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Visible-Light-Induced, Catalyst-Free Radical Cross-Coupling Cyclization of *N*-Allylbromodifluoroacetamides with Disulfides or Diselenides

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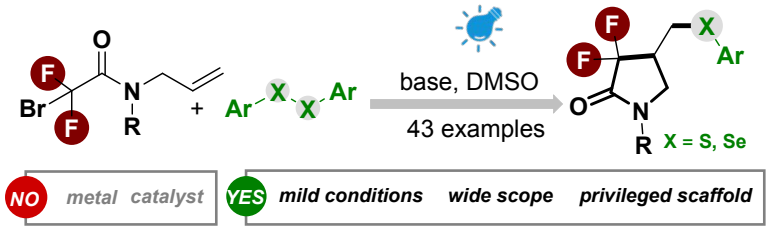
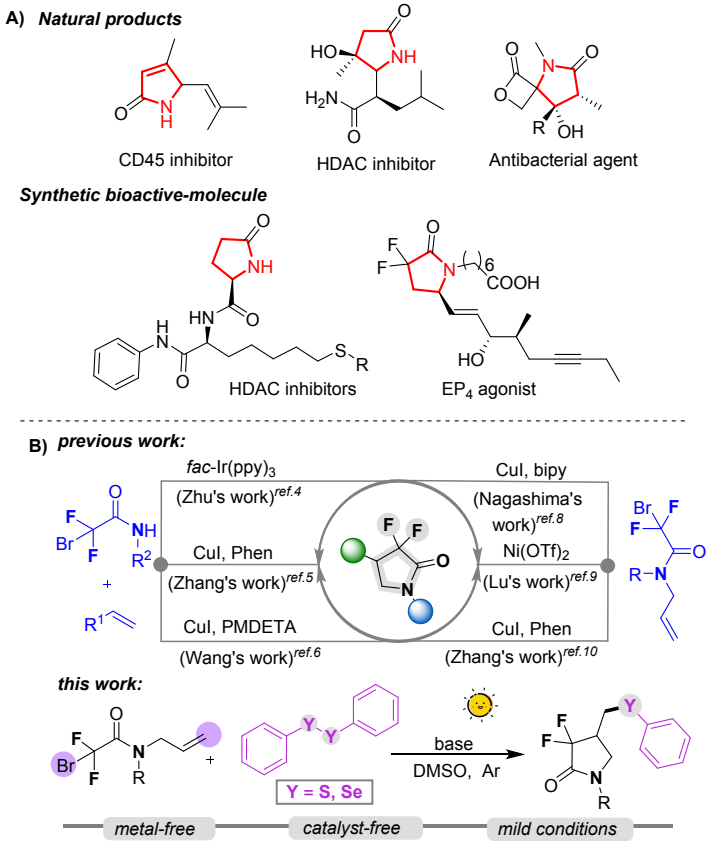


ABSTRACT: A visible-light-induced, catalyst-free radical cross-coupling cyclization of diselenides or disulfides with *N*-allylbromodifluoroacetamide has been developed. This developed protocol exhibits good functional group tolerance and affords a variety of 4-thio-, 4-seleno-substituted 3,3-difluoro-*γ*-lactams in moderate to good yields. Based on control experiments, a plausible radical-radical cross coupling pathway is proposed.

Owing to their unique physical and chemical properties, *gem*-difluoro scaffolds have found increasing utilizations in agricultural, medicinal, and materials sciences.[1] Therefore, new synthesis methods for synthesizing difluoro group-containing compounds have attracted widespread attention in synthetic chemistry over the past few years.[2] In particular, incorporation of difluoromethylene group (CF_2) into *γ*-lactams has been intensively studied in

recent years as γ-lactams usually possess interesting biological profiles (Scheme 1A).[3]

Scheme 1 Representative Examples of Bioactive γ-Lactams and Synthetic Profiles Accessing 3,3-Difluoropyrrolidin-2-ones

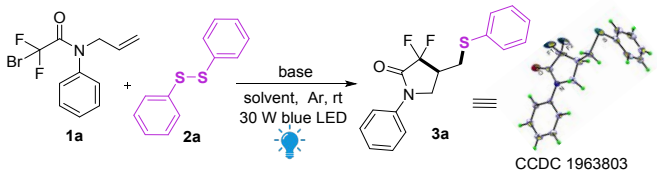


The current strategies mainly rely on transition-metal or visible-light-induced photoredox-catalyzed radical difluoromethylation *via* intramolecular or intermolecular pathways, resulting in a range of 3,3-difluoro-γ-lactams. Recently, Zhu,[4] Zhang[5] and Wang[6] group reported the synthesis of 3,3-difluoro-γ-lactams *via* visible-light photoredox and copper-catalysed cyclizations between α-bromodifluoroacetamides and alkenes. More recently, indoles bearing a C-3 bromodifluoroacetamide moiety acted as a CF_2 radical precursor were employed to construct 3,3-difluoro-γ-lactams under visible-light photocatalysis.[7] Alternatively, *N*-allylhalodifluoroacetamides were utilized to proceed a intramolecular cyclization to generate 3,3-difluoro-γ-lactams developed by Nagashima,[8] Zhang,[9] and Lu[10] group. Given the fact that the current strategies heavily rely on the transition-metal catalysis or high temperature, new efficient

and environmentally benign synthetic protocols accessing CF_2-containing γ-lactams are still highly desirable, especially for catalyst- and metal-free processes (Scheme 1B).

Organosulfides and organoselenides have received increasing attention because of their interesting biological and medicinal properties.[11] In the context of photocatalysis, disulfides (BDE = 46 kcal/mol) and diselenides (BDE = 41 kcal/mol)[12] are able to serve as facile organochalcogen agents in radical-involved coupling with various pre-functionalized substrates, such as thiols,[13] alkynes,[14] Olefins,[15] indoles,[16] *etc.*. Given their advantageous feature, we envisioned that the homolytic cleavage of diselenides or disulfides under mild conditions is expected to facilely generate RS· and RSe·, which would subsequently proceed tandem radical addition/radical coupling process with *N*-allylhalodifluoroacetamides. Notably, compared to the previous thermal copper-catalyzed protocol,[9] this metal-free, photo-induced strategy for the construction of *sulfo*- or *seleno*-engineered 3,3-difluoro-γ-lactams is more environmentally benign due to its mild and green reaction conditions. Herein, we disclose an catalyst-/metal-free strategy for the synthesis of 4-sulfo/seleno-α,α-difluoro-γ-lactams through a radical-initiated tandem cyclization.

Table 1 Optimization of reaction conditions[a]

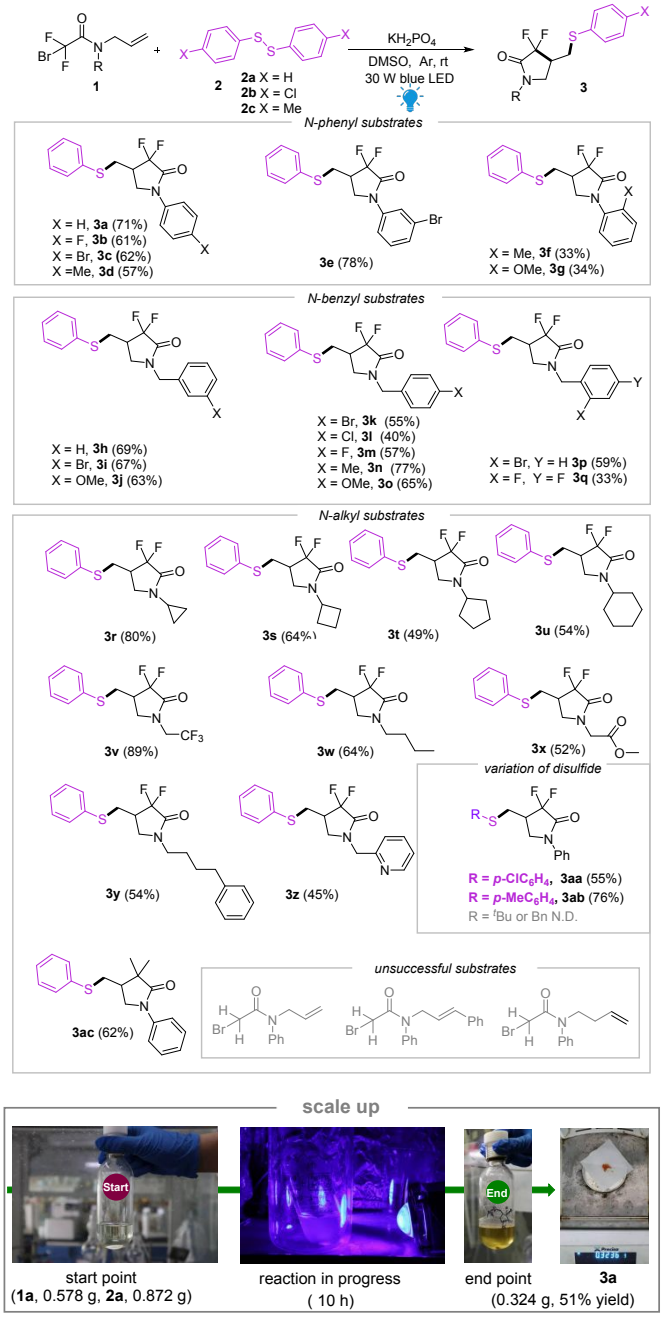


Entry	Base	Solvent	Yield[b]
1	K_2HPO_4	DMF	Trace
2	K_2HPO_4	CH_3CN	Trace
3	K_2HPO_4	DMSO	71%
4	K_2HPO_4	THF	NR
5	K_2HPO_4	CH_2Cl_2	NR
6	K_2CO_3	DMSO	38%
7	CH_3COOK	DMSO	Trace
8	DMAP	DMSO	69%

9	Et_3N	DMSO	60%
10[c]	K_2HPO_4	DMSO	26%
11[d]	K_2HPO_4	DMSO	54%
12	-	DMSO	ND
13[e]	K_2HPO_4	DMSO	ND
14[f]	K_2HPO_4	DMSO	63%

[a]Unless otherwise noted, the reaction was carried out at 0.2 mmol scale in solvent (2 mL) at rt with a molar ratio of 1a/2a = 1:2; w or w/o base (2 equiv.). [b]Isolated yields. [c]With $Ru(bpy)_3PF_6$ (5 mol%). [d]With $Ir(ppy)_2(dtbbpy)PF_6$ (5 mol%). [e]In the dark. [f]Irradiated by 30W white LED.

Scheme 2 Substrate Scope for the Cyclization of 1 and 2[a]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol, 2equiv.) and K_2HPO_4 (0.4 mmol, 2

equiv.) and DMSO (2 mL) were irradiated with 30 W blue LED in Ar at rt for 10 h; isolated yields. Gram scale: **1** (2 mmol), **2** (4 mmol, 2 equiv.), K_2HPO_4 (4 mmol, 2 equiv.) and DMSO (20 mL) were irradiated with 30 W blue LED in Ar at rt for 10 h; isolated yield.

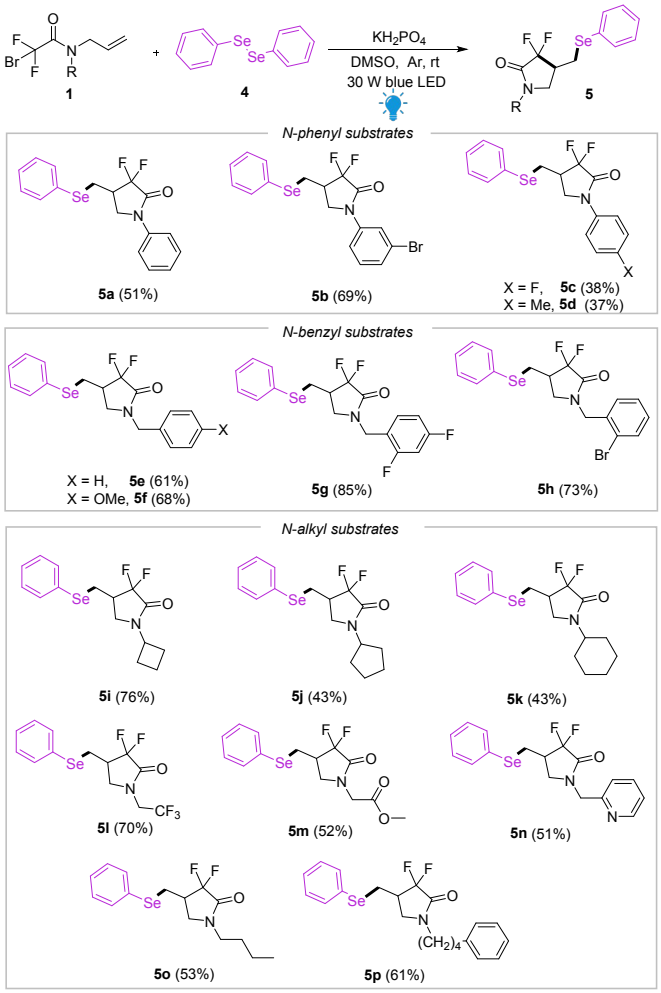
Originally, *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide (**1a**) and diphenyl disulfide (**2a**) was chosen as the model substrates to verify the designed visible-light-driven radical tandem cyclization under irradiation of blue light emitting diode (LED). In the presence of K_2HPO_4 as a base, a careful survey of different solvents disclosed that DMSO performed best in this protocol (Table1, entries 1-5). Moreover, K_2HPO_4 was proven to be the optimal base through cogitative screening of various bases (K_2CO_3, CH_3COOK, DMAP, Et_3N) (Table1, entries 6-9). It is worth mentioning that addition of $Ru(bpy)_3PF_6$ or $Ir(ppy)_2(dtbbpy)PF_6$ led to relatively lower yields of **3a** (Table1, entries 10-11). Control experiments demonstrated that base and visible light are all essential to this transformation (Table1, entries 12-13). This reaction can also occur under irradiation of 3 W blue LEDs but with a prolonged reaction time. Presumably, wide emission band for white LEDs is more likely to cause the unexpected side reactions, and irradiation with white LED gave a lower reaction efficiency relative to blue LEDs (Table1, entry 14). Interestingly, for this photo-induced transformation, the five-*exo*-*trig* cyclization dominated in the process and no six-*endo*-*trig* cyclization product was isolated.

With the optimized reaction conditions in hand, various substituted bromodifluoroacetamides **1** were examined to evaluate the substrate scope of this protocol (Scheme 2). As for *o*-, *m*- and *p*-substituted of *N*-phenyl substrates **1** were tested to give the corresponding *sulfo*-α,α-difluoro-γ-lactams in moderate to good chemical yields (**3b-3g**), whereas *ortho*-substitution obviously led to relatively lower yields (**3f** and **3g**). In addition, *N*-benzyl **3h** was also obtained in good yield (69%). Thus, diverse *N*-benzyl groups bearing electron-donating (Me, OMe) and electron-withdrawing (F, Cl, Br) groups were well tolerated and good yields were generally achieved (**3i-3p**), except for the *ortho*-substituted **3q** (33% yield). It is noteworthy that *N*-cycloalkyl-2-bromo-2,2-difluoro-*N*-

phenylacetamides were also suitable for this transformation, providing the corresponding products **3r-3u** in 49%-80% yields. Moreover, *N*-alkyl substrates including 2,2,2-trifluoroethyl, butyl, glycine methyl ester, phenylbutyl, pyridin-2-ylmethyl were all compatible with the reaction conditions, giving the corresponding products **3v-3z** in 45%-89% yields. Ultimately, 4-Cl- and 4-Me-diphenyl disulfides are also applicable in this protocol, delivering the corresponding products **3aa** and **3ab** in good yields (55% and 76%). Unfortunately, dialkyl disulfides were examined as well in this protocol, which were unsuitable for this photo-induced process. Possibly, the aryl groups were essential to stabilize the S/Se-radicals in this transformation. Replacing the *gem*-fluoro group with *gem*-methyl group in **1a** had no significant effect on this procedure, leading to the desired product **3ac** in a moderate yield. Otherwise, *N*-allyl-2-bromo-*N*-phenylacetamide was unsuitable substrate. Regrettably, in contrast to unsubstituted olefin substrate, the Ph-substituted counterpart was unable to proceed the cyclization, which is probably due to the demanding steric effect of Ph group. Pleasingly, a scale-up reaction for the synthesis of **3a** was conducted under the standard reaction conditions, which afforded the desired product **3a** in 51% yield.

Encouraged by the above results, diphenyl diselenide (**4**) was also tested to further evaluate the generality of this protocol and the results are summarized in Scheme 3. Pleasingly, diverse *N*-phenyl substituted bromodifluoroamides were employed in the reaction to afford the corresponding products **5a**-**5d** in moderate to good chemical yields (37%-69%). Otherwise, good yields (61%-85%) were obtained for various *N*-benzyl bromodifluoroamides (**5e**-**5h**). Gratifyingly, *N*-alkyl substrates were all tolerated well to proceed the title reaction smoothly, though *N*-cyclopentyl and *N*-cyclohexyl analogues (**5j** and **5k**) were achieved in comparably lower yields. Moreove, *N*-alkyl substrates including 2,2,2-trifluoroethyl, glycine methyl ester, pyridin-2-ylmethyl, butyl, phenylbutyl were applied in reaction conditions to afforded **5l-5p** in moderate to good chemical yields (51%-70%)

Scheme 3 Substrate Scope for the Cyclization of 1 and Diphenyl Diselenide (4)[a]



[a]Reaction conditions: **1** (0.2 mmol), **4** (0.4 mmol, 2 equiv.) and K_2HPO_4 (0.4 mmol, 2 equiv.) were irradiated with 30 W blue LED in Ar at rt for 10 h; isolated yield.

To gain mechanistic insights into this process, several control experiments were implemented (Figure 1a). The radical inhibition experiments were conducted by adding 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) under the standard reaction conditions and the mass analysis of the reaction mixture indicates that the formation of **TEMPO-1a** (m/z = 389.1990, calcd 389.2011) and **TEMPO-2a** (m/z = 288.1378, calcd 288.1393) can be clearly identified. Mixing **2a** with 2 equiv. of TEMPO under the standard conditions gave the corresponding **TEMPO-2a** in 19% yield, while no reaction was observed in the case of **1a** with 2 equiv. of TEMPO. On the other hand, the emission quenching experiments of **1a** and **2a** in DMSO were recorded. The **2a** solutions was excited at

340 nm and the emission intensity was collected at 405 nm, moreover, the **1a** solutions was acted as quencher. The *Io* and *I* represent the emission in absence and presence of the quencher. The relevant graph was plotted *via* the modified Stern–Volmer equation (Figure 1b).[17] The UV-visible spectroscopy studies on **1a** and **2a** (1×10^{-4} M, in DMSO) demonstrate that an absorption at 258 nm can be observed for **1a**, whereas the absorption for **2a** shows at 257 nm (Figure 1c). No obvious bathochromic shift was observed for the mixture of **1a** and **2a,** indicating that the corresponding electron-donor−acceptor complexes (EDA) was unlikely formed.

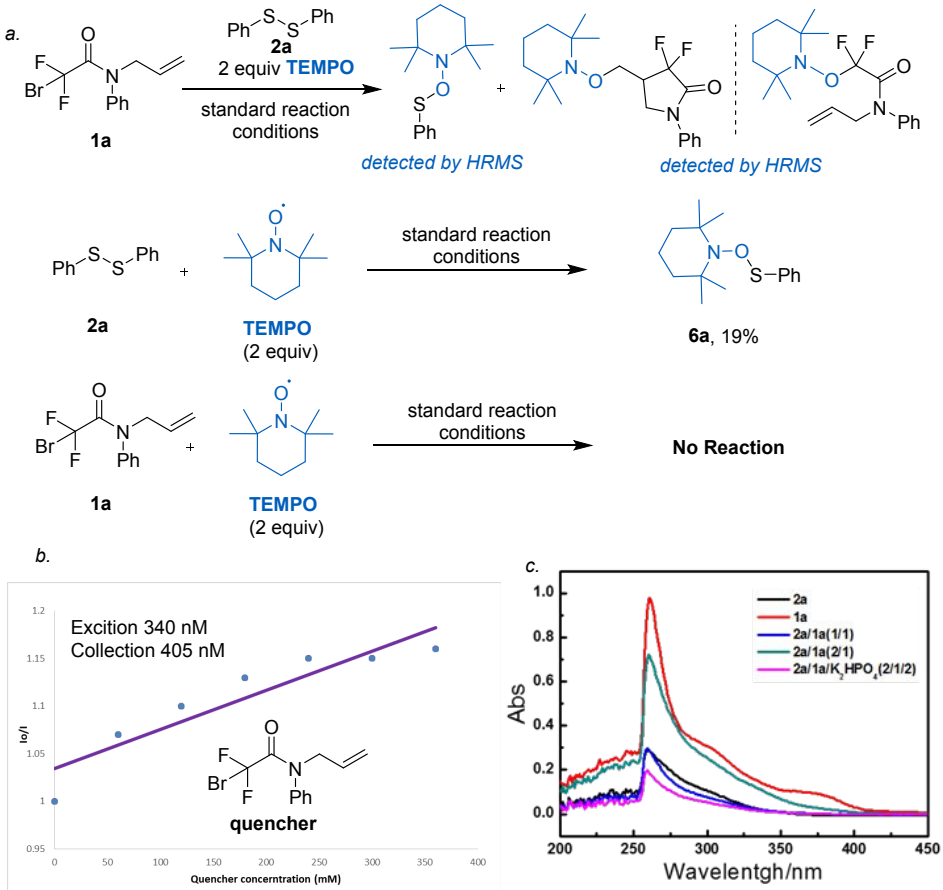
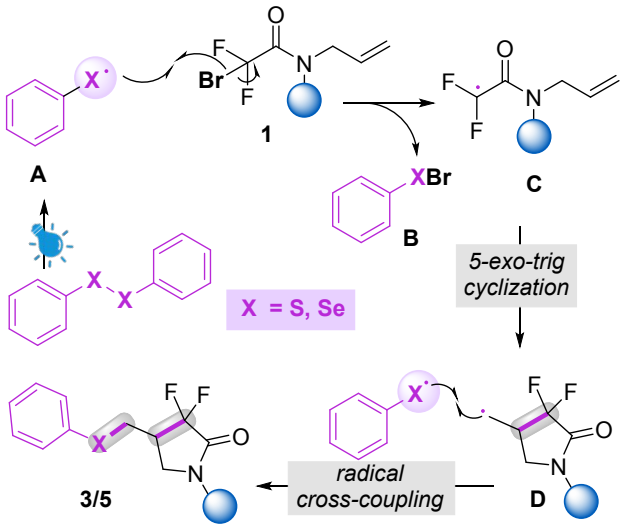


Figure 1 Control Experiments, Emission Quenching Experiments and UV–Vis Spectra for Mechanistic Studies

Based on the above-mentioned mechanistic experiments, we propose a plausible mechanism for this transformation in Scheme 4. Firstly, **Ph-X-X-Ph** was excited by visible light to proceed a homolytic cleavage to generate radical **Ph-X·** (**A**) and **Ph-XBr** (**B**). Presumably, the base K_2HPO_4 would consume the resulting PhXBr to promote this transformation. Subsequently, the abstraction of

bromine atom from **1a** by **Ph-X**· provided radical **C**, which would proceed a rapid 5-*exo-trig* cyclization to give radical the intermediate **D**. Finally, a radical-radical cross-coupling between radical intermediate **D** and **Ph-X**· facilely delivered the final product **3** or **5**. Nevertheless, an alternative radical chain mechanism was unable to be completely ruled out, as the accumulation of the desired product was observed albeit at an extremely low speed (see Supporting Information for details).

Scheme 4 Proposed Mechanism.



In summary, we successfully developed a visible-light-induced, catalyst-free radical cross-coupling cyclization of diselenides or disulfides with *N*-allylbromodifluoroacetamide. As a result, a wide range of sulfo- or seleno-engineered 3,3-difluoro-*γ*-lactams were facilely installed under mild conditions. Furthermore, the straightforwardness and environmental benignity of this developed method would inspire broad exploitation of the hidden potentials of *N*-allylhalodifluoroacetamides in the visible-light-induced transformations, enabling their practical applications in the preparation of valuable fluorinated heterocycles.

EXPERIMENTAL SECTION

General Experimental Methods. Unless otherwise noted, all the reagents were purchased

from commercial suppliers and used without further purification. And the light source used for illuminating the reaction vessel (commercial supplier: Synthware) consisted of blue LEDs (λ_{max} = 460 nm) purchased from Taobao (https://gpiled.taobao.com). ^{1}H NMR spectra were recorded at 400 MHz. The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz), integration. ^{13}C NMR data were collected at 100 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. ^{19}F NMR data were collected at 376 MHz with complete proton decoupling. UV–Vis spectra were recorded using a shimadzu UV-2600. Infrared spectra (IR) were measured by FT-IR apparatus. High resolution mass spectroscopy (HRMS) was recorded on TOF MS ES+ mass spectrometer and acetonitrile was used to dissolve the sample. Cyclic Voltammetry (CV) experiments were recorded on a CHI650D electrochemical workstation. Emission intensities were recorded using Perkin-Elemer LS 55 Fluorescence Spectrometer. Column chromatography was carried out on silica gel (200-300 mesh).

General procedure for the preparation of 1a-1z. Step A: To a mixture of amines (5.0 mmol, 1.0 equiv.) and ytterbium (III) trifluoromethanesulfonate was added ethyl bromodifluoroacetate (0.5 mmol, 1.0 equiv.). The mixture was stirred until the reaction was judged to be completed by TLC analysis. The obtained crude product was purified by column chromatography (PE:EA = 19:1) on silica gel to give the corresponding product.

Step B: To a solution of 2-bromo-2,2-difluoro-*N*-amines (5.0 mmol, 1.0 equiv.) in CH_3CN (15 mL) were added K_2CO_3 (2.07 g, 15 mmol, 3.0 equiv.) and allyl bromide (1.82 g, 15 mmol, 3.0 equiv.). The mixture was heated to reflux under argon atmosphere, until the reaction was judged to be completed by TLC analysis. The solvent was removed and the obtained residue was purified by column chromatography (PE:EA = 19:1) on silica gel to give the corresponding product **1**.

General procedure for the synthesis of compounds 3a and 5a

Under argon atmosphere, a mixture of *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide **1** (0.2 mmol, 1equiv.), K_2HPO_4 (0.4 mmol, 2.0 equiv.), diphenyldisulfide (**2a**) or diphenyldiselenide (**2b**) (0.4 mmol, 2 equiv.) in DMSO (2.0 mL) was stirred at room temperature under irradiation of 30 W blue LEDs (distance app. 3 cm) for 10 h. Thereafter, EtOAc (60 mL) was added to the reaction

mixture. And the obtained organic layer was washed with brine (3×20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was further purified by flash chromatography using silica gel (EtOAc/PE = 1:19 - 1:1) to afford the desired product **3** or **5**.

Scale-up reaction Under argon atmosphere, a mixture of N-allyl-2-bromo-2,2-difluoro-N-phenylacetamide 1a (2.0 mmol, 1.0 equiv.), K_2HPO_4 (4.0 mmol, 2.0 equiv.), diphenyldisulfide 2a (4.0 mmol, 2.0 equiv.) in DMSO (20 mL) was stirred at room temperature under irradiation of 30 W blue LEDs (distance app. 8 cm) for 10 h. Thereafter, EtOAc (150 mL) was added to the reaction mixture. And the obtained organic layer was washed with brine (3×40 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude products were further purified by flash chromatography using silica gel (EtOAc/PE = 1:19 - 1:1) to afford the desired products 3a in 50% yield (326 mg, 1.0 mmol).

Characterization data of starting materials 1a-1d[9,10] 1e-1y

*N-allyl-2-bromo-N-(3-bromophenyl)-2,2-difluoroacetamide **(1e)***. Pale yellow oil (789 mg, 2.2 mmol, overall yield 43%); IR (neat) *v* 1731, 1588, 1439, 1104, 995, 780, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.0 Hz, 1H), 7.44 (s, 1H), 7.30 (*J* = 8.0 Hz, 1H), 7.21 (d, *J* = 7.8 Hz, 1H), 5.91 – 5.81 (m, 1H), 5.25 (d, *J* = 10.1 Hz, 1H), 5.16 (d, *J* = 17.1 Hz, 1H), 4.30 – 4.29 (m, 2H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -52.12; ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 158.6 (t, J_{C-F} = 25.3 Hz), 140.8, 132.2, 131.9, 130.4, 127.6, 122.4, 120.3, 111.3 (t, J_{C-F} = 317.3 Hz), 55.4; HRMS (ESI): $C_{11}H_9Br_2F_2NNaO^+$ $[M+Na]^+$ Calcd 389.8911, found 389.8891.

*N-allyl-2-bromo-2,2-difluoro-N-(o-tolyl)acetamide **(1f).*** as an mixture of inseparable atropisomers: Pale yellow oil (727 mg, 2.4 mmol, overall yield 48%); IR (neat) *v* 1686, 1492, 1399, 1150, 981, 899, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.23 – 7.17 (m, 2H), 5.98 – 5.84 (m, 1H), 5.23 – 5.13 (m, 2H), 4.75 (dd, *J* = 14.1, 5.8 Hz, 1H), 3.69 (dd, *J* = 14.1, 7.4 Hz, 1H), 2.26 (s, 3H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -51.78 (d, *J* = 156.0 Hz, 1.00F), -51.70 (d, *J* = 157.4 Hz, 0.11F), -55.84 (d, *J* = 157.4 Hz, 0.09F), -55.41 (d, *J* = 155.9 Hz, 1.00F); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 159.1 (dd, J_{C-F} = 26.5, 25.2 Hz), 138.2, 136.0, 131.2, 130.5, 129.6, 129.2, 126.3, 120.1, 111.8 (dd, J_{C-F} = 320.5, 314.5 Hz), 54.5, 17.9; HRMS (ESI): $C_{12}H_{12}BrF_2NNaO^+$ $[M+Na]^+$ Calcd 325.9963, Found 325.9946.

*N-allyl-2-bromo-2,2-difluoro-N-(2-methoxyphenyl)acetamide **(1g)***. Pale yellow oil (893 mg, 2.8 mmol, overall yield 56%); IR (neat) *v* 1687, 1499, 1281, 1150, 924, 938, 662 cm^{-1}; ^1H NMR

(400 MHz, $CDCl_3$) δ 7.38 – 7.34 (m, 1H), 7.20 (d, J = 7.7 Hz, 1H), 6.96 – 6.93 (m, 2H), 5.90 – 5.80 (m, 1H), 5.16 – 4.64 (m, 2H), 4.69 – 4.64 (dd, J = 14.5, 5.6 Hz, 1H), 3.83 – 3.80 (m, 4H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -52.09 (d, J = 154.9 Hz), -54.70 (d, J = 155.1 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 155.4, 131.3, 130.4, 127.9, 120.1, 119.2, 111.4, 55.5, 54.0; HRMS (ESI): $C_{12}H_{12}BrF_2NNaO_2^+$ $[M+Na]^+$ Calcd 341.9912, Found 341.9890.

N-allyl-N-benzyl-2-bromo-2,2-difluoroacetamide ***(1h).*** as an mixture of inseparable atropisomers: Pale yellow oil (909 mg, 3.0 mmol, overall yield 60%); IR (neat) v 1681, 1442, 1153, 1129, 929, 868, 635 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 3H), 7.25 – 7.21 (m, 2H), 5.83 – 5.70 (m, 1H), 5.33 – 5.13 (m, 2H), 4.72 (s, 0.80 H), 4.63 (s, 1.29 H), 4.03 (d, J = 5.6 Hz, 1.28H), 4.03 (d, J = 5.6 Hz, 0.79H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -53.78 (s, 1.16F), -54.21 (s, 2.00F); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 159.7 (t, $J_{C\text{-}F}$ = 26.1 Hz), 135.5, 134.8, 131.6, 130.6, 128.9, 128.8, 128.1, 127.9, 127.2, 119.4, 118.8, 111.0 (t, $J_{C\text{-}F}$ = 316.2 Hz), 50.82 (t, $J_{C\text{-}F}$ = 3.6 Hz), 49.72 (t, $J_{C\text{-}F}$ = 3.5 Hz), 48.8, 48.5; HRMS (ESI): $C_{12}H_{12}BrF_2NNaO^+$ $[M+Na]^+$ Calcd 325.9963, Found 325.9940.

N-allyl-2-bromo-N-(3-bromobenzyl)-2,2-difluoroacetamide ***(1i).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.33 g, 3.5 mmol, overall yield 70%); IR (neat) v 1681, 1419, 1155, 1071, 930, 873, 641 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.36 (m, 1H), 7.39 – 7.36 (m, 1H), 7.27 – 7.14 (m, 2H), 5.84 – 5.71 (m, 1H), 5.35 – 5.14 (m, 2H), 4.69 (s, 0.67H), 4.59 (s, 1.32H), 4.05 (d, J = 5.3 Hz, 1.33H), 4.05 (d, J = 5.6 Hz, 0.69H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -53.96 (s, 1.00F), -54.39 (s, 2.00F); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 159.7 (t, $J_{C\text{-}F}$ = 26.8 Hz), 137.8, 137.2, 131.4, 131.3, 131.1, 131.0, 130.5, 130.4, 130.3, 130.2, 126.6, 125.7, 123.1, 122.9, 119.7, 119.1, 110.8 (t, $J_{C\text{-}F}$ = 315.0 Hz), 50.4 – 49.9 (m), 48.7, 48.3; HRMS (ESI): $C_{12}H_{11}Br_2F_2NNaO^+$ $[M+Na]^+$ Calcd 403.9068, Found 403.9064.

N-allyl-2-bromo-2,2-difluoro-N-(3-methoxybenzyl)acetamide ***(1j).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.43 g, 4.3 mmol, overall yield 86%); IR (neat) v 1681, 1436, 1262, 1150, 1008, 871, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 1H), 6.86 – 6.75 (m, 3H), 5.83 – 5.71 (m, 1H), 5.33 – 5.14 (m, 2H), 4.69 (s, 0.74H), 4.61 (s, 1.33H), 4.03 (d, J = 5.3 Hz, 1.30H), 3.94 (d, J = 5.6 Hz, 0.77H), 3.80 – 3.79 (m, 3H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -53.77 (s, 1.15F), -54.28 (s, 2.00F); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 160.1 – 159.1 (m), 137.0, 136.4, 131.1, 130.4, 130.0, 129.9, 120.3, 119.5, 119.4, 118.8, 113.5, 113.4, 113.2, 113.0,

111.0 (t, J_{C-F} = 315.2 Hz), 55.3, 55.2, 50.7 (t, J_{C-F} = 3.7 Hz), 49.8 (t, J_{C-F} = 3.6 Hz), 48.6, 48.5; HRMS (ESI): $C_{13}H_{14}BrF_2NNaO_2^+$ $[M+Na]^+$ Calcd 356.0068, Found 356.0045.

N-allyl-2-bromo-N-(4-bromobenzyl)-2,2-difluoroacetamide ***(1k).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.49 g, 3.9 mmol, overall yield 78%); IR (neat) *v* 1686, 1492, 1399, 1150, 981, 899, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.49 (m, 2H), 7.14 – 7.09 (m, 2H), 5.83 – 5.69 (m, 1H), 5.34 – 5.12 (m, 2H), 4.67 (s, 0.65H), 4.57 (s, 1.32H), 4.02 (d, *J* = 5.3 Hz, 1.35H), 3.94 (d, *J* = 5.6 Hz, 0.67H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -53.90 (s, 0.98F), -54.35 (s, 2.00F); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.7 (t, J_{C-F} = 26.8 Hz), 134.6, 133.9, 132.1, 132.0, 131.5, 130.4, 129.9, 128.9, 122.1, 122.0, 119.7, 119.0, 110.9 (t, J_{C-F} = 315.0 Hz), 50.2 (t, J_{C-F} = 3.7 Hz), 50.0 (t, J_{C-F} = 3.7 Hz), 48.5, 48.4; HRMS (ESI):$C_{12}H_{11}Br_2F_2NNaO^+$ $[M+Na]^+$ Calcd 403.9068, Found 403.9051.

N-allyl-2-bromo-N-(4-chlorobenzyl)-2,2-difluoroacetamide ***(1l).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.01 g, 3.0 mmol, overall yield 60%); IR (neat) *v* 1681, 1407, 1130, 1015, 924, 800, 682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 2H), 7.20 – 7.15 (m, 2H), 5.83 – 5.69 (m, 1H), 5.34 – 5.12 (m, 2H), 4.69 (s, 0.68H), 4.59 (s, 1.36H), 4.02 (d, *J* = 5.3 Hz, 1.34H), 3.92 (d, *J* = 5.6 Hz, 0.67H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -53.90 (s, 0.98F), -54.35 (s, 2.00F); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.7 (t, J_{C-F} = 26.6 Hz), 134.0, 133.9, 133.3, 131.5, 130.4, 129.5, 129.2, 129.1, 128.6, 119.6, 119.0, 110.9 (t, J_{C-F} = 315.0 Hz), 50.2 (t, J_{C-F} = 3.7 Hz), 49.9 (t, J_{C-F} = 3.7 Hz), 48.5, 48.3; HRMS (ESI): $C_{12}H_{11}BrClF_2NNaO^+$ $[M+Na]^+$ Calcd 359.9573, Found 359.9551.

N-allyl-2-bromo-2,2-difluoro-N-(4-fluorobenzyl)acetamide ***(1m).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.09 g, 3.4 mmol, overall yield 68%); IR (neat) *v* 1681, 1415, 1224, 115, 923, 820, 621 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.19 (m, 2H), 7.09 – 7.01 (m, 2H), 5.83 – 5.69 (m, 1H), 5.34 – 5.12 (m, 2H), 4.69 (s, 0.66H), 4.59 (s, 1.37H), 4.02 (d, *J* = 5.4 Hz, 1.40H), 3.91 (d, *J* = 5.7 Hz, 0.69H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -53.80 (s, 1.55F), -54.31 (s, 3.15F), -113.83 (s, 0.50F), -114.10 (s, 1.01F); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.5 (d, J_{C-F} = 247.3 Hz), 162.5 (d, J_{C-F} = 246.7 Hz), 159.6 (d, J_{C-F} = 26.6 Hz), 159.3 (d, J_{C-F} = 26.5 Hz), 131.5, 131.3 (d, J_{C-F} = 3.3 Hz), 130.51, 130.47, 130.0 (d, J_{C-F} = 8.2 Hz), 129.0 (d, J_{C-F} = 8.2 Hz), 119.5, 118.9, 115.9 (d, J_{C-F} = 21.7 Hz), 115.8 (d, J_{C-F} = 21.5 Hz), 110.9 (t, *J* = 315.0 Hz), 50.1 (t, J_{C-F} =

3.6 Hz), 49.8 (t, J_{C-F} = 3.7 Hz), 48.3, 48.2; HRMS (ESI): $C_{12}H_{11}BrF_3NNaO^+$ $[M+Na]^+$ Calcd 343.9868, Found 343.9844.

N-allyl-2-bromo-2,2-difluoro-N-(4-methylbenzyl)acetamide ***(1m).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.32 g, 4.2 mmol, overall yield 83%); IR (neat) *v* 1681, 1443, 1155, 1008, 923, 868, 677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.19 – 7.09 (m, 4H), 5.83 – 5.69 (m, 1H), 5.32 – 5.13 (m, 2H), 4.67 (s, 0.80H), 4.59 (s, 1.26H), 4.00 (d, *J* = 5.5 Hz, 1.24H), 3.91 (d, *J* = 5.7 Hz, 0.80H), 2.35 (s, 1.18H), 2.34 (s, 1.77H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -53.63 (s, 1.27F), -54.01 (s, 2.00F); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.6 (t, J_{C-F} = 26.1 Hz), 137.9, 137.7, 132.4, 131.7, 130.6, 129.6, 129.5, 128.2, 127.2, 119.4, 118.7, 111.1 (t, J_{C-F} = 315.0 Hz), 111.0 (t, J_{C-F} = 315.0 Hz), 50.6 (t, J_{C-F} = 3.8 Hz), 49.6 (t, J_{C-F} = 3.7 Hz), 48.5, 48.3, 21.13, 21.09; HRMS (ESI): $C_{13}H_{14}BrF_2NNaO^+$ $[M+Na]^+$ Calcd 340.0119, Found 340.0101.

N-allyl-2-bromo-2,2-difluoro-N-(4-methoxybenzyl)acetamide ***(1o).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.02 g, 3.1 mmol, overall yield 61%); IR (neat) *v* 1681, 1435, 1260, 1150, 927, 781, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.19 – 7.13 (m, 2H), 6.9 – 6.87 (m, 2H), 5.83 – 5.68 (m, 1H), 5.33 – 5.12 (m, 2H), 4.65 (s, 0.74H), 4.56 (s, 1.25H), 4.00 (d, *J* = 5.5 Hz, 1.25H), 3.91 (d, *J* = 5.7 Hz, 0.76H), 3.81 (s, 1.18H), 3.80 (s, 1.79H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -53.63 (s, 1.19F), -54.01 (s, 2.00F); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.6 (d, J_{C-F} = 26.5 Hz), 159.5, 159.4, 159.1 (d, J_{C-F} = 26.2 Hz), 159.6 – 159.3 (m), 131.7, 130.7, 129.7, 128.7, 127.5, 126.6, 119.3, 118.7, 114.3, 114.2, 111.1 (t, J_{C-F} = 315.1 Hz), 111.0 (t, J_{C-F} = 315.0 Hz), 55.3, 55.2, 50.3 (t, J_{C-F} = 3.9 Hz), 49.4 (t, J_{C-F} = 3.7 Hz), 48.2, 48.1; HRMS (ESI): $C_{13}H_{14}BrF_2NNaO_2^+$ $[M+Na]^+$ Calcd 356.0068, Found 356.0041.

N-allyl-2-bromo-N-(2-bromobenzyl)-2,2-difluoroacetamide ***(1p).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.51 g, 4.0 mmol, overall yield 79%); IR (neat) *v* 1692, 1440, 1132, 1027, 873, 746, 682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.56 (m, 1H), 7.36 – 7.30 (m, 1H), 7.21 – 7.13 (m, 2H), 5.86 – 5.75 (m, 1H), 5.32 – 5.19 (m, 2H), 4.79 (s, 0.73H), 4.74 (s, 1.37H), 4.07 (d, *J* = 5.4 Hz, 1.33H), 3.98 (d, *J* = 5.7 Hz, 0.74H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -54.22 (s, 2.00F), -54.58 (s, 1.08F); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.9 (d, J_{C-F} = 26.6 Hz), 159.6 (d, J_{C-F} = 26.5 Hz), 134.6, 134.3, 133.2, 133.1, 131.4, 130.3, 129.3, 128.5, 127.9, 127.8, 127.4, 123.6, 122.7, 119.6, 119.1, 111.8 (t, J_{C-F} = 315.1 Hz), 111.7 (t, J_{C-F} = 315.0 Hz), 51.2 (t, J_{C-F} = 3.8 Hz), 50.5 (t, J_{C-F} = 3.6 Hz), 49.7, 49.2; HRMS (ESI): $C_{12}H_{11}Br_2F_2NNaO^+$ $[M+Na]^+$ Calcd 403.9068,

Found 403.9045.

N-allyl-2-bromo-N-(2,4-difluorobenzyl)-2,2-difluoroacetamide ***(1q).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.46 g, 4.3 mmol, overall yield 86%); IR (neat) *v* 1682, 1505, 1136, 1092, 967, 849, 606 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 0.80H), 6.93 – 6.80 (m, 0.27H), 6.93 – 6.80 (m, 2H), 5.84 – 5.72 (m, 1H), 5.34 – 5.24 (m, 2H), 4.74 (s, 0.55H), 4.62 (s, 1.60H), 4.07 (d, J = 5.6 Hz, 1.60H), 3.93 (d, J = 5.7 Hz, 0.56H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -54.11 (s, 0.66F), -54.36 (s, 1.97F), -109.76 (d, J = 7.6 Hz, 0.24F), -109.82 (d, J = 7.7 Hz, 0.65F), -114.02 (d, J = 7.6 Hz, 0.87F), -114.06 (d, J = 7.6 Hz, 0.31F); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.1 – 161.2 (m), 160.2 – 159.3 (m), 131.5 (dd, $J_{C\text{-}F}$ = 9.7, 5.4 Hz), 131.3, 130.2, 129.5 – 129.3 (m), 119.7, 119.0, 118.6 (dd, $J_{C\text{-}F}$ = 15.2, 4.0 Hz), 111.9 (dd, $J_{C\text{-}F}$ = 21.3, 3.6 Hz), 109.3 (t, $J_{C\text{-}F}$ = 315.0 Hz), 104.2 (t, $J_{C\text{-}F}$ = 25.4 Hz), 103.9 (t, $J_{C\text{-}F}$ = 25.7 Hz), 50.4, 49.0, 44.3 – 44.2 (m), 42.4 (d, $J_{C\text{-}F}$ = 3.5 Hz); HRMS (ESI): $C_{12}H_{10}BrF_4NNaO^+$ $[M+Na]^+$ Calcd 361.9774, Found 361.9758.

N-allyl-2-bromo-N-cyclopropyl-2,2-difluoroacetamide ***(1r).*** as an mixture of inseparable atropisomers with EtOAc : Pale yellow oil (924 mg, 3.7 mmol, overall yield 73%); IR (neat) *v* 1682, 1405, 1148, 986, 912, 841, 665 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 – 5.79 (m, 1H), 5.21 – 5.18 (m, 2H), 4.15 – 4.08 (m, 2H), 3.04 – 2.93 (m, 0.66H), 2.81 – 2.70 (m, 0.31H), 1.00 – 0.72 (m, 4H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -53.01 (s, 2.00F), -54.26 (s, 0.96F); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 132.5, 132.2, 118.4, 117.3, 51.6, 31.2, 30.8, 8.7, 7.4; HRMS (ESI): $C_8H_{10}BrF_2NNaO^+$ $[M+Na]^+$ Calcd 275.9806, Found 275.9789.

N-allyl-2-bromo-N-cyclobutyl-2,2-difluoroacetamide ***(1s).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.18 g, 4.4 mmol, overall yield 88%); IR (neat) *v* 1681, 1418, 1269, 1106, 985, 877, 686 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 – 5.76 (m, 1H), 5.23 – 5.13 (m, 2H), 4.74 (p, J = 8.3 Hz, 0.66H), 4.42 (p, J = 8.7 Hz, 0.35H), 4.12 – 4.11 (m, 2H), 2.32 – 2.14 (m, 4H), 1.80 – 1.60 (m, 2H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -54.13 (s, 2.00F), -54.16 (s, 1.08F); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.2 (t, $J_{C\text{-}F}$ = 26.4 Hz), 158.6 (t, $J_{C\text{-}F}$ = 26.4 Hz), 133.7, 133.6, 117.3, 116.2, 111.1 (t, $J_{C\text{-}F}$ = 315.1 Hz), 110.8 (t, $J_{C\text{-}F}$ = 315.1 Hz), 53.0, 52.0 (t, $J_{C\text{-}F}$ = 4.2 Hz), 47.6 (t, $J_{C\text{-}F}$ = 3.5 Hz), 44.8, 28.9, 28.2, 15.1, 14.4; HRMS (ESI): $C_9H_{12}BrF_2NNaO^+$ $[M+Na]^+$ Calcd 289.9963, Found 289.9941.

N-allyl-2-bromo-N-cyclopentyl-2,2-difluoroacetamide ***(1t).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.15 g, 4.1 mmol, overall yield 82%); IR (***neat***) *v* 1682, 1444, 1108,

1008, 923, 800, 645 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.91 – 5.78 (m, 1H), 5.24 – 5.16 (m, 2H), 4.62 – 4.48 (m, 0.73H), 4.19 – 4.13 (m, 0.28H), 4.08 (d, J = 3.4 Hz, 0.60H), 3.90 (d, J = 4.6 Hz, 1.47H), 1.98 – 1.93 (m, 2H), 1.78 – 1.74 (m, 2H), 1.57 – 1.55 (m, 4H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -53.72 (s, 2.00F), -54.09 (s, 0.78F); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 159.1 (t, J_{C-F} = 26.4 Hz), 158.9 (t, J_{C-F} = 26.4 Hz), 133.9, 133.7, 117.5, 116.5, 111.3 (t, J_{C-F} = 315.1 Hz), 110.9 (t, J_{C-F} = 315.1 Hz), 60.6, 59.3 (t, J_{C-F} = 3.7 Hz), 49.6 (t, J_{C-F} = 3.6 Hz), 45.5, 29.5, 28.5, 24.2, 24.0; HRMS (ESI): $C_{10}H_{14}BrF_2NNaO^+$ $[M+Na]^+$ Calcd 304.0119, Found 304.0103.

N-allyl-2-bromo-N-cyclohexyl-2,2-difluoroacetamide ***(1u).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.18 g, 4.0 mmol, overall yield 80%); IR (neat) *v* 1675, 1420, 1171, 1119, 901, 844, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.87 – 5.77 (m, 1H), 5.24 – 5.15 (m, 2H), 4.08 – 3.99 (m, 1H), 3.95 – 3.93 (m, 2H), 1.88 – 1.81 (m, 4H), 1.77 – 1.63 (m, 2H), 1.54 – 1.47 (m, 1H), 1.39 – 1.47 (m, 2H), 1.17 – 1.05 (m, 1H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -53.83 (s, 0.73F), -54.10 (s, 2.00F); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 159.0 (t, J_{C-F} = 26.4 Hz), 158.7 (t, J_{C-F} = 26.4 Hz), 134.6, 132.9, 117.5, 117.0, 111.3 (t, J_{C-F} = 315.1 Hz), 110.8 (t, J_{C-F} = 315.1 Hz), 58.4, 58.1 (t, J_{C-F} = 3.7 Hz), 48.1 (t, J_{C-F} = 3.7 Hz), 45.5, 31.2, 29.6, 25.8, 25.6, 25.3, 25.0; HRMS (ESI): $C_{11}H_{16}BrF_2NNaO^+$ $[M+Na]^+$ Calcd 318.0276, Found 318.0254.

N-allyl-2-bromo-2,2-difluoro-N-(2,2,2-trifluoroethyl)acetamide ***(1v).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.25 g, 4.3 mmol, overall yield 85%); IR (neat) *v* 1695, 1417, 1106, 1011, 991, 875, 685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.82 – 5.72 (m, 1H), 5.41 – 5.28 (m, 2H), 4.27 (d, J = 5.7 Hz, 1.58H), 4.19 (d, J = 5.3 Hz, 0.43H), 4.09 – 4.01 (m, 2H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -53.92 (q, J = 7.5 Hz, 0.50F), -55.03 (s, 2.00F), -68.57 (t, J = 7.5 Hz, 0.72F), -68.72 (s, 3.11F); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$, major) δ 160.1 (t, J_{C-F} = 27.8 Hz), 130.5, 124.1 (q, J_{C-F} = 280.9 Hz), 120.8, 110.2 (t, J_{C-F} = 314.3 Hz), 51.5, 45.7 (q, J_{C-F} = 34.5 Hz); HRMS (ESI): $C_7H_7BrF_5NNaO^+$ $[M+Na]^+$ Calcd 317.9523, Found 317.9498.

Methyl N-allyl-N-(2-bromo-2,2-difluoroacetyl)glycinate ***(1x).*** as an mixture of inseparable atropisomers: Pale yellow oil (613 mg, 2.2 mmol, overall yield 43%); IR (neat) *v* 1685, 1439, 1214, 1118, 991, 876, 674 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.79 – 5.65 (m, 1H), 5.26 – 5.15 (m, 2H), 4.17 – 4.01 (m, 4H), 3.71 – 3.69 (m, 3H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -55.09 (s, J = 0.86F), -55.10 (s, J = 2.00F); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 168.3, 168.2, 161.5 – 157.4 (m), 131.2,

130.6, 119.9, 119.4, 110.7, 110.4 (t, J_{C-F} = 314.3 Hz), 52.7, 52.5, 52.3 (t, J_{C-F} = 3.8 Hz), 51.0, 48.4 (t, J_{C-F} = 4.1 Hz), 47.6; HRMS (ESI): $C_8H_{10}BrF_2NNaO_3^+$ $[M+Na]^+$ Calcd 307.9704, Found 307.9681.

N-allyl-2-bromo-2,2-difluoro-N-(4-phenylbutyl)acetamide ***(1y).*** as an mixture of inseparable atropisomers: Pale yellow oil (1.19 g, 3.5 mmol, overall yield 69%); IR (neat) *v* 1681, 1452, 1143, 983, 868, 745, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.12 (m, 2H), 7.21 – 7.16 (m, 3H), 5.81 – 5.70 (m, 1H), 5.28 – 5.17 (m, 2H), 4.05 (d, *J* = 5.4 Hz, 1.14H), 3.97 (d, *J* = 5.6 Hz, 0.91H), 3.44 – 3.38 (m, 2H), 2.68 – 2.56 (m, 2H), 1.64 – 1.63 (m, 4H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -54.07 (s, 2.00F), -54.13 (s, 1.58F); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1 (t, J_{C-F} = 26.4 Hz), 159.0 (t, J_{C-F} = 26.3 Hz), 141.9, 141.5, 132.1, 131.2, 128.44, 128.40, 128.38, 128.33, 126.0, 125.9, 118.9, 118.2, 111.1 (t, J_{C-F} = 315.1 Hz), 110.0 (t, J_{C-F} = 315.0 Hz), 50.8 (t, J_{C-F} = 3.8 Hz), 49.4, 48.0 (t, J_{C-F} = 3.5 Hz), 46.7, 35.5, 35.4, 28.4, 28.3, 27.9, 26.0; HRMS (ESI): $C_{15}H_{18}BrF_2NNaO^+$ $[M+Na]^+$ Calcd 368.0432, Found 368.0411.

N-allyl-2-bromo-2,2-difluoro-N-(pyridin-2-ylmethyl)acetamide ***(1z).*** as an mixture of inseparable atropisomers: Pale yellow oil (897 mg, 295 mmol, overall yield 59%); IR (neat) *v* 1681, 1436, 1133, 993, 930, 750, 603 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 – 8.55 (m, 1H), 7.73 – 7.66 (m, 1H), 7.27 – 7.19 (m, 2H), 5.87 – 5.74 (m, 1H), 5.31 – 5.17 (m, 2H), 4.84 (s, 0.72H), 4.71 (s, 1.28H), 4.22 (d, *J* = 5.4 Hz, 1.28H), 4.07 (d, *J* = 5.6 Hz, 0.74H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -54.11 (s, *J* = 1.09F), -54.31 (s, *J* = 2.00F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 159.6, 155.7, 155.4, 149.7, 149.4, 137.0, 131.4, 130.4, 122.8, 122.7, 122.2, 120.9, 119.5, 118.9, 111.0, 52.6 (t, *J* = 3.3 Hz), 51.2 – 51.1 (m), 49.9; HRMS (ESI): $C_{11}H_{11}BrF_2N_2NaO^+$ $[M+Na]^+$ Calcd 326.9915, Found 326.9894.

Characterization data of products 3 and 5

3,3-difluoro-1-phenyl-4-((phenylthio)methyl)pyrrolidin-2-one ***(3a).*** Pale yellow solid (45 mg, 0.14 mmol, yield 71%); m.p. 82 – 83 ℃; IR (neat) *v* 2924, 1722, 1494, 1202, 1147, 1022, 757, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.61 (m, 2H), 7.43 – 7.41 (m, 4H), 7.36 – 7.32 (m, 2H), 7.29 – 7.28 (m, 1H), 7.24 – 7.23 (m, 1H), 4.02 – 3.97 (m, 1H), 3.72 – 3.68 (m, 1H), 3.50 (dd, *J* = 13.6, 4.0 Hz, 1H), 2.99 (dd, *J* = 13.5, 11.0 Hz, 1H), 2.91 – 2.76 (m, 1H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -109.46 (d, *J* = 268.8 Hz), -116.89 (d, *J* = 268.5 Hz); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.1 – 161.3 (m), 137.8, 133.7, 130.6, 129.5, 129.2, 127.5, 126.3, 112.0, 116.9 (dd, J_{C-F} = 255.2, 250.0 Hz), 48.1 (d, J_{C-F} = 5.9 Hz), 39.3 (t, J_{C-F} = 20.9 Hz), 30.2 (d, J_{C-F} = 7.6 Hz); HRMS (ESI):

$C_{17}H_{15}F_2NNaOS^+$ $[M+Na]^+$ Calcd 342.0735, Found 342.0729.

3,3-difluoro-1-(4-fluorophenyl)-4-((phenylthio)methyl)pyrrolidin-2-one ***(3b).*** Pale yellow oil (40 mg, 0.12 mmol, yield 61%); IR (neat) *v* 2917, 1728, 1509, 1230, 1024, 833, 741, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 7.43 – 7.41 (m, 2H), 7.36 – 7.33 (m, 2H), 7.30 – 7.28 (m, 1H), 7.13 – 7.08 (m, 2H), 3.97 (t, *J* = 9.0 Hz, 1H), 3.68 (t, *J* = 8.7 Hz, 1H), 3.50 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.99 (dd, *J* = 13.4, 11.1 Hz, 1H), 2.92 – 2.77 (m, 1H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -109.47 (d, *J* = 269.2 Hz), -114.87, -116.80 (d, *J* = 269.0 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 160.4 (d, J_{C-F} = 246.9 Hz), 133.9, 133.6, 130.6, 129.5, 127.5, 121.8 (d, J_{C-F} = 8.2 Hz), 116.1 (d, J_{C-F} = 22.7 Hz), 48.3 (d, J_{C-F} = 5.9 Hz), 39.4 (t, J_{C-F} = 21.0 Hz), 30.22 (d, J_{C-F} = 7.6 Hz); HRMS (ESI): $C_{17}H_{14}F_3NNaOS^+$ $[M+Na]^+$ Calcd 360.0640, Found 360.0645.

1-(4-bromophenyl)-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3c)*** Pale yellow oil (48 mg, 0.12 mmol, yield 62%); IR (neat) *v* 2918, 1710, 1493, 1296, 1075, 970, 750, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.51 (m, 4H), 7.42 (d, *J* = 7.3 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 3.96 (t, *J* = 9.0 Hz, 1H), 3.67 (t, *J* = 8.4 Hz, 1H), 3.50 (dd, *J* = 13.8, 4.1 Hz, 1H), 2.99 (dd, *J* = 13.4, 11.2 Hz, 1H), 2.91 – 2.76 (m, 1H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -109.58 (d, *J* = 269.6 Hz), -116.73 (d, *J* = 269.2 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 161.9 (t, J_{C-F} = 31.2 Hz), 136.8, 133.5, 132.2, 130.6, 129.5, 127.6, 121.3, 119.3, 116.7 (dd, J_{C-F} = 255.6, 250.1 Hz), 47.9 (d, J_{C-F} = 6.0 Hz), 39.2 (t, J_{C-F} = 21.0 Hz), 30.1 (d, J_{C-F} = 7.6 Hz); HRMS (ESI): $C_{17}H_{14}BrF_2NNaOS^+$ $[M+Na]^+$ Calcd 419.9840, Found 419.9863.

3,3-difluoro-4-((phenylthio)methyl)-1-(p-tolyl)pyrrolidin-2-one ***(3d).*** Pale yellow solid (38 mg, 0.11 mmol, yield 57%); m.p. 82 – 83 ℃; IR (neat) *v* 2922, 1725, 1439, 1252, 1100, 1000, 739, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J*= 7.2 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 3.96 (t, *J* = 9.1 Hz, 1H), 3.67 (t, *J* = 8.7 Hz, 1H), 3.49 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.98 (dd, *J* = 13.5, 11.0 Hz, 1H), 2.90 – 2.75 (m, 1H), 2.35 (s, 3H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -109.33 (d, *J* = 268.5 Hz), -116.82 (d, *J* = 268.4 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 161.7 (t, J_{C-F} = 31.2 Hz), 136.2, 135.3, 133.7, 130.6, 129.7, 129.4, 127.5, 120.0, 117.0 (dd, J_{C-F} = 255.0, 249.9 Hz), 48.1 (d, J_{C-F} = 5.9 Hz), 39.4 (t, J_{C-F} = 21.1 Hz), 30.3 (d, J_{C-F} = 7.7 Hz), 20.9; HRMS (ESI): $C_{18}H_{17}F_2NNaOS^+$ $[M+Na]^+$ Calcd 356.0891, Found 356.0889.

1-(3-bromophenyl)-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3e)***. Pale yellow oil

(62 mg, 0.16 mmol, yield 78%); IR (neat) *v* 2922, 1731, 1478, 1147, 1024, 934, 741, 679 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 7.3 Hz, 2H), 7.39 – 7.33 (m, 3H), 7.30 – 7.27 (m, 2H), 3.97 (t, *J* = 9.0 Hz, 1H), 3.67 (t, *J* = 8.6 Hz, 1H), 3.49 (dd, *J* = 13.8, 4.2 Hz, 1H), 2.99 (dd, *J* = 13.5, 11.1 Hz, 1H), 2.91 – 2.76 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -109.58 (d, *J* = 269.2 Hz), -116.86 (d, *J* = 269.5 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.0 (t, J_{C-F} = 31.4 Hz) 139.0, 133.6, 130.7, 130.5, 129.5, 129.2, 127.6, 122.9, 122.7, 118.4, 116.6 (dd, J_{C-F} = 255.7, 250.3 Hz), 47.9 (d, J_{C-F} = 5.9 Hz), 39.3 (t, J_{C-F} = 20.8 Hz), 30.2 (d, J_{C-F} = 7.4 Hz); HRMS (ESI): $C_{17}H_{14}BrF_2NNaOS^+$ $[M+Na]^+$ Calcd 419.9840, Found 419.9870.

3,3-difluoro-4-((phenylthio)methyl)-1-(o-tolyl)pyrrolidin-2-one ***(3f)***. Pale yellow oil (22 mg, 0.070 mmol, yield 33%); IR (neat) *v* 2919, 1732, 1493, 1195, 1023, 851, 762, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.30 – 7.28 (m, 4H), 7.11 (d, *J* = 7.1 Hz, 1H), 3.86 – 3.81 (m, 1H), 3.63 – 3.59 (m, 1H), 3.52 (dd, *J* = 13.6, 4.0 Hz, 1H), 3.04 – 2.98 (m, 1H), 2.94 – 2.83 (m, 1H), 2.20 (s, 3H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.28 (d, *J* = 269.4 Hz), -117.20 (d, *J* = 269.1 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.2, 135.5, 135.2, 133.9, 131.5, 130.5, 129.4, 129.0, 127.4, 127.1, 126.1, 50.4 (d, J_{C-F} = 5.8 Hz), 40.4 (t, J_{C-F} = 21.0 Hz), 30.4 (d, J_{C-F} = 7.9 Hz), 17.7; HRMS (ESI): $C_{18}H_{17}F_2NNaOS^+$ $[M+Na]^+$ Calcd 356.0891, Found 356.0893.

3,3-difluoro-1-(2-methoxyphenyl)-4-((phenylthio)methyl)pyrrolidin-2-one ***(3g)***. Pale yellow oil (24 mg, 0.070 mmol, yield 34%); IR (neat) *v* 2954, 1733, 1504, 1160, 1022, 851, 741, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.6 Hz, 2H), 7.36 – 7.29 (m, 4H), 7.25 (s, 1H), 7.01 – 6.96 (m, 2H), 3.89 – 3.87 (m, 1H), 3.82 (s, 3H), 3.73 – 3.68 (m, 1H), 3.48 (dd, *J* = 13.5, 4.2 Hz, 1H), 3.04 – 2.98 (m, 1H), 2.91 – 2.80 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.33 (d, *J* = 268.5 Hz), -117.84 (d, *J* = 268.5 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.4, 134.1, 130.5, 129.8, 129.3, 127.9, 127.3, 125.2, 121.0, 112.2, 55.7, 49.6 (d, J_{C-F} = 5.3 Hz), 40.3 (t, J_{C-F} = 21.0 Hz), 30.3 (d, J_{C-F} = 7.9 Hz); HRMS (ESI): $C_{18}H_{17}F_2NNaO_2S^+$ $[M+Na]^+$ Calcd 372.0840, Found 372.0866.

1-benzyl-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3h).*** Pale yellow oil (46 mg, 0.14 mmol, yield 69%); IR (neat) *v* 2918, 1735, 1251, 1080, 1025, 995, 739, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 7H), 7.23 – 7.21 (m, 3H), 4.55 (d, *J* = 14.6 Hz, 1H), 4.45 (d, *J* = 14.6 Hz, 1H), 3.44 – 3.36 (m, 2H), 3.10 – 3.06 (m, 1H), 2.85 – 2.79 (m, 1H), 2.74 – 2.57 (m, 1H);

^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.01 (d, J = 268.8 Hz), -116.88 (d, J = 269.1 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.1 (t, J_{C-F} = 30.4 Hz), 134.4, 133.8, 130.4, 129.3, 129.1, 128.3, 127.3, 47.4, 46.5 (d, J_{C-F} = 6.2 Hz) 39.6 (t, J_{C-F} = 21.1 Hz), 30.4 (d, J_{C-F} = 8.2 Hz); HRMS (ESI): $C_{18}H_{17}F_2NNaOS^+$ $[M+Na]^+$ Calcd 356.0891, Found 356.0909.

1-(3-bromobenzyl)-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3i).*** Pale yellow oil (55 mg, 0.13 mmol, yield 67%); IR (neat) *v* 2918, 1727, 1439, 1251, 1134, 997, 741, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.8 Hz, 1H), 7.39 – 7.29 (m, 6H), 7.23 – 7.21 (m, 1H), 7.15 (d, J = 7.6 Hz, 1H), 4.50 (d, J = 14.7 Hz, 1H), 4.42 (d, J = 14.7 Hz, 1H), 3.44 – 3.36 (m, 2H), 3.11 – 3.07 (m, 1H), 2.88 – 2.81 (m, 1H), 2.76 – 2.61 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.17 (d, J = 269.7 Hz), -116.91 (d, J = 269.4 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.2 (t, J_{C-F} = 31.1 Hz), 136.7, 133.8, 131.6, 131.3, 130.7, 130.5, 129.4, 127.4, 126.9, 123.0, 117.1 (dd, J_{C-F} = 249.5, 253.9 Hz), 46.9, 46.6 (d, J_{C-F} = 6.1 Hz), 39.8 (t, J_{C-F} = 21.2 Hz), 30.4 (d, J_{C-F} = 7.0 Hz); HRMS (ESI): $C_{18}H_{16}BrF_2NNaOS^+$ $[M+Na]^+$ Calcd 433.9996, Found 434.0009.

3,3-difluoro-1-(3-methoxybenzyl)-4-((phenylthio)methyl)pyrrolidin-2-one ***(3j).*** Pale yellow oil (46 mg, 0.13 mmol, yield 63%); IR (neat) *v* 2925, 1726, 1438, 1042, 1255, 995, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.24 (m, 6H), 6.86 (d, J = 8.3 Hz, 1H), 6.79 (d, J = 7.2 Hz, 1H), 6.74 (s, 1H), 4.51 (d, J = 14.6 Hz, 1H), 4.42 (d, J = 14.5 Hz, 1H), 3.79 (s, 3H), 3.44 – 3.35 (m, 2H), 3.11 – 3.06 (m, 1H), 2.86 – 2.80 (m, 1H), 2.74 – 2.59 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.00 (d, J = 269.0 Hz), -116.94 (d, J = 269.4 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.1 (t, J_{C-F} = 30.8 Hz), 160.1, 135.9, 133.9, 130.4, 130.1, 129.3, 127.3, 120.5, 117.3 (dd, J_{C-F} = 255.7, 250.9 Hz), 113.8, 113.7, 55.3, 47.4, 46.5 (d, J_{C-F} = 6.1 Hz), 39.7 (t, J_{C-F} = 21.1 Hz), 30.4 (d, J_{C-F} = 8.1 Hz); HRMS (ESI): $C_{19}H_{19}F_2NNaO_2S^+$ $[M+Na]^+$ Calcd 386.0997, Found 386.1011.

1-(4-bromobenzyl)-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3k).*** Pale yellow oil (45 mg, 0.11 mmol, yield 55%); IR (neat) *v* 2924, 1725, 1488, 1252, 1069, 739, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 2H), 7.34 – 7.27 (m, 5H), 7.10 (d, J = 8.4 Hz, 2H), 4.50 (d, J = 14.7 Hz, 1H), 4.39 (d, J = 14.7 Hz, 1H), 3.42 – 3.36 (m, 2H), 3.10 – 3.05 (m, 1H), 2.86 – 2.79 (m, 1H), 2.74 – 2.59 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.13 (d, J = 269.7 Hz), -116.97 (d, J = 269.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.8, 133.4, 132.2, 130.4, 130.0, 129.4, 127.4, 122.5, 46.4, 46.5 (d, J_{C-F} = 6.1 Hz), 39.7 (t, J_{C-F} = 21.3 Hz), 30.4 (d, J_{C-F} = 8.0 Hz); HRMS (ESI): $C_{18}H_{16}BrF_2NNaOS^+$ $[M+Na]^+$ Calcd 433.9996, Found 434.0013.

1-(4-chlorobenzyl)-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3l).*** Pale yellow oil (29 mg, 0.080 mmol, yield 40%); IR (neat) *v* 2920, 1726, 1491, 1253, 1015, 802, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 7H), 7.16 (d, *J* = 8.3 Hz, 2H), 4.51 (d, *J* = 14.7 Hz, 1H), 4.41 (d, *J* = 14.7 Hz, 1H), 3.42 – 3.36 (m, 2H), 3.11 – 3.05 (m, 1H), 2.85 – 2.79 (m, 1H), 2.74 – 2.59 (m, 1H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -110.12 (d, *J* = 269.2 Hz), -116.99 (d, *J* = 269.3 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 163.2 (t, J_{C-F} = 32.0 Hz), 134.4, 133.8, 132.9, 130.5, 129.7, 129.4, 129.3, 127.4, 46.8, 46.5 (d, J_{C-F} = 7.4 Hz), 39.7 (t, J_{C-F} = 21.5 Hz), 30.4 (d, J_{C-F} = 8.0 Hz); HRMS (ESI): $C_{18}H_{16}ClF_2NNaOS^+$ $[M+Na]^+$ Calcd 390.0501, Found 390.0501.

3,3-difluoro-1-(4-fluorobenzyl)-4-((phenylthio)methyl)pyrrolidin-2-one ***(3m).*** Pale yellow oil (40 mg, 0.11 mmol, yield 57%); IR (neat) *v* 2918, 1725, 1509m 1223, 1096, 819, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 5H), 7.22 – 7.19 (m, 2H), 7.04 (t, *J* = 8.5 Hz, 2H), 4.52 (d, *J* = 14.6 Hz, 1H), 4.42 (d, *J* = 14.6 Hz, 1H), 3.43 – 3.36 (m, 2H), 3.10 – 3.05 (m, 1H), 2.85 – 2.79 (m, 1H), 2.74 – 2.59 (m, 1H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -110.10 (d, *J* = 269.4 Hz), -113.39, -117.03 (d, *J* = 269.2 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 163.1 (t, J_{C-F} = 30.3 Hz), 162.7 (d, J_{C-F} = 247.3 Hz), 133.8, 130.5, 130.3 (d, *J* = 3.3 Hz), 130.1 (d, *J* = 8.4 Hz), 129.4, 127.4, 116.05 (d, J_{C-F} = 21.7 Hz), 46.7, 46.4 (d, J_{C-F} = 6.2 Hz), 39.7 (t, J_{C-F} = 20.6 Hz), 30.39 (d, J_{C-F} = 8.1 Hz); HRMS (ESI): $C_{18}H_{16}F_3NNaOS^+$ $[M+Na]^+$ Calcd 374.0797, Found 374.0813.

3,3-difluoro-1-(4-methylbenzyl)-4-((phenylthio)methyl)pyrrolidin-2-one ***(3n)****.* Pale yellow oil (53 mg, 0.15 mmol, yield 77%); IR (neat) *v* 2918, 1726, 1439, 1210, 1060, 740, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 5H), 7.16 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 4.50 (d, *J* = 14.5 Hz, 1H), 4.41 (d, *J* = 14.5 Hz, 1H), 3.43-3.35 (m, 2H), 3.09 – 3.04 (m, 1H), 2.85 – 2.78 (m, 1H), 2.73 – 2.57 (m, 1H), 2.35 (s, 3H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -109.91 (d, *J* = 269.0 Hz), -116.93 (d, *J* = 268.9 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 163.0 (t, J_{C-F} = 30.7 Hz), 138.1, 133.9, 131.3, 130.4, 129.7, 129.3, 128.3, 127.3, 47.2, 46.4 (d, J_{C-F} = 6.1 Hz), 39.6 (t, J_{C-F} = 21.1 Hz), 30.4 (d, J_{C-F} = 8.1 Hz), 21.1; HRMS (ESI): $C_{19}H_{19}F_2NNaOS^+$ $[M+Na]^+$ Calcd 370.1048, Found 370.1057.

3,3-difluoro-1-(4-methoxybenzyl)-4-((phenylthio)methyl)pyrrolidin-2-one **3o**: Pale yellow oil (47 mg, 0.13 mmol, yield 65%); IR (neat) *v* 2918, 1727, 1489, 1257, 1042, 876, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.28 (m, 4H), 7.24 – 7.22 (m, 1H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.48 (d, *J* = 14.5 Hz, 1H), 4.39 (d, *J* = 14.5 Hz, 1H), 3.81 (s, 3H), 3.42 – 3.31 (m,

2H), 3.08 – 3.03 (s, 1H), 2.86 – 2.78 (m, 1H), 2.71 – 2.57 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -109.86 (d, J = 268.9 Hz), -116.94 (d, J = 30.5 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.0 (t, $J_{C\text{-}F}$ = 30.6 Hz), 159.6, 133.9, 130.42, 129.8, 129.3, 127.8, 126.4, 117.3 (dd, $J_{C\text{-}F}$ = 249.5, 254.0 Hz), 114.4, 55.3, 46.9, 46.3 (d, $J_{C\text{-}F}$ = 6.0 Hz), 39.6 (t, $J_{C\text{-}F}$ = 21.1 Hz), 30.4 (d, $J_{C\text{-}F}$ = 8.1 Hz); HRMS (ESI): $C_{19}H_{19}F_2NNaO_2S^+$ $[M+Na]^+$ Calcd 386.0997, Found 386.1011.

1-(2-bromobenzyl)-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3p)***. Pale yellow oil (49 mg, 0.12 mmol, yield 59%); IR (neat) *v* 2926, 1728, 1439, 1252, 1136, 992, 741, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.9 Hz, 1H), 7.36 – 7.29 (m, 5H), 7.24 – 7.18 (m, 3H), 4.70 (d, J = 15.0 Hz, 1H), 4.62 (d, J = 15.0 Hz, 1H), 3.50 – 3.41 (m, 1H), 3.38 (dd, J = 13.6, 4.5 Hz, 1H), 3.13 – 3.08 (m, 1H), 2.86 (dd, J = 13.3, 10.9 Hz, 1H), 2.77 – 2.61 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.17 (d, J = 269.1 Hz), -117.02 (d, J = 269.5 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.2 (t, $J_{C\text{-}F}$ = 30.6 Hz), 133.9, 133.7, 133.2, 130.5, 130.4, 130.0, 129.3, 128.1, 127.3, 124.0, 117.1 (dd, $J_{C\text{-}F}$ = 255.7, 251.0 Hz), 47.2, 46.8 (d, $J_{C\text{-}F}$ = 6.0 Hz), 39.9 (t, $J_{C\text{-}F}$ = 20.8 Hz), 30.4 (d, $J_{C\text{-}F}$ = 8.1 Hz); HRMS (ESI): $C_{18}H_{16}BrF_2NNaOS^+$ $[M+Na]^+$ Calcd 433.9996, Found 434.0022.

1-(2,4-difluorobenzyl)-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3q)***. Pale yellow oil (25 mg, 0.07 mmol, yield 33%); IR (neat) *v* 2920, 1728, 1506, 1254, 1095, 850, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 6H), 6.91 – 6.82 (m, 2H), 4.57 (d, J = 14.7 Hz, 1H), 4.48 (d, J = 14.7 Hz, 1H), 3.47 (t, J = 9.1 Hz, 1H), 3.38 (dd, J = 13.6, 4.3 Hz, 1H), 3.15 – 3.11 (m, 1H), 2.84 (dd, J = 13.3, 11.1 Hz, 1H), 2.76 – 2.60 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -108.73 (d, J = 7.9 Hz), -110.25 (d, J = 269.8 Hz), -114.14 (d, J = 7.8 Hz), -117.12 (d, J = 269.4 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.3 – 159.8 (m), 133.8, 131.95 (dd, $J_{C\text{-}F}$ = 9.7, 5.2 Hz), 130.5, 129.4, 127.4, 120.20 – 113.52 (m), 112.18 (dd, $J_{C\text{-}F}$ = 21.4, 3.8 Hz), 104.19 (t, $J_{C\text{-}F}$ = 25.5 Hz), 46.8 (d, $J_{C\text{-}F}$ = 5.9 Hz), 40.4 (d, $J_{C\text{-}F}$ = 3.2 Hz), 39.8 (t, $J_{C\text{-}F}$ = 20.7 Hz), 30.4 (d, $J_{C\text{-}F}$ = 8.1 Hz); HRMS (ESI): $C_{18}H_{15}F_4NNaOS^+$ $[M+Na]^+$ Calcd 392.0703, Found 392.0721.

1-cyclopropyl-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3r).*** Pale yellow oil (45 mg, 0.16 mmol, yield 80%); IR (neat) *v* 2928, 1724, 1439, 1208, 1101, 984, 740, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.38 (m, 2H), 7.35 – 7.32 (m, 2H), 7.28 – 7.25 (m, 1H), 3.50 – 3.45 (m, 1H), 3.39 (dd, J =13.7, 4.4 Hz, 1H), 3.18 – 3.13 (m, 1H), 2.86 (dd, J = 13.2, 11.3 Hz, 1H), 2.75 – 2.57 (m, 2H), 0.85 – 0.81 (m, 2H), 0.79 – 0.73 (m, 2H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -109.84 (d, J = 268.9 Hz), -117.16 (d, J = 268.6 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.0 (t,

$J_{C\text{-}F}$ = 30.3 Hz), 133.9, 130.4, 129.4, 127.3, 117.4 (dd, J = 255.4, 250.7 Hz), 47.4 (d, $J_{C\text{-}F}$ = 6.0 Hz), 39.7 (t, $J_{C\text{-}F}$ = 20.9 Hz), 30.3 (d, $J_{C\text{-}F}$ = 8.2 Hz), 26.2, 5.1, 4.9; HRMS (ESI): $C_{14}H_{15}F_2NNaOS^+$ $[M+Na]^+$ Calcd 306.0735, Found 306.0747.

1-cyclobutyl-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3r).*** Pale yellow oil (38 mg, 0.13 mmol, yield 64%); IR (neat) ν 2921, 1717, 1480, 1269, 1100, 1012, 971, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.40 (m, 2H), 7.37 – 7.33 (m, 2H), 7.29 – 7.27 (m, 1H), 4.61 (p, J = 8.8 Hz, 1H), 3.66 (ddd, J = 10.0, 8.1, 1.8 Hz, 1H), 3.43 (dd, J = 13.7, 4.3 Hz, 1H), 3.33 – 3.19 (m, 1H), 2.89 (dd, J = 13.4, 11.2 Hz, 1H), 2.76 – 2.62 (m, 1H), 2.22 – 2.14 (m, 4H), 1.78 – 1.70 (m, 2H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -109.87 (d, J = 268.4 Hz), -116.96 (d, J = 268.6 Hz); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.4 (t, $J_{C\text{-}F}$ = 30.7 Hz), 133.9, 130.4, 129.4, 127.3, 117.6 (dd, $_{C\text{-}F}$ = 255.5, 250.5 Hz), 47.1, 43.6 (d, $J_{C\text{-}F}$ = 6.2 Hz), 39.6 (t, $J_{C\text{-}F}$ = 21.0 Hz), 30.4 (d, $J_{C\text{-}F}$ = 8.1 Hz), 27.0, 26.8, 15.1; HRMS (ESI): $C_{15}H_{17}F_2NNaOS^+$ $[M+Na]^+$ Calcd 320.0891, Found 320.0909.

1-cyclopentyl-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3t).*** Pale yellow oil (30 mg, 0.10 mmol, yield 49%); IR (neat) ν 2918, 1720, 1439, 1254, 1133, 991, 741, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.39 (m, 2H), 7.36 – 7.32 (m, 2H), 7.29 – 7.25 (m, 1H), 4.47 (p, J = 8.1 Hz, 1H), 3.52 (t, J = 8.9 Hz, 1H), 3.42 (dd, J = 13.7, 4.2 Hz, 1H), 3.18 – 3.14 (m, 1H), 2.91 – 2.85 (m, 1H), 2.75 – 2.60 (m, 1H), 1.94 – 1.82 (m, 2H), 1.76 – 1.62 (m, 4H), 1.56 – 1.46 (m, 2H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -110.04 (d, J = 268.3 Hz), -117.37 (d, J = 268.3 Hz); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.9 (t, $J_{C\text{-}F}$ = 30.3 Hz), 134.0, 130.4, 129.3, 127.3, 53.4, 43.2 (d, $J_{C\text{-}F}$ = 6.1 Hz), 39.8 (t, $J_{C\text{-}F}$ = 21.3 Hz), 31.5 (d, $J_{C\text{-}F}$ = 8.0 Hz), 28.7, 24.1; HRMS (ESI): $C_{16}H_{19}F_2NNaOS^+$ $[M+Na]^+$ Calcd 334.1048, Found 334.1047.

1-cyclohexyl-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one **(3t).** Pale yellow oil (35 mg, 0.11 mmol, yield 54%); IR (neat) ν 2918, 1711, 1453, 1257, 1056, 976, 733, 688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.38 (m, 2H), 7.36 – 7.32 (m, 2H), 7.28 – 7.24 (m, 1H), 3.99 – 3.95 (m, 1H), 3.55 (t, J = 9.0 Hz, 1H), 3.42 (dd, J = 13.6, 4.2 Hz, 1H), 3.16 (t, J = 8.2 Hz, 1H), 2.89 – 2.83 (m, 1H), 2.73 – 2.58 (m, 1H), 1.83 – 1.81 (m, 2H), 1.74 – 1.68 (m, 3H), 1.43 – 1.34 (m, 5H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -110.13 (d, J = 268.1 Hz), -117.30 (d, J = 267.9 Hz); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 134.0, 130.3, 129.4, 127.3, 51.6, 43.1 (d, $J_{C\text{-}F}$ = 6.2 Hz), 39.7 (t, $J_{C\text{-}F}$ = 21.5 Hz), 30.3 (d, $J_{C\text{-}F}$ = 8.3 Hz), 29.8, 29.6, 25.2, 25.1; HRMS (ESI): $C_{17}H_{21}F_2NNaOS^+$ $[M+Na]^+$ Calcd 348.1204, Found 348.1216.

3,3-difluoro-4-((phenylthio)methyl)-1-(2,2,2-trifluoroethyl)pyrrolidin-2-one ***(3v)***. Pale yellow oil (58 mg, 0.18 mmol, yield 89%); IR (neat) *v* 2918, 1743, 1489, 1259, 1081, 905, 742, 659 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.39 (m, 2H), 7.36 – 7.33 (m, 2H), 7.30 – 7.28 (m, 1H), 4.02 (dq, *J* = 17.7, 8.9 Hz, 1H), 3.85 (dq, *J* = 17.2, 8.7 Hz, 1H), 3.70 (t, *J* = 9.0 Hz, 1H), 3.41 (dt, *J* = 16.0, 7.9 Hz, 2H), 2.91 (dd, *J* = 13.4, 11.0 Hz, 1H), 2.83 – 2.68 (m, 1H); $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -69.45, -111.43 (d, *J* = 271.0 Hz), -117.56 (d, *J* = 271.3 Hz); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.9 (t, J_{C-F} = 31.6 Hz), 133.6, 130.7, 129.5, 127.6, 123.4 (q, J_{C-F} = 280.4 Hz), 116.2 (dd, J_{C-F} = 255.9, 250.9 Hz), 48.1 (d, J_{C-F} = 5.9 Hz), 44.8 (q, J_{C-F} = 35.1 Hz), 40.1 (t, J_{C-F} = 20.9 Hz), 30.1 (d, 7.8 Hz); HRMS (ESI): $C_{13}H_{12}F_5NNaOS^+$ $[M+Na]^+$ Calcd 348.0452, Found 348.0455.

1-butyl-3,3-difluoro-4-((phenylthio)methyl)pyrrolidin-2-one ***(3w).*** Pale yellow oil (38 mg, 0.13 mmol, yield 64%); IR (neat) *v* 2917, 1727, 1510, 1293, 1098, 836, 739, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.29 – 7.25 (m, 1H), 3.55 – 3.50 (m, 1H), 3.42 (ddd, *J* = 16.6, 11.3, 5.8 Hz, 2H), 3.30 – 3.21 (m, 2H), 2.91 – 2.85 (m, 1H), 2.77 – 2.58 (m, 1H), 1.53 (p, *J* = 7.4 Hz, 2H), 1.34 – 1.28 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -110.10 (d, *J* = 268.5 Hz), -116.98 (d, *J* = 268.5 Hz); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.0 (t, J_{C-F} = 30.0 Hz), 133.9, 130.4, 129.4, 127.3, 117.4 (dd, J_{C-F} = 255.0, 250.4 Hz), 46.9 (d, J_{C-F} = 6.6 Hz), 43.2, 39.7 (t, J_{C-F} = 21.2 Hz), 30.4 (d, J_{C-F} = 8.4 Hz), 28.8, 19.9, 13.6; HRMS (ESI): $C_{15}H_{19}F_2NNaOS^+$ $[M+Na]^+$ Calcd 322.1048, Found 322.1031.

Methyl 2-(3,3-difluoro-2-oxo-4-((phenylthio)methyl)pyrrolidin-1-yl)acetate ***(3x).*** Pale yellow oil (33 mg, 0.10 mmol, yield 52%); IR (neat) *v* 2920, 1728, 1438, 1207, 1101, 1023, 852, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.29 – 7.25 (m, 1H), 4.18 (d, *J* = 17.5 Hz, 1H), 4.06 (d, *J* = 17.6 Hz, 1H), 3.76 (s, 3H), 3.65 (t, *J* = 8.9 Hz, 1H), 3.45 – 3.40 (m, 2H), 2.94 (dd, *J* = 13.2, 11.4 Hz, 1H), 2.85 – 2.70 (m, 1H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -110.38 (d, *J* = 270.4 Hz), -117.37 (d, *J* = 270.3 Hz); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.7, 163.7 (t, J_{C-F} = 30.8 Hz), 133.8, 130.5, 129.4, 127.4, 116.8 (dd, J_{C-F} = 255.1, 251.4 Hz), 52.6, 47.78 (d, J_{C-F} = 5.8 Hz), 44.3, 39.8 (t, J_{C-F} = 21.3 Hz), 30.3 (d, J_{C-F} = 8.0 Hz); HRMS (ESI): $C_{14}H_{15}F_2NNaO_3S^+$ $[M+Na]^+$ Calcd 338.0633, Found 338.0637.

3,3-difluoro-1-(4-phenylbutyl)-4-((phenylthio)methyl)pyrrolidin-2-one ***(3y).*** Pale yellow oil (41 mg, 0.11 mmol, yield 54%); IR (neat) *v* 2919, 1725, 1439, 1253, 1143, 1066, 980, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.37 (m, 2H), 7.34 – 7.31 (m, 2H), 7.29 – 7.26 (m, 4H), 7.20 –

7.18 (m, 1H), 7.16 – 7.14 (m, 1H), 3.48 – 3.38 (m, 3H), 3.31 – 3.24 (m, 1H), 3.17 – 3.13 (m, 1H), 2.85 (dd, J = 13.3, 11.2 Hz, 1H), 2.74 – 2.61 (m, 3H), 1.62 – 1.56 (m, 4H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.05 (d, J = 268.4 Hz), -116.89 (d, J = 268.6 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.1 (t, J_{C-F} = 30.0 Hz), 141.6, 133.9, 130.4, 129.4, 128.42, 128.40, 127.3, 126.0, 117.3 (dd, J_{C-F} = 255.3, 250.3 Hz), 47.0 (d, J_{C-F} = 6.2 Hz), 43.2, 39.7 (t, J_{C-F} = 21.1 Hz), 35.2, 30.4 (d, J_{C-F} = 8.1 Hz), 28.2, 26.1; HRMS (ESI): $C_{21}H_{23}F_2NNaOS^+$ $[M+Na]^+$ Calcd 398.1361, Found 398.1367.

3,3-difluoro-4-((phenylthio)methyl)-1-(pyridin-2-ylmethyl)pyrrolidin-2-one ***(3z).*** Pale yellow oil (30 mg, 0.90 mmol, yield 45%); IR (neat) v 2919, 1726, 1437, 1210, 1097, 1001, 741, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 4.4 Hz, 1H), 7.68 (td, J = 7.7, 1.6 Hz, 1H), 7.37 – 7.29 (m, 4H), 7.26 – 7.22 (m, 3H), 4.68 (d, J = 15.0 Hz, 1H), 4.57 (d, J = 15.0 Hz, 1H), 3.76 – 3.55 (m, 1H), 3.40 (dd, J = 13.6, 4.4 Hz, 1H), 3.34 – 3.31 (m, 1H), 2.89 (dd, J = 13.2, 11.0 Hz, 1H), 2.80 – 2.66 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.00 (d, J = 269.1 Hz), -117.09 (d, J = 269.1 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.3 (t, J_{C-F} = 30.1 Hz), 154.6, 149.6, 137.2, 134.0, 130.5, 129.3, 127.3, 123.0, 122.5, 117.3 (dd, J_{C-F} = 255.5, 251.1 Hz), 49.0, 47.5 (d, J_{C-F} = 5.8 Hz), 39.8 (t, J_{C-F} = 21.1 Hz), 30.4 (d, J_{C-F} = 8.1 Hz); HRMS (ESI): $C_{17}H_{16}F_2N_2NaOS^+$ $[M+Na]^+$ Calcd 357.0844, Found 357.0853.

4-(((4-chlorophenyl)thio)methyl)-3,3-difluoro-1-phenylpyrrolidin-2-one ***(3aa).*** Pale yellow solid (39 mg, 0.11 mmol, yield 55%); m.p. 116 – 117 ℃; IR (neat) v 2918, 1722, 1476, 1202, 1057, 809, 760, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.0 Hz, 2H), 7.42 (t, J = 8.0 Hz, 2H), 7.36 – 7.30 (m, 4H), 7.27 – 7.23 (m, 1H), 4.00 (t, J = 8.8 Hz, 1H), 3.70 (t, J = 8.4 Hz, 1H), 3.46 (dd, J = 13.7, 4.4 Hz, 1H), 2.99 (dd, J = 13.5, 10.9 Hz, 1H), 2.89 – 2.74 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -109.26 (d, J = 269.0 Hz), -116.85 (d, J = 268.7 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.8 (t, J_{C-F} = 31.1 Hz), 137.7, 133.7, 132.2, 131.9, 129.6, 129.2, 126.3, 119.9, 116.8 (dd, J_{C-F} = 255.4, 250.3 Hz), 48.0 (d, J_{C-F} = 5.8 Hz), 39.2 (t, J_{C-F} = 20.8 Hz), 30.5 (d, J_{C-F} = 7.6 Hz); HRMS (ESI): $C_{17}H_{14}ClF_2NNaOS^+$ $[M+Na]^+$ Calcd 376.0345, Found 376.0371.

3,3-difluoro-1-phenyl-4-((p-tolylthio)methyl)pyrrolidin-2-one ***(3ab).*** Pale yellow solid (51 mg, 0.15 mmol, yield 76%); m.p. 72 – 73 ℃; IR (neat) v 2920, 1723, 1494, 1200, 1035, 802, 756, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.4 Hz, 2H), 7.41 (t, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.24 – 7.23 (m, 1H), 7.15 (d, J = 8.0 Hz, 2H), 3.99 (t, J = 8.8 Hz, 1H), 3.70 (t, 8.4 Hz, 1H), 3.44 (dd, J = 13.7, 4.1 Hz, 1H), 2.94 (dd, J = 13.6, 11.1 Hz, 1H),, 2.87 – 2.71 (m, 1H), 2.34 (s,

3H); ^{19}F {^{1}H} {^{1}H} NMR (376 MHz, $CDCl_3$) δ -109.46 (d, J = 268.7 Hz), -116.87 (d, J = 268.5 Hz); ^{13}C {^{1}H} {^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.0 (t, J_{C-F} = 31.1 Hz), 137.90, 137.85, 131.3, 130.2, 129.8, 129.2, 126.2, 119.9, 117.0 (dd, J_{C-F} = 254.9, 250.1 Hz), 48.1 (d, J_{C-F} = 5.9 Hz), 39.3 (t, J_{C-F} = 20.9 Hz), 30.9 (d, J_{C-F} = 7.4 Hz), 21.1; HRMS (ESI): $C_{18}H_{17}F_2NNaOS^+$ $[M+Na]^+$ Calcd 356.0891, Found 356.0909.

3,3-dimethyl-1-phenyl-4-((phenylthio)methyl)pyrrolidin-2-one (**3ac**) Yellow oil (39 mg, 0.12 mmol, yield 62%); IR (neat) *v* 2963, 1693, 1492, 1394, 1298, 1022, 759, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, J = 8.2 Hz, 2H), 7.46 – 7.20 (m, 7H), 7.13 (t, J = 7.4 Hz, 1H), 3.92 (dd, J = 9.8, 7.5 Hz, 1H), 3.54 (t, J = 9.5 Hz, 1H), 3.23 (dd, J = 12.9, 4.3 Hz, 1H), 2.87 (dd, J = 12.9, 10.8 Hz, 1H), 2.35 (tdd, J = 11.0, 8.1, 4.2 Hz, 1H), 1.27 (s, 3H), 1.11 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 178.2, 139.5, 135.3, 129.8, 129.2, 128.8, 126.7, 124.4, 119.7, 50.4 , 44.8, 42.3, 33.2, 24.1, 18.8; HRMS (ESI): $C_{19}H_{21}NNaOS^+$ $[M+Na]^+$ Calcd 334.1236, Found 3334.1211.

3,3-difluoro-1-phenyl-4-((phenylselanyl)methyl)pyrrolidin-2-one ***(5a).*** Pale yellow solid (37 mg, 0.10 mmol, yield 51%); m.p. 86 – 87 ℃; IR (neat) *v* 2917, 1724, 1495, 1285, 1098, 848, 765, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 2H), 7.57 – 7.55 (m, 2H), 7.41 (t, J = 8.0 Hz, 2H), 7.33 – 7.332 (m, 3H), 7.24 – 7.23 (m, 1H), 3.90 (t, J = 8.8 Hz, 1H), 3.63 (t, J = 8.4 Hz, 1H), 3.39 (dd, J = 12.7, 3.9 Hz, 1H), 2.94 (t, J = 11.7 Hz, 1H), 2.89 – 2.73 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -109.86 (d, J = 268.0 Hz), -116.89 (d, J = 267.9 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.1 (t, J_{C-F} = 31.0 Hz), 137.8, 133.6, 126.9, 129.2, 128.1, 127.9, 126.3, 119.9, 116.9 (dd, J_{C-F} = 253.3, 248.0 Hz), 48.9 (d, J_{C-F} = 6.1 Hz), 40.3 (t, J_{C-F} = 21.1 Hz), 22.3 (d, J_{C-F} = 7.0 Hz); HRMS (ESI): $C_{17}H_{15}F_2NNaOSe^+$ $[M+Na]^+$ Calcd 390.0179, Found 390.0153.

1-(3-bromophenyl)-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one ***(5b).*** Pale yellow oil (62 mg, 0.14 mmol, yield 69%); IR (neat) *v* 2954, 1729, 1478, 1209, 1036, 851, 737, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.63 – 7.60 (m, 1H), 7.57 – 7.55 (m, 2H), 7.38-7.36 (m, 1H), 7.33 – 7.32 (m, 3H), 7.29 – 7.27 (m, 1H)，3.95 (t, J = 9.2 Hz, 1H), 3.58 (t, J = 8.8 Hz, 1H), 3.38 (dd, J = 12.7, 4.0 Hz, 1H), 2.93 (t, J = 11.8 Hz, 1H), 2.87 – 2.74 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.00 (d, J = 268.7 Hz), -116.84 (d, J = 268.5 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.1 (t, J_{C-F} = 31.0 Hz), 139.0, 133.6, 130.5, 129.6, 129.2, 128.2, 127.8, 122.9, 122.6,

118.3, 116.7 (dd, J_{C-F} = 254.4, 249.0 Hz), 48.7 (d, J = 6.0 Hz), 40.2 (t, J_{C-F} = 21.1 Hz), 22.2 (d, J_{C-F} = 6.9 Hz); HRMS (ESI): $C_{17}H_{14}BrF_2NNaOSe^+$ $[M+Na]^+$ Calcd 467.9284, Found 467.9305.

3,3-difluoro-1-(4-fluorophenyl)-4-((phenylselanyl)methyl)pyrrolidin-2-one ***(5c).*** Pale yellow oil (29 mg, 0.08 mmol, yield 38%); IR (neat) *v* 2918, 1725, 1509, 1223, 1096, 819, 739, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 4H), 7.33 – 7.32 (m, 3H), 7.12 – 7.08 (m, 2H), 3.96 (t, J = 9.2 Hz, 1H), 3.61 (t, J = 8.4 Hz, 1H), 3.39 (dd, J = 12.8, 4.0 Hz, 1H), 2.96 – 2.90 (m, 1H), 2.88 – 2.75 (m, 1H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -109.88 (d, J = 268.2 Hz), -114.90, -116.75 (d, J = 268.4 Hz);^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.0 (t, J_{C-F} = 31.1 Hz), 160.4 (d, J = 245.3 Hz), 133.9 (d, J_{C-F} = 3.1 Hz), 133.5, 129.6, 128.1, 127.8, 121.7 (d, J_{C-F} = 8.2 Hz), 116.9 (dd, J_{C-F} = 255.2, 249.7 Hz), 116.1 (d, J_{C-F} = 22.7 Hz), 49.1 (d, J_{C-F} = 6.1 Hz), 40.2 (t, J_{C-F} = 21.1 Hz), 22.3 (d, J_{C-F} = 7.0 Hz); HRMS (ESI): $C_{17}H_{14}F_3NNaOSe^+$ $[M+Na]^+$ Calcd 408.0085, Found 408.0105.

3,3-difluoro-4-((phenylselanyl)methyl)-1-(p-tolyl)pyrrolidin-2-one ***(5d).*** Pale yellow solid (28 mg, 0.07 mmol, yield 37%); m.p. 91 – 92 ℃; IR (neat) *v* 2918, 1706, 1514, 1284, 1028, 829, 739, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.55 (m, 2H), 7.47 (d, J = 8.0 Hz, 2H), 7.33 – 7.31 (m, 3H), 7.20 (d, J = 8.4 Hz, 2H), 3.96 (t, J = 9.2 Hz, 1H), 3.60 (t, J = 8.8 Hz, 1H), 3.39 (dd, J = 12.8, 4.0 Hz, 1H), 2.96 – 2.90 (m, 1H), 2.88 – 2.73 (m, 1H), 2.35 (s, 3H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -109.77 (d, J = 267.8 Hz), -116.80 (d, J = 267.8 Hz); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.9 (t, J_{C-F} = 30.6 Hz), 136.1, 135.3, 133.5, 129.7, 129.6, 128.1, 127.9, 119.9, 116.9 (dd, J_{C-F} = 255.2, 249.7 Hz), 49.9 (d, J_{C-F} = 6.0 Hz), 40.2 (t, J_{C-F} = 21.1 Hz), 22.4 (d, J_{C-F} = 7.1 Hz), 21.0; HRMS (ESI): $C_{18}H_{17}F_2NNaOSe^+$ $[M+Na]^+$ Calcd 404.0336, Found 404.0363.

1-benzyl-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one ***(5e).*** Pale yellow oil (47 mg, 0.12 mmol, yield 61%); IR (neat) *v* 2919, 1724, 1437, 1249, 1057, 994, 737, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.45 (m, 2H), 7.36 – 7.33 (m, 3H), 7.28 – 7.27 (m, 3H), 7.22 – 7.20 (m, 2H), 4.53 (d, J = 14.6 Hz, 1H), 4.45 (d, J = 14.6 Hz, 1H), 3.43 – 3.38 (m, 1H), 3.27 (dd, J = 12.6, 4.3 Hz, 1H), 3.04 – 3.00 (m, 1H), 2.77 (t, J = 11.7 Hz, 1H), 2.74 – 2.57 (m, 1H); ^{19}F $\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ -110.43 (d, J = 268.2 Hz), -116.89 (d, J = 268.2 Hz); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.3 (t, J_{C-F} = 30.1 Hz), 134.4, 133.4, 129.5, 129.1, 128.3, 128.0, 127.9, 117.4 (dd, J_{C-F} = 255.8, 250.7 Hz), 47.1, 47.3 (d, J_{C-F} = 6.2 Hz), 40.6 (t, J_{C-F} = 21.2 Hz), 22.6 (d, J_{C-F} = 7.5 Hz); HRMS (ESI): $C_{18}H_{17}F_2NNaOSe^+$ $[M+Na]^+$ Calcd 404.0336, Found 404.0357.

*3,3-difluoro-1-(4-methoxybenzyl)-4-((phenylselanyl)methyl)pyrrolidin-2-one (**5f**).* Pale yellow oil (56 mg, 0.14 mmol, yield 68%); IR (neat) *v* 2918, 1724, 1513, 1245, 1029, 818, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.45 (m, 2H), 7.31 – 7.28 (m, 3H), 7.14 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 4.47 (d, *J* = 14.5 Hz, 1H), 4.37 (d, *J* = 14.4 Hz, 1H), 3.81 (s, 3H), 3.41 – 3.36 (m, 1H), 3.26 (dd, *J* = 12.6, 4.3 Hz, 1H), 3.01 – 2.96 (m, 1H), 2.76 (t, *J* = 11.7 Hz, 1H), 2.71 – 2.56 (m, 1H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -110.25 (d, *J* = 268.2 Hz), -116.88 (d, *J* = 267.9 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 163.1 (t, J_{C-F} = 30.7 Hz), 159.5, 133.4, 129.7, 129.4, 128.0, 127.9, 126.4, 117.4 (dd, J_{C-F} = 255.8, 250.8 Hz), 114.4, 55.3, 47.1 (d, J_{C-F} = 6.3 Hz), 46.8, 40.5 (t, J_{C-F} = 21.2 Hz), 22.6 (d, J_{C-F} = 7.6 Hz); HRMS (ESI): $C_{19}H_{19}F_2NNaO_2Se^+$ $[M+Na]^+$ Calcd 434.0441, Found 434.0464.

*1-(2,4-difluorobenzyl)-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one (**5g**).* Pale yellow oil (71 mg, 0.17 mmol, yield 85%); IR (neat) *v* 2918, 1728, 1505, 966, 850, 737, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.47 (m, 2H), 7.29-7.24 (m, 4H), 6.90 – 6.81 (m, 2H), 4.56 (d, *J* = 14.7 Hz, 1H), 4.46 (d, *J* = 14.7 Hz, 1H), 3.46 (t, *J* = 9.0 Hz, 1H), 3.27 (dd, *J* = 12.6, 4.2 Hz, 1H), 3.05 (t, *J* = 8.4 Hz, 1H), 2.78 (t, *J* = 11.7 Hz, 1H), 2.69 – 2.59 (m, 1H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -108.76 (d, *J* = 8.0 Hz), -110.63 (d, *J* = 268.6 Hz), -114.09 (d, *J* = 7.7 Hz), -117.02 (d, *J* = 268.8 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 163.3 (t, J_{C-F} = 30.8 Hz), 162.9 (dd, J_{C-F} = 250.5, 11.9 Hz), 161.1 (dd, J_{C-F} = 249.7, 12.0 Hz), 133.5, 131.9 (dd, J_{C-F} = 9.8, 5.3 Hz), 129.5, 128.0, 117.6 (dd, J_{C-F} = 15.4, 3.8 Hz), 117.1 (dd, J_{C-F} = 256.2, 250.9 Hz), 112.2 (dd, J_{C-F} = 21.3, 3.8 Hz), 104.2 (t, J_{C-F} = 25.5 Hz), 47.5 (d, J_{C-F} = 6.3 Hz), 40.7 (t, J_{C-F} = 21.2 Hz), 40.4 (d, J_{C-F} = 3.3 Hz), 22.5 (d, J_{C-F} = 7.5 Hz); HRMS (ESI): $C_{18}H_{15}F_4NNaOSe^+$ $[M+Na]^+$ Calcd 440.0147, Found 440.0163.

*1-(2-bromobenzyl)-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one (**5h**).* Pale yellow oil (67 mg, 0.15 mmol, yield 73%); IR (neat) *v* 2919, 1437, 1251, 1134, 1026, 737, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 1H), 7.48 – 7.47 (m, 2H), 7.35 – 7.31 (m, 2H), 7.27 – 7.26 (m, 2H), 7.24 – 7.18 (m, 2H), 4.67 (d, *J* = 15.0 Hz, 1H), 4.61 (d, *J* = 14.9 Hz, 1H), 3.45 (t, *J* = 9.0 Hz, 1H), 3.27 (dd, *J* = 12.6, 4.3 Hz, 1H), 3.03 (t, *J* = 8.5 Hz, 1H), 2.80 (t, *J* = 11.6 Hz, 1H), 2.76 – 2.61 (m, 1H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -110.59 (d, *J* = 268.3 Hz), -116.94 (d, *J* = 268.3 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 163.4 (t, J_{C-F} = 30.1 Hz), 133.7, 133.5, 133.2, 130.4, 130.0, 129.5, 128.2, 128.04, 127.99, 124.0, 117.2 (dd, J_{C-F} = 254.3, 249.0 Hz), 47.6 (d, J_{C-F}

= 6.2 Hz), 47.2, 40.8 (t, J_{C-F} = 21.2 Hz), 22.5 (d, J_{C-F} = 7.5 Hz); HRMS (ESI): $C_{18}H_{16}BrF_2NNaOSe^+$ Calcd 481.9441, Found 481.9466.

1-cyclobutyl-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one ***(5i).*** Pale yellow oil (52 mg, 0.15 mmol, yield 76%); IR (neat) *v* 2917, 1721, 1438, 1268, 1065, 968, 738, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.51 (m, 2H), 7.33 – 7.31 (m, 3H), 4.61 (p, *J* = 8.6 Hz, 1H), 3.70 – 3.59 (m, 1H), 3.33 (dd, *J* = 12.8, 4.3 Hz, 1H), 3.22 – 3.09 (m, 1H), 2.90 – 2.78 (m, 1H), 2.74 – 2.60 (m, 1H), 2.20 – 2.11 (m, 4H), 1.77 – 1.70 (m, 2H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -110.24 (d, *J* = 267.8 Hz), -116.97 (d, *J* = 268.0 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 162.3 (t, J_{C-F} = 30.6 Hz), 133.4, 129.5, 128.0, 47.0, 44.4 (d, J_{C-F} = 6.4 Hz), 40.5 (t, J_{C-F} = 21.2 Hz), 27.0, 26.9, 22.7 (d, J_{C-F} = 7.4 Hz), 15.1; HRMS (ESI): $C_{15}H_{17}F_2NNaOSe^+$ $[M+Na]^+$ Calcd 368.0336, Found 368.0357.

1-cyclopentyl-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one ***(5j)***. Pale yellow oil (31 mg, 0.09 mmol, yield 43%); IR (neat) ν 2918, 1717, 1250, 1080, 851, 775, 738, 691 cm^{-1};^1H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.53 (m, 2H), 7.33 – 7.31 (m, 3H), 4.47 (p, *J* = 8.1 Hz, 1H), 3.53 – 3.49 (m, 1H), 3.32 (dd, *J* = 12.8, 4.3 Hz, 1H), 3.11 – 3.06 (m, 1H), 2.86 – 2.80 (m, 1H), 2.74 – 2.59 (m, 1H), 1.88 – 1.83 (m, 2H), 1.75 – 1.61 (m, 4H), 1.54 – 1.45 (m, 2H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -110.43 (d, *J* = 267.6 Hz), -117.34 (d, *J* = 267.6 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 163.1 (t, J_{C-F} = 30.6 Hz), 133.4, 129.5, 128.2, 128.0, 117.52 (dd, J_{C-F} = 255.0, 250.2 Hz), 53.3, 44.0 (d, J_{C-F} = 6.2 Hz), 40.8 (t, J_{C-F} = 21.2 Hz), 28.7, 24.1, 22.7 (d, J_{C-F} = 7.5 Hz); HRMS (ESI): $C_{16}H_{19}F_2NNaOSe^+$ $[M+Na]^+$ Calcd 382.0492, Found 382.0501.

1-cyclohexyl-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one ***(5k).*** Pale yellow oil (32 mg, 0.09 mmol, yield 43%); IR (neat) *v* 2927, 1716, 1438, 1248, 1057, 976, 739, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.52 (m, 2H), 7.32 – 7.31 (m, 3H), 3.98 – 3.93 (m, 1H), 3.56 – 3.51 (m, 1H), 3.32 (dd, *J* = 12.7, 4.3 Hz, 1H), 3.11 – 3.06 (m, 1H), 2.81 (t, *J* = 11.9 Hz, 1H), 2.71 – 2.56 (m, 1H), 1.82-1.80 (m, 2H), 1.73 – 1.67 (m, 3H), 1.37 – 1.32 (m, 4H), 1.26 (m, 1H); ^{19}F {^1H} NMR (376 MHz, $CDCl_3$) δ -110.46 (d, *J* = 267.0 Hz), -117.33 (d, *J* = 267.3 Hz); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 162.6 (t, J_{C-F} = 30.3 Hz), 133.4, 129.5, 128.2, 127.9, 117.7 (dd, J_{C-F} = 255.3, 250.6 Hz), 51.6, 43.9 (d, J_{C-F} = 6.2 Hz), 40.7 (t, J_{C-F} = 21.2 Hz), 29.8, 29.5, 25.18, 25.16, 25.10, 22.8 (d, J_{C-F} = 7.5 Hz); HRMS (ESI): $C_{17}H_{21}F_2NNaOSe^+$ $[M+Na]^+$ Calcd 396.0649, Found 396.0663.

3,3-difluoro-4-((phenylthio)methyl)-1-(2,2,2-trifluoroethyl)pyrrolidin-2-one ***(5l).*** Pale yellow oil (46 mg, 0.14 mmol, yield 70%); IR (neat) *v* 2918, 1741, 1439, 1256, 1081, 851, 738, 691 cm^{-1};

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.53 (m, 2H), 7.33 – 7.32 (m, 3H), 4.01 (dq, J = 17.6, 8.9 Hz, 1H), 3.84 (dq, J = 17.2, 8.7 Hz, 1H), 3.69 (t, J = 8.9 Hz, 1H), 3.35 – 3.30 (m, 2H), 2.85 (t, J = 11.8 Hz, 1H), 2.79 – 2.66 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -69.45, -111.98 (d, J = 271.0 Hz), -117.50 (d, J = 270.9 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.0 (t, J_{C-F} = 31.7 Hz), 133.5, 129.6, 128.1, 127.7, 124.8 (q, J_{C-F} = 280.3 Hz), 116.3 (dd, J_{C-F} = 249.3, 254.8 Hz), 48.9 (d, J_{C-F} = 6.2 Hz), 44.7 (q, J_{C-F} = 35.2 Hz), 40.9 (t, J_{C-F} = 21.2 Hz), 22.0 (d, J_{C-F} = 7.2 Hz); HRMS (ESI): $C_{13}H_{12}F_5NNaOSe^+$ [M+Na]$^+$ Calcd 395.9896, Found 395.9915.

Methyl 2-(3,3-difluoro-2-oxo-4-((phenylselanyl)methyl)pyrrolidin-1-yl)acetate ***(5m).*** Pale yellow oil (39 mg, 0.10 mmol, yield 52%); IR (neat) v 2918, 1737, 1208, 1068, 1020, 738, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.52 (m, 2H), 7.3 – 7.31 (m, 3H), 4.17 (d, J = 17.7 Hz, 1H), 4.06 (d, J = 17.6 Hz, 1H), 3.76 (s, 3H), 3.37 – 3.31 (m, 1H), 3.37 – 3.31 (m, 2H), 2.88 (t, J = 11.7 Hz, 1H), 2.82 – 2.68 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.83 (d, J = 269.7 Hz), -117.30 (d, J = 269.7 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.7, 163.8 (t, J_{C-F} = 31.2 Hz), 133.4, 129.5, 127.99, 127.96, 116.8 (dd, J_{C-F} = 255.6, 251.1 Hz), 52.6, 48.6 (d, J_{C-F} = 6.0 Hz), 44.3, 40.7 (t, J_{C-F} = 21.1 Hz), 22.4 (d, J_{C-F} = 7.5 Hz); HRMS (ESI): $C_{14}H_{15}F_2KNO_3Se^+$ [M+Na]$^+$ Calcd 401.9817, Found 401.9833.

3,3-difluoro-4-((phenylselanyl)methyl)-1-(pyridin-2-ylmethyl)pyrrolidin-2-one ***(5n).*** Pale yellow oil (39 mg, 0.10 mmol, yield 51%); IR (neat) v 2918, 1731, 1437, 1208, 1020, 846, 738, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 4.1 Hz, 1H), 7.68 (t, J = 7.4 Hz, 1H), 7.50 – 7.48 (m, 2H), 7.29 – 7.23 (m, 5H), 4.67 (d, J = 15.0 Hz, 1H), 4.57 (d, J = 15.0 Hz, 1H), 3.64 (t, J = 8.9 Hz, 1H), 3.32 – 3.23 (m, 2H), 2.83 (t, J = 11.7 Hz, 1H), 2.78 – 2.63 (m, 1H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.48 (d, J = 268.3 Hz), -117.01 (d, J = 268.4 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.48 (t, J_{C-F} = 30.7 Hz), 154.6, 149.6, 137.2, 133.4, 129.5, 128.1, 127.9, 123.0, 122.5, 117.3 (dd, J_{C-F} = 255.6, 250.9 Hz), 48.9, 48.3 (d, J_{C-F} = 6.2 Hz), 40.7 (t, J_{C-F} = 21.2 Hz), 22.5 (d, J_{C-F} = 7.5 Hz); HRMS (ESI): $C_{17}H_{16}F_2N_2NaOSe^+$ [M+Na]$^+$ Calcd 405.0288, Found 405.0308.

1-butyl-3,3-difluoro-4-((phenylselanyl)methyl)pyrrolidin-2-one ***(5o).*** Pale yellow oil (40 mg, 0.11 mmol, yield 53%); IR (neat) v 2920, 1724, 1438, 1250, 1080, 850, 737, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.52 (m, 2H), 7.32 – 7.31 (m, 3H), 3.55 – 3.50 (m, 1H), 3.44 – 3.22 (m, 3H), 3.19 – 3.14 (m, 1H), 2.83 (t, J = 11.9 Hz, 1H), 2.75 – 2.60 (m, 1H), 1.51 (p, J = 7.3 Hz, 2H), 1.35 – 1.26 (m, 2H), 0.93 (t, J = 7.2 Hz, 3H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.50 (d, J =

267.7 Hz), -116.98 (d, J = 267.7 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.2 (t, J_{C-F} = 30.1 Hz), 133.4, 129.5, 128.1, 128.0, 117.4 (dd, J_{C-F} = 253.8, 248.6 Hz), 47.8 (d, J_{C-F} = 6.3 Hz), 43.2, 40.6 (t, J_{C-F} = 21.3 Hz), 28.8, 22.6 (d, J_{C-F} = 7.6 Hz), 19.8, 13.6; HRMS (ESI): $C_{15}H_{19}F_2NNaOSe^+$ $[M+Na]^+$ Calcd 370.0492, Found 370.0505.

3,3-difluoro-1-(4-phenylbutyl)-4-((phenylselanyl)methyl)pyrrolidin-2-one ***(5p).*** Pale yellow oil (52 mg, 0.12 mmol, yield 61%); IR (neat) *v* 2920, 1724, 1438, 1250, 1080, 851, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.50 (m, 2H), 7.31-7.26 (m, 5H), 7.21 – 7.19 (m, 1H), 7.16 – 7.14 (m, 2H), 3.47 – 3.37 (m, 2H), 3.32 – 3.25 (m, 2H), 3.11 – 3.06 (m, 1H), 2.83 – 2.77 (m, 1H), 2.73 – 2.61 (m, 3H), 1.66 – 1.51 (m, 4H); ^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ -110.45 (d, J = 267.7 Hz), -116.82 (d, J = 267.8 Hz); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.3 (t, J_{C-F} = 30.6 Hz), 141.7, 133.4, 129.5, 128.43, 128.42, 128.1, 128.0, 126.0, 117.37 (dd, J_{C-F} = 255.5, 250.4 Hz), 47.8 (d, J_{C-F} = 6.4 Hz), 43.2, 40.6 (t, J_{C-F} = 21.3 Hz), 35.2, 28.2, 26.1, 22.6 (d, J_{C-F} = 7.5 Hz); HRMS (ESI): $C_{21}H_{23}F_2NNaOSe^+$ $[M+Na]^+$ Calcd 446.0805, Found 446.0832.

ASSOCIATED CONTEN

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

10.1021/acs.joc.xxxxxxx

The setup for the photocatalytic procedure.

Mechanistic studies.

NMR spectra for compounds **1e-1v, 1x-1z, 3, 5** and **6a.**

X-ray crystallographic data and CIF file of compound 3a

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Notes

The authors declare no competing financial interest.

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