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1,3-Difunctionalization of Aminocyclopropanes via Dielectrophilic Intermediates

Ming-Ming Wang and Jérôme Waser^{*[a]}

Abstract: We report an oxidative ring-opening strategy to transform acyl, sulfonyl or carbamate protected aminocyclopropanes into 1,3-dielectrophilic carbon intermediates bearing a halide atom (Br, I) and a N,O-acetal. Replacing the alkoxy group of the N,O-acetal can be achieved under acidic conditions via an elimination-addition pathway, while substitution of the halides by nucleophiles can be done under basic conditions via a S_N2 pathway, generating a wide range of 1,3-difunctionalized propylamines. A proof of concept for asymmetric induction was realized using a chiral phosphoric acid (CPA) as catalyst, highlighting the potential of the method in enantioselective synthesis of important building blocks.

Aminocyclopropanes are important building blocks in synthetic chemistry.^[1] They can be incorporated into organic compounds simply by amidation or S_N2 reaction. As structural units, they are found in potential lead compounds for new drugs and herbicides.^[2] Although the biological activity of aminocyclopropanes is well recognized, their reactivity in ring-opening reaction has been less explored. Our group, followed by others, showed that donor-acceptor substituted aminocyclopropanes (D-A aminocyclopropanes) are very useful intermediates, acting as zwitterionic nucleophile/electrophile synthons in the presence of Lewis acid catalysts (Scheme 1A).^[3] Although D-A aminocyclopropanes exhibit excellent reactivity, it usually takes extra steps to remove the electron-withdrawing groups or to transform them into other functionalities. For simple aminocyclopropanes lacking electron-withdrawing substituents at the vicinal position, current activation strategies focus mainly on: 1) oxidizing the amino group to a radical cation by strong oxidants or using photoredox chemistry;^[4] and 2) utilizing transition-metal catalysts to form metalcyclobutane intermediates.^[5] In both cases, the reported transformations were mostly limited to annulations. When considering the importance of 1,3-difunctionalized propylamines in medicinal chemistry, with already commercialized drugs such as amprenavir (**1**) and proglumide (**2**) (Scheme 1B), the development of new synthetic methods starting from aminocyclopropanes appears therefore highly desirable.^[6]

Inspired by the Hofmann–Löffler–Freitag (HLF) reaction and recent progress in the area (Scheme 1C),^[7] we wondered whether generation of a N-halogen bond on an aminocyclopropane followed by formation of the N-centered radical could lead to C–C bond activation instead of the hydrogen abstraction observed in the HLF reaction. Indeed, a single report on the photolysis of N-bromo aminocyclopropanes indicated that such a process may be possible.^[8]

Herein, we report that aminocyclopropanes can indeed be opened under mild conditions by reaction with halogenation reagents such as N-bromo and iodo succinimide (NBS and NIS). The obtained N–X cyclopropanes **I** then spontaneously open to give highly reactive 1,3-dielectrophilic imines **II** (Scheme 1D).^[9] Imines **II** can then either be isolated in high yield in the form of the more stable N,O-acetal, or reacted in a sequential nucleophilic addition and S_N2 reaction, leading to a wide range of α,γ-difunctionalized amines.

A. Previous work from our group involving D-A aminocyclopropanes

B. Drug molecules containing 1,3-difunctionalized propyl amines

C. Hofmann–Löffler–Freitag reaction

D. This work: 1,3-difunctionalization of aminocyclopropanes

Scheme 1. Our previous work with D-A aminocyclopropanes (A). Bioactive compounds featuring α,γ-difunctionalized amines (B). Hofmann–Löffler–Freitag reaction (C). And this work: oxidative ring opening strategy towards α,γ-difunctionalized amines (D).

[a] Ming-Ming Wang and Prof. Dr. Jérôme Waser
Laboratory of Catalysis and Organic Synthesis
Institute of Chemical Sciences and Engineering
Ecole Polytechnique Fédérale de Lausanne
EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne (CH)
Fax: (+)41 21 693 97 00
E-mail: jerome.waser@epfl.ch
Homepage: <http://lcsso.epfl.ch/>

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We started our investigation by reacting *N*-*para*-methoxybenzoyl protected aminocyclopropane **3a** with a stoichiometric amount of NIS in CDCl_3 (Table 1, entry 1). To our delight, formation of an imine intermediate **II** was observed by NMR, though accompanied by degradation. Due to the instability of this intermediate, it could not be isolated in pure form. Since N,O-acetals are stable precursors of imines,^[10] we then trapped **II** by adding methanol as nucleophile affording N,O-acetal **4a** in 86% NMR yield (Table 1, entry 2). The yield could be further improved to 92% by adding 10 mol% diphenyl phosphate and by performing the reaction in MeCN (Table 1, entry 3). N,O-acetal **4a** was stable enough to allow isolation in 84% yield. NBS also promoted ring opening, giving **5** in 65% yield (Table 1, entry 4). In contrast, NCS (*N*-chloro-succinimide) and NFSI (*N*-fluorobenzenesulfonimide) failed to yield the ring-opening products **6** and **7** (Table 1, entries 5 and 6).

Table 1. Optimization of the ring-opening of aminocyclopropane **3a**^[a]

Entry	Oxidant	Nucleophile	Yield ^[b]
1	NIS	-	35% ^[c]
2	NIS	MeOH	86% (74%) ^[d]
3 ^[e]	NIS	MeOH	92% (84%) ^[d]
4	NBS	MeOH	65%
5	NCS	MeOH	0%
6	NFSI	MeOH	0%

^[a]Reaction conditions: reactions were run at a 0.10 mmol scale in 0.50 mL of CDCl_3 at room temperature for 0.5 h. Ar = *p*-MeO-Ph. ^[b]The yield was determined by ^1H NMR using CH_2Br_2 as internal standard. ^[c]The ring-opening imine intermediate was formed. ^[d]Yield of isolated product. ^[e]Diphenyl phosphate (10 mol%) was added as additive, MeCN (0.50 mL) was used as solvent.

With the optimal conditions in hand, we then examined the scope of the reaction (Scheme 2). A series of benzoyl protected aminocyclopropanes with electron-withdrawing or electron-donating groups in the *para* position of the benzene ring all underwent the ring-opening well to give products **4a-f** in yields ranging between 70 and 85%. Under these conditions, bromide **5** was isolated with an improved yield of 90%. With substituents on the *ortho*, *meta* or 2,4,6-positions, no erosion of the yield was observed (products **4g-i**). Furyl-substituted amide **4j** was obtained in 96% yield. With a cinnamoyl protected aminocyclopropane, N,O-acetal **4k** was isolated in 80% yield with the double bond staying untouched. 2-Phenylacetyl, naphthoyl and pivaloyl amides were also well tolerated and gave products **4l-n** in 75–88% yield. In addition to amides-, sulfonyl amides and carbamates-substituted cyclopropanes could also be used, giving the desired products **4o-q** in good yields. N-alkyl substituted aminocyclopropanes were also converted to the corresponding products **4r** and **4s** in high yield.^[11] For non-protected aminocyclopropane (**8**), the ring was also opened but the imine was further oxidized to give cyanide **9**. Finally, more complex

aminocyclopropanes were investigated. Aminocyclopropanes incorporated into an amino acid and the drugs isoxepac and indomethacin underwent the ring-opening well to give N,O-acetals **4t-v**, showing the potential utility of this method in the late-stage functionalization of bioactive compounds.

Scheme 2 Scope of aminocyclopropanes in the ring-opening reaction. ^[a]Reaction conditions: **3** (0.30 mmol), NIS (0.315 mmol), MeOH (0.36 mmol), diphenyl phosphate (0.030 mmol) in MeCN (1.50 mL) at room temperature. ^[b]No diphenyl phosphate. ^[c]Reaction scale: 0.10 mmol. ^[d]NIS (2.1 equiv).

We then explored the scope for the O-nucleophiles (Scheme 3). Apart from methanol, other primary alcohols (products **10a-c**), secondary alcohols (products **10d-e**) or even a diol (product **10f**) were compatible with the reaction conditions. For optically pure menthol, the reaction proceeded with good yield albeit with poor diastereoselectivity to give product **10e**. For *tert*-butyl hydroperoxide (TBHP), molecular iodine was used as oxidant instead of NIS as it gave better yield, affording α -amino peroxide **10g**. Peroxides are an important class of bioactive compounds.^[12] The reaction also worked for hydrogen peroxide, though more equivalents of H_2O_2 were needed in order to obtain a good yield of **10h**.

Scheme 3. Scope of O-nucleophiles, Ar = *p*-MeO-Ph. Reaction conditions: **3a** (0.30 mmol), NIS (0.315 mmol), ROH (0.36 mmol), diphenyl phosphate (0.030 mmol) in MeCN (1.50 mL) at room temperature, 0.5–1 h. ^[a]I₂ (1.1 equiv) was used instead of NIS. ^[b]I₂ (1.1 equiv) was used instead of NIS with 2.0 equiv. of H₂O₂.

Our next objective was to exploit the full potential of our dielectrophilic synthons by adding a broad variety of other nucleophiles (Scheme 4). However, when other nucleophiles including TMSCN, MsNH₂, 1-naphthol and indole derivatives were used instead of alcohols, very low yields were obtained, as side reactions between NIS and those nucleophiles were observed. Therefore, one-pot addition of nucleophiles to the N,O-acetals under acidic conditions was attempted. The addition of MsNH₂ provided N,N-aminal **11** in 69% yield. The use of C-nucleophiles was also possible, including cyanide, 2-naphthol and 3-methyl indole (products **12–14**). When adding NaBH₃CN, N,O-acetal **4a** was reduced to give **15**.

Next, the iodide was replaced through an S_N2 reaction either in a one-pot procedure after addition of a base and solvent switch, or in two steps after isolation of the N,O-acetal, depending on the strength of the nucleophile (Scheme 4B). For benzoic acid and benzyl thiol, no isolation of the N,O-acetal was necessary. Ester **16** and thioether **17** were isolated in 81% and 79% yield respectively. When using aniline as nucleophile, N,O-acetal **4o** has to be isolated and purified, otherwise addition of succinimide originating from NIS rather than aniline was observed. Nevertheless, amine **18** was obtained in an excellent 86% yield over two steps. The same procedure was successful for malonate and NaCN, giving products **19** and **20** in good yields. In absence of external nucleophiles, α-methoxy azetidine **21**, which is an interesting building block for the synthesis of α-substituted azetidine derivatives,^[13] was obtained in 25% yield. The low yield is due to the formation of a 6-membered ring side product by attack of the oxygen of the carbamate. Finally, the one-pot addition of two different nucleophiles was investigated. Addition of 3-methyl-indole and a thiol or cyclopropylamine gave products **22** and **23** in 79% and 55% yield respectively.

Scheme 4. Conversion of aminocyclopropanes into a variety of α,γ-difunctionalized amines. Ar = *p*-MeO-Ph. See supporting Information for detailed reaction conditions.

Enantioselective addition of alcohols or peroxides to imines has been explored mainly by using two different types of catalysts: chiral phosphoric acids (CPA) and cinchona alkaloid derivatives.^[14] In order to obtain the product with enantiomeric excess, we utilized CPA **24** as catalyst (Scheme 5). N,O-acetal **4a** could be obtained in 82% yield and 78% ee, which is highly promising for the future development of enantioselective transformations.

Scheme 5. Enantioselective ring-opening of cyclopropane **3a** using CPA **24**.

In order to understand the mechanism better, we performed several control experiments (Scheme 6). When mixing **3q** and

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NXS (X = Br, I) in CDCl_3 for two hours, we observed formation of compounds **25** and **26**, corresponding to the initially postulated intermediates **I** and **II** (Scheme 6, equation 1). In the case of NIS, compounds **25a** was unstable and converted directly into imine **26a**. With NBS, only few conversion of **25b** into **26b** was also observed after two hours. Longer reaction times led to non-reproducible results, with varying amounts of **26b** being formed. In order to get more reliable results, we synthesized *N*-bromo cyclopropane **25b** using a reported procedure.^[8] Pure **25b** was converted quantitatively to **26b** in 6 h under ambient light (Scheme 6, equation 2). In contrast, nearly no conversion was observed in the dark. The fact that the reaction of the *N*-bromo compound is mediated by light could rationalize the low reproducibility of the results obtained in the one-pot transformation. Imine **26b** could then be transformed to N,O acetal **27** in the dark. The presence of methanol since the start of the reaction led to the same result, with only a small amount of competing debromination (Scheme 6, equation 3). Again, no reaction was observed in absence of light. Interestingly, when **25b** was treated with NIS, the formation of both bromination and iodination products **26b** and **26a** was observed, indicating that a cross-over pathway is operative (Scheme 6, equation 4). Finally, when using 2-methyl substituted aminocyclopropane **28** (d.r. = 4:1), difunctionalization product **29** was isolated as a mixture of two diastereoisomers in a 1:1 ratio after one-pot substitution of iodide with benzoate (Scheme 6, equation 5).^[15]

Scheme 6. Mechanistic investigations. NMR yields are reported, except for compound **29** (isolated yield).

Based on those results, we propose the mechanism depicted in Scheme 7. Halogenation of the aminocyclopropane by NXS provides *N*-X cyclopropane **I**, which undergoes homolytic cleavage of the N-X bond to form two radical species (**III**). Due to the ring strain of the cyclopropane, ring-opening occurs to form the primary alkyl radical which recombines with the halogen radical (**IV**) to give imine **II**. A radical chain process with the primary radical reacting with a further molecule of **I** can be envisaged. The incorporation of iodine in presence of NIS further support the presence of a primary radical such as **IV**. However, it is not possible at this stage to exclude other reaction mechanisms, such as direct halogenation of the C-C bond or a concerted rearrangement of **I** to **II**. Further studies will be needed to better establish the reaction mechanism. In the presence of MeOH, the N,O-acetal product is then formed. This last step can be accelerated by a Brønsted acid catalyst.

Scheme 7. Speculative reaction mechanism.

In summary, we have developed a practical and general strategy for the ring-opening and 1,3-difunctionalization of aminocyclopropanes. A series of stable 3-iodo N,O-acetal products were isolated. From these 1,3-dielectrophiles, a wide range of α,γ -difunctionalized products were rapidly accessed in one pot or in two steps. By using a chiral phosphoric acid as catalyst, a proof-of-concept for asymmetric induction was achieved. Based on the simple reaction procedure and the structural diversity of nitrogen-containing building blocks obtained, we believe that this new methodology will be useful in synthetic and medicinal chemistry.

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Keywords: aminocyclopropanes • ring-opening • amines • 1,3-dielectrophile intermediate • synthetic methodology

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Choose your nucleophiles: We report an oxidative ring-opening strategy to transform aminocyclopropanes into 1,3-dielectrophilic halogenated N,O-acetals. Substitution of either the alkoxy group of the N,O-acetal or the halide by a series of nucleophiles then generates a broad range of 1,3-difunctionalized propylamines.

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1. General Methods

For quantitative flash chromatography, distilled technical grade solvents were used. THF, Et₂O, toluene, hexane and CH₂Cl₂ were dried by passage over activated alumina under nitrogen atmosphere (H₂O content < 7 ppm, Karl-Fischer titration). All chemicals were purchased and used as received unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, or aluminium oxide, basic, Brockmann I, 50-200, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC plastic or aluminium plates and visualized with UV light, permanganate CAN or p-anisaldehyde stains. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ¹H-NMR spectra were recorded at room temperature on a Bruker DPX-400 400 MHz spectrometer in CDCl₃, Acetone-*d*₆, CD₃CN or CD₃OD, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal acetone signal at 2.09 ppm, the internal acetonitrile signal at 1.94 ppm and the internal methanol signal at 3.34 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, p = quintet, m = multiplet or unresolved, br = broad signal, integration, coupling constant(s) in Hz, interpretation). ¹³C-NMR spectra were recorded with 1H-decoupling on a Bruker DPX-400 100 MHz spectrometer in CDCl₃, Acetone-*d*₆, CD₃CN or CD₃OD, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, Acetone-*d*₆ signal at 29.8 ppm, CD₃CN signal at 1.3 ppm or CD₃OD signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 or a Bruker Alpha-P spectrophotometer with an ATR device and a ZnSe prism and are reported as cm⁻¹ (w = weak, m = medium, s = strong). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. HPLC measurements were done on a Agilent 1260 Infinity autosampler using a CHIRALPAK IA, IB, IC or IF column from DAICEL Chemical. Optical rotations were measured on a polarimeter using a 10 cm cell with a Na 589 nm filter. The specific solvents and concentrations (in g/100 mL) are indicated.

2. Preparation of starting materials

2.1 Synthesis of the aminocyclopropanes

General Procedure A (GP A):

Following a modified version of a reported procedure,^[1] to a solution of cyclopropylamine (0.70 mL, 10 mmol, 1.1 equiv.) and triethylamine (1.40 mL, 10.0 mmol, 1.1 equiv.) in dichloromethane (10 mL) was slowly added a solution of acyl chloride (9.09 mmol, 1.0 equiv.) in dichloromethane (10 mL) at 0 °C. The reaction mixture was stirred at room temperature usually for 16 hours. Upon completion, the mixture was quenched by the addition of 1 N HCl (10 mL). The aqueous layer was then extracted with dichloromethane. The organic extract was washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. In most cases, the crude product was pure enough to be used as such, without further purification.

N-Cyclopropyl-4-methoxybenzamide (3a)

Following GP A, using 4-methoxybenzoyl chloride (1.55 g, 9.09 mmol), N-cyclopropyl-4-methoxybenzamide (**3a**) was obtained as a white solid (1.90 g, 8.99 mmol, 99%).

¹H NMR (400 MHz, CDCl₃) δ 7.74 – 7.66 (d, *J* = 8.8 Hz, 2H, ArH), 6.94 – 6.85 (d, *J* = 8.8 Hz, 2H, ArH), 6.21 (s, 1H, NH), 3.84 (s, 3H, OCH₃), 2.88 (tq, *J* = 7.1, 3.6 Hz, 1H, CH), 0.85 (td, *J* = 7.0, 5.3 Hz, 2H, CH₂), 0.65 – 0.55 (m, 2H, CH₂).

¹H NMR data correspond to the reported values.^[1]

N-Cyclopropyl-4-(methylthio)benzamide (3b).

¹ Baburajan, P.; Elango, K. P. *Tetrahedron Lett.* **2014**, 55, 1006-1010.

Following GP A, using 4-(methylthio)benzoyl chloride (1.70 g, 9.09 mmol), N-cyclopropyl-4-(methylthio)benzamide (**3b**) was obtained as an off-white solid (1.41 g, 6.80 mmol, 75%).

R_f: 0.33 (silica, pentanes:ethyl acetate 1:1);

Mp: 158-160 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.68 – 7.61 (m, 2H, ArH), 7.25 – 7.20 (m, 2H, ArH), 6.24 (s, 1H, NH), 2.89 (dq, *J* = 7.0, 3.4 Hz, 1H, CH), 2.50 (s, 3H, SCH₃), 0.91 – 0.80 (m, 2H, CH₂), 0.66 – 0.54 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 168.3, 143.4, 130.4, 127.2, 125.3, 23.1, 15.0, 6.8;

IR (film): $\tilde{\nu}$ = 3271 (m), 3006 (w), 1622 (s), 1556 (s), 1486 (m), 1315 (m), 1121 (w), 840 (m), 761 (m);

HRMS (ESI) calcd. for C₁₁H₁₃NNaOS⁺ [M+Na]⁺ 230.0610; Found 230.0613.

N-Cyclopropyl-4-fluorobenzamide (3c).

Following GP A, using 4-fluorobenzoyl chloride (1.44 g, 9.09 mmol), N-cyclopropyl-4-fluorobenzamide (**3c**) was obtained as a white solid (1.50 g, 8.36 mmol, 92%).

¹H NMR (400 MHz, CDCl₃): δ = 7.79 – 7.70 (m, 2H, ArH), 7.12 – 7.01 (m, 2H, ArH), 6.37 (s, 1H, NH), 2.87 (tq, *J* = 7.1, 3.6 Hz, 1H, CH), 0.84 (td, *J* = 7.0, 5.3 Hz, 2H, CH₂), 0.65 – 0.56 (m, 2H, CH₂).

¹H NMR data correspond to the reported values.^[2]

4-Chloro-N-cyclopropylbenzamide (3d).

² Kondo, H.; Itami, K.; Yamaguchi, J. *Chem. Sci.* **2017**, *8*, 3799-3803.

Following GP A, using 4-chlorobenzoyl chloride (1.59 g, 9.09 mmol), 4-chloro-N-cyclopropylbenzamide (**3d**) was obtained as a white solid (1.65 g, 8.43 mmol, 93%).

R_f: 0.59 (silica, pentanes:ethyl acetate 2:3);

Mp: 133-135 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.70 – 7.64 (m, 2H, ArH), 7.41 – 7.35 (m, 2H, ArH), 6.27 (s, 1H, NH), 2.88 (tt, *J* = 7.1, 3.5 Hz, 1H, CH), 0.90 – 0.83 (m, 2H, CH₂), 0.66 – 0.55 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 167.8, 137.7, 132.7, 128.8, 128.3, 23.2, 6.8;

IR (film): $\tilde{\nu}$ = 3309 (m), 1639 (s), 1528 (m), 1484 (m), 1312 (m), 1093 (m), 847 (m);

HRMS (ESI) calcd. for C₁₀H₁₀ClNNaO⁺ [M+Na]⁺ 218.0343; Found 218.0344.

4-Cyano-N-cyclopropylbenzamide (**3e**).

Following GP A, using 4-cyanobenzoyl chloride (1.51 g, 9.09 mmol), 4-cyano-N-cyclopropylbenzamide (**3e**) was obtained as a white solid (1.60 g, 8.59 mmol, 95%).

R_f: 0.33 (silica, pentanes:ethyl acetate 1:1);

Mp: 159-161 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.84 (d, *J* = 8.1 Hz, 2H, ArH), 7.77 – 7.64 (m, 2H, ArH), 6.34 (d, *J* = 38.4 Hz, 1H, NH), 2.91 (tq, *J* = 7.0, 3.6 Hz, 1H, CH), 1.09 – 0.73 (m, 2H, CH₂), 0.70 – 0.52 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 167.0, 138.3, 132.4, 127.6, 118.0, 115.1, 23.3, 6.8;

IR (film): $\tilde{\nu}$ = 3275 (m), 3015 (w), 2230 (m), 1632 (s), 1532 (s), 1499 (m), 1313 (m), 1284 (m), 1018 (w), 858 (m);

HRMS (ESI) calcd. for C₁₁H₁₁N₂O⁺ [M+H]⁺ 187.0866; Found 187.0862.

N-Cyclopropyl-4-nitrobenzamide (**3f**).

Following GP A, using 4-nitrobenzoyl chloride (1.69 g, 9.09 mmol), N-cyclopropyl-4-nitrobenzamide (**3f**) was obtained as a pale yellow solid (1.71 g, 8.27 mmol, 91%).

R_f: 0.31 (silica, pentanes:ethyl acetate 1:1);

Mp: 176-177 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.30 – 8.22 (m, 2H, ArH), 7.94 – 7.86 (m, 2H, ArH), 6.41 (s, 1H, NH), 2.92 (tq, *J* = 7.2, 3.7 Hz, 1H, CH), 0.91 (td, *J* = 7.1, 5.4 Hz, 2H, CH₂), 0.70 – 0.59 (m, 2H, CH₂);
¹³C NMR (101 MHz, CDCl₃): δ = 166.8, 149.6, 139.9, 128.0, 123.8, 23.4, 6.8;
IR (film): $\tilde{\nu}$ = 3280 (m), 1639 (s), 1597 (w), 1533 (m), 1514 (s), 1350 (m), 1308 (m);
HRMS (ESI) calcd. for C₁₀H₁₁N₂O₃⁺ [M+H]⁺ 207.0764; Found 207.0761.

N-Cyclopropyl-3-methoxybenzamide (3g).

Following GP A, using 3-methoxybenzoyl chloride (1.55 g, 9.09 mmol), N-cyclopropyl-3-methoxybenzamide (**3g**) was obtained as a pale yellow solid (1.88 g, 8.90 mmol, 98%).

R_f: 0.31 (silica, pentanes:ethyl acetate 1:1);

Mp: 74-76 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.29 (s, 1H, ArH), 7.23 (d, *J* = 7.7 Hz, 1H, ArH), 7.19 (d, *J* = 7.7 Hz, 1H, ArH), 6.96 (ddd, *J* = 8.0, 2.7, 1.2 Hz, 1H, ArH), 6.39 (s, 1H, NH), 3.78 (s, 1H, OCH₃), 2.84 (tt, *J* = 7.2, 3.5 Hz, 1H, CH), 0.92 – 0.69 (m, 2H, CH₂), 0.65 – 0.43 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 168.8, 159.7, 135.8, 129.4, 118.6, 117.6, 112.2, 55.4, 23.1, 6.7;

IR (film): $\tilde{\nu}$ = 3295 (w), 1638 (m), 1582 (m), 1527 (m), 1485 (m), 1286 (m), 1247 (m), 1040 (m), 732 (s);

HRMS (ESI) calcd. for C₁₁H₁₃NNaO₂⁺ [M+Na]⁺ 214.0838; Found 214.0842.

N-Cyclopropyl-2-methoxybenzamide (3h).

Following GP A, using 2-methoxybenzoyl chloride (0.853 g, 5.00 mmol), N-cyclopropyl-2-methoxybenzamide (**3h**) was obtained as a colorless solid (0.586 g, 3.06 mmol, 61%) after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.36 (silica, pentanes:ethyl acetate 1:1);

Mp: 56-58 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.19 (dq, *J* = 7.8, 1.7 Hz, 1H, ArH), 7.89 (s, 1H, NH), 7.40 (ddq, *J* = 8.7, 7.3, 1.6 Hz, 1H, ArH), 7.04 (ddt, *J* = 8.9, 7.6, 1.5 Hz, 1H, ArH), 6.92 (dq, *J* = 8.3, 1.2 Hz, 1H, ArH), 3.91 (s, 3H, OCH₃), 2.91 (tq, *J* = 7.4, 3.8 Hz, 1H, CH), 0.86 – 0.78 (m, 2H, CH₂), 0.61 – 0.52 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.5, 157.3, 132.6, 132.1, 121.3, 121.2, 111.2, 55.8, 22.7, 6.7;

IR (film): $\tilde{\nu}$ = 3393 (w), 3002 (w), 1651 (s), 1600 (m), 1525 (s), 1484 (s), 1295 (m), 1240 (s), 1020 (m), 756 (m);

HRMS (ESI) calcd. for C₁₁H₁₃NNaO₂⁺ [M+Na]⁺ 214.0838; Found 214.0843.

N-Cyclopropyl-2,4,6-trimethylbenzamide (3i).

Following GP A, using 2,4,6-trimethylbenzoyl chloride (1.66 g, 9.09 mmol), N-cyclopropyl-2,4,6-trimethylbenzamide (**3i**) was obtained as a white solid (1.70 g, 8.36 mmol, 92%).

R_f: 0.40 (silica, dichloromethane);

Mp: 133-135 °C;

¹H NMR (400 MHz, CDCl₃): δ = 6.81 (s, 2H, ArH), 5.76 (s, 1H, NH), 2.90 (dq, *J* = 7.2, 3.5, 1.4 Hz, 1H, CH), 2.25 (s, 9H, CH₃), 0.92 – 0.79 (m, 2H, CH₂), 0.63 – 0.52 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 172.0, 138.4, 134.6, 134.1, 128.1, 22.6, 21.0, 19.0, 6.8;

IR (film): $\tilde{\nu}$ = 3223 (w), 1633 (m), 1536 (m), 1310 (w), 1265 (m), 856 (m), 734 (s);

HRMS (ESI) calcd. for C₁₃H₁₇NNaO⁺ [M+Na]⁺ 226.1202; Found 226.1206.

N-Cyclopropylfuran-2-carboxamide (3j).

Following GP A, using 2-furoyl chloride (1.19 g, 9.09 mmol), N-cyclopropylfuran-2-carboxamide (**3j**) was obtained as an off-white solid (1.31 g, 8.67 mmol, 95%).

¹H NMR (400 MHz, CDCl₃): δ = 7.39 (t, *J* = 3.1 Hz, 1H, ArH), 7.13 – 7.03 (m, 1H, ArH), 6.53 – 6.40 (m, 2H, ArH, NH), 2.85 (tq, *J* = 7.2, 3.7 Hz, 1H, CH), 0.84 (tt, *J* = 6.7, 4.1 Hz, 2H, CH₂), 0.66 – 0.54 (m, 2H, CH₂).

¹H NMR data correspond to the reported values.^[2]

N-Cyclopropylcinnamamide (3k).

Following GP A, using cinnamoyl chloride (1.52 g, 9.09 mmol), N-cyclopropylcinnamamide (**3k**) was obtained as a white solid (1.25 g, 6.68 mmol, 73%) after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.32 (silica, pentanes:ethyl acetate 3:2);

¹H NMR (400 MHz, CDCl₃): δ = 7.63 (d, *J* = 15.6 Hz, 1H, vinylH), 7.51 – 7.45 (m, 2H, ArH), 7.38 – 7.31 (m, 3H, ArH), 6.35 (d, *J* = 15.6 Hz, 1H, vinylH), 5.90 (brs, 1H, NH), 2.86 (tq, *J* = 7.1, 3.6 Hz, 1H, CH), 0.87 – 0.80 (m, 2H, CH₂), 0.62 – 0.52 (m, 2H, CH₂).

¹H NMR data correspond to the reported values.^[3]

N-Cyclopropyl-2-phenylacetamide (3l).

Following GP A, using 2-phenylacetyl chloride (1.41 g, 9.09 mmol), N-cyclopropyl-2-phenylacetamide (**3l**) was obtained as a white solid (1.52 g, 8.67mmol, 95%).

R_f: 0.36 (silica, dichloromethane:ethyl acetate 4:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.38 – 7.27 (m, 3H, ArH), 7.23 (dd, *J* = 6.8, 1.8 Hz, 2H, ArH), 5.44 (s, 1H, NH), 3.54 (s, 2H, CH₂), 2.66 (tq, *J* = 7.1, 3.6 Hz, 1H, CH), 0.75 – 0.67 (m, 2H, CH₂), 0.44 – 0.33 (m, 2H, CH₂).

¹H NMR data correspond to the reported values.^[4]

N-Cyclopropyl-2-naphthamide (3m).

Following GP A, using 2-naphthoyl chloride (1.73 g, 9.09 mmol), N-cyclopropyl-2-naphthamide (**3m**) was obtained as a white solid (1.90 g, 8.99 mmol, 99%).

R_f: 0.32 (silica, dichloromethane);

Mp: 179-181 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.24 (d, *J* = 1.7 Hz, 1H, ArH), 7.92 – 7.83 (m, 3H, ArH), 7.80 (dd, *J* = 8.5, 1.8 Hz, 1H, ArH), 7.54 (pd, *J* = 6.9, 1.6 Hz, 2H, ArH), 6.45 (s, 1H, NH), 2.97 (tq, *J* = 7.2, 3.7 Hz, 1H, CH), 0.90 (td, *J* = 7.0, 5.2 Hz, 2H, CH₂), 0.77 – 0.59 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 168.9, 134.7, 132.6, 131.6, 128.9, 128.4, 127.7, 127.6, 127.2, 126.7, 123.5, 23.2, 6.8;

IR (film): $\tilde{\nu}$ = 3243 (m), 3056 (w), 1623 (s), 1538 (s), 1314 (m), 1043 (w), 870 (m), 782 (m);

HRMS (ESI) calcd. for C₁₄H₁₃NNaO⁺ [M+Na]⁺ 234.0889; Found 234.0890.

N-Cyclopropylpivalamide (3n).

³ Zhang, B.; Feng, P.; Cui, Y.; Jiao, N. *Chem. Commun.* **2012**, 48, 7280-7282.

⁴ Tam, E.; Rita.; Liu, Y.; Chen, A. *Eur. J. Org. Chem.* **2015**, 1100-1107.

Following GP A, using pivaloyl chloride (1.10 g, 9.09 mmol), N-cyclopropylpivalamide (**3n**) was obtained as a white solid (1.22 g, 8.64 mmol, 95%).

R_f: 0.36 (silica, pentanes:ethyl acetate 3:2) KMnO₄;

¹H NMR (400 MHz, CDCl₃): δ = 5.71 (s, 1H, NH), 2.74 – 2.59 (m, 1H, CH), 1.16 (s, 9H, CH₃), 0.83 – 0.65 (m, 2H, CH₂), 0.61 – 0.34 (m, 2H, CH₂).

¹H NMR data correspond to the reported values.^[5]

tert-Butyl cyclopropylcarbamate (3o).

Following a modified version of a reported procedure,^[6] to a solution of cyclopropylamine (1.40 mL, 20.0 mmol, 1.0 equiv.) in dichloromethane (20 mL) was slowly added a solution of di-*tert*-butyl dicarbonate (4.85 g, 22.0 mmol, 1.1 equiv.) in dichloromethane (20 mL) at 0 °C. The reaction mixture was stirred at for 16 hours room temperature. Upon completion, the mixture was quenched by addition of 1 N HCl (10 mL). The aqueous layer was then extracted with dichloromethane. The organic layer was washed with brine (10 mL), and dried over Na₂SO₄, filtered and concentrated *in vacuo*. *tert*-Butyl cyclopropylcarbamate (**3o**) was obtained as a white solid (3.11 g, 19.8 mmol, 99%), which was pure enough to be used without further purification.

¹H NMR (400 MHz, CDCl₃): δ = 4.70 (brs, 1H, NH), 2.57 – 2.47 (m, 1H, CH), 1.44 (s, 9H, CH₃), 0.72 – 0.63 (m, 2H, CH₂), 0.53 – 0.39 (m, 2H, CH₂).

¹H NMR data correspond to the reported values.^[6]

Benzyl cyclopropylcarbamate (3p).

Following GP A, using benzyl chloroformate (1.55 g, 9.09 mmol), benzyl cyclopropylcarbamate (**3p**) was obtained as a colorless solid (1.72 g, 9.00 mmol, 99%).

¹H NMR (400 MHz, CDCl₃): δ = 7.41 – 7.29 (m, 5H, ArH), 5.10 (s, 2H, CH₂), 5.01 – 4.80 (m, 1H, NH), 2.60 (ttd, *J* = 7.0, 3.6, 2.0 Hz, 1H, CH), 0.76 – 0.69 (m, 2H, CH₂), 0.55 – 0.49 (m, 2H, CH₂).

⁵ Zhou, L.; Lu, W. *Org. Lett.* **2014**, *16*, 508-511.

⁶ Tars, K.; Leitan, J.; Kazaks, A.; Zelencova, D.; Liepinsh, E.; Kuka, J.; Makrecka, M.; Lola, D.; Andrianovs, V.; Gustina, D.; Grinberga, S.; Liepinsh, E.; Kalvinsh, I.; Dambrova, M.; Loza, E.; Pugovics, O. *J. Med. Chem.* **2014**, *57*, 2213-2236.

¹H NMR data correspond to the reported values.^[7]

N-(1-Cyano-3-iodopropyl)-4-methylbenzenesulfonamide (3q).

Following GP A, using tosyl chloride (1.73 g, 9.09 mmol), N-(1-Cyano-3-iodopropyl)-4-methylbenzenesulfonamide (**3q**) was obtained as a colorless solid (1.90 g, 9.00 mmol, 99%).

¹H NMR (400 MHz, CDCl₃): δ = 7.79 (d, *J* = 8.4 Hz, 2H, ArH), 7.32 (d, *J* = 8.0 Hz, 2H, ArH), 4.94 (s, 1H, NH), 2.43 (s, 3H, CH₃), 2.23 (tt, *J* = 6.6, 3.7 Hz, 1H, CH), 0.65 – 0.52 (m, 4H, CH₂).

¹H NMR data correspond to the reported values.^[8]

N-Cyclopropyl-N,4-dimethylbenzenesulfonamide (3r).

Following a modified version of a reported procedure,^[1] to a solution of N-cyclopropyl-methylamine hydrochloride (0.323 g, 3.00 mmol, 1.1 equiv.) and triethylamine (0.84 mL, 6.0 mmol, 2.2 equiv.) in dichloromethane (10 mL) was slowly added a solution of tosyl chloride (0.535 g, 2.80 mmol, 1.0 equiv.) in dichloromethane (10 mL) at 0 °C. The reaction mixture was stirred for 16 hours at room temperature. Upon completion, the mixture was quenched by addition of 1 N HCl (10 mL). The aqueous layer was then extracted with dichloromethane. The organic layer was washed with brine (10 mL), and dried over Na₂SO₄, filtered and concentrated *in vacuo*. N-cyclopropyl-N,4-dimethylbenzenesulfonamide (**3r**) was obtained as a yellow solid (0.580 g, 2.58 mmol, 92%), which was pure enough to be used without further purification.

R_f: 0.60 (silica, pentanes:ethyl acetate 3:1);

Mp: 73–76 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.73 (d, *J* = 8.3 Hz, 2H, ArH), 7.34 (d, *J* = 7.7 Hz, 2H, ArH), 2.73 (s, 3H, CH₃), 2.44 (s, 3H, CH₃), 1.78 (tt, *J* = 6.9, 3.6 Hz, 1H, CH), 0.90 – 0.83 (m, 2H, CH₂), 0.72 – 0.64 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 143.5, 132.8, 129.5, 128.0, 37.5, 32.1, 21.5, 7.5;

⁷ Shaw, M. H.; McCreanor, N. G.; Whittingham, W. G.; Bower, J. F. *J. Am. Chem. Soc.* **2015**, *137*, 463–468.

⁸ O'Sullivan, S.; Doni, E.; Tuttle, T.; Murphy, J. A. *Angew. Chem. Int. Ed.* **2014**, *53*, 474–478.

IR (film): $\tilde{\nu}$ = 2963 (w), 1596 (w), 1456 (m), 1365 (m), 1338 (s), 1151 (s), 1089 (s), 1034 (m), 817 (s), 691 (s);

HRMS (ESI) calcd. for $C_{11}H_{15}NNaO_2S^+$ $[M+Na]^+$ 248.0716; Found 248.0721.

***tert*-Butyl benzyl(cyclopropyl)carbamate (3s).**

Following a modified version of a reported procedure,^[9] to a solution of benzyl bromide (0.616 g, 3.60 mmol, 1.2 equiv.) and NaH (60% dispersion in mineral oil, 156 mg, 3.90 mmol, 1.3 equiv.) in DMF (10 mL) was slowly added a solution of *tert*-butyl cyclopropylcarbamate (0.472 g, 3.00 mmol, 1.0 equiv.) in DMF (5 mL) at 0 °C. The reaction mixture was stirred at room temperature for 16 hours. Upon completion, the mixture was quenched by addition of 1 N HCl (10 mL). The aqueous layer was then extracted with dichloromethane. The organic layer was washed with brine (10 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. *tert*-Butyl benzyl(cyclopropyl)carbamate (3s) was obtained as a bright yellow oil (0.540 g, 2.18 mmol, 73%) after purification by column chromatography on silica using 8:1 pentanes:ethyl acetate as eluent.

¹H NMR (400 MHz, $CDCl_3$): δ = 7.35 – 7.15 (m, 5H, ArH), 4.39 (s, 2H, NCH_2), 2.42 (s, 1H, CH), 1.42 (s, 9H, CH_3), 0.74 – 0.53 (m, 4H, CH_2).

¹H NMR data correspond to the reported values.^[9]

Benzyl (S)-(1-(cyclopropylamino)-1-oxo-3-phenylpropan-2-yl)carbamate (3t).

Following a modified version of a reported procedure,^[10] Boc-L-phenylalanine (898 mg, 3.00 mmol, 1.0 equiv.) and CDI (486 mg, 3.00 mmol, 1.0 equiv.) were suspended in THF (15 mL). The resulting mixture was stirred for 2 hour before adding cyclopropylamine (185 mg, 3.30 mmol, 1.1 equiv.). The reaction mixture was stirred at room temperature for another 16 hours. Upon completion, the mixture was quenched by addition of 2 M NaOH (5 mL x 2). The aqueous layer was then extracted with dichloromethane. The organic layer was washed with 1 N HCl (10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Benzyl (S)-(1-(cyclopropylamino)-1-oxo-3-phenylpropan-2-yl)carbamate (3t) was obtained as a white solid (480 mg, 1.44 mmol, 48%) after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.35 (silica, pentane:ethyl acetate 1:1);

⁹ Park, Y.; Beak, P. *Tetrahedron* **1996**, 52, 12333-12350.

¹⁰ Shang, M.; Wang, M.-M.; Saint-Denis, T. G.; Li, M.-H.; Dai, H.-X.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2017**, 56, 5317-5321.

Mp: 161-163 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.38 – 7.22 (m, 8H, ArH), 7.17 (d, *J* = 7.2 Hz, 2H, ArH), 5.69 (s, 1H, NH), 5.43 (d, *J* = 8.1 Hz, 1H, NH), 5.07 (s, 2H, OCH₂), 4.28 (q, *J* = 7.6 Hz, 1H, CHN), 3.11 (dd, *J* = 13.6, 6.1 Hz, 1H, CH₂), 2.96 (dd, *J* = 13.6, 8.1 Hz, 1H, CH₂), 2.58 (tq, *J* = 7.1, 3.6 Hz, 1H, CHN), 0.72 – 0.60 (m, 2H, CH₂), 0.34 – 0.19 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 171.9, 155.8, 136.5, 136.1, 129.3, 128.7, 128.5, 128.2, 128.0, 127.1, 67.1, 56.3, 38.9, 22.4, 6.5, 6.3;

IR (film): $\tilde{\nu}$ = 3298 (m), 1690 (m), 1652 (s), 1533 (m), 1286 (w), 1261 (w), 1040 (w), 747 (w), 698 (w);

HRMS (APPI) calcd. for C₂₀H₂₂N₂NaO₃⁺ [M+Na]⁺ 361.1523; Found 361.1518.

N-Cyclopropyl-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetamide (3u).

Following a modified version of a reported procedure,^[10] Isoxepac (536 mg, 2.00 mmol, 1.0 equiv.) and CDI (324 mg, 2.00 mmol, 1.0 equiv.) were suspended in DCM (10 mL). The resulting mixture was stirred for 1 hour before adding cyclopropylamine (123 mg, 2.20 mmol, 1.1 equiv.). The reaction mixture was stirred at room temperature for another 2 hours. Upon completion, the mixture was quenched by addition of 2 M NaOH (5 mL x 2). The aqueous layer was then extracted with dichloromethane. The organic layer was washed with 1 N HCl (10 mL). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. N-Cyclopropyl-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetamide (**3u**) was obtained as a white solid (550 mg, 1.79 mmol, 90%), which was found pure enough to be used without further purification.

R_f: 0.35 (silica, pentane:ethyl acetate 1:3);

Mp: 161-163 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.05 (d, *J* = 2.3 Hz, 1H, ArH), 7.88 (d, *J* = 7.6 Hz, 1H, ArH), 7.57 (t, *J* = 7.5 Hz, 1H, ArH), 7.48 (t, *J* = 7.6 Hz, 1H, ArH), 7.43 (dd, *J* = 8.4, 2.4 Hz, 1H, ArH), 7.37 (d, *J* = 7.4 Hz, 1H, ArH), 7.04 (d, *J* = 8.4 Hz, 1H, ArH), 5.72 (s, 1H, NH), 5.19 (s, 2H, OCH₂), 3.53 (s, 2H, CH₂), 2.68 (tq, *J* = 7.3, 3.6 Hz, 1H, CH), 0.73 (td, *J* = 7.1, 5.3 Hz, 2H, CH₂), 0.52 – 0.35 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 190.8, 172.1, 160.5, 140.3, 136.3, 135.4, 132.9, 132.3, 129.4, 129.3, 128.6, 127.9, 125.2, 121.5, 73.6, 42.5, 22.9, 6.6;

IR (film): $\tilde{\nu}$ = 3272 (w), 3057 (w), 1643 (s), 1609 (m), 1541 (m), 1487 (s), 1412 (m), 1300 (s), 1138 (m), 1016 (m), 801 (w), 735 (m);

HRMS (ESI) calcd. for C₁₉H₁₇NNaO₃⁺ [M+Na]⁺ 330.1101; Found 330.1104.

2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N-cyclopropylacetamide (3v).

Following a modified version of a reported procedure,^[10] indomethacin (1.07 g, 3.00 mmol, 1.0 equiv.) and CDI (486 mg, 3.00 mmol, 1.0 equiv.) were suspended in THF (10 mL). The resulting mixture was

stirred for 2 hours before adding cyclopropylamine (188 mg, 3.30 mmol, 1.1 equiv.). The reaction mixture was stirred at room temperature for another 2 hours. Upon completion, the mixture was quenched by addition of 2 M NaOH (5 mL x 2). The aqueous layer was extracted with dichloromethane. The combined organic layers were then washed with 1 N HCl (10 mL) and extracted with dichloromethane. The combined organic extracts were washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. 2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N-cyclopropylacetamide (**3v**) was obtained as a yellow solid (1.14 g, 2.88 mmol, 96%), which was found pure enough to be used without further purification.

R_f: 0.20 (silica, pentanes:ethyl acetate 3:7);

Mp: 166-168 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.65 (d, *J* = 8.5 Hz, 2H, ArH), 7.48 (d, *J* = 8.5 Hz, 2H, ArH), 6.88 – 6.82 (m, 2H, ArH), 6.69 (dd, *J* = 9.0, 2.5 Hz, 1H, ArH), 5.70 (s, 1H, NH), 3.82 (s, 3H, OCH₃), 3.61 (s, 2H, CH₂), 2.65 (tq, *J* = 7.1, 3.6 Hz, 1H, CH), 2.36 (s, 3H, CH₃), 0.76 – 0.68 (m, 2H, CH₂), 0.42 – 0.33 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 171.3, 168.3, 156.3, 139.6, 136.2, 133.5, 131.2, 130.8, 130.2, 129.2, 115.1, 112.8, 112.3, 100.7, 55.7, 32.2, 22.7, 13.2, 6.7;

IR (film): $\tilde{\nu}$ = 3268 (w), 3006 (w), 2929 (w), 1676 (s), 1644 (s), 1541 (m), 1476 (s), 1356 (s), 1314 (s), 1223 (s), 1147 (m), 1088 (m), 908 (m), 832 (m), 730 (s);

HRMS (APPI) calcd. for C₂₂H₂₁ClN₂O₃⁺ [M]⁺ 396.1235; Found 396.1242.

tert-Butyl ((1S*,2S*)-2-methylcyclopropyl)carbamate (28**).**

Following a reported procedure,^[11] to a solution of (1S*,2S*)-2-methylcyclopropanecarboxylic acid (1.00 g, 10.0 mmol, 4:1 d.r.) and Et₃N (1.40 mL, 10.0 mmol) in anhydrous *t*-BuOH (6 mL) was added diphenylphosphoryl azide (2.37 mL, 11.0 mmol) dropwise. The reaction was heated to 80 °C and stirred for 72 h before cooling to r.t. The reaction mixture was concentrated in vacuo and the residue was dissolved in Et₂O (20 mL). Water (20 mL) was added and the aqueous portion was extracted with Et₂O (3 x 20 mL). The organics extracts were combined, washed with sat. aq. sodium bicarbonate (20 mL) and brine (20 mL), dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography on silica using 10:1 pentanes:ethyl acetate as eluent. *tert*-Butyl ((1S*,2S*)-2-methylcyclopropyl)carbamate (**28**) was obtained as a colorless oil (1.02 g, 5.96 mmol, 60 %), which was a mixture of diastereoisomers A and B in a 4:1 (A:B) ratio.

¹H NMR (400 MHz, CDCl₃): δ = 4.68 (2H, br s, N-H, A+B), 2.51 (1H, br m, C1-H, B), 2.18 (1H, br m, C1-H, A), 1.43 (18H, br s, 3 x C7-H₃, A+B), 1.09-1.07 (6H, m, C4-H₃, A+B), 0.91-0.83 (3H, m, C2-H (A+B) and 1 x C3-H₂ (B)), 0.60 (1H, m, C3-H₂, A), 0.45 (1H, m, C3-H₂, A), 0.09 (1H, m, C3-H₂, B).

¹H NMR data correspond to the reported values.^[11]

¹¹ Shaw, M. H.; Melikhova, E. Y.; Kloer, D. P.; Whittingham, W. G.; Bower, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 4992-4995.

3. Scope of the ring-opening reaction

General Procedure B (GP B):

In a glass vial, the correspondent aminocyclopropane (0.300 mmol, 1.0 equiv.), N-Iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.), methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) and diphenyl phosphate (7.5 mg, 0.030 mmol, 0.10 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes, if not specified otherwise. After the completion of the reaction, the crude product was directly submitted to column chromatography on silica using pentanes:ethyl acetate as eluent.

Note: The obtained products were found heat-sensitive; in order to avoid their degradation, they were concentrated maintaining the heating bath of the rotatory evaporator below 30 °C and they were stored at -20 °C in the freezer. It is recommended that they are used for further transformations following a one-pot protocol, without isolation.

N-(3-Iodo-1-methoxypropyl)-4-methoxybenzamide (4a).

Following GP B, starting from N-cyclopropyl-4-methoxybenzamide **3a** (57.3 mg, 0.300 mmol), N-(3-iodo-1-methoxypropyl)-4-methoxybenzamide **4a** (88.8 mg, 0.255 mmol, 85%) was obtained as a yellow solid after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

For enantioselective version: in an oven dried microwave vial, N-cyclopropyl-4-methoxybenzamide **3a** (19.1 mg, 0.100 mmol, 1.0 equiv.), N-Iodosuccinimide (23.6 mg, 0.105 mmol, 1.05 equiv.), methanol (4.8 μ L, 0.12 mmol, 1.2 equiv.) and CPA **24** (3.8 mg, 0.0050 mmol, 0.05 equiv.) were dissolved in 0.5 mL of MeCN (0.20 M). The reaction mixture was stirred at -15 °C in a cryostat for 6 hours. After the completion of the reaction, N-(3-iodo-1-methoxypropyl)-4-methoxybenzamide **4a** (28.6 mg, 0.0819 mmol, 82%) was obtained as a yellow solid after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent. Chiral HPLC conditions: er = 88.9:11.1; Chiralpak IC 90:10 Hexane/iPrOH, 1.0 mL/min, 31 min. t_r (minor) = 17.4 min. and t_r (major) = 19.9 min. λ = 260 cm^{-1} .

R_f: 0.30 (silica, pentanes:ethyl acetate 3:1);

Mp: 92-95 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.80 – 7.74 (m, 2H, ArH), 6.96 – 6.90 (m, 2H, ArH), 6.36 (d, J = 9.5 Hz, 1H, NH), 5.44 (ddd, J = 9.6, 7.0, 5.3 Hz, 1H, CH), 3.85 (s, 3H, OCH₃), 3.41 (s, 3H, OCH₃), 3.29 – 3.17 (m, 2H, CH₂I), 2.25 (dddd, J = 17.7, 12.0, 7.4, 3.2 Hz, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 166.8, 162.6, 128.9, 125.7, 113.8, 81.6, 56.2, 55.4, 39.5, -0.9;

IR (film): $\tilde{\nu}$ = 3308 (w), 2933 (w), 2836 (w), 1641 (s), 1606 (s), 1532 (m), 1502 (s), 1307 (m), 1255 (s), 1175 (s), 1104 (m), 844 (m), 768 (w);

HRMS (ESI) calcd. for C₁₂H₁₆INNaO₃⁺ [M+Na]⁺ 372.0067; Found 372.0066.

N-(3-iodo-1-methoxypropyl)-4-(methylthio)benzamide (4b).

Following GP B, starting from N-cyclopropyl-4-(methylthio)benzamide **3b** (62.1 mg, 0.300 mmol), N-(3-iodo-1-methoxypropyl)-4-methoxybenzamide **4b** (81.4 mg, 0.223 mmol, 74%) was obtained as a yellow solid after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.31 (silica, pentanes:ethyl acetate 3:1);

Mp: 99-102 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.71 (d, *J* = 8.2 Hz, 2H, ArH), 7.27 (d, *J* = 8.0 Hz, 2H, ArH), 6.32 (d, *J* = 9.6 Hz, 1H, NH), 5.45 (dt, *J* = 9.7, 6.2 Hz, 1H, CH), 3.42 (s, 3H, OCH₃), 3.30 – 3.19 (m, 2H, CH₂I), 2.51 (s, 3H, SCH₃), 2.26 (ddd, *J* = 13.9, 8.8, 6.7 Hz, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 166.8, 144.3, 129.5, 127.4, 125.4, 81.7, 56.3, 39.5, 15.0, -1.0;

IR (film): $\tilde{\nu}$ = 3317 (w), 2928 (w), 1644 (s), 1596 (m), 1520 (s), 1488 (m), 1318 (w), 1107 (m), 837 (w);

HRMS (ESI) calcd. for C₁₂H₁₆INNaO₂S⁺ [M+Na]⁺ 387.9839; Found 387.9842.

4-Fluoro-N-(3-iodo-1-methoxypropyl)benzamide (4c).

Following GP B, starting from N-cyclopropyl-4-fluorobenzamide **3c** (62.1 mg, 0.300 mmol), 4-fluoro-N-(3-iodo-1-methoxypropyl)benzamide **4c** (83.6 mg, 0.248 mmol, 83%) was obtained as a yellow solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.48 (silica, pentanes:ethyl acetate 3:1);

Mp: 78-81 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.87 – 7.77 (m, 2H, ArH), 7.12 (t, *J* = 8.6 Hz, 2H, ArH), 6.48 (d, *J* = 9.5 Hz, 1H, NH), 5.43 (ddd, *J* = 9.5, 7.1, 5.2 Hz, 1H, CH), 3.41 (s, 3H, OCH₃), 3.30 – 3.15 (m, 2H, CH₂I), 2.34 – 2.16 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 166.3, 165.0 (d, *J* = 252.8 Hz), 129.7 (d, *J* = 3.1 Hz), 129.4 (d, *J* = 9.0 Hz), 115.7 (d, *J* = 21.9 Hz), 81.8, 56.3, 39.4, -1.0;

¹⁹F NMR (376 MHz, CDCl₃) δ = -107.1;

IR (film): $\tilde{\nu}$ = 3292 (w), 2933 (w), 1643 (s), 1602 (s), 1530 (m), 1496 (s), 1285 (m), 1233 (s), 1157 (s), 1100 (s), 1064 (s), 848 (s);

HRMS (ESI) calcd. for $C_{11}H_{13}FINNaO_2^+$ $[M+Na]^+$ 359.9867; Found 359.9868.

4-Chloro-N-(3-iodo-1-methoxypropyl)benzamide (4d).

Following GP B, starting from 4-chloro-N-cyclopropylbenzamide **3d** (58.5 mg, 0.300 mmol), 4-chloro-N-(3-iodo-1-methoxypropyl)benzamide **4d** (74.5 mg, 0.211 mmol, 70%) was obtained as an off-white solid after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.48 (silica, pentanes:ethyl acetate 3:1);

Mp: 110-114 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.75 (d, J = 8.5 Hz, 2H, ArH), 7.44 (dd, J = 8.5, 1.9 Hz, 2H, ArH), 6.29 (d, J = 11.6 Hz, 1H, NH), 5.50 – 5.38 (m, 1H, CH), 3.43 (d, J = 1.2 Hz, 3H, CH₃), 3.32 – 3.15 (m, 2H, CH₂), 2.33 – 2.18 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.3, 138.4, 132.0, 129.0, 128.5, 81.8, 56.4, 39.4, -1.2;

IR (film): $\tilde{\nu}$ = 3209 (w), 2930 (w), 1645 (s), 1594 (m), 1527 (s), 1485 (s), 1314 (m), 1092 (s), 1065 (m), 844 (m);

HRMS (ESI) calcd. for $C_{11}H_{13}ClINNaO_2^+$ $[M+Na]^+$ 375.9572; Found 375.9577.

4-Cyano-N-(3-iodo-1-methoxypropyl)benzamide (4e).

Following GP B, starting from 4-cyano-N-cyclopropylbenzamide **3e** (55.8 mg, 0.300 mmol) and after stirring for 2 hours, N-(3-iodo-1-methoxypropyl)-4-nitrobenzamide **4e** (79.6 mg, 0.231 mmol, 77%) was obtained as a yellow oil after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.35 (silica, pentanes:ethyl acetate 3:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.91 (d, J = 8.4 Hz, 2H, ArH), 7.77 (d, J = 8.4 Hz, 2H, ArH), 6.44 (d, J = 9.5 Hz, 1H, NH), 5.45 (ddd, J = 9.5, 6.9, 5.2 Hz, 1H, CH), 3.44 (s, 3H, OCH₃), 3.31 – 3.18 (m, 2H, CH₂I), 2.33 – 2.20 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 165.6, 137.5, 132.6, 127.7, 117.8, 115.6, 82.0, 56.6, 39.2, -1.3;
IR (film): $\tilde{\nu}$ = 3307 (m), 2927 (m), 2853 (w), 2231 (m), 1651 (s), 1531 (s), 1496 (s), 1312 (m), 1284 (m), 1104 (m), 1065 (m), 856 (m), 764 (m);
HRMS (ESI) calcd. for C₁₁H₁₀IN₂O⁺ [M-OCH₃]⁺ 312.9832; Found 312.9835.

N-(3-Iodo-1-methoxypropyl)-4-nitrobenzamide (4f).

Following GP B, starting from N-cyclopropyl-4-nitrobenzamide **3f** (61.8 mg, 0.300 mmol) and after stirring for 2 hours, N-(3-iodo-1-methoxypropyl)-4-nitrobenzamide **4f** (88.0 mg, 0.242 mmol, 81%) was obtained as a yellow solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.50 (silica, pentanes:ethyl acetate 3:1);

Mp: 65-68 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.34 – 8.29 (m, 2H, ArH), 8.00 – 7.96 (m, 2H, ArH), 6.48 (d, *J* = 9.4 Hz, 1H, NH), 5.47 (ddd, *J* = 9.4, 6.9, 5.2 Hz, 1H, CH), 3.45 (s, 3H, OCH₃), 3.30 – 3.20 (m, 2H, CH₂I), 2.33 – 2.23 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 165.3, 149.9, 139.1, 128.3, 123.9, 82.1, 56.7, 39.2, -1.3;

IR (film): $\tilde{\nu}$ = 3293 (w), 2930 (w), 1652 (m), 1601 (m), 1522 (s), 1487 (m), 1346 (s), 1105 (m), 1065 (m), 868 (m), 838 (m);

HRMS (APCI) calcd. for C₁₀H₁₀IN₂O₃⁺ [M-OCH₃]⁺ 332.9731; Found 332.9733.

N-(3-Iodo-1-methoxypropyl)-3-methoxybenzamide (4g).

Following GP B, starting from N-cyclopropyl-3-methoxybenzamide **3g** (57.3 mg, 0.300 mmol), N-(3-iodo-1-methoxypropyl)-3-methoxybenzamide **4g** (96.0 mg, 0.275 mmol, 92%) was obtained as a yellow oil after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.36 (silica, pentanes:ethyl acetate 3:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.38 (s, 1H, ArH), 7.32 (d, *J* = 4.9 Hz, 2H, ArH), 7.04 (td, *J* = 4.9, 2.7 Hz, 1H, ArH), 6.61 (d, *J* = 9.5 Hz, 1H, NH), 5.42 (ddd, *J* = 9.5, 7.1, 5.2 Hz, 1H, CH), 3.82 (s, 3H, OCH₃), 3.40 (s, 3H, OCH₃), 3.27 – 3.14 (m, 2H, CH₂I), 2.30 – 2.17 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 167.3, 159.8, 135.0, 129.6, 118.7, 118.1, 112.5, 81.7, 56.2, 55.4, 39.3, - 1.0;

IR (film): $\tilde{\nu}$ = 3297 (w), 2934 (w), 2833 (w), 1645 (s), 1583 (s), 1524 (s), 1485 (s), 1358 (w), 1310 (m), 1290 (m), 1251 (m), 1103 (m), 1145 (s), 994 (w), 746 (m);

HRMS (ESI) calcd. for C₁₂H₁₆INNaO₃⁺ [M+Na]⁺ 372.0067; Found 372.0069.

N-(3-Iodo-1-methoxypropyl)-2-methoxybenzamide (4h).

Following GP B, starting from N-cyclopropyl-2-methoxybenzamide **3h** (57.3 mg, 0.300 mmol) and after stirring for 1 hour, N-(3-iodo-1-methoxypropyl)-2-methoxybenzamide **4h** (87.5 mg, 0.251 mmol, 84%) was obtained as a yellow oil after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.45 (silica, pentanes:ethyl acetate 3:1);

¹H NMR (400 MHz, CDCl₃): δ = 8.19 (dd, *J* = 7.8, 1.9 Hz, 1H, *ArH*), 7.99 (d, *J* = 9.4 Hz, 1H, *ArH*), 7.48 (ddd, *J* = 8.8, 7.4, 1.9 Hz, 1H, *ArH*), 7.09 (t, *J* = 7.6 Hz, 1H, *ArH*), 6.99 (d, *J* = 8.3 Hz, 1H, *NH*), 5.47 (ddd, *J* = 9.3, 7.0, 5.3 Hz, 1H, *CH*), 3.97 (s, 3H, OCH₃), 3.42 (s, 3H, OCH₃), 3.30 – 3.18 (m, 2H, CH₂I), 2.34 – 2.19 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 165.5, 157.5, 133.3, 132.5, 121.4, 120.8, 111.4, 81.5, 56.2, 56.0, 39.9, - 0.9;

IR (film): $\tilde{\nu}$ = 3376 (w), 2932 (w), 2834 (w), 1656 (s), 1600 (m), 1516 (s), 1482 (s), 1464 (m), 1293 (m), 1237 (s), 1098 (s), 1019 (m), 843 (w), 755 (s);

HRMS (ESI) calcd. for C₁₂H₁₆INNaO₃⁺ [M+Na]⁺ 372.0067; Found 372.0078.

N-(3-Iodo-1-methoxypropyl)-2,4,6-trimethylbenzamide (4i).

Following GP B, starting from N-cyclopropyl-2,4,6-trimethylbenzamide **3i** (61.0 mg, 0.300 mmol) and after stirring for 1 hour, N-(3-iodo-1-methoxypropyl)-2,4,6-trimethylbenzamide **4i** (76.7 mg, 0.212 mmol, 71%) was obtained as a pale yellow solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.50 (silica, pentanes:ethyl acetate 3:1);

Mp: 97-99 °C;

¹H NMR (400 MHz, CDCl₃): δ = 6.85 (s, 2H, ArH), 5.84 (d, *J* = 9.5 Hz, 1H, NH), 5.40 (ddd, *J* = 9.7, 6.8, 5.6 Hz, 1H, CH), 3.52 (s, 3H, OCH₃), 3.23 (td, *J* = 7.5, 7.1, 1.5 Hz, 2H, CH₂I), 2.31 (s, 6H, CH₃), 2.27 (s, 3H, CH₃), 2.19 (qd, *J* = 7.4, 2.0 Hz, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 170.6, 138.7, 134.4, 133.8, 128.3, 81.4, 56.7, 39.6, 21.0, 19.3, -1.2;

IR (film): $\tilde{\nu}$ = 3252 (w), 2924 (m), 2854 (w), 1644 (s), 1523 (s), 1442 (m), 1310 (w), 1176 (m), 1099 (m), 1067 (m), 847 (w);

HRMS (ESI) calcd. for C₁₄H₂₀INNaO₂⁺ [M+Na]⁺ 384.0431; Found 384.0436.

N-(3-Iodo-1-methoxypropyl)furan-2-carboxamide (4j).

Following GP B, starting from N-cyclopropylfuran-2-carboxamide **3j** (45.3 mg, 0.300 mmol), N-(3-iodo-1-methoxypropyl)furan-2-carboxamide **4j** (88.7 mg, 0.287 mmol, 96%) was obtained as a yellow oil after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.29 (silica, pentanes:ethyl acetate 3:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.49 – 7.43 (m, 1H, ArH), 7.16 (d, *J* = 3.1 Hz, 1H, ArH), 6.57 (d, *J* = 9.9 Hz, 1H, NH), 6.52 (dd, *J* = 3.5, 1.8 Hz, 1H, ArH), 5.37 (ddd, *J* = 9.8, 7.2, 5.2 Hz, 1H, CH), 3.39 (s, 3H, OCH₃), 3.25 – 3.14 (m, 2H, CH₂I), 2.33 – 2.15 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 158.2, 147.1, 144.3, 115.3, 112.4, 80.9, 56.2, 39.5, -1.1;

IR (film): $\tilde{\nu}$ = 3285 (w), 2930 (w), 1650 (w), 1589 (s), 1512 (s), 1471 (s), 1310 (m), 1291 (m), 1174 (s), 1103 (s), 1065 (s), 1010 (s);

HRMS (ESI) calcd. for C₉H₁₂INNaO₃⁺ [M+Na]⁺ 331.9754; Found 331.9762.

N-(3-Iodo-1-methoxypropyl)cinnamamide (4k).

Following GP B, starting from N-cyclopropylcinnamamide **3k** (56.2 mg, 0.300 mmol), N-(3-iodo-1-methoxypropyl)cinnamamide **4k** (83.1 mg, 0.241 mmol, 80%) was obtained as a yellow solid after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.40 (silica, pentanes:ethyl acetate 3:1);

Mp: 93–95 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.69 (d, *J* = 15.6 Hz, 1H, vinylH), 7.51 (dd, *J* = 6.6, 2.9 Hz, 2H, ArH), 7.42 – 7.33 (m, 3H, ArH), 6.41 (d, *J* = 15.6 Hz, 1H, vinylH), 5.91 (d, *J* = 9.8 Hz, 1H, NH), 5.38 (ddd, *J* = 9.7, 7.1, 5.3 Hz, 1H, CH), 3.41 (s, 3H, OCH₃), 3.27 – 3.16 (m, 2H, CH₂I), 2.21 (ddt, *J* = 14.3, 11.9, 6.7 Hz, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 165.9, 142.6, 134.4, 130.0, 128.9, 127.9, 119.8, 81.3, 56.3, 39.6, -1.0;

IR (film): $\tilde{\nu}$ = 3264 (m), 3028 (w), 2926 (m), 2853 (w), 1657 (s), 1623 (s), 1530 (s), 1449 (m), 1358 (m), 1336 (m), 1203 (s), 1110 (s), 1068 (s), 976 (m), 862 (w), 765 (m);

HRMS (ESI) calcd. for $C_{13}H_{16}INNaO_2^+$ $[M+Na]^+$ 368.0118; Found 368.0118.

N-(3-Iodo-1-methoxypropyl)-2-phenylacetamide (4l).

Following GP B, starting from N-cyclopropyl-2-phenylacetamide **3l** (52.6 mg, 0.300 mmol), N-(3-iodo-1-methoxypropyl)-2-phenylacetamide **4l** (75.0 mg, 0.225 mmol, 75%) was obtained as a yellow solid after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.40 (silica, pentanes:ethyl acetate 3:1);

Mp: 84-87 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.40 – 7.34 (m, 2H, ArH), 7.33 – 7.28 (m, 1H, ArH), 7.26 (dd, *J* = 6.1, 2.3 Hz, 2H, ArH), 5.60 (d, *J* = 9.5 Hz, 1H, NH), 5.19 (ddd, *J* = 9.6, 7.1, 5.2 Hz, 1H, CH), 3.61 (d, *J* = 3.7 Hz, 2H, CH₂), 3.29 (s, 3H, OCH₃), 3.08 (td, *J* = 7.6, 7.1, 1.4 Hz, 2H, CH₂I), 2.10 – 1.97 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 171.3, 134.3, 129.3, 129.2, 127.6, 81.2, 56.1, 43.9, 39.2, -1.3;

IR (film): $\tilde{\nu}$ = 3279 (w), 3062 (w), 3030 (w), 2930 (w), 1654 (s), 1535 (m), 1496 (m), 1176 (m), 1111 (m), 1068 (m), 724 (m);

HRMS (ESI) calcd. for $C_{12}H_{16}INNaO_2^+$ $[M+Na]^+$ 356.0118; Found 356.0123.

N-(3-Iodo-1-methoxypropyl)-2-naphthamide (4m).

Following GP B, starting from N-cyclopropyl-2-naphthamide **3m** (63.4 mg, 0.300 mmol), N-(3-iodo-1-methoxypropyl)-2-naphthamide **4m** (97.5 mg, 0.264 mmol, 88%) was obtained as a yellow solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.58 (silica, pentanes:ethyl acetate 3:1);

Mp: 96-98 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.32 (s, 1H, ArH), 7.95 – 7.83 (m, 4H, ArH), 7.57 (pd, *J* = 6.9, 1.5 Hz, 2H, ArH), 6.54 (d, *J* = 9.6 Hz, 1H, NH), 5.52 (ddd, *J* = 9.6, 7.0, 5.2 Hz, 1H, CH), 3.47 (s, 3H, OCH₃), 3.34 – 3.20 (m, 2H, CH₂I), 2.39 – 2.24 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 167.4, 134.9, 132.5, 130.8, 129.0, 128.7, 128.0, 127.8, 127.7, 126.9, 123.4, 81.8, 56.4, 39.6, -1.0;

IR (film): $\tilde{\nu}$ = 3296 (w), 3058 (w), 2925 (m), 2852 (w), 1645 (s), 1527 (s), 1503 (m), 1309 (m), 1066 (m), 863 (w);

HRMS (ESI) calcd. for $C_{15}H_{16}INNaO_2^+$ $[M+Na]^+$ 392.0118; Found 392.0115.

N-(3-Iodo-1-methoxypropyl)pivalamide (4n).

Following GP B, starting from N-cyclopropylpivalamide **3n** (42.4 mg, 0.300 mmol), N-(3-iodo-1-methoxypropyl)pivalamide **4n** (78.6 mg, 0.263 mmol, 88%) was obtained as a dark yellow solid after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.48 (silica, pentanes:ethyl acetate 3:1);

Mp: 76–78 °C;

¹H NMR (400 MHz, CDCl₃): δ = 5.81 (d, *J* = 9.5 Hz, 1H, NH), 5.23 (ddd, *J* = 9.5, 7.1, 5.2 Hz, 1H, CH), 3.33 (s, 3H, OCH₃), 3.26 – 3.05 (m, 2H, CH₂I), 2.21 – 2.08 (m, 2H, CH₂CH₂I), 1.22 (s, 9H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 178.7, 81.1, 56.0, 39.5, 38.9, 27.5, -1.1;

IR (film): $\tilde{\nu}$ = 3329 (w), 2961 (m), 2934 (m), 1650 (s), 1518 (s), 1367 (w), 1190 (m), 1110 (m), 1069 (m);

HRMS (ESI) calcd. for C₉H₁₈INNaO₂⁺ [M+Na]⁺ 322.0274; Found 322.0282.

***tert*-Butyl (3-iodo-1-methoxypropyl)carbamate (4o).**

Following GP B, starting from *tert*-butyl cyclopropylcarbamate **3o** (47.2 mg, 0.300 mmol) and without the addition of diphenyl phosphate, *tert*-butyl (3-iodo-1-methoxypropyl)carbamate **4o** (89.0 mg, 0.282 mmol, 94%) was obtained as a pale yellow oil after purification by column chromatography on silica using 4:1 pentanes:ethyl acetate as eluent. K₂CO₃ (0.300 mmol, 1.00 equiv.) has to be added to the reaction mixture before purification.

R_f: 0.45 (silica, pentanes:ethyl acetate 6:1);

¹H NMR (400 MHz, Methanol-*d*₄): δ = 4.85 – 4.80 (m, 2H, NH + CH), 3.27 (s, 3H, OCH₃), 3.16 (td, *J* = 7.1, 2.5 Hz, 2H, CH₂I), 2.12 – 2.03 (m, 1H, CH₂CH₂I), 1.95 (dtd, *J* = 14.4, 7.4, 5.7 Hz, 1H, CH₂CH₂I), 1.42 (s, 9H, CH₃);

¹³C NMR (101 MHz, Methanol-*d*₄): δ = 157.9, 84.2, 80.5, 55.5, 39.7, 28.6, 0.4;

IR (film): $\tilde{\nu}$ = 3335 (w), 2977 (w), 2931 (w), 2832 (w), 1698 (s), 1513 (m), 1366 (m), 1244 (s), 1161 (s), 1086 (m), 994 (m), 865 (m);

HRMS (ESI) calcd. for C₉H₁₈INNaO₃⁺ [M+Na]⁺ 338.0224; Found 338.0226.

Benzyl (3-iodo-1-methoxypropyl)carbamate (4p).

Following GP B, starting from benzyl cyclopropylcarbamate **3p** (57.4 mg, 0.300 mmol) and without the addition of diphenyl phosphate, benzyl (3-iodo-1-methoxypropyl)carbamate **4p** (84.0 mg, 0.241 mmol, 80%) was obtained as a colorless oil after purification by column chromatography on silica using 4:1 pentanes:ethyl acetate as eluent. K_2CO_3 (0.300 mmol, 1.00 equiv.) has to be added to the reaction mixture before purification.

R_f: 0.40 (silica, pentanes:ethyl acetate 4:1);

¹H NMR (400 MHz, $CDCl_3$): δ = 7.48 – 7.28 (m, 5H, ArH), 5.13 (s, 2H, OCH_2), 5.07 (d, J = 10.0 Hz, 1H, NH), 4.99 (td, J = 10.3, 8.6, 5.8 Hz, 1H, CH), 3.38 (s, 3H, OCH_3), 3.17 (t, J = 7.1 Hz, 2H, CH_2I), 2.14 (tt, J = 14.1, 7.8 Hz, 2H, CH_2CH_2I);

¹³C NMR (101 MHz, $CDCl_3$): δ = 155.8, 136.0, 128.6, 128.3, 128.1, 83.6, 67.0, 55.9, 39.4, -0.7;

IR (film): $\tilde{\nu}$ = 3317 (w), 3033 (w), 2934 (w), 2831 (w), 1698 (s), 1521 (s), 1453 (m), 1227 (s), 1200 (s), 1089 (s), 1036 (s), 979 (s), 855 (w), 735 (m), 696 (s);

HRMS (ESI) calcd. for $C_{12}H_{16}INaO_3^+$ $[M+Na]^+$ 372.0067; Found 372.0078.

N-(3-Iodo-1-methoxypropyl)-4-methylbenzenesulfonamide (4q).

Following GP B, starting from N-cyclopropyl-4-methylbenzenesulfonamide **3q** (63.4 mg, 0.300 mmol), without the addition of diphenyl phosphate. After stirring for 20 hours, N-(3-iodo-1-methoxypropyl)-4-methylbenzenesulfonamide **4q** (101 mg, 0.274 mmol, 91%) was obtained as a yellow oil after purification by column chromatography on silica using 4:1 pentanes:ethyl acetate as eluent.

R_f: 0.29 (silica, pentanes:ethyl acetate 3:1);

¹H NMR (400 MHz, Methanol- d_4): δ = 7.72 (d, J = 8.4 Hz, 2H, ArH), 7.33 (d, J = 7.9 Hz, 2H, ArH), 4.52 (dd, J = 7.5, 4.9 Hz, 1H, CH), 3.17 (s, 3H, OCH_3), 3.09 – 2.96 (m, 2H, CH_2I), 2.39 (s, 3H, CH_3), 2.00 (dddd, J = 14.1, 7.5, 6.5, 5.6 Hz, 1H, CH_2CH_2I), 1.71 (dddd, J = 14.5, 8.3, 7.0, 5.0 Hz, 1H, CH_2CH_2I), NH signal was not resolved;

¹³C NMR (101 MHz, Methanol- d_4): δ = 144.7, 140.6, 130.7, 127.8, 87.3, 55.4, 40.2, 21.4, 0.4;

IR (film): $\tilde{\nu}$ = 3272 (m), 2932 (w), 2832 (w), 1598 (w), 1495 (w), 1449 (m), 1324 (m), 1245 (w), 1155 (s), 1114 (m), 1032 (m), 985 (m), 860 (m), 812 (m);

HRMS (ESI) calcd. for $C_{11}H_{16}INaO_3S^+$ $[M+Na]^+$ 391.9788; Found 391.9792.

N-(3-Iodo-1-methoxypropyl)-N,4-dimethylbenzenesulfonamide (4r).

Following GP B, starting from N-cyclopropyl-N,4-dimethylbenzenesulfonamide **3r** (67.6 mg, 0.300 mmol), without the addition of diphenyl phosphate. After stirring for 20 hours, N-(3-iodo-1-methoxypropyl)-N,4-dimethylbenzenesulfonamide **4r** (104 mg, 0.282 mmol, 94%) was obtained as a pale yellow oil after purification by column chromatography on silica using 4:1 pentanes:ethyl acetate as eluent.

R_f: 0.50 (silica, pentanes:ethyl acetate 6:1);

¹H NMR (400 MHz, Acetone-*d*₆): δ = 7.77 (d, *J* = 8.3 Hz, 2H, ArH), 7.44 (d, *J* = 8.0 Hz, 2H, ArH), 5.10 (dd, *J* = 8.3, 4.4 Hz, 1H, CH), 3.21 (s, 3H, OCH₃), 3.19 – 3.13 (m, 2H, CH₂I), 2.68 (s, 3H, NCH₃), 2.43 (s, 3H, ArCH₃), 2.12 (ddd, *J* = 14.2, 8.2, 5.9 Hz, 1H, CH₂CH₂I), 1.68 (dtd, *J* = 14.6, 7.9, 4.4 Hz, 1H, CH₂CH₂I);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 144.4, 138.0, 130.6, 127.9, 89.3, 56.0, 37.4, 27.5, 21.4, 1.3;

IR (film): $\tilde{\nu}$ = 2938 (w), 2831 (w), 1597 (w), 1494 (w), 1449 (w), 1340 (s), 1216 (m), 1185 (m), 1153 (s), 1099 (m), 932 (s), 814 (m);

HRMS (ESI) calcd. for C₁₂H₁₈INNaO₃S⁺ [M+Na]⁺ 405.9944; Found 405.9960.

***tert*-Butyl benzyl(3-iodo-1-methoxypropyl)carbamate (4s).**

Following GP B, starting from *tert*-butyl benzyl(cyclopropyl)carbamate **3s** (74.2 mg, 0.300 mmol) and without the addition of diphenyl phosphate, *tert*-butyl benzyl(3-iodo-1-methoxypropyl)carbamate **4s** (110 mg, 0.271 mmol, 90%) was obtained as a colorless oil after purification by column chromatography on silica using 6:1 pentanes:ethyl acetate as eluent. K₂CO₃ (0.300 mmol, 1.00 equiv.) has to be added to the reaction mixture before purification.

R_f: 0.44 (silica, pentanes:ethyl acetate 8:1);

¹H NMR (400 MHz, Acetone-*d*₆): δ = 7.47 – 7.14 (m, 5H, ArH), 5.61 – 5.34 (m, 1H, CH), 4.62 – 4.42 (m, 1H, ArCH₂), 4.24 (d, *J* = 16.2 Hz, 1H, ArCH₂), 3.10 (m, 5H, OCH₃ + CH₂I), 2.06 – 2.02 (m, 1H, CH₂), 1.97 – 1.85 (m, 1H, CH₂), 1.59 – 1.31 (m, 9H, CH₃);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = ¹³C NMR (101 MHz,) δ 156.4, 140.9, 129.1, 129.0, 128.4, 128.2, 127.8, 127.5, 88.7, 87.5, 80.8, 80.6, 55.7, 45.1, 44.3, 38.5, 28.4, 1.9, 1.6; Mixture of 2 rotamers with almost 1:1 ratio. They are not completely resolved.

IR (film): $\tilde{\nu}$ = 2975 (w), 2933 (w), 1695 (s), 1453 (w), 1403 (m), 1379 (m), 1366 (m), 1252 (m), 1158 (s), 1074 (m), 956 (w), 889 (w);

HRMS (ESI) calcd. for C₁₆H₂₄INNaO₃⁺ [M+Na]⁺ 428.0693; Found 428.0700.

Benzyl ((2S)-1-((3-iodo-1-methoxypropyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (4t).

Following GP B, starting from benzyl (S)-1-(cyclopropylamino)-1-oxo-3-phenylpropan-2-yl)carbamate **3t** (33.8 mg, 0.100 mmol), N-Iodosuccinimide (23.6 mg, 0.105 mmol, 1.05 equiv.), methanol (4.8 μ L, 0.120 mmol, 1.2 equiv.) and diphenyl phosphate (2.5 mg, 0.010 mmol, 0.10 equiv.) were dissolved in 0.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 3 hours. Benzyl ((2S)-1-((3-iodo-1-methoxypropyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate **4t** (34.2 mg, 0.0690 mmol, 69%) was obtained as a beige solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.30 (silica, pentanes:ethyl acetate 3:1);

Mp: 120-122 °C;

¹H NMR (400 MHz, Acetone-*d*₆; mixture of diastereoisomers in a 1 :1 ratio: the signals corresponding to the two diastereoisomers are partially resolved): δ = 7.56 (d, *J* = 9.4 Hz, 1H, NH), 7.50 (d, *J* = 9.5 Hz, 1H, NH), 7.39 – 7.15 (m, 10H, ArH), 6.59 (d, *J* = 8.1 Hz, 1H, NH), 6.53 (d, *J* = 8.4 Hz, 1H, NH), 5.20 – 5.08 (m, 1H, CH), 5.02 (s, 2H, OCH₂), 4.41 (dtd, *J* = 20.8, 8.4, 6.2 Hz, 1H, CH), 3.28 – 3.17 (m, 3H, OCH₃), 3.18 – 3.10 (m, 2H, PhCH₂), 3.10 – 3.03 (m, 1H, CH₂I), 3.02 – 2.93 (m, 1H, CH₂I), 2.19 – 2.10 (m, 1H, CH₂CH₂I), 2.09 – 2.07 (m, 1H, CH₂CH₂I), 1.97 – 1.85 (m, 1H, CH₂CH₂I);

¹³C NMR (101 MHz, Acetone-*d*₆; mixture of diastereoisomers in a 1 :1 ratio: the signals corresponding to the two diastereoisomers are partially resolved): δ = 172.7, 172.6, 156.8, 138.5, 138.4, 138.2, 138.1, 130.2, 129.2, 129.2, 129.1, 128.6, 128.6, 128.6, 128.5, 127.4, 127.4, 81.9, 81.6, 66.7, 66.7, 57.7, 57.7, 55.7, 55.7, 40.0, 39.8, 38.8, 38.7, 1.0, 0.9;

IR (film): $\tilde{\nu}$ = 3289 (m), 3030 (w), 2932 (w), 1664 (s), 1537 (s), 1256 (m), 1066 (m), 745 (m), 698(m);

HRMS (APPI) calcd. for C₂₁H₂₅IN₂NaO₄⁺ [M+Na]⁺ 519.0751; Found 519.0751.

N-(3-Iodo-1-methoxypropyl)-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetamide (4u).

Following GP B, starting from N-cyclopropyl-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetamide **3u** (30.7 mg, 0.100 mmol), N-Iodosuccinimide (23.6 mg, 0.105 mmol, 1.05 equiv.), methanol (4.8 μ L, 0.120 mmol, 1.2 equiv.) and diphenyl phosphate (2.5 mg, 0.010 mmol, 0.10 equiv.) were dissolved in 0.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 1 hour. N-(3-Iodo-1-methoxypropyl)-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetamide **4u** (40.7 mg, 0.0880 mmol, 88%) was obtained as a yellow oil after purification by column chromatography on silica, using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.50 (silica, pentanes:ethyl acetate 1:1);

¹H NMR (400 MHz, Acetone-*d*₆): δ = 8.09 (s, 1H, ArH), 7.84 (d, *J* = 7.6 Hz, 1H, ArH), 7.69 – 7.58 (m, 2H, ArH), 7.58 – 7.49 (m, 3H, ArH + NH), 7.04 (d, *J* = 8.4 Hz, 1H, ArH), 5.29 (s, 2H, OCH₂), 5.18 (dt, *J* = 9.4, 6.3 Hz, 1H, CH), 3.61 (d, *J* = 2.4 Hz, 2H, CH₂), 3.31 – 3.16 (m, 5H, OCH₃ + CH₂I), 2.17 (dd, *J* = 14.0, 6.9 Hz, 1H, CH₂CH₂I), 2.11 – 2.06 (m, 1H, CH₂CH₂I);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 190.8, 171.6, 161.1, 141.4, 137.2, 137.1, 133.7, 132.7, 130.8, 129.9, 129.9, 128.9, 125.9, 121.5, 81.7, 74.1, 55.8, 42.7, 40.0, 1.0;

IR (film): $\tilde{\nu}$ = 3292 (w), 2930(w), 1647 (s), 1609 (m), 1530 (m), 1487 (s), 1378 (m), 1299 (s), 1253 (m), 1120 (m), 1069 (m), 1015 (m), 831 (w), 760 (m);

HRMS (APCI) calcd. for C₂₀H₂₀INNaO₄⁺ [M+Na]⁺ 488.0329; Found 488.0335.

2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N-(3-iodo-1-methoxypropyl)acetamide (4v).

Following GP B, starting from 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N-cyclopropylacetamide **3v** (39.6 mg, 0.100 mmol), N-Iodosuccinimide (47.3 mg, 0.210 mmol, 2.1 equiv.), methanol (4.8 μ L, 0.120 mmol, 1.2 equiv.) and diphenyl phosphate (2.5 mg, 0.010 mmol, 0.10 equiv.) were dissolved in 0.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 4 hours. 2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N-(3-iodo-1-methoxypropyl)acetamide **4v** (24.4 mg, 0.0440 mmol, 44%) was obtained as a pale yellow solid after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.30 (silica, pentanes:ethyl acetate 2:1);

Mp: 135-138 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 7.77 – 7.72 (m, 2H, ArH), 7.66 – 7.61 (m, 2H, ArH), 7.47 (d, *J* = 10.0 Hz, 1H, NH), 7.14 (d, *J* = 2.6 Hz, 1H, ArH), 7.02 (d, *J* = 9.0 Hz, 1H, ArH), 6.71 (dd, *J* = 9.0, 2.6 Hz, 1H, ArH), 5.24 – 5.14 (m, 1H, CH), 3.81 (s, 3H, OCH₃), 3.68 (s, 2H, ArCH₂), 3.25 (s, 3H, OCH₃), 3.20 (t, *J* = 7.2 Hz, 2H, CH₂I), 2.33 (s, 3H, CH₃), 2.12 (dt, *J* = 13.8, 7.0 Hz, 1H, CH₂CH₂I), 2.03 – 1.97 (m, 1H, CH₂CH₂I);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 171.0, 168.8, 157.1, 139.2, 136.6, 135.6, 132.1, 131.9, 131.8, 129.9, 115.7, 114.6, 112.5, 102.2, 81.8, 55.9, 55.8, 39.9, 32.5, 13.7, 1.0;

IR (film): $\tilde{\nu}$ = 3296 (w), 2931 (w), 2832 (w), 1680 (s), 1591 (w), 1521 (w), 1477 (s), 1358 (m), 1321 (s), 1224 (m), 1088 (m), 835 (w);

HRMS (APPI) calcd. for C₂₃H₂₄ClIN₂O₄⁺ [M]⁺ 554.0464; Found 554.0463.

N-(3-Bromo-1-methoxypropyl)-4-methoxybenzamide (5).

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (0.300 mmol, 1.0 equiv.), N-bromosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.), methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) and diphenyl phosphate (7.5 mg, 0.030 mmol, 0.10 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. After the completion of the reaction, the crude was directly submitted to column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent. N-(3-Bromo-1-methoxypropyl)-4-methoxybenzamide **5** (81.2 mg, 0.270 mmol, 90%) was obtained as a white solid.

R_f: 0.29 (silica, pentanes:ethyl acetate 2:1);

Mp: 76-78 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.78 (d, J = 8.8 Hz, 2H, ArH), 6.94 (d, J = 8.8 Hz, 2H, ArH), 6.42 (d, J = 9.6 Hz, 1H, NH), 5.53 (ddd, J = 9.6, 6.7, 5.3 Hz, 1H, CH), 3.85 (s, 3H, OCH₃), 3.54 – 3.46 (m, 2H, CH₂Br), 3.42 (s, 3H, OCH₃), 2.34 – 2.20 (m, 2H, CH₂CH₂Br);

¹³C NMR (101 MHz, CDCl₃): δ = 166.8, 162.6, 128.9, 125.8, 113.9, 80.0, 56.2, 55.4, 38.6, 27.9;

IR (film): $\tilde{\nu}$ = 3304 (w), 2936 (w), 2837 (w), 1641 (m), 1605 (s), 1532 (m), 1501 (s), 1310 (m), 1252 (s), 1177 (m), 1106 (m), 1030 (m), 844 (m), 769 (m);

HRMS (ESI) calcd. for C₁₂H₁₆BrNNaO₃⁺ [M+Na]⁺ 324.0206; Found 324.0206.

3-Iodopropanenitrile (9).

Following GP B, starting from cyclopropyl amine (7.0 μ L, 0.10 mmol), N-Iodosuccinimide (23.6 mg, 0.105 mmol, 1.05 equiv.) and methanol (4.8 μ L, 0.12 mmol, 1.2 equiv.) were dissolved in 0.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 0.5 hour. 3-Iodopropanenitrile **9** (7.6 mg, 0.042 mmol, 42%) was obtained as a pale yellow oil after purification by column chromatography on silica, using 4:1 pentanes:ethyl acetate as eluent.

R_f: 0.40 (silica, pentanes:ethyl acetate 4:1);

¹H NMR (400 MHz, CDCl₃): δ = 3.28 (t, J = 7.1 Hz, 2H, CH₂I), 3.01 (t, J = 7.1 Hz, 2H, CH₂CN);

¹³C NMR (101 MHz, CDCl₃): δ = 118.1, 22.5, -6.9;

IR (film): $\tilde{\nu}$ = 2957 (w), 2921 (m), 2852 (w), 2252 (w), 1413 (s), 1250 (s), 1174 (s), 883 (s);

¹³C NMR and IR data correspond to the reported values.^[12]

General Procedure C (GP C):

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (57.3 mg, 0.300 mmol, 1.0 equiv.), N-Iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.), alcohol (0.360 mmol, 1.2 equiv.) and diphenyl phosphate (7.5 mg, 0.030 mmol, 0.10 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The

¹² Irifune, S.; Kibayashi, T.; Ishii, Y.; Ogawa, M. *Synthesis* **1998**, 5, 366-369.

reaction mixture was stirred at room temperature for 30 minutes, if not specified otherwise. After the completion of the reaction, the crude product was directly submitted to column chromatography on silica using pentanes:ethyl acetate as eluent.

N-(1-(Benzyloxy)-3-iodopropyl)-4-methoxybenzamide (10a).

Following GP C, using from phenylmethanol (38.9 mg, 0.360 mmol, 1.2 equiv.), N-(1-(benzyloxy)-3-iodopropyl)-4-methoxybenzamide **10a** (120 mg, 0.282 mmol, 94%) was obtained as a yellow oil after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.33 (silica, pentanes:ethyl acetate 3:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.74 (d, *J* = 8.8 Hz, 2H, ArH), 7.40 – 7.26 (m, 5H, ArH), 6.94 (d, *J* = 8.8 Hz, 2H, ArH), 6.36 (d, *J* = 9.7 Hz, 1H, NH), 5.68 (ddd, *J* = 9.7, 7.3, 4.9 Hz, 1H, CH), 4.72 – 4.60 (m, 2H, CH₂), 3.86 (s, 3H, OCH₃), 3.32 – 3.13 (m, 2H, CH₂I), 2.40 – 2.21 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 166.7, 162.6, 137.8, 128.9, 128.5, 127.9, 127.8, 125.7, 113.9, 80.1, 70.8, 55.5, 39.8, -0.8;

IR (film): $\tilde{\nu}$ = 3306 (w), 3030 (w), 2938 (w), 2837 (w), 1640 (s), 1606 (s), 1532 (m), 1501 (s), 1307 (m), 1255 (s), 1177 (s), 1100 (m), 1063 (m), 1028 (s), 844 (m), 737 (m);

HRMS (ESI) calcd. for C₁₈H₂₀INNaO₃⁺ [M+Na]⁺ 448.0380; Found 448.0384.

N-(3-Iodo-1-(prop-2-yn-1-yloxy)propyl)-4-methoxybenzamide (10b).

Following GP C, using from prop-2-yn-1-ol (20.2 mg, 0.360 mmol, 1.2 equiv.) and after stirring for 1 hour, N-(3-iodo-1-(prop-2-yn-1-yloxy)propyl)-4-methoxybenzamide **10b** (91.2 mg, 0.244 mmol, 81%) was obtained as a yellow solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.40 (silica, pentanes:ethyl acetate 3:1);

Mp: 78-80 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.77 (d, *J* = 8.8 Hz, 2H, ArH), 6.94 (d, *J* = 8.8 Hz, 2H, ArH), 6.39 (d, *J* = 9.6 Hz, 1H, NH), 5.67 (ddd, *J* = 9.6, 7.3, 5.0 Hz, 1H, CH), 4.34 – 4.24 (m, 2H, CH₂), 3.86 (s, 3H, OCH₃), 3.33 – 3.16 (m, 2H, CH₂I), 2.43 (t, *J* = 2.4 Hz, 1H, alkynylH), 2.38 – 2.22 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 166.8, 162.7, 129.0, 125.5, 113.9, 80.1, 79.7, 74.4, 56.3, 55.5, 39.5, -1.3;

IR (film): $\tilde{\nu}$ = 3291 (w), 2957 (w), 2924 (w), 2854 (w), 1642 (m), 1605 (s), 1530 (m), 1498 (s), 1307 (m), 1253 (s), 1176 (s), 1062 (s), 1029 (s), 909 (w), 843 (m), 607 (m);

HRMS (ESI) calcd. for C₁₄H₁₆INNaO₃⁺ [M+Na]⁺ 396.0067; Found 396.0077.

N-(1-(Allyloxy)-3-iodopropyl)-4-methoxybenzamide (10c).

Following GP C, using from prop-2-en-1-ol (20.9 mg, 0.360 mmol, 1.2 equiv.) and after stirring for 1 hour, N-(1-(allyloxy)-3-iodopropyl)-4-methoxybenzamide **10c** (71.1 mg, 0.189 mmol, 63%) was obtained as a yellow oil after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.41 (silica, pentanes:ethyl acetate 3:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.76 (d, *J* = 8.9 Hz, 2H, ArH), 6.94 (d, *J* = 8.9 Hz, 2H, ArH), 6.38 (d, *J* = 9.6 Hz, 1H, NH), 5.91 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H, vinylH), 5.58 (ddd, *J* = 9.6, 7.2, 5.1 Hz, 1H, CH), 5.29 (dq, *J* = 17.2, 1.7 Hz, 1H, vinylH), 5.18 (dq, *J* = 10.4, 1.4 Hz, 1H, vinylH), 4.21 – 4.05 (m, 2H, CH₂), 3.85 (s, 3H, OCH₃), 3.33 – 3.14 (m, 2H, CH₂I), 2.41 – 2.14 (m, 2H, CH₂CH₂I);

¹³C NMR (101 MHz, CDCl₃): δ = 166.7, 162.6, 134.1, 128.9, 125.7, 117.4, 113.9, 79.9, 69.5, 55.4, 39.7, -0.9;

IR (film): $\tilde{\nu}$ = 3305 (w), 2933 (w), 2839 (w), 1640 (s), 1606 (s), 1532 (m), 1501 (s), 1308 (m), 1255 (s), 1178 (s), 1032 (s), 927 (w), 844 (m), 768 (w);

HRMS (ESI) calcd. for C₁₄H₁₈INNaO₃⁺ [M+Na]⁺ 398.0224; Found 398.0224.

N-(3-Iodo-1-isopropoxypropyl)-4-methoxybenzamide (10d).

Following GP C, using from propan-2-ol (21.6 mg, 0.360 mmol, 1.2 equiv.), N-(3-iodo-1-isopropoxypropyl)-4-methoxybenzamide **10d** (94.6 mg, 0.251 mmol, 84%) was obtained as a yellow oil after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.40 (silica, pentanes:ethyl acetate 3:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.75 (d, *J* = 8.8 Hz, 2H, ArH), 6.92 (d, *J* = 8.9 Hz, 2H, ArH), 6.40 (d, *J* = 9.3 Hz, 1H, NH), 5.60 (ddd, *J* = 9.4, 7.4, 5.0 Hz, 1H, CH), 3.90 (p, *J* = 6.1 Hz, 1H, CH), 3.84 (s, 3H, OCH₃), 3.29 – 3.14 (m, 2H, CH₂I), 2.22 (qd, *J* = 7.4, 5.3 Hz, 2H, CH₂CH₂I), 1.22 (d, *J* = 6.1 Hz, 3H, CH₃), 1.13 (d, *J* = 6.2 Hz, 3H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 166.4, 162.5, 128.8, 125.9, 113.8, 78.1, 69.5, 55.4, 40.0, 23.4, 21.8, -0.4;

IR (film): $\tilde{\nu}$ = 3303 (w), 2969 (w), 2933 (w), 2838 (w), 1638 (s), 1606 (s), 1532 (m), 1501 (s), 1442 (w), 1336 (w), 1255 (s), 1175 (s), 1033 (s), 844 (m);

HRMS (ESI) calcd. for C₁₄H₂₀INNaO₃⁺ [M+Na]⁺ 400.0380; Found 400.0388.

N-(3-Iodo-1-(((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)propyl)-4-methoxybenzamide (10e).

Following GP C, using from (-)-menthol (56.3 mg, 0.360 mmol, 1.2 equiv.), N-(3-iodo-1-(((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)propyl)-4-methoxybenzamide **10e** (120 mg, 0.253 mmol, 84%) was obtained as an off-white solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.45 (silica, pentanes:ethyl acetate 4:1);

Mp: 89-91 °C;

¹H NMR (400 MHz, CDCl₃; mixture of diastereoisomers in a 1.5 :1 ratio: the signals corresponding to the two distereoisomers are partially resolved): δ = 7.79 – 7.70 (m, 4H, ArH, *major+minor*), 6.99 – 6.86 (m, 4H, ArH, *major+minor*), 6.31 (d, *J* = 9.4 Hz, 1H, NH *minor*), 6.25 (d, *J* = 9.4 Hz, 1H, NH *major*), 5.70 – 5.52 (m, 2H, CH, *major+minor*), 3.85 (d, *J* = 1.2 Hz, 6H, OCH₃, *major+minor*), 3.48 (td, *J* = 10.5, 4.3 Hz, 1H, OCH ring *minor*), 3.36 (td, *J* = 10.5, 4.3 Hz, 1H, OCH ring *major*), 3.29 – 3.09 (m, 4H, CH₂I, *major+minor*), 2.40 – 2.07 (m, 8H, CH₂CH₂I *major+minor* + CH₂ ring, *major+minor*), 2.01 – 1.93 (m, 1H, CH ring *minor*), 1.69 – 1.55 (m, 6H, CH₂ ring, *major+minor* + CH₂ ring *minor*), 1.44 – 1.27 (m, 3H, CH *major+minor* + CH ring *major*), 1.22 – 1.12 (m, 2H, CH₂ ring *major*), 1.00 – 0.94 (m, 2H, CH *major+minor*), 0.92 (d, *J* = 6.0 Hz, 6H, CH₃, *major+minor*), 0.88 (d, *J* = 7.1 Hz, 6H, CH₃, *major+minor*), 0.80 (d, *J* = 6.5 Hz, 3H, CH₃ *minor*), 0.62 (d, *J* = 6.9 Hz, 3H, CH₃ *major*);

¹³C NMR (101 MHz, CDCl₃; mixture of diastereoisomers in a 1.5 :1 ratio: the signals corresponding to the two distereoisomers are partially resolved): δ = 166.4, 166.0, 162.5, 128.8, 126.2, 125.9, 113.9, 113.8, 81.0, 79.5, 75.7, 55.4, 55.4, 49.1, 47.8, 43.3, 40.9, 40.7, 40.3, 34.4, 34.2, 31.6, 31.3, 25.5, 25.4, 22.9, 22.8, 22.3, 21.3, 21.1, 16.1, 15.9, -0.5, -0.9;

IR (film): $\tilde{\nu}$ = 3317 (w), 2953 (m), 2922 (m), 2868 (w), 1636 (m), 1606 (s), 1501 (m), 1257 (s), 1178 (m), 1026 (m), 844 (m);

HRMS (ESI) calcd. for C₂₁H₃₂INNaO₃⁺ [M+Na]⁺ 496.1319; Found 496.1323.

N-(1-(2-Hydroxyethoxy)-3-iodopropyl)-4-methoxybenzamide (10f).

Following GP C, using from ethane-1,2-diol (22.3 mg, 0.360 mmol, 1.2 equiv.) and after stirring for 1 hour, N-(1-(2-hydroxyethoxy)-3-iodopropyl)-4-methoxybenzamide **10f** (65.0 mg, 0.171 mmol, 57%) was obtained as a yellow oil after purification by column chromatography on silica using 2:3 pentanes:ethyl acetate as eluent.

R_f: 0.22 (silica, pentanes:ethyl acetate 2:3);

¹H NMR (400 MHz, Acetone-*d*₆): δ = 7.98 – 7.81 (m, 3H, *ArH* + *NH*), 7.05 – 6.93 (m, 2H, *ArH*), 5.55 (ddd, *J* = 9.2, 7.2, 5.4 Hz, 1H, *CH*), 3.86 (s, 3H, *OCH*₃), 3.70 – 3.59 (m, 4H, *OCH*₂*CH*₂*O*), 3.35 (t, *J* = 7.2 Hz, 2H, *CH*₂*I*), 2.35 (dq, *J* = 13.9, 6.9 Hz, 1H, *CH*₂*CH*₂*I*), 2.26 – 2.16 (m, 1H, *CH*₂*CH*₂*I*);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 167.3, 163.4, 130.2, 127.3, 114.3, 81.3, 70.6, 62.0, 55.8, 40.1, 1.5; **IR** (film): $\tilde{\nu}$ = 3307 (w), 2934 (w), 2872 (w), 2839 (w), 1708 (m), 1640 (m), 1605 (s), 1534 (m), 1501 (s), 1255 (s), 1177 (s), 1106 (m), 1027 (s), 844 (m), 768 (w);

HRMS (ESI) calcd. for C₁₃H₁₈INNaO₄⁺ [*M*+*Na*]⁺ 402.0173; Found 402.0181.

N-(1-(*tert*-Butylperoxy)-3-iodopropyl)-4-methoxybenzamide (10g).

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (0.300 mmol, 1.0 equiv.), iodine (83.8 mg, 0.330 mmol, 1.1 equiv.), a *tert*-butyl hydroperoxide solution, 5.0-6.0 M in decane (72.0 μL, 0.360 mmol, 1.2 equiv.) and diphenyl phosphate (7.5 mg, 0.030 mmol, 0.10 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. After the completion of the reaction, the crude product was directly submitted to column chromatography on silica using 4:1 pentanes:ethyl acetate as eluent. N-(1-(*tert*-Butylperoxy)-3-iodopropyl)-4-methoxybenzamide **10g** (83.2 mg, 0.204 mmol, 68%) was obtained as a yellow oil.

R_f: 0.38 (silica, pentanes:ethyl acetate 4:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.77 (d, *J* = 8.8 Hz, 2H, *ArH*), 6.93 (d, *J* = 8.8 Hz, 2H, *ArH*), 6.58 (d, *J* = 8.8 Hz, 1H, *NH*), 5.91 (ddd, *J* = 8.9, 7.1, 5.7 Hz, 1H, *CH*), 3.85 (s, 3H, *OCH*₃), 3.30 – 3.16 (m, 2H, *CH*₂*I*), 2.51 – 2.39 (m, 1H, *CH*₂*CH*₂*I*), 2.35 – 2.24 (m, 1H, *CH*₂*CH*₂*I*), 1.23 (s, 9H, *CH*₃);

¹³C NMR (101 MHz, CDCl₃): δ = 166.4, 162.5, 129.0, 126.0, 113.8, 83.7, 80.9, 55.4, 37.2, 26.4, -1.6;

IR (film): $\tilde{\nu}$ = 3312 (w), 2976 (m), 2933 (w), 2838 (w), 1647 (s), 1606 (s), 1534 (m), 1503 (s), 1363 (m), 1255 (s), 1177 (s), 1031 (m), 845 (m);

HRMS (ESI) calcd. for $C_{15}H_{22}INNaO_4^+$ $[M+Na]^+$ 430.0486; Found 430.0483.

N-(1-Hydroperoxy-3-iodopropyl)-4-methoxybenzamide (10h).

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (57.3 mg, 0.300 mmol, 1.0 equiv.), iodine (83.8 mg, 0.330 mmol, 1.1 equiv.), a hydrogen peroxide 30% aqueous solution (61.3 μ L, 0.600 mmol, 2.0 equiv.) and diphenyl phosphate (7.5 mg, 0.030 mmol, 0.10 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. After the completion of the reaction, the crude product was directly submitted to column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent. N-(1-Hydroperoxy-3-iodopropyl)-4-methoxybenzamide **10h** (94.6 mg, 0.269 mmol, 90%) was obtained as a grey solid.

R_f: 0.30 (silica, pentanes:ethyl acetate 3:2);

¹H NMR (400 MHz, Acetone-*d*₆): δ = 10.94 (s, 1H, OOH), 8.08 (d, *J* = 8.9 Hz, 1H, NH), 7.93 (d, *J* = 8.8 Hz, 2H, ArH), 6.99 (d, *J* = 8.8 Hz, 2H, ArH), 5.90 (dt, *J* = 8.8, 6.7 Hz, 1H, CH), 3.86 (s, 3H, OCH₃), 3.34 (t, *J* = 7.2 Hz, 2H, CH₂I), 2.52 (dq, *J* = 14.0, 7.0 Hz, 1H, CH₂CH₂I), 2.27 (dq, *J* = 14.2, 7.5 Hz, 1H, CH₂CH₂I);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 167.0, 163.4, 130.3, 127.4, 114.3, 85.5, 55.8, 36.8, 0.9;

IR (film): $\tilde{\nu}$ = 3280 (w), 2963 (w), 2837 (w), 1635 (m), 1605 (s), 1500 (s), 1254 (s), 1176 (s), 1027 (m), 842 (m), 768 (m);

HRMS (ESI) calcd. for $C_{11}H_{14}INNaO_4^+$ $[M+Na]^+$ 373.9860; Found 373.9857.

4. Flexible conversion of aminocyclopropanes

N-(3-Iodo-1-(methylsulfonamido)propyl)-4-methoxybenzamide (11).

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (57.3 mg, 0.300 mmol, 1.0 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.), diphenyl phosphate (7.5 mg, 0.030 mmol, 0.1 equiv.), and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. Methanesulfonamide (85.6 mg, 0.900 mmol, 3.0 equiv.) was then added and the reaction mixture was stirred at room temperature for another 10 minutes. After the completion of the reaction, the crude product was directly submitted to column chromatography on silica using 2:3 pentanes:Et₂O as eluent. N-(3-Iodo-1-(methylsulfonamido)propyl)-4-methoxybenzamide **11** (84.9 mg, 0.206 mmol, 69%) was obtained as a pale yellow solid.

R_f: 0.26 (silica, pentanes:diethyl ether 2:3);

Mp: 102-105 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.86 – 7.65 (m, 2H, ArH), 7.03 – 6.83 (m, 2H, ArH), 6.24 (d, J = 9.6 Hz, 1H, NH), 5.45 (ddd, J = 9.6, 7.0, 5.3 Hz, 1H, CH), 3.86 (s, 3H, OCH₃), 3.42 (s, 3H, CH₃), 3.32 – 3.15 (m, 2H, CH₂I), 2.37 – 2.14 (m, 2H, CH₂CH₂I); 1 NH is not resolved.

¹³C NMR (101 MHz, CDCl₃): δ = 166.8, 162.6, 128.9, 125.8, 113.9, 81.6, 56.3, 55.5, 39.6, -1.0;

IR (film): $\tilde{\nu}$ = 3308 (w), 2933 (w), 2835 (w), 1642 (s), 1606 (s), 1532 (m), 1502 (s), 1255 (s), 1176 (m), 1104 (m), 1066 (m), 844 (m);

HRMS (ESI) calcd. for C₁₂H₁₇I₂NaO₄S⁺ [M+Na]⁺ 434.9846; Found 434.9855.

N-(1-Cyano-3-iodopropyl)-4-methylbenzenesulfonamide (12).

Starting from N-cyclopropyl-4-methylbenzenesulfonamide **3q** (21.1 mg, 0.100 mmol, 1.0 equiv.), N-iodosuccinimide (23.6 mg, 0.105 mmol, 1.05 equiv.) and methanol (4.8 μ L, 0.12 mmol, 1.2 equiv.) were dissolved in 0.5 mL of CDCl₃ (0.20 M). After stirring for 20 hours at room temperature, TMSCN (18.8 μ L, 0.150 mmol, 1.5 equiv.) was added to the reaction crude and kept stirring at room

temperature for another 20 hours. N-(1-Cyano-3-iodopropyl)-4-methylbenzenesulfonamide **12** (23.5 mg, 0.0650 mmol, 65%) was obtained as a beige solid after purification by preparative TLC on silica using 4:1 pentanes:ethyl acetate as eluent.

Note: It was later found that N-(1-cyano-3-iodopropyl)-4-methylbenzenesulfonamide **12** can be synthesized simply by replacing methanol with TMSCN. Starting from N-cyclopropyl-4-methylbenzenesulfonamide **3a** (84.4 mg, 0.400 mmol, 1.0 equiv.), NIS (108 mg, 0.480 mmol, 1.2 equiv.) and TMSCN (75.1 μ L, 0.600 mmol, 1.5 equiv.) were dissolved in 2.0 mL of CHCl_3 (0.20 M). After stirring at room temperature for 24 hours, N-(1-cyano-3-iodopropyl)-4-methylbenzenesulfonamide **12** (109 mg, 0.300 mmol, 75%) was obtained as a beige solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

R_f: 0.25 (silica, pentanes:ethyl acetate 4:1);

Mp: 132-133 °C;

¹H NMR (400 MHz, CDCl_3): δ = 7.80 (d, J = 8.4 Hz, 2H, ArH), 7.38 (d, J = 8.0 Hz, 2H, ArH), 5.49 (d, J = 9.8 Hz, 1H, NH), 4.40 (dt, J = 9.9, 7.4 Hz, 1H, CH), 3.21 (t, J = 6.7 Hz, 2H, CH_2I), 2.45 (s, 3H, CH_3), 2.29 (q, J = 6.9 Hz, 2H, $\text{CH}_2\text{CH}_2\text{I}$);

¹³C NMR (101 MHz, CDCl_3): δ = 144.9, 135.6, 130.2, 127.3, 116.6, 45.1, 37.2, 21.7, -2.5;

IR (film): $\tilde{\nu}$ = 3267 (w), 1436 (w), 1337 (m), 1164 (s), 1090 (m), 936 (w), 819 (w), 757 (m);

HRMS (ESI) calcd. for $\text{C}_{11}\text{H}_{13}\text{IN}_2\text{NaO}_2\text{S}^+$ $[\text{M}+\text{Na}]^+$ 386.9635; Found 386.9633.

N-(1-(1-Hydroxynaphthalen-2-yl)-3-iodopropyl)-4-methoxybenzamide (**13**).

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (57.3 mg, 0.300 mmol, 1.0 equiv.), diphenyl phosphate (7.5 mg, 0.030 mmol, 0.1 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of CHCl_3 (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. 1-Naphthol (47.2 mg, 0.360 mmol, 1.2 equiv.) and TFA (23.0 μ L, 0.300 mmol, 1.0 equiv.) were added and the reaction mixture was stirred at room temperature for another 1 hour. After the completion of the reaction, the crude product was directly submitted to column chromatography on silica using 2:1 pentanes: ethyl acetate as eluent. N-(3-Iodo-1-(3-methyl-1H-indol-2-yl)propyl)-4-methoxybenzamide **13** (73.0 mg, 0.159 mmol, 53%) was obtained as a yellow oil.

R_f: 0.44 (silica, pentanes:ethyl acetate 2:1);

¹H NMR (400 MHz, Acetone- d_6): δ = 10.64 (s, 1H, OH), 8.61 (d, J = 8.1 Hz, 1H, NH), 8.43 – 8.25 (m, 1H, ArH), 7.92 (d, J = 8.9 Hz, 2H, ArH), 7.82 – 7.72 (m, 1H, ArH), 7.50 – 7.36 (m, 4H, ArH), 6.98 (d, J = 8.9 Hz, 2H, ArH), 5.65 (td, J = 8.5, 6.3 Hz, 1H, CH), 3.83 (s, 3H, OCH_3), 3.51 – 3.29 (m, 2H, CH_2I), 2.98 – 2.86 (m, 1H, $\text{CH}_2\text{CH}_2\text{I}$), 2.64 (dq, J = 14.1, 7.0 Hz, 1H, $\text{CH}_2\text{CH}_2\text{I}$);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 169.7, 163.7, 152.5, 135.2, 130.4, 128.1, 127.4, 127.2, 126.0, 125.9, 124.8, 123.9, 121.9, 120.5, 114.5, 55.8, 50.0, 37.5, 3.2;
IR (film): $\tilde{\nu}$ = 3253 (brs), 3055 (w), 1695 (w), 1605 (s), 1500 (s), 1257 (s), 1178 (s), 1028 (m), 843 (w);
HRMS (ESI) calcd. for C₂₁H₂₁INO₃⁺ [M+H]⁺ 462.0561; Found 462.0557.

N-(3-Iodo-1-(3-methyl-1H-indol-2-yl)propyl)-4-methoxybenzamide (14).

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (57.3 mg, 0.300 mmol, 1.0 equiv.), diphenyl phosphate (7.5 mg, 0.030 mmol, 0.1 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of CHCl₃ (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. 3-Methylindole (47.2 mg, 0.360 mmol, 1.2 equiv.) and TFA (23.0 μ L, 0.300 mmol, 1.0 equiv.) were added and the reaction mixture was stirred at room temperature for another 20 minutes. After the completion of the reaction, the crude product was directly submitted to column chromatography on silica using 2:1 pentanes: ethyl acetate as eluent. N-(3-Iodo-1-(3-methyl-1H-indol-2-yl)propyl)-4-methoxybenzamide **14** (110 mg, 0.246 mmol, 82%) was obtained as a dark yellow solid.

R_f: 0.33 (silica, pentanes:ethyl acetate 2:1);

Mp: 83-86 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 9.99 (s, 1H, indole-NH), 8.04 (d, *J* = 7.6 Hz, 1H, NH), 7.91 – 7.83 (m, 2H, ArH), 7.47 (d, *J* = 7.8 Hz, 1H, ArH), 7.30 (d, *J* = 8.0 Hz, 1H, ArH), 7.08 – 7.03 (m, 1H, ArH), 7.02 – 6.97 (m, 1H, ArH), 6.96 – 6.89 (m, 2H, ArH), 5.63 (q, *J* = 7.7 Hz, 1H, CH), 3.81 (s, 3H, OCH₃), 3.30 (ddd, *J* = 9.8, 7.6, 6.5 Hz, 1H, CH₂I), 3.21 (dt, *J* = 9.7, 7.2 Hz, 1H, CH₂I), 2.65 (ddt, *J* = 26.6, 14.3, 6.9 Hz, 2H, CH₂CH₂I), 2.39 (s, 3H, CH₃);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 166.7, 163.1, 136.9, 135.0, 130.0, 129.8, 127.7, 122.2, 119.5, 119.2, 114.3, 111.7, 108.5, 55.8, 48.0, 39.5, 9.0, 2.9;

IR (film): $\tilde{\nu}$ = 3303 (m), 2959 (w), 2924 (m), 2854 (w), 1606 (s), 1539 (m), 1504 (s), 1460 (m), 1302 (m), 1256 (s), 1177 (m), 1130 (m), 907 (m), 842 (m);

HRMS (ESI) calcd. for C₂₀H₂₁IN₂NaO₂⁺ [M+Na]⁺ 471.0540; Found 471.0546.

N-(3-Iodopropyl)-4-methoxybenzamide (15).

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (57.3 mg, 0.300 mmol, 1.0 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of acetic acid (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. Sodium cyanoborohydride (28.3 mg, 0.450 mmol, 1.5 equiv.) was added and the reaction mixture was stirred at room temperature for another 30 minutes. After the completion of the reaction, the crude product was directly submitted to column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent. N-(3-iodopropyl)-4-methoxybenzamide **15** (75.0 mg, 0.235 mmol, 78%) was obtained as a pale yellow solid.

R_f: 0.34 (silica, pentanes:ethyl acetate 1:1);

Mp: 84-86 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.73 (d, J = 8.8 Hz, 2H, ArH), 6.92 (d, J = 8.8 Hz, 2H, ArH), 6.27 (s, 1H, NH), 3.85 (s, 3H, OCH₃), 3.54 (q, J = 6.4 Hz, 2H, CH₂), 3.24 (t, J = 6.8 Hz, 2H, CH₂), 2.15 (p, J = 6.7 Hz, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 167.2, 162.2, 128.7, 126.5, 113.8, 55.4, 40.5, 32.9, 3.4;

IR (film): $\tilde{\nu}$ = 3289 (w), 2932 (w), 1633 (m), 1606 (s), 1543 (m), 1504 (s), 1299 (m), 1254 (s), 1179 (m), 1029 (w), 844 (w);

HRMS (APCI) calcd. for C₁₁H₁₅INO₂⁺ [M+H]⁺ 320.0142; Found 320.0138.

3-((*tert*-Butoxycarbonyl)amino)-3-methoxypropyl benzoate (**16**).

In a glass vial, *tert*-butyl cyclopropylcarbamate **3o** (47.1 mg, 0.300 mmol, 1.0 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. After the completion of the reaction, K₂CO₃ (82.8 mg, 0.600 mmol, 2.0 equiv.) was added to the reaction mixture and then solvent was removed under reduced pressure. The crude was dissolved in 1.5 mL of DMF, and benzoic acid (73.2 mg, 0.600 mmol, 2.0 equiv.) was added. The resulting mixture was stirred at room temperature for 16 hours and then diluted with brine (10.0 mL). The aqueous layer was extracted with EtOAc (10.0 mL x 2). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by column

chromatography on silica using 3:1 pentanes:ethyl acetate as eluent. 3-((*tert*-Butoxycarbonyl)amino)-3-methoxypropyl benzoate **16** (75.1 mg, 0.243 mmol, 81%) was obtained as a yellow oil.

R_f: 0.33 (silica, pentanes:ethyl acetate 4:1);

¹H NMR (400 MHz, CDCl₃): δ = 8.03 (d, *J* = 7.4 Hz, 2H, ArH), 7.55 (t, *J* = 7.4 Hz, 1H, ArH), 7.43 (t, *J* = 7.6 Hz, 2H, ArH), 5.12 – 4.83 (m, 2H, NH + CH), 4.42 (t, *J* = 6.2 Hz, 2H, OCH₂), 3.36 (s, 3H, OCH₃), 2.08 – 2.04 (m, 2H, CH₂CH₂O), 1.43 (s, 9H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 166.4, 155.3, 133.0, 130.1, 129.6, 128.4, 80.4, 79.9, 61.1, 55.5, 34.6, 28.2;

IR (film): $\tilde{\nu}$ = 3354 (w), 2977 (w), 2933 (w), 1716 (s), 1513 (m), 1367 (m), 1274 (s), 1167 (s), 1114 (m), 861 (w), 712 (s);

HRMS (APCI) calcd. for C₁₆H₂₃NNaO₅⁺ [M+Na]⁺ 332.1468; Found 332.1469.

***tert*-Butyl (3-(benzylthio)-1-methoxypropyl)carbamate (17).**

In a glass vial, *tert*-butyl cyclopropylcarbamate **3o** (47.1 mg, 0.300 mmol, 1.0 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. After the completion of the reaction, K₂CO₃ (82.8 mg, 0.600 mmol, 2.0 equiv.) was added to the reaction mixture and then solvent was removed under reduced pressure. The crude was dissolved in 1.5 mL of DMF, and phenylmethanethiol (52.7 μ L, 0.450 mmol, 1.5 equiv.) was added. The resulting mixture was stirred at room temperature for 3 hours and then diluted with brine (10.0 mL). The aqueous layer was extracted with EtOAc (10.0 mL x 2). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica using 4:1 pentanes:ethyl acetate as eluent. *tert*-Butyl (3-(benzylthio)-1-methoxypropyl)carbamate **17** (74.1 mg, 0.238 mmol, 79%) was obtained as a colorless oil.

R_f: 0.37 (silica, pentanes:ethyl acetate 6:1);

¹H NMR (400 MHz, Acetonitrile-*d*₃): 7.33 – 7.26 (m, 4H, ArH), 7.23 (h, *J* = 4.3 Hz, 1H, ArH), 5.61 (d, *J* = 10.0 Hz, 1H, NH), 4.78 (dt, *J* = 10.2, 6.4 Hz, 1H, CH), 3.69 (s, 2H, PhCH₂), 3.19 (s, 3H, OCH₃), 2.40 (t, *J* = 7.4 Hz, 2H, SCH₂), 1.81 (dt, *J* = 14.0, 7.0 Hz, 1H, CH₂CH₂S), 1.69 (dq, *J* = 14.0, 7.3 Hz, 1H, CH₂CH₂S), 1.40 (s, 9H, CH₃);

¹³C NMR (101 MHz, Acetonitrile-*d*₃): δ = 156.5, 139.9, 129.8, 129.4, 127.8, 82.7, 79.7, 55.2, 36.5, 35.5, 28.5, 27.5;

IR (film): $\tilde{\nu}$ = 3337 (w), 2977 (w), 2930 (w), 1703 (s), 1495 (s), 1453 (m), 1366 (s), 1248 (m), 1163 (s), 1047 (m), 700 (m);

HRMS (ESI) calcd. for C₁₆H₂₅NNaO₃S⁺ [M+Na]⁺ 334.1447; Found 334.1455.

***tert*-Butyl (1-methoxy-3-(phenylamino)propyl)carbamate (18).**

In a glass vial, *tert*-butyl cyclopropylcarbamate **3o** (47.1 mg, 0.300 mmol, 1.0 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. After the completion of the reaction, K_2CO_3 (41.4 mg, 0.300 mmol, 1.0 equiv.) was added to the mixture before purification by column chromatography on silica using 4:1 pentanes:ethyl acetate as eluent. The obtained *tert*-Butyl (3-iodo-1-methoxypropyl)carbamate **4o** was then dissolved in 1.5 mL of DMF, K_2CO_3 (82.8 mg, 0.600 mmol, 2.0 equiv.) and aniline (54.8 μ L, 0.600 mmol, 2.0 equiv.) were added. The resulting mixture was stirred at room temperature for 16 hours and then diluted with brine (10.0 mL). The aqueous layer was extracted with EtOAc (10.0 mL x 2). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent. *tert*-Butyl (1-methoxy-3-(phenylamino)propyl)carbamate **18** (72.1 mg, 0.258 mmol, 86%) was obtained as a pale yellow oil.

R_f: 0.45 (silica, pentanes:ethyl acetate 3:1);

¹H NMR (400 MHz, $CDCl_3$): δ = 7.18 (t, J = 7.8 Hz, 2H, ArH), 6.70 (t, J = 7.3 Hz, 1H, ArH), 6.62 (d, J = 8.0 Hz, 2H, ArH), 5.06 – 4.80 (m, 2H, NH + CH), 3.94 (s, 1H, NH), 3.36 (s, 3H, OCH_3), 3.25 (td, J = 6.5, 3.4 Hz, 2H, NCH_2), 1.99 – 1.82 (m, 2H, CH_2CH_2N), 1.46 (s, 9H, CH_3);

¹³C NMR (101 MHz, $CDCl_3$): δ = 155.4, 148.1, 129.2, 117.4, 112.9, 81.8, 80.0, 55.5, 40.1, 35.1, 28.3;

IR (film): $\tilde{\nu}$ = 3377 (w), 2977 (w), 2932 (w), 2832 (w), 1699 (s), 1603 (s), 1504 (s), 1366 (m), 1251 (m), 1168 (s), 1080 (m), 749 (m);

HRMS (APCI) calcd. for $C_{15}H_{24}N_2NaO_3^+$ [$M+Na$] $^+$ 303.1679; Found 303.1677.

Dimethyl 2-(3-((*tert*-butoxycarbonyl)amino)-3-methoxypropyl)malonate (**19**).

In a glass vial, *tert*-butyl cyclopropylcarbamate **3o** (47.1 mg, 0.300 mmol, 1.0 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. After the completion of the reaction, K_2CO_3 (41.4 mg, 0.300 mmol, 1.0 equiv.) was added to the mixture before purification by column chromatography on silica using 4:1 pentanes:ethyl acetate as eluent. The obtained *tert*-butyl (3-iodo-1-methoxypropyl)carbamate **4o** was then dissolved in 1.5 mL of DMF, K_2CO_3 (82.8 mg, 0.600 mmol, 2.0 equiv.) and dimethyl malonate (70.0 μ L, 0.600 mmol, 2.0 equiv.) were added. The resulting mixture was stirred at room temperature

for 16 hours and then diluted with brine (10.0 mL). The aqueous layer was extracted with EtOAc (10.0 mL x 2). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent. Dimethyl 2-(3-((*tert*-butoxycarbonyl)amino)-3-methoxypropyl)malonate **19** (76.6 mg, 0.240 mmol, 80%) was obtained as a pale yellow oil.

R_f: 0.35 (silica, pentanes:ethyl acetate 3:1) KMnO₄;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 6.33 (d, *J* = 9.9 Hz, 1H, NH), 4.78 (dt, *J* = 10.0, 6.4 Hz, 1H, CH), 3.69 (s, 6H, CO₂CH₃), 3.45 (t, *J* = 7.5 Hz, 1H, CH), 3.25 (s, 3H, OCH₃), 1.97 – 1.85 (m, 2H, CH₂), 1.75 – 1.65 (m, 1H, CH₂), 1.62 – 1.54 (m, 1H, CH), 1.42 (s, 9H, CH₃);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 170.3, 170.2, 156.5, 83.3, 79.1, 55.0, 52.6, 51.7, 33.3, 28.5, 25.5;

IR (film): $\tilde{\nu}$ = 3367 (w), 2977 (w), 2955 (w), 2833 (w), 1733 (s), 1717 (s), 1511 (m), 1437 (m), 1366 (m), 1245 (m), 1162 (m), 1110 (m), 1048 (m), 863 (w);

HRMS (ESI) calcd. for C₁₄H₂₅NNaO₇⁺ [M+Na]⁺ 342.1523; Found 342.1530.

***tert*-Butyl (3-cyano-1-methoxypropyl)carbamate (20).**

In a glass vial, *tert*-butyl cyclopropylcarbamate **3o** (47.1 mg, 0.300 mmol, 1.0 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μL, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. After the completion of the reaction, K₂CO₃ (41.4 mg, 0.300 mmol, 1.0 equiv.) was added to the mixture before purification by column chromatography on silica using 4:1 pentanes:ethyl acetate as eluent. The obtained *tert*-butyl (3-iodo-1-methoxypropyl)carbamate **4o** was then dissolved in 1.5 mL of DMF. K₂CO₃ (82.8 mg, 0.600 mmol, 2.0 equiv.) and NaCN (29.4 mg, 0.600 mmol, 2.0 equiv.) were added. The resulting mixture was stirred at room temperature for 2 hours and then diluted with EtOAc (10.0 mL) and extracted with brine (10.0 mL x 6). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. *tert*-Butyl (3-cyano-1-methoxypropyl)carbamate **20** (60.4 mg, 0.282 mmol, 94%) was obtained as a colorless oil without any further purification.

R_f: 0.48 (silica, pentanes:ethyl acetate 2:1) KMnO₄;

Mp: 49–52 °C;

¹H NMR (400 MHz, CDCl₃): δ = 4.90 (dt, *J* = 12.6, 6.1 Hz, 1H, CH), 4.80 (d, *J* = 10.5 Hz, 1H, NH), 3.35 (s, 3H, OCH₃), 2.44 (td, *J* = 7.4, 4.6 Hz, 2H, CH₂CN), 1.93 (q, *J* = 7.1 Hz, 2H, CH₂CH₂CN), 1.46 (s, 9H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 155.1, 119.0, 81.3, 80.3, 55.6, 31.4, 28.2, 13.3;

IR (film): $\tilde{\nu}$ = 3341 (w), 2979 (w), 2936 (w), 2834 (w), 2247 (w), 1700 (s), 1515 (s), 1367 (s), 1214 (m), 1169 (s), 1050 (s), 892 (w);

HRMS (APCI) calcd. for C₁₀H₁₈N₂NaO₃⁺ [M+Na]⁺ 237.1210; Found 237.1214.

***tert*-Butyl 2-methoxyazetidine-1-carboxylate (21).**

In a glass vial, *tert*-butyl cyclopropylcarbamate **3o** (47.1 mg, 0.300 mmol, 1.0 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of MeCN (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. After the completion of the reaction, *t*-BuOK (101 mg, 0.900 mmol, 3.0 equiv.) was added. The resulting mixture was stirred at room temperature for 16 hours and then diluted with brine (10.0 mL). The aqueous layer was extracted with DCM (10.0 mL x 2). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by column chromatography on basic aluminium oxide. *tert*-Butyl 2-methoxyazetidine-1-carboxylate **21** (14.1 mg, 0.075 mmol, 25%) was obtained as a pale yellow oil by using dichloromethane as eluent. 4-Methoxy-1,3-oxazinan-2-one **21'** (11.8 mg, 0.090 mmol, 30%) was obtained as a yellow oil by using 20:1 dichloromethane:methanol as eluent.

***tert*-Butyl 2-methoxyazetidine-1-carboxylate (21).**

R_f: 0.50 (silica, pentanes:ethyl acetate 6:1);

¹H NMR (400 MHz, CDCl₃): δ = 5.17 (dd, *J* = 6.8, 4.0 Hz, 1H, CH), 3.74 (dt, *J* = 8.7, 4.3 Hz, 1H, NCH₂), 3.64 (td, *J* = 8.5, 6.2 Hz, 1H, NCH₂), 3.49 (s, 3H, OCH₃), 2.42 (dddd, *J* = 12.2, 8.9, 6.8, 5.4 Hz, 1H, CH₂), 2.17 – 2.08 (m, 1H, CH₂), 1.46 (s, 9H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 156.4, 91.2, 80.0, 56.2, 43.5, 28.3, 24.8;

IR (film): $\tilde{\nu}$ = 2974(w), 2931 (w), 2900 (w), 1702 (s), 1456 (w), 1381 (m), 1349 (m), 1257 (w), 1154 (m), 1092 (s), 999 (w), 925 (w), 853 (w);

HRMS (ESI) calcd. for C₉H₁₇NNaO₃⁺ [M+Na]⁺ 210.1101; Found 210.1107.

4-Methoxy-1,3-oxazinan-2-one (21').

R_f: 0.37 (silica, dichloromethane:methanol 20:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.70 (s, 1H, NH), 4.57 (q, *J* = 3.6 Hz, 1H, CH), 4.49 (ddd, *J* = 12.6, 10.9, 2.9 Hz, 1H, OCH₂), 4.26 (dddd, *J* = 10.9, 4.8, 2.5, 1.1 Hz, 1H, OCH₂), 3.36 (s, 3H, OCH₃), 2.05 – 1.99 (m, 1H, CH₂), 1.97 – 1.90 (m, 1H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 153.8, 79.8, 63.1, 54.6, 26.9;

IR (film): $\tilde{\nu}$ = 3269 (w), 2939 (w), 2182 (w), 1698 (s), 1284 (s), 1087 (s);

HRMS (ESI) calcd. for C₅H₁₀NO₃⁺ [M+H]⁺ 132.0655; Found 132.0651.

N-(3-((4-Fluorophenyl)thio)-1-(3-methyl-1H-indol-2-yl)propyl)-4-methoxybenzamide (22).

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (57.3 mg, 0.300 mmol, 1.0 equiv.), diphenyl phosphate (7.5 mg, 0.030 mmol, 0.1 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of CHCl₃ (0.20 M). The reaction mixture was stirred at room temperature for 30 minutes. 3-Methylindole (47.2 mg, 0.360 mmol, 1.2 equiv.) and TFA (23.0 μ L, 0.300 mmol, 1.0 equiv.) were added to the reaction mixture and the reaction mixture was stirred at room temperature for another 20 minutes. Then the solvent was removed under reduced pressure. K₂CO₃ (124 mg, 0.900 mmol, 3.0 equiv.), 4-fluorobenzenethiol (64.0 μ L, 0.600 mmol, 2.0 equiv.) and 1.5 mL of DMF were added to the residue. After stirring at room temperature for 16 hours, the crude product was diluted with DCM (20.0 mL) and extracted with brine (20.0 mL x 3). The combined organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent. N-(3-((4-Fluorophenyl)thio)-1-(3-methyl-1H-indol-2-yl)propyl)-4-methoxybenzamide **22** (106 mg, 0.240 mmol, 79%) was obtained as a pale yellow solid.

R_f: 0.41 (silica, pentanes:ethyl acetate 2:1);

Mp: 143-146 °C;

¹H NMR (400 MHz, CDCl₃): δ = 9.01 (s, 1H, indole-NH), 7.73 – 7.62 (m, 2H, ArH), 7.51 (d, J = 7.8 Hz, 1H, ArH), 7.30 (ddd, J = 8.7, 5.4, 2.7 Hz, 2H, ArH), 7.27 – 7.25 (m, 1H, ArH), 7.15 (ddd, J = 8.1, 7.0, 1.3 Hz, 1H, ArH), 7.11 – 7.06 (m, 1H, ArH), 6.99 – 6.91 (m, 2H, ArH), 6.89 – 6.83 (m, 2H, ArH), 6.69 (d, J = 7.4 Hz, 1H, NH), 5.28 (q, J = 7.5 Hz, 1H, CH), 3.81 (s, 3H, OCH₃), 2.86 (t, J = 7.0 Hz, 2H, CH₂S), 2.55 (dq, J = 14.3, 7.1 Hz, 1H, CH₂CH₂S), 2.38 (dt, J = 14.0, 7.3 Hz, 1H, CH₂CH₂S), 2.31 (s, 3H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 167.6, 162.4, 161.9 (d, J = 246.7 Hz), 135.4, 133.4, 132.6 (d, J = 8.0 Hz), 130.4 (d, J = 3.4 Hz), 128.8, 128.6, 126.2, 122.1, 118.9 (d, J = 51.0 Hz), 116.2, 116.0, 113.8, 111.0, 108.2, 55.4, 47.1, 33.1, 32.1, 8.8;

¹⁹F NMR (376 MHz, CDCl₃): δ = -115.1;

IR (film): $\tilde{\nu}$ = 3313 (m), 2924 (w), 2856 (w), 1606 (s), 1540 (m), 1490 (s), 1460 (m), 1306 (m), 1255 (s), 1178 (m), 1029 (m), 832 (m), 734 (m);

HRMS (ESI) calcd. for C₂₆H₂₅FN₂NaO₂S⁺ [M+Na]⁺ 471.1513; Found 471.1505.

N-(3-(Cyclopropylamino)-1-(3-methyl-1H-indol-2-yl)propyl)-4-methoxybenzamide (23).

In a glass vial, N-cyclopropyl-4-methoxybenzamide **3a** (57.3 mg, 0.300 mmol, 1.0 equiv.), diphenyl phosphate (7.5 mg, 0.030 mmol, 0.1 equiv.), N-iodosuccinimide (70.8 mg, 0.315 mmol, 1.05 equiv.) and methanol (14.4 μ L, 0.360 mmol, 1.2 equiv.) were dissolved in 1.5 mL of CHCl_3 (0.20 M). The reaction mixture was stirred for 30 minutes. 3-Methylindole (47.2 mg, 0.360 mmol, 1.2 equiv.) and TFA (23.0 μ L, 0.300 mmol, 1.0 equiv.) were added to the reaction mixture and the reaction mixture was stirred for another 20 minutes. Then the solvent was removed under reduced pressure, K_2CO_3 (124 mg, 0.900 mmol, 3.0 equiv.), cyclopropyl amine (42.0 μ L, 0.600 mmol, 2.0 equiv.) and 1.5 mL of DMF were added to the residue. After stirring at room temperature for 16h, the crude product was diluted with DCM (20.0 mL) and extracted with brine (20.0 mL x 3). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica using 8:1 dichloromethane:methanol as eluent. N-(3-(Cyclopropylamino)-1-(3-methyl-1H-indol-2-yl)propyl)-4-methoxybenzamide **23** (62.2 mg, 0.165 mmol, 55%) was obtained as a yellow solid.

R_f: 0.28 (silica, dichloromethane:methanol 8:1);

Mp: 177-179 $^{\circ}\text{C}$;

^1H NMR (400 MHz, Acetone- d_6): δ = 10.19 (s, 1H, indole-NH), 8.45 (d, J = 7.6 Hz, 1H, NH), 7.93 – 7.84 (m, 2H, ArH), 7.45 (d, J = 7.1 Hz, 1H, ArH), 7.27 (d, J = 7.8 Hz, 1H, ArH), 7.02 (td, J = 8.0, 7.5, 1.4 Hz, 1H, ArH), 6.99 – 6.96 (m, 1H, ArH), 6.96 – 6.92 (m, 2H, ArH), 5.67 – 5.54 (m, 1H, CH), 3.83 (s, 3H, OCH_3), 2.84 (t, J = 6.3 Hz, 2H, CH_2N), 2.31 (s, 3H, CH_3), 2.24 (qd, J = 6.5, 1.7 Hz, 2H, $\text{CH}_2\text{CH}_2\text{N}$), 2.21 – 2.15 (m, 1H, CH), 0.47 – 0.33 (m, 4H, CH_2); 1 NH was not resolved.

^{13}C NMR (101 MHz, Acetone- d_6): δ = 166.3, 163.0, 136.4, 136.3, 130.0, 129.9, 127.9, 121.7, 119.2, 118.9, 114.2, 111.6, 107.0, 55.7, 47.0, 46.1, 34.8, 31.1, 8.8, 6.2, 6.2;

IR (film): $\tilde{\nu}$ = 3296 (m), 2933 (w), 1606 (s), 1504 (s), 1256 (s), 1179 (m), 1030 (m), 844 (m), 742 (m);

HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{28}\text{N}_3\text{O}_2^+$ $[\text{M}+\text{H}]^+$ 378.2176; Found 378.2171.

3-((*tert*-Butoxycarbonyl)amino)-3-methoxy-2-methylpropyl benzoate (**29**).

In a glass vial, *tert*-butyl (2-methylcyclopropyl)carbamate **28** (17.1 mg, 0.100 mmol, 1.0 equiv.), *N*-iodosuccinimide (23.6 mg, 0.105 mmol, 1.05 equiv.) and methanol (4.8 μ L, 0.12 mmol, 1.2 equiv.) were dissolved in 0.5 mL of dichloromethane (0.20 M). The reaction mixture was stirred for 30 minutes. After the completion of the reaction, K_2CO_3 (27.6 mg, 0.200 mmol, 2.0 equiv.) was added to the reaction mixture and then solvent was removed under reduced pressure. The crude was dissolved in 0.5 mL of DMF, and benzoic acid (24.4 mg, 0.200 mmol, 2.0 equiv.) was added. The resulting mixture was stirred at room temperature for 16 hours. The crude was then diluted with brine (5.0 mL). The aqueous layer was extracted with EtOAc (5.0 mL x 2). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by preparative TLC on silica using 3:1 pentanes:ethyl acetate as eluent. 3-((*tert*-Butoxycarbonyl)amino)-3-methoxy-2-methylpropyl benzoate **29** (10.3 mg, 0.032 mmol, 32%) was obtained as a colorless oil.

R_f: 0.30 (silica, pentanes:ethyl acetate 6:1);

¹H NMR (400 MHz, $CDCl_3$; mixture of two diastereoisomers in a 1:1 ratio: the signals corresponding to the two diastereoisomers are not resolved): δ = 8.09 – 7.99 (m, 2H, ArH), 7.60 – 7.53 (m, 1H, ArH), 7.45 (dd, J = 8.4, 7.0 Hz, 2H, ArH), 5.09 (dd, J = 20.7, 10.4 Hz, 1H, NH), 4.89 (ddd, J = 13.2, 10.4, 5.3 Hz, 1H, CH), 4.41 – 4.22 (m, 2H, OCH_2), 3.35 (d, J = 1.0 Hz, 3H, OCH_3), 2.19 (dq, J = 13.2, 6.4 Hz, 1H, CHCH₃), 1.45 (d, J = 2.6 Hz, 9H, CH₃), 1.07 (dd, J = 7.0, 1.8 Hz, 3H, CH₃);

¹³C NMR (101 MHz, $CDCl_3$; mixture of two diastereoisomers in a 1:1 ratio: the signals corresponding to the two diastereoisomers are partially resolved): δ = 166.4, 155.6, 133.0, 130.2, 130.1, 129.5, 128.4, 84.1, 83.8, 79.8, 66.0, 55.8, 55.7, 38.0, 37.7, 28.3, 12.8, 12.2;

IR (film): $\tilde{\nu}$ = 3355 (w), 2977 (w), 2932 (w), 1718 (s), 1508 (m), 1367 (m), 1273 (s), 1170 (s), 1083 (m), 712 (m);

HRMS (ESI) calcd. for $C_{17}H_{25}NNaO_5^+$ [$M+Na$]⁺ 346.1625; Found 346.1634.

5. Mechanistic studies

5.1 In-situ analysis of reaction intermediates

N-cyclopropyl-4-methylbenzenesulfonamide **3q** (21.1 mg, 0.100 mmol, 1.0 equiv.) and NXS (0.200 mmol, 2.0 equiv.) were dissolved in 0.5 mL of CDCl₃ (0.20 M). After stirring for 2 hours at room temperature, the reaction crude mixture was submitted to ¹H NMR analysis directly.

25a was not isolated because of low yield as well as low stability.

Due to the stability issue, we were not able to isolate **26a** and its structure was only assumed based on the crude ¹H NMR spectra.

26a ¹H NMR (400 MHz, CDCl₃): δ = 8.51 (t, J = 3.5 Hz, 1H, CH), 7.81 (d, J = 8.3 Hz, 2H, ArH), 7.34 (d, J = 8.0 Hz, 2H, ArH), 3.34 – 3.26 (m, 2H, CH₂I), 3.22 – 3.14 (m, 2H, CH₂), 2.43 (s, 3H, CH₃).

5.2 Efforts towards the isolation of intermediate **25b**

In 5.1 experiment part, **25b** was isolated with 80% purity, accompanied by **26b** as a major impurity.

25b ^1H NMR (400 MHz, CD_2Cl_2): δ = 7.92 – 7.82 (m, 2H, ArH), 7.43 (d, J = 8.0 Hz, 2H, ArH), 2.48 (s, 3H, CH_3), 2.43 – 2.38 (m, 1H, CH), 1.04 – 0.93 (m, 4H, CH_2).

26b ^1H NMR (400 MHz, CD_2Cl_2): δ = 8.53 (t, J = 3.7 Hz, 1H, CH), 7.81 – 7.77 (m, 2H, ArH), 7.38 (d, J = 8.0 Hz, 2H, ArH), 3.61 (t, J = 6.6 Hz, 2H, CH_2Br), 3.13 (td, J = 6.6, 3.7 Hz, 2H, CH_2), 2.45 (s, 3H, CH_3).

In fact, **25b** was a reported compound but the spectra was not given in the original paper.^[13] Therefore, we synthesized **25b** by following the modified reported protocol and found that in these two cases, the ^1H NMR data corresponds well to each other.

A solution of 2 mmol of **3q** in 3 ml dichloromethane was added to a 25 mL flask covered by foil paper, then bromine (0.4 mL) in 10 mL of 2 N NaOH (aq) was added drop by drop to the solution above. The temperature was kept at 0 °C and the reaction mixture was stirred for an additional 2 hours. The organic layer was washed twice with ice water. The organic layer was dried over Na_2SO_4 at -20 °C, after which the Na_2SO_4 was filtered off. The crude product was obtained after concentration under reduced pressure at room temperature, covered by foil paper. Beige solid was obtained as product albeit with some dichloromethane.

¹³ Dekker, E. E. J.; Engberts, J. B. F. N.; de Boer, Th. J. Recl. Trav. Chim. Pays-Bas, **1978**, 97, 39-41.

5.3 Reactivity of intermediate **25b** and **26b**

N-bromo-N-cyclopropyl-4-methylbenzenesulfonamide **25b** (14.5 mg, 0.050 mmol, 1.0 equiv.) was added in 0.5 mL of CD₂Cl₂ (0.10 M). After stirring for 6 hours at room temperature, the reaction crude was submitted to ¹H NMR analysis directly. In this case, full conversion of **25b** was observed and the structure of **26b** was assumed based on the crude ¹H NMR spectra as it is not stable enough to be isolated. Note: under the same conditions, no conversion was observed when the vial was covered with foil paper.

To the crude solution of **26b** in CD₂Cl₂ was added MeOH (8.1 μL , 0.200 mmol, 4.0 equiv.), then the vial was covered with foil paper to exclude any role of light in this reaction. After stirring for 16 hours at room temperature, the reaction crude was submitted to ^1H NMR and HRMS analysis directly. In this case, full conversion of **26b** was observed and the structure of **27** was assumed based on the crude ^1H NMR spectra as this Ts protected N,O-acetal is not stable.

Methanol (8.1 μ L, 0.200 mmol, 4.0 equiv.) was added to the solution of N-bromo-N-cyclopropyl-4-methylbenzenesulfonamide **25b** (14.5 mg, 0.050 mmol, 1.0 equiv.) in 0.5 mL of CD₂Cl₂ (0.10 M). After stirring for 16 hours under ambient light at room temperature, the reaction crude was submitted to ¹H NMR and HRMS analysis directly. . Note: under the same conditions, no conversion was observed when the vial was covered with foil paper.

27 ¹H NMR (400 MHz, CD₂Cl₂): δ = 7.75 (dd, J = 8.4, 1.9 Hz, 2H, ArH), 7.35 – 7.31 (m, 2H, ArH), 5.51 (d, J = 9.7 Hz, 1H, NH, note: this proton is not resolved sometimes), 4.66 (ddd, J = 9.7, 7.5, 4.9 Hz, 1H, CH), 3.37 – 3.27 (m, 2H, CH₂Br), 3.22 (s, 3H, OCH₃), 2.13 – 2.05 (m, 1H, CH₂), 1.92 – 1.85 (m, 1H, CH₂).

HRMS (ESI) calcd. for C₁₁H₁₆BrNNaO₃S⁺ [M+Na]⁺ 343.9926; Found 343.9920.

5.4 Crossover experiment

N-bromo-N-cyclopropyl-4-methylbenzenesulfonamide **25b** (14.5 mg, 0.050 mmol, 1.0 equiv.) and NIS (22.5 mg, 0.100 mmol, 2.0 equiv.) was added in 0.5 mL of CD_2Cl_2 (0.10 M). After stirring for 2 hours at room temperature, the reaction crude was submitted to ^1H NMR analysis directly.

6. Spectra of new compounds

N-Cyclopropyl-4-(methylthio)benzamide (3b)

^1H -NMR (400 MHz, CDCl_3)

¹³C-NMR (101 MHz, CDCl₃)

IR

4-Chloro-N-cyclopropylbenzamide (3d)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

4-Cyano-N-cyclopropylbenzamide (3e)

^1H -NMR (400 MHz, CDCl_3)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-Cyclopropyl-4-nitrobenzamide (3f)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-Cyclopropyl-3-methoxybenzamide (3g)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-Cyclopropyl-2-methoxybenzamide (3h)
¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

N-Cyclopropyl-2,4,6-trimethylbenzamide (3i)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-Cyclopropyl-2-naphthamide (3m)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-Cyclopropyl-N,4-dimethylbenzenesulfonamide (3r)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

Benzyl (S)-1-(cyclopropylamino)-1-oxo-3-phenylpropan-2-yl carbamate (3t)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-Cyclopropyl-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetamide (3u)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N-cyclopropylacetamide (3v)
¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(3-Iodo-1-methoxypropyl)-4-methoxybenzamide (4a)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

HPLC

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.000	BB	0.4742	262.42535	8.45173	49.8710
2	20.743	BB	0.5242	263.78317	7.80741	50.1290

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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1	17.402	BB	0.4508	157.17209	5.25709	11.0808
2	19.928	BB	0.4757	1261.24243	38.95499	88.9192

N-(3-Iodo-1-methoxypropyl)-4-(methylthio)benzamide (4b)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

4-Fluoro-N-(3-iodo-1-methoxypropyl)benzamide (4c)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

4-Chloro-N-(3-iodo-1-methoxypropyl)benzamide (4d)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

4-Cyano-N-(3-iodo-1-methoxypropyl)benzamide (4e)

$^1\text{H-NMR}$ (400 MHz, CDCl_3)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(3-Iodo-1-methoxypropyl)-4-nitrobenzamide (4f)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(3-Iodo-1-methoxypropyl)-3-methoxybenzamide (4g)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(3-Iodo-1-methoxypropyl)-2-methoxybenzamide (4h)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(3-Iodo-1-methoxypropyl)-2,4,6-trimethylbenzamide (4i)

$^1\text{H-NMR}$ (400 MHz, CDCl_3)

^{13}C -NMR (101 MHz, CDCl_3)

IR

¹H-NMR (400 MHz, CDCl₃)

IR

N-(3-Iodo-1-methoxypropyl)cinnamamide (4k)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(3-Iodo-1-methoxypropyl)-2-phenylacetamide (4l)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(3-Iodo-1-methoxypropyl)-2-naphthamide (4m)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(3-Iodo-1-methoxypropyl)pivalamide (4n)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

tert-Butyl (3-iodo-1-methoxypropyl)carbamate (4o)

¹H-NMR (400 MHz, CD₃OD)

^{13}C -NMR (101 MHz, CD_3OD)

IR

Benzyl (3-iodo-1-methoxypropyl)carbamate (4p)
¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(3-Iodo-1-methoxypropyl)-4-methylbenzenesulfonamide (4q)

¹H-NMR (400 MHz, CD₃OD)

^{13}C -NMR (101 MHz, CD_3OD)

IR

N-(3-Iodo-1-methoxypropyl)-N,4-dimethylbenzenesulfonamide (4r)

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

IR

tert-Butyl benzyl(3-iodo-1-methoxypropyl)carbamate (4s)

¹H-NMR (400 MHz, Acetone-*d*₆)

^{13}C -NMR (101 MHz, Acetone- d_6)

IR

Benzyl ((2S)-1-((3-iodo-1-methoxypropyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (4t)

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

IR

N-(3-Iodo-1-methoxypropyl)-2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetamide (4u)

$^1\text{H-NMR}$ (400 MHz, Acetone- d_6)

^{13}C -NMR (101 MHz, Acetone- d_6)

IR

2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N-(3-iodo-1-methoxypropyl)acetamide (4v)
¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

IR

N-(3-Bromo-1-methoxypropyl)-4-methoxybenzamide (5)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

3-Iodopropanenitrile (9)
¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(1-(Benzyloxy)-3-iodopropyl)-4-methoxybenzamide (10a)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(3-Iodo-1-(prop-2-yn-1-yloxy)propyl)-4-methoxybenzamide (10b)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(1-(Allyloxy)-3-iodopropyl)-4-methoxybenzamide (10c)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(3-Iodo-1-isopropoxypropyl)-4-methoxybenzamide (10d)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(3-Iodo-1-(((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)propyl)-4-methoxybenzamide (10e)
¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(1-(2-Hydroxyethoxy)-3-iodopropyl)-4-methoxybenzamide (10f)

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

IR

N-(1-(*tert*-Butylperoxy)-3-iodopropyl)-4-methoxybenzamide (10g)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(1-Hydroperoxy-3-iodopropyl)-4-methoxybenzamide (10h)

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

IR

N-(3-Iodo-1-(methylsulfonamido)propyl)-4-methoxybenzamide (11)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

N-(1-Cyano-3-iodopropyl)-4-methylbenzenesulfonamide (12)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(1-(1-Hydroxynaphthalen-2-yl)-3-iodopropyl)-4-methoxybenzamide (13)
¹H-NMR (400 MHz, Acetone-*d*₆)

^{13}C -NMR (101 MHz, Acetone- d_6)

IR

¹H-NMR (400 MHz, Acetone-*d*₆)

IR

N-(3-Iodopropyl)-4-methoxybenzamide (15)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

3-((*tert*-Butoxycarbonyl)amino)-3-methoxypropyl benzoate (16)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

tert-Butyl (3-(benzylthio)-1-methoxypropyl)carbamate (17)

^1H -NMR (400 MHz, CD_3CN)

^{13}C -NMR (101 MHz, CD_3CN)

IR

***tert*-Butyl (1-methoxy-3-(phenylamino)propyl)carbamate (18)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

Dimethyl 2-(3-((*tert*-butoxycarbonyl)amino)-3-methoxypropyl)malonate (19)

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

IR

***tert*-Butyl (3-cyano-1-methoxypropyl)carbamate (20)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

tert-Butyl 2-methoxyazetidine-1-carboxylate (20)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR

4-Methoxy-1,3-oxazinan-2-one (21')

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(3-((4-Fluorophenyl)thio)-1-(3-methyl-1H-indol-2-yl)propyl)-4-methoxybenzamide (22)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

N-(3-(Cyclopropylamino)-1-(3-methyl-1H-indol-2-yl)propyl)-4-methoxybenzamide (23)

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

IR

3-((tert-Butoxycarbonyl)amino)-3-methoxy-2-methylpropyl benzoate (29)

¹H-NMR (400 MHz, CDCl₃)

^{13}C -NMR (101 MHz, CDCl_3)

IR