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Facile access to oxazolidin-2-imine, thiazolidin-2-imine and imidazolidin-2-imine derivatives bearing an exocyclic haloalkyliene via direct halocyclization between propargylamines, heterocumulenes and I_2 (NBS)

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ABSTRACT

A simple, cheap, efficient, and metal-free method for one-step synthesis of a library of 1,3-diheteroatom five-membered heterocycles with exocyclic C=N and C=C double bonds was presented. The convenient reactions proceed via the direct three-component halocyclization of propargylamines, heterocumulenes and I_2 (NBS).

1. Introduction

Substituted oxazoles,[1] thiazoles[2] and imidazoles[3] are important structural components of a vast array of naturally occurring and pharmacologically active molecules. Furthermore, these types of heterocycles are also valuable intermediates[4] in organic synthesis and useful ligands[5] for organometallic compounds with interesting properties. There has been a longstanding interest in the development of new oxazole-, thiazole- and imidazole-based structures for the fine-tuning of the biological or physical properties of these molecules and new methods for their construction.[6–8] Among a variety of oxazole, thiazole and imidazole derivatives, oxazolidin-2-imines,[9] thiazolidin-2-imines[10] and imidazolidin-2-imines[11] are currently attracting considerable attention due to their therapeutic value in diseases, such as methicillin-resistant *Staphylococcus aureus* (MRSA)[12] and *Mycobacterium tuberculosis*.[13] Several synthetic approaches to substituted oxazolidin-2-imines, thiazolidin-2-imines and imidazolidin-2-imines have recently been reported.[14,15] Recently, Campbell and Toste found that (L)AuCl/$AgNTf_2$ can catalyze the cyclization of the in situ generated propargylamines with a tosyl isocyanate to form oxazolidin-2-imines as major products while the application of AgOTf provided imidazolidin-2-ones as major products (Scheme 1).[14d] Furthermore, it has been found that replacement of the tosyl isocyanate by aryl or alkyl isocyanates in the presence of $Ph_3PAuCl/AgOTf$ or Rh^{2+} led to the formation of tetrasubstituted 3,4-dihydropyrimidin-2(1H)-ones (Scheme 1). Remarkably, both chemo- and regioselectivity of cyclization of propargylamines and isocyanates are dependent on the catalyst, and the nature of isocyanates and propargylamines.[16] Consequently, further insights into the reactivity of propargylamines toward isocyanates are essential. In particular on the industrial scale for medicinal chemistry applications the catalyst- and additive-free method is highly desirable.

Vinyl halides are versatile building blocks in organic synthesis due to their applicability toward a vast range of cross-coupling reactions.[17] Iodocyclization has been successfully employed in synthesis of various kinds of iodo-substituted carbocycles and heterocycles.[18] Among these transformations, however, examples that form products containing the exocyclic iodoalkylidene functionality are still rare.[14b,19] Very recently, one viable protocol for synthesis of 5-iodomethyleneoxazolidin-2-imines and 5-methylenethiazolidin-2-imines from the CuI-catalyzed multicomponent, one-pot, three-step reaction between aldehyde, amine, alkyne, iso(thio)cyanate and I_2 is reported.[14b] Although this method employs the readily available starting materials aldehyde, amine, alkyne, and iso(thio)cyanate, the iodocyclization procedure suffers from more stoichiometric amounts of I_2 in the presence of large

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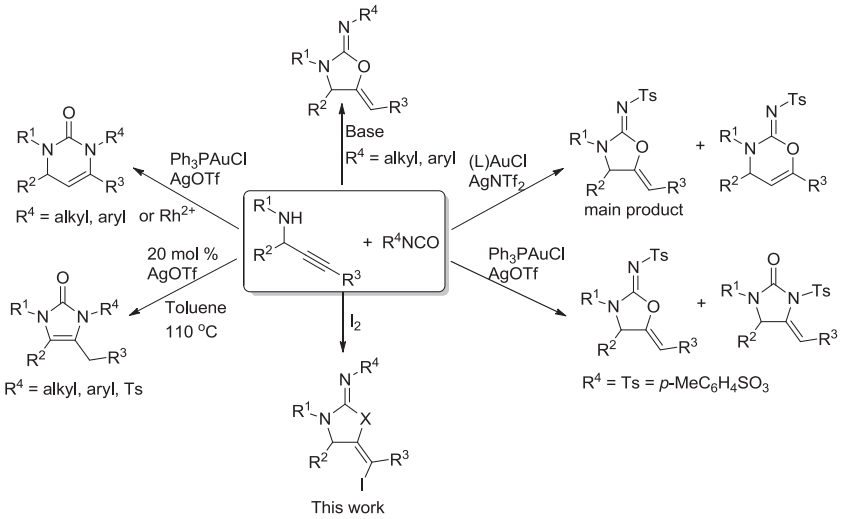


Scheme 1. Direction reaction between substituted propargylamine and isocyanate.

excess of Na_2CO_3, and moderate yields. Here, we describe a direct reaction between propargylamines, I_2, and heteroallenes such as RNCO, RNCS and RN=C=NR, which provides an efficient method for the synthesis of oxazolidin-2-imines, thiazolidin-2-imines and imidazolidin-2-imines bearing an exocyclic iodoalkylidene and significantly increase the reaction substrate scope. This methodology is also general in preparing oxazolidin-2-imines bearing an exocyclic bromoalkylidene.

2. Results and discussion

In our initial screening experiments, the three-component reaction between propargylamine **1a**, phenyl isocyanate **2a** and I_2 was selected as the model reaction. A mixture of **1a** (0.3 mmol) and **2a** (0.3 mmol) in ethyl acetate (EA) was treated with molecular iodine (0.3 mmol) at room temperature, providing the desired product **3aa** in 75% yield (Table 1, entry 1). Increasing reaction temperature to 50 °C gave **3aa** in 97% yield, while a higher temperature showed a little improvement (Table 1, entries 2 and 3). Afterwards, evaluation of different solvents (dichloromethane, acetonitrile, methanol) reveled that ethyl acetate was among the most suitable solvents for this iodocyclization (Table 1, entries 4–7). The structure of **3aa** was further confirmed by the X-ray crystal structure analysis (Fig. 1).

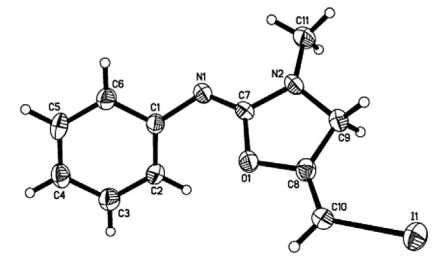
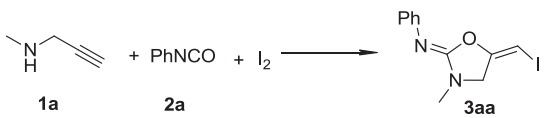


Fig. 1. ORTEP drawing of **3aa** with 30% probability thermal ellipsoids.

On the basis of the optimized conditions, the scope of this protocol was initially examined by applying an array of different isocyanates **2**. The results showed that aryl isocyanates bearing electron-donating and electron-neutral groups afforded the corresponding oxazolidine derivatives **3ab**–**3ae** in good to excellent yields (Table 2, entries 2–5). Products **3af**–**3ai** bearing halogens (fluorine, chlorine, bromine) were also obtained with excellent yields (Table 2, entries 6–9). However, the presence of the strong

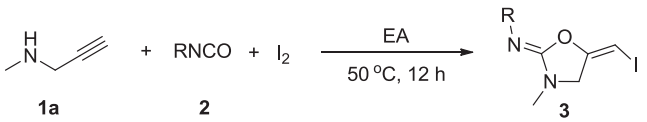
Table 1
Optimization of reaction conditions for the synthesis of oxazolidine derivative **3aa**[a]



Entry	Solvent	T/°C	Time/h	Yield/%[b]
1	EA	25	24	75
2	EA	50	24	97
3	EA	75	24	99
4	EA	50	12	98
5	DCM	50	12	89
6	MeCN	50	12	75
7	MeOH	50	12	Complicated

[a] Reactions were carried out with **1a** (0.30 mmol), **2** (0.30 mmol), I_2 (0.3 mmol), and solvent (3 mL).
[b] Isolated yield.

Table 2
Isocyanates scope[a]



Entry	R	Product	Yield (%)[b]
1	Ph (**2a**)	**3aa**	97
2	4-$CH_3C_6H_4$ (**2b**)	**3ab**	92
3	4-$CH_3OC_6H_4$ (**2c**)	**3ac**	96
4	2-$CH_3OC_6H_4$ (**2d**)	**3ad**	93
5	2-$CH_3C_6H_4$ (**2e**)	**3ae**	86
6	4-FC_6H_4 (**2f**)	**3af**	99
7	3-FC_6H_4 (**2g**)	**3ag**	96
8	4-ClC_6H_4 (**2h**)	**3ah**	90
9	4-BrC_6H_4 (**2i**)	**3ai**	91
10	4-$CF_3C_6H_4$ (**2j**)	**3aj**	88
11	2-$CF_3C_6H_4$ (**2k**)	**3ak**	65

[a] Reactions were carried out with **1a** (0.30 mmol), **2** (0.30 mmol), I_2 (0.3 mmol) in EA (3 mL) at 50 °C for 12 h.
[b] Isolated yield.

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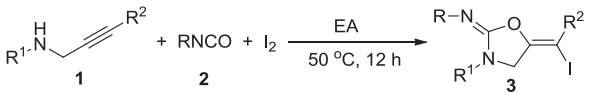
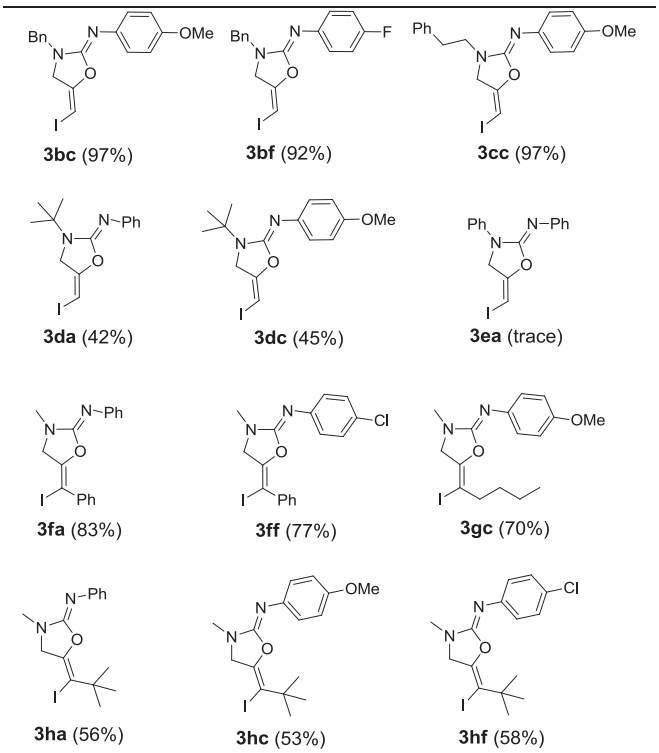
electro-withdrawing CF_3 group in aryl isocyanates (Table 2, entries 10 and 11) and the substituent shift from the *para*-to *ortho*-position (e.g., **3ab** vs **3ae**, **3aj** vs **3ak**) have a slightly negative impact on the yields.

To our delight, this protocol is also effective for the transformation of variously substituted propargylamines (Table 3). In general, the nature of *N*-substituents has a significant effect on the yields. For example, *N*-benzyl and *N*-(2-phenyl)ethyl substituted propargylamines gave the desired oxazolidine derivatives **3bc**, **3bf**, and **3cc** in excellent yields. In contrast, *N*-*tert*-butyl substituted propargylamine (**1d**) was found to have a lower activity for iodocyclization (**3da** and **3dc**) compared to **1a**–**1c**, due to the increased steric hindrance. Furthermore, the results show that propargylamines with an internal/terminal C≡C bond are all compatible with this protocol. Arylalkynes seem to be more reactive than alkylalkynes (**3fa** and **3ff** vs **3gc**, **3ha** and **3hc**), presumably as aryl substituents facilitate the stability of the iodonium cation intermediate (vide infra). Noticeably, the presence of the large sterically demanding *tert*-butyl group at another alkyne terminus also had a negative impact on the reaction outcomes, leading to the decrease of yields (**3ha**, **3hc**, and **3hf**).

Table 3
Propargylamine scope[a,b]

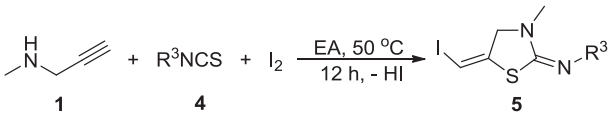


1a: R^1 = Me, R^2 = H; **1b**: R^1 = Bn, R^2 = H;
1c: R^1 = $PhCH_2CH_2$, R^2 = H;
1d: R^1 = *t*-Bu, R^2 = H; **1e**: R^1 = Ph, R^2 = H;
1f: R^1 = CH_3, R^2 = Ph; **1g**: R^1 = Me, R^2 = *n*-Bu;
1h: R^1 = Me, R^2 = *t*-Bu



[a] Reactions were carried out with **1** (0.30 mmol), **2** (0.30 mmol), I_2 (0.3 mmol) in EA (3 mL) at 50 °C. [b] isolated yield.

Given the fact that substituted thiazoles display a very promising antitumor activity,[2,10] we made an extension of this protocol to synthesis of thiazolidin-2-imines (Scheme 2). It was found that **4a**–**4d** were suitable reactants, and desirable products **5aa**–**5ad** were generated in good to quantitative yields.

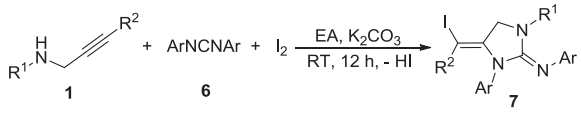


R^3 = Ph (**5aa**, 99%),
3-ClC_6H_4 (**5ab**, 99%),
4-ClC_6H_4 (**5ac**, 98%),
4-$CH_3C_6H_4$ (**5ad**, 86%)

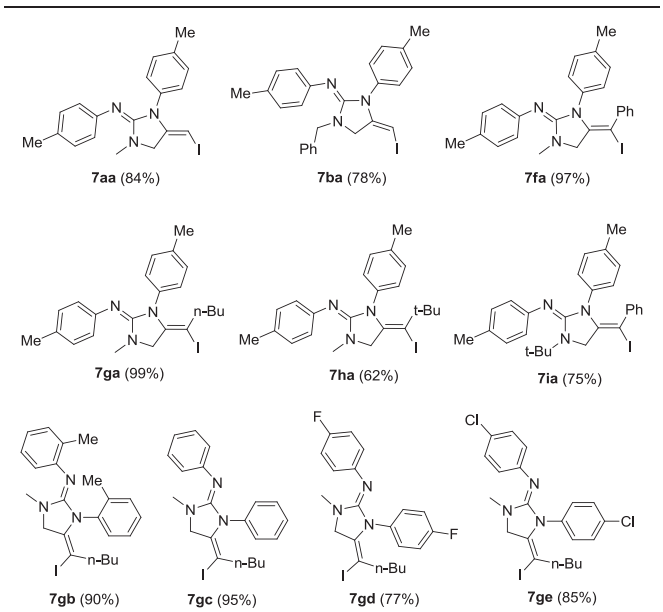
Scheme 2. Iodocyclization between propargylamines, isothiocyanates and I_2.

Encouraged by the above results, we further explored the application of this method in synthesis of imidazoline derivatives and envisioned that combination of **1** with carbodiimides **6** and I_2 could subject to some tandem transformation in the current experimental conditions. Surprisingly, no desired iodocyclization product **7aa** was obtained, when the optimal conditions described above were applied to the cyclization between **1a**, diarylcarbodiimide **6a** and I_2. After adding K_2CO_3 as an additive, the desirable reaction proceeded smoothly, affording **7aa** in a satisfactory yield (Table 4). The sluggishness of such reaction likely resulted from larger steric hindrance and weaker electrophilicity of carbodiimides compared to isocyanates and isothiocyanates and the decreasing acidity of the multisubstituted guanidine intermediate compared with the urea and thioureas ones. Subsequently, we investigated the generality and the

Table 4
Three-component iodocyclization between propargylamines, carbodiimides and I_2[a,b]



Ar = 4-MeC_6H_4 (**6a**); 2-MeC_6H_4 (**6b**); C_6H_5 (**6c**); 4-FC_6H_4 (**6d**); 4-ClC_6H_4 (**6e**)



[a] Reactions were carried out with **1** (0.36 mmol), **2** (0.30 mmol), I_2 (0.36 mmol), K_2CO_3 (0.45 mmol) in EA (3 mL) at 25 °C; [b] isolated yield.

scope of this transformation via variation of both propargylamines and carbodiimides. As illustrated in Table 4, a series of propargylamines **1a**–**1i** were investigated by coupling reaction with di(*p*-methylphenyl)carbodiimide **6a** and I_2 in the presence of 1.5 equiv of K_2CO_3. To our delight, various electron-rich, electron-neutral, and electron-deficient substituents were well tolerated, and the standard reaction conditions were compatible to substrates with both aryl and alkyl groups at another terminus of propargylamines. In general, the steric effect of substituents on propargylamines has an impact on the yield. For example, reaction of **6a** with *N*-methyl substituted propargylamine **1f** gave **7fa** in 97% yield, while the *N*-*tert*-butyl substituted propargylamine **1i** gave the corresponding product **7ia** in 75% yield. Similarly, the introduction of sterically larger encumbered substituents at another alkyne terminus led to the decrease of the yield too (**7ga** vs **7ha**). The structure of **7ha** was further confirmed by the X-ray crystal structure analysis (Fig. 2). Noticeably, the position of the methyl group in the benzene ring has some effect on the reaction. For example, the diarylcarbodiimide with the methyl at the *para*-position (**6a**) gave the expected product in a higher yield than the *ortho*-position isomer (**6b**) (**7ga** vs **7gb**).

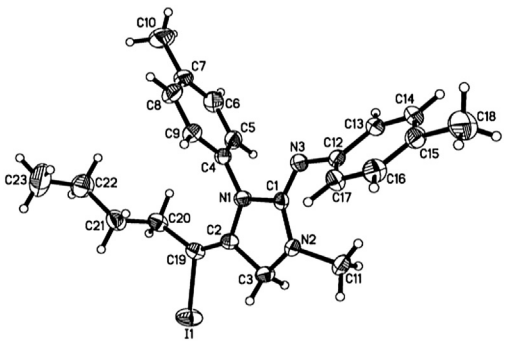
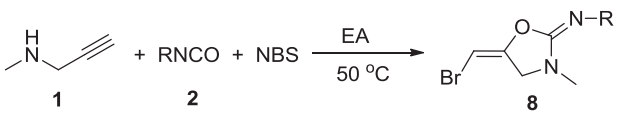


Fig. 2. ORTEP drawing of **7ga** with 30% probability thermal ellipsoids.

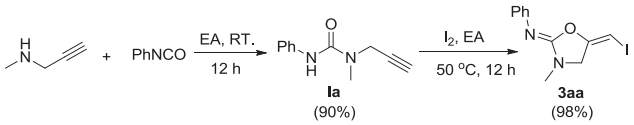
In addition, this protocol also allows the bromocyclization between propargylamines, isocyanate and *N*-bromosuccinimide (NBS). As shown in Scheme 3, products **8ah** and **8ac** were successfully accessed with moderate to good yields, which provides an efficient method for bromoalkylidene-substituted oxazolidine derivatives.



R = *4*-ClC_6H_4 (**8ah**, 79%);
4-$CH_3OC_6H_4$ (**8ac**, 57%)

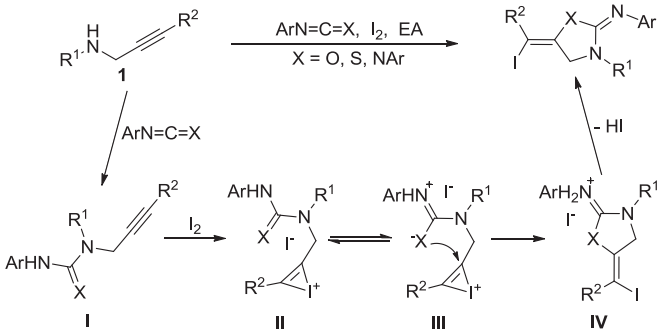
Scheme 3. Bromocyclization between propargylamines, isocyanates and NBS.

To shed light on the mechanism of the reaction, the following experiments were conducted. Firstly, the reaction of propargylamine **1a** with PhNCO **2a** gave the urea **Ia** in 90% yield. Subsequently, the cyclization of **Ia** with I_2 was performed under the aforementioned conditions, giving the desired product **3aa** in almost quantitative yield (Scheme 4).



Scheme 4. Mechanism study of stepwise reactions.

Based on the results described above, a plausible mechanism for the present iodocyclization of propargylamines with isocyanates and I_2 is illustrated in Scheme 5. Initially, propargylamine reacts with isocyanate (isothiocyanate) to form a urea (thiourea) intermediate (**I**). Next, the electrophilic addition of I_2 to alkyne of **I** results in the formation of a three-membered cyclic iodonium cation (**II**). The isomerization of intermediate **II** gives intermediate **III** as observed previously,[19b] which subsequently undergo the intramolecular cyclization through an attack of the oxygen (sulfur) atom upon the three-membered cyclic iodonium cation, forming the ammonium intermediate (**IV**). Finally, the release of HI of **IV** in the presence of base gives the corresponding iodocyclization product. Since the addition of carbodiimides to propargylamines is sluggish, the additive K_2CO_3, which is promotor for guanidination of carbodiimides with propargylamines and sequent intramolecular cyclization, is required.[20]



Scheme 5. The plausible mechanism for the formation of **3**, **5** and **7**.

3. Conclusions

In summary, we have developed a simple, cheap, efficient, and metal-free method for one-step synthesis of a library of 1,3-diheteroatom five-membered heterocycles with exocyclic C=N and C=C double bonds via the direct three-component iodocyclization of propargylamines, heterocumulenes and I_2. This method allows access to a wide range of 5-iodoalkylidenated oxazolidin-2-imines, thiazolidin-2-imines and imidazolidin-2-imines in moderate to excellent yields under mild conditions. The present procedure is also suitable for the synthesis of 5-bromoalkylidenated oxazolidin-2-imines from readily available propargylamines, isocyanates and NBS, which are potential pharmacological interest and synthetic potential in organometallic and organic chemistry. The advantages of the present method are easy access to the reagents, simple operation, high chemo- and regioselectivity, without the need of catalyst and additives (except carbodiimides).

4. Experimental section

4.1. General

Propargylamines[21] and carbodiimides[22] were prepared according to the literature procedures. ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL ECA-400 NMR spectrometer (FT, 400 MHz for ^1H; 100 MHz for ^{13}C) in $CDCl_3$ at room temperature. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. GC–MS were obtained on a Focus GC-ISQ MS instrument. High resolution mass spectrometry (HRMS) spectra were obtained on a micro TOF II Instrument using ESI ionization source. X-ray diffraction data for **3aa** (CCDC no. 1047709) and **7ga** (CCDC no. 1047710) were collected on a SMART APEX CCD diffractometer (graphite-monochromated Mo*Kα* radiation, φ-ω scan technique, λ=0.71073 Å). The intensity data were integrated by means of the

SAINT program. SADABS was used to perform area-detector scaling and absorption corrections. The structure was solved by direct methods and was refined against F^2 using all reflections with the aid of the SHELXTL package. All non-hydrogen atoms were found from the difference Fourier syntheses and refined anisotropically. The H atoms were included in calculated positions with isotropic thermal parameters related to those of the supporting carbon atoms but were not included in the refinement. All calculations were performed using the Bruker Smart program.

4.2. General procedure for the synthesis of oxazolidine derivatives 3

A mixture of isocyanate (0.3 mmol) and propargylamine (0.3 mmol) was treated with iodine (0.3 mmol) in ethyl acetate (3 mL). The reaction tube was stirred for 12 h at 50 °C (oil bath temperature) with the gradual formation of white precipitation. Subsequently, the reaction was quenched with K_2CO_3 aqueous solution to make the PH beyond 9. The mixture was extracted with EA (3×10 mL) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. Pure products **3** were obtained by column chromatography (silica gel, with a mixture of hexane/ethyl acetate (4:1) as eluent).

*4.2.1. N-((E)-5-(Iodomethylene)-3-methyloxazolidin-2-yliden-e)-4-methylaniline (**3ab**).* Light yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.06 (d, J=8.0 Hz, 2H), 6.93–6.91 (m, 2H), 5.63 (t, J=2.8 Hz, 1H), 4.12 (d, J=2.8 Hz, 2H), 3.06 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 150.90, 150.08, 143.71, 132.02, 129.37, 123.24, 53.60, 49.07, 31.83, 20.99. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{12}H_{14}N_2OI$ 329.0151, found 329.0162.

*4.2.2. N-((E)-5-(Iodomethylene)-3-methyloxazolidin-2-yliden-e)-4-methoxyaniline (**3ac**).* Brown solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.00–6.96 (m, 2H), 6.83–6.80 (m, 2H), 5.64 (t, J=2.8 Hz, 1H), 4.11 (d, J=2.8 Hz, 2H), 3.78 (s, 3H), 3.03 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 155.34, 150.90, 150.00, 139.43, 124.22, 114.02, 55.53, 53.55, 49.01, 31.83. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{12}H_{14}N_2O_2I$ 345.0100, found 345.0117.

*4.2.3. N-((E)-5-(Iodomethylene)-3-methyloxazolidin-2-yliden-e)-2-methoxyaniline (**3ad**).* Light yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.01–6.89 (m, 4H), 5.58 (t, J=2.8 Hz, 1H), 4.13 (d, J=2.8 Hz, 2H), 3.82 (s, 3H), 3.08 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 152.15, 150.88, 150.67, 135.89, 124.16, 123.63, 120.68, 111.37, 55.88, 53.89, 48.94, 31.39. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{12}H_{14}N_2O_2I$ 345.0100, found 345.0093.

*4.2.4. N-((E)-5-(Iodomethylene)-3-methyloxazolidin-2-yliden-e)-2-methylaniline (**3ae**).* Light yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.16–6.93 (m, 4H), 5.61 (t, J=2.8 Hz, 1H), 4.14 (d, J=2.8 Hz, 2H), 3.06 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 150.87, 149.34, 145.19, 131.00, 130.13, 126.11, 126.11, 122.79, 63.76, 49.03, 31.87, 18.29. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{12}H_{14}N_2OI$ 329.0151, found 329.0152.

*4.2.5. 4-Fluoro-N-((E)-5-(iodomethylene)-3-methyloxazolidin-2-ylidene)aniline (**3af**).* Light yellow oil. ^{1}H NMR (400M, $CDCl_3$): δ 6.98–6.91 (m, 4H), 5.66 (t, J=2.8 Hz, 1H), 4.13 (d, J=2.8 Hz, 2H), 3.02 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 160.16, 157.77, 150.80, 150.39, 142.46, 124.67, 124.59, 115.46, 115.24, 53.62, 49.41, 31.85. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{11}H_{11}N_2OFI$ 332.9900, found 332.9915.

*4.2.6. 3-Fluoro-N-((E)-5-(iodomethylene)-3-methyloxazolidin-2-ylidene)aniline (**3ag**).* Light yellow oil. ^{1}H NMR (400M, $CDCl_3$): δ 7.21–7.16 (m, 1H), 6.82–6.70 (m, 3H), 5.70 (t, J=2.8 Hz, 1H), 4.14 (d, J=2.8 Hz, 2H), 3.04 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 164.41, 161.98, 150.58, 150.49, 148.26, 148.26, 148.17, 129.59, 129.50, 119.46, 110.77, 110.55, 109.50, 109.29, 53.48, 49.59, 31.72. ^{19}F NMR (376M, $CDCl_3$): δ 114.18. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{11}H_{11}N_2OFI$ 332.9900, found 332.9909.

*4.2.7. 4-Chloro-N-((E)-5-(iodomethylene)-3-methyloxazolidin-2-ylidene)aniline (**3ah**).* Dark brown oil. ^{1}H NMR (400M, $CDCl_3$): δ 7.21–7.19 (m, 2H), 6.97–6.95 (m, 2H), 5.67 (t, J=2.8 Hz, 1H), 4.13 (d, J=2.8 Hz, 2H), 3.03 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 150.62, 150.40, 145.03, 128.72, 124.83, 55.83, 49.48, 31.75. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{11}H_{11}N_2OICl$ 348.9605, found 348.9612.

*4.2.8. 4-Bromo-N-((E)-5-(iodomethylene)-3-methyloxazolidin-2-ylidene)aniline (**3ai**).* Dark brown solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.35–7.33 (m, 2H), 6.92–6.89 (m, 2H), 5.67 (t, J=2.4 Hz, 1H), 4.14 (d, J=2.4 Hz, 2H), 3.03 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 150.69, 150.39, 131.67, 125.33, 115.44, 53.54, 49.52, 31.75. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{11}H_{11}N_2OBrI$ 392.9099, found 392.9091.

*4.2.9. N-((E)-5-(Iodomethylene)-3-methyloxazolidin-2-yliden-e)-4-(trifluoromethyl)aniline (**3aj**).* Yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.49 (d, J=8.3 Hz, 2H), 7.10 (d, J=8.3 Hz, 2H), 5.69 (t, J=2.8 Hz, 1H), 4.15 (d, J=2.8 Hz, 2H), 3.05 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 150.70, 150.45, 145.87, 125.90, 125.87, 123.68, 123.68, 53.49, 49.73, 31.69. ^{19}F NMR (376M, $CDCl_3$): δ −61.59. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{12}H_{11}F_3N_2OI$ 382.9868, found 382.9862.

*4.2.10. N-((E)-5-(Iodomethylene)-3-methyloxazolidin-2-ylide-ne)-2-(trifluoromethyl)aniline (**3ak**).* Dark brown oil. ^{1}H NMR (400M, $CDCl_3$): δ7.56 (d, J=8.0 Hz, 1H), 7.40 (t, J=8.0 Hz, 1H), 7.10–7.04 (m, 2H), 5.65 (t, J=2.8 Hz, 1H), 4.15 (d, J=2.8 Hz, 2H), 3.06 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 150.62, 150.02, 145.39, 132.12, 126.29, 126.24, 125.76, 124.69, 123.04, 122.16, 55.58, 49.60, 31.66. ^{19}F NMR (376M, $CDCl_3$): δ 62.24. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{12}H_{11}F_3N_2OI$ 382.9868, found 382.9862.

*4.2.11. N-((E)-3-Benzyl-5-(iodomethylene)oxazolidin-2-yliden-e)-4-methoxyaniline (**3bc**).* Yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.41–7.35 (m, 5H), 7.08–7.06 (m, 2H), 6.87–6.85 (m, 2H), 5.66 (t, J=2.8 Hz, 1H), 4.63 (s, 3H), 3.98 (d, J=2.8 Hz, 2H), 3.80 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 155.38, 151.00, 149.50, 139.32, 135.95, 128.95, 128.35, 128.04, 124.28, 114.05, 55.54, 50.78, 49.21, 48.78. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{18}H_{18}N_2O_2I$ 421.0413, found 421.0417.

*4.2.12. N-((E)-3-Benzyl-5-(iodomethylene)oxazolidin-2-yliden-e)-4-fluoroaniline (**3bf**).* Yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.44–7.35 (m, 5H), 7.09–6.97 (m, 4H), 5.69 (t, J=2.6 Hz, 1H), 4.64 (s, 2H), 4.00 (d, J=2.8 Hz, 2H) ^{3}C NMR (100M, $CDCl_3$): δ 160.07, 157.68, 150.79, 149.82, 142,23, 135.77, 129.00, 128.33, 124.62, 124.54, 115.37, 115.15, 50.76, 49.52, 48.72. ^{19}F NMR (376M, $CDCl_3$): δ −121.80. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{17}H_{15}FN_2O_2I$ 409.0213, found 409.0205.

*4.2.13. N-((E)-5-(Iodomethylene)-3-phenethyloxazolidin-2-ylidene)-4-methoxyaniline (**3cc**).* Yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.31–7.24 (m, 5H), 6.97–6.95 (m, 2H), 6.82–6.79 (m, 2H), 5.58 (t, J=2.8 Hz, 1H), 3.93 (d, J=2.8 Hz, 2H), 3.76 (s, 3H), 3.65 (t, J=3.6 Hz, 2H). 2.96 (t, J=3.6 Hz, 2H). ^{13}C NMR (100M, $CDCl_3$): δ 155.25, 151.00, 149.11, 139.45, 138.58, 128.84, 128.74, 126.69, 124.21, 113.96, 55.50, 51.85, 48.91, 46.18, 33.48. HRMS (EI) (m/z): $[M+H]^+$ Calcd for $C_{19}H_{20}N_2O_2I$ 435.0569, found 435.0567.

*4.2.14. N-((E)-3-(tert-Butyl)-5-(iodomethylene)oxazolidin-2-y-lidene)aniline (**3da**).* Dark brown oil. ^{1}H NMR (400M, $CDCl_3$): δ 7.24–7.22 (m, 2H), 6.99–6.97 (m, 3H), 5.49 (t, J=2.8 Hz, 1H), 4.16

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(d, *J*=2.8 Hz, 2H), 1.51 (s, 9H). ^{13}C NMR (100M, $CDCl_3$): δ 151.03, 147.41, 146.82, 128.63, 122.39, 54.43, 50.19, 47.72, 27.31. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{14}H_{18}N_2OI$ 357.0464, found 357.0462.

*4.2.15. N-((E)-3-(tert-Butyl)-5-(iodomethylene)oxazolidin-2-y-lidene)-4-methoxyaniline (**3dc**).* Dark brown oil. ^{1}H NMR (400M, $CDCl_3$): δ 6.96–6.94 (m, 2H), 6.82–6.80 (m, 2H), 5.51 (t, *J*=2.8 Hz, 1H), 4.17 (d, *J*=2.8 Hz, 2H), 3.78 (s, 3H), 1.52 (s, 9H). ^{13}C NMR (100M, $CDCl_3$): δ 155.06, 151.12, 147.26, 124.12, 114,17, 113.94, 55.58, 54.34, 50.12, 47.53, 27.29. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{15}H_{22}N_2O_2I$ 387.0569, found 387.0573.

*4.2.16. N-((E)-5-(Iodo(phenyl)methylene)-3-methyloxazolidin-2-ylidene)aniline (**3fa**).* Yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.57 (d, *J*=7.4 Hz, 2H), 7.29–7.19 (m, 5H), 7.08 (d, *J*=7.6 Hz, 2H), 6.98 (t, *J*=7.4 Hz, 1H), 4.33 (s, 2H), 3.07 (s, 2H). ^{13}C NMR (100M, $CDCl_3$): δ 150.30, 146.04, 145.26, 136.55, 129.76, 128.55, 128.16, 128.12, 123.65, 122.60, 73.25, 56.80, 31.65. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{17}H_{16}N_2O_2I$ 391.0307, found 391.0300.

*4.2.17. 4-Chloro-N-((E)-5-(iodo(phenyl)methylene)-3-methylo-xazolidin-2-ylidene)aniline (**3ff**).* Yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ7.53–7.51 (m, 2H), 7.29–7.20 (m, 3H), 7.14–7.12 (m, 2H), 6.99–6.97 (m, 2H), 4.31 (s, 2H), 3.04 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 150.53, 144.98, 144.67, 136.52, 129.66, 128.51, 128.36, 128.20, 127.54, 124.93, 73.38, 55.62, 31.58. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{17}H_{15}N_2O_2ICl$ 424.9918, found 424.9917.

*4.2.18. N-((E)-5-(1-Iodopentylidene)-3-methyloxazolidin-2-y-lidene)-4-methoxyaniline (**3gc**).* Yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.01 (d, *J*=8.0 Hz, 2H), 6.79 (d, *J*=8.0 Hz, 2H), 4.09 (s, 2H), 3.77 (s, 3H), 3.00 (s, 3H), 2.45 (t, *J*=6.8 Hz, 2H), 1.47–1.40 (m, 2H), 1.33–1.24 (m, 2H), 0.90 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 155.11, 150.32, 144.41, 139.53, 124.29, 113.88, 76.84, 55.51, 54.91, 34.95, 31.71, 31.07, 21.39, 13.86. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{16}H_{22}N_2O_2I$ 385.0777, found 385.0802.

*4.2.19. N-((E)-5-(1-Iodo-2,2-dimethylpropylidene)-3-methylo-xazolidin-2-ylidene)aniline (**3ha**).* Yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.24 (t, *J*=8.0 Hz, 2H), 7.02 (d, *J*=8.0 Hz, 2H), 6.98 (t, *J*=8.0 Hz, 1H), 4.16 (s, 2H), 3.01 (s, 3H), 1.22 (s, 9H). ^{13}C NMR (100M, $CDCl_3$): δ 150.89, 146.66, 142.29, 128.50, 123.55, 122.34, 93.29, 58.28, 38.26, 31.45, 29.80. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{15}H_{20}N_2OI$ 371.0620, found 371.0637.

*4.2.20. N-((E)-5-(1-Iodo-2,2-dimethylpropylidene)-3-methylo-xazolidin-2-ylidene)-4-methoxyaniline (**3hc**).* Yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 6.96 (d, *J*=8.0 Hz, 2H), 6.77 (d, *J*=8.0 Hz, 2H), 4.15 (s, 2H), 3.77 (s, 3H), 2.99 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (100M, $CDCl_3$): δ 150.78, 142.48, 139.86, 124.33, 113.89, 99.22, 58.38, 55.59, 38.34, 31.58, 29.89. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{16}H_{22}N_2O_2I$ 401.0726, found 401.0737.

*4.2.21. 4-Chloro-N-((E)-5-(1-iodo-2,2-dimethylpropylidene)-3-methyloxazolidin-2-ylidene)aniline (**3hf**).* Light yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ7.17 (d, *J*=8.0 Hz, 2H), 6.98 (d, *J*=8.0 Hz, 2H), 4.17 (s, 2H), 3.00 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (100M, $CDCl_3$): δ 151.13, 145.38, 124.04, 128.51, 127.31, 124.83, 93.63, 58.25, 38.31, 31.47, 31.34, 29.81. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{15}H_{19}N_2OICl$ 405.0231, found 405.0239.

4.3. General procedure for the synthesis of thiazolidine derivatives 5

A mixture of isothiocyanate (0.3 mmol) and propargylamines (0.3 mmol) was treated with iodine (0.3 mmol) in ethyl acetate (3 mL). The reaction tube was stirred for 12 h in a 50 °C oil bath with the gradual formation of white precipitation. Subsequently, the reaction was quenched with K_2CO_3 aqueous solution to make the PH beyond 9. The mixture was extracted with EA (3×10 mL) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. Pure products **5** were obtained by column chromatography (silica gel, with a mixture of hexane/ethyl acetate (10:1) as eluent).

*4.3.1. N-((E)-5-(Iodomethylene)-3-methylthiazolidin-2-yliden-e)aniline (**5aa**).* Dark brown oil. ^{1}H NMR (400M, $CDCl_3$): δ 7.29–7.26 (m, 2H), 7.08–7.04 (m, 1H), 6.92–6.90 (m, 2H), 5.93 (t, *J*=2.8 Hz, 1H), 4.16 (d, *J*=2.8 Hz, 2H), 3.10 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 156.15, 151.24, 137.32, 129.09, 123.62, 122.15, 62.88, 61.88, 33.21. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{11}H_{12}N_2SI$ 330.9766, found 330.9763.

*4.3.2. 3-Chloro-N-((E)-5-(iodomethylene)-3-methylthiazolidin-2-ylidene)aniline (**5ab**).* Dark brown oil. ^{1}H NMR (400M, $CDCl_3$): δ 7.18 (t, *J*=8.0 Hz, 1H), 7.03–7.00 (m, 1H), 6.92 (t, *J*=2.0 Hz, 1H), 6.80–6.78 (m, 1H), 5.97 (t, *J*=2.8 Hz, 1H), 4.16 (d, *J*=2.8 Hz, 2H), 3.10 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 156.52, 152.33, 136.65, 134.35, 130.02, 123.49, 122.42, 120.41, 63.40, 61.83, 33.13. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{11}H_{11}N_2SICl$ 364.9376, found 364.9387.

*4.3.3. 4-Chloro-N-((E)-5-(iodomethylene)-3-methylthiazolidin-2-ylidene)aniline (**5ac**).* Dark brown oil. ^{1}H NMR (400M, $CDCl_3$): δ 7.24–7.20 (m, 2H), 6.85–6.82 (m, 2H), 5.96 (t, *J*=2.8 Hz, 1H), 4.16 (d, *J*=2.8 Hz, 2H), 3.11 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 156.53, 149.69, 136.72, 129.10, 128.72, 123.49, 63.38, 61.88, 33.17. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{11}H_{11}N_2SICl$ 364.9376, found 364.9367.

*4.3.4. N-((E)-5-(Iodomethylene)-3-methylthiazolidin-2-yliden-e)-4-methylaniline (**5ad**).* Dark brown oil. ^{1}H NMR (400M, $CDCl_3$): δ 7.07 (d, *J*=8.0 Hz, 2H), 6.80 (d, *J*=8.0 Hz, 2H), 5.92 (t, *J*=2.8 Hz, 1H), 4.15 (d, *J*=2.8 Hz, 2H), 3.11 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 156.16, 148.63, 137.34, 132.99, 129.66, 121.87, 62.83, 61.82, 33.18, 21.00. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{12}H_{14}N_2SI$ 344.9922, found 344.9912.

4.4. General procedure for the synthesis of imidazolidine derivatives 7

A mixture of propargylamine (0.36 mmol), carbodiimide (0.3 mmol), and K_2CO_3 (0.45 mmol, 61.4 mg) in ethyl acetate (3 mL) was treated with iodine (0.3 mmol). After stirring for 12 h at 25 °C, the reaction mixture was quenched with $Na_2S_2O_3$ aqueous solution (0.1 mol/L) and extracted with EA (3×10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Pure products **7** were obtained by column chromatography (silica gel, with a mixture of hexane/ethyl acetate (20:1) as eluent).

*4.4.1. N-((E)-4-(Iodomethylene)-1-methyl-3-(p-tolyl)imidazo-ledin-2-ylidene)-4-methylaniline (**7aa**).* Light yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.05 (q, *J*=8.0 Hz, 4H), 6.79 (d, *J*=8.0 Hz, 2H), 6.57 (d, *J*=9.0 Hz, 2H), 4.57 (t, *J*=2.5 Hz, 1H), 4.11 (d, *J*=2.5 Hz, 2H), 2.75 (s, 3H), 2.28 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 150.05, 145.39, 145.31, 137.59, 133.74, 130.12, 129.96, 128.78, 128.37, 122.42, 58.02, 40.22, 34.65, 21.19, 20.75. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{19}H_{21}N_3I$ 418.0780, found 418.0770.

*4.4.2. N-((E)-1-Benzyl-4-(iodomethylene)-3-(p-tolyl)imidazo-lidin-2-ylidene)-4-methylaniline (**7ba**).* Light yellow solid. ^{1}H NMR (400M, $CDCl_3$): δ 7.41–7.36 (m, 2H), 7.34–7.31 (m, 3H), 6.77 (d, *J*=8.0 Hz, 2H), 6.59 (d, *J*=8.0 Hz, 2H), 4.60 (t, *J*=2.4 Hz, 1H),4.46 (s, 2H), 4.01 (d, *J*=2.4 Hz, 2H), 2.29 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 148.89, 145.66, 145.10, 137.50, 136.95, 133.79, 130.03,

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129.83, 128.77, 128.44, 128.12, 127.83, 127.61, 122.18, 54.53, 49.86, 40.88, 21.16, 20.72. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{25}H_{25}N_3I$ 494.1093, found 494.1124.

*4.4.3. N-((E)-4-(Iodo(phenyl)methylene)-1-methyl-3-(p-tolyl) imidazoledin-2-ylidene)-4-methylaniline (**7fa**).* Yellow solid. ^1H NMR (400M, $CDCl_3$): δ 6.88−6,81 (m, 7H), 6.67−6.57 (m, 6H), 4.34 (s, 2H), 2.72 (s, 3H), 2.23 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 151.60, 145.85, 141.08, 138.35, 136.27, 134.92, 129.99, 129.86, 128.89, 128.77, 128.52, 127.52, 126.32, 122.28, 83.78, 62.81, 35.02, 21.05, 20.88. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{25}H_{25}N_3I$ 494.1093, found 494.1128.

*4.4.4. N-((E)-4-(1-Iodopentylidene)-1-methyl-3-(p-tolyl)imida-zolidin-2-ylidene)-4-methylaniline (**7ga**).* Light yellow solid. ^1H NMR (400M, $CDCl_3$): δ 7.08−7.03 (m, 4H), 6.83 (d, *J*=8.0 Hz, 2H), 6.54 (d, *J*=8.0 Hz, 2H), 4.11 (s, 2H), 2.67 (s, 3H), 2.30 (s, 3H), 2.21 (s, 3H), 1.78 (t, *J*=7.9 Hz, 2H), 1.17−1.09 (m, 2H), 0.90−0.83 (m, 2H), 0.66 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 152.20, 146.14, 137.74, 137.70, 137.14, 129.85, 129.61, 129.50, 128.81, 122.34, 76.06, 62.52, 37.48, 34.63, 32.05, 21.65, 21.24, 20.81, 13.85. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{23}H_{28}N_3I$ 474.1406, found 474.1436.

*4.4.5. N-((E)-4-(1-Iodo-2,2-dimethylpropylidene)-1-methyl-3-(p-tolyl)imidazolidin-2-ylidene)-4-methylaniline (**7ha**).* Light yellow solid. ^1H NMR (400M, $CDCl_3$): δ 6.93 (t, *J*=8.0 Hz, 4H), 6.82 (d, *J*=8.0 Hz, 2H), 6.62 (d, *J*=8.0 Hz, 2H), 4.22 (s, 2H), 2.81 (s, 3H), 2.27 (s, 3H), 2.25 (s, 3H), 0.99 (s, 9H). ^{13}C NMR (100M, $CDCl_3$): δ 146.99, 145.41, 136.99, 134.72, 132.57, 129.38, 128.66, 128.39, 128.23, 122.14, 57.12, 54.82, 52.13, 40.36, 27.61, 21.06, 20.61. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{23}H_{28}N_3I$ 474.1406, found 474.1416.

*4.4.6. N-((E)-1-(tert-Butyl)-4-(iodo(phenyl)methylene)-3-(p-to-lyl) imidazolidin-2-ylidene)-4-methylaniline (**7ia**).* Light yellow solid. ^1H NMR (400M, $CDCl_3$): δ 6.80−6.73 (m, 3H), 6.67 (d, *J*=8.0 Hz, 2H), 6.46 (d, *J*=8.0 Hz, 2H), 6.22 (s, 4H), 6.10 (d, *J*=8.0 Hz, 2H), 4.37 (s, 2H), 2.02 (s, 3H), 1.96 (s, 3H), 1.57 (s, 9H), ^{13}C NMR (100M, $CDCl_3$): δ 149.33, 145.88, 141.80, 140.97, 136.74, 135.81, 129.85, 129.72, 128.54, 128.10, 127.86, 127.33, 126.29, 121.76, 64.92, 56.50, 54.55, 27.61, 20.86, 20.60. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{28}H_{31}N_3I$ 536.1563, found 536.1558.

*4.4.7. N-((E)-4-(1-Iodopentylidene)-1-methyl-3-(o-tolyl)imida-zolidin-2-ylidene)-2-methylaniline (**7gb**).* Light yellow solid. ^1H NMR (400M, $CDCl_3$): δ 7.20−7.17 (m, 3H), 7.13−7.10 (m, 1H), 6.97−6.90 (m, 2H), 6.74 (t, *J*=7.3 Hz, 1H), 6.54 (d, *J*=7.6 Hz, 1H), 4.15 (s, 2H), 2.60 (s, 3H), 2.33 (s, 3H), 2.08 (s, 3H), 1.76−1.69 (m, 2H), 1.17−1.10 (m, 2H), 0.89−0.83 (m, 2H), 0.67 (t, *J*=7.1 Hz, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 150.05, 147.33, 138.26, 137.59, 135.81, 130.77, 130.29, 129.69, 129.63, 128.78, 126.82, 125.90, 122.19, 121.27, 74.86, 62.66, 37.02, 34.07, 32.53, 21.80, 18.62, 18.03, 14.00. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{23}H_{29}N_3I$ 474.1406, found 474.1440.

*4.4.8. N-((E)-4-(1-Iodopentylidene)-1-methyl-3-phenylimidaz-olidin-2-ylidene)aniline (**7gc**).* Light yellow solid. ^1H NMR (400M, $CDCl_3$): δ 7.24−7.15 (m, 5H), 7.01−6.97 (m, 2H), 6.75−6.72 (m, 1H), 6.63−6.61 (m, 2H), 4.12 (s, 2H), 2.69 (s, 3H), 1.75 (t, *J*=7.7 Hz, 2H), 1.11−1.07 (m, 2H), 0.86−0.81 (m, 2H), 0.64 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (100M, $CDCl_3$): δ151.95, 148.71, 140.12, 137.18, 129.93, 129.03, 128.36, 127.97, 122.63, 120.84, 62.30, 37.64, 34.39, 32.04, 21.71, 13.96. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{21}H_{25}N_3I$ 446.1093, found 446.1121.

*4.4.9. 4-Fluoro-N-((E)-3-(4-fluorophenyl)-4-(1-iodopentyliden-e)-1-methylimidazolidin-2-ylidene)aniline (**7gd**).* Light yellow solid. ^1H NMR (400M, $CDCl_3$): δ 7.14−7.10 (m, 2H), 6.94−6.90 (m, 2H), 6.74−6.70 (m, 2H), 6.56−6.52 (m, 2H), 4.13 (s, 2H), 2.73 (s, 3H), 1.78 (t, *J*=7.7 Hz, 2H), 1.14−1.06 (m, 2H), 0.92−0.84 (m, 2H), 0.67 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 163.27, 160.80, 159.31, 156.94, 152.44, 144.55, 137.08, 136.13, 135.14, 131.75, 131.66, 123.58, 123.50, 121.41, 116.17, 115.94, 115.08, 114.86, 62.11, 37.62, 34.19, 32.04, 21.78, 13.95. ^{19}F NMR (376M, $CDCl_3$): δ −113.27, −123.98. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{21}H_{23}N_3IF_2$ 482.0905, found 482.0931.

*4.4.10. 4-Chloro-N-((E)-3-(4-chlorophenyl)-4-(1-iodopentyli-dene)-1-methylimidazolidin-2-ylidene)aniline (**7ge**).* Light yellow solid. ^1H NMR (400M, $CDCl_3$): δ 7.24−7.22 (m, 2H), 7.12−7.09 (m, 2H), 7.00−6.98 (m, 2H), 6.56−6.54 (m, 2H), 4.13 (s, 2H), 2.69 (s, 3H), 1.80 (t, *J*=7.7 Hz, 2H), 1.16−1.08 (m, 2H), 0.93−0.86 (m, 2H), 0.68 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 152.05, 147.24, 138.53, 136.62, 134.02, 131.14, 129.33, 128.40, 126.11, 123.84, 76.94, 62.20, 37.61, 34.43, 31.97, 21.73, 13.93. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{21}H_{23}Cl_2N_3I$ 514.0314, found 514.0347.

4.5. General procedure for the synthesis of oxazolidine derivatives 8

A mixture of isocyanate (0.3 mmol) and propargylamine (0.3 mmol) was treated with NBS (0.3 mmol) in ethyl acetate (3 mL). After stirring for 12 h at 50 °C, the reaction mixture was quenched with $Na_2S_2O_3$ aqueous solution (0.1 mol/L) and extracted with EA (3×10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Pure products **8** were obtained by column chromatography (silica gel, with a mixture of hexane/ethyl acetate (4:1) as eluent).

*4.5.1. N-((E)-5-(Bromomethylene)-3-methyloxazolidin-2-ylide-ne)-4-chloroaniline (**8ah**).* Brown oil. ^1H NMR (400M, $CDCl_3$): δ 7.20 (d, *J*=8.6 Hz, 2H), 6.97 (d, *J*=8.6 Hz, 2H), 5.85 (t, *J*=2.7 Hz, 1H), 4.16 (d, *J*=2.7 Hz, 2H), 3.03 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 152.12, 148.49, 144.71, 128.67, 127.79, 124.80, 82.63, 51.19, 31.75. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{11}H_{11}N_2OBr$ 300.9743, found 300.9736.

*4.5.2. N-((E)-5-(Bromomethylene)-3-methyloxazolidin-2-ylide-ne)-4-methoxyaniline (**8ac**).* Brown oil. ^1H NMR (400M, $CDCl_3$): δ 6.98 (d, *J*=9.0,Hz, 2H), 6.81 (d, *J*=9.0 Hz, 2H), 5.84 (t, *J*=2.7 Hz, 1H), 4.15 (d, *J*=2.7 Hz, 2H), 3.78 (s, 3H), 3.03 (s, 3H). ^{13}C NMR (100M, $CDCl_3$): δ 155.32, 149.55, 148.87, 193.43, 124.18, 113.99, 82.07, 55.50, 51.19, 31.83. HRMS (EI) (*m*/*z*): $[M+H]^+$ Calcd for $C_{12}H_{13}N_2O_2Br$ 296.0160, found 296.0169.

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