COMMUNICATION

Oxidative Fluorination of Cyclopropylamides via Organic Photoredox Catalysis

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

Abstract: We report an oxidative ring-opening strategy to transform cyclopropylamides and cyclobutylamides into fluorinated imines. The imines can be isolated in their more stable hemiaminal form, with the fluorine atom installed selectively at the γ or δ position. Both cheap benzophenone with UV A light or organic and inorganic dyes with blue light could be used as photoredox catalysts to promote this process. Various fluorinated amines were then obtained by nucleophilic attack on the hemiaminals in one pot, giving access to a broad range of useful building blocks for medicinal chemistry.

Tremendous efforts have been devoted to the development of site-selective fluorination methods, given the significance of fluorinated compounds in medicine and agrochemistry.^[1] Among these methods, the formation of C(sp³)-F bonds via ring opening fluorination of carbocycles is an attractive route.^[2] While success has been achieved in ring opening fluorination of arylcyclopropanes (Scheme 1A),^[3] cyclopropanols^[4] and cyclobutanols^[4a,b] (Scheme 1B), their nitrogen-substituted counterparts were not studied yet, despite the importance of nitrogen-containing fluorinated drugs and agrochemicals.

Previous studies on ring-opening of aminocyclopropanes and aminocyclobutanes focused on Donor-Acceptor systems, which are more reactive.^[5] Simple systems lacking electron-withdrawing groups have been less exploited, with most approaches using transition-metal catalyst for C-C activation.^[6] Oxidative methods proceeding via radical pathways constitute an interesting alternative.^[7] Zheng and co-workers demonstrated that cyclopropylanilines and cyclobutylanilines can be oxidized to a radical cation species **I** using photoredox catalysis (Scheme 1C).^[8] After ring opening, the resulting iminium radical **II** underwent (3+2) annulation with alkenes or alkynes. Our group later extended this approach to cyclopropenes^[9] and Stephenson and co-workers applied it to the synthesis of 1-aminonorbornanes.^[10] They also developed an alternative strategy involving the activation of cyclopropylimines through their triplet excited state.^[11] Our group exploited another approach based on a Hofmann–Löffler–Freitag (HLF)-inspired reaction to

generate a nitrogen-centered radical from *N*-halogen aminocyclopropane **III** (Scheme 1D).^[12] The N radical then underwent ring-opening and radical recombination to generate γ -halogenated imines isolable in their *N*,*O*-acetal form **IV**. However, this approach failed in the case of fluorination.

Scheme 1. Oxidative ring-opening fluorination of cyclopropanes (A). Fluorination of cyclopropanols and cyclobutanols (B). Photoredox catalysis enabled (3+2) annulation of cyclopropylanilines (C). 1,3-Difunctionalization of aminocyclopropanes (D). This work: oxidative fluorination of cyclopropylamides (E).

We envisioned that a highly oxidizing excited photocatalyst should be able to activate cyclopropylamides via single electron transfer (SET) oxidation to give amidium radical **V** (Scheme 1E).^[13] After ring-opening, the formed alkyl radical could be trapped by a fluorination reagent, and the imine stabilized as a hemiaminal **VI**. Herein, we report the successful implementation of this strategy, using either cheap benzophenone with black light (365 nm) or organic/inorganic dyes with blue LEDs, and Selectfluor acting as both oxidant and fluorination reagent. The reaction is complementary to the method of Lectka for the synthesis of fluorinated amines (Scheme 1A, $\text{R} = \text{NR}_3^+$),^[3a] as a reversed regioselectivity is observed for fluorination compared with arylcyclopropanes. The obtained hemiaminals were easily converted into diverse products by reaction with nucleophiles.

With benzamide cyclopropane **1a** as substrate, the combination of benzophenone and Selectfluor under irradiation at 365 nm in MeCN/H₂O was optimal, yielding 3-fluorinated hemiaminal **2a** in 74% yield (Table 1, entry 1).^[14] Control experiments showed no

[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/>

Supporting information for this article is given via a link at the end of the document. Raw data for NMR, IR and MS is available at zenodo.org, DOI: 10.5281/zenodo.3895605

COMMUNICATION

conversion in the absence of benzophenone or irradiation (Table 1, entries 2 and 3). Only 10% of product was observed when using NFSI as fluorinating reagent (Table 1, entry 4). 9-Fluorenone, which is efficient for the ring-opening fluorination of arylcyclopropanes, [3a] failed in this case (Table 1, entry 5). Other photocatalysts such as $[\text{Ir}(\text{dF-CF}_3\text{ppy})_2(\text{dtbbpy})]\text{PF}_6$ and Mes-Acr^+ can also be utilized to achieve similar results using visible light (Table 1, entries 6 and 7). Lower yields were obtained with substrates containing less electron-donating substituents on the benzene ring of the amide (Table 1, entries 8 and 9). No conversion was observed with a strong electron-withdrawing substituent such as a nitrobenzoyl (Table 1, entry 10) or a tosyl (Ts) group (Table 1, entry 11). With a Boc group, no product was isolated due to fast decomposition of the hemiaminal (Table 1, entry 12). With a pivaloyl group, the yield dropped to 29% with incomplete conversion (Table 1, entry 13). When mixing cyclopropyl aniline **1h** with Selectfluor, fast degradation was observed even prior to UV irradiation (Table 1, entry 14).

Table 1. Optimization of the reaction conditions^[a]

Entry	Deviation from standard condition	Yield ^[b]
1	none	74%
2	no benzophenone	0
3	no irradiation	0
4	NFSI instead of Selectfluor	10% ^[c]
5	9-fluorenone instead of benzophenone	6% ^[c]
6	$[\text{Ir}(\text{dF-CF}_3\text{ppy})_2(\text{dtbbpy})]\text{PF}_6$ with blue LED ^[d]	76% ^[c]
7	Mes-Acr^+ with blue LED ^[e]	75% ^[c]
8	1b as substrate ^[f]	48%
9	1c as substrate ^[f]	43%
10	1d as substrate	0
11	1e as substrate	0
12	1f as substrate	decomposed
13	1g as substrate	29% ^[g]
14	1h as substrate	decomposed

1a, R = OMe
1b, R = Me
1c, R = F
1d, R = NO₂
1e, R = Ts
1f, R = Boc
1g, R = tBu
1h, R = 4-chlorophenyl

^[a]Reaction conditions: 0.30 mmol scale for 45 min. ^[b]Yield of isolated product. ^[c]Yield determined by ¹H NMR using CH₂Br₂ as internal standard. ^[d]With 1 mol% $[\text{Ir}(\text{dF-CF}_3\text{ppy})_2(\text{dtbbpy})]\text{PF}_6$ and 1.5 equiv. Selectfluor for 1 h. ^[e]With 2 mol% 9-mesityl-10-methylacridiniumperchlorate (Mes-Acr^+) and 1.5 equiv. Selectfluor for 3 h. ^[f]Reaction run for 4 h. ^[g]Reaction run for 10 h and product **2g** converted to an indole adduct to simplify purification.

We then developed one pot protocols to replace the hydroxy group by adding nucleophiles to the reaction mixture (Scheme 2). We focused on benzophenone as catalyst, because of its broad availability and low price. *N,O*-, *N,S*- or *N,N*- acetals can be accessed in 39–73% yield (products **3a–f**). The hemiaminal can also be reduced by NaBH₃CN, affording **3g** in 83% yield. A Petasis reaction^[15] gave allylic amine **3h** in 42% yield. 1,3,5-Trimethoxybenzene afforded **3i** in 69% yield while only 22% yield of **3j** was observed when using 1,3-dimethoxybenzene. With pyrrole, C2 addition product **3k** was isolated in 46% yield.

Scheme 2. Scope of nucleophiles in the one-pot ring-opening fluorination reaction. ^[a]Reactions were run at a 0.30 mmol scale for 45 min, then a solution of nucleophile (1.2 equiv.) in 0.5 mL MeCN was added and the mixture was kept stirring at room temperature for the indicated time, Ar = *p*-MeO-Ph. ^[b]MeOH (1.0 mL, 82 equiv.) was used. ^[c]1,2,4-1*H*-Triazole (2.0 equiv.) was used. ^[d]1,2,3,4-1*H*-Tetrazole (2.0 equiv.) was used. ^[e]Potassium *trans*-styryltrifluoroborate (2.0 equiv.) was used.

The addition of indole provided **3l** in 67% yield. Upon scaling up this reaction to 10 mmol, 1.86 grams (57% yield) of **3l** were

COMMUNICATION

obtained. Indoles bearing a *N*-methyl or a 2-phenyl group provided the corresponding products **3m** and **3n** in 64 and 67% yield. With 3-methyl indole, **3o** and **3p** resulting from *C* and *N* alkylation were isolated in 65% yield in 2:1 ratio. 4-Fluoro indole was well tolerated, giving **3q** in 57% yield. Indoles bearing electron-donating substituents like methoxy (**3r**) and methyl (**3s**), as well as electron-withdrawing substituents like a chloro (**3t**) and an ester groups (**3u**) at the C5 position gave yields ranging from 45% to 69%. A methyl (**3v**), a CF₃ (**3w**) and a bromo (**3x**) group at C6 or a methyl at C7 position (**3y**) led to product formation in 50–66% yield.

We then examined the scope of aminocyclopropanes and aminocyclobutanes (Scheme 3). When using 2-methyl substituted aminocyclopropane **4a** (d.r.= 4:1), **5a** was isolated as a mixture of two diastereoisomers in a 1:1 ratio. With 2-phenyl substituted aminocyclopropane **4b**, **5b** was obtained in 90% yield after reduction by NaBH₃CN. When using bicyclic compound **4c**, a mixture of two diastereoisomers in a ratio of 1.4:1 was isolated in 60% yield. 2,2-Difluoro aminocyclopropane **4d** afforded trifluoromethyl hemiaminal **5d** in 68% yield.

Scheme 3. Scope of multi-substituted aminocyclopropanes and aminocyclobutanes in the ring-opening fluorination reaction. Ar = *p*-MeO-Ph. See supporting Information for detailed reaction conditions.

With aminocyclobutane **4e**, a series of products **5ea–5ec** was obtained in 56–64% yield, by simply adding different nucleophiles

(hydride, indole or pyrazole) for the second step. When using 3-phenyl aminocyclobutane **4f**, **5f** resulting from selective C1–C2 bond cleavage next to nitrogen was obtained in 63% yield, while C3–C4 bond cleavage was observed only in traces by ¹⁹F NMR in the reaction mixture. With cyclopropylbenzene (**6**) oxyfluorinated product **7** was isolated in 63% yield, with the same regioselectivity as previously observed for aminofluorination (Scheme 4).^[3] This shows that selectivity for ring-opening is substrate controlled and not originating from our different reaction conditions.

Scheme 4. Oxy-fluorination of cyclopropylbenzene (**6**).

In order to better understand the mechanism, we performed several control experiments (Scheme 5). When the *trans* and the *cis* isomers of **4a** were submitted separately to the reaction conditions, the same diastereomeric ratio was observed for product **5a**, supporting the formation of a ring-opened intermediate (Scheme 5, equation 1). When adding TEMPO, we obtained product **8** in 13% yield and recovered 84% **1a**, suggesting that a primary alkyl radical was formed (Scheme 5, equation 2). In order to exclude initiation by hydrogen atom transfer (HAT) to form a neutral amidyl radical, we tested the reaction of *N*-cyclopropyl-4-methoxy-*N*-methylbenzamide (**9**). Products **11** and **12** were obtained, resulting probably from the hydrolysis of unstable hemiaminal intermediate **10** (Scheme 5, equation 3). Attempts to synthesize a *N*-fluorinated aminocyclopropane corresponding to **1a** were unsuccessful,^[16] and an independently synthesized *N*-fluoro amide did not react under our reaction conditions (See Supporting Information for details).^[17] This makes N–H fluorination as a first step highly improbable.

Scheme 5. Mechanistic investigations.

Based on these results and literature precedence, a first speculative reaction mechanism can be proposed (Scheme 6). Photo-excited ketones such as benzophenone (BP) in their triplet state can initiate processes such as hydrogen atom transfer (HAT),^[18] triplet energy transfer (EnT)^[19] and single electron transfer (SET).^[20] By comparing the reduction potentials of cyclopropylamide **1a**, Selectfluor and triplet state benzophenone (BP^{3*}), neither Selectfluor ($E_{1/2}^{\text{red}} = +0.33$ V)^[21,22] nor triplet state benzophenone ($E_{1/2}^{\text{BP}^3*/\text{BP}^-} = +1.27$ V)^[23] are able to oxidize cyclopropylamide **1a** (measured $E_{1/2}^{\text{red}} = +1.67$ V). However, Selectfluor or the Selectfluor-derived radical cation (**I**, $E_{1/2}^{\text{red}} = +0.79$ V)^[24] could oxidize triplet state benzophenone (BP^{3*}, $E_{1/2}^{\text{BP}^3*/\text{BP}^-} = -0.62$ V) to the benzophenone radical cation BP^{•+}, which is oxidizing enough to convert **1a** to radical cation intermediate **III** ($E_{1/2}^{\text{BP}^+/ \text{BP}^-} = +2.37$ V). For [Ir(dF-CF₃ppy)₂(dtbbpy)]PF₆, a similar catalytic cycle could be proposed when considering its redox properties ($E_{1/2}^{\text{Ir(III)}/\text{Ir(II)}} = +1.21$ V, $E_{1/2}^{\text{Ir(III)}/\text{Ir(IV)}} = -0.89$ V and $E_{1/2}^{\text{Ir(IV)}/\text{Ir(III)}} = +1.69$ V).^[21] For the stronger oxidizing Mes-Acr⁺ dye ($E_{1/2}^{\text{red}} = +2.06$ V),^[25] another mechanism may be operative. After SET oxidation, **III** would undergo ring opening to form **IV**, followed by radical fluorination with Selectfluor and nucleophilic addition of water to the iminium to yield **2a**. The reversal of regiochemistry observed compared to the work of Lectka can be tentatively attributed to the low stability of **III** leading to ring-opening, whereas the radical cation obtained from arylcyclopropanes is more stable and undergoes first nucleophilic addition.

Scheme 6. Speculative reaction mechanism.

In summary, we have developed a strategy for the ring-opening fluorination of cyclopropylamides and cyclobutylamides using cheap benzophenone as organophotoredox catalyst. The hemiaminal products can be converted to other building blocks by

substituting the hydroxy group with diverse nucleophiles. Based on the simple reaction procedure and the structural diversity of nitrogen- and fluorine-containing building blocks obtained, we believe that this methodology will be useful in synthetic and medicinal chemistry.

Acknowledgements

We thank the Swiss National Science Foundation (SNSF, grant nos. 200021_165788 and 200020_182798) and EPFL for financial support. We thank Dr. Luca Buzzetti, Dr. Zhikun Zhang and Ms. Stephanie Amos from ISIC EPFL for helpful discussion. We thank Mr. Bastian Muriel from our laboratory for the synthesis of compound **1h**.

Keywords: aminocyclopropanes • ring-opening • photoreaction • fluorination • benzophenone

- [1] a) Organofluorine chemistry (Eds.: R. E. Banks, B. E. Smart, J. C. Tatlow) Springer US: Boston, MA, **1994**. b) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, 317, 1881; c) P. A. Champagne, J. Desroches, J.-D. Hamel, M. Vandamme, J.-F. Paquin, *Chem. Rev.* **2015**, 115, 9073; d) Q. Cheng, T. Ritter, *Trends Chem.* **2019**, 1, 461; e) R. Szpera, D. F. J. Moseley, L. B. Smith, A. J. Sterling, V. Gouverneur, *Angew. Chem., Int. Ed.* **2019**, 58, 14824.
- [2] a) H. Yan, C. Zhu, *Sci. China Chem.* **2017**, 60, 214; b) X. Wu, C. Zhu, *Chem. Rev.* **2018**, 18, 587; c) Y. Liu, Q.-L. Wang, Z. Chen, C.-S. Zhou, B.-Q. Xiong, P.-L. Zhang, C.-A. Yang, Q. Zhou, *Beilstein J. Org. Chem.* **2019**, 15, 256; d) S. P. Morcillo, *Angew. Chem., Int. Ed.* **2019**, 58, 14044.
- [3] a) C. R. Pitts, B. Ling, J. A. Snyder, A. E. Bragg, T. Lectka, *J. Am. Chem. Soc.* **2016**, 138, 6598; b) S. M. Banik, K. M. Mennie, E. N. Jacobsen, *J. Am. Chem. Soc.* **2017**, 139, 9152; c) N. O. Ilchenko, M. Hedberg, K. J. Szabó, *Chem. Sci.* **2017**, 8, 1056.
- [4] a) H. Zhao, X. Fan, J. Yu, C. Zhu, *J. Am. Chem. Soc.* **2015**, 137, 3490; b) N. Ishida, S. Okumura, Y. Nakanishi, M. Murakami, *Chem. Lett.* **2015**, 44, 821; c) S. Ren, C. Feng, T.-P. Loh, *Org. Biomol. Chem.* **2015**, 13, 5105; d) S. Bloom, D. D. Bume, C. R. Pitts, T. Lectka, *Chem. Eur. J.* **2015**, 21, 8060; e) Y. Deng, N. I. Kauser, S. M. Islam, J. T. Mohr, *Eur. J. Org. Chem.* **2017**, 2017, 5872; f) Y. A. Konik, M. Kudrjashova, N. Konrad, S. Kaabel, I. Järving, M. Lopp, D. G. Kananovich, *Org. Biomol. Chem.* **2017**, 15, 4635.
- [5] General reviews on donor-acceptor cyclopropanes: a) H.-U. Reissig, R. Zimmer, *Chem. Rev.* **2003**, 103, 1151; b) T. F. Schneider, J. Kaschel, D. B. Werz, *Angew. Chem., Int. Ed.* **2014**, 53, 5504; Selected examples of aminocyclopropanes: c) F. de Nanteuil, J. Waser, *Angew. Chem., Int. Ed.* **2011**, 50, 12075; d) A. R. Rivero, I. Fernández, M. Á. Sierra, *Org. Lett.* **2013**, 15, 4928; e) F. de Nanteuil, E. Serrano, D. Perrotta, J. Waser, *J. Am. Chem. Soc.* **2014**, 136, 6239; f) S. Racine, F. de Nanteuil, E. Serrano, J. Waser, *Angew. Chem., Int. Ed.* **2014**, 53, 8484; g) D. Perrotta, M.-M. Wang, J. Waser, *Angew. Chem., Int. Ed.* **2018**, 57, 5120; h) M. Zhu, D.-C. Wang, M.-S. Xie, G.-R. Qu, H.-M. Guo, *Chem. Eur. J.* **2018**, 24, 15512; i) E.-J. Hao, D.-D. Fu, D.-C. Wang, T. Zhang, G.-R. Qu, G.-X. Li, Y. Lan, H.-M. Guo, *Org. Chem. Front.* **2019**, 6, 863; j) T. Liang, M.-S. Xie, G.-R. Qu, H.-M. Guo, *Asian J. Org. Chem.* **2019**, 8, 1405; k) M.-C. Zhang, D.-C. Wang, M.-S. Xie, G.-R. Qu, H.-M. Guo, S.-L. You, *Chem* **2019**, 5, 156; For a comparison of the reactivity of different donor-acceptor cyclopropanes, see: l) A. Kreft, A. Lucht, J. Grunenberg, P. G. Jones, D. B. Werz, *Angew. Chem., Int. Ed.* **2019**, 58, 1955.

- [6] a) S. Rousseaux, B. Liégault, K. Fagnou, *Chem. Sci.* **2012**, 3, 244; b) M. H. Shaw, E. Y. Melikhova, D. P. Kloer, W. G. Whittingham, J. F. Bower, *J. Am. Chem. Soc.* **2013**, 135, 4992; c) M. H. Shaw, R. A. Croft, W. G. Whittingham, J. F. Bower, *J. Am. Chem. Soc.* **2015**, 137, 8054; d) M. H. Shaw, N. G. McCreanor, W. G. Whittingham, J. F. Bower, *J. Am. Chem. Soc.* **2015**, 137, 463; e) N. G. McCreanor, S. Stanton, J. F. Bower, *J. Am. Chem. Soc.* **2016**, 138, 11465; f) M. H. Shaw, W. G. Whittingham, J. F. Bower, *Tetrahedron* **2016**, 72, 2731; g) H. Kondo, K. Itami, J. Yamaguchi, *Chem. Sci.* **2017**, 8, 3799; h) G.-W. Wang, J. F. Bower, *J. Am. Chem. Soc.* **2018**, 140, 2743; i) Y.-L. Zhang, R.-T. Guo, J.-H. He, X.-C. Wang, *Org. Lett.* **2019**, 21, 4239; j) G.-W. Wang, O. Boyd, T. A. Young, S. M. Bertrand, J. F. Bower, *J. Am. Chem. Soc.* **2020**, 142, 1740.
- [7] a) J. Lee, J. S. U, S. C. Blackstock, J. K. Cha, *J. Am. Chem. Soc.* **1997**, 119, 10241; b) J. D. Ha, J. Lee, S. C. Blackstock, J. K. Cha, *J. Org. Chem.* **1998**, 63, 8510; c) Y. Takemoto, S. Yamagata, S.-i. Furuse, C. Iwata, *Chem. Commun.* **1998**, 651; d) C. Madelaine, Y. Six, O. Buriez, *Angew. Chem., Int. Ed.* **2007**, 46, 8046.
- [8] a) S. Maity, M. Zhu, R. S. Shinabery, N. Zheng, *Angew. Chem., Int. Ed.* **2012**, 51, 222; b) T. H. Nguyen, S. Maity, N. Zheng, *Beilstein J. Org. Chem.* **2014**, 10, 975; c) T. H. Nguyen, S. A. Morris, N. Zheng, *Adv. Synth. Catal.* **2014**, 356, 2831; d) J. Wang, N. Zheng, *Angew. Chem., Int. Ed.* **2015**, 54, 11424.
- [9] B. Muriel, A. Gagnebin, J. Waser, *Chem. Sci.* **2019**, 10, 10716.
- [10] D. Staveness, T. M. Sadano, K. Li, E. A. Burnham, K. D. Jackson, C. R. J. Stephenson, *Chem* **2019**, 5, 215.
- [11] D. Staveness, J. L. Collins, R. C. McAtee, C. R. J. Stephenson, *Angew. Chem., Int. Ed.* **2019**, 58, 19000.
- [12] a) N. C. Mancey, N. Sardon, A.-L. Auvinet, R. J. Butlin, W. Czechtizky, J. P. A. Harrity, *Chem. Commun.* **2011**, 47, 9804; b) M.-M. Wang, J. Waser, *Angew. Chem., Int. Ed.* **2019**, 58, 13880; c) Q. Wang, N. Zheng, *Org. Lett.* **2019**, 21, 9999.
- [13] J. B. McManus, N. P. R. Onuska, D. A. Nicewicz, *J. Am. Chem. Soc.* **2018**, 140, 9056.
- [14] See Supporting Information for details of tested reaction conditions. It is interesting to note that standard borosilicate glass tubes can be used, as less than 10% light is absorbed at 365 nm, see: <https://www.pgo-online.com/intl/borofloat.html>.
- [15] D. E. Carrera, *Chem. Commun.* **2017**, 53, 11185.
- [16] B. J. Groendyke, D. I. AbuSalim, S. P. Cook, *J. Am. Chem. Soc.* **2016**, 138, 12771.
- [17] In addition, light on/off and Stern-Volmer experiments were performed, but they did not allow clear cut conclusions, see Supporting Information for details.
- [18] a) S. Kamijo, T. Hoshikawa, M. Inoue, *Org. Lett.* **2011**, 13, 5928; b) T. Hoshikawa, S. Kamijo, M. Inoue, *Org. Biomol. Chem.* **2013**, 11, 164; c) Y. Masuda, N. Ishida, M. Murakami, *J. Am. Chem. Soc.* **2015**, 137, 14063; d) N. Ishida, Y. Masuda, S. Uemoto, M. Murakami, *Chem. Eur. J.* **2016**, 22, 6524; e) Y. Shen, Y. Gu, R. Martin, *J. Am. Chem. Soc.* **2018**, 140, 12200; f) N. Ishida, Y. Masuda, Y. Imamura, K. Yamazaki, M. Murakami, *J. Am. Chem. Soc.* **2019**, 141, 19611.
- [19] a) E. Arceo, E. Montroni, P. Melchiorre, *Angew. Chem. Int. Ed.* **2014**, 53, 12064; b) A. Tröster, R. Alonso, A. Bauer, T. Bach, *J. Am. Chem. Soc.* **2016**, 138, 7808.
- [20] Photoexcited triplet state ketones are known to be oxidants, see: a) C. G. Schaefer, K. S. Peters, *J. Am. Chem. Soc.* **1980**, 102, 7566; b) L. Li, X. Mu, W. Liu, Y. Wang, Z. Mi, C.-J. Li, *J. Am. Chem. Soc.* **2016**, 138, 5809; Their application as reductants is much less frequent. For a rare example, see: c) C. B. Tripathi, T. Ohtani, M. T. Corbett, T. Ooi, *Chem. Sci.* **2017**, 8, 5622. For other possible pathways to generate benzophenone radical cations, see: d) X. Cai, Z. Han, S. Yao, N. Lin, *Sci China Ser B* **2001**, 44, 582; e) K. Ohkubo, T. Nanjo, S. Fukuzumi, *Org. Lett.* **2005**, 7, 4265.
- [21] S. Ventre, F. R. Petronijevic, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2015**, 137, 5654.
- [22] All redox values indicated in this manuscript are vs SCE in MeCN.
- [23] W. L. Wallace, R. P. Van Duyne, F. D. Lewis, *J. Am. Chem. Soc.* **1976**, 98, 5319.
- [24] D.-M. Yan, Q.-Q. Zhao, L. Rao, J.-R. Chen, W.-J. Xiao, *Chem. Eur. J.* **2018**, 24, 16895.
- [25] K. A. Margrey, D. A. Nicewicz, *Acc. Chem. Res.* **2016**, 49, 1997.

Ming-Ming Wang and Jérôme Waser*

Page No. – Page No.

**Oxidative Fluorination of
Cyclopropylamides via Organic
Photoredox Catalysis**

Make it shine: We report a photocatalyzed ring-opening fluorination of cyclopropylamides and cyclobutylamides. Both cheap benzophenone with UV A light or organic and inorganic dyes with blue light could be used to promote this process. Various fluorinated amines were then obtained by nucleophilic attack on the formed hemiaminals in one pot, giving access to a broad range of useful building blocks for medicinal chemistry.

Table of Contents

1. General methods	S2
2. Optimisation of the ring-opening fluorination reaction	S3
3. Preparation of starting materials	S4
4. Scope of ring-opening fluorination of mono-substituted cyclopropanes	S13
5. Scope of the nucleophiles for elimination-addition of hemiaminals	S17
6. Scope of ring-opening fluorination for multi-substituted aminocyclopropanes or aminocyclobutanes	S31
7. Scale-up synthesis of compound 3l	S37
8. Mechanistic studies	S38
9. Spectra for new compounds	S46

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, 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 or CD₃CN, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, Acetone-*d*₆ signal at 29.8 ppm or CD₃CN signal at 1.3 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. Fluorescence quenching experiment was conducted on a Varian Cary Eclipse machine. UV/Vis spectroscopy was performed on an Agilent Cary 60 UV-Vis machine. Cyclic voltammetry was performed with a Biologic SP-150 Potentiostat.

For reactions under the irradiation of UV light (365 nm), reactions were performed in 12*75 mm borosilicate glass tubes which were placed around 7 cm far away from lamps (CAMAG UV Lamp 4, long-wave UV light 365 nm) in Rayonet RPR-100 photochemical reactor. For reactions under the irradiation of blue light, reactions were performed in 12*75 mm borosilicate glass tubes which were held using a rack for test tubes placed at the center of a crystallization flask. On this flask were attached the blue LEDs (Ruban LED avec câble à extrémités ouvertes Barthelme Y51516414 182405 24 V 502 cm bleu 1 pc(s), bought directly on www.conrad.ch/fr). The distance between the LEDs and the test tubes was approximatively 3 to 4 cm. Long irradiation for more than 2 h resulted in temperature increasing up to 34 °C.

2. Optimisation of the ring-opening fluorination reaction

2.1 Screening of protecting group

For substrates **1a-k**, reactions were carried out by following General Procedure B (GP B). It is worth attention that **1h** underwent quick degradation as soon as solvent was added, before UV irradiation.

Entry	Substrate	Reaction time	Isolated yield
1	1a	45 min	74%
2	1b	4 h	48%
3	1c	4 h	43%
4	1d	4 h	0
5	1e	4 h	0
6	1f	45 min	decomposed
7	1g	10 h	31% ^[a]
8	1h	45 min	decomposed
7	1i	45 min	quantitative formation of a sulfoxide
8	1j	4 h	40%
9	1k	4 h	41%

^[a] ¹H NMR yield using fluorobenzene as internal standard. Product **2g** was converted to an indole adduct **2g-indole** by following General Procedure C, in order to simplify purification.

2.2 Catalyst screening

Entry	Catalyst	Deviation	Isolated yield
1	Benzophenone	-	74%
2	9-Fluorenone	-	6% ^[a]
3	9-Fluorenone	No water	0
4	Benzophenone	No water	0
5	[Ir(dF-CF ₃ ppy) ₂ (dtbbpy)]PF ₆ (1 mol%)	Selectfluor (1.5 equiv), 1.5 h, blue LED	76% ^[a]
6	9-Mesityl-10-methylacridinium perchlorate (2 mol%)	Selectfluor (1.5 equiv), 3 h, blue LED	75% ^[a]

^[a] ¹H NMR yield using CH₂Br₂ or fluorobenzene as internal standard.

2.3 Solvent screening

Entry	Solvent	NMR yield ^[a]
1	MeCN	<5%
2	CD ₂ Cl ₂	0
3	Acetone- <i>d</i> ₆	10
4	DMSO- <i>d</i> ₆	0
5	Methanol- <i>d</i> ₄	0
6	MeCN-H ₂ O (4:6)	76%
7	CD ₂ Cl ₂ -D ₂ O (4:6)	<5%
8	Acetone-H ₂ O (4:6)	53%
9	DMSO-H ₂ O (4:6)	0

^[a] ¹H NMR yield using fluorobenzene as internal standard.

3. Preparation of starting materials

3.1 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 1 M NaOH (10 mL) and 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.

The synthesis of **1a-1i** has already been described by our group. The procedures are taken from the indicated publications to facilitate reproduction of the results by having all data in the same file.

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

***N*-Cyclopropyl-4-methoxybenzamide (1a)**

Following GP A, using 4-methoxybenzoyl chloride (1.55 g, 9.09 mmol), *N*-cyclopropyl-4-methoxybenzamide **1a** 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-methylbenzamide (1b).**

Following GP A, using 4-methylbenzoyl chloride (1.41 g, 9.09 mmol), *N*-cyclopropyl-4-methylbenzamide **1b** was obtained as a white solid (1.51 g, 8.62 mmol, 95%).

¹H NMR (400 MHz, CDCl₃): δ = 7.72 – 7.55 (m, 2H, ArH), 7.23 – 7.11 (m, 2H, ArH), 6.33 (d, *J* = 39.2 Hz, 1H, NH), 2.88 (tt, *J* = 7.2, 3.5 Hz, 1H, CH), 2.37 (d, *J* = 3.1 Hz, 3H, CH₃), 0.92 – 0.75 (m, 2H, CH₂), 0.68 – 0.54 (m, 2H, CH₂).

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

***N*-Cyclopropyl-4-fluorobenzamide (1c).**

² Zhang, Y.; Liu, B.; Gou, Z.; Li, Y.; Zhang, X.; Wang, Y.; Yu, S.; Li, Y.; Sun, D. *Bioorg. Med. Chem. Lett.* **2015**, *25*, 791-794.

Following GP A, using 4-fluorobenzoyl chloride (1.44 g, 9.09 mmol), *N*-cyclopropyl-4-fluorobenzamide **1c** 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.^[3]

***N*-Cyclopropyl-4-nitrobenzamide (1d).**

Following GP A, using 4-nitrobenzoyl chloride (1.69 g, 9.09 mmol), *N*-cyclopropyl-4-nitrobenzamide **1d** 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*-(1-Cyano-3-iodopropyl)-4-methylbenzenesulfonamide (1e).**

³ Kondo, H.; Itami, K.; Yamaguchi, J. *Chem. Sci.* **2017**, *8*, 3799-3803.

Following GP A, using tosyl chloride (1.73 g, 9.09 mmol), *N*-(1-Cyano-3-iodopropyl)-4-methylbenzenesulfonamide **1e** 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.^[4]

***tert*-Butyl cyclopropylcarbamate (**1f**).**

Following a modified version of a reported procedure,^[5] 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 1 M NaOH (10 mL) and brine (10 mL), and dried over Na₂SO₄, filtered and concentrated *in vacuo*. *tert*-Butyl cyclopropylcarbamate **1f** 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.^[5]

***N*-Cyclopropylpivalamide (**1g**).**

Following GP A, using pivaloyl chloride (1.32 g, 11.0 mmol), *N*-cyclopropylpivalamide **1g** was obtained as a white solid (0.90 g, 6.37 mmol, 64%).

¹H NMR (400 MHz, CDCl₃): δ = 5.71 (s, 1H, NH), 2.76 – 2.60 (m, 1H, CH), 1.16 (s, 9H, CH₃), 0.86 – 0.71 (m, 2H, CH₂), 0.57 – 0.36 (m, 2H, CH₂).

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

4-Chloro-*N*-cyclopropylaniline (1h**).**

⁴ O'Sullivan, S.; Doni, E.; Tuttle, T.; Murphy, J. A. *Angew. Chem. Int. Ed.* **2014**, *53*, 474-478.

⁵ 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.

⁶ Miyamura, S.; Araki, M.; Suzuki, T.; Yamaguchi, J.; Itami, K. *Angew. Chem. Int. Ed.* **2015**, *54*, 846-851.

This compound was synthesized for another project in our group. For its synthesis and characterization, please refer to: *Chem. Sci.* **2019**, *10*, 10716, SI page 17.

***N*-Cyclopropyl-4-(methylthio)benzamide (1i).**

Following GP A, using 4-(methylthio)benzoyl chloride (1.70 g, 9.09 mmol), *N*-cyclopropyl-4-(methylthio)benzamide **1i** 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.

4-Chloro-*N*-cyclopropylbenzamide (1j).

Following GP A, using 4-chlorobenzoyl chloride (1.59 g, 9.09 mmol), 4-chloro-*N*-cyclopropylbenzamide **1j** 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 $C_{10}H_{10}ClNNaO^+$ $[M+Na]^+$ 218.0343; Found 218.0344.

***N*-cyclopropylbenzamide (1k).**

Following GP A, using benzoyl chloride (1.28 g, 9.09 mmol), *N*-cyclopropylbenzamide **1k** was obtained as a white solid (1.38 g, 8.57 mmol, 94%).

1H NMR (400 MHz, $CDCl_3$): δ = 7.76 – 7.67 (m, 2H, ArH), 7.49 – 7.43 (m, 1H, ArH), 7.41 – 7.34 (m, 2H, ArH), 6.46 (s, 1H, NH), 2.88 (tq, J = 7.1, 3.7 Hz, 1H, CH), 0.87 – 0.78 (m, 2H, CH_2), 0.66 – 0.50 (m, 2H, CH_2).

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

4-Methoxy-*N*-2-methylcyclopropyl)benzamide (4a).

Following a modified version of a reported procedure,^[1] to a solution of 2-methylcyclopropan-1-amine (250 mg, 3.52 mmol, 4:1 d.r., ordered from Fluorochem) and Et_3N (0.54 mL, 3.9 mmol, 1.1 equiv.) in dichloromethane (10 mL) was slowly added a solution of 4-methoxybenzoyl chloride (658 mg, 3.87 mmol, 1.1 equiv.) in dichloromethane (5 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 Na_2SO_4 , filtered and concentrated *in vacuo*. 4-Methoxy-*N*-2-methylcyclopropyl)benzamide **4a** was obtained as a white solid (655 mg, 3.20 mmol, 4:1 d.r., 91%) after first purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent. Second purification was performed by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent, **trans-4a** (272 mg) and **cis-4a** (79 mg) were obtained separately, together with the rest of product **4a** recovered as a mixture of diastereomers.

4-Methoxy-*N*-trans-2-methylcyclopropyl)benzamide (*trans*-4a)

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

Mp: 94-96 °C;

⁷ Sureshbabu, P.; Sadaf, A.; Chaudhary, P.; Kandasamy, J. *Org. Biomol. Chem.* **2019**, *17*, 845-850.

¹H NMR (400 MHz, CDCl₃): δ = 7.75 – 7.62 (m, 2H, ArH), 6.94 – 6.83 (m, 2H, ArH), 6.20 (s, 1H, NH), 3.83 (s, 3H, OCH₃), 2.56 (dq, *J* = 6.9, 3.4 Hz, 1H, NCH), 1.13 (d, *J* = 6.1 Hz, 3H, CH₃), 0.95 (ddt, *J* = 12.2, 6.2, 3.2 Hz, 1H, CHCH₃), 0.73 (ddd, *J* = 9.2, 5.4, 3.8 Hz, 1H, CH₂), 0.61 (dt, *J* = 7.2, 5.7 Hz, 1H, CH₂).

¹³C NMR (101 MHz, CDCl₃): δ = 168.1, 162.1, 128.6, 126.7, 113.6, 55.4, 30.4, 17.2, 14.9 (signals of C2 and C3 are overlapped).

IR (film): $\tilde{\nu}$ = 3274 (m), 3003 (w), 2952 (w), 1624 (s), 1606 (s), 1574 (m), 1541 (s), 1254 (s), 1031 (m), 843 (m);

HRMS (APCI) calcd. for C₁₂H₁₅NNaO₂⁺ [M+Na]⁺ 228.0995; Found 228.0993.

4-Methoxy-*N*-cis-2-methylcyclopropylbenzamide (cis-4a)

R_f: 0.26 (silica, pentanes:ethyl acetate 1:1);

Mp: 89-91 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.76 – 7.69 (m, 2H, ArH), 6.92 – 6.87 (m, 2H, ArH), 6.07 (s, 1H, NH), 3.84 (s, 3H, OCH₃), 2.90 (dddd, *J* = 9.9, 7.0, 4.0, 3.0 Hz, 1H, NCH), 1.15 – 1.07 (m, 4H, CH₃ + CH₂), 1.03 (dddd, *J* = 8.8, 5.4, 3.2, 1.2 Hz, 1H, CH₂), 0.26 – 0.15 (m, 1H, CHCH₃).

¹³C NMR (101 MHz, CDCl₃): δ = 168.7, 162.1, 128.6, 126.9, 113.7, 55.4, 27.5, 13.2, 12.5, 11.7.

IR (film): $\tilde{\nu}$ = 3292 (m), 2958 (w), 1631 (s), 1606 (s), 1499 (s), 1252 (s), 1178 (m), 1028 (m), 844 (m);

HRMS (APCI) calcd. for C₁₂H₁₅NNaO₂⁺ [M+Na]⁺ 228.0995; Found 228.0993.

4-Methoxy-*N*-(trans-2-phenylcyclopropyl)benzamide (4b).

Following a modified version of a reported procedure,^[1] to a solution of *trans*-2-phenylcyclopropylamine hydrochloride (635 mg, 3.74 mmol, 1.1 equiv., ordered from Acros) and triethylamine (1.0 mL, 7.2 mmol, 2.0 equiv.) in dichloromethane (10 mL) was slowly added a solution of 4-methoxybenzoyl chloride (607 mg, 3.56 mmol, 1.0 equiv.) in dichloromethane (10 mL) at 0 °C. The reaction mixture was stirred at room temperature 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 1 M NaOH (10 mL) and brine (10 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. 4-Methoxy-*N*-(*trans*-2-phenylcyclopropyl)benzamide **4b** was obtained as a white solid (0.92 g, 3.4 mmol, 97%).

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

Mp: 153-155 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.81 – 7.65 (m, 2H, ArH), 7.31 – 7.26 (m, 2H, ArH), 7.24 – 7.15 (m, 3H, ArH), 6.97 – 6.83 (m, 2H, ArH), 6.39 (s, 1H, NH), 3.84 (s, 3H, OCH₃), 3.06 (tt, *J* = 7.4, 3.4 Hz, 1H, NCH), 2.16 (ddd, *J* = 9.8, 6.3, 3.4 Hz, 1H, PhCH), 1.29 (dddd, *J* = 27.6, 10.0, 6.0, 4.4 Hz, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 168.1, 162.2, 140.4, 128.7, 128.4, 126.6, 126.5, 126.1, 113.7, 55.4, 32.5, 24.9, 16.3;

IR (film): $\tilde{\nu}$ = 3291 (w), 1632 (s), 1606 (s), 1500 (s), 1255 (s), 1029 (m), 845 (m);

HRMS (ESI) calcd. for C₁₇H₁₇NNaO₂⁺ [M+Na]⁺ 290.1151; Found 290.1151.

(1*R*,5*S*,6*S*)-tert-Butyl 6-(4-methoxybenzamido)-3-azabicyclo[3.1.0]hexane-3-carboxylate (4c).

Following a modified version of a reported procedure,^[1] to a solution of (1*R*,5*S*,6*S*)-*tert*-butyl 6-amino-3-azabicyclo[3.1.0]hexane-3-carboxylate (495 mg, 2.50 mmol, 1.0 equiv., ordered from Spirochem) and triethylamine (0.40 mL, 2.9 mmol, 1.1 equiv.) in dichloromethane (10 mL) was slowly added a solution of 4-methoxybenzoyl chloride (470 mg, 2.76 mmol, 1.1 equiv.) in dichloromethane (5 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*. (1*R*,5*S*,6*S*)-*tert*-butyl 6-(4-methoxybenzamido)-3-azabicyclo[3.1.0]hexane-3-carboxylate (**4c**) was obtained as a beige solid (740 mg, 2.23 mmol, 89%) after purification by column chromatography on silica using 2:3 pentanes:ethyl acetate as eluent.

R_f: 0.29 (silica, pentanes:ethyl acetate 2:3);

Mp: 160-162 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.74 – 7.64 (m, 2H, ArH), 6.93 – 6.82 (m, 2H, ArH), 6.41 – 6.24 (m, 1H, NH), 3.82 (d, *J* = 1.9 Hz, 3H, OCH₃), 3.77 – 3.65 (m, 2H, CH₂), 3.45 – 3.34 (m, 2H, CH₂), 2.60 – 2.55 (m, 1H, NCH), 1.79 – 1.68 (m, 2H, CH), 1.42 (d, *J* = 1.4 Hz, 9H, CH₃); Mixture of 2 rotamers with almost 1:1 ratio. They are not completely resolved.

¹³C NMR (101 MHz, CDCl₃): δ = 168.0, 162.2, 154.5, 128.7, 126.3, 113.7, 79.5, 55.4, 47.8, 47.5, 33.1, 28.4, 25.2, 23.7; Mixture of 2 rotamers with almost 1:1 ratio. They are not completely resolved.

IR (film): $\tilde{\nu}$ = 3302 (w), 2974 (w), 2931 (w), 2873 (w), 1694 (s), 1606 (s), 1502 (s), 1393 (s), 1253 (s), 1172 (s), 1115 (s), 1029 (m), 844 (w), 769 (w), 730 (w);

HRMS (ESI) calcd. for C₁₈H₂₄N₂NaO₄⁺ [M+Na]⁺ 355.1628; Found 355.1631.

***N*-(2,2-Difluorocyclopropyl)-4-methoxybenzamide (4d).**

Following a modified version of a reported procedure,^[1] to a solution of 2,2-difluorocyclopropylamine hydrochloride (250 mg, 1.93 mmol, 1.0 equiv., ordered from Fluorochem) and triethylamine (0.60 mL, 4.3 mmol, 2.2 equiv.) in dichloromethane (10 mL) was slowly added a solution of 4-methoxybenzoyl chloride (370 mg, 2.17 mmol, 1.1 equiv.) in dichloromethane (5 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*. *N*-(2,2-

difluorocyclopropyl)-4-methoxybenzamide (**4d**) was obtained as a white solid (320 mg, 1.41 mmol, 73%) after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.25 (silica, pentanes:ethyl acetate 2:1);

Mp: 128-129 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.73 (d, *J* = 8.7 Hz, 2H, ArH), 6.91 (d, *J* = 8.7 Hz, 2H, ArH), 6.39 (s, 1H, NH), 3.84 (s, 3H, OCH₃), 3.51 (dtq, *J* = 12.1, 5.9, 3.4, 3.0 Hz, 1H, CH), 1.87 (dtd, *J* = 13.5, 9.3, 6.4 Hz, 1H, CH₂), 1.50 – 1.35 (m, 1H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = ¹³C NMR (101 MHz, Chloroform-*d*) δ 167.8, 162.6, 128.9, 125.5, 113.8, 111.1 (dd, *J* = 291.4, 284.3 Hz), 55.4, 30.8 (dd, *J* = 15.0, 9.4 Hz), 19.3 (t, *J* = 9.9 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -131.2 (d, *J* = 162.2 Hz, 1F), -143.6 (d, *J* = 162.2 Hz, 1F);

IR (film): $\tilde{\nu}$ = 3307 (m), 1638 (s), 1608 (m), 1500 (s), 1471 (m), 1257 (s), 1222 (s), 1014 (m), 845 (m);

HRMS (ESI) calcd. for C₁₁H₁₂F₂NO₂⁺ [M+H]⁺ 228.0831; Found 228.0843.

***N*-Cyclobutyl-4-methoxybenzamide (**4e**)**

Following GP A, using cyclobutylamine (523 mg, 7.40 mmol, 1.1 equiv.) and 4-methoxybenzoyl chloride (1.19 g, 7.00 mmol, 1.0 equiv.), *N*-cyclobutyl-4-methoxybenzamide **4e** was obtained as a white solid (1.08 g, 5.27 mmol, 75%).

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

Mp: 126-128 °C;

¹H NMR (400 MHz, CDCl₃) δ = 7.84 – 7.61 (m, 2H, ArH), 7.00 – 6.82 (m, 2H, ArH), 6.16 (s, 1H, NH), 4.58 (h, *J* = 8.1 Hz, 1H, CH), 3.84 (s, 3H, OCH₃), 2.53 – 2.32 (m, 2H, CH₂CH₂CH₂), 2.02 – 1.86 (m, 2H, CH₂), 1.76 (tt, *J* = 11.4, 6.5 Hz, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.0, 162.1, 128.6, 126.8, 113.7, 55.4, 45.1, 31.4, 15.2;

IR (film): $\tilde{\nu}$ = 3305 (w), 2941 (w), 1628 (s), 1607 (s), 1503 (s), 1253 (s), 1030 (m), 844 (m);

HRMS (ESI) calcd. for C₁₂H₁₆NO₂⁺ [M+H]⁺ 206.1176; Found 206.1175.

4-Methoxy-*N*-(*trans*-3-phenylcyclobutyl)benzamide (4f**).**

Following a modified version of a reported procedure,^[1] to a solution of *trans*-3-phenylcyclobutan-1-amine (250 mg, 1.70 mmol, 1.0 equiv., ordered from Fluorochem) and triethylamine (0.27 mL, 1.9 mmol, 1.1 equiv.) in dichloromethane (10 mL) was slowly added a solution of 4-methoxybenzoyl chloride (320 mg, 1.88 mmol, 1.1 equiv.) in dichloromethane (5 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*. 4-

Methoxy-*N*-(*trans*-3-phenylcyclobutyl)benzamide **4f** was obtained as a white solid (448 mg, 1.59 mmol, 94%) 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);

Mp: 164-166 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.83 – 7.71 (m, 2H, ArH), 7.39 – 7.26 (m, 4H, ArH), 7.26 – 7.17 (m, 1H, ArH), 6.98 – 6.87 (m, 2H, ArH), 6.36 (d, *J* = 6.9 Hz, 1H, NH), 4.71 (ddtd, *J* = 14.2, 7.9, 6.3, 1.3 Hz, 1H, NCH), 3.86 (s, 3H, OCH₃), 3.71 – 3.57 (m, 1H, PhCH), 2.74 – 2.61 (m, 2H, CH₂), 2.55 – 2.43 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ 166.5, 162.1, 144.8, 128.7, 128.5, 126.8, 126.5, 126.0, 113.7, 55.4, 43.7, 36.9, 34.6;

IR (film): $\tilde{\nu}$ = 3338 (m), 2938 (w), 1628 (s), 1605 (m), 1499 (s), 1251 (s), 1031 (m);

HRMS (ESI) calcd. for C₁₈H₂₀NO₂⁺ [M+H]⁺ 282.1489; Found 282.1480.

***N*-Cyclopropyl-4-methoxy-*N*-methylbenzamide (9).**

Following GP D, *N*-cyclopropyl-methylamine hydrochloride (323 mg, 3.00 mmol, 1.1 equiv.) was used as starting material. *N*-cyclopropyl-4-methoxy-*N*-methylbenzamide **9** (560 mg, 2.73 mmol, 97%) was obtained as a yellow oil which solidified during storage.

R_f: 0.40 (silica, pentanes:ethyl acetate 2:3);

Mp: 59-61 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.55 – 7.43 (m, 2H, ArH), 6.94 – 6.82 (m, 2H, ArH), 3.83 (s, 3H, OCH₃), 3.07 (s, 3H, NCH₃), 2.82 (tt, *J* = 7.0, 3.9 Hz, 1H, CH), 0.63 (d, *J* = 6.7 Hz, 2H, CH₂), 0.47 (p, *J* = 5.8, 5.0 Hz, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 172.2, 160.6, 129.4, 129.4, 113.1, 55.2, 35.6, 33.1, 9.4;

IR (film): $\tilde{\nu}$ = 3010 (w), 2936(w), 1626 (s), 1607 (s), 1381 (s), 1250 (s), 1172 (m), 1027 (m), 842 (m);

HRMS (ESI) calcd. for C₁₂H₁₅NNaO₂⁺ [M + Na]⁺ 228.0995; Found 228.0999.

4. Scope of ring-opening fluorination of mono-substituted cyclopropanes

General Procedure B (GP B):

In a 12*75 mm Borosilicate glass tube, the corresponding aminocyclopropane (0.300 mmol, 1.0 equiv.), selectfluor (117 mg, 0.330 mmol, 1.1 equiv.) and benzophenone (5.4 mg, 0.030 mmol, 0.10 equiv.) were dissolved in 0.75 mL of MeCN-H₂O (v:v 4:6, 0.40 M). The reaction mixture was degassed by three freeze-pump-thaw cycles and backfilled with N₂. The mixture was then stirred at room temperature under 365 nm irradiation in Rayonet Reactor for 45 minutes, if not specified otherwise. The distance between glass tube and lamp was 7 cm. After the completion of the reaction, the crude product was directly submitted to column chromatography on silica using pentanes:ethyl acetate as eluent.

***N*-(3-Fluoro-1-hydroxypropyl)-4-methoxybenzamide (2a).**

Following GP B, starting from *N*-cyclopropyl-4-methoxybenzamide **1a** (57.3 mg, 0.300 mmol), *N*-(3-fluoro-1-hydroxypropyl)-4-methoxybenzamide **2a** (50.5 mg, 0.222 mmol, 74%) was obtained as a white solid after purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent.

R_f: 0.27 (silica, pentanes:ethyl acetate 1:1);

Mp: 119-121 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.78 – 7.69 (m, 2H, ArH), 7.19 – 7.05 (m, 1H, NH), 6.96 – 6.87 (m, 2H, ArH), 5.71 (dt, *J* = 7.3, 5.3 Hz, 1H, CH), 4.96 – 4.58 (m, 2H, FCH₂), 4.27 (s, 1H, OH, peak was not splitted), 3.85 (s, 3H, OCH₃), 2.27 – 2.06 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 168.1, 162.7, 128.9, 125.5, 113.8, 80.7 (d, *J* = 161.6 Hz), 72.8 (d, *J* = 2.1 Hz), 55.4, 35.1 (d, *J* = 18.8 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.0;

IR (film): $\tilde{\nu}$ = 3318 (br, s), 2968 (w), 1640 (m), 1606 (s), 1503 (s), 1256 (s), 1179 (m), 1029 (m), 846 (m);

HRMS (APPI) calcd. for C₁₁H₁₄FNO₃⁺ [*M*]⁺ 227.0952; Found 227.0949.

***N*-(3-Fluoro-1-hydroxypropyl)-4-methylbenzamide (2b).**

Following GP B, starting from *N*-cyclopropyl-4-methylbenzamide **1b** (52.5 mg, 0.300 mmol) and after stirring for 4 hours, *N*-(3-fluoro-1-hydroxypropyl)-4-methylbenzamide **2b** (30.3 mg, 0.144 mmol, 48%) was obtained as a white solid after purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent.

R_f: 0.32 (silica, pentanes:ethyl acetate 1:1);

Mp: 103-105 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 8.04 (s, 1H, NH), 7.85 – 7.75 (m, 2H, ArH), 7.26 (d, *J* = 8.0 Hz, 2H, ArH), 5.72 (dtd, *J* = 8.3, 6.5, 4.3 Hz, 1H, CH), 4.99 (d, *J* = 4.3 Hz, 1H, OH), 4.74 – 4.50 (m, 2H, FCH₂), 2.37 (s, 3H, CH₃), 2.18 – 2.07 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 167.4, 142.6, 132.7, 129.7, 128.2, 81.5 (d, *J* = 161.8 Hz), 71.9 (d, *J* = 6.6 Hz), 37.5 (d, *J* = 19.5 Hz), 21.3;

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -222.2;

IR (film): $\tilde{\nu}$ = 3301 (br, s), 1643 (s), 1532 (m), 1504 (m), 1281 (w), 756 (m);

HRMS (APCI) calcd. for C₁₁H₁₄FNNaO₂⁺ [*M*+Na]⁺ 234.0901; Found 234.0899.

4-Fluoro-*N*-(3-fluoro-1-hydroxypropyl)benzamide (2c).

Following GP B, starting from *N*-cyclopropyl-4-fluorobenzamide **1c** (62.1 mg, 0.300 mmol) and after stirring for 4 hours, 4-fluoro-*N*-(3-fluoro-1-hydroxypropyl)benzamide **2c** (27.6 mg, 0.128 mmol, 43%) was obtained as a white solid after purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent.

R_f: 0.42 (silica, pentanes:ethyl acetate 1:1);

Mp: 80-82 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.78 (dd, *J* = 8.9, 5.2 Hz, 2H, ArH), 7.20 – 7.08 (m, 3H, ArH + NH), 5.72 (dtd, *J* = 7.1, 5.2, 3.2 Hz, 1H, CH), 5.11 – 4.43 (m, 2H, FCH₂), 4.17 (d, *J* = 3.2 Hz, 1H, OH), 2.44 – 1.92 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 167.5, 165.1 (d, *J* = 253.0 Hz), 129.5, 129.5 (d, *J* = 9.0 Hz), 115.8 (d, *J* = 21.9 Hz), 80.7 (d, *J* = 161.4 Hz), 72.9 (d, *J* = 8.9 Hz), 35.0 (d, *J* = 18.6 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -107.0, -217.8;

IR (film): $\tilde{\nu}$ = 3315 (br, s) 1644 (s), 1604 (s), 1501 (s), 1236 (m), 852 (m);

HRMS (APCI) calcd. for C₁₀H₁₁F₂NNaO₂⁺ [M+Na]⁺ 238.0650; Found 238.0648.

***N*-(3-Fluoro-1-(1*H*-indol-3-yl)propyl)pivalamide (2*g*-indole).**

Following GP B, starting from *N*-cyclopropylpivalamide **1g** (42.3 mg, 0.300 mmol) and after stirring for 10 hours for the first step, 1*H*-indole (42.2 mg, 0.360 mmol, 1.2 equiv.) in 0.5 mL MeCN was then added to the reaction crude. After the reaction mixture was stirred for another 16 hours, *N*-(3-fluoro-1-(1*H*-indol-3-yl)propyl)pivalamide **2g-indole** (8.0 mg, 0.029 mmol, 29%) was obtained as a yellow solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.47 (silica, pentanes:ethyl acetate 1:1);

Mp: 76-79 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.23 (s, 1H, indole NH), 7.59 (d, *J* = 7.9 Hz, 1H, ArH), 7.38 (d, *J* = 8.2 Hz, 1H, ArH), 7.22 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H, ArH), 7.15 – 7.10 (m, 2H, ArH), 6.04 (d, *J* = 7.8 Hz, 1H, NH), 5.51 (q, *J* = 7.2 Hz, 1H, CH), 4.67 – 4.41 (m, 2H, FCH₂), 2.48 – 2.32 (m, 2H, CH₂), 1.20 (s, 9H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 177.8, 136.6, 125.7, 122.5, 121.7, 119.9, 119.1, 116.2, 111.5, 82.0 (d, *J* = 163.9 Hz), 43.8 (d, *J* = 5.7 Hz), 38.7, 35.4 (d, *J* = 19.2 Hz), 27.5;

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.0;

IR (film): $\tilde{\nu}$ = 3411 (w), 3287 (m), 2965 (m), 1640 (s), 1510 (s), 1197 (w), 1011 (w), 743 (s);

HRMS (ESI) calcd. for C₁₆H₂₁FN₂NaO⁺ [M+Na]⁺ 299.1530; Found 299.1536.

4-Chloro-*N*-(3-fluoro-1-hydroxypropyl)benzamide (2j).

Following GP B, starting from 4-chloro-*N*-cyclopropylbenzamide **1j** (58.5 mg, 0.300 mmol) and after stirring for 4 hours, 4-chloro-*N*-(3-fluoro-1-hydroxypropyl)benzamide **2j** (27.7 mg, 0.120 mmol, 40%)

was obtained as a white solid after purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent.

R_f: 0.32 (silica, pentanes:ethyl acetate 1:1);

Mp: 114-116 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.75 – 7.64 (m, 2H, ArH), 7.45 – 7.34 (m, 2H, ArH), 7.21 (s, 1H, NH), 5.72 (td, *J* = 6.9, 4.8 Hz, 1H, CH), 5.00 – 4.55 (m, 2H, FCH₂), 4.30 (d, *J* = 3.0 Hz, 1H, OH), 2.30 – 2.01 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 167.4, 138.5, 131.7, 129.0, 128.5, 80.7 (d, *J* = 161.6 Hz), 72.8 (d, *J* = 2.0 Hz), 35.1 (d, *J* = 18.6 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.1;

IR (film): $\tilde{\nu}$ = 3299 (m) 1644 (s), 1532 (s), 1487 (m), 1094 (m), 847 (w);

HRMS (APCI) calcd. for C₁₀H₁₁ClFNNaO₂⁺ [M+Na]⁺ 254.0355; Found 254.0352.

***N*-(3-Fluoro-1-hydroxypropyl)benzamide (2k).**

Following GP B, starting from *N*-cyclopropylbenzamide **1k** (48.3 mg, 0.300 mmol) and after stirring for 4 hours, *N*-(3-fluoro-1-hydroxypropyl)benzamide **2k** (24.2 mg, 0.123 mmol, 41%) was obtained as a yellow solid after purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent.

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

Mp: 114-116 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 8.14 (s, 1H, NH), 7.94 – 7.87 (m, 2H, ArH), 7.56 – 7.50 (m, 1H, ArH), 7.49 – 7.42 (m, 2H, ArH), 5.81 – 5.66 (m, 1H, CH), 5.07 (d, *J* = 4.2 Hz, 1H, OH), 4.73 – 4.52 (m, 2H, FCH₂), 2.19 – 2.08 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 167.5, 135.5, 132.3, 129.1, 128.2, 81.5 (d, *J* = 161.8 Hz), 71.9 (dd, *J* = 10.0, 6.7 Hz), 37.5 (d, *J* = 19.5 Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -222.2;

IR (film): $\tilde{\nu}$ = 3315 (br, s) 1644 (s), 1530 (s), 1489 (m), 1283 (m), 1035 (m), 713 (m);

HRMS (APCI) calcd. for C₁₀H₁₂FNNaO₂⁺ [M+Na]⁺ 220.0744; Found 220.0742.

***N*-Cyclopropyl-4-(methylsulfinyl)benzamide (2i).**

Following GP B, starting from *N*-cyclopropyl-4-(methylthio)benzamide **1i** (62.1 mg, 0.300 mmol) and after stirring for 3 hours, *N*-cyclopropyl-4-(methylsulfinyl)benzamide **2i** (63.5 mg, 0.285 mmol, 95%) was obtained as a white solid after purification by column chromatography on silica using 10:1 dichloromethane:methanol as eluent.

R_f: 0.42 (silica, dichloromethane:methanol 10:1);

Mp: 175-177 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.92 – 7.85 (m, 2H, ArH), 7.66 – 7.59 (m, 2H, ArH), 6.71 (s, 1H, NH), 2.92 (tq, *J* = 6.4, 3.3 Hz, 1H, CH), 2.71 (s, 3H, CH₃), 0.87 (td, *J* = 7.0, 5.3 Hz, 2H, CH₂), 0.69 – 0.60 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 167.7, 148.9, 137.2, 128.0, 123.6, 43.8, 23.3, 6.7;

IR (film): $\tilde{\nu}$ = 3269 (m), 2994 (w), 2918 (w), 1638 (s), 1535 (s), 1303 (m), 1044 (s), 856 (m);

HRMS (ESI) calcd. for C₁₁H₁₄NO₂S⁺ [M+H]⁺ 224.0740; Found 224.0740.

5. Scope of the nucleophiles for elimination-addition of hemiaminals

General Procedure C (GP C):

In a 12*75 mm borosilicate glass tube, *N*-cyclopropyl-4-methoxybenzamide **1a** (57.3 mg, 0.300 mmol), selectfluor (117 mg, 0.330 mmol, 1.1 equiv.) and benzophenone (5.4 mg, 0.030 mmol, 0.10 equiv.) were dissolved in 0.75 mL of MeCN-H₂O (v:v 4:6, 0.40 M). The reaction mixture was degassed by three freeze-pump-thaw cycles and backfilled with N₂. The mixture was then stirred at room temperature under 365 nm irradiation in Rayonet Reactor for 45 minutes. Then the tube was taken out from the Rayonet Reactor and a solution of nucleophile (0.360 mmol, 1.2 equiv.) in 0.50 mL MeCN was added dropwise. The reaction mixture was stirred at room temperature for 3 hours, 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*-(3-Fluoro-1-methoxypropyl)-4-methoxybenzamide (3a).**

Following GP C, methanol (1.0 mL, 25 mmol, 82 equiv.) was used as nucleophile. After the reaction mixture was stirred for 1 hours, *N*-(3-fluoro-1-methoxypropyl)-4-methoxybenzamide (**3a**) (53.0 mg, 0.220 mmol, 73%) was obtained as a white solid after purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent.

R_f: 0.46 (silica, pentanes:ethyl acetate 1:1);

Mp: 110-112 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.82 – 7.68 (m, 2H, ArH), 7.01 – 6.85 (m, 2H, ArH), 6.56 (d, *J* = 8.8 Hz, 1H, NH), 5.55 (dt, *J* = 10.1, 5.3 Hz, 1H, CH), 4.85 – 4.52 (m, 2H, FCH₂), 3.85 (s, 3H, ArOCH₃), 3.42 (s, 3H, OCH₃), 2.24 – 2.01 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.8, 162.5, 128.9, 125.9, 113.8, 80.6 (d, *J* = 162.9 Hz), 78.4 (d, *J* = 3.4 Hz), 56.0, 55.4, 35.9 (d, *J* = 19.0 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -219.3;

IR (film): $\tilde{\nu}$ = 3304 (w), 2937 (w), 2839 (w), 1642 (s), 1606 (s), 1531 (m), 1503 (s), 1257 (s), 1178 (m), 845 (m);

HRMS (ESI) calcd. for C₁₂H₁₆FNNaO₃⁺ [M+Na]⁺ 264.1006; Found 264.1014.

***N*-(3-Fluoro-1-hydroperoxypropyl)-4-methoxybenzamide (3b).**

Following GP C, hydrogen peroxide solution 30% (w/w) in water (37 μ L, 0.36 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(3-fluoro-1-hydroperoxypropyl)-4-methoxybenzamide (**3b**) (46.5 mg, 0.191 mmol, 64%) was obtained as a white solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.41 (silica, pentanes:ethyl acetate 2:3);

Mp: 93–95 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 10.95 (s, 1H, OOH), 8.09 (d, *J* = 7.7 Hz, 1H, NH), 7.94 – 7.91 (m, 2H, ArH), 7.01 – 6.97 (m, 2H, ArH), 5.95 (dt, *J* = 8.9, 6.8 Hz, 1H, CH), 4.69 – 4.51 (m, 2H, FCH₂), 3.86 (s, 3H, OCH₃), 2.39 – 2.09 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 167.0, 163.3, 130.2, 127.4, 114.3, 82.3 (d, *J* = 5.9 Hz), 81.2 (d, *J* = 163.0 Hz), 55.8, 33.7 (d, *J* = 20.0 Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -221.6;

IR (film): $\tilde{\nu}$ = 3305 (br, s), 2971 (w), 1644 (s), 1606 (s), 1503 (s), 1258 (s), 1178 (m), 1028 (m), 845 (m);

HRMS (ESI) calcd. for C₁₁H₁₄FNNaO₄⁺ [M+Na]⁺ 266.0799; Found 266.0798.

***N*-(3-Fluoro-1-(*p*-tolylthio)propyl)-4-methoxybenzamide (**3c**).**

Following GP C, 4-methylthiophenol (44.6 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(3-fluoro-1-(*p*-tolylthio)propyl)-4-methoxybenzamide (**3c**) (68.5 mg, 0.206 mmol, 69%) was obtained as a white solid 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);

Mp: 97–99 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.66 – 7.59 (m, 2H, ArH), 7.40 – 7.33 (m, 2H, ArH), 7.12 – 7.06 (m, 2H, ArH), 6.90 – 6.86 (m, 2H, ArH), 6.45 (d, *J* = 9.4 Hz, 1H, NH), 5.69 (ddd, *J* = 9.4, 7.4, 5.7 Hz, 1H, CH), 4.86 – 4.52 (m, 2H, FCH₂), 3.83 (s, 3H, OCH₃), 2.39 – 2.09 (m, 5H, CH₃ + CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 165.8, 162.3, 138.4, 133.9, 129.9, 128.7, 128.2, 126.0, 113.7, 81.2 (d, *J* = 165.6 Hz), 55.4, 55.1 (d, *J* = 3.9 Hz), 36.1 (d, *J* = 19.5 Hz), 21.1;

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.7;

IR (film): $\tilde{\nu}$ = 3293 (w), 2963 (w), 1636 (s), 1605 (s), 1500 (s), 1293 (s), 1028 (m), 843 (m), 810 (m);

HRMS (ESI) calcd. for C₁₈H₂₀FNNaO₂S⁺ [M+Na]⁺ 356.1091; Found 356.1095.

***N*-(3-Fluoro-1-(1*H*-pyrazol-1-yl)propyl)-4-methoxybenzamide (**3d**).**

Following GP C, 1*H*-pyrazole (24.5 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, *N*-(3-fluoro-1-(1*H*-pyrazol-1-yl)propyl)-4-methoxybenzamide (**3d**) (58.2 mg, 0.210 mmol, 70%) was obtained as a white solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.26 (silica, pentanes:ethyl acetate 1:1);

Mp: 146-148 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.77 – 7.71 (m, 2H, ArH + NH), 7.71 – 7.66 (m, 2H, ArH), 7.56 (d, *J* = 1.7 Hz, 1H, ArH), 6.84 – 6.79 (m, 2H, ArH), 6.57 (q, *J* = 7.8 Hz, 1H, CH), 6.25 (t, *J* = 2.1 Hz, 1H, ArH), 4.63 – 4.07 (m, 2H, FCH₂), 3.80 (s, 3H, OCH₃), 2.72 – 2.54 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.4, 162.5, 140.4, 130.8, 129.1, 125.2, 113.6, 105.2, 79.9 (d, *J* = 165.7 Hz), 62.3 (d, *J* = 3.9 Hz), 55.4, 35.0 (d, *J* = 19.8 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -221.8;

IR (film): $\tilde{\nu}$ = 3304 (w), 2970 (w), 1645 (m), 1606 (m), 1502 (s), 1252 (s), 1027 (m), 845 (m), 767 (m);

HRMS (ESI) calcd. for C₁₄H₁₆FN₃NaO₂⁺ [M+Na]⁺ 300.1119; Found 300.1124.

***N*-(3-Fluoro-1-(1*H*-1,2,4-triazol-1-yl)propyl)-4-methoxybenzamide (3e).**

Following GP C, 1,2,4-1*H*-triazole (41.4 mg, 0.600 mmol, 2.0 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, *N*-(3-fluoro-1-(1*H*-1,2,4-triazol-1-yl)propyl)-4-methoxybenzamide (**3e**) (59.1 mg, 0.213 mmol, 71%) was obtained as a white solid after purification by column chromatography on silica using 100% ethyl acetate as eluent.

R_f: 0.26 (silica, 100% ethyl acetate);

Mp: 156-158 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 8.60 (d, *J* = 8.4 Hz, 1H, NH), 8.55 (s, 1H, ArH), 7.94 – 7.86 (m, 3H, ArH), 7.02 – 6.93 (m, 2H, ArH), 6.61 (q, *J* = 7.7 Hz, 1H, CH), 4.75 – 4.33 (m, 2H, FCH₂), 3.85 (s, 3H, OCH₃), 2.69 (ddt, *J* = 25.7, 7.5, 5.7 Hz, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 167.1, 163.7, 152.6, 144.9, 130.3, 126.4, 114.4, 80.8 (d, *J* = 163.7 Hz), 61.8 (d, *J* = 5.7 Hz), 55.8, 35.0 (d, *J* = 20.0 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -221.2;

IR (film): $\tilde{\nu}$ = 3303 (w), 1653 (m), 1606 (m), 1503 (s), 1256 (s), 1178 (m), 1025 (m), 846 (m);

HRMS (ESI) calcd. for C₁₃H₁₅FN₄NaO₂⁺ [M+Na]⁺ 301.1071; Found 301.1064.

***N*-(3-Fluoro-1-(1*H*-tetrazol-1-yl)propyl)-4-methoxybenzamide (**3f**).**

Following GP C, 1*H*-tetrazole (42.0 mg, 0.600 mmol, 2.0 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, *N*-(3-fluoro-1-(1*H*-tetrazol-1-yl)propyl)-4-methoxybenzamide (**3f**) (33.0 mg, 0.118 mmol, 39%) was obtained as a white solid after purification by column chromatography on silica using 2:3 pentanes:ethyl acetate as eluent.

R_f: 0.26 (silica, pentanes:ethyl acetate 2:3);

Mp: 157-159 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 9.30 (s, 1H, ArH), 8.86 (d, *J* = 8.4 Hz, 1H, NH), 7.93 – 7.87 (m, 2H, ArH), 7.03 – 6.97 (m, 2H, ArH), 6.87 (q, *J* = 8.1 Hz, 1H, CH), 4.85 – 4.49 (m, 2H, FCH₂), 3.85 (s, 3H, OCH₃), 2.89 – 2.79 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 167.3, 163.9, 144.1, 130.4, 126.0, 114.5, 80.7 (d, *J* = 164.3 Hz), 62.5 (d, *J* = 5.2 Hz), 55.9, 35.0 (d, *J* = 20.1 Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -223.2;

IR (film): $\tilde{\nu}$ = 3294 (w), 2971 (w), 1650 (m), 1605 (s), 1503 (s), 1256 (s), 1177 (m), 1025 (m), 845 (m);

HRMS (ESI) calcd. for C₁₂H₁₄FN₅NaO₂⁺ [M+Na]⁺ 302.1024; Found 302.1017.

***N*-(3-Fluoropropyl)-4-methoxybenzamide (**3g**).**

Following GP C, NaBH₃CN (22.6 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(3-fluoropropyl)-4-methoxybenzamide (**3g**) (52.4 mg, 0.248 mmol, 83%) was obtained as a beige solid after purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent.

R_f: 0. (silica, pentanes:ethyl acetate 1:1);

Mp: 71-73 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.79 – 7.64 (m, 2H, ArH), 6.97 – 6.85 (m, 2H, ArH), 6.38 (s, 1H, NH), 4.59 (dt, *J* = 47.3, 5.6 Hz, 2H, FCH₂), 3.84 (s, 3H, OCH₃), 3.60 (q, *J* = 6.3 Hz, 2H, NCH₂), 2.03 (dddd, *J* = 28.2, 12.1, 6.5, 5.5 Hz, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 167.1, 162.1, 128.6, 126.7, 113.7, 82.9 (d, *J* = 163.8 Hz), 55.4, 37.1 (d, *J* = 4.2 Hz), 30.2 (d, *J* = 19.1 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -219.9;

IR (film): $\tilde{\nu}$ = 3298 (m), 2967 (w), 1630 (s), 1607 (s), 1542 (m), 1505 (s), 1299 (m), 1256 (s), 1179 (m), 848 (m);

HRMS (ESI) calcd. for C₁₁H₁₅FNO₂⁺ [M+H]⁺ 212.1081; Found 212.1083.

(E)-N-(5-Fluoro-1-phenylpent-1-en-3-yl)-4-methoxybenzamide (3h).

Following GP C, potassium *trans*-styryltrifluoroborate (126 mg, 0.600 mmol, 2.0 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, (E)-N-(5-fluoro-1-phenylpent-1-en-3-yl)-4-methoxybenzamide (**3h**) (39.0 mg, 0.125 mmol, 42%) was obtained as a white solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

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

Mp: 121-123 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 7.96 – 7.86 (m, 2H, ArH), 7.70 (d, *J* = 8.4 Hz, 1H, NH), 7.47 – 7.39 (m, 2H, ArH), 7.36 – 7.27 (m, 2H, ArH), 7.26 – 7.19 (m, 1H, ArH), 7.01 – 6.93 (m, 2H, ArH), 6.65 (dd, *J* = 16.0, 1.2 Hz, 1H, vinyl CH), 6.40 (dd, *J* = 16.0, 6.7 Hz, 1H, vinyl CH), 4.99 (h, *J* = 7.3, 6.8 Hz, 1H, CH), 4.73 – 4.48 (m, 2H, FCH₂), 3.84 (s, 3H, OCH₃), 2.18 (ddt, *J* = 24.8, 7.2, 6.0 Hz, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 165.4, 162.1, 137.1, 130.2, 130.1, 129.0, 128.5, 127.4, 127.3, 126.3, 113.4, 81.1 (d, *J* = 163.3 Hz), 54.9, 48.2 (d, *J* = 5.7 Hz), 35.6 (d, *J* = 19.6 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -220.4;

IR (film): $\tilde{\nu}$ = 3316 (w), 2963 (w), 1630 (s), 1606 (s), 1538 (m), 1504 (s), 1255 (s), 1178 (m), 1030 (m), 749 (m);

HRMS (ESI) calcd. for C₁₉H₂₁FNO₂⁺ [M + H]⁺ 314.1551; Found 314.1539.

N-(3-Fluoro-1-(2,4,6-trimethoxyphenyl)propyl)-4-methoxybenzamide (3i).

Following GP C, 1,3,5-trimethoxybenzene (60.5 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, N-(3-fluoro-1-(2,4,6-trimethoxyphenyl)propyl)-4-methoxybenzamide (**3i**) (77.8 mg, 0.206 mmol, 69%) was obtained as a white solid after purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent.

R_f: 0.44 (silica, pentanes:ethyl acetate 3:2);

Mp: 133-135 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.75 – 7.66 (m, 2H, ArH), 7.55 (d, *J* = 9.6 Hz, 1H, NH), 6.95 – 6.85 (m, 2H, ArH), 6.16 (s, 2H, ArH), 5.98 (dt, *J* = 9.6, 7.4 Hz, 1H, CH), 4.47 (dt, *J* = 47.1, 6.6 Hz, 2H, FCH₂), 3.88 (s, 6H, OCH₃), 3.84 (s, 3H, OCH₃), 3.81 (s, 3H, OCH₃), 2.39 – 2.11 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 165.6, 161.9, 160.5, 158.6, 128.6, 127.4, 113.6, 109.7, 91.1, 82.2 (d, *J* = 164.2 Hz), 55.9, 55.4 (there are two ¹³C signals for four methoxy groups, meaning signals for the two *para* methoxy groups are overlapped), 41.7 (d, *J* = 8.1 Hz), 36.1 (d, *J* = 19.0 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.4;

IR (film): $\tilde{\nu}$ = 3445 (w), 2962 (w), 2839 (w), 1653 (m), 1606 (s), 1493 (s), 1252 (s), 1124 (s), 1030 (m), 844 (w), 814 (w);

HRMS (ESI) calcd. for C₂₀H₂₄FNNaO₅⁺ [M+Na]⁺ 400.1531; Found 400.1522.

***N*-(1-(2,4-Dimethoxyphenyl)-3-fluoropropyl)-4-methoxybenzamide (3j).**

Following GP C, 1,3-dimethoxybenzene (49.7 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, *N*-(1-(2,4-dimethoxyphenyl)-3-fluoropropyl)-4-methoxybenzamide (**3j**) (22.4 mg, 0.0646 mmol, 22%) was obtained as a white solid after purification by column chromatography on silica using 3:2 pentanes:ethyl acetate as eluent.

R_f: 0.43 (silica, pentanes:ethyl acetate 1:1);

Mp: 133-134 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 7.90 – 7.83 (m, 2H, ArH), 7.74 (d, *J* = 8.8 Hz, 1H, NH), 7.27 (d, *J* = 8.4 Hz, 1H, ArH), 7.01 – 6.91 (m, 2H, ArH), 6.58 (d, *J* = 2.4 Hz, 1H, ArH), 6.48 (dd, *J* = 8.4, 2.4 Hz, 1H, ArH), 5.52 (td, *J* = 8.6, 6.2 Hz, 1H, CH), 4.62 – 4.36 (m, 2H, FCH₂), 3.90 (s, 3H, OCH₃), 3.84 (s, 3H, OCH₃), 3.78 (s, 3H, OCH₃), 2.33 – 2.18 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 166.0, 163.0, 161.2, 159.0, 129.8, 129.2, 128.4, 123.7, 114.3, 105.3, 99.6, 82.4 (d, *J* = 163.3 Hz), 55.9, 55.8, 55.6, 47.3 (d, *J* = 6.1 Hz), 37.0 (d, *J* = 19.4 Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -220.2;

IR (film): $\tilde{\nu}$ = 3325 (w), 2962 (w), 1632 (s), 1607 (s), 1504 (s), 1254 (s), 1031 (m), 843 (m);

HRMS (ESI) calcd. for C₁₉H₂₃FNO₄⁺ [M+H]⁺ 348.1606; Found 348.1603.

***N*-(3-Fluoro-1-(1*H*-pyrrol-2-yl)propyl)-4-methoxybenzamide (3k).**

Following GP C, 1*H*-pyrrole (24.1 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 2 hours, *N*-(3-fluoro-1-(1*H*-pyrrol-2-yl)propyl)-4-methoxybenzamide

(**3k**) (38.2 mg, 0.138 mmol, 46%) was obtained as a red solid after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

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

Mp: 150-152 °C;

¹H NMR (400 MHz, CDCl₃): δ = 9.37 (s, 1H, pyrrole NH), 7.78 – 7.61 (m, 2H, ArH), 6.98 – 6.82 (m, 2H, ArH), 6.74 (td, *J* = 2.6, 1.5 Hz, 1H, ArH), 6.56 (d, *J* = 7.6 Hz, 1H, NH), 6.12 (q, *J* = 2.9 Hz, 1H, ArH), 6.05 (qd, *J* = 2.9, 1.8 Hz, 1H, ArH), 5.31 (dt, *J* = 8.3, 6.2 Hz, 1H, CH), 4.87 – 4.52 (m, 2H, FCH₂), 3.84 (s, 3H, OCH₃), 2.65 – 2.31 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 167.9, 162.4, 132.6, 128.8, 126.1, 118.0, 113.8, 107.5, 104.4, 82.0 (d, *J* = 164.2 Hz), 55.4, 45.5 (d, *J* = 3.5 Hz), 33.3 (d, *J* = 19.5 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -217.2;

IR (film): $\tilde{\nu}$ = 3320 (br,s), 2965 (w), 1621 (s), 1606 (s), 1533 (m), 1503 (s), 1255 (s), 1178 (m), 1027 (m), 728 (w);

HRMS (ESI) calcd. for C₁₅H₁₇FN₂NaO₂⁺ [M+Na]⁺ 299.1166; Found 299.1174.

***N*-(3-Fluoro-1-(1*H*-indol-3-yl)propyl)-4-methoxybenzamide (**3l**).**

Following GP C, 1*H*-indole (42.2 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(3-fluoro-1-(1*H*-indol-3-yl)propyl)-4-methoxybenzamide (**3l**) (65.2 mg, 0.200 mmol, 67%) was obtained as a dark solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.46 (silica, pentanes:ethyl acetate 1:1);

Mp: 63-66 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.28 (s, 1H, indole NH), 7.74 – 7.69 (m, 2H, ArH), 7.67 (dd, *J* = 8.0, 1.0 Hz, 1H, ArH), 7.38 (dt, *J* = 8.2, 1.0 Hz, 1H, ArH), 7.21 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H, ArH), 7.16 (dd, *J* = 2.6, 0.7 Hz, 1H, ArH), 7.12 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, ArH), 6.92 – 6.85 (m, 2H, ArH), 6.48 (d, *J* = 8.0 Hz, 1H, NH), 5.72 (q, *J* = 7.1 Hz, 1H, CH), 4.75 – 4.46 (m, 2H, FCH₂), 3.82 (s, 3H, OCH₃), 2.59 – 2.42 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.3, 162.2, 136.7, 128.7, 126.7, 125.7, 122.5, 122.0, 120.0, 119.1, 116.0, 113.7, 111.5, 82.0 (d, *J* = 163.9 Hz), 55.4, 44.3 (d, *J* = 5.7 Hz), 35.5 (d, *J* = 19.2 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.2;

IR (film): $\tilde{\nu}$ = 3408 (w), 3292 (m), 2965(w), 1631 (s), 1606 (s), 1499 (s), 1254 (s), 1178 (m), 1029 (m), 745 (m);

HRMS (ESI) calcd. for C₁₉H₁₉FN₂NaO₂⁺ [M+Na]⁺ 349.1323; Found 349.1322.

***N*-(3-Fluoro-1-(1-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (**3m**).**

Following GP C, 1-methylindole (47.2 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(3-fluoro-1-(1-methyl-1H-indol-3-yl)propyl)-4-methoxybenzamide (**3m**) (65.5 mg, 0.193 mmol, 64%) was obtained as a beige solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

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

Mp: 168-169 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 7.90 – 7.84 (m, 2H, ArH), 7.72 (dt, *J* = 7.9, 1.0 Hz, 2H, ArH + NH), 7.35 (dt, *J* = 8.3, 0.9 Hz, 1H, ArH), 7.27 (d, *J* = 0.8 Hz, 1H, ArH), 7.16 (ddd, *J* = 8.3, 7.0, 1.1 Hz, 1H, ArH), 7.01 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H, ArH), 6.95 – 6.89 (m, 2H, ArH), 5.80 – 5.70 (m, 1H, CH), 4.74 – 4.46 (m, 2H, FCH₂), 3.81 (s, 3H, OCH₃), 3.79 (s, 3H, NCH₃), 2.63 – 2.30 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 166.2, 162.9, 138.2, 129.9, 128.2, 127.8, 127.5, 122.4, 120.2, 119.7, 116.7, 114.2, 110.3, 82.4 (d, *J* = 163.0 Hz), 55.7, 43.3 (d, *J* = 6.5 Hz), 36.6 (d, *J* = 19.5 Hz), 32.8;

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -220.0;

IR (film): $\tilde{\nu}$ = 3306 (w), 2961 (m), 1626 (s), 1606 (s), 1502 (s), 1253 (s), 1178 (m), 1030 (m), 743 (m);

HRMS (ESI) calcd. for C₂₀H₂₁FN₂NaO₂⁺ [M+Na]⁺ 363.1479; Found 363.1481.

***N*-(3-Fluoro-1-(2-phenyl-1H-indol-3-yl)propyl)-4-methoxybenzamide (3n).**

Following GP C, 2-phenylindole (69.5 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(3-fluoro-1-(2-phenyl-1H-indol-3-yl)propyl)-4-methoxybenzamide (**3n**) (80.6 mg, 0.200 mmol, 67%) was obtained as a pink solid after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.31 (silica, pentanes:ethyl acetate 2:1);

Mp: 105-107 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.32 (s, 1H, indole NH), 7.81 – 7.77 (m, 1H, ArH), 7.69 – 7.61 (m, 4H, ArH), 7.50 – 7.44 (m, 2H, ArH), 7.44 – 7.37 (m, 2H, ArH), 7.25 (ddd, *J* = 8.1, 7.1, 1.3 Hz, 1H, ArH), 7.20 (td, *J* = 7.4, 1.2 Hz, 1H, ArH), 6.90 – 6.83 (m, 2H, ArH), 6.74 (d, *J* = 7.1 Hz, 1H, NH), 5.75 (q, *J* = 7.2 Hz, 1H, CH), 4.61 – 4.32 (m, 2H, FCH₂), 3.82 (s, 3H, OCH₃), 2.76 – 2.35 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.1, 162.1, 136.2, 136.1, 132.2, 129.1, 128.8, 128.7, 128.5, 126.7, 126.6, 122.5, 120.3, 119.1, 113.7, 111.6, 111.5, 82.0 (d, *J* = 164.3 Hz), 55.4, 45.1 (d, *J* = 5.7 Hz), 36.6 (d, *J* = 19.4 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.2;

IR (film): $\tilde{\nu}$ = 3428 (w), 3274 (w), 2962 (w), 1637 (s), 1605 (s), 1491 (s), 1253 (s), 1177 (m), 1029 (m), 843 (m), 745 (m);

HRMS (ESI) calcd. for $C_{25}H_{23}FN_2NaO_2^+$ $[M+Na]^+$ 425.1636; Found 425.1631.

***N*-(3-Fluoro-1-(3-methyl-1*H*-indol-2-yl)propyl)-4-methoxybenzamide (3o).**

Following GP C, 3-methylindole (47.2 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 20 hours, *N*-(3-fluoro-1-(3-methyl-1*H*-indol-2-yl)propyl)-4-methoxybenzamide (**3o**) (44.8 mg, 0.132 mmol, 44%) and *N*-(3-fluoro-1-(3-methyl-1*H*-indol-1-yl)propyl)-4-methoxybenzamide (**3p**) (21.4 mg, 0.063 mmol, 21%) were obtained as beige solids after purification by column chromatography on silica using 3:1 pentanes:ethyl acetate as eluent.

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

Mp: 170-172 °C;

¹H NMR (400 MHz, CDCl₃): δ = 9.17 (s, 1H, indole NH), 7.76 – 7.68 (m, 2H, ArH), 7.53 (d, J = 7.9 Hz, 1H, ArH), 7.31 (d, J = 8.0 Hz, 1H, ArH), 7.16 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H, ArH), 7.09 (td, J = 7.4, 6.8, 1.1 Hz, 1H, ArH), 6.93 – 6.86 (m, 2H, ArH), 6.81 (d, J = 7.1 Hz, 1H, NH), 5.25 (q, J = 7.2 Hz, 1H, CH), 4.67 – 4.38 (m, 2H, FCH₂), 3.84 (s, 3H, OCH₃), 2.77 – 2.45 (m, 2H, CH₂), 2.33 (s, 3H, CH₃);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 165.7, 162.2, 135.9, 134.6, 129.0, 128.9, 126.9, 121.2, 118.5, 118.2, 113.4, 110.8, 107.1, 81.1 (d, J = 163.6 Hz), 54.9, 43.0 (d, J = 5.5 Hz), 35.3 (d, J = 19.9 Hz), 7.7;

¹⁹F NMR (376 MHz, CDCl₃): δ = -220.1;

IR (film): $\tilde{\nu}$ = 3312 (m), 2963 (w), 2919 (w), 1607 (s), 1504 (s), 1257 (s), 1028 (m), 844 (w), 740 (m);

HRMS (APCI) calcd. for $C_{20}H_{22}FN_2O_2^+$ $[M+H]^+$ 341.1660; Found 341.1654.

***N*-(3-Fluoro-1-(3-methyl-1*H*-indol-1-yl)propyl)-4-methoxybenzamide (3p).**

R_f: 0.36 (silica, pentanes:ethyl acetate 2:1);

Mp: 278-280 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.72 – 7.65 (m, 2H, ArH), 7.58 – 7.51 (m, 2H, ArH), 7.26 – 7.20 (m, 1H, ArH), 7.16 – 7.09 (m, 1H, ArH), 7.06 (d, J = 1.3 Hz, 1H, ArH), 6.90 – 6.85 (m, 2H, ArH), 6.78 (d, J = 8.0 Hz, 1H, NH), 6.71 (q, J = 7.1 Hz, 1H, CH), 4.66 – 4.35 (m, 2H, FCH₂), 3.82 (s, 3H, OCH₃), 2.61 (ddtd, J = 26.5, 11.2, 6.7, 4.5 Hz, 2H, CH₂), 2.31 (d, J = 1.1 Hz, 3H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 166.2, 162.6, 135.7, 129.2, 128.9, 125.6, 122.3, 121.4, 119.5, 119.1, 113.8, 112.3, 109.9, 80.4 (d, *J* = 165.7 Hz), 58.6 (d, *J* = 4.5 Hz), 55.4, 35.4 (d, *J* = 19.9 Hz), 9.7;

¹⁹F NMR (376 MHz, CDCl₃): δ = -222.2;

IR (film): $\tilde{\nu}$ = 3282 (w), 2967 (w), 1635 (s), 1606 (s), 1504 (s), 1257 (s), 1177 (m), 1030 (m), 745 (m);

HRMS (ESI) calcd. for C₂₀H₂₁FN₂NaO₂⁺ [M+Na]⁺ 363.1479; Found 363.1469.

***N*-(3-Fluoro-1-(4-fluoro-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3q).**

Following GP C, 4-fluoro-1*H*-indole (48.6 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 20 hours, *N*-(3-fluoro-1-(4-fluoro-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (**3q**) (59.2 mg, 0.172 mmol, 57%) was obtained as a beige solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.33 (silica, pentanes:ethyl acetate 2:3);

Mp: 82-84 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 10.45 (s, 1H, indole NH), 7.93 – 7.80 (m, 2H, ArH), 7.59 (d, *J* = 8.4 Hz, 1H, NH), 7.42 (s, 1H, ArH), 7.25 (d, *J* = 8.2 Hz, 1H, ArH), 7.08 (td, *J* = 8.0, 5.2 Hz, 1H, ArH), 6.99 – 6.92 (m, 2H, ArH), 6.75 (ddd, *J* = 11.6, 7.8, 0.6 Hz, 1H, ArH), 5.76 (q, *J* = 7.8 Hz, 1H, CH), 4.73 – 4.40 (m, 2H, FCH₂), 3.83 (s, 3H, OCH₃), 2.52 – 2.34 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 166.1, 162.9, 157.3 (d, *J* = 242.8 Hz), 140.8 (dd, *J* = 15.5, 12.2 Hz), 129.8, 128.3, 124.1 (d, *J* = 15.9 Hz), 122.9 (d, *J* = 8.1 Hz), 115.9 (t, *J* = 4.1 Hz), 115.3 (dd, *J* = 20.8, 2.8 Hz), 114.3, 108.9 (t, *J* = 4.4 Hz), 104.8 (d, *J* = 20.2 Hz), 82.4 (d, *J* = 163.1 Hz), 55.7, 44.8 (d, *J* = 6.4 Hz), 38.1 (dd, *J* = 19.5, 2.8 Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -121.5, -220.2;

IR (film): $\tilde{\nu}$ = 3273 (w), 2964 (w), 1634 (s), 1606 (s), 1499 (s), 1255 (s), 1032 (m), 848 (m), 738 (m);

HRMS (ESI) calcd. for C₁₉H₁₉F₂N₂O₂⁺ [M+H]⁺ 345.1409; Found 345.1406.

***N*-(3-Fluoro-1-(5-methoxy-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3r).**

Following GP C, 5-methoxy-1*H*-indole (52.9 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(3-fluoro-1-(5-methoxy-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (**3r**) (58.0 mg, 0.163 mmol, 54%) was obtained as a beige solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

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

Mp: 133-136 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 10.01 (s, 1H, indole NH), 7.93 – 7.84 (m, 2H, ArH), 7.70 (d, *J* = 8.8 Hz, 1H, NH), 7.33 (d, *J* = 2.1 Hz, 1H, ArH), 7.30 – 7.23 (m, 2H, ArH), 6.97 – 6.91 (m, 2H, ArH), 6.75 (dd, *J* = 8.7, 2.5 Hz, 1H, ArH), 5.75 (td, *J* = 8.6, 6.0 Hz, 1H, CH), 4.74 – 4.50 (m, 2H, FCH₂), 3.81 (s, 3H, OCH₃), 3.73 (s, 3H, OCH₃), 2.61 – 2.39 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆, mixture of two rotamers, minor rotamer omitted for clarity): δ = 166.4, 162.9, 154.8, 132.9, 129.9, 128.3, 127.8, 123.7, 117.4, 114.2, 112.9, 112.6, 101.8, 82.4 (d, *J* = 162.9 Hz), 55.8, 55.7, 43.4 (d, *J* = 6.6 Hz), 36.3 (d, *J* = 19.8 Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -219.9;

IR (film): $\tilde{\nu}$ = 3311 (w), 2962 (w), 1625 (s), 1606 (s), 1500 (s), 1255 (s), 1174 (m), 1029 (m), 844 (m);

HRMS (ESI) calcd. for C₂₀H₂₁FN₂NaO₃⁺ [M+Na]⁺ 379.1428; Found 379.1428.

***N*-(3-Fluoro-1-(5-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3s).**

Following GP C, 5-methyl-1*H*-indole (47.2 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 4 hours, *N*-(3-fluoro-1-(5-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (**3s**) (64.0 mg, 0.188 mmol, 63%) was obtained as a pink solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

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

Mp: 140-142 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.14 (s, 1H, indole NH), 7.77 – 7.66 (m, 2H, ArH), 7.44 (s, 1H, ArH), 7.27 (d, *J* = 6.7 Hz, 1H, ArH), 7.13 (d, *J* = 2.5 Hz, 1H, ArH), 7.04 (dd, *J* = 8.3, 1.6 Hz, 1H, ArH), 6.92 – 6.85 (m, 2H, ArH), 6.45 (d, *J* = 7.9 Hz, 1H, NH), 5.67 (q, *J* = 7.1 Hz, 1H, CH), 4.72 – 4.47 (m, 2H, FCH₂), 3.83 (s, 3H, OCH₃), 2.57 – 2.45 (m, 2H, CH₂), 2.43 (s, 3H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 166.3, 162.1, 135.0, 129.3, 128.7, 126.8, 125.9, 124.2, 122.1, 118.7, 115.4, 113.7, 111.2, 82.0 (d, *J* = 164.0 Hz), 55.4, 44.3 (d, *J* = 5.9 Hz), 35.5 (d, *J* = 19.2 Hz), 21.5;

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.2;

IR (film): $\tilde{\nu}$ = 3407 (w), 3307 (br, m), 2962 (w), 2917 (w), 1630 (s), 1605 (s), 1497 (s), 1254 (s), 1177 (m), 1029 (m), 731 (m);

HRMS (ESI) calcd. for C₂₀H₂₁FN₂NaO₂⁺ [M+Na]⁺ 363.1479; Found 363.1473.

***N*-(1-(5-Chloro-1*H*-indol-3-yl)-3-fluoropropyl)-4-methoxybenzamide (3t).**

Following GP C, 5-chloro-1*H*-indole (54.4 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, *N*-(1-(5-chloro-1*H*-indol-3-yl)-3-fluoropropyl)-4-

methoxybenzamide (**3t**) (74.3 mg, 0.206 mmol, 69%) was obtained as a pink solid after purification by column chromatography on silica using 1:2 pentanes:ethyl acetate as eluent.

R_f: 0.46 (silica, pentanes:ethyl acetate 1:2);

Mp: 103-105 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.57 (s, 1H, indole NH), 7.75 – 7.69 (m, 2H, ArH), 7.60 (s, 1H, ArH), 7.23 (d, *J* = 8.7 Hz, 1H, ArH), 7.11 (dd, *J* = 8.6, 2.0 Hz, 2H, ArH), 6.88 (d, *J* = 8.6 Hz, 2H, ArH), 6.59 (d, *J* = 7.8 Hz, 1H, NH), 5.64 (q, *J* = 7.0 Hz, 1H, CH), 4.71 – 4.44 (m, 2H, FCH₂), 3.82 (s, 3H, OCH₃), 2.45 (dq, *J* = 26.2, 6.1 Hz, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.6, 162.3, 135.0, 128.7, 126.6, 126.5, 125.5, 123.5, 122.7, 118.4, 115.6, 113.8, 112.6, 82.0 (d, *J* = 163.7 Hz), 55.4, 44.5 (d, *J* = 4.6 Hz), 35.4 (d, *J* = 19.2 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.0;

IR (film): $\tilde{\nu}$ = 3430 (w), 3271 (m), 2960 (w), 1630 (s), 1605 (s), 1498 (s), 1253 (s), 1177 (m), 1029 (m), 731 (m);

HRMS (ESI) calcd. for C₁₉H₁₈ClFN₂NaO₂⁺ [M+Na]⁺ 383.0933; Found 383.0930.

Methyl 3-(3-fluoro-1-(4-methoxybenzamido)propyl)-1H-indole-5-carboxylate (3u**).**

Following GP C, methyl-1H-indole-5-carboxylate (63.0 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 40 hours, methyl 3-(3-fluoro-1-(4-methoxybenzamido)propyl)-1H-indole-5-carboxylate (**3u**) (51.4 mg, 0.134 mmol, 45%) was obtained as a yellow solid after purification by column chromatography on silica using 1:2 pentanes:ethyl acetate as eluent.

R_f: 0.28 (silica, pentanes:ethyl acetate 1:2);

Mp: 147-149 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 10.56 (s, 1H, indole NH), 8.54 (dd, *J* = 1.6, 0.7 Hz, 1H, ArH), 7.96 – 7.90 (m, 1H, NH), 7.90 – 7.86 (m, 2H, ArH), 7.81 (dd, *J* = 8.6, 1.6 Hz, 1H, ArH), 7.53 (d, *J* = 0.9 Hz, 1H, ArH), 7.47 (dd, *J* = 8.7, 0.7 Hz, 1H, ArH), 6.96 – 6.90 (m, 2H, ArH), 5.82 (q, *J* = 7.8 Hz, 1H, CH), 4.63 (dddt, *J* = 47.1, 37.7, 9.3, 6.0 Hz, 2H, FCH₂), 3.84 (s, 3H, OCH₃), 3.81 (s, 3H, OCH₃), 2.63 – 2.47 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆, mixture of two rotamers, ratio = ca. 1:1): δ = 168.3, 166.6, 162.9, 140.3, 140.1, 129.9, 128.2, 126.9, 126.9, 125.2, 125.0, 123.6, 122.9, 122.1, 119.1, 119.1, 114.2, 112.1, 112.0, 82.3 (d, *J* = 163.2 Hz), 55.7, 51.9, 43.4 (d, *J* = 6.2 Hz), 36.7 (d, *J* = 19.7 Hz);

¹³C NMR (151 MHz, Acetonitrile-*d*₃, 70 °C): δ = 169.0, 167.5, 163.6, 140.6, 130.2, 128.6, 127.2, 125.4, 124.2, 123.0, 122.9, 119.5, 115.0, 112.6, 83.1 (d, *J* = 162.2 Hz), 56.5, 52.5, 44.3 (d, *J* = 5.9 Hz), 37.0 (d, *J* = 19.6 Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -220.1;

IR (film): $\tilde{\nu}$ = 3315 (w), 2952 (w), 1695 (s), 1607 (s), 1502 (s), 1435 (m), 1252 (s), 1178 (m), 1112 (m), 770 (m);

HRMS (ESI) calcd. for C₂₁H₂₁FN₂NaO₄⁺ [M+Na]⁺ 407.1378; Found 407.1381.

N-(3-Fluoro-1-(6-methyl-1H-indol-3-yl)propyl)-4-methoxybenzamide (3v**).**

Following GP C, 6-methyl-1*H*-indole (47.2 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, *N*-(3-fluoro-1-(6-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide **3v** (65.8 mg, 0.194 mmol, 65%) was obtained as a red solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

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

Mp: 153-156 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 10.01 (s, 1H, indole NH), 7.93 – 7.82 (m, 2H, ArH), 7.69 (d, *J* = 8.7 Hz, 1H, NH), 7.60 (d, *J* = 8.1 Hz, 1H, ArH), 7.28 (dd, *J* = 2.5, 0.8 Hz, 1H, ArH), 7.19 (dt, *J* = 1.6, 0.8 Hz, 1H, ArH), 6.96 – 6.89 (m, 2H, ArH), 6.87 – 6.80 (m, 1H, ArH), 5.75 (td, *J* = 8.6, 6.2 Hz, 1H, CH), 4.74 – 4.45 (m, 2H, FCH₂), 3.81 (s, 3H, OCH₃), 2.56 – 2.42 (m, 2H, CH₂), 2.38 (s, 3H, CH₃);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 166.3, 162.9, 138.3, 131.8, 129.9, 128.3, 125.3, 122.4, 121.6, 119.7, 117.4, 114.2, 112.1, 82.4 (d, *J* = 163.0 Hz), 55.7, 43.5 (d, *J* = 6.4 Hz), 36.6 (d, *J* = 19.7 Hz), 21.7;

¹⁹F NMR (376 MHz, CDCl₃): δ = -219.9;

IR (film): $\tilde{\nu}$ = 3295 (w), 2963 (w), 1629(s), 1606 (s), 1500 (s), 1254 (s), 1178 (m), 1030 (m), 802 (m);

HRMS (ESI) calcd. for C₂₀H₂₁FN₂NaO₂⁺ [M+Na]⁺ 363.1479; Found 363.1480.

***N*-(3-Fluoro-1-(6-(trifluoromethyl)-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3w).**

Following GP C, 6-trifluoromethyl-1*H*-indole (66.6 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, *N*-(3-fluoro-1-(6-(trifluoromethyl)-1*H*-indol-3-yl)propyl)-4-methoxybenzamide **3w** (61.5 mg, 0.156 mmol, 52%) was obtained as a pink solid 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: 78-80 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.91 (s, 1H, indole NH), 7.76 – 7.69 (m, 3H, ArH), 7.57 (s, 1H, ArH), 7.29 (d, *J* = 8.4 Hz, 1H, ArH), 7.21 (d, *J* = 2.5 Hz, 1H, ArH), 6.93 – 6.86 (m, 2H, ArH), 6.63 (d, *J* = 7.5 Hz, 1H, NH), 5.73 (q, *J* = 7.1 Hz, 1H, CH), 4.74 – 4.44 (m, 2H, FCH₂), 3.82 (s, 3H, OCH₃), 2.56 – 2.37 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.7, 162.4, 135.5, 128.7, 127.9, 126.3, 125.0 (q, *J* = 271.7 Hz), 124.7, 124.4 (q, *J* = 31.9 Hz), 119.3, 116.5 (q, *J* = 3.5 Hz), 116.2, 113.9, 109.1 (q, *J* = 4.4 Hz), 81.9 (d, *J* = 164.0 Hz), 55.4, 44.5 (d, *J* = 4.4 Hz), 35.4 (d, *J* = 19.3 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -60.7, -217.9;

IR (film): $\tilde{\nu}$ = 3272 (w), 2965 (w), 1628(s), 1606 (s), 1499 (s), 1355 (s), 1255 (s), 1111 (s), 734 (m);
HRMS (ESI) calcd. for $C_{20}H_{19}F_4N_2O_2^+$ $[M+H]^+$ 395.1377; Found 395.1372.

***N*-(1-(6-Bromo-1*H*-indol-3-yl)-3-fluoropropyl)-4-methoxybenzamide (3x).**

Following GP C, 6-bromo-1*H*-indole (70.2 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 24 hours, *N*-(1-(6-bromo-1*H*-indol-3-yl)-3-fluoropropyl)-4-methoxybenzamide **3x** (61.0 mg, 0.151 mmol, 50%) was obtained as a yellow solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

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

Mp: 175-178 °C;

¹H NMR (400 MHz, CDCl₃): δ = 8.34 (s, 1H, indole NH), 7.73 – 7.68 (m, 2H, ArH), 7.53 – 7.45 (m, 2H, ArH), 7.18 (dd, J = 8.4, 1.7 Hz, 1H, ArH), 7.09 (d, J = 2.4 Hz, 1H, ArH), 6.92 – 6.87 (m, 2H, ArH), 6.50 (d, J = 8.1 Hz, 1H, NH), 5.69 (q, J = 7.1 Hz, 1H, CH), 4.70 – 4.49 (m, 2H, FCH₂), 3.82 (s, 3H, OCH₃), 2.56 – 2.33 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.5, 162.3, 137.4, 128.7, 126.4, 124.6, 123.2, 122.4, 120.3, 116.3, 116.1, 114.4, 113.8, 81.9 (d, J = 164.0 Hz), 55.4, 44.2 (d, J = 4.8 Hz), 35.4 (d, J = 19.1 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -217.9;

IR (film): $\tilde{\nu}$ = 3269 (w), 2962 (w), 1630 (s), 1605 (s), 1497 (s), 1254 (s), 1177 (m), 1029 (m), 730 (m);

HRMS (ESI) calcd. for $C_{19}H_{18}^{79}BrFN_2NaO_2^+$ $[M+Na]^+$ 427.0428; Found 427.0424.

***N*-(3-Fluoro-1-(7-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3y).**

Following GP C, 7-methyl-1*H*-indole (47.2 mg, 0.360 mmol, 1.2 equiv.) was used as nucleophile. After the reaction mixture was stirred for 16 hours, *N*-(3-fluoro-1-(7-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (**3y**) (67.4 mg, 0.198 mmol, 66%) was obtained as a beige solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

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

Mp: 175-176 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 10.13 (s, 1H, indole NH), 7.93 – 7.81 (m, 2H, ArH), 7.70 (d, J = 8.7 Hz, 1H, NH), 7.57 (dd, J = 5.7, 3.5 Hz, 1H, ArH), 7.36 (d, J = 2.6 Hz, 1H, ArH), 6.96 – 6.85 (m, 4H, ArH),

5.77 (td, $J = 8.4, 6.4$ Hz, 1H, CH), 4.76 – 4.46 (m, 2H, FCH₂), 3.81 (s, 3H, OCH₃), 2.58 – 2.42 (m, 5H, CH₂ + CH₃);

¹³C NMR (101 MHz, Acetone-*d*₆): $\delta = 166.3, 162.9, 137.2, 129.9, 128.3, 127.1, 123.0, 122.8, 121.4, 120.1, 117.9, 117.7, 114.2, 82.4$ (d, $J = 163.1$ Hz), 55.7, 43.5 (d, $J = 6.6$ Hz), 36.7 (d, $J = 19.6$ Hz), 16.9;

¹⁹F NMR (376 MHz, Acetone-*d*₆): $\delta = -220.0$;

IR (film): $\tilde{\nu} = 3293$ (w), 2964 (w), 1632 (s), 1606 (s), 1499 (s), 1254 (s), 1177 (m), 1029 (m), 844 (m);

HRMS (ESI) calcd. for C₂₀H₂₁FN₂NaO₂⁺ [M+Na]⁺ 363.1479; Found 363.1480.

6. Scope of ring-opening fluorination for multi-substituted aminocyclopropanes or aminocyclobutanes

General Procedure D (GP D):

In a 12*75 mm borosilicate glass tube, substituted cyclopropylamides or cyclobutylamides (0.100 mmol, 1.0 equiv.), selectfluor (39.0 mg, 0.110 mmol, 1.1 equiv.) and benzophenone (1.8 mg, 0.010 mmol, 0.10 equiv.) were dissolved in 0.50 mL of MeCN-H₂O (v:v 4:6, 0.20 M). The reaction mixture was degassed by three freeze-pump-thaw cycles and backfilled with N₂. Then the mixture was stirred at room temperature under 365 nm irradiation in Rayonet Reactor until the reaction was complete. The tube was taken out from the Rayonet Reactor and a solution of nucleophile (0.120 mmol, 1.2 equiv.) in 0.20 mL MeCN was added dropwise. The reaction mixture was stirred at room temperature for 3 hours, 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*-(3-Fluoro-1-hydroxybutyl)-4-methoxybenzamide (5a).**

Following GP D, 4-methoxy-*N*-(2-methylcyclopropyl)benzamide (**4a**) (20.5 mg, 0.100 mmol, 1.0 equiv.) was used as starting material and the reaction was kept stirring under irradiation for 45 minutes. *N*-(3-fluoro-1-hydroxybutyl)-4-methoxybenzamide (**5a**) (20.6 mg, 0.0855 mmol, 85%, 1:1 d.r., diastereomeric value was determined by integration of the two peaks in ¹⁹F NMR) was obtained as a white solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

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

Mp: 136-138 °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): $\delta = 7.99$ (s, 1H, NH), 7.93 – 7.81 (m, 2H, ArH), 7.01 – 6.91 (m, 2H, ArH), 5.76 – 5.63 (m, 1H, NCH), 5.06 – 4.77 (m, 2H, FCH + OH), 3.85 (s, 3H, OCH₃), 2.20 – 2.07 (m, 1H, CH₂), 1.99 – 1.88 (m, 1H, CH₂), 1.35 (ddd, $J = 23.8, 6.2, 4.9$ Hz, 3H, CH₃);

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): $\delta = 167.1, 166.9, 163.2, 163.2, 130.0, 130.0, 127.6, 114.3, 114.3, 88.8$ (d, $J = 162.5$ Hz), 88.5 (d, $J = 163.2$ Hz), 72.2 (d, $J = 6.4$ Hz), 72.1 (d, $J = 5.5$ Hz), 55.8, 44.0 (d, $J = 20.6$ Hz), 43.5 (d, $J = 20.6$ Hz), 21.5 (d, $J = 22.4$ Hz), 21.2 (d, $J = 22.4$ Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): $\delta = -173.3, -175.4$;

IR (film): $\tilde{\nu} = 3317$ (br, s), 2979 (w), 1638 (m), 1606 (s), 1503 (s), 1255 (s), 1029 (m), 846 (w);

HRMS (APCI) calcd. for C₁₂H₁₆FNNaO₃⁺ [M + Na]⁺ 264.1006; Found 264.1001.

***N*-(3-Fluoro-3-phenylpropyl)-4-methoxybenzamide (5b).**

Following GP D, 4-methoxy-*N*-(trans-2-phenylcyclopropyl)benzamide (**4b**) (26.7 mg, 0.100 mmol, 1.0 equiv.) was used as starting material and the reaction was kept stirring under irradiation for 1 hour. Then NaBH₃CN (7.6 mg, 0.12 mmol, 1.2 equiv.) was added as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(3-fluoro-3-phenylpropyl)-4-methoxybenzamide (**5b**) (25.8 mg, 0.0900 mmol, 90%) was obtained as a white solid 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);

Mp: 71-73 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.72 – 7.63 (m, 2H, ArH), 7.42 – 7.28 (m, 5H, ArH), 6.94 – 6.84 (m, 2H, ArH), 6.45 (t, *J* = 5.8 Hz, 1H, NH), 5.61 (ddd, *J* = 47.9, 7.3, 5.2 Hz, 1H, CH), 3.83 (s, 3H, OCH₃), 3.71 – 3.55 (m, 2H, NCH₂), 2.30 – 2.16 (m, 2H, NCH₂CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 167.0, 162.1, 139.5 (d, *J* = 19.7 Hz), 128.6, 128.6, 128.4 (d, *J* = 2.0 Hz), 126.7, 125.3 (d, *J* = 7.0 Hz), 113.6, 93.5 (d, *J* = 170.1 Hz), 55.3, 36.7 (d, *J* = 24.8 Hz), 36.6 (d, *J* = 1.8 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -176.3;

IR (film): $\tilde{\nu}$ = 3315 (w), 2932(w), 1629 (m), 1605 (m), 1542 (m), 1502 (s), 1252 (s), 1178 (m), 1028 (m), 844 (m);

HRMS (ESI) calcd. for C₁₇H₁₈FNNaO₂⁺ [*M* + Na]⁺ 310.1214; Found 310.1212.

***tert*-Butyl 3-fluoro-4-((4-methoxybenzamido)methyl)pyrrolidine-1-carboxylate (5c).**

Following GP D, *tert*-Butyl (1*R*,5*S*,6*S*)-6-(4-methoxybenzamido)-3-azabicyclo[3.1.0]hexane-3-carboxylate (**4c**) (33.2 mg, 0.100 mmol, 1.0 equiv.) was used as starting material and the reaction was kept stirring under irradiation for 45 minutes. Then NaBH₃CN (7.6 mg, 0.12 mmol, 1.2 equiv.) was added as nucleophile. After the reaction mixture was stirred for 3 hours, *tert*-butyl 3-fluoro-4-((4-methoxybenzamido)methyl)pyrrolidine-1-carboxylate (**5c**) (21.1 mg, 0.0599 mmol, 60%, 1.4:1 d.r., diastereomeric value was determined by integration of FCH signals from ¹H NMR at 70 °C in CD₃CN) was obtained as a colorless gel which solidified during storage after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

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

Mp: 56-59 °C;

¹H NMR (400 MHz, CDCl₃; mixture of diastereoisomers and rotamers: the signals corresponding to the two diastereoisomers and two rotamers are partially resolved): δ = 7.86 – 7.63 (m, 2H, ArH), 7.04 – 6.80 (m, 2H, ArH), 6.35 (s, 1H, NH), 5.10 (dd, *J* = 53.0, 37.7 Hz, 1H, FCH), 3.85 (s, 3H, OCH₃), 3.80 – 3.10 (m, 6H, 3 x NCH₂), 2.69 (t, *J* = 27.2 Hz, 1H, FCHCH), 1.46 (d, *J* = 2.9 Hz, 9H, C(CH₃)₃);

¹H NMR (400 MHz, Acetonitrile-*d*₃, 70 °C; mixture of two diastereoisomers: the signals corresponding to the two diastereoisomers are partially resolved, diastereomeric ratio was determined by integration of FCH signals): δ = 7.81 – 7.73 (m, 4H, ArH, *major + minor*), 7.02 – 6.97 (m, 4H, ArH, *major + minor*), 6.94 (s, 2H, NH, *major + minor*), 5.17 (dt, *J* = 53.6, 3.3 Hz, 1H, FCH, *major*), 5.07 (ddd, *J* = 50.9, 4.5, 2.4 Hz, 1H, FCH, *minor*), 3.85 (s, 6H, OCH₃, *major + minor*), 3.69 – 3.46 (m, 8H, 2* NCH₂, *major + minor*), 3.41 – 3.27 (m, 2H, NCH₂, *major*), 3.15 (t, *J* = 10.7 Hz, 2H, NCH₂, *minor*), 2.74 – 2.55 (m, 2H, FCHCH, *major + minor*), 1.45 (s, 18H, 3* CH₃, *major + minor*);

¹³C NMR (101 MHz, CDCl₃; mixture of diastereoisomers in a 1.4:1 ratio: the signals corresponding to the two diastereoisomers are partially resolved): δ = 167.4, 167.3, 162.4, 162.3, 154.3, 154.2, 128.7, 128.7, 126.3, 126.1, 113.9, 113.8, 93.6 (d, *J* = 178.8 Hz), 93.0 (d, *J* = 177.8 Hz), 79.9, 79.8, 55.4, 52.9 (d, *J* = 23.3 Hz), 52.5 (d, *J* = 22.3 Hz), 46.8, 46.6, 43.3 (d, *J* = 19.4 Hz), 42.5 (d, *J* = 19.1 Hz), 37.5 (d, *J* = 6.8 Hz), 37.2 (d, *J* = 6.5 Hz), 28.4;

¹⁹F NMR (376 MHz, CDCl₃): δ = -176.1, -177.5, -193.4, -193.5;

IR (film): $\tilde{\nu}$ = 3339 (w), 2974 (w), 1695 (s), 1606 (s), 1505 (s), 1411 (s), 1255 (s), 1175 (s), 845 (m);

HRMS (ESI) calcd. for C₁₈H₂₅FN₂NaO₄⁺ [*M* + Na]⁺ 375.1691; Found 375.1698.

4-Methoxy-*N*-(3,3,3-trifluoro-1-hydroxypropyl)benzamide (5d).

Following GP D, *N*-(2,2-difluorocyclopropyl)-4-methoxybenzamide (**4d**) (22.7 mg, 0.100 mmol, 1.0 equiv.) was used as starting material and the reaction was kept stirring under irradiation for 6 hours. 4-methoxy-*N*-(3,3,3-trifluoro-1-hydroxypropyl)benzamide (**5d**) (18.0 mg, 0.0684 mmol, 68%) was obtained as a white solid after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.26 (silica, pentanes:ethyl acetate 3:2);

Mp: 104-106 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 8.20 (d, *J* = 8.3 Hz, 1H, NH), 7.91 – 7.83 (m, 2H, ArH), 7.02 – 6.95 (m, 2H, ArH), 5.93 (dtd, *J* = 8.4, 6.2, 4.6 Hz, 1H, CH), 5.33 (d, *J* = 4.7 Hz, 1H, OH), 3.85 (s, 3H, OCH₃), 2.73 (qdd, *J* = 10.9, 6.3, 1.5 Hz, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 166.6, 163.4, 130.0, 127.3, 126.8 (q, *J* = 277.1 Hz), 114.4, 70.1 (q, *J* = 4.4 Hz), 55.8, 40.5 (q, *J* = 27.1 Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -64.2;

IR (film): $\tilde{\nu}$ = 3304 (br, s), 1642 (s), 1607 (s), 1505 (s), 1254 (s), 1140 (s), 1029 (m), 843 (m);

HRMS (ESI) calcd. for C₁₁H₁₂F₃NNaO₃⁺ [*M* + Na]⁺ 286.0661; Found 286.0653.

N-(4-Fluorobutyl)-4-methoxybenzamide (5ea).

Following GP D, *N*-cyclobutyl-4-methoxybenzamide (**4e**) (20.5 mg, 0.100 mmol, 1.0 equiv.) was used as starting material and the reaction was kept stirring under irradiation for 45 minutes. Then NaBH₃CN (7.6 mg, 0.12 mmol, 1.2 equiv.) was added as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(4-fluorobutyl)-4-methoxybenzamide (**5ea**) (14.3 mg, 0.0636 mmol, 64%) was obtained as a colorless oil after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.28 (silica, pentanes:ethyl acetate 1:1);

¹H NMR (400 MHz, CDCl₃): δ = 7.79 – 7.65 (m, 2H, ArH), 6.98 – 6.83 (m, 2H, ArH), 6.20 (s, 1H, NH), 4.55 (t, *J* = 5.7 Hz, 1H, FCH₂), 4.43 (td, *J* = 5.6, 4.7, 2.5 Hz, 1H, FCH₂), 3.84 (s, 3H, OCH₃), 3.49 (q, *J* = 6.7 Hz, 2H, NCH₂), 1.85 – 1.72 (m, 4H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ 167.1, 162.1, 128.6, 126.8, 113.7, 83.8 (d, *J* = 164.4 Hz), 55.4, 39.4, 27.8 (d, *J* = 19.9 Hz), 25.8 (d, *J* = 4.3 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.2;

IR (film): $\tilde{\nu}$ = 3317 (w), 2962 (w), 1632 (s), 1606 (s), 1504 (m), 1254 (s), 1179 (m), 1030 (m), 845 (m);

HRMS (ESI) calcd. for C₁₂H₁₇FN₂O₂⁺ [M+H]⁺ 226.1238; Found 226.1232.

***N*-(4-Fluoro-1-(1*H*-indol-3-yl)butyl)-4-methoxybenzamide (5eb).**

Following GP D, *N*-cyclobutyl-4-methoxybenzamide (**4e**) (20.5 mg, 0.100 mmol, 1.0 equiv.) was used as starting material and the reaction was kept stirring under irradiation for 45 minutes. Then 1*H*-indole (14.0 mg, 0.120 mmol, 1.2 equiv.) was added as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(4-fluoro-1-(1*H*-indol-3-yl)butyl)-4-methoxybenzamide (**5eb**) (20.1 mg, 0.0591 mmol, 59%) was obtained as a orange oil after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

R_f: 0.43 (silica, pentanes:ethyl acetate 1:1);

¹H NMR (400 MHz, CDCl₃): δ = 8.39 (s, 1H, indole NH), 7.73 – 7.65 (m, 3H, ArH), 7.38 (dt, *J* = 8.2, 0.9 Hz, 1H, ArH), 7.21 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H, ArH), 7.17 – 7.14 (m, 1H, ArH), 7.11 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, ArH), 6.90 – 6.83 (m, 2H, ArH), 6.31 (d, *J* = 8.2 Hz, 1H, NH), 5.56 (q, *J* = 7.6 Hz, 1H, CH), 4.62 – 4.38 (m, 2H, FCH₂), 3.81 (s, 3H, OCH₃), 2.23 (dddd, *J* = 15.3, 14.2, 8.6, 4.4 Hz, 2H, CH₂), 1.93 – 1.77 (m, 2H, CH₂CH₂F);

¹³C NMR (101 MHz, CDCl₃): δ = 166.4, 162.1, 136.6, 128.7, 126.7, 126.0, 122.5, 121.8, 119.9, 119.2, 116.5, 113.7, 111.4, 83.9 (d, *J* = 164.6 Hz), 55.4, 46.4, 30.7 (d, *J* = 4.2 Hz), 27.6 (d, *J* = 19.7 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -218.4;

IR (film): $\tilde{\nu}$ = 3413 (w), 3273 (w), 2960 (w), 1630 (s), 1606 (s), 1498 (s), 1253 (s), 1178 (m), 1030 (m), 745 (m);

HRMS (ESI) calcd. for C₂₀H₂₁FN₂NaO₂⁺ [M+Na]⁺ 363.1479; Found 363.1477.

***N*-(4-Fluoro-1-(1*H*-pyrazol-1-yl)butyl)-4-methoxybenzamide (5ec).**

Following GP D, *N*-cyclobutyl-4-methoxybenzamide (**4e**) (20.5 mg, 0.100 mmol, 1.0 equiv.) was used as starting material and the reaction was kept stirring under irradiation for 45 minutes. Then 1*H*-pyrazole (8.2 mg, 0.12 mmol, 1.2 equiv.) was added as nucleophile. After the reaction mixture was stirred for 16 hours, *N*-(4-fluoro-1-(1*H*-pyrazol-1-yl)butyl)-4-methoxybenzamide (**5ec**) (16.2 mg, 0.0556 mmol, 56%) was obtained as a white solid 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: 157-158 °C;

¹H NMR (400 MHz, Acetone-*d*₆): δ = 8.37 (d, *J* = 8.7 Hz, 1H, NH), 7.96 – 7.84 (m, 2H, ArH), 7.81 (dd, *J* = 2.3, 0.7 Hz, 1H, ArH), 7.45 (d, *J* = 1.7 Hz, 1H, ArH), 7.01 – 6.91 (m, 2H, ArH), 6.37 (q, *J* = 7.9 Hz, 1H, CH), 6.20 (dd, *J* = 2.3, 1.7 Hz, 1H, ArH), 4.47 (dtd, *J* = 47.4, 6.0, 0.9 Hz, 2H, FCH₂), 3.84 (s, 3H, OCH₃), 2.46 – 2.19 (m, 2H, CH₂), 1.87 – 1.53 (m, 2H, CH₂);

¹³C NMR (101 MHz, Acetone-*d*₆): δ = 166.7, 163.4, 139.9, 130.2, 130.1, 126.9, 114.3, 105.3, 84.0 (d, *J* = 163.6 Hz), 66.2, 55.8, 31.0 (d, *J* = 5.2 Hz), 27.3 (d, *J* = 20.0 Hz);

¹⁹F NMR (376 MHz, Acetone-*d*₆): δ = -219.5;

IR (film): $\tilde{\nu}$ = 3302 (w), 2965 (w), 1644 (m), 1606 (s), 1503 (s), 1254 (s), 1176 (m), 1031 (m), 762 (m);

HRMS (ESI) calcd. for C₁₅H₁₈FN₃NaO₂⁺ [M+Na]⁺ 314.1275; Found 314.1270.

***N*-(4-Fluoro-3-phenylbutyl)-4-methoxybenzamide (5f).**

Following GP D, 4-methoxy-*N*-(3-phenylcyclobutyl)benzamide (**6f**) (28.1 mg, 0.100 mmol, 1.0 equiv.) was used as starting material and the reaction was kept stirring under irradiation for 2 hours. Then NaBH₃CN (7.6 mg, 0.12 mmol, 1.2 equiv.) was added as nucleophile. After the reaction mixture was stirred for 3 hours, *N*-(4-fluoro-3-phenylbutyl)-4-methoxybenzamide (**5f**) (19.0 mg, 0.0631 mmol, 63%) was obtained as a colorless oil after purification by column chromatography on silica using 1:1 pentanes:ethyl acetate as eluent.

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

¹H NMR (400 MHz, CDCl₃): δ = 7.60 – 7.52 (m, 2H, ArH), 7.38 – 7.32 (m, 2H, ArH), 7.27 (tt, *J* = 7.8, 1.3 Hz, 3H, ArH), 6.93 – 6.83 (m, 2H, ArH), 5.95 (s, 1H, NH), 4.66 – 4.40 (m, 2H, FCH₂), 3.83 (s, 3H, OCH₃), 3.55 – 3.31 (m, 2H, NCH₂), 3.06 (dddd, *J* = 24.0, 10.3, 6.8, 5.3 Hz, 1H, PhCH), 2.26 – 1.92 (m, 2H, CH₂);

¹³C NMR (101 MHz, CDCl₃): δ = 166.8, 162.0, 140.1 (d, *J* = 6.1 Hz), 129.0, 128.5, 127.9, 127.3, 126.7, 113.6, 86.9 (d, *J* = 173.8 Hz), 55.4, 44.9 (d, *J* = 18.7 Hz), 38.4, 31.4 (d, *J* = 4.0 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -217.8;

IR (film): $\tilde{\nu}$ = 3315 (m), 2960 (m), 1630 (s), 1605 (s), 1502 (s), 1253 (s), 1026 (s), 700 (m);

HRMS (ESI) calcd. for C₁₈H₂₁FNO₂⁺ [M+H]⁺ 302.1551; Found 302.1556.

3-Fluoro-3-phenylpropan-1-ol (7).

Following GP B, starting from Cyclopropylbenzene **6** (35.4 mg, 0.300 mmol) and after stirring for 45 minutes, 3-fluoro-3-phenylpropan-1-ol **7** (29.1 mg, 0.189 mmol, 63%) was obtained as a colorless oil after purification by column chromatography on silica using 2:1 pentanes:ethyl acetate as eluent.

R_f: 0.44 (silica, pentanes:ethyl acetate 2:1, KMnO₄);

¹H NMR (400 MHz, CDCl₃): δ = 7.49 – 7.30 (m, 5H, ArH), 5.68 (ddd, *J* = 48.1, 9.1, 4.0 Hz, 1H, FCH), 3.94 – 3.74 (m, 2H, OCH₂), 2.32 – 1.97 (m, 2H, CH₂), 1.53 (t, *J* = 5.5 Hz, 1H, OH);

¹³C NMR (101 MHz, CDCl₃): δ = 139.9 (d, *J* = 19.6 Hz), 128.5, 128.4 (d, *J* = 1.3 Hz), 125.5 (d, *J* = 6.9 Hz), 92.4 (d, *J* = 169.3 Hz), 59.1 (d, *J* = 4.3 Hz), 39.9 (d, *J* = 23.1 Hz);

¹⁹F NMR (376 MHz, CDCl₃): δ = -177.5;

IR (film): $\tilde{\nu}$ = 3339 (br,s), 2953 (w), 2926 (w), 1454 (w), 1048 (s), 759 (m), 698 (s).

¹H/¹⁹F NMR data correspond to the reported values. ^[8]

⁸ Remli, M.; Ayi, A. I.; Condom, R.; Guedj, R. *Bull. Soc. Chim. Fr.* **1986**, 6, 864-867.

7. Scale-up synthesis of compound **3l**

Procedure:

In a 30*200 mm borosilicate glass tube, *N*-cyclopropyl-4-methoxybenzamide **1a** (1.91 g, 10.0 mmol), selectfluor (3.89 g, 11.0 mmol, 1.1 equiv.) and benzophenone (182 mg, 1.00 mmol, 0.10 equiv.) were dissolved in 12.5 mL of MeCN-H₂O (v:v 4:6, 0.40 M). The reaction mixture was degassed by three freeze-pump-thaw cycles and backfilled with N₂. The mixture was then stirred at room temperature under 365 nm irradiation in Rayonet Reactor for 45 minutes. Then the tube was taken out from the Rayonet Reactor and a solution of 1*H*-indole (1.40 g, 12.0 mmol, 1.2 equiv.) in 7.50 mL MeCN was added dropwise. The reaction mixture was stirred at room temperature for 3 hours. After the completion of the reaction, the crude product was washed with water (30 mL) and extracted with dichloromethane (30 mL x 3). Then the organic phases were combined, dried over Na₂SO₄, concentrated. After purification by column chromatography on silica using pentanes:ethyl acetate as eluent, **3l** (1.86 g, 5.71 mmol, 57%) was obtained as product.

- A. After freeze-pump-thaw cycles
- B. Put the reaction tube into Rayonet Reactor
- C. Fix the reaction tube (with books)
- D. After irradiation
- E. Add a solution of indole dropwise

8. Mechanistic studies

8.1 TEMPO experiment

In a 12*75 mm borosilicate glass tube, *N*-cyclopropyl-4-methoxybenzamide (**1a**) (19.1 mg, 0.100 mmol, 1.0 equiv.), selectfluor (39.0 mg, 0.110 mmol, 1.1 equiv.), benzophenone (1.8 mg, 0.010 mmol, 0.10 equiv.) and TEMPO (31.2 mg, 0.200 mmol, 2.0 equiv.) were dissolved in 0.50 mL of MeCN-H₂O (v:v 4:6, 0.20 M). The reaction mixture was degassed by three freeze-pump-thaw cycles and backfilled with N₂. The mixture was then stirred at room temperature under 365 nm irradiation in Rayonet Reactor for 45 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 and *N*-(1-Hydroxy-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)-4-methoxybenzamide (**8**) (4.7 mg, 0.013 mmol, 13%) was obtained as a white solid. *N*-cyclopropyl-4-methoxybenzamide (**1a**) (16.0 mg, 0.084 mmol, 84%) was recovered using 1:1 pentanes:ethyl acetate as eluent.

N-(1-Hydroxy-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)-4-methoxybenzamide (**8**).

R_f: 0.39 (silica, pentanes:ethyl acetate 1:1);

Mp: 118-121 °C;

¹H NMR (400 MHz, CDCl₃): δ = 7.81 – 7.71 (m, 2H, ArH), 7.58 (d, *J* = 6.5 Hz, 1H, NH), 6.95 – 6.86 (m, 2H, ArH), 5.65 (q, *J* = 5.5 Hz, 1H, CH), 4.21 (ddd, *J* = 9.6, 8.3, 3.6 Hz, 1H, OCH₂), 4.12 (d, *J* = 2.8 Hz, 1H, OH), 3.93 (ddd, *J* = 9.8, 6.1, 3.7 Hz, 1H, OCH₂), 3.85 (s, 3H, OCH₃), 2.10 – 1.95 (m, 2H, OCH₂CH₂), 1.49 – 1.40 (m, 4H, CH₂), 1.33 – 1.24 (m, 2H, CH₂CH₂CH₂), 1.23 – 0.99 (m, 12H, CH₃);

¹³C NMR (101 MHz, CDCl₃): δ = 168.2, 162.5, 129.0, 126.0, 113.7, 74.2, 72.6, 59.8, 55.4, 39.7, 39.6, 33.5, 33.0, 32.9, 20.5, 20.3, 17.0;

IR (film): $\tilde{\nu}$ = 3341 (m), 2930 (m), 1643 (m), 1606 (m), 1503 (s), 1255 (s), 1177 (m), 987 (m), 845 (w);

HRMS (ESI) calcd. for C₂₀H₃₃N₂O₄⁺ [M + H]⁺ 365.2435; Found 365.2418.

8.2 Light-dark interval experiment

Procedure: The reaction was run similar with the standard procedure, except that fluorobenzene (28.8 mg, 0.300 mmol, 1.0 equiv.) was added as internal standard at the beginning. After 10 minutes, 20 μ L of the reaction mixture was extracted by micro syringe under N₂ flow. The aliquot was then diluted in 0.4 mL CDCl₃ and was then measured the substrate recovery rate (yield of product was not accounted as the hemiaminal could undergo hydrolysis slowly over time) by crude ¹H NMR. The reaction mixture was stirred under ambient light for 1 hour and an aliquot was prepared and analyzed by the above mentioned methods. Then the reaction mixture was kept stirring under irradiation in the Rayonet reactor for a second 10 minutes and an aliquot was prepared and analyzed. The reaction mixture was stirred under ambient light for a second hour and an aliquot was prepared and analyzed. Next the reaction mixture was kept stirring under irradiation in the Rayonet reactor for a third 10 minutes and an aliquot was prepared and analyzed. The reaction mixture was stirred under ambient light for a third hour and an aliquot was prepared and analyzed. The reaction mixture was kept stirring under irradiation in the Rayonet reactor for a fourth 10 minutes and an aliquot was prepared and analyzed.

Finally the reaction mixture was stirred under ambient light for a forth hour and an aliquot was prepared and analyzed.

Discussion: The light–dark interval experiments cannot exclude the chain process totally, but from the above figure, we can see the light is essential to the generation of product. If there is some chain propagation after stopping of irradiation, its contribution to the product should be small.

8.3 UV-vis spectra

The UV-vis spectra was measured by using the solution of corresponding compound in MeCN-water (v:v 4:6).

8.4 Cyclic voltammetry experiment

Procedure: Cyclic voltammetry was performed with a Biologic SP-150 Potentiostat, with a three-electrode cell configuration: a glassy carbon electrode as the working electrode, Pt wire as the counter electrode and a Ag/Ag⁺ quasi-reference electrode with 0.01 M AgBF₄ in acetonitrile. Bu₄NPF₆ was employed as the electrolyte and acetonitrile was used as solvent.

Ferrocene was used to calibrate the potential of Ag/Ag⁺ quasi-reference electrode.

Result: $E_{1/2}^{\text{red}}(\mathbf{1a}) = +1.67$ V vs SCE in MeCN.

8.5 Stern-Volmer quenching experiments

Procedure: Stern-Volmer fluorescence quenching experiments were conducted on a Varian Cary Eclipse machine. Benzophenone was recrystallized from ethanol. Selectfluor was recrystallized from acetonitrile/diethyl ether. **1a** was recrystallized from ethyl acetate.

For Ir photocatalyst:

Stock solution of [Ir(dF-CF₃ppy)₂(dtbbpy)]PF₆ (0.45 mg in volumetric flask of 100 mL with MeCN-H₂O v:v 4:6, 4.0×10⁻⁶ M). Four samples of **1a** (11.5 mg, 22.9 mg, 34.4 mg, 45.8 mg) were measured and dissolved respectively with 3.0 mL stock solution of [Ir(dF-CF₃ppy)₂(dtbbpy)]PF₆ to prepare solutions of **1a** as 0.02 M, 0.04 M, 0.06 M, 0.08 M. Similarly, four samples of selectfluor (21.2 mg, 42.5 mg, 63.7 mg, 85.0 mg) were measured and dissolved respectively with 3.0 mL stock solution of [Ir(dF-CF₃ppy)₂(dtbbpy)]PF₆ to prepare solutions of selectfluor as 0.02 M, 0.04 M, 0.06 M, 0.08 M.

The above solutions were transferred to quartz cuvettes and were bubbled with N₂ for 2 minutes before analysis. The solution was excited at 365 nm and the emission intensity was recorded at 475 nm.

For benzophenone photocatalyst:

Stock solution of benzophenone (82.0 mg in volumetric flask of 50.0 mL with MeCN-H₂O v:v 4:6, 0.009 M). Four samples of **1a** (1.33 mg, 2.29 mg, 3.44 mg, 5.73 mg) were measured and dissolved respectively with 3.0 mL stock solution of benzophenone to prepare solutions of **1a** as 0.0023 M, 0.004 M, 0.006 M, 0.01 M. Similarly, five samples of selectfluor (10.6 mg, 21.2 mg, 42.5 mg, 63.7 mg, 85.0 mg) were measured and dissolved respectively with 3.0 mL stock solution of benzophenone to prepare solutions of selectfluor as 0.01 M, 0.02 M, 0.04 M, 0.06 M, 0.08 M.

The above solutions were transferred to quartz cuvettes and were bubbled with N₂ for 2 minutes before analysis. The solution was excited at 365 nm and the emission intensity was recorded at 475 nm.

Note: It is well known that fluorescence of triplet state benzophenone can be quenched by multifunctional aromatics due to the formation of exciplexes.^[9]

Therefore, we further performed Stern-Volmer quenching with substrate **1g**, results showed no obvious quenching of fluorescence of triplet state benzophenone by **1g**.

⁹ Yamada, T. K. (1989) Photochemistry of aromatic ketones. I. Quenching of the benzophenone triplet state by multifunctional aromatics. II. Sensitized fluorescence of 9,10-dibromoanthracene and 1,3-dibromo-9,10-bis(phenylethynyl) anthracene by energy transfer from the triplet state of benzophenone and acetophenone. Doctoral dissertation. University of Southern California.

8.6 Reaction of *N*-Cyclopropyl-4-methoxy-*N*-methylbenzamide (**9**)

Following GP B, starting from *N*-Cyclopropyl-4-methoxy-*N*-methylbenzamide **9** (20.5 mg, 0.100 mmol), 4-methoxy-*N*-methylbenzamide **11** (12.0 mg, 0.073 mmol, 73%) was obtained as a white solid after purification by column chromatography on silica using 1:2 pentanes:ethyl acetate as eluent.

R_f: 0.25 (silica, pentanes:ethyl acetate 1:2);

¹H NMR (400 MHz, Acetone-*d*₆): δ = 7.85 (d, *J* = 8.8 Hz, 2H, ArH), 7.58 (s, 1H, NH), 7.12 – 6.79 (m, 2H, ArH), 3.84 (s, 3H, OCH₃), 2.88 (d, *J* = 2.9 Hz, 3H, NCH₃).

¹H NMR data correspond to the reported values.^[10]

3-Fluoropropanal **12** was observed from crude ¹H NMR and peaks correspond to the reported values.^[11]

8.7 *N*-fluoroamide synthesis

Although we did not observe any *N*-fluorination when mixing **1a** with Selectfluor, we still tried to synthesis *N*-cyclopropyl-*N*-fluoro-4-methoxybenzamide **13** in order to exclude the possibility of involving it as an intermediate. However, this goal was not achieved when we followed a reported protocol from Cook group.^[12] It is indicated in Cook's paper that their protocol for *N*-fluorination is limited to *N*-*tert* butyl amides since less-hindered amides undergo *N*-sulfonation when treated with NFSI.

¹⁰ Xia, Q.; Liu, X.; Zhang, Y.; Chen, C.; Chen, W. *Org. Lett.* **2013**, *15*, 3326-3329.

¹¹ Linclau, B.; Peron, F.; Bogdan, E.; Wells, N.; Wang, Z.; Compain, G.; Fontenelle, C.; Galland, N.; Le Questel, J.-Y.; Graton, J. *Chem. Eur. J.* **2015**, *21*, 17808-17816.

¹² Groendyke, B. J.; AbuSalim, D. I.; Cook, S. P. *J. Am. Chem. Soc.* **2016**, *138*, 12771-12774.

We were still curious about the stability of *N*-fluoroamides under our reaction conditions. Therefore, we synthesized one of the substrates **15** reported by the Cook group by following their protocol and then test it under irradiation with stoichiometric amount of benzophenone. However, no conversion of the starting material **15** was observed based on crude $^1\text{H}/^{19}\text{F}$ NMR. As a result, involvement of a *N*-fluoroamide intermediate can probably be ruled out.

9. Spectra

4-Methoxy-N-(trans-2-methylcyclopropyl)benzamide (trans-4a)

^1H -NMR (400 MHz, CDCl_3)

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

4-Methoxy-N-(cis-2-methylcyclopropyl)benzamide (cis-4a)
¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

4-Methoxy-N-(trans-2-phenylcyclopropyl)benzamide (4b)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

(1R,5S,6S)-tert-Butyl 6-(4-methoxybenzamido)-3-azabicyclo[3.1.0]hexane-3-carboxylate (4c)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

***N*-(2,2-Difluorocyclopropyl)-4-methoxybenzamide (4d)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

IR

***N*-Cyclobutyl-4-methoxybenzamide (4e)**

4-Methoxy-N-(trans-3-phenylcyclobutyl)benzamide (4f).

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

***N*-Cyclopropyl-4-methoxy-*N*-methylbenzamide (9)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

N-(3-Fluoro-1-hydroxypropyl)-4-methoxybenzamide (2a)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

***N*-(3-Fluoro-1-hydroxypropyl)-4-methylbenzamide (2b)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

4-Fluoro-N-(3-fluoro-1-hydroxypropyl)benzamide (2c)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

N-(3-Fluoro-1-(1*H*-indol-3-yl)propyl)pivalamide (2*g*-indole)

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

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

IR

4-Chloro-N-(3-fluoro-1-hydroxypropyl)benzamide (2j)

^1H -NMR (400 MHz, CDCl_3)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

***N*-(3-Fluoro-1-hydroxypropyl)benzamide (2k)**

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

N-Cyclopropyl-4-(methylsulfinyl)benzamide (2i)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR

***N*-(3-Fluoro-1-methoxypropyl)-4-methoxybenzamide (3a)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

***N*-(3-Fluoro-1-hydroperoxypropyl)-4-methoxybenzamide (3b)**

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

IR

***N*-(3-Fluoro-1-(*p*-tolylthio)propyl)-4-methoxybenzamide (3c)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

***N*-(3-Fluoro-1-(1*H*-pyrazol-1-yl)propyl)-4-methoxybenzamide (3d)**

^1H -NMR (400 MHz, CDCl_3)

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

***N*-(3-Fluoro-1-(1*H*-1,2,4-triazol-1-yl)propyl)-4-methoxybenzamide (3e)**
¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

***N*-(3-Fluoro-1-(1*H*-tetrazol-1-yl)propyl)-4-methoxybenzamide (3f)**

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

***N*-(3-Fluoropropyl)-4-methoxybenzamide (3g)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

IR

(*E*)-*N*-(5-Fluoro-1-phenylpent-1-en-3-yl)-4-methoxybenzamide (3h)
¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

IR

***N*-(3-Fluoro-1-(2,4,6-trimethoxyphenyl)propyl)-4-methoxybenzamide (3i)**

^1H -NMR (400 MHz, CDCl_3)

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

¹⁹F-NMR (376 MHz, CDCl₃)

IR

***N*-(1-(2,4-Dimethoxyphenyl)-3-fluoropropyl)-4-methoxybenzamide (3j)**

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

IR

***N*-(3-Fluoro-1-(1*H*-pyrrol-2-yl)propyl)-4-methoxybenzamide (3k)**
¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

***N*-(3-Fluoro-1-(1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3l)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

***N*-(3-Fluoro-1-(1-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3m)**
¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

***N*-(3-Fluoro-1-(2-phenyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3n)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

IR

***N*-(3-Fluoro-1-(3-methyl-1*H*-indol-2-yl)propyl)-4-methoxybenzamide (3o)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, Acetone-d₆)

***N*-(3-Fluoro-1-(4-fluoro-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3q)**
¹H-NMR (400 MHz, Acetone-d₆)

¹³C-NMR (101 MHz, Acetone-d₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

IR

***N*-(3-Fluoro-1-(5-methoxy-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3r)**
¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

IR

***N*-(3-Fluoro-1-(5-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3s)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

^{19}F -NMR (376 MHz, CDCl_3)

IR

***N*-(1-(5-Chloro-1*H*-indol-3-yl)-3-fluoropropyl)-4-methoxybenzamide (3t)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

IR

Methyl 3-(3-fluoro-1-(4-methoxybenzamido)propyl)-1H-indole-5-carboxylate (3u)
¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

***N*-(3-Fluoro-1-(6-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3v)**
¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

***N*-(3-Fluoro-1-(6-(trifluoromethyl)-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3w)**
¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

***N*-(1-(6-Bromo-1*H*-indol-3-yl)-3-fluoropropyl)-4-methoxybenzamide (3x)**
¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

***N*-(3-Fluoro-1-(7-methyl-1*H*-indol-3-yl)propyl)-4-methoxybenzamide (3y)**
¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

N-(3-Fluoro-1-hydroxybutyl)-4-methoxybenzamide (5a)

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

***N*-(3-Fluoro-3-phenylpropyl)-4-methoxybenzamide (5b)**
¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

IR

tert-Butyl 3-fluoro-4-((4-methoxybenzamido)methyl)pyrrolidine-1-carboxylate (5c)
¹H-NMR (400 MHz, CDCl₃)

^{19}F -NMR (376 MHz, CDCl_3)

IR

4-Methoxy-N-(3,3,3-trifluoro-1-hydroxypropyl)benzamide (5d).

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

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

¹⁹F-NMR (376 MHz, Acetone-d₆)

IR

***N*-(4-Fluorobutyl)-4-methoxybenzamide (5ea)**

^1H -NMR (400 MHz, CDCl_3)

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

***N*-(4-Fluoro-1-(1*H*-indol-3-yl)butyl)-4-methoxybenzamide (5eb)**

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

***N*-(4-Fluoro-1-(1*H*-pyrazol-1-yl)butyl)-4-methoxybenzamide (5ec)**

¹H-NMR (400 MHz, Acetone-*d*₆)

¹³C-NMR (101 MHz, Acetone-*d*₆)

¹⁹F-NMR (376 MHz, Acetone-*d*₆)

IR

***N*-(4-Fluoro-3-phenylbutyl)-4-methoxybenzamide (5f)**

¹H-NMR (400 MHz, CDCl₃)

¹⁹F-NMR (376 MHz, CDCl₃)

IR

3-Fluoro-3-phenylpropan-1-ol (7)

¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

^{19}F -NMR (376 MHz, CDCl_3)

IR

***N*-(1-Hydroxy-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)-4-methoxybenzamide (8)**
¹H-NMR (400 MHz, CDCl₃)

¹³C-NMR (101 MHz, CDCl₃)

IR