EurJOC
European Journal of Organic Chemistry

A Journal of
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Accepted Article

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201900685

Link to VoR: http://dx.doi.org/10.1002/ejoc.201900685

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Site-specific Synthesis of β-Fluorinated γ-Butyrolactams via Decarboxylative Fluorination of β-Carboxyl-γ-Butyrolactams

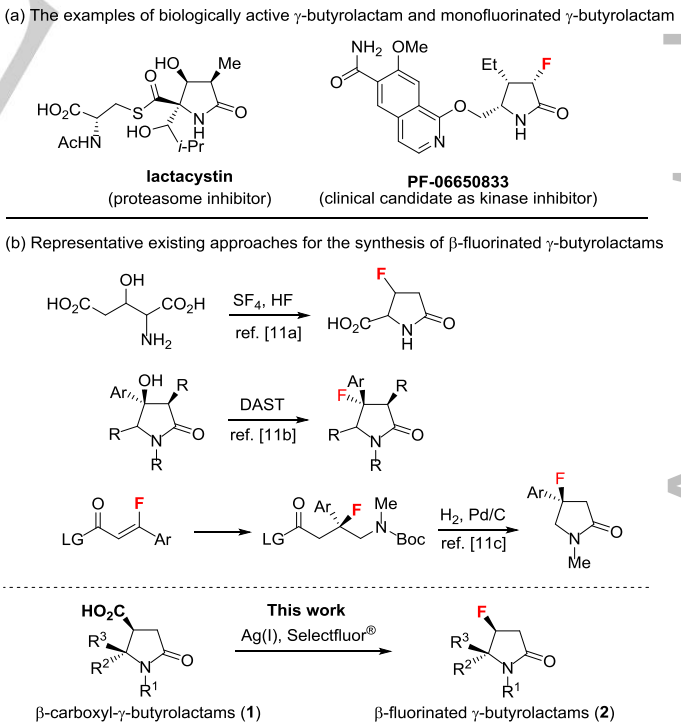
Supasorn Phae-nok,[a] Manat Pohmakotr,[a] Chutima Kuhakarn,[a] Vichai Reutrakul,[a] and Darunee Soorukram*[a]

Abstract: Monofluorinated cyclic nitrogen-containing compounds are synthetically useful scaffolds in organic synthesis and medicinal applications. In this report, $AgNO_3$ mediated decarboxylative fluorination of β-carboxyl-γ-butyrolactams using Selectfluor® as a fluorine source was described to achieve a site-specific synthesis of β-fluorinated γ-butyrolactams.

Introduction

There has been growing interest in organofluorine compounds in various fields, including agrochemical, materials, and pharmaceutical sciences. The presence of fluorine atoms or fluorine-containing motifs in organic molecules was realized to enhance physical, chemical, and biological properties of non-fluorinated parent compounds.[1] As a result, there were tremendous progresses in fluorination methods, including electrophilic fluorination, using electrophilic fluorinating reagents,[2] and nucleophilic fluorination, using fluoride ion sources.[3] Recently, radical fluorination[4] using the radical reactivity of the traditionally nitrogen-based electrophilic reagents such as Selectfluor®, *N*-fluorobis(phenylsulfonyl)amine (NFSI), and *N*-fluoropyridinium salts (NFPy's) has also gained much attentions. Among synthetic methodologies developed for radical fluorination toward fluorination of alkenes,[5] fluorination of boronic acid derivatives,[6] C(sp^3)–H fluorination,[7] and C–C bond activation,[8] decarboxylative fluorination (or fluorodecarboxylation) of carboxylic acids has proved to be a powerful and complementary approach for the formation of C(sp^3)–F bonds.[9] The salient features of decarboxylative fluorination include stability of the carboxylic acid precursors, the ready availability of the fluorinating agents, and most importantly, the site-specific formation of the C(sp^3)–F bond.

Monofluorinated γ-butyrolactams (or pyrrolidin-2-ones)[10][11] bearing fluorine atom within functionalized structures are of increasing demand in both academic researches and industrial sections, particularly in pharmaceutical industry.[12] This attributed to the profound effects that the incorporation of fluorine atoms at specific position of cyclic nitrogen-containing compounds can lead to the improved biological activities. A recent example is PF-06650833, a chiral α-fluorinated γ-butyrolactam which exhibited potent and selective inhibitory activity toward interleukin‐1 receptor associated kinase 4 (IRAK4) (Scheme 1a).[10a] Therefore, the development of efficient and site-specific stereoselective synthesis of chiral fluorinated γ-butyrolactams is of considerable importance. Although synthetic methods for the synthesis of α-fluorinated carbonyl compounds are available,[10] those for selective synthesis of β-fluorinated carbonyl compounds are still limited (Scheme 1b).[11] Encouraged by our previous results on decarboxylative fluorination of paraconic acids to access β-fluorinated γ-butyrolactones,[13] we envisioned that β-fluorinated γ-butyrolactams could be synthesized with a direct and site-specific manner employing β-carboxyl-γ-butyrolactams **1** as precursors. We report herein $AgNO_3$ mediated decarboxylative fluorination of **1** employing Selectfluor® as a fluorine source to access a series of β-fluorinated γ-butyrolactams **2** including chiral derivatives that might be useful in organic synthesis and drug discovery.



Scheme 1. a) Biologically active compounds containing γ-butyrolactam cores; b) representative existing approaches and our method for the synthesis of β-fluorinated γ-butyrolactams.

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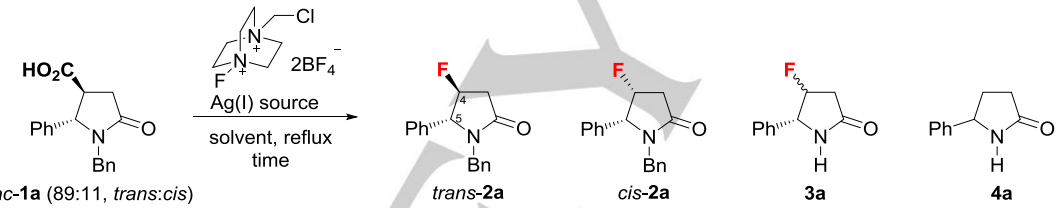
Results and Discussion

Primarily, the racemic mixture of β-carboxyl-γ-butyrolactam **1a** (*rac*-**1a**) was used as a model substrate to find an optimal reaction conditions and the results are summarized in Table 1. Treatment of *rac*-**1a** (89:11, *trans*:*cis*)[14a] with Selectfluor® (2 equiv.) and $AgNO_3$ (1 equiv.) in refluxing acetone/H_2O (1:1 v/v) for 12 h yielded a mixture of β-fluorinated γ-butyrolactams **2a** and **3a** as well as γ-butyrolactam **4a** in a ratio of 5:1:1 (^{1}H-NMR analysis of the crude reaction mixture); 74% conversion based on the recovery of *rac*-**1a** (Table 1, entry 1). Although **3a** could be removed from the obtained mixture, the separation of **2a** and **4a** proved to be difficult. Next, various reaction parameters, including solvents, reaction time, and the additive were investigated with the goal to suppress the formation of **4a**. After through screening, it was found that treatment of *rac*-**1a** with Selectfluor® and $AgNO_3$ (1.5 equiv. each) in refluxing MeCN/H_2O (1:4 v/v) for 6 h gave the best results; 82% conversion with **2a**:**3a**:**4a** in a ratio of 15:2:1 (Table 1, entry 9). After chromatographic separation, *trans*-**2a**, *cis*-**2a**, and **3a** were isolated in 48%, 6%, and 5% yields, respectively. The relative stereochemistries of *trans*-**2a** and *cis*-**2a** were assigned on the basis of the analysis of coupling constants between H-4 and H-5 of **2a**.[15] Attempts to use $AgNO_3$ as a catalyst (20 mol%) or employing $NaHCO_3$ (1 equiv.) as an additive gave inferior results (Table 1, entries 10-12). The reaction did not proceed when either $AgNO_3$ or Selectfluor® was excluded from the reaction; *rac*-**1a** was recovered in quantitative yields (86–99% yields; Table 1, entries 13 and 14). These results emphasized the crucial roles of both Selectfluor® or Ag(I) in the present reaction. Lastly, other Ag(I) salts, including AgOAc and $AgBF_4$ were also evaluated but the results obtained were less satisfactory (Table1, entries 15 and 16). After extensive investigation, the optimum reaction conditions were chosen as follows: **1** (1 equiv.), $AgNO_3$ (1.5 equiv.), Selectfluor® (1.5 equiv.) in refluxing MeCN/H_2O (1:4 v/v) for 6 h (Table 1, entry 9).

On the basis of the precedent works[9b] and the above observation, a mechanistic pathway for the decarboxylative fluorination of *rac*-**1a** is proposed (Scheme 2). The oxidation of Ag(I) by Selectfluor® generates an Ag(III)-F intermediate (**A**).

Table 1. Optimization of the reaction conditions for the decarboxylative fluorination of *rac*-**1a**.

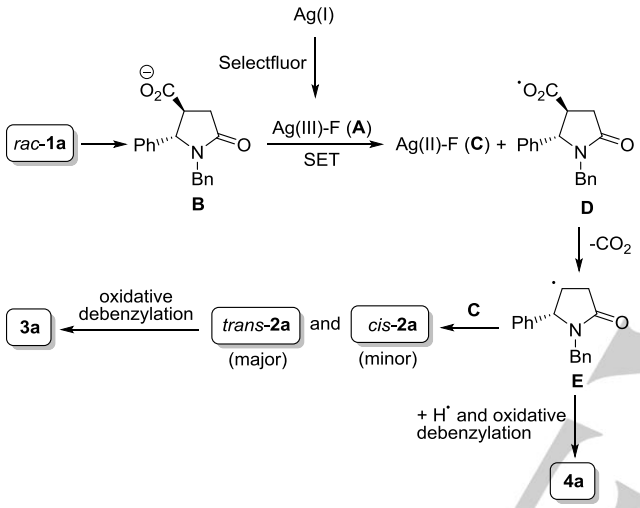


rac-**1a** (89:11, *trans*:*cis*) *trans*-**2a** *cis*-**2a** **3a** **4a**

Entry	Ag(I) source (equiv.)	Selectfluor® (equiv.)	Solvent (ratio, v/v)	Time (h)	% Conversion[a] (**2a**:**3a**:**4a**)[b]	% Yield of **2a** (*trans*:*cis*)[c]
1	$AgNO_3$ (1)	2	acetone/H_2O (1:1)	12	74 (5:1:1)	N.D.
2	$AgNO_3$ (1)	2	MeCN/H_2O (1:1)	12	82 (4:1:trace)	42 (6:1)
3	$AgNO_3$ (1)	2	H_2O	12	63 (4:1:0)	39 (6:1)
4[d]	$AgNO_3$ (1)	2	CH_2Cl_2/H_2O (1:1)	12	57 (1:0:trace)[e]	38 (4:1)
5[d]	$AgNO_3$ (1)	2	DCE/H_2O (1:1)	12	32 (1:0:trace)[e]	28 (4:1)
6[d]	$AgNO_3$ (1)	2	benzene/H_2O (1:1)	12	41 (1:0:0)	32 (5:1)
7	$AgNO_3$ (1)	2	MeCN/H_2O (1:4)	6	84 (3:1:trace)[e]	56 (4:1)
8	$AgNO_3$ (1)	1	MeCN/H_2O (1:4)	6	53 (19:6:1)	28 (5:1)
9	$AgNO_3$ (1.5)	1.5	MeCN/H_2O (1:4)	6	82 (15:2:1)	48 (*trans*-**2a**), 6 (*cis*-**2a**)[f]
10	$AgNO_3$ (0.2)	1.5	MeCN/H_2O (1:4)	6	40 (6:1:0)	N.D.
11[d]	$AgNO_3$ (1.5)	1.5	MeCN/H_2O (1:4)	6	53 (1:0:trace)	50 (4:1)
12[d]	$AgNO_3$ (1.5)	1.5	MeCN/H_2O (1:4)	12	61 (1:0:trace)	51 (4:1)
13	-	1.5	MeCN/H_2O (1:4)	6	_[g]	_[g]
14	$AgNO_3$ (1.5)	-	MeCN/H_2O (1:4)	6	_[h]	_[h]
15	AgOAc (1.5)	1.5	MeCN/H_2O (1:4)	6	16 (11:1:0)	9 (N.D.)
16	$AgBF_4$ (1.5)	1.5	MeCN/H_2O (1:4)	6	31 (3:1:0)	21 (N.D.)

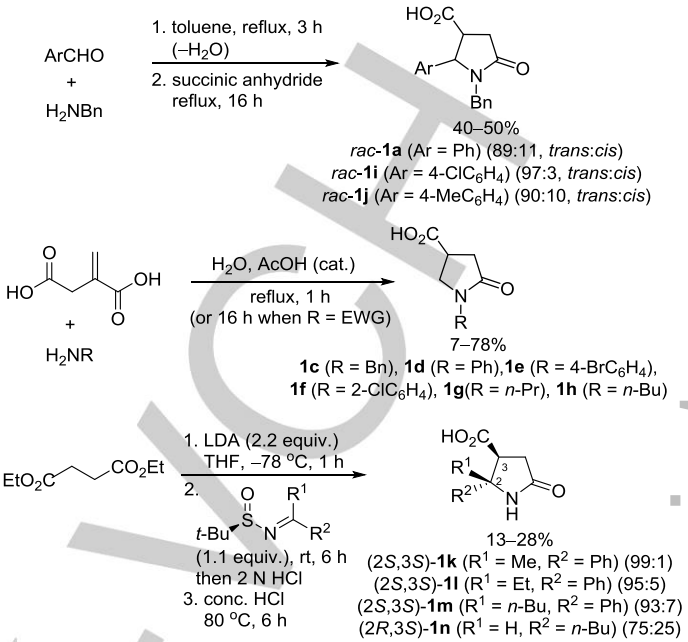
[a] Based on the recovery of *rac*-**1a**. [b] The ratio of **2a**, **3a**, and **4a** was determined by ^{1}H NMR analysis of the crude mixture. [c] *Trans*:*cis* ratio of **2a** was determined by ^{1}H NMR analysis after column chromatography (SiO_2). [d] $NaHCO_3$ (1 equiv.) was added. [e] Trace of the corresponding α,β-unsaturated γ-butyrolactam was observed. [f] *Trans*-**3a** was isolated in 5% yield. See the Experimental Section. [g] *rac*-**1a** was recovered (99% yield). [h] *rac*-**1a** was recovered (86% yield). N.D. = not determined.

Intermediate **A** then undergoes a single electron-transfer (SET) process with a carboxylate anion **B** derived from *rac*-**1a** to give an Ag(II)-F intermediate (**C**) and the corresponding carboxyl radical **D**. Radical **D** then undergoes decarboxylation to give alkyl radical **E**. Subsequent abstraction of a fluorine atom from **C** by **E** leads to β-fluorinated γ-butyrolactams **2a** as a mixture of *trans*-**2a** (major) and *cis*-**2a** (minor). The β-fluorinated γ-butyrolactam **3a** was proposed to arise from the competitive oxidative debenzylation[16] while **4** could be formed from trapping a hydrogen atom of **E** and the oxidative debenzylation processes. Notably, the formation of **A** derived from Ag(I) and Selectfluor® is crucial for this transformation since the reaction did not proceed if either Selectfluor® or Ag(I) was excluded from the reaction (Table 1, entries 13 and 14).



Scheme 2. Proposed mechanism for the decarboxylative fluorination of *rac*-**1a**.

With the optimized reaction conditions in hand, we next explored the generality and functional group compatibility of the reaction. Substrates **1** were synthesized as shown in Scheme 3.[14] The results of the decarboxylative fluorination of **1** are summarized in Table 2. Under standard reaction conditions, the decarboxylative fluorination of *rac*-**1b**-**1j** gave the corresponding products **2b**-**2j** in moderate to good yields (21-83% yields) (Table 2, entries 2-10). It was found that substituents on the nitrogen atom and the aromatic ring located at the γ position of the lactam ring had significant effect on the reaction efficiency. While the reaction of **1d** suffers from a competing fluorination on the phenyl ring, the reactions of **1c** and **1e**-**1h** bearing a benzyl, an electron-withdrawing, and an alkyl substituent, respectively, gave the corresponding products **2c** and **2e**-**2h** in moderate to good yields. In addition, while *rac*-**1i** (97:3, *trans*:*cis*) possessing a *p*-ClC_6H_4 group, gave **2i** (21% yield;[17] *trans*-**2i**:*cis*-**2i** = 91:9 by ^{1}H-NMR analysis) (Table 2, entry 9), compounds **1**, bearing *p*-$MeOC_6H_4$ or 3,4,5-$(MeO)_3C_6H_2$ group did not provide the expected products (not shown) but were found decomposed under the reaction conditions. This possibly attributed to the ease of the electron rich aromatic system to undergo competitive



Scheme 3. Synthesis of starting materials **1**.

oxidative cleavage.[16] In addition, the reaction of *rac*-**1j** (90:10, *trans*:*cis*), bearing a *p*-Tol group at the γ position of the lactam ring, gave **2j** (45% yield, *trans*-**2j**:*cis*-**2j** = 93:7, ^{1}H-NMR analysis) (Table 2, entry 10) along with a mixture of compounds derived from competitive oxidation at a methyl group on the aromatic ring being observed.

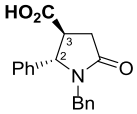
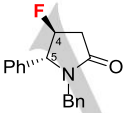
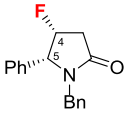
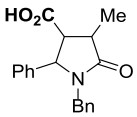
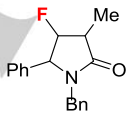
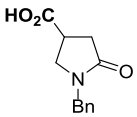
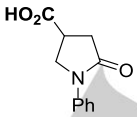
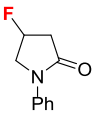
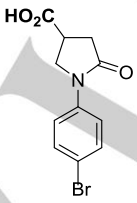
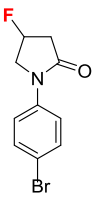
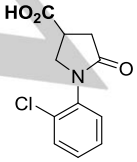
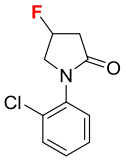
It is worth mentioning that compounds **1** with a N-H lactam scaffold readily underwent the decarboxylative fluorination. Thus, the reaction of *rac*-**1k** (99:1, *trans*:*cis*) gave a mixture of *trans*-**2k** and *cis*-**2k**. Delightfully, the mixture of *trans*-**2k** and *cis*-**2k** were readily separated by means of chromatographic methods (SiO_2) to give *trans*-**2k** (37% yield) and *cis*-**2k** (25% yield) (Table 2, entry 11). The reaction could also be applied with a chiral substrate. Under standard reaction conditions, (2*S*,3*S*)-**1k** (dr = 99:1) gave (4*S*,5*R*)-**2k** (42% yield) and (4*R*,5*R*)-**2k** (29% yield) (Table 2, entry 12). Similarly, chiral substrates **1l**-**1n** also gave the corresponding chiral β-fluorinated γ-butyrolactams **2l**-**2n** in 37-50% yields with moderate ratios of the two diastereomers (*trans*:*cis* = 4:1) (Table 2, entries 13–15). For the products **2l**-**2n**, each pair of the two diastereomers can be readily separated by chromatographic methods (SiO_2) to yield the respective chiral fluorinated compounds each as a single isomer. Notably, chiral β-fluorinated γ-butyrolactams possessing a N-H lactam scaffold might be useful for further transformation to fluorinated pyrrolidine drugs and related fluorinated nitrogen-containing derivatives which may be found useful in pharmaceutical sciences.

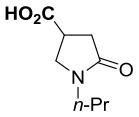
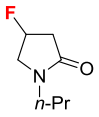
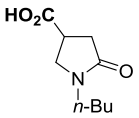
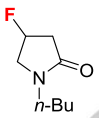
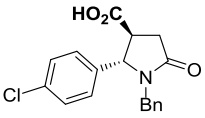
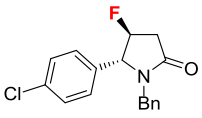
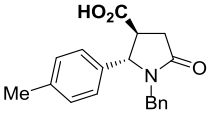
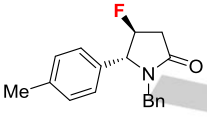
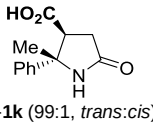
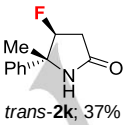
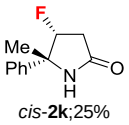
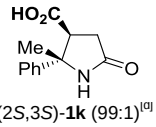
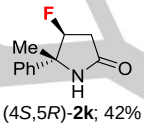
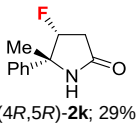
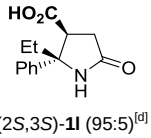
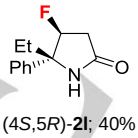
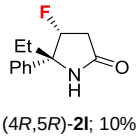
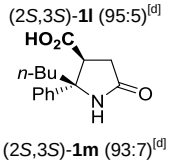
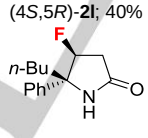
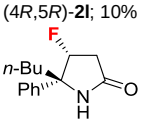
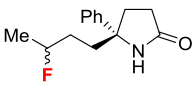
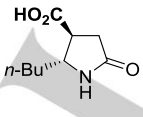
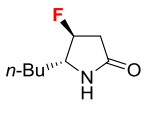
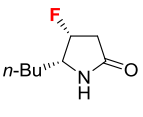
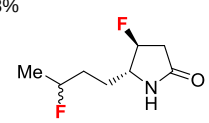
The relative stereochemistries of **2** were established on the basis of the NMR analysis (see the Experimental Section). In addition, for the minor isomer (*cis* isomer) of **2a**, **2i**, **2j**, and **2k** as well as (4*R*,5*R*)-**2k**-(4*R*,5*R*)-**2m**, the relative stereochemistry

was also established on the basis of the high-field shift of the fluorine signal, which is a result of an anisotropic effect of the benzene ring.[18] Finally, the stereochemistries of (4*S*,5*R*)-**2n** and (4*R*,5*R*)-**2n** were assigned on the basis of the coupling constant between H-4 and H-5 of the lactam ring. It is worth to emphasize that in all cases, the major diastereomer of **2** is the one in which the fluorine atom located on the opposite side to the larger substituent at the γ position. This implied that fluorination took place from the less sterically hindered face of the radical intermediate **E** (Scheme 2).

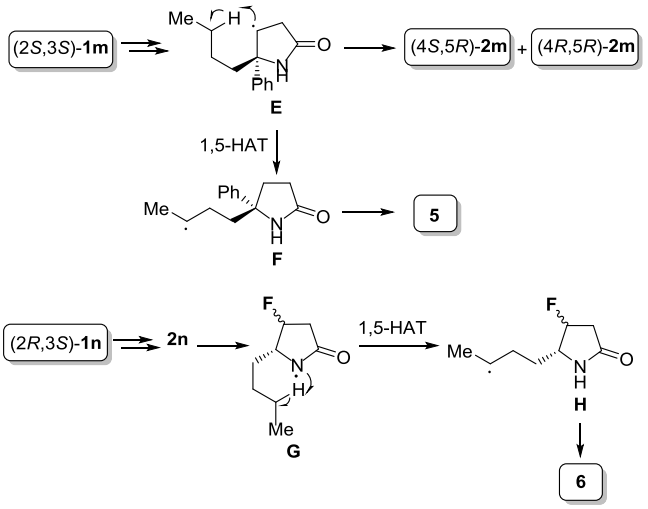
Interestingly, when (2*S*,3*S*)-**1m** and (2*R*,3*S*)-**1n** were used as substrates, a competitive remote C(sp^3)–H fluorination took place, leading to fluorinated γ-butyrolactams **5** and **6**, each as a mixture of diastereomers (11-12% yields) (Table 2, entries 14 and 15). The structures of **5** and **6** were established on the basis of 1D and 2D NMR spectroscopy and mass spectrometry. The position of fluorine atom on the side chain of **5** and **6** was also confirmed by using the magnitude of the coupling constants between carbons and fluorine (See the Experimental Section). The formation of **5** and **6** can be explained. A competitive remote intramolecular hydrogen atom abstraction of the alkyl radical **E** derived from (2*S*,3*S*)-**1m** via a six-membered-ring transition state leads to the corresponding alkyl radical **F** which after abstraction of a fluorine atom gives the observed compound **5** (Scheme 4). For the formation of difluorinated derivative **6**, it was proposed that, under the oxidation conditions employed, the amidyl radical **G** was generated[19] and undergoes site-selective remote radical generation via 1,5-hydrogen atom transfer (1,5-HAT) providing alkyl radical **H**. Upon trapping with a second fluorine atom, the difluorinated derivative **6** was obtained. Further exploration of the observed site-selective remote fluorination is under investigation.

Table 2. Decarboxylative fluorination of β-carboxyl-γ-butyrolactams **1**.

Entry	**1** (dr)[a]	Product **2**; Yield (dr)[a]	
1	 *rac*-**1a** (89:11, *trans*:*cis*)	 *trans*-**2a**; 48%	 *cis*-**2a**; 6%
2	 *rac*-**1b** (61:21:15:3)[b]	 *rac*-**2b**; 65% (52:22:16:10)[b]	
3	 **1c**	 **2c**; 60%	
4	 **1d**	 **2d**; 29%[c]	
5	 **1e**	 **2e**; 33%	
6	 **1f**	 **2f**; 83%	

7	 **1g**	 **2g**; 75%
8	 **1h**	 **2h**; 68%
9	 *rac*-**1i** (97:3, *trans*:*cis*)	 *trans*-**2i** and *cis*-**2i**; 21% (91:9)
10	 *rac*-**1j** (90:10, *trans*:*cis*)	 *trans*-**2j** and *cis*-**2j**; 45% (93:7)
11	 *rac*-**1k** (99:1, *trans*:*cis*)[d]	 *trans*-**2k**; 37%	 *cis*-**2k**;25%
12	 (2*S*,3*S*)-**1k** (99:1)[d]	 (4*S*,5*R*)-**2k**; 42%	 (4*R*,5*R*)-**2k**; 29%
13	 (2*S*,3*S*)-**1l** (95:5)[d]	 (4*S*,5*R*)-**2l**; 40%	 (4*R*,5*R*)-**2l**; 10%
14	 (2*S*,3*S*)-**1m** (93:7)[d]	 (4*S*,5*R*)-**2m**; 30%	 (4*R*,5*R*)-**2m**; 7%
		 **5**; 12% (1:1)
15	 (2*R*,3*S*)-**1n** (75:25)[d]	 (4*S*,5*R*)-**2n**; 38%	 (4*R*,5*R*)-**2n**; 10%
		 **6**; 11% (1:1)

[a] The diastereomeric ratio (dr) was determined by ^{1}H NMR analysis. [b] A mixture of four diastereomers of *rac*-**1b** was used as a substrate. [c] A mixture of products derived from the fluorination on the phenyl ring was observed. [d] The diastereomeric ratio (dr) was determined by ^{1}H NMR analysis. The stereochemistry was assigned based on the transition state proposed in the literatures.[14]



Scheme 4. Proposed mechanism for the observed remote C(sp^3)–H fluorination.

Conclusions

In conclusion, the direct and site-specific synthesis of β-fluorinated γ-butyrolactams via $AgNO_3$ mediated decarboxylative fluorination of β-carboxyl-γ-butyrolactams using Selectfluor® as a fluorine source was described. The developed methods should be found useful and applicable to the synthesis of β-fluorinated γ-butyrolactams and related fluorinated nitrogen-containing compounds which are an important class of compounds toward organic synthesis and pharmaceutical science.

Experimental Section

General: The ^{1}H, ^{13}C and ^{19}F NMR were recorded on either Bruker Ascend™400 (400 MHz) or JNM-ECZS (400 MHz) spectrometer in $CDCl_3$ or $CDCl_3$/CD_3OD using tetramethylsilane as an internal standard. The IR spectra were recorded on ALPHA FT-IR Spectrometer. The mass spectra were recorded on a Thermo Finnigan Polaris Q mass spectrometer. The high-resolution mass spectra were recorded on an HR-TOF-MS Micromass model VQ-TOF2 mass spectrometer. Melting points were recorded on a Büchi M-565 Melting Point Apparatus and uncorrected. The specific optical rotation values were recorded on a Jasco P-1020 polarimeter. Tetrahydrofuran (THF) was freshly distilled under argon from sodium-benzophenone ketyl. Column chromatography was performed by using Merck silica gel 60 (Art 7734). Other common solvents [dichloromethane (CH_2Cl_2), ethyl acetate (EtOAc) and hexanes] were distilled before use. Compounds *rac*-**1a**–*rac*-**1j** were synthesized according to the literature procedures.[14]

1-Benzyl-5-oxo-2-phenylpyrrolidine-3-carboxylic acid (*rac*-1a): dr = 89:11 (*trans:cis*); ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD, interpreted equally for both isomers, major one marked*): δ 7.38−7.25 (m, 7H, Ar*H** and Ar*H*), 7.25−7.16 (m, 7H, Ar*H** and Ar*H*), 7.14−7.02 (m, 4H, Ar*H** and Ar*H*), 7.01−6.90 (m, 2H, Ar*H**), 5.06 (d, *J* = 14.8 Hz, 1H, CH*H*), 5.00 (d, *J* = 14.8 Hz, 1H, CH*H**), 4.68 (d, *J* = 9.0 Hz, 1H, C*H*), 4.63 (d, *J* = 5.4 Hz, 1H, C*H**), 3.48 (d, *J* = 14.8 Hz, 1H, C*H*H*), 3.42 (d, *J* = 14.8 Hz, 1H, C*H*H), 3.56−3.47 (m, 1H, C*H*), 3.10 (dd, *J* = 10.7, 17.4 Hz, 1H, CH_2), 3.06−2.95 (m, 1H, C*H**), 2.91−2.73 (m, 2H, CH_2*), 2.57 (dd, *J* = 9.2, 17.4 Hz, 1H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD, major one marked*): δ 174.0 (CO*), 173.6 (CO*), 138.6 (C*), 137.7 (C), 135.1 (C* and C), 128.9 (2 × CH* and 2 × CH), 128.4 (3 × CH* and 3 × CH), 128.1 (2 × CH* and 2 × CH), 127.5 (CH* and CH), 126.7 (2 × CH* and 2 × CH), 63.8 (CH*), 62.4 (CH), 45.6 (CH*), 44.3 (CH_2* and CH), 43.0 (CH_2), 33.4 (CH_2*), 31.9 (CH_2) ppm. Due to low intensity, some proton and carbon peaks of *cis*-**1a** could not be detected.

1-Benzyl-4-methyl-5-oxo-2-phenylpyrrolidine-3-carboxylic acid (*rac*-1b): Methylation of *rac*-**1a** (89:11, *trans*:*cis*) gave *rac*-**1b** as a mixture of four diastereomers (**A**–**D**) (73% yield, dr = 61:21:15:3) after column chromatography (SiO_2, 50%EtOAc in hexanes with a small amount of formic acid); viscous oil; IR (neat): ν_{max} 3030, 1728, 1643 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, integrated equally for all isomers): δ 7.35−6.85 (m, Ar*H* of all isomers), 5.08 (d, *J* = 14.7 Hz, 1H, CH*H* of **C**), 5.02 (d, *J* = 14.4 Hz, 1H, CH*H* of **A**), 4.98 (d, *J* = 14.2 Hz, 1H, CH*H* of **B**), 4.80 (d, *J* = 5.2 Hz, 1H, C*H* of **C**), 4.56 (d, *J* = 6.9 Hz, 1H, C*H* of **A**), 4.46 (d, *J* = 8.1 Hz, 1H, C*H* of **B**), 4.34 (d, *J* = 3.8 Hz, 1H, C*H* of **D**), 3.39 (d, *J* = 14.6 Hz, 1H, C*H*H of **A**), 3.14 (dd, *J* = 7.0, 9.2 Hz, 1H, C*H* of **A**), 3.10−2.93 (m, 3H, 3 × C*H* of **A** and **C**), 2.75 (m, 1H, C*H* of **B**), 2.66 (m, 1H, C*H* of **B**), 1.35 (d, *J* = 7.0 Hz, 3H, CH_3 of **B**), 1.15 (d, *J* = 7.4 Hz, 3H, CH_3 of **A**), 1.10 (d, *J* = 7.2 Hz, 3H, CH_3 of **C**) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.0 (CO of **B**), 175.9 (CO of **A**), 175.2 (CO of **B**), 174.7 (CO of **A**), 139.0 (C of **C**), 138.3 (C of **B**), 138.0 (C of **A**), 135.5 (C of **B**), 135.4 (C of **A**), 129.1 (2 × CH of **A**), 128.6 (4 × CH of **A**), 128.5 (2 × CH of **A**), 127.3 (2 × CH of **A**), 61.8 (CH of **B**), 61.1 (CH of **A**), 55.0 (CH of **B**), 51.8 (CH of **C**), 51.4 (CH of **A**), 44.8 (CH_2 of **C**), 44.6 (CH_2 of **B**), 44.5 (CH_2 of **A**), 40.8 (CH of **B**), 38.4 (CH of **A**), 38.2 (CH of **C**), 16.0 (CH_3 of **B**), 12.0 (CH_3 of **C**), 12.3 (CH_3 of **A**) ppm. Due to low intensity, some proton and carbon peaks of minor isomers of **1b** could not be detected. MS: *m/z* (%) relative intensity 309 [(M)$^+$, 34], 218 (100), 175 (37), 160 (51), 146 (37), 132 (34), 118 (40), 106 (31), 91 (43), 77 (21). HRMS (ESI-TOF) *m/z*: [M − H] calcd. for $C_{19}H_{18}NO_3$: 308.1287, found 308.1298.

1-Benzyl-5-oxopyrrolidine-3-carboxylic acid (1c): ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 7.30−7.17 (m, 3H, Ar*H*), 7.17−7.08 (m, 2H, Ar*H*), 4.43 (d, *J* = 14.8 Hz, 1H, CH*H*), 4.32 (d, *J* = 14.8 Hz, 1H, C*H*H), 3.50−3.33 (m, 2H, CH_2), 3.17−3.03 (m, 1H, C*H*), 2.78−2.56 (m, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ 174.6 (CO), 173.2 (CO), 135.5 (C), 128.6 (2 × CH), 127.9 (2 × CH), 127.7 (CH), 48.7 (CH_2), 46.5 (CH_2), 35.6 (CH), 34.0 (CH_2) ppm.

5-Oxo-1-phenylpyrrolidine-3-carboxylic acid (1d): ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 7.56−7.44 (m, 2H, Ar*H*), 7.34−7.26 (m, 2H, Ar*H*), 7.15−7.08 (m, 1H, Ar*H*), 4.08 (dd, *J* = 6.6, 9.8 Hz, 1H, CH*H*), 4.05−3.90 (m, 1H, C*H*H), 3.36−3.23 (m, 1H, C*H*), 2.88 (dd, *J* = 7.6, 17.6 Hz, 1H, CH*H*), 2.80 (dd, *J* = 9.6, 17.6 Hz, 1H, C*H*H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ 174.3 (C), 172.4 (C), 138.2 (C), 128.8 (2 × CH), 125.2 (CH), 120.5 (2 × CH), 50.7 (CH_2), 35.6 (CH), 35.3 (CH_2) ppm.

1-(4-Bromophenyl)-5-oxopyrrolidine-3-carboxylic acid (1e): white solid; m.p. 164−166 °C (CH_3OH/hexanes). IR (neat): ν_{max} 3093, 1728, 1642 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 7.42 (s, 4H, Ar*H*), 4.05 (dd, *J* = 6.2, 9.8 Hz, 1H, CH*H*), 3.96 (dd, *J* = 8.8, 10.0 Hz, 1H, CH*H*), 3.33−3.23 (m, 1H, C*H*), 2.93−2.75 (m, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ 174.2 (CO), 172.3 (CO), 137.5 (C), 131.8 (2 × CH), 121.6 (2 × CH), 117.9 (C), 50.4 (CH_2), 35.4 (CH), 35.3 (CH_2) ppm. MS: *m/z* (%) relative intensity 285 [(M+H)$^+$, 21], 284 (M$^+$, 10), 186 (90), 184 (100), 172 (70), 77 (20). HRMS (ESI-TOF) *m/z*: [M − H] calcd. for $C_{11}H_9BrNO_3$: 281.9771, found 281.9775.

1-(2-Chlorophenyl)-5-oxopyrrolidine-3-carboxylic acid (1f): white solid; m.p. 166−168 °C (CH_3OH/hexanes). IR (neat): ν_{max} 3276, 1694, 1657 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 7.44−7.38 (m, 1H, Ar*H*), 7.30−7.20 (m, 3H, Ar*H*), 3.97−3.90 (m, 2H, CH_2), 3.44−3.32 (m, 1H, C*H*), 2.92−2.72 (m, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ 174.3 (CO), 173.3 (CO), 135.0 (C), 132.0 (C), 130.3

(CH), 129.5 (CH), 129.2 (CH), 127.8 (CH), 51.7 (CH_2), 36.7 (CH), 33.8 (CH_2) ppm. MS: *m/z* (%) relative intensity 239 (M^+, 4), 204 (61), 127 (100), 90 (7). HRMS (ESI-TOF) *m/z*: [M − H] calcd. for $C_{11}H_9ClNO_3$: 238.0276, found 238.0263.

5-Oxo-1-propylpyrrolidine-3-carboxylic acid (1g): pale yellow oil; IR (neat): ν_{max} 1720, 1631 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.63 (dd, *J* = 6.2, 10.2 Hz, 1H, CH*H*), 3.54 (dd, *J* = 8.2, 10.6 Hz, 1H, CH*H*), 3.29−3.10 (m, 2H, CH_2 and 1H, C*H*), 2.80−2.63 (m, 2H, CH_2), 1.56−1.42 (m, 2H, CH_2), 0.83 (t, *J* = 7.4 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.8 (CO), 173.5 (CO), 49.2 (CH_2), 44.3 (CH_2), 35.9 (CH), 34.1 (CH_2), 20.3 (CH_2), 11.1 (CH_3) ppm. MS: *m/z* (%) relative intensity 172 [$(M+H)^+$, 61], 171 (M^+, 1), 142 (4). HRMS (ESI-TOF) *m/z*: [M − H] calcd. for $C_8H_{12}NO_3$: 170.0823, found 170.0820.

1-Butyl-5-oxopyrrolidine-3-carboxylic acid (1h): pale yellow oil; IR (neat): ν_{max} 1722, 1633 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.68 (dd, *J* = 6.0, 10.0 Hz, 1H, CH*H*), 3.60 (dd, *J* = 9.2, 9.6 Hz, 1H, CH*H*), 3.39−3.19 (m, 2H, CH_2 and 1H, C*H*), 2.84−2.69 (m, 2H, CH_2), 1.57−1.44 (m, 2H, CH_2), 1.38−1.24 (m, 2H, CH_2), 0.91 (t, *J* = 7.4 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.1 (CO), 173.3 (CO), 49.1 (CH_2), 42.5 (CH_2), 35.9 (CH), 34.1 (CH_2), 29.1 (CH_2), 19.9 (CH_2), 13.7 (CH_3) ppm. MS: *m/z* (%) relative intensity 186 [$(M+H)^+$, 63], 182 (M^+, 2), 142 (100), 96 (82). HRMS (ESI-TOF) *m/z*: [M − H] calcd. for $C_9H_{14}NO_3$: 184.0979, found 184.0978.

1-Benzyl-2-(4-chlorophenyl)-5-oxopyrrolidine-3-carboxylic acid (*rac*-1i): dr = 97:3 (*trans*:*cis*); white solid; m.p. 190−194 °C (CH_2Cl_2/hexanes). IR (neat): ν_{max} 3061, 1726, 1649 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 7.35−7.27 (m, 2H, Ar*H*), 7.25−7.17 (m, 3H, Ar*H*), 7.06 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.00−6.92 (m, 2H, Ar*H*), 4.99 (d, *J* = 14.8 Hz, 1H, C*H*H), 4.59 (d, *J* = 5.9 Hz, 1H, C*H*), 3.46 (d, *J* = 14.8 Hz, 1H, CH*H*), 3.02−2.93 (m, 1H, C*H*), 2.90−2.76 (m, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ 173.6 (CO), 173.5 (CO), 137.2 (C), 134.9 (C), 134.2 (C), 129.1 (2 × CH), 128.5 (2 × CH), 128.2 (2 × CH), 128.1 (2 × CH), 127.6 (CH), 63.2 (CH), 45.6 (CH), 44.3 (CH_2), 33.4 (CH_2) ppm. MS: *m/z* (%) relative intensity 329 [$(M)^+$, 47], 238 (100), 146 (66), 118 (44), 104 (49), 91 (44), 77 (2). HRMS (ESI-TOF) *m/z*: [M − H] calcd. for $C_{18}H_{15}ClNO_3$: 328.0746, found 328.0748.

1-Benzyl-5-oxo-2-(*p*-tolyl)pyrrolidine-3-carboxylic acid (*rac*-1j): dr = 90:10 (*trans*:*cis*); ^1H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 7.27−7.18 (m, 2H, Ar*H*), 7.17−7.12 (m, 2H, Ar*H*), 7.04−6.95 (m, 5H, Ar*H*), 4.99 (d, *J* = 14.7 Hz, 1H, CH*H*), 4.58 (d, *J* = 5.6 Hz, 1H, C*H*), 3.44 (d, *J* = 14.7 Hz, 1H, C*H*H), 3.05−2.97 (m, 1H, C*H*), 2.90−2.75 (m, 2H, CH_2), 2.32 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ 174.1 (C), 173.5 (C), 138.3 (C), 135.7 (C), 135.3 (C), 129.7 (2 × CH), 128.4 (2 × CH), 128.2 (2 × CH), 127.5 (CH), 126.8 (2 × CH), 63.6 (CH), 45.7 (CH), 44.2 (CH_2), 33.6 (CH_2), 20.9 (CH_3) ppm.

(2*S*,3*S*)-2-Methyl-5-oxo-2-phenylpyrrolidine-3-carboxylic acid [(2*S*,3*S*)-1k]: A solution of diethyl succinate (0.87 g, 5 mmol) in dry THF (5 mL) was added dropwise to a solution of LDA (2.2 equiv.) at −78 °C. After stirring for 1 h, a solution of (*R*,*E*)-2-methyl-*N*-(1-phenylethylidene)propane-2-sulfinamide (5.5 mmol, 1.1 equiv.) in dry THF (5 mL) was added dropwise at −78 °C. The reaction was allowed to stir at room temperature for 6 h then the obtained dark purple solution was quenched with 2N HCl (30 mL) at −78 °C and allowed to stir for 4 h at room temperature. The resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic phase was washed with saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated to provide a crude mixture. Filtration through a short column (SiO_2, 60% EtOAc/hexanes) gave a mixture of ester products which was subsequently subjected to hydrolysis using conc. HCl (10 mL) at 80 °C for 6 h. After cooling to room temperature, the reaction mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layer was extracted with saturated $NaHCO_3$ (3 × 20 mL). The aqueous phase was collected, acidified with 6N HCl (to pH 4-5), and extracted with CH_2Cl_2 (3 × 30 mL). The combine organic phase was washed with water, brine, dried over anhydrous Na_2SO_4, and concentrated to give (2*S*,3*S*)-**1k**: dr = 99:1; yellow solid; m.p. 160−162 °C (Et_2O/hexanes). $[\alpha]_D^{25}$ −80.4° (*c* 1.5, CH_3OH). IR (neat): ν_{max} 3247, 1706, 1650 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 7.26−7.08 (m, 5H, Ar*H*), 3.21 (dd, *J* = 9.1, 9.1 Hz, 1H, C*H*), 2.75 (dd, *J* = 9.1, 17.4 Hz, 1H, C*H*H), 2.36 (dd, *J* = 9.1, 17.4 Hz, 1H, CH*H*), 1.79 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ 176.8 (CO), 172.3 (CO), 140.9 (C), 128.2 (2 × CH), 127.7 (CH), 125.7 (2 × CH), 63.6 (C), 52.6 (CH), 32.7 (CH_2), 28.7 (CH_3) ppm. MS: *m/z* (%) relative intensity 220 [$(M + H)^+$, 1], 204 (68), 176 (26), 132 (100), 104 (21), 77 (12). HRMS (ESI-TOF) *m/z*: [M − H] calcd. for $C_{12}H_{12}NO_3$: 218.0823, found 218.0822.

(2*S*,3*S*)-2-Ethyl-5-oxo-2-phenylpyrrolidine-3-carboxylic acid [(2*S*,3*S*)-1l]: According to the procedure described for (2*S*,3*S*)-**1k**, the reaction of (*R*,*E*)-2-methyl-*N*-(1-phenylpropylidene)propane-2-sulfinamide gave (2*S*,3*S*)-**1l**: dr = 95:5, white powder, m.p. 144−146 °C (EtOAc); $[\alpha]_D^{27}$ −10.2° (*c* 0.6, CH_3OH). IR (neat): ν_{max} 3202, 1688, 1648 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 7.72 (s, 1H, N*H*), 7.30−7.10 (m, 5H, Ar*H*), 3.21 (dd, *J* = 8.6, 8.6 Hz, 1H, C*H*), 2.70 (dd, *J* = 8.6, 17.6 Hz, 1H, C*H*H), 2.45−2.30 (m, 2H, 2 × CH*H*), 2.00−1.85 (m, 1H, C*H*H), 0.65 (t, *J* = 7.4 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ 178.0 (CO), 174.2 (CO), 138.8 (C), 128.3 (2 × CH), 127.8 (CH), 126.1 (2 × CH), 68.1 (C), 52.2 (CH), 33.7 (CH_2), 32.8 (CH_2), 8.5 (CH_3) ppm. MS: *m/z* (%) relative intensity 233 [$(M)^+$, 6], 204 (40), 178 (51), 149 (100), 95 (64), 81 (71), 67 (44), 55 (57). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{13}H_{15}NO_3Na$: 256.0944, found 256.0943.

(2*S*,3*S*)-2-Butyl-5-oxo-2-phenylpyrrolidine-3-carboxylic acid [(2*S*,3*S*)-1m]: According to the procedure described for (2*S*,3*S*)-**1k**, the reaction of (*R*,*E*)-2-methyl-*N*-(1-phenylpentylidene)propane-2-sulfinamide gave (2*S*,3*S*)-**1m**: dr = 93:7, yellow powder; m.p. 80−82 °C (EtOAc). $[\alpha]_D^{26}$ −34.7° (*c* 0.5, $CHCl_3$). IR (neat): ν_{max} 3217, 1705, 1643 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.26−7.14 (m, 5H, Ar*H*), 3.24 (dd, *J* = 8.6, 8.6 Hz, 1H, C*H*), 2.70 (dd, *J* = 8.6, 17.2 Hz, 1H, C*H*H), 2.45−2.30 (m, 2H, 2 × CH*H*), 1.92−1.80 (m, 1H, CH*H*), 1.30−1.15 (m, 2H, CH_2), 1.04−0.90 (m, 2H, CH_2), 0.79 (t, 7.2 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4 (CO), 173.9 (CO), 139.1 (C), 128.4 (2 × CH), 127.8 (CH), 126.0 (2 × CH), 67.5 (C), 51.9 (CH), 40.8 (CH_2), 32.6 (CH_2), 26.2 (CH_2), 22.7 (CH_2), 13.8 (CH_3) ppm. MS: *m/z* (%) relative intensity 204 (100), 132 (81), 115 (4). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd. for $C_{15}H_{20}NO_3$: 262.1438, found 262.1439.

(2*R*,3*S*)-2-Butyl-5-oxopyrrolidine-3-carboxylic acid [(2*R*,3*S*)-1n]: According to the procedure described for (2*S*,3*S*)-**1k**, the reaction of (*R*,*E*)-2-methyl-*N*-pentylidenepropane-2-sulfinamide gave (2*R*,3*S*)-**1n**: dr = 75:25, sticky oil; $[\alpha]_D^{26}$ +16.2° (*c* 0.9, $CHCl_3$). IR (neat): ν_{max} 3221, 1718, 1649 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, interpret equally for both isomers, major one marked*): δ 7.60 (s, 1H, N*H*), 7.54 (s, 1H, N*H**), 3.90−3.77 (m, 2H, C*H* and C*H**), 3.37 (dt, *J* = 8.2, 8.3 Hz, 1H, C*H*), 2.90−2.80 (m, 1H, C*H**), 2.80−2.60 (m, 2H, CH*H* and CH*H**), 2.60−2.54 (m, 1H, CH*H**), 2.48−2.36 (m, 1H, C*H*H), 1.70−1.58 (m, 1H, C*H*H*), 1.56−1.44 (m, 2H, CH*H** and C*H*H), 1.44−1.36 (m, 1H, CH*H*), 1.36−1.20 (m, 8H, CH_2* and CH_2), 0.90−0.77 (m, 6H, CH_3* and CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major one marked*): δ 178.2 (CO), 177.4 (CO*), 176.5 (CO*), 175.0 (CO), 58.0 (CH*), 56.1 (CH), 44.7 (CH*), 43.4 (CH), 36.0 (CH_2*), 33.5 (CH_2*), 32.7 (CH_2), 31.2 (CH_2), 28.3 (CH_2), 27.8 (CH_2*), 22.4 (CH_2 and CH_2*), 13.9 (CH_3 and CH_3*) ppm. MS: *m/z* (%) relative intensity 185 [$(M + H)^+$, 1], 128 (13), 115 (32), 70 (15), 56 (100), 55 (7). HRMS (ESI-TOF) *m/z*: [M − H] calcd. for $C_9H_{14}NO_3$: 184.0979, found 184.0978.

General procedure for the synthesis of β-fluorinated-γ-butyrolactams 2: Compound **1** (0.5 mmol), $AgNO_3$ (1.5 equiv.) and Selectfluor® (1.5 equiv.) were dissolved in a mixture of acetonitrile and water (0.05 M, 1:4 %v/v). The resulting solution was stirred at reflux for 6

h then it was cooled to room temperature and extracted with EtOAc (3 × 20 mL). The combined organic layer was washed with water, a saturated aqueous $NaHCO_3$ (30 mL), brine, and dried with anhydrous Na_2SO_4. Purification by column chromatography (SiO_2) gave compound **2**.

1-Benzyl-4-fluoro-5-phenylpyrrolidin-2-one (2a): The reaction of *rac*-**1a** (dr = 89:11) (147.7 mg, 0.5 mmol) with $AgNO_3$ (127.4 mg, 0.75 mmol) and Selectfluor® (265.7 mg, 0.75 mmol) gave *trans*-**2a** (64.4 mg, 48% yield), *cis*-**2a** (8.2 mg, 6% yield), and *trans*-**3a** (4.5 mg, 5% yield) after column chromatography (SiO_2, 30% EtOAc/hexanes).

trans-**2a**: white solid; m.p. 67−69 °C (Et_2O/hexanes). IR (neat): ν_{max} 1678 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.28 (m, 3H, Ar*H*), 7.28−7.17 (m, 3H, Ar*H*), 7.11−7.00 (m, 4H, Ar*H*), 5.18 (d, *J* = 15.0 Hz, 1H, CH*H*), 4.86 (dd, *J* = 5.5, 53.0 Hz, 1H, C*H*F), 4.55 (d, *J* = 23.6 Hz, 1H, C*H*), 3.53 (d, *J* = 15.0 Hz, 1H, C*H*H), 2.87 (ddd, *J* = 5.5, 18.4, 35.2 Hz, 1H, C*H*H), 2.67 (dd, *J* = 18.4, 26.4 Hz, 1H, CH*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8 (CO), 135.5 (d, $^3J_{CF}$ = 9.6 Hz, C), 135.4 (C), 129.4 (2 × CH), 128.8 (CH), 128.7 (2 × CH), 128.0 (2 × CH), 127.7 (CH), 126.4 (2 × CH), 92.2 (d, $^1J_{CF}$ = 184.1 Hz, CHF), 68.0 (d, $^2J_{CF}$ = 25.9 Hz, CH), 44.2 (CH_2), 37.1 (d, $^2J_{CF}$ = 23.0 Hz, CH_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −167.1 to −167.7 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 270 [(M + H)$^+$, 45], 269 [(M)$^+$, 1], 249 (40), 132 (90), 117 (100), 91 (37), 77 (9). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd. for $C_{17}H_{17}FNO$: 270.1289, found 270.1286.

cis-**2a**: pale yellow oil; IR (neat): ν_{max} 1681 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39−7.31 (m, 3H, Ar*H*), 7.23−7.15 (m, 3H, Ar*H*), 7.15−7.09 (m, 2H, Ar*H*), 6.96−6.88 (m, 2H, Ar*H*), 5.14−4.98 (m, 1H, C*H*F), 5.12 (d, *J* = 14.6 Hz, 1H, C*H*H), 4.46 (dd, *J* = 5.0, 21.0 Hz, 1H, C*H*), 3.49 (d, *J* = 14.6 Hz, 1H, CH*H*), 2.84−2.66 (m, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3 (CO), 135.6 (C), 132.4 (d, $^3J_{CF}$ = 10.0 Hz, C), 129.1 (2 × CH), 128.9 (CH), 128.7 (2 × CH), 128.6 (2 × CH), 128.5 (2 × CH), 127.8 (CH), 86.9 (d, $^1J_{CF}$ = 185.6 Hz, CHF), 65.6 (d, $^2J_{CF}$ = 20.2 Hz, CH), 44.2 (CH_2), 38.4 (d, $^2J_{CF}$ = 24.9 Hz, CH_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −184.7 to −185.2 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 249 (33), 178 (6), 160 (8), 132 (29), 117 (32), 106 (100), 91 (35), 77 (24). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd. for $C_{17}H_{17}FNO$: 270.1289, found 270.1298.

trans-**3a**: yellow solid; m.p. 97−108 °C (Et_2O/hexanes). IR (neat): ν_{max} 3207, 1710 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.30 (m, 2H, Ar*H*), 7.30−7.25 (m, 1H, Ar*H*), 7.25−7.17 (m, 2H, Ar*H*), 6.82 (s, 1H, N*H*), 4.96 (dd, *J* = 5.8, 53.6 Hz, 1H, C*H*F), 4.85 (d, *J* = 23.6 Hz, 1H, C*H*), 2.71 (ddd, *J* = 5.8, 18.2, 32.5 Hz, 1H, C*H*H), 2.49 (ddd, *J* = 1.3, 18.2, 26.2 Hz, 1H, CH*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0 (CO), 137.8 (d, $^3J_{CF}$ = 8.6 Hz, C), 129.2 (2 × CH), 128.6 (CH), 125.6 (2 × CH), 94.8 (d, $^1J_{CF}$ = 184.7 Hz, CHF), 64.7 (d, $^2J_{CF}$ = 25.7 Hz, CH), 36.7 (d, $^2J_{CF}$ = 23.2 Hz, CH_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −167.6 to −168.1 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 179 [(M)$^+$, 83], 149 (44), 121 (49), 104 (100), 91 (51), 81 (82), 77 (39). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{10}H_{10}FNONa$: 202.0639, found 202.0638.

1-Benzyl-4-fluoro-3-methyl-5-phenylpyrrolidin-2-one (*rac*-2b): The reaction of *rac*-**1b** (dr = 61:21:15:3) (309.4 mg, 1 mmol) with $AgNO_3$ (254.3 mg, 1.5 mmol) and Selectfluor® (531.4 mg, 1.5 mmol) gave *rac*-**2b** as four diastereomers [3,4-*trans*-4,5-*cis* (*t*,*c*); 3,4-*trans*-4,5-*trans* (*t*,*t*); 3,4-*cis*-4,5-*trans* (*c*,*t*); and 3,4-*cis*-4,5-*cis* (*c*,*c*)]. Purification by column chromatography (SiO_2, 20% EtOAc/hexanes) gave a mixture of *t*,*c*-**2b**, *t*,*t*-**2b**, *c*,*t*-**2b**, and *c*,*c*-**2b** (52:22:16:10, determined by ^{19}F-NMR analysis) (183.4 mg, 65% yield) as a viscous oil; IR (neat): ν_{max} 1695, 1418 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, integrated equally for all isomers): δ 7.36−7.25 (m, 2H, Ar*H* of *t*,*c*-**2b**), 7.25−7.17 (m, 3H, Ar*H* of *t*,*c*-**2b**), 7.12−7.02 (m, 5H, Ar*H* of *t*,*c*-**2b**), 5.19 (d, *J* = 15.0 Hz, 1H, C*H*H of *t*,*c*-**2b**), 5.14 (d, *J* = 14.4 Hz, 1H, C*H*H of *t*,*t*-**2b**), 5.13 (d, *J* = 16.4 Hz, 1H, C*H*H of *c*,*c*-**2b**), 5.10 (d, *J* = 12.9 Hz, 1H, C*H*H of *c*,*t*-**2b**), 4.76 (dd, *J* = 4.8, 53.2 Hz, 1H, C*H*F of *t*,*c*-**2b**), 4.70 (ddd, *J* = 4.3, 6.0, 53.5 Hz, 1H, C*H*F of *t*,*t*-**2b**), 4.69 (d, *J* = 22.3 Hz, 1H, C*H* of *c*,*t*-**2b**), 4.68 (dd, *J* = 4.6, 58.0 Hz, 1H, C*H*F of *c*,*c*-**2b**), 4.65 (dd, *J* = 4.2, 53.7 Hz, 1H, C*H*F of *c*,*t*-**2b**), 4.50 (d, *J* = 22.5 Hz, 1H, C*H* of *t*,*c*-**2b**), 4.44 (dd, *J* = 6.0, 14.3, 1H, C*H* of *t*,*t*-**2b**), 4.37 (dd, *J* = 3.5, 23.1 Hz, 1H, C*H* of *c*,*c*-**2b**), 3.59 (d, *J* = 15.0 Hz, 1H, CH*H* of *t*,*c*-**2b**), 3.48 (d, *J* = 14.4 Hz, 1H, CH*H* of *t*,*t*-**2b**), 2.87−2.65 (m, 4H, 4 × C*H* of *t*,*c*-**2b**, *t*,*t*-**2b**, *c*,*t*-**2b**, and *c*,*c*-**2b**), 1.28 (d, *J* = 7.6 Hz, 3H, CH_3 of *c*,*c*-**2b**), 1.24 (dd, *J* = 1.6, 7.5 Hz, 3H, CH_3 of *t*,*c*-**2b**), 1.22 (dd, *J* = 2.9, 8.7 Hz, 3H, CH_3 of *t*,*t*-**2b**) 1.18 (dd, *J* = 1.6, 7.2 Hz, 3H, CH_3 of *c*,*t*-**2b**), ppm. Due to low intensity, some proton peaks of minor isomers could not be detected by ^1H NMR spectroscopy. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5 (CO of *t*,*c*-**2b**), 135.5 (C of *t*,*c*-**2b**), 135.2 (d, $^3J_{CF}$ = 9.0 Hz, C of *t*,*c*-**2b**), 129.3 (CH of *t*,*c*-**2b**), 128.7 (3 × CH of *t*,*c*-**2b**), 128.6 (2 × CH of *t*,*c*-**2b**), 128.0 (CH of *t*,*c*-**2b**), 127.6 (2 × CH of *t*,*c*-**2b**), 126.3 (CH of *t*,*c*-**2b**), 99.6 (d, $^1J_{CF}$ = 188.6 Hz, CHF of *c*,*c*-**2b**), 95.4 (d, $^1J_{CF}$ = 188.5 Hz, CHF of *c*,*t*-**2b**), 94.7 (d, $^1J_{CF}$ = 188.0 Hz, CHF of *t*,*c*-**2b**), 93.0 (d, $^1J_{CF}$ = 189.5 Hz, CHF of *t*,*t*-**2b**), 66.3 (d, $^2J_{CF}$ = 25.1 Hz, CH of *c*,*t*-**2b**), 66.1 (d, $^2J_{CF}$ = 26.0 Hz, CH of *t*,*c*-**2b**), 65.9 (d, $^2J_{CF}$ = 19.9 Hz, CH of *c*,*c*-**2b**), 62.3 (d, $^2J_{CF}$ = 21.1 Hz, CH of *t*,*t*-**2b**), 44.5 (CH_2 of *t*,*c*-**2b** and CH_2 of *c*,*c*-**2b**), 44.3 (CH_2 of *t*,*t*-**2b**), 44.2 (CH_2 of *c*,*t*-**2b**), 43.7 (d, $^2J_{CF}$ = 19.2 Hz, CH of *c*,*c*-**2b**), 42.5 (d, $^2J_{CF}$ = 21.4 Hz, CH of *t*,*t*-**2b**), 39.5 (d, $^2J_{CF}$ = 22.0 Hz, CH of *c*,*t*-**2b**), 39.2 (d, $^2J_{CF}$ = 21.8 Hz, CH of *t*,*c*-**2b**), 14.1 (d, $^3J_{CF}$ = 4.6 Hz, CH_3 of *c*,*c*-**2b**), 13.0 (d, $^3J_{CF}$ = 4.8 Hz, CH_3 of *t*,*t*-**2b**), 8.0 (d, $^3J_{CF}$ = 10.4 Hz, CH_3 of *t*,*c*-**2b**), 7.8 (d, $^3J_{CF}$ = 11.7 Hz, CH_3 of *c*,*t*-**2b**) ppm. Due to low intensity, some proton peaks of minor isomers could not be detected by ^{13}C NMR spectroscopy. ^{19}F NMR (376 MHz, $CDCl_3$): δ −175.5 to −176.0 (m, 1F, CHF of *c*,*c*-**2b**), −184.4 to −184.9 (m, 1F, CHF of *t*,*t*-**2b**), −185.6 to −186.1 (m, 1F, CHF of *t*,*c*-**2b**), −186.8 to −187.3 (m, 1F, CHF of *c*,*t*-**2b**) ppm. MS: *m/z* (%) relative intensity 284 [(M + H)$^+$, 7], 131 (100), 91 (21), 77 (7). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd. for $C_{18}H_{19}FNO$: 284.1445, found 284.1447.

1-Benzyl-4-fluoropyrrolidin-2-one (2c): The reaction of **1c** (219.2 mg, 1 mmol) with $AgNO_3$ (254.3 mg, 1.5 mmol) and Selectfluor® (531.4 mg, 1.5 mmol) gave **2c** (116.7 mg, 60% yield) after column chromatography (SiO_2, 50% EtOAc/hexanes); pale-yellow oil; IR (neat): ν_{max} 1685 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32−7.10 (m, 5H, Ar*H*), 5.28−5.03 (m, 1H, C*H*F), 4.44 (ABq, *J* = 14.9 Hz, 2H, CH_2), 3.48 (ddd, *J* = 4.7, 12.2, 32.2 Hz, 1H, C*H*H), 3.40 (dd, *J* = 12.2, 26.6 Hz, 1H, CH*H*), 2.79−2.58 (m, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3 (CO), 135.6 (C), 128.8 (2 × CH), 128.0 (2 × CH), 127.8 (CH), 85.9 (d, $^1J_{CF}$ = 177.7 Hz, CHF), 53.5 (d, $^2J_{CF}$ = 25.2 Hz, CH_2), 46.2 (CH_2), 38.8 (d, $^2J_{CF}$ = 23.7 Hz, CH_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −172.8 to −173.4 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 194 [(M + H)$^+$, 100], 146 (27), 118 (22), 104 (14), 91 (45). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{11}H_{12}FNONa$: 216.0795, found 216.0793.

1-Phenyl-4-fluoropyrrolidin-2-one (2d): The reaction of **1d** (205.2 mg, 1.0 mmol) with $AgNO_3$ (254.2 mg, 1.5 mmol) and Selectfluor® (531.4 mg, 1.5 mmol) gave **2d** (51.6 mg, 29% yield) after column chromatography (SiO_2, 50% EtOAc/hexanes); yellow solid; m.p. 66−70 °C (Et_2O/hexanes). IR (neat): ν_{max} 1696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.65−7.60 (m, 2H, Ar*H*), 7.45−7.38 (m, 2H, Ar*H*), 7.25−7.18 (m, 1H, Ar*H*), 5.39 (dt, *J* = 4.8, 53.3 Hz, 1H, C*H*F), 4.20 (ddd, *J* = 4.6, 12.1, 32.4 Hz, 1H, C*H*H), 4.07 (dd, *J* = 12.1, 25.2 Hz, 1H, CH*H*), 3.07−2.82 (m, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5 (CO), 138.5 (C), 129.0 (2 × CH), 125.1 (CH), 120.1 (2 × CH), 85.3 (d, $^1J_{CF}$ = 177.7 Hz, CHF), 55.4 (d, $^2J_{CF}$ = 25.2 Hz, CH_2), 40.1 (d, $^2J_{CF}$ = 23.6 Hz, CH_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −172.8 to −173.5 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 179 [(M)$^+$, 71], 130 (11), 106 (100), 77 (28). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{10}H_{10}FNONa$: 202.0644, found 202.0638.

1-(4-Bromophenyl)-4-fluoropyrrolidin-2-one (2e): The reaction of **1e** (142.1 mg, 0.5 mmol) with $AgNO_3$ (127.8 mg, 0.75 mmol) and Selectfluor® (265.9 mg, 0.75 mmol) gave **2e** (42.1 mg, 33% yield) after column chromatography (SiO_2, 50% EtOAc/hexanes); brown semi-solid; IR (neat): ν_{max} 1696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.48−7.40 (m, 4H, Ar*H*), 5.30 (dt, *J* = 5.1, 54.0 Hz, 1H, C*H*F), 4.07 (ddd, *J* = 4.6, 11.8,

32.0 Hz, 1H, C*H*H), 3.95 (dd, *J* = 12.2, 25.0 Hz, 1H, CH*H*), 2.96−2.72 (m, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5 (CO), 137.6 (C), 132.0 (2 × CH), 121.4 (2 × CH), 117.9 (C), 85.1 (d, $^1J_{CF}$ = 178.3 Hz, CHF), 55.2 (d, $^2J_{CF}$ = 25.9 Hz, CH_2), 40.1 (d, $^2J_{CF}$ = 24.0 Hz, CH_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −173.0 to −173.5 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity MS: *m/z* (%) relative intensity 257 [(M+H)$^+$, 17], 184 (80), 105 (100). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{10}H_9BrFNONa$: 279.9744, found 279.9741.

1-(2-Chlorophenyl)-4-fluoropyrrolidin-2-one (2f): The reaction of **1f** (119.7 mg, 0.5 mmol) with $AgNO_3$ (127.8 mg, 0.75 mmol) and Selectfluor® (265.7 mg, 0.75 mmol) gave **2f** (88.7 mg, 83% yield) after column chromatography (SiO_2, 50% EtOAc/hexanes); brown semi-solid; IR (neat): ν_{max} 1688 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.38 (m, 1H, Ar*H*), 7.32−7.20 (m, 3H, Ar*H*), 5.34 (dt, *J* = 5.0, 53.1 Hz, 1H, C*H*F), 4.11 (ddd, *J* = 4.7, 12.1, 32.7 Hz, 1H, C*H*H), 3.85 (dd, *J* = 12.0, 25.2 Hz, 1H, CH*H*), 2.86 (ddd, *J* = 5.3, 18.1, 35.1 Hz, 1H, C*H*H), 2.76 (dd, *J* = 18.0, 26.4 Hz, 1H, C*H*H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4 (CO), 135.1 (C), 132.2 (C), 130.6 (CH), 129.6 (2 × CH), 127.9 (CH), 86.4 (d, $^1J_{CF}$ = 178.3 Hz, CHF), 56.5 (d, $^2J_{CF}$ = 24.9 Hz, CH_2), 38.6 (d, $^2J_{CF}$ = 23.9 Hz, CH_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −173.0 to −173.6 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 214 [(M+H)$^+$, 17], 178 (100), 140 (30), 77 (11). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{10}H_9ClFNONa$: 236.0249, found 236.0250.

4-Fluoro-1-propylpyrrolidin-2-one (2g): The reaction of **1g** (85.7 mg, 0.5 mmol) with $AgNO_3$ (127.8 mg, 0.75 mmol) and Selectfluor® (265.9 mg, 0.75 mmol) gave **2g** (54.6 mg, 75% yield) after column chromatography (SiO_2, 50% EtOAc/hexanes); pale-yellow oil; IR (neat): ν_{max} 1668 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.19 (dt, *J* = 5.1, 53.2 Hz, 1H, C*H*F), 3.61 (ddd, *J* = 4.8, 12.2, 32.2 Hz, 1H, C*H*H), 3.51 (dd, *J* = 11.0, 25.0 Hz, 1H, CH*H*), 3.32−3.21 (m, 1H, CH*H*), 3.21−3.12 (m, 1H, CH*H*), 2.76−2.52 (m, 2H, CH_2), 1.55−1.45 (m, 2H, CH_2), 0.85 (t, *J* = 7.4 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4 (CO), 86.1 (d, $^1J_{CF}$ = 178.2 Hz, CHF), 54.0 (d, $^2J_{CF}$ = 25.9 Hz, CH_2), 43.8 (CH_2), 38.9 (d, $^2J_{CF}$ = 23.9 Hz, CH_2), 20.4 (CH_2), 11.1 (CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −172.6 to −173.2 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 146 [(M+H)$^+$, 100], 145 (M$^+$, 10), 116 (36), 96 (65), 53 (79). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_7H_{12}FNONa$: 168.0795, found 168.0791.

1-Butyl-4-fluoropyrrolidin-2-one (2h): The reaction of **1h** (92.6 mg, 0.5 mmol) with $AgNO_3$ (127.4 mg, 0.75 mmol) and Selectfluor® (265.9 mg, 0.75 mmol) gave **2g** (54.2 mg, 68% yield) after column chromatography (SiO_2, 50% EtOAc/hexanes); pale-yellow oil; IR (neat): ν_{max} 1678 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.19 (dt, *J* = 4.9, 53.7 Hz, 1H, C*H*F), 3.61 (ddd, *J* = 4.7, 12.1, 32.1 Hz, 1H, C*H*H), 3.51 (dd, *J* = 11.8, 26.6 Hz, 1H, CH*H*), 3.36−3.25 (m, 1H, CH*H*), 3.25−3.16 (m, 1H, CH*H*), 2.74−2.50 (m, 2H, CH_2), 1.50−1.39 (m, 2H, CH_2), 1.32−1.19 (m, 2H, CH_2), 0.87 (t, *J* = 7.4 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2 (CO), 86.1 (d, $^1J_{CF}$ = 177.3 Hz, CHF), 54.0 (d, $^2J_{CF}$ = 24.9 Hz, CH_2), 41.9 (CH_2), 38.9 (d, $^2J_{CF}$ = 23.9 Hz, CH_2), 29.2 (CH_2), 19.9 (CH_2), 13.7 (CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −172.6 to −173.2 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 160 [(M+H)$^+$, 100], 117 (30), 96 (39), 53 (51). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_8H_{14}FNONa$: 182.0952, found 182.0954.

1-Benzyl-5-(4-chlorophenyl)-4-fluoropyrrolidin-2-one (2i): The reaction of *rac*-**1i** (dr = 97:3) (165 mg, 0.5 mmol) with $AgNO_3$ (127.4 mg, 0.75 mmol) and Selectfluor® (265.7 mg, 0.75 mmol) gave a mixture of *trans*-**2i** and *cis*-**2i** (62.7 mg, 21% yield, 91:9) after column chromatography (SiO_2, 20% acetone/hexanes); pale-yellow oil; IR (neat): ν_{max} 1692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, integrated equally for both isomers, *trans*-**2i** marked*): δ 7.37−7.28 (m, 2H, Ar*H**), 7.27−7.15 (m, 3H, Ar*H**), 7.06 (d, *J* = 6.6 Hz, 2H, Ar*H**), 6.98 (d, *J* = 8.3 Hz, 2H, Ar*H**), 5.18 (d, *J* = 14.7 Hz, 1H, C*H*H of *cis*-**2i**), 5.16 (d, *J* = 15.0 Hz, 1H, C*H*H*), 4.87 (dd, *J* = 5.4, 52.8 Hz, 1H, C*H*F of *cis*-**2i**), 4.83 (dd, *J* = 5.3, 52.6 Hz, 1H, CH*F**), 4.51 (d, *J* = 23.5 Hz, 1H, C*H**), 4.43 (dd, *J* = 4.9, 21.6 Hz, 1H, C*H* of *cis*-**2i**), 3.51 (d, *J* = 15.0 Hz, 1H, CH*H**), 3.45 (d, *J* = 14.7 Hz, 1H, CH*H*), 2.85 (ddd, *J* = 5.5, 18.3, 34.8 Hz, 1H, C*H*H*), 2.67 (dd, *J* = 18.3, 26.5 Hz, 1H, CH*H**) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, *trans*-**2i** marked*): δ 171.6 (CO*), 135.1 (C*), 134.8 (C*), 134.1 (d, $^3J_{CF}$ = 9.1 Hz, C*), 130.4 (2 × CH of *cis*-**2i**), 129.6 (2 × CH*), 129.4 (2 × CH of *cis*-**2i**), 129.2 (CH of *cis*-**2i**), 128.8 (2 × CH*), 128.7 (2 × CH of *cis*-**2i**), 128.0 (2 × CH*), 127.8 (CH*), 127.7 (2 × CH*), 126.3 (2 × CH of *cis*-**2i**), 92.1 (d, $^1J_{CF}$ = 184.0 Hz, CHF of *cis*-**2i**), 91.9 (d, $^1J_{CF}$ = 184.6 Hz, CHF*), 68.0 (d, $^2J_{CF}$ = 25.8 Hz, CH of *cis*-**2i**), 67.3 (d, $^2J_{CF}$ = 26.2 Hz, CH*), 44.3 (CH_2*), 43.6 (CH_2 of *cis*-**2i**), 38.4 (d, $^2J_{CF}$ = 24.5 Hz, CH_2 of *cis*-**2i**), 36.9 (d, $^2J_{CF}$ = 23.6 Hz, CH_2*) ppm. Due to low intensity, some proton and carbon peaks of *cis*-**2i** could not be detected. ^{19}F NMR (376 MHz, $CDCl_3$): δ −167.4 to −168.0 (m, 1F, CHF of *trans*-**2i**), −184.7 to −185.2 (m, 1F, CHF of *cis*-**2i**) ppm. MS: *m/z* (%) relative intensity 304 [(M + H)$^+$, 23], 283 (10), 151 (17), 132 (100), 91 (12). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{17}H_{15}ClFNONa$: 326.0718, found 326.0720.

1-Benzyl-4-fluoro-5-(*p*-tolyl)pyrrolidin-2-one (2j): The reaction of *rac*-**1j** (dr = 90:10) (309.1 mg, 1 mmol) with $AgNO_3$ (254.3 mg, 1.5 mmol) and Selectfluor® (531.4 mg, 1.5 mmol) gave a mixture of *trans*-**2j** and *cis*-**2j** (127.6 mg, 45% yield, 93:7) after column chromatography (SiO_2, 20% acetone/hexanes); brown oil; IR (neat): ν_{max} 1693 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, integrated equally for both isomers, *trans*-**2j** marked*): δ 7.38−7.29 (m, 3H, Ar*H**), 7.23 (d, *J* = 7.8 Hz, 2H, Ar*H**), 7.17 (d, *J* = 6.9 Hz, 2H, Ar*H**), 7.02 (d, *J* = 7.9 Hz, 2H, Ar*H**), 5.27 (d, *J* = 15.0 Hz, 1H, C*H*H*), 5.21 (d, *J* = 14.4 Hz, 1H, C*H*H of *cis*-**2j**), 4.94 (dd, *J* = 5.3, 52.8 Hz, 1H, CH*F**), 4.61 (d, *J* = 23.8 Hz, 1H, C*H**), 4.53 (dd, *J* = 5.0, 21.2 Hz, 1H, C*H* of *cis*-**2j**), 3.60 (d, *J* = 15.0 Hz, 1H, CH*H**), 2.96 (ddd, *J* = 5.4, 18.3, 35.6 Hz, 1H, C*H*H*), 2.75 (dd, *J* = 18.2, 26.4 Hz, 1H, CH*H**), 2.42 (s, 3H, CH_3 of *cis*-**2j**), 2.39 (s, 3H, CH_3*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, *trans*-**2j** marked*): δ 171.7 (CO*), 138.7 (C*), 135.5 (C*), 132.4 (d, $^3J_{CF}$ = 9.4 Hz, C*), 130.0 (2 × CH*), 129.6 (CH of *cis*-**2j**), 129.3 (2 × CH of *cis*-**2j**), 129.0 (CH of *cis*-**2j**), 128.7 (2 × CH*), 128.6 (2 × CH of *cis*-**2j**), 128.5 (2 × CH of *cis*-**2j**), 128.0 (2 × CH*), 127.6 (CH*), 126.7 (CH of *cis*-**2j**), 126.3 (2 × CH*), 92.2 (d, $^1J_{CF}$ = 183.7 Hz, CHF*), 86.9 (d, $^1J_{CF}$ = 185.6 Hz, CHF of *cis*-**2j**), 67.7 (d, $^2J_{CF}$ = 25.7 Hz, CH*), 65.3 (d, $^2J_{CF}$ = 20.3 Hz, CH of *cis*-**2j**), 44.1 (CH_2*), 43.9 (CH_2 of *cis*-**2j**), 38.4 (d, $^2J_{CF}$ = 24.2 Hz, CH_2 of *cis*-**2j**), 37.1 (d, $^2J_{CF}$ = 23.7 Hz, CH_2*), 21.1 (CH_3*) ppm. Due to low intensity, some proton and carbon peaks of *cis*-**2j** could not be detected. ^{19}F NMR (376 MHz, $CDCl_3$): δ −167.2 to −167.8 (m, 1F, CHF of *trans*-**2j**), −184.9 to −185.3 (m, 1F, CHF of *cis*-**2j**) ppm. MS: *m/z* (%) relative intensity 284 [(M + H)$^+$, 3], 91 (100), 83 (51), 81 (30), 77 (20). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd. for $C_{18}H_{19}FNO$: 283.1445, found 284.1448.

(4*S*,5*R*)- and (4*R*,5*R*)-4-Fluoro-5-methyl-5-phenylpyrrolidin-2-one [(4*S*,5*R*)- and (4*R*,5*R*)-2k]: The reaction of (2*S*,3*S*)-**1j** (dr >99:1) (109.7 mg, 0.5 mmol) with $AgNO_3$ (127.5 mg, 0.75 mmol) and Selectfluor® (265.7 mg, 0.75 mmol) gave (4*S*,5*R*)-**2k** (40 mg, 42% yield) and (4*R*,5*R*)-**2k** (28.6 mg, 29% yield) after column chromatography (SiO_2, 60% EtOAc/hexanes).

(4*S*,5*R*)-**2k**: semi-solid; $[\alpha]_D^{25}$ −233.7° (*c* 1.0, $CHCl_3$). IR (neat): ν_{max} 3206, 1689 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.30 (m, 4H, Ar*H*), 7.30−7.24 (m, 1H, Ar*H*), 6.91 (br, 1H, N*H*), 4.96 (dd, *J* = 4.2, 53.0 Hz, 1H, C*H*F), 2.83 (ddd, *J* = 5.2, 18.0, 31.4 Hz, 1H, CH*H*), 2.59 (ddd, *J* = 1.9, 18.0, 23.7 Hz, 1H, C*H*H), 1.60 (d, *J* = 1.6 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1 (CO), 139.0 (d, $^3J_{CF}$ = 5.7 Hz, C), 128.5 (2 × CH), 127.9 (CH), 125.9 (2 × CH), 93.9 (d, $^1J_{CF}$ = 188.8 Hz, CHF), 65.8 (d, $^2J_{CF}$ = 20.1 Hz, C), 37.6 (d, $^2J_{CF}$ = 23.9 Hz, CH_2), 27.0 (d, $^3J_{CF}$ = 2.9 Hz, CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −174.6 to −175.1 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 194 [(M + H)$^+$, 4], 178 (100), 158 (18), 130 (23), 104 (31), 77 (11). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{11}H_{12}FNONa$: 216.0795, found 216.0796.

(4*R*,5*R*)-**2k**: yellow semi-solid; $[\alpha]_D^{26}$ −177.4° (*c* 1.0, $CHCl_3$). IR (neat): ν_{max} 3211, 1695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.22 (m, 4H, Ar*H*), 7.28−7.22 (m, 1H, Ar*H*), 6.62 (br, 1H, N*H*), 5.01 (dd, *J* = 4.8, 53.6 Hz, 1H, C*H*F), 2.56 (ddd, *J* = 4.8, 18.0, 34.4 Hz, 1H, C*H*H), 2.43 (dd, *J* = 18.0, 23.2 Hz, 1H, CH*H*), 1.63 (d, *J* = 4.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4 (CO), 142.9 (C), 129.0 (2 × CH), 128.0 (CH), 124.9 (2 × CH), 95.6 (d, $^1J_{CF}$ = 191.7 Hz, CHF), 66.1 (d, $^2J_{CF}$ = 21.0 Hz, C), 37.3 (d, $^2J_{CF}$ = 23.0 Hz, CH_2), 22.8 (d, $^3J_{CF}$ = 10.6 Hz, CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −180.1 to −180.7 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 194 [(M + H)$^+$, 1], 178 (100), 158 (13), 130 (15), 104 (18), 77 (3). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{11}H_{12}FNONa$: 216.0795, found 216.0798.

(4*S*,5*R*)- and (4*R*,5*R*)-5-Ethyl-4-fluoro-5-phenylpyrrolidin-2-one [(4*S*,5*R*)- and (4*R*,5*R*)-2l]: The reaction of (2*S*,3*S*)-**1h** (dr = 95:5) (116.6 mg, 0.5 mmol) with $AgNO_3$ (127.4 mg, 0.75 mmol) and Selectfluor® (265.8 mg, 0.75 mmol) gave (4*S*,5*R*)-**2l** (40.9 mg, 40% yield) and (4*R*,5*R*)-**2l** (9.8 mg, 10% yield) after column chromatography (SiO_2, 60% EtOAc/hexanes).

(4*S*,5*R*)-**2l**: white solid; m.p. 130−131 °C (Et_2O/hexanes). $[\alpha]_D^{26}$ −123.7° (*c* 1.0, $CHCl_3$). IR (neat): ν_{max} 3184, 1698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (br, 1H, N*H*), 7.38−7.21 (m, 5H, Ar*H*), 5.02 (dd, *J* = 4.4, 53.2 Hz, 1H, C*H*F), 2.83 (ddd, *J* = 5.6, 18.2, 31.8 Hz, 1H, C*H*H), 2.59 (ddd, *J* = 1.6, 18.0, 24.6 Hz, 1H, CH*H*), 2.15−1.98 (m, 1H, C*H*H), 1.75−1.63 (m, 1H, CH*H*), 0.75 (t, *J* = 7.2 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7 (CO), 137.1 (d, $^3J_{CF}$ = 5.7 Hz, C), 128.5 (2 × CH), 127.6 (CH), 126.1 (2 × CH), 93.5 (d, $^1J_{CF}$ = 187.8 Hz, CHF), 70.2 (d, $^2J_{CF}$ = 20.2 Hz, C), 37.8 (d, $^2J_{CF}$ = 23.9 Hz, CH_2), 32.3 (CH_2), 7.7 (CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −174.7 to −175.2 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 178 (100), 158 (19), 149 (33), 130 (5), 81 (7), 55 (8). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{12}H_{14}FNONa$: 230.0952, found 230.0953.

(4*R*,5*R*)-**2l**: semi-solid; $[\alpha]_D^{26}$ −62.0° (*c* 0.6, $CHCl_3$). IR (neat): ν_{max} 3182, 1698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (br, 1H, N*H*), 7.38−7.21 (m, 5H, Ar*H*), 5.08 (ddt, *J* = 1.5, 4.8, 53.9 Hz, 1H, C*H*F), 2.54 (ddd, *J* = 5.0, 17.8, 33.4 Hz, 1H, C*H*H), 2.44 (ddd, *J* = 1.8, 17.8, 24.2 Hz, 1H, CH*H*), 2.16−1.97 (m, 2H, CH_2), 0.69 (t, *J* = 7.6 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8 (CO), 141.0 (C), 129.0 (2 × CH), 127.8 (CH), 125.5 (2 × CH), 95.8 (d, $^1J_{CF}$ = 191.6 Hz, CHF), 70.0 (d, $^2J_{CF}$ = 20.2 Hz, C), 37.2 (d, $^2J_{CF}$ = 24.0 Hz, CH_2), 27.9 (d, $^3J_{CF}$ = 9.6 Hz, CH_2), 8.1 (CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −183.0 to −183.8 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 230 [(M + H)$^+$, 5], 178 (100), 158 (40), 130 (42), 77 (3). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd. for $C_{12}H_{15}FNO$: 208.1132, found 208.1131.

(4*S*,5*R*)- and (4*R*,5*R*)-5-Butyl-4-fluoro-5-phenylpyrrolidin-2-one [(4*S*,5*R*)- and (4*R*,5*R*)-2m]: The reaction of (2*S*,3*S*)-**1m** (dr = 93:7) (130.7 mg, 0.5 mmol) with $AgNO_3$ (127.5 mg, 0.75 mmol) and Selectfluor® (266.0 mg, 0.75 mmol) gave (4*S*,5*R*)-**2m** (35.6 mg, 30% yield) and (4*R*,5*R*)-**2m** (8.4 mg, 7% yield) along with a racemic mixture of **5** (14.6 mg, 12% yield, 1:1) after column chromatography (SiO_2, 60% EtOAc/hexanes).

(4*S*,5*R*)-**2m**: white solid; m.p. 142−143 °C (Et_2O/hexanes). $[\alpha]_D^{26}$ −132.0° (*c* 1.0, $CHCl_3$). IR (neat): ν_{max} 3173, 3090, 1702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.30 (m, 2H, Ar*H*), 7.30−7.20 (m, 3H, Ar*H*), 7.04 (br, 1H, N*H*), 4.99 (dd, *J* = 5.2, 52.8 Hz, 1H, C*H*F), 2.82 (ddd, *J* = 5.7, 17.7, 31.7 Hz, 1H, C*H*H), 2.58 (ddd, *J* = 1.4, 18.0, 24.6 Hz, 1H, CH*H*), 2.04 (dt, *J* = 4.1, 12.8 Hz, 1H, C*H*H), 1.62 (dt, *J* = 4.3, 12.7 Hz, 1H, CH*H*), 1.28−1.16 (m, 2H, CH_2), 1.16−1.06 (m, 1H, C*H*H), 1.06−0.94 (m, 1H, CH*H*), 0.77 (t, *J* = 7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3 (CO), 137.4 (C), 128.6 (2 × CH), 127.7 (CH), 126.0 (2 × CH), 93.6 (d, $^1J_{CF}$ = 188.8 Hz, CHF), 69.5 (d, $^2J_{CF}$ = 19.1 Hz, C), 39.1 (CH_2), 37.6 (d, $^2J_{CF}$ = 24.9 Hz, CH_2), 25.4 (CH_2), 22.8 (CH_2), 13.8 (CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −174.7 to −175.1 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 236 [(M + H)$^+$, 1], 167 (59), 149 (100), 55 (2). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{14}H_{18}FNONa$: 258.1265, found 258.1270.

(4*R*,5*R*)-**2m**: semi-solid; $[\alpha]_D^{26}$ −115.7° (*c* 0.5, $CHCl_3$). IR (neat): ν_{max} 3182, 1699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37−7.29 (m, 2H, Ar*H*), 7.29−7.21 (m, 3H, Ar*H*), 6.71 (br, 1H, N*H*), 5.05 (ddd, *J* = 1.2, 4.6, 54.0 Hz, 1H, C*H*F), 2.52 (ddd, *J* = 5.1, 17.7, 34.1 Hz, 1H, C*H*H), 2.43 (ddd, *J* = 1.6, 17.8, 24.6 Hz, 1H, CH*H*), 2.01 (dt, *J* = 1.6, 8.6 Hz, 2H, CH_2), 1.30−1.13 (m, 2H, CH_2), 1.07−0.95 (m, 1H, C*H*H), 0.95−0.81 (m, 1H, CH*H*), 0.76 (t, *J* = 7.2 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5 (CO), 141.2 (C), 129.0 (2 × CH), 127.8 (CH), 125.3 (2 × CH), 96.0 (d, $^1J_{CF}$ = 191.6 Hz, CHF), 69.4 (d, $^2J_{CF}$ = 20.2 Hz, C), 36.9 (d, $^2J_{CF}$ = 24.0 Hz, CH_2), 34.6 (d, $^3J_{CF}$ = 9.6 Hz, CH_2), 26.0 (CH_2), 22.9 (CH_2), 13.8 (CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −182.8 to −183.3 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 236 [(M + H)$^+$, 1], 178 (100), 160 (33), 130 (26), 77 (1). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{14}H_{18}FNONa$: 258.1265, found 258.1275.

5: yellow viscous oil; IR (neat): ν_{max} 3210, 1682 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, interpreted for two major isomers): δ 7.40−7.10 (m, 12H, Ar*H* and N*H* of two isomers), 4.65−4.39 (m, 2H, C*H*F of two isomers), 2.40−2.20 (m, 8H, 4 × CH_2), 2.23−2.12 (m, 1H, CH*H*), 2.12−1.90 (m, 2H, CH_2), 1.89−1.77 (m, 1H, C*H*H), 1.55−1.38 (m, 2H, CH_2), 1.38−1.28 (m, 2H, CH_2), 1.25−1.20 (m, 3H, CH_3), 1.20−1.15 (m, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, interpreted for two major isomers): δ 178.2 (2 × CO), 144.9 (C), 144.6 (C), 128.7 (4 × CH), 127.1 (2 × CH), 124.8 (4 × CH), 90.7 (d, $^1J_{CF}$ = 164.8 Hz, CHF), 90.6 (d, $^1J_{CF}$ = 165.8 Hz, CHF), 64.9 (C), 64.8 (C), 38.0 (d, $^3J_{CF}$ = 2.9 Hz, CH_2), 37.8 (d, $^3J_{CF}$ = 3.9 Hz, CH_2), 36.5 (CH_2), 36.3 (CH_2), 31.8 (d, $^2J_{CF}$ = 21.1 Hz, CH_2), 31.7 (d, $^2J_{CF}$ = 21.1 Hz, CH_2), 30.1 (2 × CH_2), 21.0 (d, $^2J_{CF}$ = 23.0 Hz, CH_3), 20.9 (d, $^2J_{CF}$ = 23.0 Hz, CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$, interpreted for two major isomers): δ −172.8 to −173.3 (m, 1F, CHF), −173.3 to −173.9 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 236 [(M + H)$^+$, 7], 160 (100), 117 (9), 115 (9). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_{14}H_{18}FNONa$: 258.1265, found 258.1267.

(4*S*,5*R*)- and (4*R*,5*R*)-5-Butyl-4-fluoropyrrolidin-2-one [(4*S*,5*R*)- and (4*R*,5*R*)-2n]: The reaction of (2*R*,3*S*)-**1n** (dr = 75:25) (92.6 mg, 0.5 mmol) with $AgNO_3$ (127.5 mg, 0.75 mmol) and Selectfluor® (265.8 mg, 0.75 mmol) gave (4*S*,5*R*)-**2n** (30.1 mg, 38% yield) and (4*R*,5*R*)-**2n** (8.2 mg, 10% yield) along with a racemic mixture of **6** (10 mg, 11% yield, 1:1, determined by ^{19}F NMR analysis) after column chromatography (SiO_2, 40-90% EtOAc/hexanes).

(4*S*,5*R*)-**2n**: pale yellow oil; $[\alpha]_D^{25}$ −140.1° (*c* 1.0, $CHCl_3$). IR (neat): ν_{max} 3232, 1690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.95 (br, 1H, N*H*), 4.93 (dd, *J* = 6.0, 53.2 Hz, 1H, C*H*F), 3.74 (dt, *J* = 6.8, 25.2 Hz, 1H, C*H*), 2.73 (ddd, *J* = 5.8, 18.2, 31.6 Hz, 1H, C*H*H), 2.54 (ddd, *J* = 1.6, 18.4, 26.4 Hz, 1H, CH*H*), 1.56−1.39 (m, 2H, CH_2), 1.38−1.27 (m, 4H, 2 × CH_2), 0.90 (t, *J* = 7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0 (CO), 92.5 (d, $^1J_{CF}$ = 181.1 Hz, CHF), 61.5 (d, $^2J_{CF}$ = 24.0 Hz, CH), 37.1 (d, $^2J_{CF}$ = 23.0 Hz, CH_2), 33.1 (d, $^3J_{CF}$ = 7.7 Hz, CH_2), 27.5 (CH_2), 22.3 (CH_2), 13.8 (CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −170.6 to −171.2 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 160 [(M + H)$^+$, 62], 102 (43), 82 (100), 55 (57). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd. for $C_8H_{15}FNO$: 160.1138, found 160.1130.

(4*R*,5*R*)-**2n**: semi-solid; $[\alpha]_D^{25}$ −240.8° (*c* 0.5, $CHCl_3$). IR (neat): ν_{max} 3178, 1699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.34 (br, 1H, N*H*), 5.09 (dt, *J* = 4.4, 53.6 Hz, 1H, C*H*F), 3.69 (ddt, *J* = 3.9, 7.1, 24.5 Hz, 1H, C*H*), 2.60 (ddd, *J* = 4.8, 17.8, 36.4 Hz, 1H, C*H*H), 2.52 (dd, *J* = 17.2, 25.2 Hz, 1H, CH*H*), 1.75−1.62 (m, 1H, C*H*H), 1.62−1.51 (m, 1H, CH*H*), 1.38−1.25 (m, 4H, 2 × CH_2), 0.87 (t, *J* = 7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7 (CO), 89.4 (d, $^1J_{CF}$ = 185.0 Hz, CHF), 59.3 (d, $^2J_{CF}$ = 21.1 Hz, CH), 38.8 (d, $^2J_{CF}$ = 24.9 Hz, CH_2), 28.3 (d, $^3J_{CF}$ = 9.5 Hz, CH_2), 28.1 (CH_2), 22.6 (CH_2), 13.9 (CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −193.4 to −194.3 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 160

[(M + H)$^+$, 14], 102 (33), 82 (100), 55 (55). HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd. for $C_8H_{14}FNONa$: 182.0957, found 182.0958.

6: pale-yellow oil; IR (neat): ν_{max} 3224, 1692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, interpreted for two major isomers): δ = 6.57 (br, 1H, N*H*), 6.51 (br, 1H, N*H*), 4.89 (dd, *J* = 5.4, 53.0 Hz, 2H, 2 × C*H*F of two isomers), 4.74−4.50 (m, 2H, 2 × C*H*F of two isomers), 3.74 (dt, *J* = 6.4, 24.8 Hz, 2H, 2 × C*H* of two isomers), 2.68 (ddd, *J* = 6.0, 18.4, 30.8 Hz, 2H, 2 × CH*H* of two isomers), 2.50 (dd, *J* = 18.2, 27.4 Hz, 2H, 2 × C*H*H of two isomers), 1.78−1.51 (m, 6H, 2 × C*H*H and 2 × CH_2 of two isomers), 1.51−1.38 (m, 2H, 2 × C*H*H of two isomers), 1.29 (dd, *J* = 6.0, 23.6 Hz, 6H, 2 × CH_3 of two isomers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, interpreted for two major isomers): δ = 174.5 (2 × CO of two isomers), 92.4 (d, $^1J_{CF}$ = 181.1 Hz, CHF), 92.3 (d, $^1J_{CF}$ = 181.1 Hz, CHF), 90.4 (d, $^1J_{CF}$ = 164.8 Hz, CHF), 90.0 (d, $^1J_{CF}$ = 164.8 Hz, CHF), 61.2 (d, $^2J_{CF}$ = 24.0 Hz, 2 × CH of two isomers), 37.1 (d, $^2J_{CF}$ = 23.0 Hz, CH_2), 37.0 (d, $^2J_{CF}$ = 24.1 Hz, CH_2), 32.8 (d, $^2J_{CF}$ = 21.1 Hz, CH_2), 32.6 (d, $^2J_{CF}$ = 21.1 Hz, CH_2), 29.4−29.3 (m, CH_2), 29.1−29.0 (m, CH_2), 21.1 (d, $^2J_{CF}$ = 22.1 Hz, CH_3), 20.8 (d, $^2J_{CF}$ = 22.0 Hz, CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$, interpreted for two major isomers): δ = −170.8 to −171.6 (m, 2F, 2 × CHF of two isomers), −173.0 to −173.5 (m, 1F, CHF), −173.5 to −174.1 (m, 1F, CHF) ppm. MS: *m/z* (%) relative intensity 178 [(M + H)$^+$, 54], 157 (10), 102 (48), 82 (100), 55 (58). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ calcd. for $C_8H_{14}F_2NO$: 178.1043, found 178.1041.

Acknowledgments

The authors acknowledge financial support from the Thailand Research Fund (RSA6180025 and IRN58W0005), the Center of Excellence for Innovation in Chemistry (PERCH-CIC), Ministry of Higher Education, Science, Research and Innovation, the Office of the Higher Education Commission and Mahidol University under the National Research Universities Initiative, CNRS-PICS Program (PICS6663), and The Franco-Thai Cooperation Program in Higher Education and Research (PHC-Siam 2017). National Science and Technology Development Agency (NSTDA) for financial support through student scholarship to S. P. is also gratefully acknowledged.

Keywords: γ-Butyrolactams • Decarboxylation • Fluorination • Fluorinated lactams

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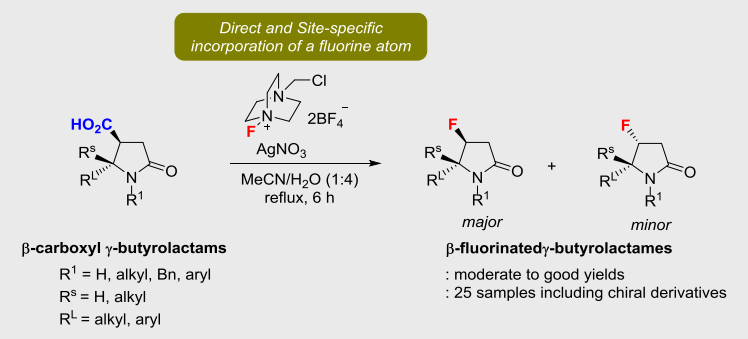

The direct and site-specific synthesis of β-fluorinated γ-butyrolactams via $AgNO_3$ mediated decarboxylative fluorination of β-carboxyl-γ-butyrolactams using Selectfluor® as a fluorine source was described. The β-fluorinated γ-butyrolactams including chiral derivatives were obtained in moderate to good yields.

β-fluorinated γ-butyrolactams*

*Supasorn Phae-nok, Manat Pohmakotr, Chutima Kuhakarn, Vichai Reutrakul, and Darunee Soorukram**

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Site-specific Synthesis of β-Fluorinated γ-Butyrolactams via Decarboxylative Fluorination of β-Carboxyl-γ-Butyrolactams