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Microwave-assisted expeditious synthesis of 5-fluoroalkyl-3-(aryl/alkyl)-oxazolidin-2-ones

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ABSTRACT

An efficient and convenient protocol for synthesis of 5-fluoroalkyl-3-(aryl/alkyl)-oxazolidin-2-ones is described. The reaction of allyl (aryl/alkyl) carbamates with fluoroalkyl iodide initiated by sodium dithionite in aqueous acetonitrile resulted in adducts that undergoes a cyclization assisted by microwave irradiation to form 5-fluoroalkyl-3-(aryl/alkyl)-oxazolidin-2-ones with high yields. It was also found that the products can be more efficiently formed via an AIBN-initiated one-pot addition–cyclization sequence from benzyl allyl(aryl/alkyl) carbamates and fluoroalkyl iodide.

1. Introduction

Oxazolidin-2-ones is a very important class of organic compounds widely used in pharmaceutical, material, and synthetic chemistry.[1] They display good antibacterial activity against Gram-positive bacteria resistant to the conventional antibiotics.[2] Oxazolidin-2-one derivatives have also been shown to serve as functional materials enduring high temperatures[3] and as an efficient auxiliary in asymmetric synthesis.[4]

To date, several protocols for the synthesis of oxazolidin-2-ones have been described, including the reactions of amino alcohols with carbonyl reagents,[5] of epoxides with isocyanates,[6] and the iodine lactonization.[7] Recently, a new method has been reported to prepare oxazolidin-2-ones from 3-substitute-2-iodopentyl arylcarbamates assisted by microwave irradiation.[8]

It is known that introduction of fluorine atom into organic compounds may greatly change their biological activities.[9] Thus, development of effective methods for the construction of fluorinated and fluoroalkylated oxazolidin-2-one framework could be of interest in organic synthesis. Recently, fluoroalkyl lactones have been obtained by a sequential addition–lactonization reaction of pent-4-enoic acids with fluoroalkyl iodide.[10] Also, preparation of fluoroalkylated furan rings has been achieved by treatment of the corresponding pent-4-enol with fluoroalkyl iodide.[11] We describe, herein, an efficient protocol for the synthesis of 5-fluoroalkyl-3-(aryl/alkyl)-oxazolidin-2-ones **1** (Fig. 1) by exploiting microwave-assisted cyclization as the key step.

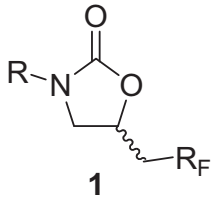

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Fig. 1. Fluorinated oxazolidin-2-one derivatives synthesized in the present study.

2. Results and discussions

To carry out our studies, we firstly synthesized benzyl allyl (aryl/alkyl) carbamates **4a**–**f** following a reported procedure (Scheme 1).[7] Aryl/alkyl amines **2a**–**2f** reacted with benzyl chloroformate (CbzCl) to give the corresponding benzyl aryl/alkyl carbamates **3a**–**3f** in 57.8%–99.7% yields, which were then treated with allyl bromide in the presence of NaH and TBAI to afford the corresponding benzyl allyl(aryl/alkyl) carbamates **4a**–**f** in 96.3%–99.9% yields.

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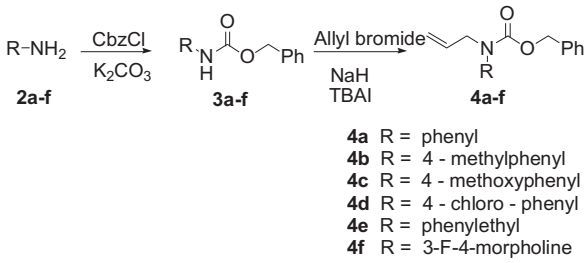
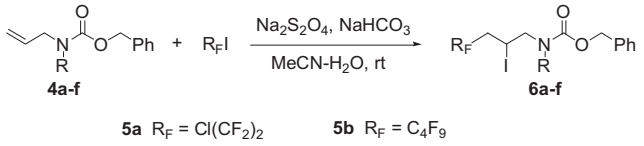


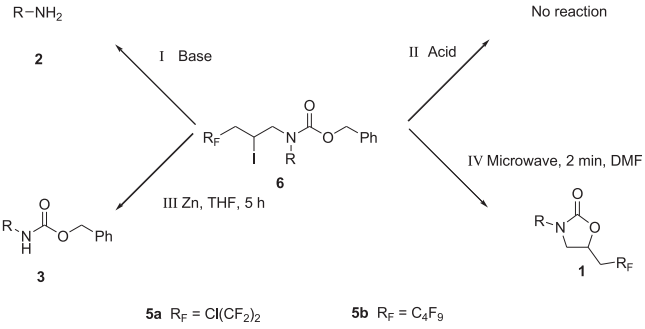
Scheme 1. Synthesis of benzyl allyl (aryl/alkyl) carbamates.

The radical addition reaction of benzyl/ethyl allyl(aryl/alkyl) carbamates **4a**–**f** with fluoroalkyl iodides **5a** or **5b** was then achieved in aqueous acetonitrile initiated by sodium dithionite[10,11] at room temperature to give the corresponding adducts **6aa**–**fb**. The yields were in the range of 44.9%–62.0% (Scheme 2).



Scheme 2. Synthesis of benzyl/ethyl 3-(fluoroalkyl)-2-iodopentyl (aryl/alkyl) carbamates.

Next, as a model reaction, the intramolecular cyclization of benzyl 5-chloro-4,4,5,5-tetrafluoro-2-iodopentyl(phenyl)carbamate (**6aa**) was investigated (Scheme 3). In our previous work, we obtained 4-(fluoroaryl)-1,3-oxazolidin-2-ones via the intramolecular N-cyclization of 3-(fluoroalkyl)-2-iodo-ethylcarbamates in the presence of NaH in THF.[10] But when the intramolecular O-cyclization of **6aa** was conducted in the presence of strong or weak bases, such as NaH, NaOH, Na_2CO_3, and $NaHCO_3$ at 25–67 °C in THF for 2 h, a decomposed byproduct, phenylamine (**2a**), instead of the cyclization product, was obtained. A further attempt was made to carry out the O-cyclization under acidic conditions. However, the reaction did not take place in the presence of various acids including HCl (aqueous), CH_3COOH, HCOOH or CF_3COOH likely due to the stability of **6aa** under acidic conditions.



Scheme 3. The different conditions for cyclization of carbamate **6aa**.

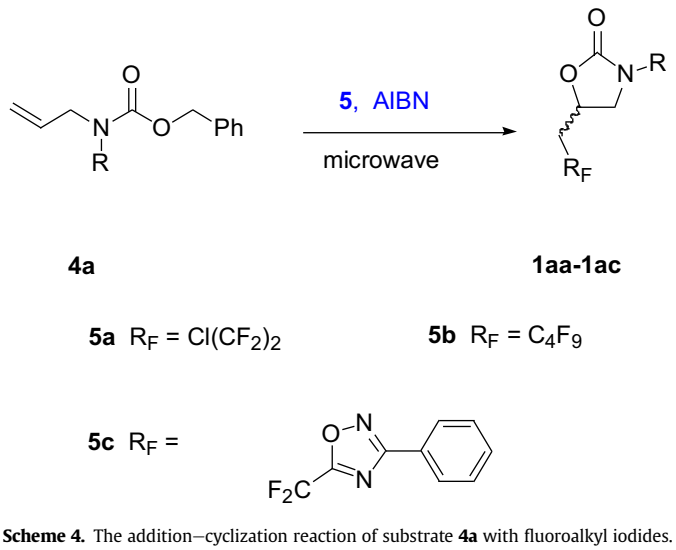
It is reported that the O-cyclization can occur at high temperatures,[12] in the presence of zinc,[13] or by assistance of microwave irradiation.[8] However, the cyclization of **6aa** by heating at reflux or at above 200 °C did not take place neither in the presence nor in the absence of solvents, such as toluene, DMF, and DMSO. On the other hand, in the presence of zinc, **6aa** was decomposed to the benzyl (phenyl) carbamate **3a**, probably due to the more cleavable nature of the C–N bond of the carbamate than its C–O bond under such a condition.

Ultimately, under microwave irradiation with a power of 250 W, the O-cyclization of **6aa** was formed in high yield in 2 min in DMF. When the substrate was ethyl 5-chloro-4,4,5,5-tetrafluoro-2-iodopentyl(phenyl)carbamate, a similar result was obtained. Different carbamates **6** were then used to probe the influence of a number of substituents on microwave-assisted intramolecular O-cyclization. The results were summarized in Table 1 indicated that all the desired fluoroalkylated oxazolidin-2-ones **1** containing a range of substituents were synthesized in good yields. An intramolecular S_N^2 cyclization step had been proposed as a fundament to the cyclization reaction, with the activation energy for the reaction being very high owing to multiple bond breaking-forming processes.

Table 1
The synthesis of 5-fluoroalkyl-3-(aryl/alkyl)-oxazolidin-2-ones

Entry	Substrates	Products	Yields (%)
1	**6aa**	**1aa**	72.6
2	**6ba**	**1ba**	80.4
3	**6ca**	**1ca**	84.8
4	**6da**	**1da**	90.4
5	**6ea**	**1ea**	61.1
6	**6fa**	**1fa**	73.6
7	**6ab**	**1ab**	81.8
8	**6bb**	**1bb**	81.3
9	**6cb**	**1cb**	81.6
10	**6db**	**1db**	86.1
11	**6eb**	**1eb**	67.7
12	**6fb**	**1fb**	78.9

We then sought to test the addition of benzyl allyl (aryl/alkyl) carbamates (**4a**–**f**) with fluoroalkyl iodides directly followed by a cyclization in one pot to obtain the target product **1** in order to avoid some additional purification effort (Scheme 4). It turned out that either at a high temperature or room temperature the addition reaction of **4a** with **5b** in DMF, initiated by sodium dithionite, resulted in a low yield of product **1ab**. Since the radical addition of unsaturated compounds with fluoroalkyl iodides can be initiated



Scheme 4. The addition–cyclization reaction of substrate **4a** with fluoroalkyl iodides.

by azodiisobutyronitrile (AIBN) at high temperature,[14] AIBN was thus chosen to act as a potential initiator.

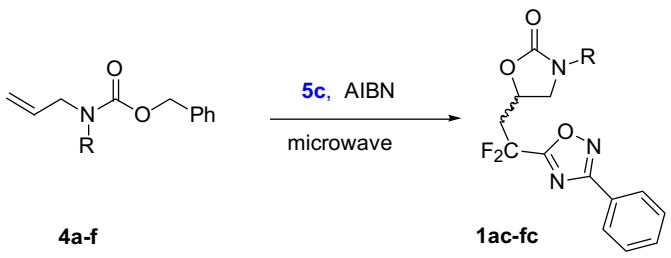
However, the reaction of **4a** with **5a** initiated by AIBN in DMF (with reflux for 2 h) did not yield any products, possibly due to the evaporation of **5a** because of its low boiling point. When the fluoroalkyl iodides 1,1,1,2,2,3,3,4,4-nonafluoro-4-iodobutane (**5b**) and 3-(difluoroiodomethyl)-5-phenyl-1,2,4-oxadiazole (**5c**), with relatively higher boiling points, were used as the starting materials, the corresponding adducts **6ab** and **6ac** were formed. Upon exciting the mixture at a microwave power of 250 W for 2 min, 5-(5-chloro-2,2,3,3,4,4,5,5-octafluoropentyl)-3-phenyloxazolidin-2-one (**1ab**) and 5-(2,2-difluoro-2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl)-3-phenyloxazo-lidin-2-one (**1ac**) were obtained in the yields of 30.7% and 62.8%, respectively (Scheme 4, Table 2, entries 2, 3). When the sequential addition–cyclization reaction of **4a** with **5c** was conducted in one pot by microwave irradiation for 2 h, **1ac** was obtained in 63.5% yield (Table 2, entry 4). These results suggested that the reaction rate was mainly dependent on the rate of the addition reaction.

Table 2
The addition–cyclization reaction of substrate **4a**

Entry	Fluoroalkyl iodide	Bp (°C)	Product	Time[c] (h)	Time[d] (min)	Yield of **1** (%)
1[a]	**5a**	55	**1aa**	2.0	2	0
2[a]	**5b**	104	**1ab**	2.0	2	30.7
3[a]	**5c**	>154	**1ac**	2.0	2	62.8
4[b]	**5c**	>154	**1ac**	2.0	120	63.5

[a] The addition reactions were initiated by AIBN in DMF at reflux.
[b] The reaction was carried out by microwave heating of 250 W in 2 h in DMF.
[c] Addition time.
[d] Cyclization time.

Encouraged by the preliminary results, we attempted to optimize the condition for the one-pot addition–cyclization using allyl(phenyl)carbamate **4a** as a model substrate for the synthesis of 5-fluoroalkyl-3-phenyloxazolidin-2-ones **1** using microwave heating (Scheme 5). The concentration of **4a** was set at 1 M for ease of comparison. The results were summarized in Table 3. With a microwave power of 250 W, the reaction occurred in 2.5 h in DMF when 2 equiv AINB was present, giving **1ac** in a relatively yield (i.e., of 72.3%) (Table 3, entry 6) compared to the yield under the other conditions used. When the solvent was changed to acetonitrile or toluene, **1ac** was obtained in lower yields (Table 4, entries 6, 8, and 9); reduction of the amount of AIBN also lowered the reaction efficiency (Table 3, entry 10). Under the optimized condition, the one-pot addition–cyclization of different substrates **4b**–**4f** with 3-(difluoroiodomethyl)-5-phenyl-1,2,4-oxadiazole (**5c**) proceeded smoothly, affording the desired products **1** in good yields of 71.6–84.3% (Table 4). When 5-(bromodifluoromethyl)-3-phenyl-1,2,4-oxadiazole was used as the substrate, the addition–lactonization reaction occurred in low yield, e.g., 92.0% of **4a** was recovered.



Scheme 5. The addition–cyclization reaction of substrate **4a** with **5c**.

Table 3
The addition–cyclization reaction of **4aa** under different conditions by microwave heating

Entry	Power (W)	Solvent	Time (h)	AIBN (N)	Yield (%) of **1**
1	100	DMF	1.0	2	19.6
2	250	DMF	1.0	2	38.7
3	400	DMF	1.0	2	37.9
4	250	DMF	1.5	2	51.5
5	250	DMF	2.0	2	63.5
6	250	DMF	2.5	2	72.3
7	250	DMF	3.0	2	72.2
8	250	CH_3CN	2.5	2	19.4
9	250	Toluene	2.5	2	35.7
10	250	DMF	2.5	1	54.2
11	250	DMF	2.5	3	71.9

Table 4
Results of the addition–cyclization reaction of substrate **4** by microwave heating

Entry	Substrates	Products	Yields (%)
1	**4ac**	**1ac**	72.3
2	**4bc**	**1bc**	71.6
3	**4cc**	**1cc**	82.4
4	**4dc**	**1dc**	84.3
5	**4ec**	**1ec**	74.3
6	**4fc**	**1fc**	78.0

3. Conclusion

In conclusion, we have developed a novel expeditious synthetic protocol for the synthesis of 5-fluoroalkyl-3-(aryl/alkyl)-oxazolidin-2-ones, which affords the title products via a radical addition and then a microwave-assisted cyclization in moderate to good yields. Notably, the target compounds can also be obtained from benzyl allyl(aryl/alkyl) carbamates by a one-pot sequential addition–cyclization reaction using AIBN as an initiator with good yields.

4. Experimental section

4.1. General

All melting points were uncorrected. IR spectra were measured on a Nicolet Magna IR-550 spectrometer using potassium bromide pellets. High resolution mass spectra were carried out on a Finnigan GC–MS-4021 spectrometer. ^1H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded with a Brucker AM-400 spectrometer with Me_4Si as the internal standard. ^{19}F NMR spectra were obtained on a Brucker AM-400 (367.5 MHz) spectrometer in $CDCl_3$ with $CFCl_3$ as the external standard; downfield shifts are designated as negative. All chemical shifts (δ) are expressed in parts per million and coupling constants (J) given in Hertz. Microwave heating was accomplished using a WBFY-205 microwave reactor.

4.2. Typical procedure for synthesis of allyl phenylcarbamate

To a flame-dried screw-caped reaction tube was added a mixture of the amine (1.84 g, 20.00 mmol), powdered K_2CO_3 (3.31 g, 24.00 mmol, 1.20 equiv), and benzyl carbonochloridate (3.14 mL, 22.00 mmol, 1.10 equiv) in 100 mL of anhydrous THF under argon. Then the resulting mixture was stirred for 2 h at room temperature, and the product was extracted with methylene chloride (100 mL) and washed with saturated Na_2CO_3 (50 mL×3). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The solvent was then removed under reduced pressure, and the residue was purified by silica-gel chromatography (EtOAc/petroleum ether=1:4), providing **3a** (4.09 g) as a white solid.

*4.2.1. Benzyl phenylcarbamate (**3a**).* Yield: 89.9%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 (2H, s), 6.67 (1H, br), 7.06 (1H, t, J=7.40 Hz), 7.27–7.45 (9H, m).

*4.2.2. Benzyl p-tolylcarbamate (**3b**).* Yield: 57.8%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (3H, s), 5.19 (2H, s), 6.62 (1H, br), 7.10 (2H, d, J=8.80 Hz), 7.27–7.46 (7H, m).

*4.2.3. Benzyl 4-methoxyphenylcarbamate (**3c**).* Yield: 93.2%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (3H, s), 5.18 (2H, s), 6.61 (1H, br), 6.84 (2H, d, J=8.80 Hz), 7.27–7.47 (7H, m).

*4.2.4. Benzyl 4-chlorophenylcarbamate (**3d**).* Yield: 99.7%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (2H, s), 6.77 (1H, br), 7.20–7.40 (9H, m).

*4.2.5. Benzyl phenethylcarbamate (**3e**).* Yield: 99.1%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.82 (2H, t, J=6.80 Hz), 3.42–3.52 (2H, m), 4.76 (1H, br), 5.09 (2H, s), 7.16–7.40 (10H, m).

*4.2.6. Benzyl 3-fluoro-4-morpholinophenylcarbamate (**3f**).* Yield: 99.1%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.88–2.99 (4H, t, J=4.60 Hz), 3.78 (4H, t, J=4.60 Hz), 5.10 (2H, s), 6.71–6.82 (2H, m), 6.88–6.91 (1H, m), 7.24–7.34 (5H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −121.08 (1F, s).

*4.2.7. Ethyl phenylcarbamate (**3g**).* Yield: 97.3%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (3H, t, J=7.20 Hz), 4.22 (2H, q, J=7.20 Hz), 6.75 (1H, br), 7.05 (1H, t, J=7.60 Hz), 7.30 (2H, t, J=7.80 Hz), 7.38 (2H, d, J=8.00 Hz).

4.3. Typical procedure for synthesis of benzyl allyl(aryl/alkyl) carbamate

To a flame-dried screw-capped reaction tube was added a mixture of **3a** (2.27 g, 10.00 mmol) and sodium hydride (0.40 g, 10.00 mmol, 1.00 equiv, 60%) in 20 mL THF under argon. After stirring for 0.5 h at room temperature, the reaction mixture was treated with *n*-Bu_4NI (0.37 g, 1.00 mmol, 0.10 equiv) followed by addition of 1.10 equiv of allyl bromide (0.95 mL, 11.00 mmol). Then the resulting solution was stirred for another 1 h at room temperature, and then the product was poured into H_2O (50 mL) and extracted with EtOAc (50 mL×3). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The solvent was then removed under reduced pressure, and the residue was purified by silica-gel chromatography (EtOAc/petroleum ether=1:8), providing **4a** (2.62 g) as a colorless liquid.

*4.3.1. Benzyl allyl(phenyl)carbamate (**4a**).* Yield: 98.1%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 (2H, d, J=6.00 Hz), 5.09–5.19 (4H, m), 5.84–5.96 (1H, m) 7.17–7.36 (10H, m).

*4.3.2. Benzyl allyl(p-tolyl)carbamate (**4b**).* Yield: 96.3%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (3H, s), 4.25 (2H, d, J=5.60 Hz), 5.08–5.20 (4H, m), 5.81–5.96 (1H, m), 7.06–7.18(4H, m), 7.26–7.40 (5H, m).

*4.3.3. Benzyl allyl(4-methoxyphenyl)carbamate (**4c**).* Yield: 96.5%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (3H, s), 4.22 (2H, d, J=6.00 Hz), 5.05–5.17 (4H, m), 5.83–5.94 (1H, m), 6.84 (2H, d, J=8.80 Hz), 7.06–7.40 (7H, m).

*4.3.4. Benzyl allyl(4-chlorophenyl)carbamate (**4d**).* Yield: 99.1%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.26 (2H, d, J=6.00 Hz), 5.10–5.20 (4H, m), 5.80–5.96 (1H, m), 7.14–7.40 (9H, m).

*4.3.5. Benzyl allyl(phenethyl)carbamate (**4e**).* Yield: 99.8%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.75–2.90 (2H, m), 3.39–3.51 (2H, m), 3.72–3.87 (2H, m), 5.05–5.18 (4H, m), 5.70–5.76 (1H, m), 7.07–7.09 (1H, m), 7.15–7.27 (4H, m), 7.28–7.39 (5H, m).

*4.3.6. Benzyl allyl(3-fluoro-4-morpholinophenyl)carbamate (**4f**).* Yield: 99.9%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.06 (4H, t, J=4.40 Hz), 3.84 (4H, t, J=4.60 Hz), 4.22 (2H, d, J=6.00 Hz), 5.09–5.19 (4H, m), 5.81–5.94 (1H, m) 6.82–6.89 (1H, m), 6.94–6.96 (2H,m), 7.24–7.38 (5H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −121.31 (1H, s).

*4.3.7. Ethyl allyl(phenyl)carbamate (**4g**).* Yield: 98.6%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (3H, t, J=7.00 Hz), 4.16 (2H, q, J=7.20 Hz), 4.25 (2H, d, J=6.00 Hz), 5.10–5.20 (2H, m), 5.85–5.95 (1H, m), 7.16–7.25 (3H,m), 7.32 (2H, t, J=7.80 Hz).

4.4. Typical procedure for synthesis of benzyl 5-(fluoroalkyl)-2-iodopentyl arylcarbamate

To a stirred solution of benzyl allyl phenylcarbamates **4a** (1.07 g, 4 mmol) and $ClCF_2CF_2I$ (1.57 g, 6.00 mmol) in MeCN/H_2O (7:1, 32 mL) was added $Na_2S_2O_4$ (1.04 g, 6.00 mmol) and $NaHCO_3$ (0.50 g, 6.00 mmol). Then, the resulting solution was stirred for 5 h at room temperature. The resulting mixture was then poured into H_2O and extracted with EtOAc (50 mL×3). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The solvent was then removed under reduced pressure, and the residue was purified by silica-gel chromatography (EtOAc/petroleum ether=1:8), providing **6aa** (0.99 g) as a colorless liquid.

*4.4.1. Benzyl 5-chloro-4,4,5,5-tetrafluoro-2-iodopentyl(phenyl)-carbamate (**6aa**).* Yield: 46.6%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64–2.98 (2H, m), 4.05–4.15 (2H, m), 4.16–4.24 (1H, m), 5.10–5.20 (2H, s), 7.16–7.44 (10H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.30 to −112.20 (2F, m), −71.78 (2F, s).

*4.4.2. Benzyl 4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl(phenyl)-carbamate (**6ab**).* Yield: 55.3%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64–3.00 (2H, m), 4.00–4.16 (2H, m), 4.18–4.30 (1H, m), 5.16 (2H, s), 7.10–7.50 (10H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.00 to −125.80 (2F, m), −124.70 to −124.50 (2F, m), −115.00 to −113.00 (2F, m), −81.06 (3F, t, J=9.59 Hz).

*4.4.3. Benzyl 5-chloro-4,4,5,5-tetrafluoro-2-iodopentyl(p-tolyl)-carbamate (**6ba**).* Yield: 61.3%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (3H, s), 2.66–3.00 (2H, m), 4.05–4.18 (2H, m), 4.19–4.25 (1H, m), 5.16 (2H, s), 7.06–7.40 (9H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.50 to −112.00 (2F, m), −71.79 (2F, s).

*4.4.4. Benzyl 4,4,5,5,6,7,7,7-octafluoro-2-iodo-6-methylheptyl(p-tolyl)carbamate (**6bb**).* Yield: 44.9%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33–2.38 (3H, s), 2.65–2.96 (2H, m), 4.03–4.14 (2H, m), 4.16–4.25 (1H, m), 5.15 (2H, s), 7.04–7.40 (9H, m). ^{19}F NMR (376 MHz, CDCl3) δ −123.15 to −122.95 (2F, m), −119.90 to −119.70 (2F, m), −114.50 to −112.50 (2F, m), −68.05 (3F, t, J=13.16 Hz).

*4.4.5. Benzyl 5-chloro-4,4,5,5-tetrafluoro-2-iodopentyl(4-meth-oxyphenyl)carbamate (**6ca**).* Yield: 46.8%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.70–2.96 (2H, m), 3.82 (3H, s), 4.00–4.12 (2H, m), 4.13–4.22 (1H, m), 5.05–5.25 (2H, m), 6.90 (2H, d, J=8.80 Hz), 7.10–7.45 (7H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.00 to −111.00 (2F, m), −71.80 (2F, s).

*4.4.6. Benzyl 4-methoxyphenyl(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)carbamate (**6cb**).* Yield: 44.0%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60–3.00 (2H, m), 3.81 (3H, s), 4.00–4.14 (2H, m), 4.15–4.30 (1H, m), 5.00–5.24 (2H, m), 6.90 (2H, d, J=8.80 Hz), 7.08–7.40 (7H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.05 to −125.85

(2F, m), −124.70 to −124.50 (2F, m), −115.00 to −112.00 (2F, m), −80.99 (3F, t, *J*=9.59 Hz).

*4.4.7. Benzyl 5-chloro-4,4,5,5-tetrafluoro-2-iodopentyl(4-chlorophenyl)carbamate (**6da**).* Yield: 60.0%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66–3.00 (2H, m), 4.00–4.16 (2H, m), 4.17–4.40 (1H, m), 5.00–5.30 (2H, m), 7.10–7.50 (9H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.50 to −113.50 (2F, m), −71.77 (2F, s).

*4.4.8. Benzyl 4-chlorophenyl(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)carbamate (**6db**).* Yield: 62.0%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60–2.98 (2H, m), 4.00–4.16 (2H, m), 4.17–4.40 (1H, m), 5.10–5.30 (2H, m), 7.08–7.50 (9H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.00 to −125.80 (2F, m), −124.40 to −124.25 (2F, m), −112.65 to −112.47 (2F, m), −80.94 (3F, t, *J*=9.21 Hz).

*4.4.9. Benzyl 5-chloro-4,4,5,5-tetrafluoro-2-iodopentyl(3-fluoro-4-morpholinophenyl)carbamate (**6fa**).* Yield: 55.6%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.70–2.92 (2H, m), 3.12 (4H, t, *J*=4.40 Hz), 3.89 (4H, t, *J*=4.40 Hz), 4.00–4.15 (2H, m), 4.16–4.28 (1H, m), 5.16 (2H, s), 6.85–7.05 (3H, m), 7.28–7.40 (5H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −120.13 (1F, s), −114.50 to −112.40 (2F, m), −71.85 to −71.73 (2F, m).

*4.4.10. Benzyl 3-fluoro-4-morpholinophenyl(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)carbamate (**6fb**).* Yield: 55.3%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66–2.96 (2H, m), 3.12 (4H, t, *J*=4.60 Hz), 3.89 (4H, t, *J*=4.60 Hz), 4.00–4.14 (2H, m), 4.15–4.25 (1H, m), 5.16 (2H, s), 6.85–7.00 (3H, m), 7.26–7.40 (5H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.00 to −125.80 (2F, m), −124.66 to −124.46 (2F, m), −120.11 (1F, s), −115.00 to −112.00 (2F, m), −80.96 (3F, t, *J*=9.40 Hz).

*4.4.11. Ethyl 5-chloro-4,4,5,5-tetrafluoro-2-iodopentyl(phenyl)-carbamate (**6ga**).* Yield: 54.5%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10–1.30 (3H, m), 2.66–2.96 (2H, m), 4.00–4.35 (5H, m), 7.15 (2H, d, *J*=8.00 Hz), 7.22 (1H, t, *J*=7.40 Hz), 7.32 (2H, t, *J*=7.60 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.00 to −125.80 (2F, m), −114.20 to −112.00 (2F, m), −71.76 (2F, s).

4.5. Typical procedure for synthesis of benzyl 5-(fluoroalkyl)-3-aryl/alkyl oxazolidin-2-one (1aa–1fb)

To a round bottom flask was added iodopentyl arylcarbamate **6aa** (0.53 g, 1 mmol) in 30 mL DMF. Then resulting mixture was stirred for 2 min by microwave irradiation with 250 W. The solvent was then removed under reduced pressure, and the residue was purified by silica-gel chromatography (EtOAc/petroleum ether=1:5), providing **1aa** (0.23 g) as a white solid.

*4.5.1. 5-(3-Chloro-2,2,3,3-tetrafluoropropyl)-3-phenyloxazo-lidin-2-one (**1aa**).* Yield: 72.6%. White solid. Mp 108.7–109.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49–2.66 (1H, m), 2.74–2.91 (1H, m), 3.86 (1H, dd, J_1=9.20 Hz, J_2=7.60 Hz), 4.27 (1H, t, *J*=8.80 Hz), 5.00–5.10 (1H, m), 7.18 (1H, t, *J*=7.40 Hz), 7.40 (2H, t, *J*=8.00 Hz), 7.52 (2H, d, *J*=8.00 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.32 to −112.18 (2F, m), −71.78 (2F, s). ^{13}C NMR (107 MHz, $CDCl_3$) δ 35.82 (t, *J*=22.63 Hz), 50.70, 66.70, 118.37, 124.53, 129.20, 137.70, 153.79. IR (KBr) 3464, 3112, 1734, 1602, 1503, 1424, 1304, 1136, 1097, 751, 689 cm^{-1}. HRMS (EI): $C_{12}H_{10}ClF_4NO_2$ calcd: 311.0336, found: 311.0332.

*4.5.2. 5-(2,2,3,3,4,4,5,5,5-Nonafluoropentyl)-3-phenyloxazolidin-2-one (**1ab**).* Yield: 81.8%. White solid. Mp 93.0–94.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48–2.66 (1H, m), 2.72–2.90 (1H, m), 3.85 (1H, dd, J_1=8.40 Hz, J_2=8.00 Hz), 4.26 (1H, t, *J*=8.80 Hz), 5.00–5.10 (1H, m), 7.17 (1H, t, *J*=7.20 Hz), 7.39 (2H, t, *J*=7.80 Hz), 7.52 (2H, d, *J*=8.00 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.00 to −125.80 (2F, m), −124.42 to −124.26 (2F, m), −112.65 to −112.50 (2F, m), −80.96 (3F, t, *J*=9.21 Hz). ^{13}C NMR (107 MHz, $CDCl_3$) δ 36.13 (t, *J*=22.26 Hz), 50.80, 66.35, 118.38, 124.60, 129.23, 137.65, 153.69. IR (KBr) 3473, 3104, 1735, 1594, 1404, 1232, 1129, 751, 736, 515 cm^{-1}. HRMS (EI): $C_{14}H_{10}F_9NO_2$ calcd: 3 95.0568, found: 395.0559.

*4.5.3. 5-(3-Chloro-2,2,3,3-tetrafluoropropyl)-3-p-tolyloxazolidin-2-one (**1ba**).* Yield: 80.4%. White solid. Mp 141.7–142.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (3H, s), 2.44–2.62 (1H, m), 2.70–2.90 (1H, m), 3.82 (1H, dd, J_1=8.80 Hz, J_2=7.60 Hz), 4.23 (1H, t, *J*=8.80 Hz), 4.95–5.10 (1H, m), 7.19 (2H, d, *J*=8.40 Hz), 7.39 (2H, d, *J*=8.40 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −115.00 to −112.0 (2F, m), −71.79 (2F, s). ^{13}C NMR (107 MHz, $CDCl_3$) δ 20.77, 36.20 (t, *J*=22.42), 50.98, 66.40, 118.48, 129.71, 134.33, 135.14, 153.80. IR (KBr) 3116, 2925, 1733, 1610, 1520, 1434, 1303, 1149, 1135, 1099, 813, 743, 511 cm^{-1}. HRMS (EI): $C_{13}H_{12}ClF_4NO_2$ calcd: 325.0493, found: 325.0486.

*4.5.4. 5-(2,2,3,3,4,4,5,5,5-Nonafluoropentyl)-3-p-tolyloxazolidin-2-one (**1bb**).* Yield: 81.3%. White solid. Mp 150.5–152.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (3H, s), 2.45–2.65 (1H, m), 2.70–2.90 (1H, m), 3.82 (1H, dd, J_1=9.20 Hz, J_2=7.60 Hz), 4.23 (1H, t, *J*=8.80 Hz), 4.98–5.09 (1H, m), 7.19 (2H, d, *J*=8.40 Hz), 7.39 (2H, d, *J*=8.80 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −125.99 to −125.84 (2F, m), −124.45 to −124.30 (2F, m), −112.70 to −112.56 (2F, m), −80.96 (3F, t, *J*=9.40 Hz). ^{13}C NMR (107 MHz, $CDCl_3$) δ 20.78, 36.10 (t, *J*=22.31 Hz), 50.95, 66.32, 118.48, 129.73, 134.36, 135.11, 153.79. IR (KBr) 3463, 3216, 2922, 1744, 1632, 1522, 1432, 1406, 1307, 1224, 1135, 822, 753, 733, 669, 515 cm^{-1}. HRMS (EI): $C_{15}H_{12}F_9NO_2$ calcd: 409.0724, found: 409.0729.

*4.5.5. 5-(3-Chloro-2,2,3,3-tetrafluoropropyl)-3-(4-methoxy-phenyl) oxazolidin-2-one (**1ca**).* Yield: 84.8%. White solid. Mp 130.7–133.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48–2.64 (1H, m), 2.72–2.88 (1H, m), 3.78–3.88 (4H, m), 4.21 (1H, t, *J*=8.80 Hz), 4.97–5.05 (1H, m), 6.92 (2H, d, *J*=8.80 Hz), 7.41 (2H, d, *J*=8.80 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.35 to −112.50 (2F, m), −71.78 (2F, s). ^{13}C NMR (107 MHz, $CDCl_3$) δ 35.86 (t, *J*=22.63), 51.29, 55.52, 66.65, 114.40, 120.47, 130.79, 154.10, 156.71. IR (KBr) 3456, 3103, 2958, 2921, 2830, 1748, 1521, 1415, 1252, 1145, 1100, 1047, 943, 833, 753, 631, 515 cm^{-1}. HRMS (EI): $C_{13}H_{12}ClF_4NO_3$ calcd: 341.0442, found: 341.0432.

*4.5.6. 3-(4-Methoxyphenyl)-5-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)-oxazolidin-2-one (**1cb**).* Yield: 81.6%. White solid. Mp 143.2–144.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46–2.64 (1H, m), 2.70–2.88 (1H, m), 3.77–3.85 (4H, m), 4.21 (1H, t, *J*=8.60 Hz), 4.97–5.07(1H, m), 6.92 (2H, d, *J*=9.20 Hz), 7.40 (2H, d, *J*=9.20 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.60 to −125.85 (2F, m), −124.58 to −124.34 (2F, m), −112.75 to −112.60 (2F, m), −81.9 (3F, 80.97, t, *J*=9.40 Hz). ^{13}C NMR (106.6 MHz, $CDCl_3$) 36.09 (t, *J*=21.99), 51.32, 55.51, 66.32, 114.40, 120.48, 130.73, 154.04, 156.73. IR (KBr) 3467, 3166, 2951, 2349, 1949, 1736, 1611, 1521, 1401, 1308, 1229, 1124, 1028, 882, 833, 733, 641, 504 cm^{-1}. HRMS (EI): $C_{15}H_{12}F_9NO_3$ calcd: 425.0673, found: 425.0672.

*4.5.7. 5-(3-Chloro-2,2,3,3-tetrafluoropropyl)-3-(4-chlorophenyl)-oxazolidin-2-one (**1da**).* Yield: 90.4%. White solid. Mp 104.6–105.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48–2.66 (1H, m), 2.72–2.90 (1H, m), 3.83 (1H, dd, J_1=8.80 Hz, J_2=7.60 Hz), 4.23 (1H, t, *J*=8.60 Hz), 5.00–5.13 (1H, m), 7.35 (2H, d, *J*=8.80 Hz), 7.46 (2H, d, *J*=9.20 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.31.99 to −112.18 (2F, m), −71.78 (2F, s). ^{13}C NMR (107 MHz, $CDCl_3$) δ 36.16 (t, *J*=22.47), 50.71, 66.50, 119.47, 129.23, 129.83, 136.27, 153.53. IR (KBr) 3473, 3116, 2955, 1740, 1594, 1498, 1431, 1261, 1098, 953, 825, 802, 495 cm^{-1}. HRMS (EI): $C_{12}H_9Cl_2F_4NO_2$ calcd: 344.9946, found: 344.9937.

*4.5.8. 3-(4-Chlorophenyl)-5-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)-oxazolidin-2-one (**1db**).* Yield: 86.1%. White solid. Mp 83.6–84.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50–2.90 (2H, m), 3.83 (1H, dd, J_1=8.80 Hz, J_2=8.00 Hz), 4.24 (1H, t, *J*=8.60 Hz), 5.00–5.13 (1H, m), 7.35 (2H, d, *J*=9.20 Hz), 7.48 (2H, d, *J*=9.20 Hz). ^{19}F NMR (376 MHz,

$CDCl_3$) δ −125.99 to −125.80 (2F, m), −124.45 to −124.25 (2F, m), −112.62 to −112.50 (2F, m), −81.94 (3F, t, J=9.21 Hz). ^{13}C NMR (107 MHz, $CDCl_3$) δ 39.35 (m), 50.66, 66.39, 119.49, 121.43, 129.21, 136.28, 153.52. IR (KBr) 3444, 3149, 2999, 2939, 2240, 1757, 1506, 1398, 1231, 1185, 1135, 1065, 836, 749, 686, 507 cm^{-1}. HRMS (EI): $C_{14}H_9ClF_9NO_2$ calcd: 429.0178, found: 429.0160.

*4.5.9. 5-(3-Chloro-2,2,3,3-tetrafluoropropyl)-3-phenethyloxazo-lidin-2-one (**1ea**).* Yield: 61.1%. White solid. Mp 54.5–56.7 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.17–2.35 (1H, m), 2.50–2.67 (1H, m), 2.84–3.02 (2H, m), 3.11 (1H, dd, J_1=8.80 Hz, J_2=6.80 Hz), 3.46–3.64 (3H, m), 4.70–4.84 (1H, m) 7.20–7.26 (3H, m), 7.28–7.37 (2H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.50 to −112.44 (2F, m), −71.80 (2F, s). ^{13}C NMR (107 MHz, $CDCl_3$) δ 33.86, 35.70 (t, J=22.58 Hz), 45.26, 50.64, 66.93, 126.86, 128.68, 128.76, 138.00, 156.76. IR (KBr) 3476, 3113, 2956, 1747, 1450, 1405, 1259, 1151, 1089, 945, 908, 883, 801, 754, 699, 684, 494 cm^{-1}. HRMS (EI): $C_{14}H_{14}ClF_4NO_2$ calcd: 339.0649, found: 339.0647.

*4.5.10. 5-(2,2,3,3,4,4,5,5,5-Nonafluoropentyl)-3-phenethyloxazolidin-2-one (**1eb**).* Yield: 67.7%. White solid. Mp 52.7–53.9 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.16–2.34 (1H, m), 2.46–2.66 (1H, m), 2.84–2.97 (2H, m), 3.10 (1H, dd, J_1=8.80 Hz, J_2=6.80 Hz), 3.46–3.62 (3H, m), 4.70–4.84 (1H, m) 7.20–7.26 (3H, m), 7.29–7.36 (2H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.05 to −125.90 (2F, m), −124.64 to −124.40 (2F, m), −112.95 to −112.85 (2F, m), −81.01 (3F, t, J=9.59). ^{13}C NMR (106.6 MHz, $CDCl_3$) δ 33.84, 35.93, 45.24, 50.65, 66.58, 126.85, 128.68, 128.76, 138.00, 156.70. IR (KBr) 3029, 2938, 1732, 1494, 1454, 1221, 1175, 1133, 889, 745, 699, 610, 490 cm^{-1}. HRMS (EI): $C_{16}H_{14}F_9NO_2$ calcd: 423.0881, found: 423.0882.

*4.5.11. 5-(3-Chloro-2,2,3,3-tetrafluoropropyl)-3-(3-fluoro-4-morpholinophenyl)oxazolidin-2-one (**1fa**).* Yield: 73.6%. White solid. Mp 98.7–99.9 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.48–2.66 (1H, m), 2.72–2.90 (1H, m), 3.05 (4H, t, J=4.60 Hz), 3.75–3.82 (1H, dd, J_1=9.20 Hz, J_2=7.60 Hz), 3.87 (4H, t, J=4.60 Hz), 4.19 (1H, t, J=8.80 Hz), 4.97–5.07 (1H, m), 6.93 (1H, t, J=9.20 Hz), 7.09 (1H, dd, J_1=8.80 Hz, J_2=1.60 Hz), 7.41 (1H, dd, J_1=14.40 Hz, J_2=2.80 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −120.04 (1F, s), −112.34 to −112.24 (2F, m), −71.79 (2F, s). ^{13}C NMR (107 MHz, $CDCl_3$) δ 35.79 (t, J=22.63 Hz), 50.74, 50.96 (d, J=3.21 Hz), 66.70, 66.92, 107.56 (d, J=28.03 Hz), 113.99 (d, J=3.42 Hz), 118.85 (d, J=9.52 Hz), 132.70 (d, J=11.13 Hz), 136.67 (d, J=9.52 Hz), 153.62, 155.96 (d, J=155.15 Hz). IR (KBr) 3446, 3199, 2955, 2923, 2855, 2357, 1747, 1636, 1531, 1401, 1231, 1153, 1116, 952, 897, 798, 749, 665, 563 cm^{-1}. HRMS (EI): $C_{16}H_{16}ClF_5NO_3$ calcd: 414.0770, found: 414.0760.

*4.5.12. 3-(3-Fluoro-4-morpholinophenyl)-5-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)oxazolidin-2-one (**1fb**).* Yield: 78.9%. White solid. Mp 90.6–91.8 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.49–2.66 (1H, m), 2.72–2.90 (1H, m), 3.09 (4H, t, J=4.60 Hz), 3.77–3.84 (1H, dd, J_1=8.80 Hz, J_2=7.60 Hz), 3.89 (4H, t, J=4.40 Hz), 4.22 (1H, t, J=8.80 Hz), 5.00–5.10 (1H, m), 6.95–6.70 (1H, t, J=8.80 Hz), 7.10 (1H, dd, J_1=8.80 Hz, J_2=2.00 Hz), 7.44 (1H, dd, J_1=14.00 Hz, J_2=2.00 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −125.97 to −125.80(2F, m), −124.42 to −124.26(2F, m), −119.97 (1F, s), −112.64 to −112.50 (2F, m), −81.92 (3F, t, J=9.40 Hz). ^{13}C NMR (107 MHz, $CDCl_3$) δ 35.79 (t, J=22.63 Hz), 50.74, 50.90, (d, J=3.21 Hz), 66.69, 66.90, 107.54 (d, J=28.03 Hz), 113.89 (d, J=3.42 Hz), 118.85 (d, J=9.52 Hz), 132.66 (d, J=11.13 Hz), 136.68 (d, J=9.52 Hz), 153.63, 154.46 (d, J=262.15 Hz). IR (KBr) 3125, 2951, 2859, 1746, 1515, 1400, 1225, 1138, 935, 885, 744, 665 cm^{-1}. HRMS (EI): $C_{18}H_{16}F_{10}N_2O_3$ calcd: 498.1001, found: 498.0995.

4.6. Typical procedure for synthesis of 5-(fluoroalkyl)-3-aryl/alkyl oxazolidin-2-one (1ac–1fc)

To a stirred solution of benzyl allyl phenylcarbamates **4a** (0.54 g, 2 mmol) and 5-(difluoroiodomethyl)-3-phenyl-1,2,4-oxadiazole (0.97 g, 3.00 mmol) in DMF (20 mL) was added AIBN (0.66 g, 4.00 mmol). The mixture was stirred under microwave irradiation (210 W, 2.5 h), and then the solvent was evaporated under reduced pressure. The resulting residue was purified by silica-gel chromatography (EtOAc/petroleum ether=1:5), providing **1ac** (0.57 g), as a white solid.

*4.6.1. 5-(2,2-Difluoro-2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl)-3-phenyloxazolidin-2-one (**1ac**).* Yield: 72.3%. White solid. Mp 116.2–117.5 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.83–3.00 (1H, m), 3.08–3.24 (1H, m), 3.92 (1H, dd, J_1=9.20 Hz, J_2=7.20 Hz), 4.28 (1H, t, J=8.80 Hz), 5.05–5.16 (1H, m), 7.16 (1H, t, J=8.00 Hz), 7.39 (2H, t, J=8.00 Hz) 7.48–7.60 (5H, m), 8.10 (2H, d, J=6.80 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −95.08 (1F, d, J=284.25 Hz), 98.62 (1F, d, J=283.50 Hz). ^{13}C NMR (107 MHz, $CDCl_3$) δ 40.97 (t, J=24.08 Hz), 50.68, 66.95 (t, J=8.24 Hz), 114.17 (t, J=260.92 Hz) 118.33, 124.48, 125.29, 127.65, 129.09, 129.18, 132.05, 137.72, 153.74, 168.83 170.54 (J=35.95 Hz). IR (KBr) 3108, 2967, 1739, 1515, 1447, 1421, 1228, 1199, 1112, 1095, 902, 869, 747, 701 cm^{-1}. HRMS (EI): $C_{19}H_{15}F_2N_3O_3$ calcd: 371.1081, found: 371.1080.

*4.6.2. 5-(2,2-Difluoro-2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl)-3-p-tolyloxazolidin-2-one (**1bc**).* Yield: 71.6%. White solid. Mp 103.8–105.6 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.33 (3H, s), 2.82–3.00 (1H, m), 3.08–3.24 (1H, m), 3.90 (1H, dd, J_1=8.80 Hz, J_2=7.20 Hz), 4.26 (1H, t, J=8.80 Hz), 5.05–5.15 (1H, m), 7.19 (2H, d, J=8.40 Hz), 7.40 (2H, d, J=8.40 Hz), 7.48–7.60 (3H, m), 8.08–8.14 (2H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −98.95 (1F, d, J=278.99 Hz), −94.57 (1F, d, J=278.99 Hz) (2F, m). ^{13}C NMR (107 MHz, $CDCl_3$) δ 20.79, 41.07 (t, J=24.02 Hz), 50.93, 66.93, 118.49, 125.33, 127.69, 129.01, 129.71, 132.06, 132.06, 134.27, 135.23, 168.86, 170.89 (t, J=36.93 Hz). IR (KBr) 3448, 2999, 2233, 1756, 1594, 1295, 1473, 1185, 1148, 968, 764, 7, 703, 692 cm^{-1}. HRMS (EI): $C_{20}H_{17}F_2N_3O_3$ calcd: 385.1238, found: 385.1236.

*4.6.3. 5-(2,2-Difluoro-2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl)-3-(4-methoxyphenyl)oxazolidin-2-one (**1cc**).* Yield: 82.4%. White solid. Mp 64.4–66.5 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.84–3.00 (1H, m), 3.08–3.24 (1H, m), 3.80 (3H, s), 3.89 (1H, dd, J_1=8.80 Hz, J_2=7.60 Hz), 4.24 (1H, t, J=8.60 Hz), 5.05–5.15 (1H, m), 6.92 (2H, d, J=8.80 Hz), 7.41 (2H, d, J=9.20 Hz), 7.48–7.60 (3H, m), 8.08–8.14 (2H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −95.11 (1F, d, J=284.26 Hz), −98.03 (1F, d, J=283.50 Hz). ^{13}C NMR (107 MHz, $CDCl_3$) δ 40.01 (t, J=12.09 Hz), 51.23, 55.521, 66.94 (t, J=4.17 Hz), 114.38, 120.47, 125.34, 127.67, 129.10, 130.87, 132.05, 154.09, 156.66, 168.85, 170.61 (t, J=35.90 Hz). IR (KBr) 3460, 3178, 2950, 2838, 2232, 1753, 1736, 1668, 1515, 1403, 1250, 1129, 972, 831, 752, 690, 520 cm^{-1}. HRMS (EI): $C_{20}H_{17}F_2N_3O_4$ calcd: 401.1187, found: 401.1182.

*4.6.4. 3-(4-Chlorophenyl)-5-(2,2-difluoro-2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl)oxazolidin-2-one (**1dc**).* Yield: 84.3%. White solid. Mp 53.1–57.4 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.84–3.00 (1H, m), 3.10–3.24 (1H, m), 3.91 (1H, dd, J_1=8.80 Hz, J_2=7.60 Hz), 4.27 (1H, t, J=8.60 Hz), 5.06–5.18 (1H, m), 7.35 (2H, d, J=9.20 Hz), 7.46–7.60 (5H, m), 8.08–8.13 (2H, m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −95.06 (1F, d, J=284.26 Hz), −98.59 (1F, d, J=284.63 Hz). ^{13}C NMR (107 MHz, $CDCl_3$) δ 40.98 (t, J=12.09 Hz), 50.63, 67.02, 119.46, 125.27, 127.66, 129.11, 129.21, 129.75, 132.09, 136.34, 153.54, 168.86, 170.48 (t, J=35.85 Hz). IR (KBr) 3502, 3104, 2955, 1769, 1594, 1499, 1405, 1296, 1227, 1128, 1094, 956, 826, 751, 700, 516 cm^{-1}. HRMS (EI): $C_{19}H_{14}F_2N_3O_3$ calcd: 405.0692, found: 405.0670.

*4.6.5. 5-(2,2-Difluoro-2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl)-3-phenethyloxazolidin-2-one (**1ec**).* Yield: 74.3%. White solid. Mp 65.4–69.3 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.52–2.70 (1H, m), 2.84–3.02 (3H, m), 3.14–3.21 (1H, m), 3.47–3.56 (2H, t, J=7.40 Hz), 3.60 (1H, t, J=8.80 Hz), 4.79–4.88 (1H, m), 7.20–7.25 (3H, m), 7.31

(2H, t, J=7.40 Hz), 7.48–7.57 (3H, m), 8.10 (2H, d, J=8.00 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −95.26 (1F, J=283.13 Hz), −98.83 (1F, J=283.13 Hz). ^{13}C NMR (107 MHz, $CDCl_3$) δ 33.85, 40.86 (t, J=12.09 Hz), 45.25, 50.50, 67.20 (t, J=4.17 Hz), 125.35, 126.80, 127.63, 128.71 (d, J=5.14 Hz), 129.07, 132.01, 138.05, 156.73, 168.75, 170.64 (t, J=35.90 Hz). IR (KBr) 3486, 3079, 3033, 2946, 2867, 2237, 1967, 1755, 1372, 1270, 1175, 1085, 963, 905, 754, 703, 500 cm^{-1}. HRMS (EI): $C_{21}H_{19}F_2N_3O_3$ calcd: 399.1394, found: 399.1398.

*4.6.6. 5-(2,2-Difluoro-2-(5-phenyl-1,2,4-oxadiazol-3-yl)ethyl)-3-(2-fluoro-4-morpholinophenyl)-oxazolidin-2-one (**1fc**).* Yield: 78.0%. White solid. Mp 128.5–129.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.84–3.00 (1H, m), 3.07 (4H, t, J=4.60 Hz), 3.10–3.24 (1H, m), 3.82–3.99 (5H, m), 4.24 (1H, t, J=8.80 Hz), 5.08–5.16 (1H, m), 6.97 (1H, t, J=8.80 Hz), 7.11 (1H, dd, J_1=8.80 Hz, J_2=2.00 Hz), 7.43 (1H, dd, J_1=14.00 Hz, J_2=2.40 Hz), 7.49–7.60 (3H, m), 8.10 (2H, d, J=7.20 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −119.94 (1F, s), −98.60 (1F, d, J=284.26 Hz), 95.07 (1F, d, J=283.88 Hz). ^{13}C NMR (107 MHz, $CDCl_3$) δ 40.99 (t, J=24.18 Hz), 50.78, 51.03 (d, J=3.10 Hz), 66.90, 66.99, 107.56 (d, J=28.03), 107.75, 113.99 (d, J=12.78 Hz), 119.01 (d, J=4.17 Hz), 125.28, 127.67, 129.12, 132.10, 153.60, 168.86, 170.50 (t, J=41.09 Hz). IR (KBr) 3108, 2967, 1740, 1515, 1447, 1421, 1228, 1112, 902, 869, 701, 523 cm^{-1}. HRMS (EI): $C_{23}H_{21}F_3N_4O_4$ calcd: 474.1515, found: 474.1514.

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Supplementary data

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