF} = 6.5 Hz), 116.1 (CH, d, J_{CF} = 17.4 Hz), 83.7 (CH_2), 61.7 (CH), 45.1 (Cq), 45.0 (Cq), 37.1 (CH_2), 35.1 (CH_2), 34.3 (CH_2), 32.6 (CH_2), 31.7 (CH_2), 21.6 (CH_3), 21.1 (CH_3). IR υ (neat): 3198, 3077−2877, 1727, 1615, 1597 cm^{-1}. MS (ESI, m/z): 291.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{16}N_2O_3F^+$: 291.1145. Found: 291.1150. Mp = 203−207 °C.

*Methyl 4-Nitro-3-(pyridin-4-ylmethoxy)benzoate (**S22**).* Prepared according to procedure A from methyl 3-hydroxy-4-nitrobenzoate (305.3 mg, 1.55 mmol), 4-(chloromethyl)pyridine hydrochloride (279 mg, 1.7 mmol), and K_2CO_3 (470 mg, 3.4 mmol) in DMF (10.8 mL). The solvent was removed under vacuum, and the crude mixture purified through silica gel (Hept. to Hept./EtOAc 7/3) to afford a beige solid (m = 330.8 mg, 74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.67 (d, J = 5.0 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.80−7.73 (m, 2H), 7.45 (d, J = 5.0 Hz, 1H), 5.31 (s, 2H), 3.97 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 164.9 (Cq), 150.8 (Cq), 150.1 (CH), 144.1 (Cq), 135.0 (Cq), 125.7 (CH), 122.3 (CH), 121.1 (CH), 115.6 (CH), 69.3 (CH_2), 52.9 (CH_3). IR υ (neat): 3085−2958, 1719, 1293 cm^{-1}. MS (ESI, m/z): 289.1 (100) [M + H$^+$]. HMRS (ESI-

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TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{12}N_2O_5^+$: 289.0824. Found: 289.0835. Mp = 167−169 °C.

*Methyl 3-((1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-4-nitrobenzoate (**S23**).* Prepared according to procedure B from methyl 4-nitro-3-(pyridin-4-ylmethoxy)benzoate (251 mg, 0.87 mmol) in acetone (4.35 mL) and benzyl bromide (0.12 mL, 1.08 mmol). The crude pyridinium was used without purification. Pyridinium (330 mg, 0.71 mmol) in methanol (7.1 mL) and sodium borohydride (59.8 mg, 1.58 mmol). The crude product was purified by flash column chromatography (Hept. to Hept./EtOAc 7/3) to afford the title compound as a yellow oil (m = 223 mg, 67%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.81 (d, J = 8.4 Hz, 1H), 7.73 (s, 1H), 7.67 (d, J = 8.4 Hz, 1H), 5.85 (brs, 1H), 4.59 (s, 2H), 3.95 (s, 3H), 3.57 (brs, 2H), 3.60 (s, 2H), 3.03 (brs, 2H), 2.65 (t, J = 5.8 Hz, 2H), 2.25 (3, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 165.1 (Cq), 151.4 (Cq), 142.5 (Cq), 138.0 (Cq), 134.6 (Cq), 130.7 (Cq), 129.0 (CH), 128.1 (CH), 127.0 (CH), 125.2 (CH), 124.3 (CH), 121.3 (CH), 115.7 (CH), 72.7 (CH_2), 62.5 (CH_2), 52.7 (CH_3), 52.3 (CH_2), 49.2 (CH_2), 26.1 (CH_2). IR υ (neat): 2758, 1719, 1521, 1292 cm^{-1}. MS (ESI, m/z): 383.1 (100) $[M + H^+]$. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{23}N_2O_5^+$: 383.1607. Found: 383.1588.

*Methyl 4-Nitro-3-((1,2,3,6-tetrahydropyridin-4-yl)methoxy)-benzoate (**S24**).* Prepared according to procedure E from *N*-benzyl amine (286 mg, 0.748 mmol), 1,2-dichloroethane (7.5 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.16 mL, 1.5 mmol), and then MeOH (7.5 mL). The mixture was concentrated to give the title compound which was purified through silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 95/5) to afford a beige solid (m = 218.0 mg, 99%). ^{1}H NMR (300 MHz, MeOD) δ (ppm): 7.93−7.84 (m, 2H), 7.74 (dd, J = 8.4, 1.8 Hz, 1H), 6.00 (m, 1H), 4.78 (s, 2H), 3.95 (s, 3H), 3.74 (m, 2H), 3.39 (t, J = 6.2 Hz, 2H), 2.52 (m, 2H). ^{13}C NMR (75 MHz, MeOD) δ (ppm) 166.7 (Cq), 152.2 (Cq), 136.3 (Cq), 133.8 (Cq), 126.4 (CH), 123.2 (CH), 119.4 (CH), 117.0 (CH), 72.9 (CH_2), 53.5 (CH_3), 43.0 (CH_2), 41.9 (CH_2), 23.4 (CH_2). IR υ (neat): 3648, 2928−2560, 1720, 1527, 1291, 1248 cm^{-1}. MS (ESI, m/z): 293.1 (100) $[M + H^+]$. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{17}N_2O_5^+$: 293.1137. Found: 293.1150. Mp = 163−165 °C.

*Methyl 3-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-4-nitrobenzoate (**S25**).* Prepared according to procedure F from amine (240 mg, 0.82 mmol), triethylamine (0.45 mL, 3.36 mmol), 4-dimethylaminopyridine (cat.), CH_2Cl_2 (8.5 mL), and a solution of acetyl chloride (0.087 mL, 1.23 mmol) in CH_2Cl_2 (1.4 mL). The crude mixture was purified over silica gel (Hept. to Hept./EtOAc 20/80) to afford a white solid (m = 220 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers) 7.80 (dd, J = 8.2, 3.7 Hz, 1H), 7.69 (d, J = 1.5 Hz, 1H), 7.66 (dd, J = 8.2, 1.6 Hz, 1H), 5.86 (brs, 1H), 4.59 (s, 2H), 4,08 (brm, 1H, maj.), 3.98 (brm, 1H, min.), 3.92 (s, 3H), 3.70 (t, J = 5.7 Hz, 1H, min.), 3.55 (t, J = 5.8 Hz, 1H, maj.), 2.27 (brm, 1H, maj.), 2.18 (brm, 1H, min.), 2.10 (s, 3H, maj.), 2.07 (s, 3H, min.). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.3 (Cq), 169.2 (Cq), 164.9 (Cq), 151.1 (Cq), 142.4 (Cq), 134.7 (Cq), 132.2 (Cq), 130.6 (Cq), 125.3 (CH), 125.2 (CH), 123.7 (CH), 121.6 (CH), 121.0 (CH), 115.7 (CH), 115.6 (CH), 71.4 (CH_2), 71.8 (CH_2), 52.7 (CH_3), 45.1 (CH_2), 42.8 (CH_2), 41.3 (CH_2), 37.7 (CH_2), 26.0 (CH_2), 25.2 (CH_2), 21.7 (CH_3), 21.3 (CH_3). IR υ (neat): 3100−2850, 1720, 1636, 1281 cm^{-1}. MS (ESI, m/z): 335.1 (100) $[M + H^+]$. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{19}N_2O_6^+$: 335.1238. Found: 335.1236. Mp = 118−120 °C.

*3-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-N-methoxy-4-nitrobenzamide (**9h**).* Prepared according to procedure C from methyl ester (272.2 mg, 0.814 mmol), LiOH (156 mg, 6.51 mmol), MeOH (8.1 mL), and H_2O (8.1 mL). The resulting crude carboxylic acid (0.814 mmol) was dissolved in DMF (2.44 mL) and reacted with EDCI (171.6 mg, 0.895 mmol), HOBt (120.9 mg, 0.895 mmol), $MeONH_2$·HCl (68 mg, 0.814 mmol), and iPr$_2$NEt (0.33 mL, 1.87 mmol). Purification over silica gel (Hept to EtOAc) afforded the title compound as a white foam (m = 148.4 mg, 52% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers, 55/45) 10.68 (brs, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.59 (s, 1H), 7.45 (d, J = 8.6 Hz, 1H), 5.88 (s, 1H, min.), 5.84 (s, 1H, maj.), 4.59 (s, 2H), 4.07 (brm, 2H, maj.), 4.01 (brm, 2H, min.), 3.88 (s, 3H), 3.71 (t, J = 6.5 Hz, 2H, min.), 3.59 (t, J = 5.7 Hz, 2H, maj.), 2.30 (brm, 2H, maj.), 2.16 (brm, 2H, min.) 2.12 (s, 3H, maj.), 2.10 (s, 3H, min.). ^{13}C NMR (75 MHz, $CDCl_3$) (2 rotamers) δ (ppm) 169.8 (Cq), 162.7 (Cq), 151.5 (Cq), 141.5 (Cq), 136.9 (Cq), 132.3 (Cq), 131.0 (Cq), 125.5 (CH), 123.2 (CH), 120.9 (CH), 119.1 (CH), 119.0 (CH), 114.0 (CH), 72.4 (CH_2), 71.9 (CH_2), 64.1 (CH_3), 45.2 (CH_2), 43.0 (CH_2), 41.5 (CH_2), 38.0 (CH_2), 26.0 (CH_2), 25.2 (CH_2), 21.7 (CH_3), 21.3 (CH_3). IR υ (neat): 3176, 2936, 1605, 1588, 1241 cm^{-1}. MS (ESI, m/z): 350.1 (100) $[M + H^+]$. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{20}N_3O_6^+$: 350.1352 Found: 350.1339.

*1′-Acetyl-7-nitro-2′,3′-dihydro-1′H,2H-spiro[benzofuran-3,4′-pyridine]-4-carboxamide (**10h**).* Prepared according to procedure G from amide (39 mg, 0.111 mmol), $[RhCp^*Cl_2]_2$ (1.7 mg, 0.0027 mmol), and CsOAc (42. mg, 0.222 mmol) in *t*-AmOH (0.55 mL) at 60 °C overnight. The crude mixture was purified over silica gel (DCM to DCM/MeOH: 97/3) to afford a yellow solid (m = 25.3 mg, 72%). ^{1}H NMR (300 MHz, DMSO) δ (ppm): (2 rotamers, 60/40) 7.98 (d, J = 8.5 Hz, 1H, maj.), 7.94 (brs, 2H, maj.), 7.71 (brs, 2H, min.), 7.22 (d, J = 8.4 Hz, 1H, min.), 7.03 (d, J = 8.4 Hz, 1H, min.), 7.01 (d, J = 8.4 Hz, 1H, min.), 6.97 (d, J = 8.4 Hz, 1H, min.), 4.98 (dd, J = 8.4, 1.7 Hz, 1H, min.) 4.89 (dd, J = 8.3, 1.7 Hz, 1H, maj.), 4.72 (t, J = 8.9 Hz, 2H, maj. + min.), 4.34 (d, J = 10.0 Hz, 2H, maj. + min.), 4.31 (m, 1H, maj.), 3.97 (m, 1H, min.), 3.43 (dt, J = 13.1, 2.9 Hz, 1H, min.), 2.98 (dt, J = 13.5, 3.0 Hz, 1H, maj.), 2.45 (m, 1H, min.), 2.34 (dt, J = 13.3, 4.7 Hz, 1H, maj.), 1.93 (m, 2H, maj. + min.). ^{13}C NMR (75 MHz, DMSO) δ (ppm) (2 rotamers) 167.8 (Cq), 167.6 (Cq), 154.9 (Cq), 140.8 (Cq) 140.6 (Cq), 135.1 (Cq), 134.9 (Cq), 132.5 (Cq), 128.6 (CH), 125.6 (CH), 124.2 (CH), 120.0 (CH), 119.9 (CH), 107.0 (CH), 106.4 (CH), 82.6 (CH_2), 44.5 (Cq), 44.3 (Cq), 40.7 (CH_2), 37.0 (CH_2), 31.3 (CH_2), 31.0 (CH_2), 21.7 (CH_3), 21.2 (CH_3). IR υ (neat): 3359, 3166, 2927−2853, 1678, 1669, 1630 cm^{-1}. MS (ESI, m/z): 318.1 (100) $[M + H^+]$. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}N_3O_5^+$: 318.1084. Found: 318.1090. Mp = 250−254 °C.

*4-Acetyl-9-nitro-3,4,5,6-tetrahydro-7H-3,6a-methanobenzofuro-[4,3-ef][1,3]diazonin-1(2H)-one (**11h**).* Prepared according to procedure H from amide (14.7 mg, 0.046 mmol), CH_2Cl_2 (0.23 mL), and TFA (35 μL, 0.0046 mmol). The crude mixture was purified over silica gel (DCM to DCM/MeOH (95/5)) to afford a yellow solid (m = 14.0 mg, 95%). ^{1}H NMR (300 MHz, $CDCl_3$) (2 rotamers) δ (ppm): 8.98 (d, J = 6.1 Hz, 1H, maj.), 8.70 (d, J = 6.6 Hz, 1H, maj.), 8.03 (d, J = 9.0 Hz, 1H), 7.85 (d, J = 9.0 Hz, 1H), 6.08 (m, 1H, min.), 5.53 (m, 1H, maj.), 4.67 (d, J = 8.6 Hz, 1H, maj.), 4.66 (d, J = 8.6 Hz, 1H, min.), 4.45 (d, J = 8.6 Hz, 1H, maj.), 4.42 (d, J = 8.6 Hz, 1H, min.), 4.30 (m, 1H, maj.), 3.78−3.54 (m, 1H, min.), 2.83 (m, 1H, min.), 2.39−2.25 (m, 2H), 2.23 (s, 3H, maj.), 2.18 (m, 2H), 2.06 (s, 3H, min.), 1.90 (m, 1H, min.), 1.84−1.71 (m, 2H). ^{13}C NMR (75 MHz, DMSO) (2 rotamers) δ (ppm) 168.1 (Cq), 164.4 (Cq), 154.1 (Cq), 137.5 (Cq), 134.0 (Cq), 133.9 (Cq), 123.5 (CH), 123.2 (CH), 84.3 (CH_2), 61.6 (CH), 56.0 (CH), 44.3 (Cq), 44.2 (Cq), 36.6 (CH_2), 35.0 (CH_2), 34.2 (CH_2), 32.2 (CH_2), 31.3 (CH_2), 31.2 (CH_2), 21.6 (CH_3), 21.1 (CH_3). IR υ (neat): 3244, 3098−2940, 1646, 1603, 1203 cm^{-1}. MS (ESI, m/z): 318.1 (100) $[M + H^+]$. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}N_3O_5^+$: 318.1074. Found: 318.1090. Mp = 249−250 °C (decomp.).

*Methyl 3-(2-(1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)ethoxy)-benzoate (**S26**).* To a solution of alcohol[16] (101.7 mg, 0.468 mmol) in CH_2Cl_2 (4.7 mL) were added Et_3N (0.13 mL, 0.938 mmol) and DMAP (cat.) at rt. MsCl (0.054 mL, 0.7 mmol) was added at 0 °C, and the reaction mixture was stirred overnight at rt. The reaction was quenched with saturated $NaHCO_3$. The aqueous layer was extracted with EtOAc, and the combined organics were dried on Na_2SO_4, followed by solvent removal under reduced pressure. The crude mixture was used without further purification.

To a solution of phenol (71.3 mg, 0.469 mmol) in DMF (2.3 mL) was added NaH (60%, 11.2 mg, 0.469 mmol) at 0 °C. The mixture was stirred at 0 °C for 15 min, and then a solution of the crude mesylate (0.468 mmol) in DMF (2.3 mL) was added dropwise at 0 °C. After the mixture stirred overnight at rt, the reaction was quenched with saturated NaCl. The aqueous layer was extracted with EtOAc, and

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the combined organic layers were dried on Na_2SO_4, followed by solvent removal under reduced pressure. The crude mixture was purified over silica gel (Hept. to Hept./EtOAc 5/5) to afford a colorless oil (m = 87.5 mg, 53% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.62 (td, J = 7.6, 1.5 Hz, 1H), 7.54 (dd, J = 2.7, 1.5 Hz, 1H), 7.39−7.24 (m, 6H), 7.08 (ddd, J = 8.3, 2.8, 1.0 Hz, 1H), 5.51 (tt, J = 3.2, 1.6 Hz, 1H), 4.09 (t, J = 6.9 Hz, 2H), 3.91 (s, 3H), 3.60 (s, 2H), 3.01 (brs, 2H), 2.60 (t, J = 5.8 Hz, 2H), 2.48 (t, J = 7.1 Hz, 2H), 2.19 (brm, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 167.0 (Cq), 158.8 (Cq), 137.9 (Cq), 132.9 (Cq), 131.4 (Cq), 129.4 (CH), 129.3 (CH), 128.2 (CH), 127.1 (CH), 121.9 (CH), 121.1 (CH), 120.0 (CH), 114.7 (CH), 66.7 (CH_2), 62.6 (CH_2), 52.7 (CH_2), 52.1 (CH_3), 49.7 (CH_2), 36.3 (CH_2), 29.4 (CH_2). IR υ (neat): 2897−2798, 1719, 1444, 1275 cm^{-1}. MS (ESI, m/z): 352.2 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{26}NO_3^+$: 352.1913. Found: 352.1908.

*Methyl 3-(2-(1,2,3,6-Tetrahydropyridin-4-yl)ethoxy)benzoate (**S27**).* Prepared according to procedure E from *N*-benzyl amine (84.9 mg, 0.241 mmol), 1,2-dichloroethane (2.4 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.05 mL, 0.48 mmol), and then MeOH (2.4 mL). The mixture was concentrated to give the title compound which was purified through silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford an orange oil (m = 50.7 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.79 (brs, 1H), 7.61 (ddd, J = 7.6, 1.5, 1.2 Hz, 1H), 7.50 (dd, J = 2.6, 1.6 Hz, 1H), 7.31 (t, J = 7.9 Hz, 1H), 7.06 (ddd, J = 8.1, 2.7, 0.8 Hz, 1H), 5.51 (s, 1H), 4.09 (t, J = 6.3 Hz, 2H), 3.88 (s, 3H), 3.66 (brs, 2H), 3.28 (t, J = 6.0 Hz, 2H), 2.56−2.43 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 166.8 (Cq), 158.4 (Cq), 134.5 (Cq), 131.4 (Cq), 129.4 (CH), 122.2 (CH), 119.9 (CH), 115.4 (CH), 114.6 (CH), 65.8 (CH_2), 52.1 (CH_3), 41.3 (CH_2), 40.5 (CH_2), 36.1 (CH_2), 25.0 (CH_2). IR υ (neat): 3282, 2933−2765, 1713, 1444 cm^{-1}. MS (ESI, m/z): 262.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{20}NO_3^+$: 262.1443. Found: 262.1436.

*Methyl 3-(2-(1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)ethoxy)-benzoate (**S28**).* Prepared according to procedure F from amine (50.7 mg, 0.194 mmol), triethylamine (0.108 mL, 0.776 mmol), 4-dimethylaminopyridine (cat.), CH_2Cl_2 (1.9 mL), and a solution of acetyl chloride (0.021 mL, 0.29 mmol) in CH_2Cl_2 (0.32 mL). The crude mixture was purified over silica gel (DCM to DCM/MeOH 95/5) to afford a yellow oil (m = 38 mg, 64%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers: 55/45): 7.62 (td, J = 7.5, 1.4 Hz, 1H), 7.53 (dd, J = 2.7, 1.5 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.07 (d, J = 8.2, 2.8, 1.1 Hz, 1H), 5.54 (m, 1H, maj.), 5.49 (m, 1H, min.), 4.09 (dt, J = 6.7, 2.0 Hz, 2H), 4.04 (m, 2H, maj.), 3,92 (m, 2H, min.), 3.90 (s, 3H), 3.68 (t, J = 5.7 Hz, 2H, min.), 3.52 (t, J = 5.7 Hz, 2H, maj.), 2.51 (m, 2H), 2.24−2.12 (brm, 2H), 2.10 (s, 3H, maj.), 2.08 (s, 3H, min.). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.3 (Cq), 169.1 (Cq), 166.9 (Cq), 158.7 (Cq), 134.6 (Cq), 132.6 (Cq), 131.4 (Cq), 129.4 (CH), 122.0 (CH), 120.6 (CH), 119.9 (CH), 118.9 (CH), 114.6 (CH), 66.5 (CH_2), 66.3 (CH_2), 52.1 (CH_3), 45.4 (CH_2), 43.2 (CH_2), 41.6 (CH_2), 38.1 (CH_2), 36.5 (CH_2), 29.2 (CH_2), 28.3 (CH_2), 21.8 (CH_3), 21.4 (CH_3). IR υ (neat): 2949−2841, 1718, 1637, 1429, 1275, 1223 cm^{-1}. MS (ESI, m/z): 304.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{22}NO_4^+$: 304.1549. Found: 304.1536.

*3-(2-(1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)ethoxy)-N-methoxy-benzamide (**9i**).* Prepared according to procedure C from methyl ester (102.2 mg, 0.337 mmol), LiOH (63.7 mg, 2.69 mmol), MeOH (3.3 mL), and water (3.3 mL). The resulting crude carboxylic acid was dissolved in DMF (1.0 mL) and reacted with EDCI (71.2 mg, 0.371 mmol), HOBt (50.2 mg, 0.371 mmol), $MeONH_2$·HCl (31.1 mg, 0.371 mmol), and iPr$_2$NEt (0.14 mL, 0.778 mmol). Purification over silica gel (DCM to DCM/MeOH 98/2) afforded the title compound as a colorless oil (m = 87.0 mg, 81% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers) 9.92 (brs, 1H), 7.37−7.25 (m, 3H), 7.01 (td, J = 7.3, 2.2 Hz, 1H), 5.49 (m, 1H), 4.07 (t, J = 6.5 Hz, 2H), 4.01 (brs, 1H), 3.92 (brs, 1H), 3.87 (s, 3H), 3.65 (t, J = 5.8 Hz, 1H), 3.51 (t, J = 5.8 Hz, 1H), 2.48 (m, 2H), 2.18 (m, 1H), 2.11 (m, 1H), 2.09 (s, 3H, major), 2.07 (s, 3H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.7 (Cq), 169.3 (Cq), 165.9 (Cq), 158.8 (Cq), 134.6 (Cq), 133.3 (Cq), 132.7 (Cq), 129.5 (CH), 120.5 (CH), 119.2 (CH), 118.9 (CH), 118.6 (CH), 112.9 (CH), 66.3 (CH_2), 64.3 (CH_3), 45.4 (CH_2), 43.2 (CH_2), 41.6 (CH_2), 38.2 (CH_2), 36.4 (CH_2), 29.1 (CH_2), 28.3 (CH_2), 21.7 (CH_3), 21.3 (CH_3). IR υ (neat): 3190, 2933, 1614, 1580, 1428, 1237 cm^{-1}. MS (ESI, m/z): 319.2 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{23}N_2O_4^+$: 319.1652. Found: 319.1657.

*1′-Acetyl-2′,3′-dihydro-1′H-spiro[chromane-4,4′-pyridine]-5-carboxamide (**10i**).* Prepared according to procedure G from amide (24.1 mg, 0.079 mmol), $[RhCp^*Cl_2]_2$ (1.2 mg, 0.0019 mmol), and CsOAc (30.4 mg, 0.158 mmol) in *t*-AmOH (0.4 mL) at 60 °C overnight. The crude mixture was purified over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a white solid (m = 17.3 mg, 76%). ^{1}H NMR (300 MHz, methanol d^4) δ (ppm): (2 rotamers, 75/25) 7.17 (d, J = 8.3 Hz, 1H, minor), 7.13 (t, J = 15.4 Hz, 1H major), 6.82 (m, 2H major + minor), 6.76 (d, J = 8.3 Hz, 1H, major), 5.08 (dd, J = 1.9, 8.6 Hz, 1H, minor), 5.00 (dd, J = 2.0, 8.3 Hz, 1H, major), 4.37−4.14 (m, 3H), 3.89−3.77 (m, 1H, major), 3.54 (dt, J = 3.2, 12.9 Hz, 1H, minor), 3.09 (dt, J = 3.1, 13.5 Hz, 1H, major), 3.00 (dt, J = 4.6 Hz, 13.5 Hz, 1H, minor), 2.88 (dt, J = 4.4, 13.6 Hz, 1H, major), 2.21 (s, 3H, major), 2.19 (s, 3H, minor), 2.11−2.00 (m, 2H, minor), 1.98−1.90 (m, 2H, major). ^{13}C NMR (75 MHz, methanol d^4) δ (ppm) (2 rotamers) 170.6 (Cq), 156.0 (Cq), 128.8 (CH), 128.0 (CH), 125.8 (CH), 125.4 (CH), 121.7 (CH), 119.7 (CH), 119.6 (CH), 117.8 (CH), 117.5 (CH), 62.1 (CH_2), 62.0 (CH_2), 41.7 (CH_2), 37.7 (CH_2), 35.3 (CH_2), 35.2 (CH_2), 34.9 (CH_2), 33.5 (CH_2), 33.4 (CH_2), 21.8 (CH_3), 21.4 (CH_3). IR υ (neat): 3349, 2925, 2542, 1630,1422, 1394, 1294, 1230, 1070 cm^{-1}. MS (ESI, m/z): 287.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}N_2O_3^+$: 287.1390. Found: 287.1393.

*6-Acetyl-2,3,5,6,7,8-hexahydro-3a,7-methanochromeno[5,4-ef]-[1,3]diazonin-9(4H)-one (**11i**).* Prepared according to procedure H from amide (17.3 mg, 0.06 mmol), CH_2Cl_2 (0.35 mL) and TFA (46 μL, 0.006 mmol). The crude mixture was purified over silica gel (DCM to DCM/MeOH (95/5)) to afford a white solid (m = 16.9 mg, 97%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers, 85/15): 8.16 (dd, J = 2.1, 8.6 Hz, 1H, minor), 8.12 (dd, J = 1.6, 7.9 Hz, 1H, major), 7.26 (t, J = 8.1 Hz, 1H), 7.10 (dd, J = 1.7, 8.4 Hz, 1H, minor), 7.06 (dd, J = 1.5, 8.0 Hz, 1H, major), 6.92 (brs, 1H), 5.96 (dd, J = 4.6, 5.1 Hz, 1H, major), 5.45 (t, J = 5.0 Hz, 1H, minor), 4.42−4.21 (m, 2H), 3.62−3.48 (m, 1H), 3.43−3.29 (m, 1H), 4.21−4.04 (m, 2H, minor), 2.34 (s, 3H, minor), 2.25−1.99 (m, 3H, major + minor), 2.17 (s, 3H, major), 1.91−1.67 (m, 2H, major + minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.3 (Cq), 170.1 (Cq), 169.7 (Cq), 168.9 (Cq), 153.4 (Cq), 153.2 (Cq), 132.2 (Cq), 129.1 (Cq), 127.9 (CH), 127.8 (CH), 127.2 (CH), 127.1 (CH), 122.9 (CH), 122.0 (CH), 61.4 (CH), 61.1 (CH), 56.5 (CH_2), 38.1 (CH_2), 37.9 (CH_2), 37.6 (CH_2), 37.3 (CH_2), 36.5 (CH_2), 36.2 (CH_2), 35.9 (CH_2), 35.1 (CH_2), 33.6 (CH_2), 32.0 (Cq), 21.6 (CH_3), 21.0 (CH_3). IR υ (neat): 3228, 3035−2868, 1625, 1685, 1423, 1302 cm^{-1}. MS (ESI, m/z): 287.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}N_2O_3^+$: 287.1396. Found: 287.1398.

*Methyl 3-(2-(Pyridin-4-yl)ethyl)benzoate (**S29**).* To a solution of (3-(methoxycarbonyl)benzyl)triphenylphosphonium bromide (700 mg, 1.70 mmol, 1 equiv) in dry THF (7 mL) cooled at 0 °C in an ice-bath was added in one portion *t*-BuOK (230 mg, 2.05 mmol, 1.2 equiv). After the mixture stirred for 30 min at this temperature, 4-pyridinecarboxaldehyde (176 μL, 1.87 mmL, 1.1 equiv) was added. The reaction mixture was allowed to reach room temperature and stirred at this temperature for 1 h. After cooling with an ice bath, the reaction mixture was quenched with saturated NH_4Cl and then extracted with EtOAc. The combined organic layers were dried on $MgSO_4$, and the solvent was removed under reduced pressure. The crude mixture was purified through silica gel (Hept. to Hept./EtOAc 4/6) to afford the title compound as a light yellow oil (350 mg, 86% yield, mixture of Z/E diasteromers).

To a solution of methyl 3-(2-(pyridin-4-yl)vinyl)benzoate (350 mg, 1.46 mmol, 1 equiv) in anhydrous ethanol (20 mL) was added Pd/C (10% loading, 150 mg, 10% eq). The flask was purged with hydrogen and maintained under a hydrogen atmosphere for 2 h. The reaction

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mixture was then filtered on a pad of Celite. The organic layer was reduced under vacuum to give the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.50 (d, J = 5.9 Hz, 2H), 7.9 (dd, J = 1.8, 7.1 Hz, 2H), 7.35 (m, 2H), 7.09 (d, J = 5.9 Hz, 2H), 3.93 (s, 3H), 2.98 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 167.1 (Cq), 150 (Cq), 149.8 (CH), 140.9 (Cq), 133.1 (CH), 130.4 (Cq), 129.5 (CH), 128.6 (CH), 127.6 (CH), 123.9 (CH), 52.13 (CH_3), 36.8 (CH_2), 36.3 (CH_2). IR υ (neat): 2950, 1716, 1600, 1434, 1282, 1199, 1107 cm^{-1}. MS (ESI, m/z): 341.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{16}NO_2^+$: 242.1176. Found: 242.1179.

*Methyl 3-(2-(1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)ethyl)-benzoate (**S30**).* Prepared according to procedure B from methyl 3-(2-(pyridin-4-yl)ethyl)benzoate (310 mg, 1.52 mmol) in acetone (7.8 mL) and benzyl bromide (0.182 mL, 1.59 mmol). The crude pyridinium was used without purification. Pyridinium (1.52 mmol) in methanol (9.8 mL) and sodium borohydride (115 mg, 3.04 mmol). The crude product was purified by flash column chromatography (Hept. to Hept./EtOAc 4/6) to afford the title compound as a yellow oil (m = 353 mg, 69% over 2 steps). The oil turned to purple readily and was used in the next step immediately. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.81−7.71 (m, 2H), 7.35−7.10 (m, 7H), 5.50 (brs, 1H), 3.87 (s, 3H), 3.61 (s, 2H), 2.99 (brs, 2H), 2.80 (m, 2H), 2.65 (t, J = 5.7 Hz, 2H), 2.25 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 167.3 (Cq), 142.6 (Cq), 138.4 (Cq), 135.5 (CH), 133.1 (Cq), 133.0 (CH), 130.1 (Cq), 129.5 (CH), 129.4 (CH), 129.4 (CH), 129.2 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 127.1 (CH), 127.0 (CH), 119.6 (CH), 62.7 (CH_2), 52.9 (CH_2), 52.0 (CH_3), 49.8 (CH_2), 38.6 (CH_2), 33.8 (CH_2), 29.3 (CH_2). IR υ (neat): 3027−2751, 1719, 1281, 1199 cm^{-1}. MS (ESI, m/z): 336.2 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{26}NO_2^+$: 336.1958. Found: 336.1964.

*Methyl 3-(2-(1,2,3,6-Tetrahydropyridin-4-yl)ethyl)benzoate (**S31**).* Prepared according to procedure E from N-benzyl amine (348 mg, 1.04 mmol), 1,2-dichloroethane (5 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.22 mL, 2.07 mmol), and then MeOH (10.4 mL). The mixture was concentrated to give the title compound which was purified through silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a colorless oil (m = 255 mg, 99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.82 (brs, 1H), 7.90−7.85 (m, 2H), 7.38−7.35 (m, 2H), 5.40 (brs, 1H), 3.93 (s, 3H), 3.64 (brs, 2H), 5.38 (m, 2H), 2.81 (dd, J = 7.68, 9.23 Hz, 2H), 2.48−2.33 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 167.1 (Cq), 141.4 (Cq), 139.6 (Cq), 133.0 (CH), 130.3 (Cq), 129.3 (CH), 128.6 (CH), 127.5 (CH), 114.0 (CH), 52.1 (CH_3), 41.3 (CH_2), 40.6 (CH_2), 38.4 (CH_2), 33.3 (CH_2), 25.0 (CH_2). IR υ (neat): 3417, 2949, 2800, 2650, 1716, 1445, 1285, 1201 cm^{-1}. MS (ESI, m/z): 246.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{20}NO_2^+$: 246.1489. Found: 246.1494.

*Methyl 3-(2-(1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)ethyl)-benzoate (**S32**).* Prepared according to procedure F from amine (255 mg, 1.04 mmol), triethylamine (0.58 mL, 4.15 mmol), 4-dimethylaminopyridine (cat.), CH_2Cl_2 (14 mL), and a solution of acetyl chloride (0.11 mL, 1.56 mmol) in CH_2Cl_2 (1.7 mL). The crude mixture was purified over silica gel (Hept. to EtOAc) to afford a yellow oil (m = 172 mg, 55%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers, 50/50): 7.91−7.83 (m, 2H, major + minor), 7.39−7.33 (m, 2H, major + minor), 5.43 (t, J = 3.2 Hz, 1H major), 5.34 (t, J = 3.0 Hz, 1H major), 4.01 (brs, 1H), 3.92 (s, 3H), 3.89 (brs, 1H), 3.68 (t, J = 5.8 Hz, 1H), 3.51 (t, J = 5.8 Hz, 1H), 2.78 (t, J = 7.7 Hz, 2H), 2.34 (m, 2H), 2.12 (m, 2H), 2.11 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.4 (Cq), 169.2 (Cq), 167.2 (Cq), 142.0 (Cq), 137.1 (Cq), 135.1 (Cq), 133.0 (CH), 130.2 (Cq), 129.4 (CH), 128.4 (CH), 127.3 (CH), 119.1 (CH), 117.6 (CH), 52.0 (CH_3), 45.4 (CH_2), 43.2 (CH_2), 41.6 (CH_2), 38.7 (CH_2), 38.6 (CH_2), 38.2 (CH_2), 33.8 (CH_2), 33.6 (CH_2), 29.0 (CH_2), 28.1 (CH_2), 21.8 (CH_3), 21.5 (CH_3). IR υ (neat): 2922, 1718, 1641, 1432, 1284, 1201 cm^{-1}. MS (ESI, m/z): 288.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{21}NO_3Na^+$: 310.1414. Found: 310.1416.

*3-(2-(1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)ethyl)-N-methoxy-benzamide (**9j**).* Prepared according to procedure C from methyl ester (172 mg, 0.599 mmol), 3 N NaOH (2.1 mL), and EtOH (3.5 mL). The resulting crude carboxylic acid (0.336 mmol) was dissolved in DMF (1.5 mL) and reacted with EDCI·HCl (88 mg, 0.571 mmol), HOBt (88 mg, 0.571 mmol), $MeONH_2$·HCl (48 mg, 0.571 mmol), and iPr$_2$NEt (0.21 mL, 1,19 mmol). Purification over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) afforded the title compound as a colorless oil (m = 129 mg, 71% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers, 50/50) 9.15 (brs, 1H), 7.64−7.50 (m, 2H), 7.40−7.30 (m, 2H), 5.39 (brs, 1H), 5.34 (brs, 1H), 4.01 (brs, 1H), 3.90 (s, 3H), 3.88 (brs, 1H), 3.67 (t, J = 5.9 Hz, 1H), 3.52 (t, J = 5.8 Hz, 1H), 2.77 (dt, J = 1.6, 7.9 Hz, 2H), 2.33 (m, 2H), 2.12 (s, 3H), 2.09 (m, 2H), 2.07 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (presence of rotamers) 169.8 (Cq), 166.5 (Cq), 142.2 (Cq), 137.1 (Cq), 135.2 (Cq), 132.1 (CH), 132.0 (CH), 128.5 (CH), 127.3 (CH), 124.6 (CH), 119.0 (CH), 117.6 (CH), 64.3 (CH_3), 45.4 (CH_2), 43.3 (CH_2), 41.7 (CH_2), 38.6 (CH_2), 38.5 (CH_2), 38.4 (CH_2), 33.8 (CH_2), 33.7 (CH_2), 29.0 (CH_2), 28.0 (CH_2), 21.7 (CH_3), 21.4 (CH_3). IR υ (neat): 3439, 3164, 2930, 1606, 1438, 1233 cm^{-1}. MS (ESI, m/z): 303.4 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{23}N_2O_4^+$: 319.1658. Found: 319.1669.

*1′-Acetyl-2,2′,3,3′-tetrahydro-1′H-spiro[indene-1,4′-pyridine]-7-carboxamide (**10j**).* Prepared according to procedure G from amide (30 mg, 0.095 mmol), $[RhCp^*Cl_2]_2$ (1.5 mg, 0.0025 mmol), and CsOAc (36.5 mg, 0.190 mmol) in t-AmOH (0.48 mL) at 60 °C overnight. The crude mixture was purified over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a colorless oil (m = 17.9 mg, 68%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): (2 rotamers, 65/35) 7.27−7.11 (m, 4H), 6.57 (d, J = 8.3 Hz, 1H, major), 6.48 (brs, 1H, NH minor), 5.90 (brs, 1H, NH major + minor), 5.72 (brs, 1H, NH major), 4.98 (dd, J = 1.9, 8.6 Hz, 1H, minor), 4.89 (dd, J = 1.9, 8.4 Hz, 1H, major), 4.43 (ddd, J = 2.7, 4.3, 13.5 Hz, 1H major), 3.82 (dtd, J = 1.9, 4.1, 11.3 Hz, 1H, minor), 3.37 (td, J = 2.9, 12.7 Hz, 1H, minor), 3.05−2.73 (m, 2H major + minor), 2.61 (dt, J = 4.4, 13.3 Hz, 1H, minor), 2.36 (ddd, J = 4.5, 13.2, 13.7 Hz, 1H, major), 2.13 (s, 3H, major), 2.11 (s, 3H, minor), 2.07−1.88 (m, 2H major + minor), 1.81−1.70 (m, 1H major + minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers): 171.8 (Cq), 171.4 (Cq), 168.3 (Cq), 168.2 (Cq), 146.0 (Cq), 145.3 (Cq), 145.1 (Cq), 127.3 (CH), 127.1 (CH), 126.6 (CH), 126.4 (CH), 125.8 (CH), 125.5 (CH), 125.4 (CH), 123.7 (CH), 114.7 (CH), 114.1 (CH), 47.2 (Cq), 47.0 (Cq), 42.7 (CH_2), 40.9 (CH_2), 40.5 (CH_2), 38.6 (CH_2), 31.3 (CH_2), 30.5 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 21.9 (CH_3), 21.5 (CH_3). IR υ (neat): 3370, 3212, 2931−2881, 1660, 1638, 1621 cm^{-1}. MS (ESI, m/z): 271.3 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}N_2O_2^+$: 271.1447. Found: 271.1443.

*4-Acetyl-3,4,5,6,7,8-hexahydro-3,6a-methanoindeno[7,1-ef]-[1,3]diazonin-1(2H)-one (**11j**).* Prepared according to procedure H from amide (22.1 mg, 0.082 mmol), CH_2Cl_2 (0.7 mL), and TFA (63 μL, 0.008 mmol). The crude mixture was purified over silica gel (DCM to DCM/MeOH (95/5)) to afford a colorless oil (m = 20.9 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers, 80/20): 8.22 (d, J = 7.9 Hz, 1H), 7.38−7.32 (m, 1H), 7.26 (t, J = 7.61 Hz, 1H), 6.62 (brm, 1H), 6.12−6.05 (m, 1H, major), 5.36 (brm, 1H, minor), 4.46−4.35 (m, 1H, minor), 3.51 (dd, J = 4.1, 14.2 Hz, 1H, major), 3.12−2.93 (m, 2H), 2.88−2.76 (m, 1H), 2.47 (dt, J = 2.9, 13.9 Hz, 1H, minor), 2.21 (s, 3H minor), 2.24−2.07 (m, 2H), 2.03 (s, 3H major), 2.01−1.85 (m, 2H), 1.82−1.72 (m, 1H), 1.63 (dt, J = 4.3, 13.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers): 170.2 (Cq), 168.2 (Cq), 146.5 (Cq), 143.6 (Cq), 130.8 (CH), 129.5 (Cq), 129.3 (CH), 128.7 (Cq), 127.5 (CH), 62.9 (CH), 57.1 (CH), 46.9 (Cq), 41.9 (CH_2), 38.5 (CH_2), 37.6 (CH_2), 36.4 (CH_2), 35.2 (CH_2), 34.5 (CH_2), 33.2 (CH_2), 29.6 (CH_2), 21.8 (CH_3), 21.3 (CH_3). IR υ (neat): 3224, 3086−2872, 1625, 1615, 1418, 1288 cm^{-1}. MS (ESI, m/z): 271.3 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}N_2O_2^+$: 271.1447. Found: 271.1444.

*Methyl 3-(N-(Pyridin-4-ylmethyl)methylsulfonamido)benzoate (**S33**).* To a solution of methyl 3-(methylsulfonamido)benzoate (723 mg, 3.15 mmol) in DMF (22 mL) was added NaH 60% (278 mg, 6.94 mmol) at 0 °C. After the mixture stirred at 0 °C for 30 min, 4-(chloromethyl)pyridine hydrochloride (569 mg, 3.47 mmol) was

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added and the reaction was stirred overnight at room temperature. Saturated $NaHCO_3$ was added, and the aqueous layer was extracted with EtOAc (×3). The combined organic layers were washed with water and then brine and dried over Na_2SO_4. The solvent was removed under vacuum, and the crude mixture was purified through silica gel (Hept. to EtOAc) to afford the corresponding compound as a white solid (m = 335 mg, 33%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.49 (d, J = 5.4 Hz, 2H), 7.96 (t, J = 1.8 Hz, 1H), 7.92 (td, J = 7.5, 1.6 Hz, 1H), 7.48 (ddd, J = 8.0, 2.3, 1.1 Hz, 1H), 7.39 (t, J = 7.8 Hz, 1H), 7.21 (d, J = 5.5 Hz, 2H), 4.88 (s, 2H), 3.87 (s, 3H), 2.96 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 165.7 (Cq), 149.9 (CH), 145.0 (Cq), 139.0 (Cq), 133.4 (CH), 131.7 (Cq), 129.7 (CH), 129.2 (CH), 128.1 (CH), 122.8 (CH), 53.5 (CH_2), 52.3 (CH_3), 37.8 (CH_3). IR υ (neat): 3034−2913, 1727, 1333, 1287 cm^{-1}. MS (ESI, m/z): 321.1 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{16}N_2O_4S^+$: 321.0909. found: 321.0909. Mp = 130−133 °C.

*Methyl 3-(N-((1-Benzyl-1,2,3,6-tetrahydropyridin-4-yl)methyl)-methylsulfonamido)benzoate (**S34**).* Prepared according to procedure B from methyl 3-(*N*-(pyridin-4-ylmethyl)methylsulfonamido)-benzoate (335 mg, 1.04 mmol) in acetone (5.2 mL) and benzyl bromide (0.13 mL, 1.09 mmol). The crude pyridinium was used without purification. Pyridinium (1.04 mmol) in methanol (10.4 mL) and sodium borohydride (86.6 mg, 2.29 mmol). The crude product was purified by flash column chromatography (Hept. to Hept./EtOAc 5/5) to afford the title compound as a dark orange oil (m = 288 mg, 67% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.98 (dt, J = 7.6, 1.7 Hz, 1H), 7.94 (t, J = 2.0 Hz, 1H), 7.53 (dt, J = 7.6, 1.9 Hz, 1H), 7.45 (t, J = 7.8 Hz, 1H), 7.32−7.17 (m, 5H), 5.45 (brs, 1H), 4.23 (s, 2H), 3.91 (s, 3H), 3.49 (s, 2H), 2.90 (s, 3H), 2.82 (brs, 2H), 2.49 (t, J = 5.8 Hz, 2H), 2.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.0 (Cq), 139.3 (Cq), 137.8 (Cq), 133.5 (CH), 131.3 (Cq), 130.8 (Cq), 129.3 (CH), 129.0 (CH), 128.8 (CH), 128.5 (CH), 128.1 (CH), 127.0 (CH), 124.9 (CH), 62.0 (CH_2), 55.8 (CH_2), 52.3 (CH_3), 52.1 (CH_2), 49.2 (CH_2), 37.5 (CH_3), 26.5 (CH_2). IR υ (neat): 3027−2753, 1721, 1443, 1150 cm^{-1}. MS (ESI, m/z): 415.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{27}N_2O_4S^+$: 415.1692. Found: 415.1707.

*Methyl 3-(N-((1,2,3,6-Tetrahydropyridin-4-yl)methyl)methyl-sulfonamido)benzoate (**S35**).* Prepared according to procedure E from *N*-benzyl amine (288 mg, 0.695 mmol), 1,2-dichloroethane (6.9 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.15 mL, 1.39 mmol), and then MeOH (6.9 mL). The mixture was concentrated to give the title compound which was purified through silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a beige foam (m = 225 mg, 99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.76 (brs, 1H), 8.01 (td, J = 7.5, 1.5 Hz, 1H), 7.94 (dd, J = 2.2, 1.6 Hz, 1H), 7.56 (m, 1H), 7.50 (m, 1H), 5.49 (s, 1H), 4.29 (s, 2H), 3.94 (s, 3H), 3.54 (brs, 2H), 3.20 (t, J = 5.9 Hz, 2H), 2.94 (s, 3H), 2.53 (brm, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 165.9 (Cq), 139.0 (Cq), 133.7 (CH), 132.7 (Cq), 131.8 (Cq), 129.9 (CH), 129.4 (CH), 128.2 (CH), 118.6 (CH), 55.8 (CH_2), 52.4 (CH_3), 41.0 (CH_2), 40.3 (CH_2), 37.7 (CH_3), 22.5 (CH_2). IR υ (neat): 3416, 2931−2642, 1717, 1333, 1149 cm^{-1}. MS (ESI, m/z): 325.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{21}N_2O_4S^+$: 325.1222. Found: 325.1229.

*Methyl 3-(N-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methyl)-methylsulfonamido)benzoate (**S36**).* Prepared according to procedure F from amine (125.7 mg, 0.387 mmol), triethylamine (0.22 mL, 1.55 mmol), 4-dimethylaminopyridine (cat.), CH_2Cl_2 (3.8 mL), and a solution of acetyl chloride (0.041 mL, 0.581 mmol) in CH_2Cl_2 (0.64 mL). The crude mixture was purified over silica gel (DCM to DCM/MeOH 95/5) to afford a yellow oil (m = 111.4 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers): 7.97 (td, J = 7.4, 1.7 Hz, 1H), 7.91 (m, 1H), 7.55−7.40 (m, 2H), 5.46 (brs, 1H), 4.26 (s, 2H), 3.90 (s, 3H), 3.86 (brs, 1H, maj.), 3.78 (brs, 1H, min.), 3.55 (t, J = 5.7 Hz, 1H min.), 3.39 (t, J = 5.7 Hz, 1H maj.), 2.89 (s, 3H), 2.20 (brm, 1H, maj.), 2.10 (brm, 1H, min.), 2.04 (s, 3H, maj.), 1.98 (s, 3H min.). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.2 (Cq), 169.1 (Cq), 165.9 (Cq), 139.2 (Cq), 138.9 (Cq), 133.3 (CH), 133.2 (CH), 132.7 (Cq), 131.5 (Cq), 130.7 (Cq), 129.5 (CH), 129.1 (CH), 129.0 (CH), 128.3 (CH), 128.2 (CH), 124.2 (CH), 122.1 (CH), 55.8 (CH_2), 55.6 (CH_2), 52.3 (CH_3), 45.0 (CH_2), 42.8 (CH_2), 41.3 (CH_2), 37.7 (CH_2), 37.4 (CH_3), 37.3 (CH_3), 26.5 (CH_2), 25.8 (CH_2), 21.7 (CH_3), 21.3 (CH_3). IR υ (neat): 3009−2845, 1720, 1630, 1434, 1338, 1283, 1151 cm^{-1}. MS (ESI, m/z): 367.4 (100) [M + H$^+$]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{22}N_2O_5S^+$: 367.1328. Found: 367.1343.

*3-(N-((1-Acetyl-1,2,3,6-tetrahydropyridin-4-yl)methyl)methyl-sulfonamido)-N-methoxybenzamide (**9k**).* Prepared according to procedure C from methyl ester (195.9 mg, 0.535 mmol), LiOH (101.1 mg, 4.28 mmol), MeOH (5.3 mL), and water (5.3 mL). The resulting crude carboxylic acid (0.525 mmol) was dissolved in DMF (1.6 mL) and reacted with EDCI (110.6 mg, 0.577 mmol), HOBt (77.9 mg, 0.577 mmol), $MeONH_2$·HCl (43.8 mg, 0.525 mmol), and iPr$_2$NEt (0.21 mL, 1.21 mmol). Purification over silica gel (DCM to DCM/MeOH 98/2 to 95/5) afforded the title compound as a white foam (m = 126.6 mg, 63% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers: 59/41): 10.63 (brs, 1H, min.), 10.54 (brs, 1H, maj.), 7.78−7.68 (m, 2H), 7.47−7.34 (m, 2H), 5.44 (m, 1H), 4.23 (s, 2H), 3.83 (brs, 2H, maj.), 3.80 (s, 3H), 3.77 (brs, 2H, min.), 3.51 (t, J = 5.7 Hz, 2H, min.), 3.40 (t, J = 5.6 Hz, 2H, maj.), 2.87 (s, 3H), 2.18 (brm, 2H, maj.), 2.07 (brm, 2H, min.), 2.01 (s, 3H, maj.), 1.95 (s, 3H, min.). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) (2 rotamers) 169.8 (Cq), 169.6 (Cq), 164.9 (Cq), 139.2 (Cq), 139.1 (Cq), 133.4 (Cq), 132.7 (Cq), 132.0 (CH), 131.8 (CH), 129.6 (CH), 126.6 (CH), 124.0 (CH), 122.3 (CH), 63.2 (CH_3), 55.7 (CH_2), 55.6 (CH_2), 45.1 (CH_2), 43.0 (CH_2), 41.4 (CH_2), 38.0 (CH_2), 37.5 (CH_3), 37.4 (CH_3), 26.6 (CH_2), 25.7 (CH_2), 21.7 (CH_3), 21.3 (CH_3). IR υ (neat): 3197, 2930, 1613, 1331, 1150 cm^{-1}. MS (ESI, m/z): 404.1 (100) [M + Na$^+$]. HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{23}N_3O_5SNa^+$: 404.1256. Found: 404.1255.

*Methyl 3-((1-Acetyl-1,2,5,6-tetrahydropyridin-3-yl)methoxy)-benzoate (**S37**).* Prepared according to procedure E from methyl 3-((1-benzyl-1,2,5,6-tetrahydropyridin-3-yl)methoxy)benzoate **S39** (170 mg, 0.503 mmol), 1,2-dichloroethane (5 mL), 1-chloroethyl chloroformate (ACE-Cl) (0.10 mL, 1.00 mmol), and then MeOH (10 mL). The mixture was concentrated to give the free amine, which was used in the next step without purification. The title compound was prepared according to procedure F from amine (123 mg, 0.503 mmol), triethylamine (0.28 mL, 2.01 mmol), 4-dimethylaminopyridine (cat.), CH_2Cl_2 (7 mL), and a solution of acetyl chloride (0.05 mL, 0.75 mmol) in CH_2Cl_2 (1 mL). The crude mixture was purified over silica gel (Hept. to EtOAc) to afford a colorless oil (m = 130 mg, 88% yield over two steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers, 55/45): 7.70−7.63 (m, 1H), 7.61−7.56 (m, 1H), 7.41−7.31 (m, 1H), 7.15−7.08 (m, 1H), 6.07 (brs, 1H, minor), 5.99 (brs, 1H, major), 4.53 (brs, 2H, minor), 4.50 (brs, 2H, major), 4.18 (dt, J = 1.8, 2.6 Hz, 1H), 4.05 (td, J = 2.1, 2.8 Hz, 1H), 3.93 (s, 3H, minor), 3.92 (s, 3H, major), 3.70 (t, J = 5.8 Hz, 1H), 3.54 (t, J = 5.8 Hz, 1H), 2.32−2.18 (m, 2H), 2.15 (s, 3H, major), 2.13 (s, 3H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 169.6 (Cq), 169.3 (Cq), 166.8 (Cq), 166.7 (Cq), 158.5 (Cq), 158.3 (Cq), 131.9 (Cq), 131.5 (Cq), 131.4 (Cq), 130.6 (Cq), 129.5 (CH), 129.4 (CH), 126.3 (CH), 123.5 (CH), 122.4 (CH), 122.3 (CH), 120.1 (CH), 120.0 (CH), 119.9 (CH), 114.9 (CH), 70.3 (CH_2), 70.2 (CH_2), 52.2 (CH_3), 52.1 (CH_3), 46.0 (CH_2), 42.9 (CH_2), 42.4 (CH_2), 37.9 (CH_2), 25.4 (CH_2), 24.5 (CH_2), 21.9 (CH_3), 21.5 (CH_3). IR υ (neat): 3020, 1721, 1643, 1281 cm^{-1}. MS (ESI, m/z): 312.2 (100) [M + Na$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{19}NO_4Na^+$: 312.1206. Found: 312.1209.

*3-((1-Acetyl-1,2,5,6-tetrahydropyridin-3-yl)methoxy)-N-methoxy-benzamide (**9l**).* Prepared according to procedure C from methyl ester (121 mg, 0.418 mmol), LiOH (40 mg, 1.67 mmol), and THF/Water (1/1, 4 mL). The resulting crude carboxylic acid (0.418 mmol) was dissolved in DMF (3 mL) and reacted with EDCI·HCl (88 mg, 0.460 mmol), HOBt (62 mg, 0.460 mmol), $MeONH_2$·HCl (38 mg, 0.460 mmol), and iPr$_2$NEt (0.17 mL, 0.96 mmol). Purification over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) afforded the title compound as a colorless oil (m = 91 mg, 72% yield over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers, 60/40): 10.61 (brs, 1H, NH, major), 10.47 (brs, 1H, NH, minor), 7.36−7.25 (m, 2H), 7.24−7.16 (m, 1H), 6.99−6.87 (m, 1H), 5.92 (brs, 1H, minor), 5.83 (brs, 1H,

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major), 4.39 (brs, 2H, minor), 4.34 (brs, 2H, major), 4.01 (brs, 2H, major), 3.91 (brs, 2H, minor), 3.77 (s, 3H, major), 3.76 (s, 3H, minor), 3.56 (t, J = 5.6 Hz, 2H, minor), 3.43 (t, J = 5.8 Hz, 2H, major), 2.20−2.06 (m, 2H), 2.03 (s, 3H, major), 3.00 (s, 3H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 169.7 (Cq), 169.6 (Cq), 165.8 (Cq), 158.5 (Cq), 158.4 (Cq), 133.4 (Cq), 131.9 (Cq), 130.6 (Cq), 129.6 (CH), 129.5 (CH), 126.1 (CH), 123.7 (CH), 120.0 (CH), 119.7 (CH), 118.9 (CH), 118.7 (CH), 113.4 (CH), 113.2 (CH), 70.3 (CH_2), 70.2 (CH_2), 64.1 (CH_3), 46.1 (CH_2), 43.1 (CH_2), 42.3 (CH_2), 39.9 (CH_2), 25.3 (CH_2), 24.5 (CH_2), 21.9 (CH_3), 21.4 (CH_3). IR υ (neat): 3021, 2837, 1719, 1645, 1285 cm^{-1}. MS (ESI, m/z): 305.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{21}N_2O_4^+$: 305.1501. Found: 305.1502.

*1′-Acetyl-1′,6′-dihydro-2H,2′H-spiro[benzofuran-3,3′-pyridine]-4-carboxamide (**10l**).* Prepared according to procedure G from amide (33 mg, 0.108 mmol), $[RhCp^*Cl_2]_2$ (3.3 mg, 0.0054 mmol), and CsOAc (41 mg, 0.216 mmol) in t-AmOH (0.54 mL) at 60 °C overnight. The crude mixture was purified over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a colorless oil (m = 21.2 mg, 72% yield). ^{1}H NMR (300 MHz, MeOD) δ (ppm) (2 rotamers, 70/30): 7.31−7.23 (m, 1H), 7.05 (dd, J = 7.6, 8.5 Hz, 1H), 6.94 (dd, J = 8.1, 10.1 Hz, 1H), 5.98−5.79 (m, 2H), 4.62 (brm, 1H, minor), 4.54 (td, J = 1.5, 12.8 Hz, 1H), 4.44−4.31 (m, 1H), 4.21 (dd, J = 3.7, 17.9 Hz, 1H, major), 4.09−3.91 (m, 2H), 3.77 (d, J = 13.2 Hz, 1H, minor), 3.53 (dt, J = 4.0, 19.0 Hz, 1H, minor), 3.44 (dd, J = 2.1, 12.6 Hz, 1H, major), 2.16 (s, 3H, major), 2.15 (s, 3H, minor). ^{13}C NMR (75 MHz, methanol D_4) δ (ppm): (2 rotamers) 172.9 (Cq), 172.8 (Cq), 172.6 (Cq), 172.3 (Cq), 162.7 (Cq), 162.5 (Cq), 135.5 (Cq), 135.4 (Cq), 130.7 (CH), 130.6 (CH), 129.2 (Cq), 129.1 (Cq), 129.0 (CH), 127.8 (CH), 127.2 (CH), 126.6 (CH), 121.1 (CH), 120.9 (CH), 113.2 (CH), 113.1 (CH), 79.9 (CH_2), 79.3 (CH_2), 50.8 (CH_2), 50.3 (Cq), 50.2 (Cq), 46.3 (CH_2), 46.2 (CH_2), 42.5 (CH_2), 21.6 (CH_3), 21.4 (CH_3). IR υ (neat): 3337, 3195, 1777, 1664, 1619, 1439, 11468 cm^{-1}. MS (ESI, m/z): 273.1 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_{17}N_2O_3^+$: 273.1239. Found: 273.1241.

*Methyl 3-((1-Benzyl-1,2,5,6-tetrahydropyridin-3-yl)methoxy)-benzoate (**S38**).* Prepared according to procedure A from methyl 5-hydroxy-2-methylbenzoate (67 mg, 0.44 mmol), 1-benzyl-5-(chloromethyl)-1,2,3,6-tetrahydropyridine hydrochloride[17] (113 mg, 0.437 mmol), and K_2CO_3 (150 mg, 1.08 mmol) in DMF (3 mL). The solvent was removed under vacuum, and the crude mixture was purified through silica gel (Hept. to Hept./EtOAc 5/5) to afford a colorless oil (m = 96 mg, 65%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.64 (dt, J = 2.3, 7.6 Hz, 1H), 7.57 (dd, J = 1.53, 2.6 Hz, 1H), 7.41−7.24 (m, 6H), 7.10 (dd, J = 2.81, 8.19 Hz, 1H), 5.92 (brs, 1H), 4.45 (s, 2H), 3.92 (s, 3H), 3.65 (s, 2H), 3.10 (q, J = 2.3 Hz, 2H), 2.60 (t, J = 5.7 Hz, 2H), 2.29−2.20 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.9 (Cq), 158.7 (Cq), 138.1 (Cq), 133.2 (Cq), 131.4 (Cq), 129.5 (CH), 129.3 (CH), 128.3 (CH), 127.1 (CH), 124.5 (CH), 122.1 (CH), 120.1 (CH), 115.0 (CH), 70.9 (CH_2), 62.6 (CH_2), 53.3 (CH_3), 52.1 (CH_2), 49.3 (CH_2), 25.7 (CH_2). IR υ (neat): 3058−2749, 1722, 1464, 1273, 1022 cm^{-1}. MS (ESI, m/z): 338.4 (100) [M + H+]. HMRS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{24}NO_3^+$: 338.1751. Found: 338.1753.

*3-((1-Benzyl-1,2,5,6-tetrahydropyridin-3-yl)methoxy)-N-methoxybenzamide (**9m**).* Prepared according to procedure C from methyl ester (264 mg, 0.782 mmol), LiOH (37 mg, 1.56 mmol), and THF/Water (1/1, 6 mL). The resulting crude carboxylic acid (0.782 mmol) was dissolved in DMF (8 mL) and reacted with EDCI·HCl (165 mg, 0.860 mmol), HOBt (116 mg, 0.860 mmol), $MeONH_2$·HCl (72 mg, 0.860 mmol), and iPr$_2$NEt (0.31 mL, 1.8 mmol). Purification over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) afforded the title compound as a colorless oil (m = 275 mg, 80% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.17 (brs, 1H), 7.40−7.24 (m, 8H), 7.04 (td, J = 2.33, 7.08 Hz, 1H), 5.88 (brs, 1H), 4.41 (s, 2H), 3.88 (s, 3H), 3.64 (s, 2H), 3.07 (q, J = 2.3 Hz, 2H), 2.59 (t, J = 5.74 Hz, 2H), 2.27−2.17 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 159.0 (Cq), 137.9 (Cq), 133.1 (Cq), 132.0 (Cq), 129.7 (CH), 129.3 (CH), 128.3 (CH), 127.2 (CH), 124.5 (CH), 119.1 (CH), 119.0 (CH), 113.2 (CH), 70.9 (CH_2), 64.4 (CH_3), 62.6 (CH_2), 53.2 (CH_2), 49.3 (CH_2), 25.6 (CH_2). IR υ (neat): 3196, 3028−2803, 1641, 1583, 1233 cm^{-1}. MS (ESI, m/z): 353.2 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{25}N_2O_3^+$: 353.1865. Found: 353.1870.

*1′-Benzyl-1′,6′-dihydro-2H,2′H-spiro[benzofuran-3,3′-pyridine]-4-carboxamide (**10m**).* Prepared according to procedure G from amide (29 mg, 0.083 mmol), $[RhCp^*Cl_2]_2$ (1.3 mg, 0.0020 mmol), and CsOAc (31 mg, 0.165 mmol) in t-AmOH (0.41 mL) at 60 °C overnight. The crude mixture was purified over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a colorless oil (m = 23.8 mg, 91%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.76 (brs, 1H, NH), 7.35−7.15 (m, 7H), 6.90 (dd, J = 1.77, 7.4 Hz, 1H), 5.96 (td, J = 3.3, 9.8 Hz, 1H), 5.86 (brs, 1H, NH), 5.72 (td, J = 2.1, 9.9 Hz, 1H), 4.55 (d, J = 8.9 Hz, 1H), 4.19 (d, J = 8.6 Hz, 1H), 3.69 (d, J = 12.8 Hz, 1H), 3.53 (d, J = 13.0 Hz, 1H), 3.15−2.90 (m, 3H), 2.74 (d, J = 11.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 169.8 (Cq), 160.8 (Cq), 137.3 (Cq), 133.7 (Cq), 129.1 (Cq), 128.4 (CH), 127.5 (CH), 126.7 (CH), 121.1 (CH), 112.5 (CH), 81.9 (CH_2), 62.4 (CH_2), 59.9 (CH_2), 52.1 (CH_2), 49.5 (Cq). IR υ (neat): 3189, 3017−2812, 1635, 1562, 1228 cm^{-1}. MS (ESI, m/z): 319.4 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{21}H_{22}N_2ONa^+$: 341.1624. Found: 341.1625.

*3-((1-Benzyl-6-methyl-1,2,5,6-tetrahydropyridin-3-yl)methoxy)-N-methoxybenzamide (**9n**).* To a solution of (1-benzyl-6-methyl-1,2,5,6-tetrahydropyridin-3-yl)methanol (640 mg, 2.95 mmol) in THF (15 mL) were added methyl 3-hydroxybenzoate (448 mg, 2.95 mmol, 1 equiv) and triphenylphosphine (1.08 g, 4.13 mmol, 1.4 equiv). Diethyl azodicarboxylate (0.68 mmL, 4.13 mmol, 1.4 equiv) was added dropwise, and the reaction mixture was stirred overnight at room temperature. EtOAc was added, and the organic layer was washed with water and brine and dried over Na_2SO_4, followed by reduction under vacuum. The crude product was purified by flash chromatography (Hept. to hept./EtOAc 5/5) to give a colorless oil (m = 798 mg, 79%, contamined with about 5% of inseparable residual DEAD).

The amide was prepared according to procedure C from methyl ester (297 mg, 0.845 mmol), LiOH (81 mg, 3.38 mmol), and THF/Water (1/1, 8 mL). The resulting crude carboxylic acid (0.845 mmol) was dissolved in DMF (6 mL) and reacted with EDCI·HCl (178 mg, 0.930 mmol), HOBt (125 mg, 0.930 mmol), $MeONH_2$·HCl (77 mg, 0.930 mmol), and iPr$_2$NEt (0.34 mL, 1.94 mmol). Purification over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) afforded the title compound as a colorless oil (m = 236 mg, 77% yield over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.77 (brs, 1H, NH), 7.33−7.12 (m, 8H), 6.94 (td, J = 2.1, 7.7 Hz, 1H), 5.76 (brs, 1H), 4.32 (brs, 2H), 3.80 (s, 3H), 3.71 (d, J = 13.2 Hz, 1H), 3.45 (d, J = 13.2 Hz, 1H), 2.99 (m, 2H), 2.93−2.83 (m, 1H), 2.30 (m, 1H), 1.87 (m, 1H), 1.03 (d, J = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 158.9 (Cq), 131.2 (Cq), 129.7 (CH), 129.1 (CH), 128.3 (CH), 127.0 (CH), 123.5 (CH), 119.0 (CH), 113.3 (CH), 70.8 (CH_2), 64.5 (CH_3), 57.4 (CH_2), 50.9 (CH), 49.2 (CH_2), 32.0 (CH_2), 14.9 (CH_3). IR υ (neat): 3192, 2966, 2931, 1649, 1580, 1482, 1290, 1237 cm^{-1}. MS (ESI, m/z): 367.5 (100) [M + H$^+$]. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{22}H_{27}N_2O_3^+$: 367.2022. Found: 367.2024.

*1′-Benzyl-6′-methyl-1′,6′-dihydro-2H,2′H-spiro[benzofuran-3,3′-pyridine]-4-carboxamide (**10n**).* Prepared according to procedure G from amide (30.5 mg, 0.083 mmol), $[RhCp^*Cl_2]_2$ (1.3 mg, 0.002 mmol), and CsOAc (32 mg, 0.166 mmol) in t-AmOH (0.41 mL) at 60 °C overnight. The crude mixture was purified over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a colorless oil (m = 20.3 mg, 82% yield, dr: 65/35). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (major diastereomer): 7.27−7.12 (m, 5H), 7.09 (t, J = 7.8 Hz, 1H), 7.01 (d, J = 7.5 Hz, 1H), 6.75 (d, J = 7.9 Hz, 1H), 4.95 (brs, 1H, NH), 5.72 (dd, J = 2.4, 9.8 Hz, 1H), 5.65 (d, J = 10.7 Hz, 1H), 5.64 (brs, 1H, NH), 4.45 (d, J = 8.7 Hz, 1H), 4.07 (d, J = 8.8 Hz, 1H), 3.98 (d, J = 13.5 Hz, 1H), 3.18 (d, J = 13.5 Hz, 1H), 3.11−3.04 (m, 1H), 2.84 (d, J = 11.4 Hz, 1H), 2.67 (d, J = 11.4 Hz, 1H), 1.19 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 169.7 (Cq), 161.2 (Cq), 138.7 (Cq), 134.6 (CH), 133.2 (Cq), 129.2 (CH), 129.0 (CH), 128.8 (CH), 128.4 (CH), 127.1 (CH), 126.6 (CH), 120.4 (CH), 112.6 (CH), 81.4 (CH_2), 58.0 (CH_2), 56.4 (CH_2), 54.6 (CH), 49.3 (Cq), 18.8 (CH_3). IR υ (neat): 3085, 2943, 2711, 1643, 1581, 1477, 1353, 1212 cm^{-1}. MS

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(ESI, *m*/*z*): 335.2 (100) [M + H$^+$]. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{21}H_{23}N_2O_2^+$: 335.1760. Found: 335.1767.

*tert-Butyl 3-((3-(methoxycarbonyl)phenoxy)methyl)-2,5-dihydro-1H-pyrrole-1-carboxylate (**S40**).* To a solution of methyl 3-hydroxybenzoate (179 mg, 1.18 mmol) in DMF (3 mL) cooled with an ice bath was added NaH 60% (57 mg, 1.42 mmol, 1.2 equiv). After the mixture was stirred for 15 min at this temperature, a solution of *tert*-butyl 3-(chloromethyl)-2,5-dihydro-1*H*-pyrrole-1-carboxylate[18] (258 mg, 1.18 mmol, 1 equiv) in DMF (2 mL) was added dropwise. The reaction mixture was allowed to reach room temperature and, after 2 h of stirring, was quenched with saturated NH_4Cl. The aqueous layer was extracted with EtOAc (×3), and the combined organic layers were washed with water and then brine and dried with Na_2SO_4, followed by solvent removal under vacuum. The crude mixture was purified through silica gel (Hept. to Hept/EtOAc 7/4) to afford a yellow oil (*m* = 404 mg, 97% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.66 (dd, *J* = 1.6, 7.5 Hz, 1H), 7.60−7.55 (m, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.11 (dd, *J* = 2.7, 7.7 Hz, 1H), 5.82 (brm, 1H), 4.64 (brs, 2H), 4.26−4.11 (m, 4H), 3.92 (s, 3H), 1.49 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 166.8 (Cq), 158.3 (Cq), 154.3 (Cq), 135.1 (Cq), 131.5 (Cq), 129.5 (CH), 123.4 (CH), 122.9 (CH), 122.4 (CH), 121.1 (CH), 120.3 (CH), 120.1 (CH), 120.0 (CH), 116.4 (CH), 114.7 (CH), 79.6 (Cq), 65.0 (CH_2), 53.3 (CH_2), 53.1 (CH_2), 52.2 (CH_3), 28.5 (CH_3). IR υ (neat): 3015, 2812, 1754, 1622, 1381 cm^{-1}. MS (ESI, *m*/*z*): 334.4 (100) [M + H$^+$]. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{18}H_{24}NO_5^+$: 334.1654. Found: 334.1657.

*tert-Butyl 3-((3-(Methoxycarbamoyl)phenoxy)methyl)-2,5-dihydro-1H-pyrrole-1-carboxylate (**9o**).* Prepared according to procedure C from methyl ester (80 mg, 0.240 mmol), LiOH (23 mg, 0.960 mmol), and THF/Water (1/1.6 mL). The resulting crude carboxylic acid (0.240 mmol) was dissolved in DMF (3 mL) and reacted with EDCI·HCl (50 mg, 0.264 mmol), HOBt (36 mg, 0.264 mmol), $MeONH_2$·HCl (22 mg, 0.264 mmol), and *i*Pr_2NEt (0.05 mL, 0.552 mmol). Purification over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) afforded the title compound as a colorless oil (*m* = 29 mg, 39% yield over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers, 55/45): 9.88 (brs, 1H, NH), 9.73 (brs, 1H, NH), 7.41−7.26 (m, 3H), 7.04 (t, *J* = 8.2 Hz, 1H), 5.81 (brs, 1H, major), 5.77 (brs, 1H, minor), 4.61 (s, 2H), 4.16 (s, 2H), 4.14 (s, 2H), 3.86 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): (presence of rotamers) 166.0 (Cq), 158.6 (Cq), 158.5 (Cq), 154.4 (Cq), 154.3 (Cq), 135.1 (Cq), 135.0 (Cq), 133.4 (Cq), 129.7 (CH), 123.3 (CH), 122.9 (CH), 120.7 (CH), 119.6 (CH), 119.5 (CH), 119.2 (CH), 119.0 (CH), 118.7 (CH), 113.1 (CH), 111.9 (CH), 79.7 (Cq), 65.0 (CH_2), 64.4 (CH_3), 63.8 (CH_2), 53.4 (CH_2), 53.3 (CH_2), 53.1 (CH_2), 52.9 (CH_2), 28.5 (CH_3), 27.9 (CH_3). IR υ (neat): 3015, 2812, 1754, 1622, 1381 cm^{-1}. MS (ESI, *m*/*z*): 349.4 (100) [M + H$^+$]. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{18}H_{25}N_2O_5^+$: 349.1763. Found: 349.1767.

*tert-Butyl 4-Carbamoyl-2H-spiro[benzofuran-3,3′-pyrrole]-1′(2′H)-carboxylate (**10o**).* Prepared according to procedure G from amide (22 mg, 0.063 mmol), $[RhCp^*Cl_2]_2$ (1.0 mg, 0.0016 mmol), and CsOAc (24 mg, 0.126 mmol) in *t*-AmOH (0.31 mL) at 60 °C overnight. The crude mixture was purified over silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH 90/10) to afford a colorless oil (*m* = 19.4 mg, 97% yield). This product partially cyclizes in the NMR tube and was engaged in the next step without further characterization.

*tert-Butyl 1-Oxo-2,3-dihydro-1H,6H-3,5a-methanobenzofuro[3,4-ef][1,3]diazocine-4(5H)-carboxylate (**11o**).* Prepared according to procedure H from amide (19.4 mg, 0.063 mmol), CH_2Cl_2 (0.35 mL), and TFA (48 μL, 0.006 mmol). The crude mixture was filtered over a pad of basic alumina and eluted with MeOH to afford a white solid (*m* = 19.3 mg, 99% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) (2 rotamers, 55/45): 8.32 (d, *J* = 6.2 Hz, 1H, NH), 7.80 (t, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 6.2 Hz, 1H, NH), 7.27−7.18 (m, 1H), 6.98 (dd, *J* = 5.7, 8.0 Hz, 1H), 5.28−5.12 (m, 1H), 4.51 (t, *J* = 8.9 Hz, 1H), 4.40 (d, *J* = 9.3 Hz, 1H), 3.79 (d, *J* = 9.8 Hz, 1H, major), 3.71 (d, *J* = 9.7 Hz, 1H, minor), 3.35 (dd, *J* = 7.0, 10.1 Hz, 1H), 2.55−2.39 (m, 1H), 2.34−2.23 (m, 1H), 1.41 (s, 9H, major), 1.35 (s, 9H, minor). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 168.5 (Cq), 167.6 (Cq), 158.6 (Cq), 158.6 (Cq), 153.6 (Cq), 153.1 (Cq), 132.5 (Cq), 132.3 (Cq), 129.5 (CH), 129.3 (CH), 127.0 (Cq), 126.4 (Cq), 124.5 (CH), 124.5 (CH), 115.0 (CH), 114.5 (CH), 81.7 (Cq), 81.1 (Cq), 76.9 (Cq), 76.8 (Cq), 76.8 (CH), 76.9 (CH), 65.6 (CH_2), 65.5 (CH_2), 60.3 (CH_2), 60.1 (CH_2), 52.2 (Cq), 51.3 (Cq), 37.1 (CH_2), 36.7 (CH_2), 28.3 (CH_3). IR υ (neat): 3017, 2788, 1712, 1654, 1421, 1380 cm^{-1}. MS (ESI, *m*/*z*): 317.4 (100) [M + H$^+$]. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{17}H_{21}N_2O_4^+$: 317.1501. Found: 317.1498.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b03252.

Copies of ^{1}H, ^{13}C NMR and crystallographic data (PDF)
Crystallographic data for compound **11a** (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: laurent.chabaud@cnrs.fr.
*E-mail: catherine.guillou@cnrs.fr.

ORCID

Augustin Peneau: 0000-0002-8932-3732
Laurent Chabaud: 0000-0002-2590-8707

Notes

The authors declare no competing financial interest.

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