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Synthesis of organoselenyl isoquinolinium imides *via* iron(III) chloride-mediated tandem cyclization/selenation of *N*′-(2-alkynylbenzylidene)hydrazides and diselenides†

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This report describes the synthesis of organoselenyl isoquinolinium imides through a tandem cyclization between *N*′-(2-alkynylbenzylidene)hydrazides and diselenides. The reaction was carried out at room temperature under an ambient atmosphere using cheap iron(III) chloride as the metallic source. The strategy shows good tolerance to a broad range of *N*′-(2-alkynylbenzylidene)hydrazides and diselenides, and forms C–N and C–Se bonds in one step. The obtained product is further transformed into a bioactive *H*-pyrazolo[5,1-*a*]isoquinoline skeleton easily *via* a silver catalyzed [3 + 2] cycloaddition.

Introduction

Heterocycles are important elements of organic compounds and widely found in natural products, pharmaceuticals and some fine chemicals.[1] Among them, isoquinoline-based structures represent one of the most important heterocycles due to their rich biological activities.[2] Isoquinolinium imides are historically recognized as latent azomethine imines, which have been used as useful building blocks in a range of 1,3-dipolar cycloaddition events. For instance, Wu and other groups found that isoquinolinium imides could be generated *in situ*, and then used as powerful 1,3-dipoles in [3 + 2] cycloaddition with alkynes, alkenes and arynes (Fig. 1a).[3] Guo and co-workers synthesized a series of eight-membered N,O-containing heterocycles by a formal [5 + 3] cycloaddition of isoquinolinium imides with zwitterionic allylpalladium intermediates (Fig. 1b).[4] Glorius and co-workers reported an excellent strategy for the asymmetric synthesis of indolizidine derivatives by N-heterocyclic carbene (NHC) catalyzed formal [3 + 3] or [3 + 2] cycloaddition of isoquinolinium imides with enals (Fig. 1c).[5] Recently, isoquinolinium imides were applied in a copper catalyzed direct C–H bond functionalization for the efficient synthesis of phosphorus-containing isoquinolines (Fig. 1d).[6] Therefore, the development of a simple and efficient method for the divergent synthesis of isoquinolinium imides is still highly desirable.

Selenium-containing skeletons have attracted increasing attention due to their wide diversity in drug candidates and functional organic materials.[7] Moreover, they are also extensively used as catalysts, ligands and synthetic intermediates in

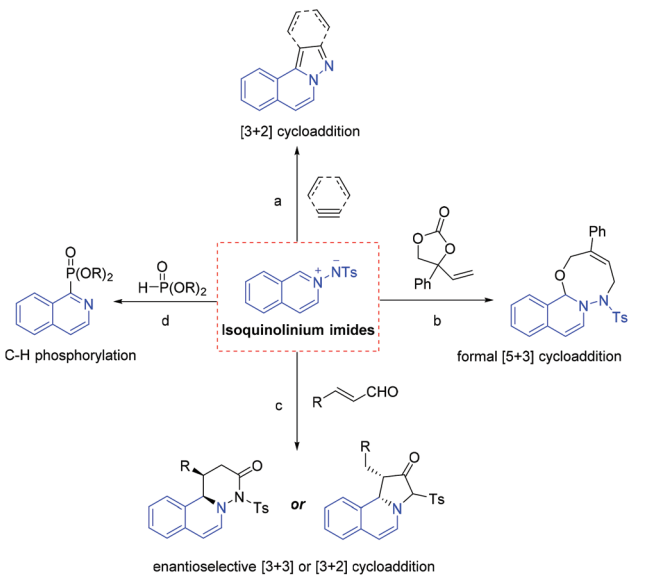

Fig. 1 Isoquinolinium imides used as useful building blocks.

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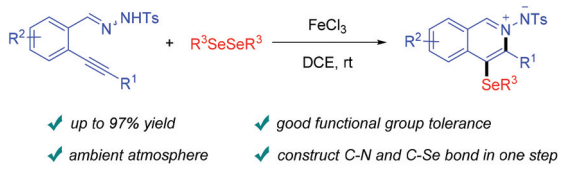


Fig. 2 Tandem cyclization/selenation.

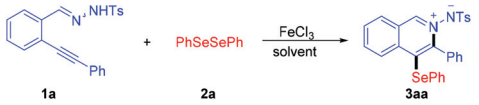
organic synthesis.[8] Regarding the indisputable significance of isoquinoline and selenoether frameworks, the development of an efficient approach for the construction of selenium-containing isoquinolinium imides is of particular interest. Tandem cyclization/cycloaddition reactions are one of the most efficient and useful methods for the synthesis of heterocycles.[9,10] The cascade strategies are always utilized as powerful tools to construct complicated molecular frameworks from relatively simple starting materials in a single vessel. Herein, we reported an efficient synthesis of organoselenyl isoquinolinium imides through a tandem cyclization (Fig. 2). The reaction used easily accessible *N*′-(2-alkynylbenzylidene)hydrazides as the starting materials, and constructed C–Se and C–N bonds in one step with the assistance of cheap iron(III) chloride.[11] The generated dipole structure provided the possibility to further access complicated molecular frameworks.

Results and discussion

We began our research with the reaction between 4-methyl-*N*′-(2-(phenylethynyl)benzylidene)benzenesulfonohydrazide (**1a**) and 1,2-diphenyldiselane (**2a**) with the assistance of $FeCl_3$. Firstly, several solvents were screened briefly. It was found that when the reaction was carried out with 0.2 mmol **1a**, 0.4 mmol **2a** and 0.4 mmol $FeCl_3$ at room temperature for 12 h, DCM, MeCN, DCE and toluene seemed to be suitable solvents (Table 1, entries 1–4), and DCE gave the corresponding product **3aa** in up to 97% yield (entry 3). THF, $MeNO_2$, and dioxane could only give the desired product **3aa** in 12–39% yields (Table 1, entries 5–7). A trace amount of the product was observed when the reaction was performed in polar solvents such as ethanol, DMF and DMA (Table 1, entries 8–10). Further decreasing the amount of **2a** (entries 11–13) or $FeCl_3$ (entries 14–16) had a significant negative influence on the reaction efficiency. The desired product was obtained in a lower yield (87%) and a trace amount of the starting material **1a** remained when the reaction was completed in a shorter time (entry 17). The tandem cyclization/selenation reaction gave **3aa** in 63% and 23% yields respectively when $FeBr_3$ or $AlCl_3$ was used to replace $FeCl_3$ (entries 18 and 19).

With the optimized reaction conditions in hand, a range of *N*′-(2-alkynylbenzylidene)hydrazides were examined first. The results are presented in Table 2. It was found that the reaction exhibited good tolerance for a range of substituted alkynes. The *ortho*-fluorine substituted substrate could also give the corresponding isoquinolinium imide **3ha** in 92% yield, and

Table 1 Optimization of the reaction conditions[a]

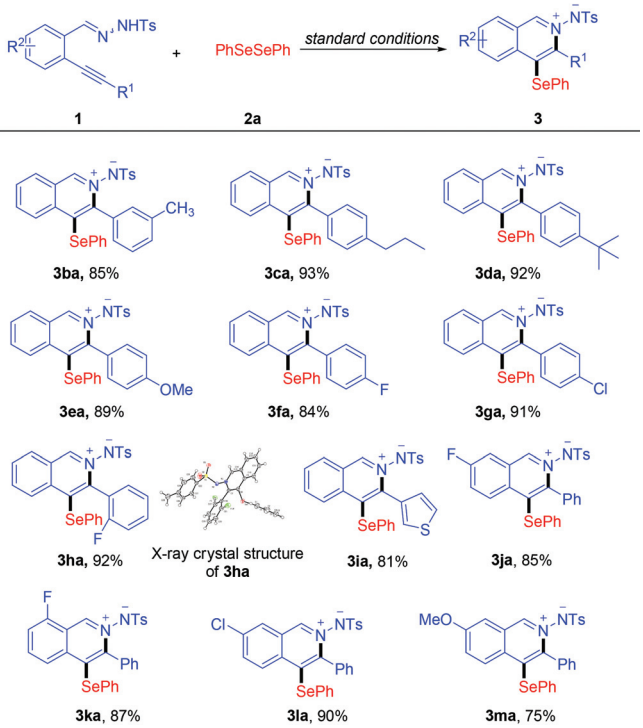


1a 2a 3aa

Entry	Solvent	2a/equiv.	[Fe]/equiv.	*T*/h	Yield[b]/%
1	DCM	2	2	12	84
2	MeCN	2	2	12	73
3	DCE	2	2	12	97
4	Toluene	2	2	12	90
5	THF	2	2	12	13
6	$MeNO_2$	2	2	12	39
7	Dioxane	2	2	12	12
8	EtOH	2	2	12	Trace
9	DMF	2	2	12	Trace
10	DMA	2	2	12	Trace
11	DCE	1.5	2	12	92
12	DCE	1	2	12	88
13	DCE	0.5	2	12	42
14	DCE	2	1	12	38
15	DCE	2	0.5	12	24
16	DCE	2	0.2	12	13
17	DCE	2	2	8	87
18[c]	DCE	2	2	12	63
19[d]	DCE	2	2	12	23

[a] Reaction conditions: **1a** (0.20 mmol, 1.0 equiv.), **2a** (*X* equiv.), $FeCl_3$ (*Y* equiv.), solvent (4.0 mL) at room temperature. [b] Isolated yield. [c] $FeCl_3$ (2 equiv.) was replaced by $FeBr_3$ (2 equiv.). [d] $FeCl_3$ (2 equiv.) was replaced by $AlCl_3$ (2 equiv.).

Table 2 Substrate scope of *N*′-(2-alkynylbenzylidene)hydrazides[a,b]



[a] The reaction was conducted with **1** (0.5 mmol), **2a** (1.0 mmol), $FeCl_3$ (1.0 mmol) and DCE (4.0 mL) at room temperature. [b] Isolated yield.

X-ray crystallographic diffraction of **3ha** further confirmed the structure of the product. Notably, the reaction was not sensitive to heterocycloalkynes, and a similar yield was observed for thiophen-3-ylethynyl hydrazide **2i**. Replacing the substituents (R^2) on the benzene ring of hydrazides with different functional groups, such as fluorine, chlorine and methoxy, resulted in a good yield of **3ja**, **3ka**, **3la** and **3ma**, respectively.

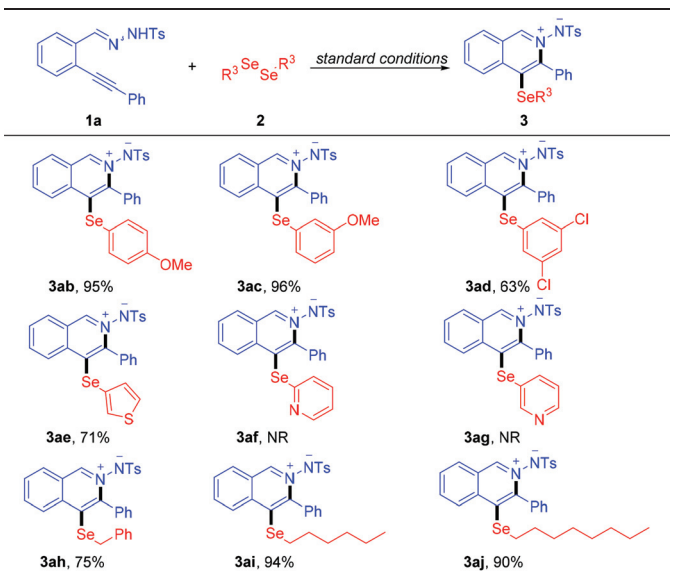
After that, we investigated the scope of the tandem cyclization/selenation with respect to diselenyl ethers (Table 3). The desired products were obtained in 63–96% yields when aromatic diselenyl ethers were subjected to the reaction of **2b–d** with hydrazide **1a**. To our delight, 1,2-di(thiophen-3-yl)diselane was also compatible for this reaction (**3ae**). Unfortunately, pyridinyldiselanes failed to generate the corresponding products, which may be due to the strong coordination ability of pyridine. To our delight, the reaction proceeded smoothly with dialkyl diselanes, which gave the desired organoselenyl isoquinolinium imides in 75–94% yields.[14]

The selenium-containing isoquinolinium imide was obtained on a gram scale easily, which further highlighted the potential application of this tandem cyclization/selenation strategy (Scheme 1).

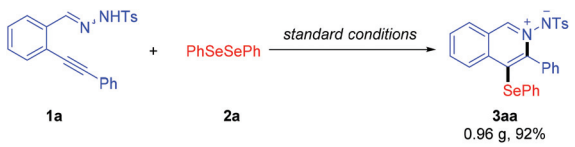
Interestingly, the isoquinolinium imide could be transformed into selenium-containing *H*-pyrazolo[5,1-*a*]isoquinoline conveniently by a [3 + 2] cycloaddition with alkyne (Scheme 2). Notably, the *H*-pyrazolo[5,1-*a*]isoquinoline skeleton exhibited important biological activities, which could be used as a CDC25B inhibitor, TC-PTP inhibitor, and PTP1B inhibitor.[12]

In order to gain a mechanistic understanding of this tandem cyclization/selenation, we conducted some control experiments (Scheme 3). It was found that no desired product **3ma** was observed when the reaction was performed in the absence of $FeCl_3$ (Scheme 3a). When PhSeCl, which was usually synthesized by the reaction of diphenyl diselenide and thionyl chloride,[13] was used instead of PhSeSePh, the selenium-containing isoquinolinium imide was isolated in 95% yield (Scheme 3b). Then we reduced the loading of $FeCl_3$ to 20 mol%; to our delight, we could still obtain the corresponding product in 74% yield (Scheme 3c). More interestingly, a tandem cyclization/selenation product was generated in 59% yield in the absence of $FeCl_3$ by using PhSeCl as the starting material (Scheme 3d). The desired product was obtained in 92% yield when the radical scavenger BHT (butylated hydroxy-

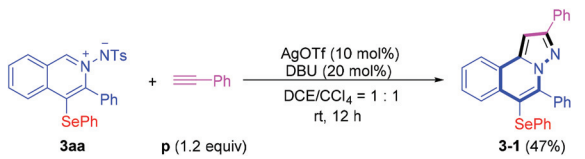
Table 3 Scope of diselanes[a,b]



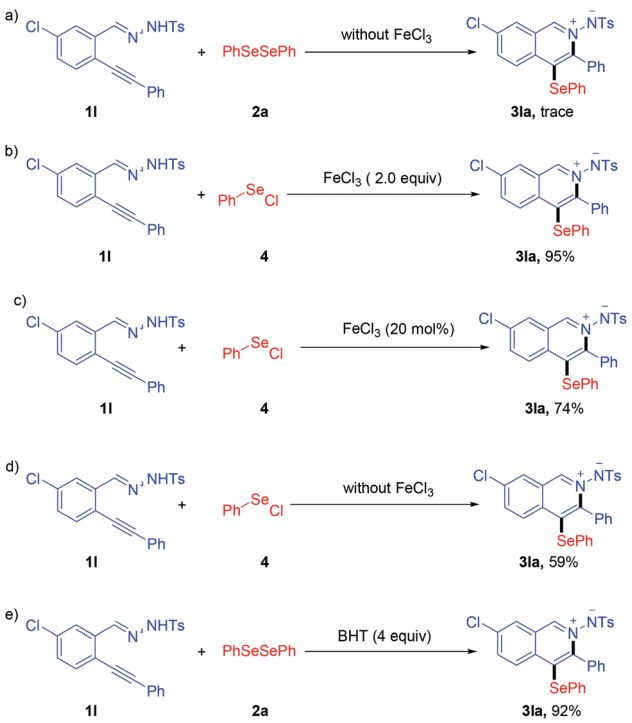
[a] The reaction was conducted with **1a** (0.5 mmol), **2** (1.0 mmol), $FeCl_3$ (1.0 mmol) and DCE (4.0 mL) at room temperature. [b] Isolated yield.



Scheme 1 Gram-scale synthesis.



Scheme 2 [3 + 2] cycloaddition with alkyne.



Scheme 3 Control experiments.

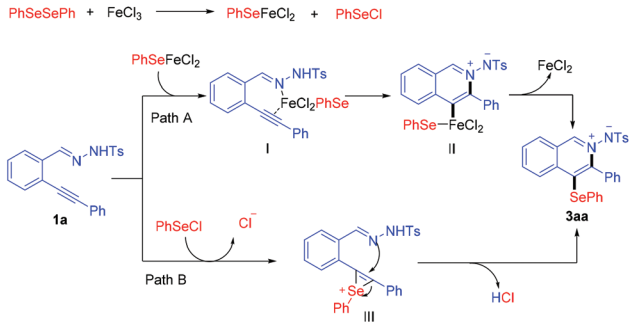


Fig. 3 The proposed mechanism for the tandem cyclization/selenation.

toluene) was added to the reaction mixture under standard conditions (Scheme 3e).

Based on the above experimental results and the previous reports,[11] we proposed two concomitant mechanistic routes for the above tandem cyclization/selenation reaction. Firstly, the reactive species $PhSeFeCl_2$ and PhSeCl were formed through the mixture of diphenyl diselenide and $FeCl_3$. Then, the triple bond of alkyne could coordinate with the iron selenolate species to generate intermediate **I**, which underwent a 6-*endo*-cyclization to afford intermediate **II**. Finally, a reductive elimination took place to give the selenium-containing isoquinolinium imide **3aa** (path A). Meanwhile, PhSeCl (**4**) exhibited higher electrophilicity than PhSeSePh, and it could activate the carbon–carbon triple bond to form intermediate **III**. Then a nucleophilic attack of the nitrogen atom to the activated triple bond could construct the final product (path B) (Fig. 3).

Experimental

General information

All the solvents for routine isolation of products and chromatography were reagent grade. Flash chromatography was performed using silica gel (200–300 mesh) with the indicated solvents. IR spectra were recorded on a spectrophotometer using KBr optics. ^{1}H NMR and ^{13}C NMR spectra were recorded on 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR) spectrometers using $CDCl_3$ as the solvent and TMS as the internal standard. The ^{1}H NMR data are reported as the chemical shift in parts per million, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant in hertz, and number of protons. High resolution mass spectra were obtained using a high resolution ESI-TOF mass spectrometer and a high resolution CI-TOF mass spectrometer.

General procedure for the generation of 3 (3ba as an example). An over-dried reaction tube equipped with a magnetic stir bar was charged with **1b** (0.5 mmol, 1 equiv.), **2a** (1.0 mmol, 2 equiv.) and $FeCl_3$ (anhydrous, 1.0 mmol, 2 equiv.). Then DCE (4 mL) was added into the mixture. Then the reaction system was kept stirring at room temperature (27 °C in an oil bath) for 12 h. After that, the system was extracted with DCM twice (15 mL × 2). The combined organic layer was dried with anhydrous Na_2SO_4. Finally, the solvent was removed by rotary evaporation and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3 to 2/1, v/v) to afford the corresponding product **3ba** as a yellow solid in 85% yield.

General procedure for the gram-scale synthesis of 3aa. An over-dried round-bottom reaction flask (100 mL) equipped with a magnetic stir bar was charged with **1a** (2.0 mmol, 1 equiv.), **2a** (4.0 mmol, 2 equiv.) and $FeCl_3$ (anhydrous, 4.0 mmol, 2 equiv.). Then DCE (20 mL) was added into the mixture. Then the reaction system was kept stirring at room temperature (27 °C in an oil bath) for 12 h. After that, the system was extracted with DCM twice (45 mL × 2). The combined organic layer was dried with anhydrous Na_2SO_4. Finally, the solvent was removed by rotary evaporation and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3 to 2/1, v/v) to afford the corresponding product **3aa** as a yellow solid in 92% yield (0.9577 g).

General procedure for further modification. An over-dried reaction tube equipped with a magnetic stir bar was charged with **3aa** (0.5 mmol, 1 equiv.), **p** (0.6 mmol, 1.2 equiv.), AgOTf (10 mol%) and DBU (20 mol%). Then a mixed solvent (4 mL) of DCE and CCl_4 in a ratio of 1 : 1 was added into the mixture. Then the reaction system was kept stirring at room temperature (27 °C in an oil bath) for 12 h. After that, the system was extracted with DCM twice (15 mL × 2). The combined organic layer was dried with anhydrous Na_2SO_4. Finally, the solvent was removed by rotary evaporation and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10 to 1/3, v/v) to afford the corresponding product **3-1** as a white solid in 47% yield.

(3-Phenyl-4-(phenylselanyl)isoquinolin-2-ium-2-yl)(tosyl)amide (3aa). Yellow solid. Yield 97% (102.7 mg). IR (neat) ν = 1371, 1280, 1132, 1087, 953, 776, 663, 589 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.84 (s, 1H), 8.48 (d, J = 8.6 Hz, 1H), 8.16 (d, J = 8.1 Hz, 1H), 7.89 (t, J = 7.2 Hz, 1H), 7.80 (t, J = 7.6 Hz, 1H), 7.28 (t, J = 7.5 Hz, 1H), 7.18–7.05 (m, 7H), 6.94 (dd, J = 19.8, 7.6 Hz, 4H), 6.72 (d, J = 7.1 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 152.6, 150.2, 140.7, 140.6, 137.1, 135.2, 133.6, 131.2, 130.8, 130.3, 130.0, 129.7, 129.5, 129.1, 129.0, 128.6, 127.4, 127.3, 126.6, 21.4 ppm. ^{77}Se NMR (76 MHz, chloroform-*d*) δ 353.2 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{22}N_2O_2SSe$ $[M + Na]^+$ 553.0459, found: 553.0461.

(4-(Phenylselanyl)-3-(*m*-tolyl)isoquinolin-2-ium-2-yl)(tosyl)-amide (3ba). Yellow solid. Yield 85% (230.0 mg). IR (neat) ν = 1477, 1373, 1281, 1082, 937, 774, 556, 457 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.85 (s, 1H), 8.50 (d, J = 9.2 Hz, 1H), 8.17 (d, J = 8.1 Hz, 1H), 7.90 (t, J = 7.1 Hz, 1H), 7.82 (t, J = 7.1 Hz, 1H), 7.16 (dd, J = 14.3, 7.7 Hz, 3H), 7.06 (dt, J = 23.5, 7.5 Hz, 4H), 6.94 (dd, J = 16.7, 7.5 Hz, 4H), 6.60 (d, J = 7.6 Hz, 1H), 6.37 (s, 1H), 2.33 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 153.0, 150.2, 140.7, 140.6, 137.3, 136.8, 135.1, 133.6, 131.5, 131.0, 130.6, 130.3, 129.9, 129.7, 129.5, 129.3, 129.0, 127.5, 127.4, 127.2, 126.7, 21.5 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{24}N_2O_2SSe$ $[M + Na]^+$ 567.0616, found: 567.0603.

(4-(Phenylselanyl)-3-(4-propylphenyl)isoquinolin-2-ium-2-yl) (tosyl)amide (3ca). Yellow solid. Yield 93% (266.1 mg). IR (neat) ν = 2359, 1281, 1136, 1086, 937, 812, 777, 659, 589 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.74 (s, 1H), 8.39 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.80 (t, *J* = 7.8 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.10–6.97 (m, 5H), 6.84 (dd, *J* = 17.7, 8.4 Hz, 6H), 6.58 (d, *J* = 8.1 Hz, 2H), 2.54–2.48 (m, 2H), 2.26 (s, 3H), 1.61 (h, *J* = 7.4 Hz, 2H), 0.93 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 152.9, 150.4, 143.3, 140.7, 140.6, 137.3, 135.1, 131.4, 131.0, 130.8, 130.2, 130.0, 129.9, 129.5, 129.2, 129.0, 127.4, 127.3, 126.7, 38.0, 24.4, 21.5, 14.0 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{31}H_{28}N_2O_2SSe$ $[M + Na]^+$ 595.0929, found: 595.0914.

(3-(4-(*tert*-Butyl)phenyl)-4-(phenylselanyl)isoquinolin-2-ium-2-yl)(tosyl)amide (3da). Yellow solid. Yield 92% (268.4 mg). IR (neat) ν = 2960, 2359, 1477, 1280, 1134, 951, 812, 736, 656, 529 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.80 (s, 1H), 8.49 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.1 Hz, 1H), 7.89 (t, *J* = 7.8 Hz, 1H), 7.80 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 3H), 7.05 (t, *J* = 7.7 Hz, 4H), 6.91 (dd, *J* = 13.0, 7.6 Hz, 4H), 6.68 (d, *J* = 8.4 Hz, 2H), 2.34 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 152.7, 151.4, 150.5, 140.7, 140.4, 137.3, 135.0, 131.2, 130.3, 130.1, 130.0, 129.4, 129.2, 129.0, 127.4, 127.3, 126.6, 124.1, 34.7, 31.3, 21.5 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{32}H_{30}N_2O_2SSe$ $[M + Na]^+$ 609.1085, found: 609.1077.

(3-(4-Methoxyphenyl)-4-(phenylselanyl)isoquinolin-2-ium-2-yl)(tosyl)amide (3ea). Yellow solid. Yield 89% (249.8 mg). IR (neat) ν = 2360, 1610, 1478, 1279, 1131, 940, 810, 734, 654, 530 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.79 (s, 1H), 8.45 (d, *J* = 8.4 Hz, 1H), 8.14 (d, *J* = 8.1 Hz, 1H), 7.89–7.84 (m, 1H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.19–7.05 (m, 5H), 6.96–6.91 (m, 4H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.61 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 160.0, 152.5, 150.4, 140.8, 140.5, 137.2, 135.1, 131.7, 131.3, 130.8, 130.1, 129.9, 129.4, 129.1, 128.9, 127.3, 127.2, 126.5, 125.8, 112.6, 55.2, 21.3 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{25}N_2O_3SSe$ $[M + H]^+$ 561.0746, found: 561.0751.

(3-(4-Fluorophenyl)-4-(phenylselanyl)isoquinolin-2-ium-2-yl)-(tosyl)amide (3fa). Yellow solid. Yield 84% (230.6 mg). IR (neat) ν = 1577, 1480, 1280, 1134, 953, 830, 730, 657, 534 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.80 (s, 1H), 8.53 (d, *J* = 8.5 Hz, 1H), 8.18 (d, *J* = 8.1 Hz, 1H), 7.94 (t, *J* = 7.8 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.16 (dd, *J* = 13.9, 7.7 Hz, 3H), 7.08 (t, *J* = 7.5 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 7.4 Hz, 2H), 6.76–6.67 (m, 4H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 162.7 (d, J_{C-F} = 247.8 Hz), 151.7, 150.6, 140.9, 140.8, 137.4, 135.4, 132.3 (d, J_{C-F} = 8.5 Hz), 131.0, 130.5, 130.2, 129.6, 129.4 (d, J_{C-F} = 3.6 Hz), 129.2, 129.1, 127.6, 127.4, 126.5, 114.4 (d, J_{C-F} = 21.9 Hz), 21.5 ppm. ^{19}F NMR (376 MHz, chloroform-*d*) δ = −111.60 ppm (s, 1F). HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{21}FN_2O_2SSe$ $[M + Na]^+$ 571.0365, found: 571.0378.

(3-(4-Chlorophenyl)-4-(phenylselanyl)isoquinolin-2-ium-2-yl)-(tosyl)amide (3ga). Pale yellow solid. Yield 91% (256.6 mg). IR (neat) ν = 1575, 1478, 1280, 1133, 938, 833, 739, 654, 532 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.77 (s, 1H), 8.54 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 7.94 (m, *J* = 8.5, 7.1, 1.3 Hz, 1H), 7.87–7.83 (m, 1H), 7.16 (t, *J* = 7.5 Hz, 3H), 7.09 (t, *J* = 7.4 Hz, 2H), 7.02–6.97 (m, 4H), 6.91–6.87 (m, 2H), 6.65 (d, *J* = 8.5 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 151.5, 150.8, 141.1, 135.5, 135.0, 131.7, 131.6, 131.1, 130.9, 130.7, 129.7, 129.2, 129.1, 127.7, 127.5, 127.4, 126.6, 21.5 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{22}ClN_2O_2SSe$ $[M + H]^+$ 565.0250, found: 565.0259.

(3-(2-Fluorophenyl)-4-(phenylselanyl)isoquinolin-2-ium-2-yl)-(tosyl)amide (3ha). Yellow solid. Yield 92% (252.1 mg). IR (neat) ν = 1613, 1438, 1280, 1132, 953, 886, 735, 666, 532 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.82 (s, 1H), 8.48 (d, *J* = 8.4 Hz, 1H), 8.14 (d, *J* = 8.1 Hz, 1H), 7.89 (t, *J* = 7.4 Hz, 1H), 7.81 (t, *J* = 7.5 Hz, 1H), 7.34–7.23 (m, 3H), 7.10 (dt, *J* = 26.0, 7.2 Hz, 3H), 7.01–6.95 (m, 4H), 6.86 (q, *J* = 8.5, 7.4 Hz, 2H), 6.56 (t, *J* = 7.3 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ160.0 (d, J_{C-F} = 241.7 Hz), 149.6, 147.3, 140.8, 140.5, 136.7, 135.1, 131.6, 131.2 (d, J_{C-F} = 7.9 Hz), 131.0, 130.7, 130.5, 129.5, 129.4, 129.1, 129.0, 127.6, 126.6, 123.2 (d, J_{C-F} = 3.3 Hz), 122.0, 115.1 (d, J_{C-F} = 21.0 Hz), 21.4 ppm. ^{19}F NMR (376 MHz, chloroform-*d*) δ = −110.31 ppm (s, 1F). HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{22}FN_2O_2SSe$ $[M + H]^+$ 549.0546, found: 549.0552.

(4-(Phenylselanyl)-3-(thiophen-3-yl)isoquinolin-2-ium-2-yl)-(tosyl)amide (3ia). Orange-red solid. Yield 81% (216.7 mg). IR (neat) ν = 1575, 1476, 1274, 1133, 943, 863, 718, 659, 530 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.80 (s, 1H), 8.49 (d, *J* = 8.5 Hz, 1H), 8.15 (d, *J* = 8.1 Hz, 1H), 7.89 (t, *J* = 7.3 Hz, 1H), 7.80 (t, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.12 (dd, *J* = 15.1, 7.5 Hz, 4H), 6.96 (dd, *J* = 13.6, 7.6 Hz, 4H), 6.80 (d, *J* = 6.0 Hz, 1H), 6.65 (dd, *J* = 2.8, 1.0 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 150.6, 148.3, 140.7, 137.3, 135.2, 132.8, 131.3, 130.8, 130.4, 129.6, 129.5, 129.3, 129.1, 128.7, 127.5, 127.2, 126.5, 123.7, 21.4 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{26}H_{20}N_2O_2S_2Se$ $[M + Na]^+$ 559.0024, found: 559.0015.

(7-Fluoro-3-phenyl-4-(phenylselanyl)isoquinolin-2-ium-2-yl)-(tosyl)amide (3ja). Yellow solid. Yield 85% (233.1 mg). IR (neat) ν = 1482, 1278, 1130, 1113, 1086, 908, 832, 713, 655, 532 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.87 (s, 1H), 8.50 (dd, *J* = 9.3, 4.9 Hz, 1H), 7.81 (dd, *J* = 7.8, 2.4 Hz, 1H), 7.63–7.57 (m, 1H), 7.32–7.27 (m, 1H), 7.19–7.05 (m, 7H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 7.5 Hz, 2H), 6.73 (d, *J* = 7.3 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 162.3 (d, J_{C-F} = 254.7 Hz), 152.0, 148.9, 140.8, 140.4, 134.1, 133.5, 132.3 (d, J_{C-F} = 8.5 Hz), 131.0, 130.9, 130.0, 129.8, 129.6, 129.1, 128.7, 128.5 (d, J_{C-F} = 10.1 Hz), 127.5, 127.4, 126.6, 125.2 (d, J_{C-F} = 25.0 Hz), 112.6 (d, J_{C-F} = 22.6 Hz), 21.4 ppm. ^{19}F NMR (376 MHz, chloroform-*d*) δ = −106.25 ppm (s, 1F). HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{21}FN_2O_2SSe$ $[M + Na]^+$ 571.0365, found: 577.0377.

(8-Fluoro-3-phenyl-4-(phenylselanyl)isoquinolin-2-ium-2-yl)-(tosyl)amide (3ka). Yellow solid. Yield 87% (238.2 mg). IR (neat) ν = 1576, 1477, 1285, 1120, 1083, 974, 860, 719, 659, 567 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.95 (d, *J* = 0.6 Hz, 1H), 8.27 (d, *J* = 8.6 Hz, 1H), 7.84 (td, *J* = 8.3, 5.6 Hz, 1H), 7.45 (t, *J* = 8.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.17–7.07 (m, 5H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 7.1 Hz, 2H), 6.77 (d, *J* = 7.1 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR

(100 MHz, chloroform-*d*) δ 158.6 (d, J_{C-F} = 262.2 Hz), 153.5, 144.1 (d, J_{C-F} = 6.6 Hz), 141.0, 140.4, 137.7, 135.6 (d, J_{C-F} = 8.6 Hz), 133.4, 131.1, 130.9, 129.9, 129.6, 129.2, 128.9, 127.7, 127.5, 126.7, 125.2 (d, J_{C-F} = 4.4 Hz), 118.6 (d, J_{C-F} = 14.8 Hz), 114.2 (d, J_{C-F} = 18.0 Hz), 21.5 ppm. ^{19}F NMR (376 MHz, chloroform-*d*) δ = −116.14 ppm (s, 1F). HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{21}FN_2O_2SSe$ $[M + H]^+$ 549.0546, found: 549.0551.

(7-Chloro-3-phenyl-4-(phenylselanyl)isoquinolin-2-ium-2-yl)-(tosyl)amide (3la). Yellow solid. Yield 90% (254.4 mg). IR (neat) ν = 1573, 1280, 1140, 1084, 891, 731, 659, 533 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.82 (s, 1H), 8.41 (d, *J* = 9.1 Hz, 1H), 8.14 (d, *J* = 1.9 Hz, 1H), 7.76 (dd, *J* = 9.1, 2.1 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.16 (dd, *J* = 17.0, 7.5 Hz, 4H), 7.11–7.06 (m, 3H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.91 (d, *J* = 7.3 Hz, 2H), 6.74 (d, *J* = 7.2 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 152.8, 148.8, 140.9, 140.4, 136.6, 135.6, 135.3, 133.4, 131.0, 130.9, 130.0, 129.7, 129.1, 128.9, 128.1, 127.7, 127.6, 127.5, 126.7, 21.5 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{22}ClN_2O_2SSe$ $[M + H]^+$ 565.0250, found: 565.0254.

(7-Methoxy-3-phenyl-4-(phenylselanyl)isoquinolin-2-ium-2-yl)(tosyl)amide (3ma). Yellow solid. Yield 75% (209.8 mg). IR (neat) ν = 1614, 1379, 1274, 1134, 1106, 807, 700, 653, 534 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.82 (s, 1H), 8.35 (d, *J* = 10.4 Hz, 1H), 7.49–7.45 (m, 2H), 7.26–7.04 (m, 8H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.89 (dd, *J* = 8.3, 1.2 Hz, 2H), 6.70–6.66 (m, 2H), 3.97 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 160.5, 150.5, 148.8, 140.7, 140.6, 133.8, 133.0, 131.4, 130.7, 130.2, 129.5, 129.2, 129.0, 128.5, 128.4, 127.3, 126.6, 106.2, 56.2, 21.4 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{24}N_2O_3SSe$ $[M + Na]^+$ 583.0565, found: 583.0566.

(4-((4-Methoxyphenyl)selanyl)-3-phenylisoquinolin-2-ium-2-yl)(tosyl)amide (3ab). Orange solid. Yield 95% (265.8 mg). IR (neat) ν = 2922, 1490, 1278, 1136, 943, 817, 759, 654, 533 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.77 (s, 1H), 8.58 (d, *J* = 8.5 Hz, 1H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.91 (t, *J* = 7.8 Hz, 1H), 7.80 (t, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.17–7.11 (m, 4H), 6.96 (d, *J* = 8.1 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 6.75 (d, *J* = 7.3 Hz, 2H), 6.62 (d, *J* = 8.8 Hz, 2H), 3.71 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 159.6, 152.2, 149.9, 140.7, 137.2, 135.0, 133.8, 133.6, 130.4, 130.2, 129.5, 129.2, 129.1, 128.7, 127.4, 126.7, 120.9, 115.2, 55.4, 21.5 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{24}N_2O_3SSe$ $[M + Na]^+$ 583.0565, found: 583.0566.

(4-((3-Methoxyphenyl)selanyl)-3-phenylisoquinolin-2-ium-2-yl)(tosyl)amide (3ac). Yellow solid. Yield 96% (269.0 mg). IR (neat) ν = 2928, 1574, 1477, 1280, 1137, 951, 833, 780, 682, 531 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.84 (s, 1H), 8.48 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.1 Hz, 1H), 7.90 (t, *J* = 7.7 Hz, 1H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.20–6.95 (m, 8H), 6.73 (d, *J* = 7.7 Hz, 2H), 6.67 (d, *J* = 8.3 Hz, 1H), 6.51–6.45 (m, 2H), 3.64 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 160.0, 152.7, 150.3, 140.7, 140.6, 137.3, 135.2, 133.6, 132.2, 130.4, 130.3, 130.0, 129.6, 129.5, 129.2, 129.1, 128.7, 127.4, 126.7, 123.1, 116.6, 112.8, 55.3, 21.5 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{24}N_2O_3SSe$ $[M + Na]^+$ 583.0565, found: 583.0565.

(4-((3,5-Dichlorophenyl)selanyl)-3-phenylisoquinolin-2-ium-2-yl)(tosyl)amide (3ad). Yellow solid. Yield 63% (188.3 mg). IR (neat) ν = 2922, 1560, 1372, 1280, 1135, 946, 881, 755, 655, 533 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.90 (s, 1H), 8.46 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 7.99 (t, *J* = 8.3 Hz, 1H), 7.89 (t, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.14 (t, *J* = 1.7 Hz, 1H), 7.09 (t, *J* = 7.8 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 1.8 Hz, 2H), 6.66 (d, *J* = 7.3 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 152.9, 150.8, 140.9, 140.5, 136.9, 135.7, 133.3, 133.1, 130.7, 129.9, 129.8, 129.2, 129.0, 128.9, 128.6, 127.9, 127.5, 126.6, 21.5 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{21}Cl_2N_2O_2SSe$ $[M + H]^+$ 598.9861, found: 598.9854.

(3-Phenyl-4-(thiophen-3-ylselanyl)isoquinolin-2-ium-2-yl)-(tosyl)amide (3ae). Orange-yellow solid. Yield 71% (191.0 mg). IR (neat) ν = 1278, 1133, 1086, 952, 881, 766, 668, 530 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.78 (s, 1H), 8.63–8.60 (m, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.97–7.92 (m, 1H), 7.84–7.80 (m, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.17–7.12 (m, 5H), 6.96 (d, *J* = 7.9 Hz, 2H), 6.81 (dd, *J* = 2.9, 1.2 Hz, 1H), 6.75 (dd, *J* = 8.2, 1.1 Hz, 2H), 6.58 (dd, *J* = 5.0, 1.2 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 152.2, 150.1, 140.8, 140.6, 137.2, 135.1, 133.5, 130.6, 130.3, 130.2, 130.0, 129.5, 129.1, 129.0, 128.8, 127.4, 127.2, 126.9, 126.7, 122.6, 21.5 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{26}H_{21}N_2O_2S_2Se$ $[M + H]^+$ 537.0204, found: 537.0207.

(3-Phenyl-4-(pyridin-2-ylselanyl)isoquinolin-2-ium-2-yl)(tosyl)-amide (3af). An unsuccessful case. We didn't get any data about it for the reaction didn't occur at all.

(3-Phenyl-4-(pyridin-3-ylselanyl)isoquinolin-2-ium-2-yl)(tosyl)-amide (3ag). An unsuccessful case. We didn't get any data about it for the reaction didn't occur at all.

(4-(Benzylselanyl)-3-phenylisoquinolin-2-ium-2-yl)(tosyl)amide (3ah). Orange solid. Yield 75% (204.9 mg). IR (neat) ν = 1275, 1134, 1085, 948, 883, 758, 657, 533 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.72 (s, 1H), 8.49 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 8.1 Hz, 1H), 7.94 (t, *J* = 7.7 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.16–7.10 (m, 4H), 7.03 (dt, *J* = 14.4, 7.0 Hz, 3H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.62 (t, *J* = 8.5 Hz, 4H), 3.70 (s, 2H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 153.0, 149.7, 140.6, 137.8, 136.8, 134.9, 133.7, 130.4, 130.2, 129.4, 129.1, 129.0, 128.6, 128.4, 127.3, 127.2, 126.9, 126.7, 33.7, 21.5 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{29}H_{25}N_2O_2SSe$ $[M + H]^+$ 545.0796, found: 545.0795.

(4-(Hexylselanyl)-3-phenylisoquinolin-2-ium-2-yl)(tosyl)amide (3ai). Pale yellow solid. Yield 94% (254.7 mg). IR (neat) ν = 2933, 1480, 1292, 1135, 943, 880, 761, 661, 534 cm^{-1}. ^{1}H NMR (400 MHz, chloroform-*d*) δ 9.75 (s, 1H), 8.63 (d, *J* = 8.5 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 8.00 (t, *J* = 7.8 Hz, 1H), 7.84 (t, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.18 (t, *J* = 8.8 Hz, 4H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 7.7 Hz, 2H), 2.46 (t, *J* = 7.3 Hz, 2H), 2.35 (s, 3H), 1.32–1.06 (m, 8H), 0.79 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 152.2, 149.4, 140.8, 140.7, 137.8, 134.9, 133.6, 130.6, 130.2, 129.9, 129.5, 129.2, 129.1, 128.7, 127.4, 127.1, 126.7, 31.1, 30.8, 30.0, 29.2, 22.5, 21.5, 14.0 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{31}N_2O_2SSe$ $[M + H]^+$ 539.1266, found: 539.1284.

(4-(Octylselanyl)-3-phenylisoquinolin-2-ium-2-yl)(tosyl)amide (3aj). Pale yellow solid. Yield 90% (255.1 mg). IR (neat) ν = 2923, 1372, 1291, 1136, 941, 879, 762, 655, 533 cm^{-1}. ^1H NMR (400 MHz, chloroform-*d*) δ 9.77 (s, 1H), 8.62 (d, *J* = 7.9 Hz, 1H), 8.16 (d, *J* = 8.1 Hz, 1H), 8.01 (t, *J* = 7.8 Hz, 1H), 7.84 (t, *J* = 8.1 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.18 (t, *J* = 8.1 Hz, 4H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 7.1 Hz, 2H), 2.47 (t, *J* = 7.3 Hz, 2H), 2.35 (s, 3H), 1.28–1.04 (m, 12H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 151.9, 149.4, 140.6, 140.5, 137.6, 134.9, 133.7, 130.4, 130.2, 129.7, 129.4, 129.0, 128.9, 128.5, 127.2, 126.9, 126.5, 31.6, 30.6, 29.8, 29.3, 28.9, 28.7, 22.5, 21.3, 14.0 ppm. HRMS (ESI) *m*/*z*: calcd for $C_{30}H_{34}N_2O_2SSe$ $[M + Na]^+$ 589.1398, found: 589.1355.

2,5-Diphenyl-6-(phenylselanyl)pyrazolo[5,1-*a*]isoquinoline (3-1). White solid. Yield 47% (56.1 mg). ^1H NMR (400 MHz, chloroform-*d*) δ 8.43 (d, *J* = 8.3 Hz, 1H), 8.20 (d, *J* = 7.0 Hz, 1H), 7.92 (d, *J* = 7.0 Hz, 2H), 7.61 (t, *J* = 6.9 Hz, 1H), 7.55 (d, *J* = 6.9 Hz, 1H), 7.51 (s, 5H), 7.43–7.39 (m, 3H), 7.37–7.33 (m, 1H), 7.14 (m, *J* = 8.2, 5.2, 2.7 Hz, 5H). ^{13}C NMR (100 MHz, chloroform-*d*) δ 153.2, 144.5, 140.9, 135.3, 133.4, 133.1, 130.5, 130.4, 129.6, 129.3, 129.1, 129.0, 128.7, 128.5, 128.0, 127.9, 126.6, 126.1, 124.4, 123.9, 112.4, 95.3 ppm. HRMS (CI) *m*/*z*: calcd for $C_{29}H_{21}N_2Se$ $[M + H]^+$ 477.0864, found: 477.0869.

Conclusions

In summary, we have developed an efficient iron(III) chloride promoted tandem cyclization/selenation method to construct a selenium-containing isoquinolinium imide skeleton. The reaction was carried out under mild and ambient atmosphere conditions by using easily accessible *N*′-(2-alkynylbenzylidene) hydrazides and diselenides as starting materials. The generated *N*-iminoisoquinolinium ylides are useful building blocks, which could be transformed into other more complex selenium-containing heterocycles easily.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

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