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# Study on the tandem synthesis of optically active 2-substituted 4 (or 5)-phenyl-1,3-oxazolines

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ABSTRACT

Optically active (*S*)-2-aryl-4 (or 5)-phenyl-1,3-oxazolines and (*S*)-2-fluoroalkyl-4-phenyl-1,3-oxazolines were synthesized from a tandem one-pot reaction of (*S*)-2-amino-2-phenylethanol with a corresponding carboxylic acid in toluene at 90 °C in the presence of $PPh_3/CBr_4$ and excess $Et_3N$. The use of aromatic carboxylic acids were determined to proceed through *N*-(2-bromo-1-phenyl-ethyl)-arylamides **5** and *N*-aroyl aziridine intermediates **6**, which resulted in the formation of (*S*)-2-aryl-4-phenyl-1,3-oxazolines and (*S*)-2-aryl-5-phenyl-1,3-oxazolines, respectively. Concurrently, the reaction with fluorinated aliphatic carboxylic acid substrates proceeded via *N*-(2-hydroxy-1-phenyl-ethyl)-fluoroalkyl amide intermediates **8**, which were converted into *N*-(2-bromo-1-phenyl-ethyl)-fluoroalkyl amide intermediates **9**, and then into (*S*)-2-fluoroalkyl-4-phenyl-1,3-oxazolines as final products. Reaction mechanisms that mainly passed through the formation of aziridine intermediates **6** in the reaction with aromatic carboxylic acids and the formation of fluoroalkyl amide intermediates **8** and **9** in the reaction with fluorinated aliphatic carboxylic acid were proposed. The acidities of the carboxylic acids that were employed were found to play a key role in the selective formation of various intermediates during this reaction.

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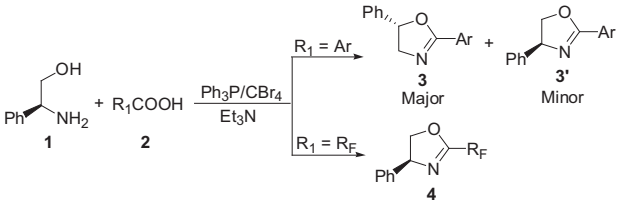
## 1. Introduction

Optically active 1,3-oxazoline heterocycles are a fundamental motif present in many bioactive molecules, natural products, and organomaterials.[1] In addition, 1,3-oxazoline heterocycles are versatile chiral ligands.[2] Many methods have been developed for the synthesis of 1,3-oxazoline;[3] however, most of these methods suffer from having complicated procedures, being multistep reactions and using harmful solvents or result in low yields.[4] Aziridines are important organic synthetic intermediates.[5] *N*-substituted aziridines have been used extensively for ring-opening, ring-expansion and cycloaddition chemical transformations because of the presence of inherent ring-strain.[6] Recently, we reported that *N*-aroyl aziridines generated in situ from the reaction of (*S*)-2-amino-3-phenylpropanol with various aromatic carboxylic acids in the presence of $PPh_3/CBr_4$ could be transformed into the optically active (*S*)-4-benzyl-1,3-oxazolines or (*S*)-5-benzyl-1,3-oxazolines via ring-opening of the aziridines and subsequent cyclization.[7] This synthetic methodology was demonstrated to be an effective tandem reaction process for the synthesis of optically active 4 or 5-benzyl-1,3-oxazoline. As part of our ongoing studies, we present a tandem reaction for the synthesis of optically active 2-aryl or fluoroalkyl-4 (or 5)-phenyl-1,3-oxazolines (Scheme 1), and explore the reason for the selective formation of different products as various types of carboxylic acids were employed.




**Scheme 1.** Synthesis of 4 (or 5)-phenyl-1,3-oxazolines.

## 2. Results and discussion

As previously reported,[7] the tandem reaction of (*S*)-2-amino-3-phenylpropanol with various aromatic acids in the presence of $PPh_3/CBr_4$ provided (*S*)-4-benzyl-1,3-oxazolines as the major products and unexpectedly produced (*S*)-5-benzyl-1,3-oxazoline as minor products. However, the use of (*S*)-2-amino-2-phenylethanol

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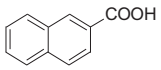
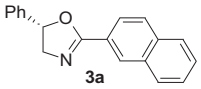
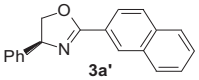
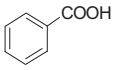
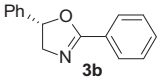
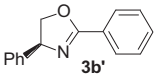
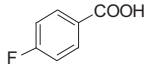
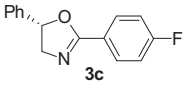
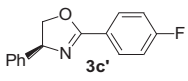
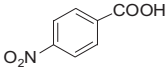
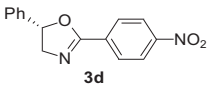
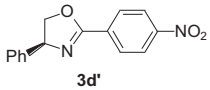
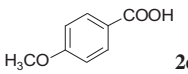
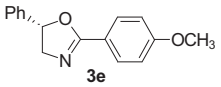
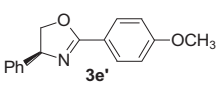
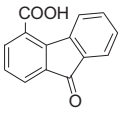
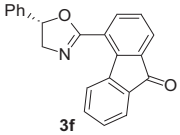
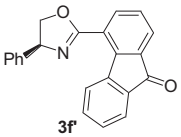
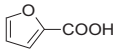
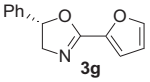
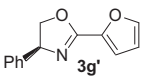
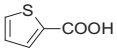
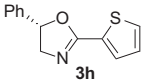
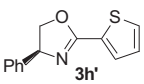
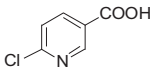
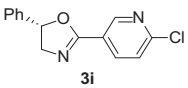
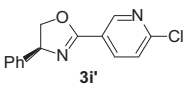
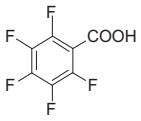
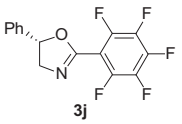
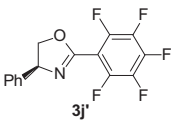
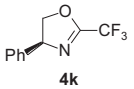
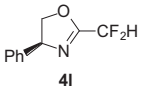
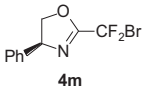
and naphthalene-2-carboxylic acid resulted in the opposite distribution of products: (*S*)-5-phenyl-1,3-oxazoline (**3a**) was the major product, while (*S*)-4-phenyl-1,3-oxazoline (**3a′**) was the minor product (entry 1, Table 1). In addition, the reaction of (*S*)-2-amino-2-phenylethanol with trifluoroacetic acid resulted in the formation of (*S*)-2-trifluoromethyl-4-phenyl-1,3-oxazoline (**4k**) (entry 11, Table 1) as the only product. The interesting experimental results prompted us to further investigate the tandem reaction and explore the transformation process.

The reaction was performed in the presence of 3 equiv of $PPh_3$/$CBr_4$ in toluene at 90 °C via a one-pot process. The reaction of the-various aromatic carboxylic acids with (*S*)-2-amino-2-phenylethanol

**Table 1**
The reaction of (*S*)-2-amino-2-phenylethanol with aromatic (or fluorinated) carboxylic acids

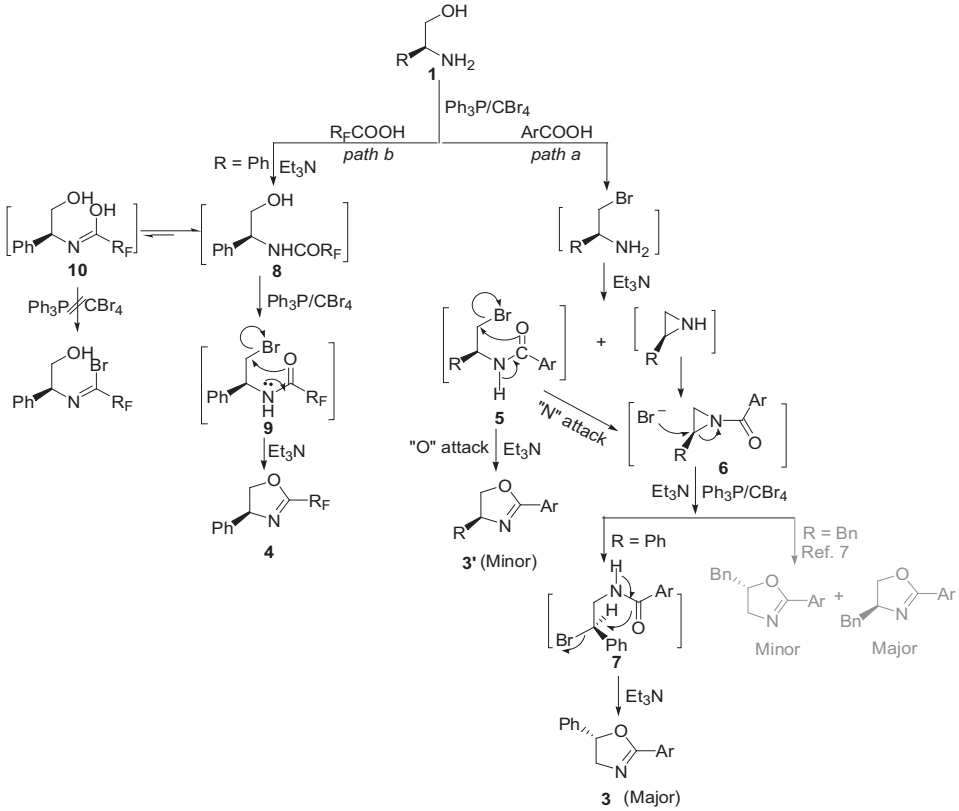
| Entry | $R_1COOH$ (**2**) | $pK_a$ | Product (**3**, **3′**, or **4**) | Time (h) | Yield[a] (%) (**3**, **3′**, or **4**) |
|---|---|---|---|---|---|
| 1 |  **2a** | 4.17 |  **3a**  **3a'** | 2 | 62, 28 |
| 2 |  **2b** | 4.19 |  **3b**  **3b'** | 6 | 48, 29 |
| 3 |  **2c** | 4.14 |  **3c**  **3c'** | 8 | 62, 31 |
| 4 |  **2d** | 3.42 |  **3d**  **3d'** | 8 | 62, 31 |
| 5 |  **2e** | 4.47 |  **3e**  **3e'** | 10 | 45, 31 |
| 6 |  **2f** | 3.51 |  **3f**  **3f'** | 14 | 53, 24 |
| 7 |  **2g** | 3.16 |  **3g**  **3g'** | 14 | 49, 21 |
| 8 |  **2h** | 3.51 |  **3h**  **3h'** | 8 | 42, 23 |
| 9 |  **2i** | 3.24 |  **3i**  **3i'** | 13 | 19, 34 |
| 10 |  **2j** | 1.6 |  **3j**  **3j'** | 20 | 43, 20 |
| 11 | $CF_3COOH$ **2k** | 0.5 |  **4k** | 42 | 61 |
| 12 | $HCF_2COOH$ **2l** | 1.3 |  **4l** | 55 | 42 |
| 13 | $BrCF_2COOH$ **2m** | 0.2 |  **4m** | 18 | 65 |
| 14 | $CH_3COOH$ **2n** | 4.75 | / | 42 | /[b] |

[a] Isolated yields.
[b] No desired product was observed.

resulted in 2-aryl-1,3-oxazolines with the retention of stereochemical configuration in excellent overall yields (Table 1). The aromatic carboxylic acids with electron-withdrawing groups resulted in comparatively higher yields (entry 3, 4) than aromatic carboxylic acids with electron-donating groups (entry 5). When perfluorinated benzoic acid was used, the reaction provided 2-pentafluorophenyl-5-phenyl-1,3-oxazoline and 2-pentafluorophenyl-4-phenyl-1,3-oxazoline in 43% and 20% yield, respectively (entry 10). Additionally, the 5-phenyl-1,3-oxazolines were the major products for all reactions that used aromatic carboxylic acids. Further experiments demonstrated that aromatic heterocyclic acids that contained either nitrogen (N), oxygen (O) or sulfur (S) could be employed in this tandem reaction to obtain optically active 1,3-oxazolines (entries 7, 8, and 9).

To expand the application of this tandem one-pot reaction, several fluorinated aliphatic carboxylic acids were used as reactants. The reaction of trifluoroacetic acid with (*S*)-2-amino-2-phenylethanol, performed in the presence of $PPh_3/CBr_4$ in toluene at 90 °C with excess $Et_3N$, resulted in one product **4k** (entry11, Table 1), which was observed as a singlet at −69.97 ppm in the $^{19}F$ NMR spectrum of the reaction mixture. This result suggested that the procedure of reaction with fluorinated aliphatic carboxylic acids is different from a reaction with aromatic carboxylic acids and aromatic heterocyclic acids. A variety of techniques (e.g., $^1H$ NMR, $^{13}C$ NMR, $^{19}F$ NMR, GC–MS, and HPLC) were used to determine that the fluorinated product was (*S*)-2-trifluoromethyl-4-phenyl-1,3-oxazoline with the retention of stereochemical configuration (99% ee). Other fluorinated aliphatic carboxylic acids (e.g., difluoroacetic acid and bromodifluoroacetic acid) provided the formation of similar (*S*)-2-fluoroalkyl-4-phenyl-1,3-oxazoline products in moderate yields (Table 1, entries 12 and 13). However, the use of non-fluorinated aliphatic carboxylic acids did not result in the desired 2-alkyl-4 (or 5)-phenyl-1,3-oxazolines under the same reaction conditions (Table 1, entries 14).

To clarify the results of the tandem reactions using (*S*)-2-amino-2-phenylethanol with various carboxylic acids, isolation, and identification of the reaction intermediates were attempted by performing the reaction of different carboxylic acids with 1 equiv of (*S*)-2-amino-2-phenylethanol and 3 equiv of $PPh_3/CBr_4$ in toluene, under a nitrogen atmosphere. The reaction with naphthalene-2-carboxylic acid was performed at room temperature for 10 min, and then heated at 90 °C. The intermediate (*S*)-1-(2-naphthoyl)-2-phenylaziridine (**6a**, Scheme 2) was observed after 0.5 h by TLC, and it was isolated in 16% yield as a white solid[7] that could be completely converted into product of (*S*)-5-phenyl-1,3-oxazolines (**3a**) with the retention of stereochemical configuration, under the reaction conditions described above. Other intermediates with the general structure of **6** were observed by GC–MS analysis of the reaction mixtures (e.g., pentafluorophenyl-(2-phenyl-aziridin-1-yl)-methanone (**6j**) ($M^+$: 313, base peak *m*/*z*: 195)). Moreover, the experiments demonstrated that pentafluorophenyl-(2-phenyl-aziridin-1-yl)-methanone (**6j**) could be completely converted into (*S*)-5-phenyl-1,3-oxazoline (**3j**, $M^+$: 313, base peak *m*/*z*: 207). This tandem reaction combines three steps in a one-pot process: the formation of *N*-aroyl aziridine intermediate **6** in the presence of $PPh_3/CBr_4$, the subsequent ring-opening reaction of **6** at the arylmethyl carbon by a $Br^-$ nucleophile generated from $PPh_3/CBr_4$,[8] followed by intramolecular nucleophilic cyclization (Scheme 2, path a). The configuration of the stereogenic center of the products was retained because inversion of the stereogenic center occurred twice during the ring-opening of the *N*-aroyl aziridine intermediate and the ring closure that formed the product in this tandem transformation. The retention of the configuration was also demonstrated by the measurement of enantiomeric purity. For example, the enantiomer excess value (ee%) of (*S*)-5-phenyl-1,3-oxazoline **3a** was 99.5%. The minor product, (*S*)-4-phenyl-1,3-oxazoline, could be obtained from the intramolecular ring closure of a noncyclized amide intermediate (**5**, Scheme 2) in the presence of $Et_3N$.[7] Although the noncyclized




**Scheme 2.** The proposed mechanism for the formation of the various products.

amide intermediate **5** in the reaction mixture of (*S*)-2-amino-2-phenylethanol with perfluorinated benzoic acid was not observed after 2 h by GC–MS, the minor product of 2-pentafluorophenyl-4-phenyl-1,3-oxazoline (**3j′**) was found ($M^+$: 313, base peak *m*/*z*: 283). The formation of the *N*-aroyl aziridine intermediate **6** may be easier than the direct ring closure of the noncyclized amide intermediate **5** in the reaction system; therefore, the 5-phenyl-1,3-oxazoline **3** was obtained as the major product.

When fluorinated aliphatic carboxylic acid, such as trifluoroacetic acid, was used as the substrate, the intermediate **8k** was observed by GC–MS and was isolated from the mixture of the reaction of (*S*)-2-amino-2-phenylethanol after 2 h. The intermediate **8k** could not be directly converted into the product **4k** in the presence of $Et_3N$. One possible reason is that the strong electron-withdrawing inductive effect of the fluoroalkyl group reduced the polarization of the C=O bond, which caused the attack of the hydroxyl group on the carbonyl carbon of intermediate **8k** to be weak and resulted in the inefficient formation of the 1,3-diazoline **4k**. 2-Trifluoromethyl-4-phenyl-1,3-diazoline (**4k**) could be obtained from **8k** only when $PPh_3/CBr_4$ and an excess $Et_3N$ were added to the isolated amide **8k** in toluene at 90 °C. This result indicates that the desired 1,3-oxazoline **4k** should be transformed via the other intermediate, which was derived from amide **8k** in the presence of $Ph_3P/CBr_4$ and excess $Et_3N$. According to Uneyama's reports,[9] amides were easily converted to imidoyl halides in the presence of $PPh_3/CX_4$. However, the reaction of (*S*)-2-amino-2-phenylethanol with trifluoroacetic acid resulted in the formation of an *N*-(2-halo-1-phenyl-ethyl)-2,2,2-trifluoro-acetamide (**9**), which was different from the imidoyl halide intermediate. GC–MS analysis indicated that there was *N*-(2-chloro-1-phenyl-ethyl)-2,2,2-trifluoro-acetamide **9k′** (wherein halo is chloro) ($M^+$: 251, *t*=9.81 min) and amide **8k** ($M^+$: 233, *t*=7.38 min) with the generation of product **4k** ($M^+$: 215, *t*=7.90 min) in the reaction system of (*S*)-2-amino-2-phenylethanol with trifluoroacetic acid in the presence of $PPh_3/CCl_4$. The structure of *N*-(2-chloro-1-phenyl-ethyl)-2,2,2-trifluoro-acetamide (**9k′**) was also further confirmed by X-ray diffraction (Fig. 1). Intermediate **9k** ($M^+$: 295, *t*=10.50 min) was also observed by GC–MS in the presence of $PPh_3/CBr_4$ after reacting for 2 h. *N*-(2-Halo-1-phenyl-ethyl)-2,2,2-trifluoro-acetamide (**9**) was obviously generated from *N*-(2-hydroxy-1-phenyl-ethyl)-2,2,2-trifluoro-acetamide (**8k**) in the presence of $PPh_3/CX_4$ and $Et_3N$. The formation of *N*-(2-halo-1-phenyl-ethyl)-2,2,2-trifluoro-acetamide (**9**) versus imidoyl halide could depend on the structure of the substrate of 2-hydroxy-ethylamine. Additionally, the isolated *N*-(2-chloro-1-phenyl-ethyl)-2,2,2-trifluoro-acetamide (**9k′**) can easily be converted into 2-trifluoromethyl-4-phenyl-1,3-oxazoline (**4k**) in 94% yield in the presence of $NEt_3$.

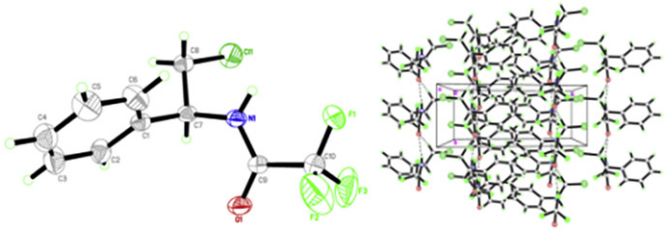


**Fig. 1.** An ORTEP plot of the intermediate **9k′** and its packing diagram.

In the reaction with aromatic carboxylic acids with relatively weak acidity, halogenation of the hydroxyl group of (*S*)-2-amino-2-phenylethanol could occur preferentially, proceeding via amidation of the amino group in this reaction condition to intermediate **5** or **6** (Scheme 2, path a), because no product of the amidation of amino group, such as *N*-(2-hydroxy-1-phenyl-ethyl)-amide, was observed by GC–MS in the reaction of (*S*)-2-amino-2-phenylethanol with perfluorinated benzoic acid after 2 h. Following the formation of intermediate **5**, there was the competition of the O or N to attack the brominated carbon for cyclization into the five-membered ring product or three-membered ring *N*-aroyl aziridine intermediate. Conjugation of the carbonyl group with the aromatic ring would reduce the nucleophilicity of the oxygen, which would cause the closure of the five-membered ring to be more difficult than that of the three-membered ring. Therefore, this tandem one-pot reaction was suggested to have mainly passed through the formation of aziridine intermediate **6** in the reaction with aromatic carboxylic acids. This was also the reason that (*S*)-5-phenyl-1,3-oxazoline **3** was the major product. On the other hand, for relatively strong fluorinated aliphatic carboxylic acids ($pK_a$=0.5–1.3), the formation of fluorinated amide **8** illustrated that this reaction preferentially underwent the amidation of amino group of (*S*)-2-amino-2-phenylethanol. Subsequently, the hydroxyl group at the $sp^3$-hybridized carbon atom of **8** was halogenated to intermediate **9** in the presence of $PPh_3/CX_4$, rather than the halogenations of the hydroxyl group at the $sp^2$-hybridized carbon atom of the imino alcohol **10** from the amide **8** tautomer to the imidoyl halide reported by Uneyama. Finally, intermediate **9** easily underwent intramolecular cyclization to form the 2-fluoroalkyl-4-phenyl-1,3-oxzaline product only.

## 3. Conclusions

In summary, the optically active (*S*)-2-aryl-4 (or 5)-phenyl-1,3-oxazolines and 2-fluoroalkyl-4-phenyl-1,3-oxazolines were efficiently prepared through a tandem one-pot reaction of (*S*)-2-amino-2-phenylethanol with a corresponding aromatic or fluorinated aliphatic carboxylic acid in toluene at 90 °C in the presence of 3 equiv of $PPh_3/CBr_4$ and excess $Et_3N$. Through the observation or isolation of reaction intermediates, the reaction with aromatic carboxylic acids was proposed to proceed via *N*-(2-bromo-1-phenyl-ethyl)-arylamide intermediates **5** and *N*-aroyl aziridine intermediates **6**. Subsequently, the *N*-aroyl aziridine intermediates **6** underwent ring-opening in the presence of $PPh_3/CBr_4$, which were followed by rapid intramolecular cyclization to form (*S*)-2-aryl-5-phenyl-1,3-oxazolines as the major products, while *N*-(2-bromo-1-phenyl-ethyl)-arylamides **5** directly cyclized to form (*S*)-2-aryl-4-phenyl-1,3-oxazolines as the minor products. When fluorinated aliphatic carboxylic acids were used as the substrates, the reaction first resulted in the formation of the *N*-(2-hydroxy-1-phenyl-ethyl)-fluoroalkyl amide intermediates **8**, and then converted **8** into *N*-(2-halo-1-phenyl-ethyl)-fluoroalkyl amide intermediates **9**, which finally underwent ring closure to form 2-fluoroalkyl-1,3-oxazolines **4** as the only products.

## 4. Experimental section

### 4.1. General methods

*4.1.1. General comments.* $^1H$, $^{13}C$, and $^{19}F$ NMR spectra were recorded on 500 MHz spectrometers. Chemical shifts for $^1H$ NMR spectra are reported in parts per million downfield from TMS, chemical shifts for $^{13}C$ NMR spectra are reported in ppm relative to internal chloroform ($\delta$ 77.2 ppm for $^{13}C$), and chemical shifts for $^{19}F$ NMR spectra are reported in ppm downfield from internal fluorotrichloromethane ($CFCl_3$). Infrared spectra (IR) were recorded with KBr pellets. Silica gel (200–400 mesh) was used for flash column chromatography. Melting points are uncorrected. Single-crystal XRD was performed with graphite-monochromatic MoKa radiation ($\lambda$=0.71073 Å) on a Bruker Smart ApexII CCD diffractometer at *T*=273 (2) K. The structures were solved by direct method with SHELXS-97 program and refined by full matrix least-squares on $F^2$ with SHELXL-97 program. All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were located and included at

their calculated position. Optical rotations were recorded on high sensitive polarimeter with 200 mm cell. The enantiomeric purity was determined by chiral HPLC (Sino-Chiral AD 0.46×25 cm column and *n*-hexane and isopropylol as mobile phase). Mass spectra were obtained using ESI or EI. High resolution mass spectra were obtained using EI at 70 eV.

CCDC 896966 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: +44 1223 336033.

### 4.2. General procedure for the preparation of (*S*)-2-aryl-4 (5)-phenyl-1,3-oxazolines 3′and 3

A 200 mL three-necked flask equipped with a condenser was charged with $Ph_3P$ (2.20 g, 8.4 mmol), $Et_3N$ (0.85 g, 8.4 mmol), $CBr_4$ (16.8 g, 8.4 mmol), substrate **1** (3.3 mmol), and aromatic acid **2** (2.8 mmol) in toluene (15.0 mL) under a nitrogen atmosphere. The solution was stirred for approximately 20 min at room temperature, then the mixture was heated at 90 °C with stirring for 6–14 h. The solvent was evaporated under reduced pressure, and the residue was diluted with petroleum ether (60–90 °C) and filtered. The residual solid $Ph_3PO$ and $Et_3N{\cdot}HBr$ was washed with petroleum ether three times. The filtrate was concentrated, and the residue was separated by column chromatography (ethyl acetate/petroleum ether, 1:8) to afford product **3** and **3′**. If the mixture was processed after stirring for 0.5 h at 90 °C, intermediate **6** was obtained by column chromatography (ethyl acetate/petroleum ether=1:8).

*4.2.1. (S)-2-(2-Naphthyl)-5-phenyl-1,3-oxazoline (**3a**).*[7] White solid; 0.47 g, 62%, mp 73.2–76.7 °C; $[\alpha]_D^{25}$ +28.4 (*c* 0.984, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.53 (s, 1H, $H_{Ar}$), 8.12 (dd, *J*=8.5, 1.5 Hz, 1H, $H_{Ar}$), 7.93–7.87 (m, 3H, $H_{Ar}$), 7.58–7.51 (m, 2H, $H_{Ar}$), 7.41–7.34 (m, 5H, $H_{Ar}$), 5.73 (dd, *J*=10.0, 10.0 Hz, 1H, $NCH_2$), 4.55 (dd, *J*=15.0, 10.0 Hz, 1H, $NCH_2$), 4.07 (dd, *J*=15.0, 8.0 Hz, 1H, CH); $^{13}C$ NMR (500 MHz, $CDCl_3$): $\delta$ 164.3, 141.2, 134.9, 132.8, 129.1, 129.0, 128.9, 128.5, 128.4, 128.0, 127.7, 126.7, 126.0, 125.0, 124.9, 81.3, 63.5; IR ($cm^{-1}$): $\nu$ 3033, 2927, 1641, 1354, 1191, 1062, 962, 761, 699.

*4.2.2. (S)-2-(2-Naphthyl)-4-phenyl-1,3-oxazoline (**3a′**).*[7] White solid; 0.21 g, 28%. Mp 110.6–112.0 °C; $[\alpha]_D^{25}$ −55.5 (*c* 1.016, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.55 (s, 1H, $H_{Ar}$), 8.14 (dd, *J*=8.5, 1.5 Hz, 1H, $H_{Ar}$), 7.94–7.88 (m, 3H, $H_{Ar}$), 7.59–7.52 (m, 2H, $H_{Ar}$), 7.40–7.31 (m, 5H, $H_{Ar}$), 5.45 (dd, *J*=10.0, 10.0 Hz, 1H, $OCH_2$), 4.87 (dd, *J*=10.0, 10.0 Hz, 1H, $OCH_2$), 4.35 (t, *J*=8.0 Hz, 1H, CH); $^{13}C$ NMR (500 MHz, $CDCl_3$): $\delta$ 165.0, 142.5, 135.0, 132.8, 129.2, 129.1, 128.9, 128.3, 127.9, 127.8, 127.7, 127.0, 126.7, 125.1, 125.0, 75.1, 70.4; IR ($cm^{-1}$): $\nu$ 3026, 2912, 1642, 1361, 1194, 1064, 757, 694.

*4.2.3. (S)-2,5-Diphenyl-1,3-oxazoline (**3b**).*[10] Clear oil; 0.30 g, 48%; $[\alpha]_D^{25}$ +21.2 (*c* 0.821, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 8.04–8.01 (m, 2H, ArH), 7.53–7.49 (m, 1H, ArH), 7.46–7.42 (m, 2H, ArH), 7.41–7.31 (m, 5H, ArH), 5.67 (dd, *J*=8.0, 10.0 Hz, 1H, CH), 4.49 (dd, *J*=10.0, 15.0 Hz, 1H, $CH_2$), 4.00 (dd, *J*=8.0, 15.0 Hz, 1H, $CH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 164.0, 141.1, 131.5, 128.8, 128.4, 128.3, 127.7, 125.8, 81.1, 63.2; IR (KBr, $cm^{-1}$): $\nu$ 3033, 2927, 1651, 1605, 1495, 1451, 1256, 1063, 778, 696.

*4.2.4. (S)-2,4-Diphenyl-1,3-oxazoline (**3b′**).*[11] Clear oil; 0.18 g, 29%; $[\alpha]_D^{25}$ −22.8 (*c* 0.690, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 8.07–8.05 (m, 2H, ArH), 7.53–7.50 (m, 1H, ArH), 7.47–7.43 (m, 2H, ArH), 7.39–7.35 (m, 2H, ArH), 7.33–7.28 (m, 3H, ArH), 5.40 (dd, *J*=8.5, 10.0 Hz, 1H, CH), 4.81 (dd, *J*=8.5, 10.5 Hz, 1H, $CH_2$), 4.29 (t, *J*=8.5 Hz, 1H, $CH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 164.8, 142.4, 131.6, 128.8, 128.5, 128.4, 127.7, 127.6, 126.8, 74.9, 70.2; IR (KBr, $cm^{-1}$): $\nu$ 3028, 2924, 1648, 1605, 1495, 1451, 1361, 1081, 780, 695.

*4.2.5. (S)-2-(4-Fluorophenyl)-5-phenyl-1,3-oxazoline (**3c**).* Pale yellow solid; mp 55.3–56.1 °C; 0.42 g, 62%; $[\alpha]_D^{25}$ −9.7 (*c* 1.066, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 8.04–8.00 (m, 2H, ArH), 7.41–7.37 (m, 2H, ArH), 7.35–7.32 (m, 3H, ArH), 7.13–7.10 (m, 2H, ArH), 5.66 (dd, *J*=8.0, 10.0 Hz, 1H, CH), 4.47 (dd, *J*=10.0, 14.5 Hz, 1H, $CH_2$), 3.99 (dd, *J*=8.0, 14.5 Hz, 1H, $CH_2$); $^{19}F$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ −107.97–108.00 (m, 1F); $^{13}C$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 164.9 (d, $^1J_{C-F}$=251.3 Hz), 163.3, 141.0, 130.7 (d, $^3J_{C-F}$=8.8 Hz), 129.0, 128.5, 125.9, 124.0 (d, $^4J_{C-F}$=3.8 Hz), 115.7 (d, $^2J_{C-F}$=21.3 Hz), 81.4, 63.3; IR (KBr, $cm^{-1}$): $\nu$ 3033, 2936, 1653, 1605, 1509, 1412, 1225, 1070, 847, 735, 699; HRMS (EI) calcd for ($M^+$) $C_{15}H_{12}FNO$: 241.0903, found 241.0901.

*4.2.6. (S)-2-(4-Fluorophenyl)-4-phenyl-1,3-oxazoline (**3c′**).* Pale yellow solid; mp 52.3–54.1 °C; 0.21 g, 31%; $[\alpha]_D^{25}$ +3.3 (*c* 0.584, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 8.07–8.03 (m, 2H, ArH), 7.38–7.35 (m, 2H, ArH), 7.31–7.28 (m, 3H, ArH), 7.14–7.10 (m, 2H, ArH), 5.38 (dd, *J*=8.5, 10.0 Hz, 1H, CH), 4.80 (dd, *J*=8.5, 10.0 Hz, 1H, $CH_2$), 4.28 (t, *J*=8.5 Hz, 1H, $CH_2$); $^{19}F$ NMR (470 MHz, $CDCl_3$, ppm): $\delta$ −107.76 to −107.80 (m, 1F); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 165.0 (d, $^1J_{C-F}$=246.4 Hz), 164.0, 142.3, 130.9 (d, $^3J_{C-F}$=8.8 Hz), 128.9, 127.8, 126.8, 123.9 (d, $^4J_{C-F}$=2.5 Hz), 115.7 (d, $^2J_{C-F}$=22.5 Hz), 75.1, 70.2; IR (KBr, $cm^{-1}$.): $\nu$ 3028, 2934, 1646, 1524, 1336, 1066, 976, 846, 700; HRMS (EI) calcd for ($M^+$) $C_{15}H_{12}FNO$: 241.0903, found 241.0903.

*4.2.7. (S)-2-(4-Nitrophenyl)-5-phenyl-1,3-oxazoline (**3d**).* Pale yellow solid; mp 133.1–134.9 °C; 0.47 g, 62%; $[\alpha]_D^{25}$ −19.9 (*c* 0.762, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 8.28 (d, *J*=9.0 Hz, 2H, ArH), 8.18 (d, *J*=9.0 Hz, 2H, ArH), 7.42–7.35 (m, 5H, ArH), 5.72 (dd, *J*=8.5, 10.0 Hz, 1H, CH), 4.53 (dd, *J*=10.0, 15.0 Hz, 1H, $CH_2$), 4.06 (dd, *J*=8.0, 15.5 Hz, 1H, $CH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 162.3, 149.7, 140.4, 133.5, 129.4, 129.1, 128.8, 128.6, 125.9, 125.8, 123.7, 81.9, 63.4; IR (KBr, $cm^{-1}$): $\nu$ 3055, 2926, 1644, 1519, 1455, 1251, 1077, 758, 700; HRMS (EI) calcd for ($M^+$) $C_{15}H_{12}N_2O_3$: 268.0848, found 268.0843.

*4.2.8. (S)-2-(4-Nitrophenyl)-4-phenyl-1,3-oxazoline (**3d′**).*[11a] Pale yellow solid; mp 88.3–90.1 °C; 0.24 g, 31%; $[\alpha]_D^{25}$ +20.7 (*c* 1.072, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 8.28 (dd, *J*=9.0 Hz, 2H, ArH), 8.20 (dd, *J*=8.5 Hz, 2H, ArH), 7.39–7.30 (m, 5H, ArH), 5.45 (dd, *J*=10.0, 9.0 Hz, 1H, CH), 4.87 (dd, *J*=8.5, 10 Hz, 1H, $CH_2$), 4.35 (t, *J*=8.5 Hz, 1H, $CH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 163.0, 149.7, 141.7, 133.4, 129.6, 129.0, 128.0, 126.8, 123.7, 75.4, 70.5; IR (KBr, $cm^{-1}$): $\nu$ 3035, 2924, 1641, 1525, 1348, 1230, 1070, 744, 699; HRMS (EI) calcd for ($M^+$) $C_{15}H_{12}N_2O_3$: 268.0848, found 268.0846.

*4.2.9. (S)-2-(4-Methoxyphenyl)-5-phenyl-1,3-oxazoline (**3e**).* Pale yellow oil; 0.32 g, 45%; $[\alpha]_D^{25}$ −8.2 (*c* 0.880, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 7.98–7.95 (m, 2H, ArH), 7.40–7.31 (m, 5H, ArH), 6.95–6.92 (m, 2H, ArH), 5.63 (dd, *J*=8.0, 10.0 Hz, 1H, CH), 4.46 (dd, *J*=10.0, 14.5 Hz, 1H, $CH_2$), 3.97 (dd, *J*=8.0, 14.5 Hz, 1H, $CH_2$), 3.85 (s, 3H, $OCH_3$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 163.8, 162.2, 141.2, 130.1, 128.8, 128.3, 125.8, 120.2, 113.8, 81.0, 63.2, 55.4; IR (KBr, $cm^{-1}$): $\nu$ 3038, 2927, 1651, 1609, 1513, 1255, 837, 763, 700; HRMS (EI) calcd for ($M^+$) $C_{16}H_{15}NO_2$: 253.1103, found 253.1097.

*4.2.10. (S)-2-(4-Methoxyphenyl)-4-phenyl-1,3-oxazoline (**3e′**).* Pale yellow solid; mp 99.2–101.5 °C; 0.22 g, 31%; $[\alpha]_D^{25}$ +41.3 (*c* 1.018, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 8.01–7.98 (m, 2H, ArH), 7.37–7.34 (m, 2H, ArH), 7.32–7.27 (m, 3H, ArH), 6.96–6.93 (m, 2H,

ArH), 5.36 (dd, *J*=8.0, 10.0 Hz, 1H, CH), 4.77 (dd, *J*=8.5, 10.0 Hz, 1H, $CH_2$), 4.25 (t, *J*=8.0 Hz, 1H, $CH_2$), 3.86 (s, 3H, $OCH_3$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): δ 164.6, 162.3, 142.7, 130.3, 128.8, 127.6, 126.8, 120.0, 113.8, 74.8, 70.1, 55.4; IR (KBr, $cm^{-1}$): ν 3033, 2959, 1648, 1608, 1256, 1030, 843, 759, 698; HRMS (EI) calcd for ($M^+$) $C_{16}H_{15}NO_2$: 253.1103, found 253.1101.

*4.2.11. (S)-4-(5-Phenyl-1,3-oxazoline-2-yl)-9H-fluoren-9-one (**3f**).* Pale yellow solid; mp 149.2–151.3 °C; 0.48 g, 53%; $[\alpha]_D^{25}$ +27.3 (*c* 1.018, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 8.45 (d, *J*=7.5 Hz, 1H, ArH), 7.97 (dd, *J*=1.5, 8.0 Hz, 1H, ArH), 7.80 (dd, *J*=1.0, 7.5 Hz, 1H, ArH), 7.71–7.69 (m, 1H, ArH), 7.45–7.40 (m, 5H, ArH), 7.39–7.30 (m, 3H, ArH), 5.76 (dd, *J*=8.0, 10.0 Hz, 1H, $CH_2$), 4.65 (dd, *J*=10.5, 15.0 Hz, 1H, $CH_2$), 4.19 (dd, *J*=8.0, 15.0 Hz, 1H, $CH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): δ 193.3, 163.1, 143.8, 143.4, 140.5, 136.3, 135.6, 135.0, 134.5, 129.6, 129.1, 128.8, 128.7, 126.5, 126.3, 126.1, 124.2, 124.1, 81.2, 63.4; IR (KBr, $cm^{-1}$): ν 3060, 2954, 1712, 1651, 1572, 1241, 1111, 752, 702; HRMS (EI) calcd for ($M^+$) $C_{22}H_{15}NO_2$: 325.1103, found 325.1102.

*4.2.12. (S)-4-(4-Phenyl-1,3-oxazoline-2-yl)-9H-fluoren-9-one (**3f′**).* Pale yellow solid; mp 114.1–115.3 °C; 0.22 g, 24%; $[\alpha]_D^{25}$ +7.2 (*c* 0.856, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 8.40 (d, *J*=7.5 Hz, 1H, ArH), 7.97 (dd, *J*=1.5, 8.0 Hz, 1H, ArH), 7.80 (dd, *J*=1.0, 7.5 Hz, 1H, ArH), 7.70–7.68 (m, 1H, ArH), 7.43–7.37 (m, 5H, ArH), 7.36–7.28 (m, 3H, ArH), 5.57 (dd, *J*=8.5, 10.0 Hz, 1H, $CH_2$), 4.90 (dd, *J*=8.5, 10.0 Hz, 1H, $CH_2$), 4.39 (t, *J*=8.5 Hz, 1H, $CH_2$); $^{13}C$ NMR (470 MHz, $CDCl_3$, ppm): δ 193.2, 163.9, 143.7, 143.4, 141.8, 136.5, 135.5, 135.0, 134.4, 129.6, 129.0, 128.8, 128.0, 126.8, 126.5, 126.2, 124.2, 124.0, 74.6, 70.8; IR (KBr, $cm^{-1}$): ν 3031, 2962, 1709, 1635, 1567, 1493, 1194, 986, 900, 739; HRMS (EI) calcd for ($M^+$) $C_{22}H_{15}NO_2$: 325.1103, found 325.1096.

*4.2.13. (S)-2-(Furan-2-yl)-5-phenyl-1,3-oxazoline (**3g**).* Yellow oil; 0.29 g, 49%; $[\alpha]_D^{25}$ −12.8 (*c* 1.242, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 7.54–7.53 (m, 1H, ArH), 7.37–7.33 (m, 2H, ArH), 7.32–7.28 (m, 3H, ArH), 6.98 (d, *J*=3.5 Hz, 1H, ArH), 6.47 (dd, *J*=1.5, 3.5 Hz, 1H, ArH), 5.59 (dd, *J*=8.0, 10.0 Hz, 1H, CH), 4.43 (dd, *J*=10.0, 14.5 Hz, 1H, $CH_2$), 3.96 (dd, *J*=8.0, 15.0 Hz, 1H, $CH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): δ 156.4, 145.4, 142.9, 140.4, 128.9, 128.5, 125.9, 114.6, 111.6, 81.3, 62.9; IR (KBr, $cm^{-1}$): ν 3032, 2939, 1672, 1482, 1262, 1089, 755, 700; HRMS (EI) calcd for ($M^+$) $C_{13}H_{11}NO_2$: 213.0790, found 213.0780.

*4.2.14. (S)-2-(Furan-2-yl)-4-phenyl-1,3-oxazoline (**3g′**).* Yellow oil; 0.13 g, 21%; $[\alpha]_D^{25}$ +28.6 (*c* 1.315, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 7.56–7.55 (m, 1H, ArH), 7.36–7.33 (m, 2H, ArH), 7.31–7.26 (m, 3H, ArH), 7.04 (d, *J*=3.5 Hz, 1H, ArH), 6.50 (dd, *J*=1.5, 3.5 Hz, 1H, ArH), 5.38 (dd, *J*=8.5, 10.0 Hz, 1H, CH), 4.76 (dd, *J*=8.5, 10.0 Hz, 1H, $CH_2$), 4.25 (t, *J*=8.5 Hz, 1H, $CH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): δ 157.0, 145.4, 142.8, 141.8, 128.7, 127.7, 126.7, 114.9, 111.6, 74.8, 70.0; IR (KBr, $cm^{-1}$): ν 3028, 2911, 1662, 1628, 1480, 1171, 1091, 970, 752, 702; HRMS (EI) calcd for ($M^+$) $C_{13}H_{11}NO_2$: 213.0790, found 213.0783.

*4.2.15. (S)-5-Phenyl-2-(thiophen-2-yl)-1,3-oxazoline (**3h**).* Yellow oil; 0.27 g, 42%; $[\alpha]_D^{25}$ −21.3 (*c* 0.721, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 7.66 (dd, *J*=1.0, 4.0 Hz, 1H, ArH), 7.48 (dd, *J*=1.0, 5.0 Hz, 1H, ArH), 7.42–7.31 (m, 5H, ArH), 7.09 (dd, *J*=3.5, 5.0 Hz, 1H, ArH), 5.65 (dd, *J*=8.0, 10.0 Hz, 1H, CH), 4.45 (dd, *J*=10.0, 14.5 Hz, 1H, $CH_2$), 3.97 (dd, *J*=8.0, 15.0 Hz, 1H, $CH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): δ 159.9, 140.7, 130.5, 130.3, 130.0, 128.9, 128.4, 127.7, 125.8, 81.6, 63.2; IR (KBr, $cm^{-1}$): ν 3031, 2928, 1648, 1524, 1432, 1251, 1059, 970, 852, 759, 700; HRMS (EI) calcd for ($M^+$) $C_{13}H_{11}NOS$: 229.0561, found 229.0556.

*4.2.16. (S)-4-Phenyl-2-(thiophen-2-yl)-1,3-oxazoline (**3h′**).*[12] Yellow oil; 0.15 g, 23%; $[\alpha]_D^{25}$ +41.5 (*c* 0.950, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 7.71 (dd, *J*=1.0, 4.0 Hz, 1H, ArH), 7.49 (dd, *J*=1.0, 5.0 Hz, 1H, ArH), 7.38–7.35 (m, 2H, ArH), 7.32–7.27 (m, 3H, ArH), 7.11 (dd, *J*=4.0, 5.0 Hz, 1H, ArH), 5.37 (dd, *J*=8.5, 10.0 Hz, 1H, CH), 4.78 (dd, *J*=8.5, 10.0 Hz, 1H, $CH_2$), 4.27 (t, *J*=8.5, 10.0 Hz, 1H, $CH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): δ 160.5, 142.1, 130.8, 130.2, 130.1, 128.8, 127.7, 127.6, 126.8, 75.3, 70.3; IR (KBr, $cm^{-1}$): ν 3028, 2924, 1646, 1432, 1251, 1059, 851, 700; HRMS (EI) calcd for ($M^+$) $C_{13}H_{11}NOS$: 229.0561, found 229.0562.

*4.2.17. (S)-2-(6-Chloropyridin-3-yl)-5-phenyl-1,3-oxazoline (**3i**).* Pale yellow solid; mp 71.3–72.6 °C; 0.14 g, 19%; $[\alpha]_D^{25}$ −16.3 (*c* 1.326, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 8.98 (d, *J*=2.0 Hz, 1H, ArH), 8.23 (dd, *J*=2.5, 8.5 Hz, 1H, ArH), 7.41–7.39 (m, 3H, ArH), 7.37–7.33 (m, 3H, ArH), 5.69 (dd, *J*=8.0, 10.0 Hz, 1H, CH), 4.49 (dd, *J*=10.5, 15.0 Hz, 1H, $CH_2$), 4.02 (dd, *J*=8.0, 15.0 Hz, 1H, $CH_2$); $^{13}C$ NMR (470 MHz, $CDCl_3$, ppm): δ 161.3, 154.3, 149.8, 140.4, 138.4, 129.1, 128.8, 125.9, 124.3, 122.9, 81.4, 63.2; IR (KBr, $cm^{-1}$): ν 3028, 2934, 1646, 1524, 1336, 1066, 976, 846, 700; HRMS (EI) calcd for ($M^+$) $C_{14}H_{11}ClN_2O$: 258.0560, found 258.0555.

*4.2.18. (S)-2-(6-Chloropyridin-3-yl)-4-phenyl-1,3-oxazoline (**3i′**).* Pale yellow solid; mp 66.3–67.1 °C; 0.24 g, 34%; $[\alpha]_D^{25}$ +9.8 (*c* 0.578, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 8.99 (d, *J*=2.5 Hz, 1H, ArH), 8.26 (dd, *J*=2.5, 8.5 Hz, 1H, ArH), 7.41–7.35 (m, 3H, ArH), 7.31–7.28 (m, 3H, ArH), 5.40 (dd, *J*=8.5, 10.5 Hz, 1H, CH), 4.83 (dd, *J*=8.5, 10.5 Hz, 1H, $CH_2$), 4.31 (t, *J*=8.5 Hz, 1H, $CH_2$); $^{13}C$ NMR (470 MHz, $CDCl_3$, ppm): δ 162.0, 154.3, 149.8, 141.7, 138.5, 129.0, 128.0, 126.8, 124.2, 122.8, 75.2, 70.3; IR (KBr, $cm^{-1}$): ν 3029, 2958, 1649, 1585, 1368, 1279, 1103, 748, 702; HRMS (EI) calcd for ($M^+$) $C_{14}H_{11}ClN_2O$: 258.0560, found 258.0557.

*4.2.19. (S)-2-(Perfluorophenyl)-5-phenyl-1,3-oxazoline (**3j**).* Yellow solid; mp 42.3–43.1 °C; 0.38 g, 43%; $[\alpha]_D^{25}$ −33.9 (*c* 1.072, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 7.43–7.35 (m, 5H, ArH), 5.72 (dd, *J*=8.5, 10.0 Hz, 1H, CH), 4.55 (dd, *J*=10.0, 15.0 Hz, 1H, $CH_2$), 4.07 (dd, *J*=8.5, 15.0 Hz, 1H, $CH_2$); $^{19}F$ NMR (470 MHz, $CDCl_3$, ppm): δ −136.74 to −136.81 (m, 2F), −149.60 to −149.69 (m, 1F), −160.68 to −160.80 (m, 2F); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): δ 154.6–154.5 (m), 145.8 (dddd, *J*=255.0, 15.0, 7.5, 3.8 Hz), 142.8 (dm, *J*=265.3 Hz), 140.0, 137.9 (dm, *J*=251.3 Hz), 129.0, 128.1, 125.8, 104.9 (td, *J*=15.0, 3.8 Hz), 81.8, 63.3; IR (KBr, $cm^{-1}$): ν 3019, 2974, 1672, 1526, 1359, 1218, 993, 701; HRMS (EI) calcd for ($M^+$) $C_{15}H_8F_5NO$: 313.0526, found 313.0522; MS (EI): *m*/*z* (%) 313 ($M^+$, 7), 207 ($M^+-C_6H_5CHO$, 100).

*4.2.20. (S)-2-(Perfluorophenyl)-4-phenyl-1,3-oxazoline (**3j′**).* Yellow solid; mp 62.3–63.1 °C; 0.18 g, 20%; $[\alpha]_D^{25}$ +28.8 (*c* 1.072, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 7.41–7.31 (m, 5H, ArH), 5.47 (t, *J*=9.5 Hz, 1H, CH), 4.83 (dd, *J*=8.5, 10.5 Hz, 1H, $CH_2$), 4.32 (t, *J*=8.5 Hz, 1H, $CH_2$); $^{19}F$ NMR (470 MHz, $CDCl_3$, ppm): δ −136.74 to −136.81 (m, 2F), −149.64 to −149.74 (m, 1F), −160.80 to −160.92 (m, 2F); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): δ 155.5–155.3 (m), 145.8 (dm, *J*=251.3 Hz), 142.9 (dddd, *J*=257.5, 17.5, 8.8, 5.0 Hz), 141.2, 137.9 (dm, *J*=252.5 Hz), 129.0, 128.1, 126.7, 104.9 (td, *J*=15.0, 3.8 Hz), 75.2, 70.5; IR (KBr, $cm^{-1}$): ν 3018, 2949, 1680, 1526, 1341, 1212, 1080, 985, 807, 699; HRMS (EI) calcd for ($M^+$) $C_{15}H_8F_5NO$: 313.0526, found 313.0527; MS (EI): *m*/*z* (%) 313 ($M^+$, 28), 283 ($M^+-CH_2O$,100).

*4.2.21. (S)-Naphthalen-2-yl-(2-phenyl-aziridin-1-yl)-methanone (**6a**).*[7] White solid; mp 106.1–107.6 °C; 0.12 g, 16%, $[\alpha]_D^{25}$ +150.6 (*c* 0.336, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): δ 8.53 (s, 1H, HAr), 8.00 (dd, *J*=8.5, 1.5 Hz, 1H, HAr), 7.85–7.78 (m, 3H, HAr), 7.57 (td, *J*=7.0, 1.5 Hz, 1H, HAr), 7.49 (td, *J*=8.5, 1.0 Hz, 1H, HAr), 7.44–7.37 (m, 5H, HAr), 3.53 (dd, *J*=6.0, 6.0 Hz, 1H, CH), 3.04 (d, *J*=6.0 Hz, 1H, $NCH_2$), 2.52 (d, *J*=3.5 Hz, 1H, $NCH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): δ 179.3, 137.3, 135.7, 132.6, 130.9, 130.1, 129.6, 129.0, 128.4, 128.3, 127.9, 126.8, 126.4, 125.1, 40.6, 35.5; IR (KBr): ν 3055, 2993, 1675, 1629, 1391, 1303, 1286, 833, 785, 705; Anal. Calcd for

$C_{19}H_{15}NO$ (273.12): C 83.49, H 5.53, N 5.12; found C 83.55, H 5.42, N 5.29.

### 4.3. General procedure for the preparation of 2-fluoroalkyl-1,3-oxazolines 4

A 200 mL three-necked flask equipped with a condenser was charged with $Ph_3P$ (2.20 g, 8.4 mmol), $Et_3N$ (1.42 g, 14.0 mmol), $CBr_4$ (16.8 g, 8.4 mmol), substrate **1** (3.3 mmol), and fluorinated carboxylic acid **2** (2.8 mmol) in toluene (15.0 mL) under a nitrogen atmosphere. The solution was stirred for about 20 min under 0 °C, then the mixture was heated at 90 °C with stirring for 18–55 h. The solvent was evaporated under reduced pressure, and the residue was diluted with petroleum ether (60–90 °C) and filtered. The residual solid $Ph_3PO$ and $Et_3N{\cdot}HBr$ was washed with petroleum ether three times. The filtrate was concentrated, and the residue was purified by column chromatography (ethyl acetate/petroleum ether, 1:8) to afford product **4**. If the mixture of $Ph_3P$ (2.20 g, 8.4 mmol), $Et_3N$ (1.42 g, 14.0 mmol), $CCl_4$ (15 mL), substrate **1** (3.3 mmol), and trifluoroacetic acid **2k** (2.8 mmol) in toluene (15.0 mL) was processed after stirring for 2 h at 90 °C, intermediate **8k** and **9k′** were obtained by column chromatography (ethyl acetate/petroleum ether=1:8).

*4.3.1. (S)-4-Phenyl-2-(trifluoromethyl)-1,3-oxazoline (**4k**).* Pale yellow oil; 0.37 g, 61%; $[\alpha]_D^{25}$ −21.8 (*c* 1.24, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 7.42–7.38 (m, 2H, ArH), 7.36–7.32 (m, 1H, ArH), 7.26–7.24 (m, 2H, ArH), 5.41 (m, 1H, CH), 4.89 (dd, *J*=8.5, 10.5 Hz, 1H, $CH_2$), 4.40 (t, *J*=8.5 Hz, 1H, $CH_2$); $^{19}F$ NMR (470 MHz, $CDCl_3$, ppm): $\delta$ −69.97 (s, $CF_3$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 155.9 (q, $^2J_{C-F}$=40.0 Hz), 139.7, 129.1, 128.3, 126.5, 116.5 (q, $^1J_{C-F}$=272.5 Hz), 76.6, 69.8; IR (KBr, $cm^{-1}$): $\nu$ 3034, 2913, 1687, 1604, 1399, 1210, 1160, 1126, 1083, 762, 700; HRMS (EI) calcd for ($M^+$) $C_{10}H_8F_3NO$: 215.0558, found 215.0561; MS (EI): *m*/*z* (%) 215 ($M^+$), 185 ($M^+$-$CH_2O$).

*4.3.2. (S)-2-(Difluoromethyl)-4-phenyl-1,3-oxazoline (**4l**).* Yellow oil; 0.23 g, 42%; $[\alpha]_D^{25}$ −42.7 (*c* 1.03, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 7.40–7.37 (m, 2H, ArH), 7.35–7.31 (m, 1H, ArH), 7.26–7.24 (m, 2H, ArH), 6.34 (t, *J*=53.0 Hz, 1H, $CF_2H$), 5.36–5.31 (m, 1H, CH), 4.80 (dd, *J*=9.0, 10.0 Hz, 1H, $CH_2$), 4.31 (t, *J*=9.0 Hz, 1H, $CH_2$); $^{19}F$ NMR (470 MHz, $CDCl_3$, ppm): $\delta$ −123.89 (d, *J*=52.0 Hz, 2F, $CF_2H$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 159.7 (t, $^2J_{C-F}$=27.5 Hz), 140.4, 129.0, 128.1, 126.6, 107.23 (t, $^1J_{C-F}$=240.0 Hz), 75.8, 69.6; IR (KBr, $cm^{-1}$): $\nu$ 3033, 2909, 1683, 1604, 1455, 1352, 1113, 1064, 761, 701; HRMS (EI) calcd for ($M^+$) $C_{10}H_9F_2NO$: 197.0652, found 197.0651.

*4.3.3. (S)-2-(Bromodifluoromethyl)-4-phenyl-1,3-oxazoline (**4m**).* Yellow oil; 0.42 g, 65%; $[\alpha]_D^{25}$ −35.1 (*c* 0.68, $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 7.43–7.39 (m, 2H, ArH), 7.38–7.35 (m, 1H, ArH), 7.29–7.27 (m, 2H, ArH), 5.44 (dd, 1H, *J*=9.0, 10.0 Hz, CH), 4.94 (dd, *J*=9.0, 10.0 Hz, 1H, $CH_2$), 4.46 (t, *J*=8.5 Hz, 1H, $CH_2$); $^{19}F$ NMR (470 MHz, $CDCl_3$, ppm): $\delta$ −55.22; $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 159.5 (t, $^2J_{C-F}$=30.0 Hz), 139.9, 129.0, 128.3, 126.5, 109.1 (t, $^1J_{C-F}$=301.3 Hz), 76.9, 69.7; IR (KBr, $cm^{-1}$): $\nu$ 3028, 2926, 1670, 1398, 1273, 1089, 754, 700; HRMS (EI) calcd for ($M^+$) $C_{10}H_8BrF_2NO$: 274.9757, found 274.9753.

*4.3.4. (S)-2,2,2-Trifluoro-N-(2-hydroxy-1-phenylethyl)acetamide (**8k**).*[13] White solid; mp 154.5–155.3 °C; $^1H$ NMR (500 MHz, $CDCl_3$, ppm): $\delta$ 7.42–7.30 (m, 5H, $H_{Ar}$), 7.12 (s, 1H, NH), 5.13–5.10 (m, 1H, CH), 4.01–3.94 (m, 2H, $CH_2$), 1.91 (s, 1H, OH); $^{19}F$ NMR (470 MHz, $CDCl_3$, ppm): $\delta$ −75.65 (s, $CF_3$); $^{13}C$ NMR (125 MHz, $CDCl_3$, ppm): $\delta$ 157.1 (q, $^2J_{C-F}$=37.5 Hz), 139.0, 138.9, 128.3, 127.5, 126.8, 116.1 (q, $^1J_{C-F}$=286.3 Hz), 64.2, 56.5; IR (KBr, $cm^{-1}$): $\nu$ 3422, 3334, 2959, 1699, 1554, 1363, 1184, 1038, 759, 701, 541; HRMS (EI) calcd for ($M^+$) $C_{10}H_{10}F_3NO_2$: 233.0664, found 233.0661; MS (ESI): *m*/*z* (%) 256 ($M^+$+$Na^+$).

*4.3.5. (S)-N-(2-Chloro-1-phenylethyl)-2,2,2-trifluoroacetamide (**9k′**).* White solid; mp 100.3–101.5 °C; $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.43–7.36 (m, 3H, ArH), 7.34–7.31 (m, 2H, ArH), 6.90 (s, 1H, NH), 5.41 (dd, *J*=5.5, 8.0 Hz, 1H, CH), 3.95–3.86 (m, 2H, $CH_2$); $^{19}F$ NMR (470 MHz, $CDCl_3$): $\delta$ −75.67 (s, $CF_3$); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 157.1 (q, $^2J_{C-F}$=37.5 Hz), 136.6, 129.2, 128.9, 126.6, 115.8 (q, $^1J_{C-F}$=286.3 Hz), 54.8, 46.4; IR (KBr): $\nu$ 3327, 3091, 1700, 1554, 1220, 1173, 728, 697, 528 $cm^{-1}$; HRMS (EI) calcd for ($M^+$) $C_{10}H_9ClF_3NO$: 251.0325, found 251.0325; MS (EI): *m*/*z* (%) 251 ($M^+$, 1), 253 ($M^+$+2, 0.32), 215 ($M^+$−HCl, 53), 202 ($M^+$−$CH_2Cl$, 100).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## Supplementary data

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