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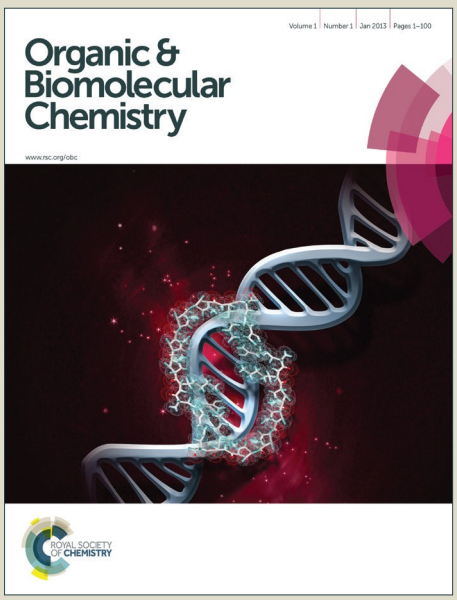

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One-Pot Synthesis of 1*H*-Isochromenes and 1,2-Dihydroisoquinolines by a Sequential Isocyanide-based Multicomponent/Wittig Reaction

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ABSTRACT: A one-pot synthesis of 1*H*-isochromenes and 1,2-dihydroisoquinolines by a I-MCR/Wittig sequence was developed. The reaction of phosphonium salt **5**, acid, amine (or without), and isocyanide gave the 1*H*-isochromenes **7** or 1,2-dihydroisoquinolines **9** in good yields by a sequential Passerini or Ugi condensation and intramolecular Wittig reaction in the presence of K_2CO_3.

Key words: 1*H*-isochromene; isoquinoline; Ugi reaction; Passerini reaction; intramolecular Wittig reaction; isocyanide

Introduction

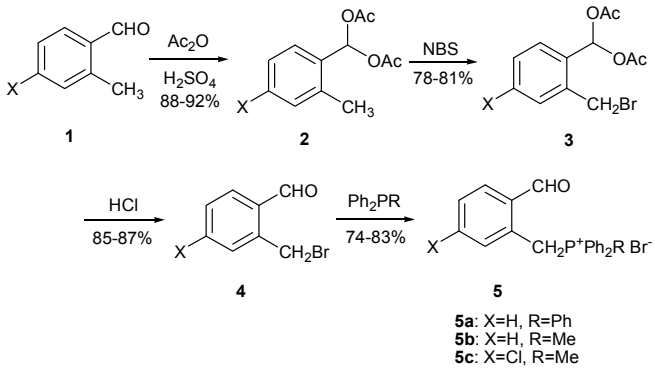
1*H*-Isochromene unit represents a useful structural motif found in natural products and biologically active compounds. Some natural products containing 1*H*-isochromene can be found in bacteria, fungi and higher plants. Recently reported natural products include banchromene,[1] indigotide A,[2] kalafungin[3] and some of their derivatives were found to show good antitumor activities.[4] The methods described for the preparation of 1*H*-isochromenes either involves tandem nucleophilic addition and cyclization of the 2-(1-alkynyl)arylaldehydes catalyzed by various late transition metal complexes involving Au,[5] Pd,[6] Cu,[7] Ag,[8] or In,[9] or cyclization of 2-(1-alkynyl)arylethanols in the presence of I_2[10] or Au complexes,[11] or intramolecular Heck[12] and Wittig reaction.[13] 1,2-Dihydroisoquinolines also play an important role in the field of medicinal chemistry due to their excellent pharmacological potential. Some

1,2-dihydroisoquinoline derivatives have been used as good β-secretase (BACE-1) inhibitors,[14] ATP-competitive inhibitors of the nod-like receptor protein (NLRP1) inflammasome,[15] brain specific and shelf-stable monoamine oxidase (MAO) inhibitors,[16] antibacterial agents[17] and novel carriers for specific delivery of drugs to the brain.[18] The reported synthetic methods for 1,2-dihydroisoquinolines include tandem nucleophilic addition and cyclization of the 2-(1-alkynyl)arylaldehydes and amine catalyzed by Ag, Cu or Au complexes,[19] $Yb(OTf)_3$,[20] $CoCl_2$,[21] I_2,[22] or no catalyst,[23] pseudo-three-component reactions of arynes with N-aryl imines,[24] cyclization of 2-(1-alkynyl)arylethylamines in the presence of Au complexes,[11] and platinum-catalyzed sequential rearrangement of amides and aminocyclization.[25] Consequently, new and convenient synthetic method to 1*H*-isochromenes and 1,2-dihydroisoquinolines would provide a valuable tool to synthetic organic and pharmaceutical chemists.

The isocyanide based multicomponent reactions (I-MCRs), mainly Ugi and Passerini reaction, have become a useful synthetic tool in organic and medicinal chemistry for rapid preparation of organic molecules.[26] The sequences of Ugi and Passerini reactions, followed by post-condensation transformations, constitute extremely powerful methods for the preparation of complex molecules, especially heterocyclic compounds with diverse structures.[27-33] For example, a post-Ugi and Buchwald-Hartwig/Michael reaction was utilized successifully to prepare functionalized spiro[indoline-3,2′-pyrrole]-2,5′-diones in moderate to good yields.[27] 3-Hydroxyisoquinolines were also obtained by sequential Ugi/reductive Heck cyclization.[28] The sequence of I-MCRs/Horner reaction has been used in preparation of butenolides, pyrrolidinones and pyridines under mild reaction condition.[32] We have recently reported an efficient synthesis of multisubstituted 2,3-dihydro-1*H*-2-benzazepin-1-ones and 3*H*-2-benzoxepin-1-ones by an I-MCR/Wittig sequence starting from phosphonium salt precursors (using as acid component in the I-MCR).[33] Continuing our interests in synthesis of various heterocycles via multicomponent reaction,[34] herein we wish to report a new efficient synthesis of 1*H*-isochromenes and 1,2-dihydroisoquinolines by an I-MCR/Wittig sequence starting from phosphonium salt precursors, which were used as aldehyde components in the I-MCR.

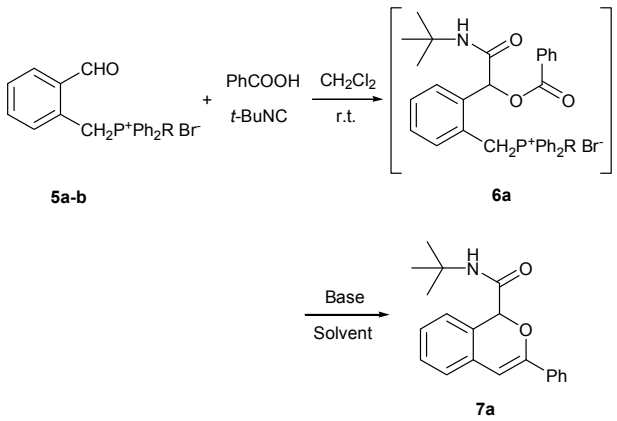
Results and Discussion

The phosphonium salt precursors **5** were prepared according to standard protocols (Scheme 1).[35] Protection of aldehydes **1** with Ac_2O in acidic condition gave compounds **2**. Bromination of **2** with the NBS led to its 2-bromomethyl derivatives **3**, which were deprotected to give 2-bromomethylbenzaldehydes **4**. Reaction of **4** with triphenylphosphine or diphenylmethylphosphine produced the corresponding phosphonium salt precursors **5**.



Scheme 1. Preparation of phosphonium salt precursors **5**

The phosphonium salts **5a-b**, benzoic acid and *t*-butylisocyanide were selected initially as the Passerini reactants (Scheme 2). When the above three components were stirred in CH_2Cl_2 at room temperature for 48 h, the Passerini product **6a** was often obtained as semi-solid or oil with high hydroscopic property which was difficult to be purified. So after washed by ether/petroleum ether (V/V = 1:1), the crude phosphonium salt **6a** was used directly without further purification for intramolecular Wittig reaction. The R group, solvent and base utilized had notable effect on this reaction. We firstly investigated the intramolecular Wittig reaction of diphenylmethyl phosphonium salt **5b** (R = Me). As the solid K_2CO_3 was used as base at 60 °C, low to moderate yields of the product **7a** were obtained when THF or methanol were used as solvents (15-45%, Table 1, entry 1-2). But when toluene was utilized as solvent, the best yield was reached (86%, Table 1, entry 3) at 110 °C. Utilizing the more basic NaOH resulted in lower yield of the product (24%, Table 1, entry 4). Moderate yields were obtained in case that NEt_3 was used in methanol or toluene (45-56%, Table 1, entry 5-6). The intramolecular Wittig reaction of triphenyl phosphonium salt **5a** (R = Ph) gave low yields in both K_2CO_3/toluene and NEt_3/MeOH system (17-23%, Table 1, entry 7-8), which implied the low reactivity of triphenyl phosphonium salt in intramolecular Wittig reaction.



Scheme 2. Optimization of the reaction condition

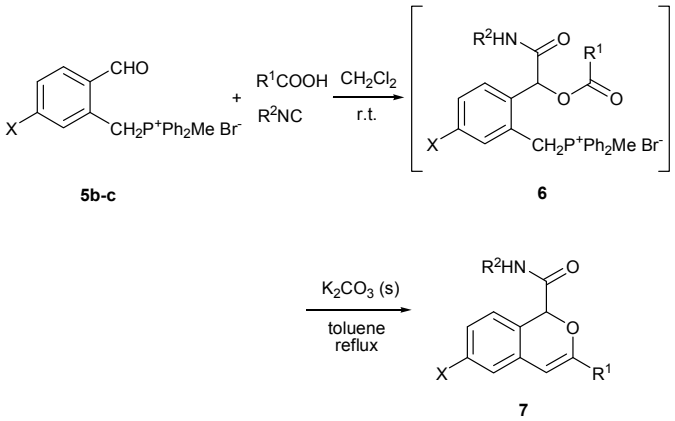
Table 1. Screening reactions conditions for intramolecular Wittig reaction

entry	R	solvent	Condition[a]	Base[b]	Yield[c] (%)
1	Me	THF	60 °C /2 h	K_2CO_3	45
2	Me	MeOH	60 °C /2 h	K_2CO_3	15
3	Me	toluene	110 °C /2 h	K_2CO_3	86
4	Me	toluene	110 °C /1 h	NaOH	24
5	Me	MeOH	60 °C /12 h	NEt_3	63
6	Me	toluene	110 °C /2 h	NEt_3	42
7	Ph	toluene	110 °C /2 h	K_2CO_3	23
8	Ph	MeOH	60 °C /12 h	NEt_3	17

[a]Condition for Ugi reaction: CH_2Cl_2, r.t., 48 hr;

[b]Two equiv. of the base was used. [c] Isolated yields.

With the optimized condition, various phosphonium salts **5b-c** (R = Me), acids and isocyanides were employed for the reaction (Scheme 3). All of the reactions were carried out smoothly to give the corresponding 1*H*-isochromenes **7** in toluene at reflux temperature, and good yields were obtained with various substituents on the reactants (Table 2). Various acids can be used in above one-pot cyclization to prepare 1*H*-isochromenes **7**. As indicated in Table 2, good yields (**7a**-**7d** and **7k**-**7o**, 81-89%, Table 2) were obtained as R^1 are aromatic groups regardless of the electro-donating or electro-withdrawing substituents on the benzene ring. Relative lower yields (**7e**-**7j**, **7p**-**q**, 68-78%, Table 2) were resulted when R^1 are alkyl, 2-furyl, 2-thiophenyl or o-substituted aromatic groups.



Scheme 3. Preparation of 1*H*-isochromenes **7**

Table 2. Preparation of 1*H*-isochromenes **7**[a]

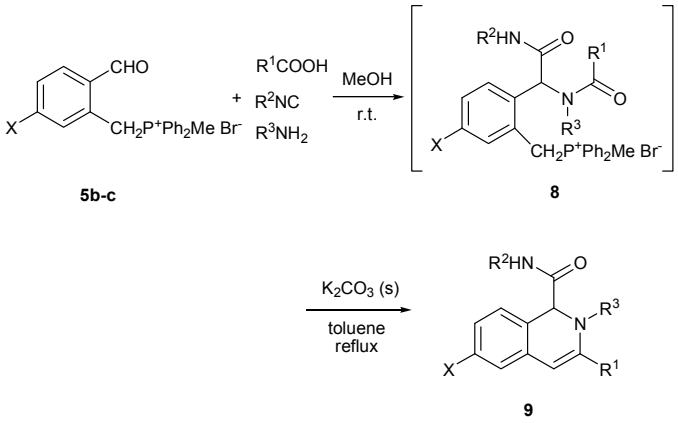
	X	R^1	R^2	Yield[b] (%)
7a	H	Ph	*t*-Bu	86
7b	H	4-$CH_3C_6H_4$	*t*-Bu	83
7c	H	4-$NO_2C_6H_4$	*t*-Bu	87
7d	H	4-ClC_6H_4	*t*-Bu	89
7e	H	2-$CH_3C_6H_4$	*t*-Bu	76
7f	H	2-FC_6H_4	*t*-Bu	78
7g	H	2-IC_6H_4	*t*-Bu	73
7h	H	CH_3	*t*-Bu	76
7i	H	H	*t*-Bu	71
7j	H	$ClCH_2$	*t*-Bu	77
7k	H	Ph	*c*-C_6H_{11}[c]	82
7l	H	4-ClC_6H_4	*c*-C_6H_{11}[c]	85
7m	H	4-$CH_3C_6H_4$	*c*-C_6H_{11}[c]	81
7n	H	4-$NO_2C_6H_4$	*c*-C_6H_{11}[c]	84
7o	Cl	Ph	*t*-Bu	82
7p	H		*t*-Bu	68
7q	H		*t*-Bu	70

[a]Reaction condition: i) CH_2Cl_2, r.t., 48 hr; ii) toluene, K_2CO_3 (s), 110 °C, 1-3 h.

[b]Isolated yields based on phosphonium **5b-c**. [c]cyclohexyl.

The Ugi reactions of phosphonium salts **5b-c**, acids, amines and isocyanides also took place to give phosphonium intermediates **8**. In the presence of K_2CO_3/toluene system, 1,2-dihydroisoquinolines **9** were obtained in moderate yields (45-57%, **9a-9o**, Table 3) via intramolecular Wittig reaction of **8**

(Scheme 4). Different acids and primary amines may be utilized in above one-pot cyclization to prepare 1,2-dihydroisoquinolines **9**. The moderate yields may be due to the low reactivity of the amide group for intramolecular Wittig reaction. As indicated in Table 3, the cyclized products can be obtained when R^1 are H and aromatic groups and R^3 are aromatic groups. The reactions failed to produce 1,2-dihydroisoquinolines **9** as aliphatic amines (R^3 = alkyl group, **9p**-**9r**, Table 3) were utilized.



Scheme 4. Preparation of 1,2-dihydroisoquinolines **9**

Table 3. Preparation of 1,2-dihydroisoquinolines **9**[a]

	X	R^1	R^2	R^3	Yield[b] (%)
9a	H	Ph	*t*-Bu	Ph	56
9b	H	Ph	*t*-Bu	4-ClC_6H_4	57
9c	H	Ph	*t*-Bu	4-$CH_3C_6H_4$	51
9d	H	4-$CH_3C_6H_4$	*t*-Bu	4-ClC_6H_4	54
9e	H	Ph	*t*-Bu	2-$CH_3C_6H_4$	45
9f	H	Ph	*t*-Bu	3-ClC_6H_4	47
9g	H	4-$NO_2C_6H_4$	*t*-Bu	4-ClC_6H_4	50
9h	H	4-ClC_6H_4	*t*-Bu	4-ClC_6H_4	55
9i	H	4-$CF_3C_6H_4$	*t*-Bu	4-ClC_6H_4	48
9j	H	4-$CH_3OC_6H_4$	*t*-Bu	4-ClC_6H_4	50
9k	H	3-$NO_2C_6H_4$	*t*-Bu	4-ClC_6H_4	51
9l	H	Ph	*t*-Bu	4-$EtOC_6H_4$	54
9m	H	H	*t*-Bu	4-ClC_6H_4	53
9n	H	Ph	*c*-C_6H_{11}[c]	4-ClC_6H_4	45
9o	Cl	4-ClC_6H_4	*t*-Bu	4-ClC_6H_4	49
9p	H	4-ClC_6H_4	*n*-Bu	*n*-Pr	0
9q	H	4-ClC_6H_4	*c*-C_6H_{11}[c]	*i*-Pr	0
9r	H	4-ClC_6H_4	*n*-Bu	*t*-Bu	0

[a]Reaction condition: i) MeOH, r.t., 48 hr; ii) toluene, K_2CO_3 (s), 110 °C, 2-4 h.

[b]Isolated yields based on phosphonium **5b-c**. [c]cyclohexyl.

Conclusions

In conclusion, the I-MCR/Wittig sequence starting from phosphonium salt precursors for preparing 1*H*-isochromenes and 1,2-dihydroisoquinolines is reported. The method was adapted to the synthesis of various multisubstituted 1*H*-isochromenes and 1,2-dihydroisoquinolines in one-pot fashion under mild reaction condition, which makes it useful in synthetic and medicinal chemistry.

Experimental Section

General

All reactions were performed in round-bottom flasks under an atmosphere of air. Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. Dichloromethane was used after distillation. Toluene was distilled from Na, and stored over 4A molecular sieves. Column chromatography purifications were performed under "flash" conditions using 400-630 mesh silica gel. Analytical thin-layer chromatography (TLC) was carried out on silica gel 60 F_{254} plates, which were visualized by exposure to ultraviolet light. Melting points were uncorrected. HRMS were measured on Angilent 6224 TOF LC/MS spectrometer. NMR were recorded in $CDCl_3$ on a Varian Mercury 400 or 600 spectrometer and resonances relative to TMS. Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR spectra were recorded on Varian Mercury 400/600 (100/150 MHz) with complete proton decoupling spectrophotometers ($CDCl_3$: 77.0 ppm).

General Procedure for the Preparation of 1*H*-Isochromenes 7

A mixture of phosphonium salt **5b-c**[31] (1 mmol), acid (1 mmol) and isocyanide (1 mmol) was stirred in methylene dichloride (5 mL) at room temperature for 48 h, and then the solvent was evaporated under reduced pressure. The residue was washed with ether/petroleum ether (10 mL, V/V = 1:1). The solid K_2CO_3 (0.27 g, 2 mmol) with toluene (5 mL) was added to the reaction system and the reaction mixture was stirred at 110 °C for 1-3 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ether/petroleum ether = 1 : 4, V/V) to give **7**.

N-(tert-butyl)-3-phenyl-1*H*-isochromene-1-carboxamide (7a). Light yellow solid (yield 0.264 g, 86%), mp 87-89 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.74 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.44-7.23 (m, 6H, Ar-H), 7.12 (d, *J* = 7.2 Hz, 1H, Ar-H), 6.52 (s, 1H, =CH), 6.38 (s, 1H, NH), 5.52 (s, 1H, CH), 1.34 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.9, 150.9, 133.5, 130.2, 129.1, 128.6, 128.5, 127.1, 126.7, 125.1, 124.7, 124.6, 124.1, 123.9, 102.1, 77.9, 51.3, 29.1, 28.6, 28.0. HRMS Calculated for $[C_{20}H_{21}NO_2+H]^+$: 308.1651, Found: 308.1643.

N-(tert-butyl)-3-(p-tolyl)-1*H*-isochromene-1-carboxamide (7b). Light yellow solid (yield 0.267 g, 83%), mp 86-87 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.62 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.39 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.27-7.20 (m, 4H, Ar-H), 7.08 (d, *J* = 7.8 Hz, 1H, Ar-H), 6.45 (s, 1H, =CH), 6.39 (s, 1H, NH), 5.48 (s, 1H, CH), 2.37 (s, 3H, CH_3), 1.32 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.9, 151.0, 139.2, 130.7, 130.3, 129.3, 129.2, 128.6, 126.8, 126.5, 125.1, 124.6, 123.7, 101.3, 77.8, 51.2, 28.6, 21.3. HRMS Calculated for $[C_{21}H_{23}NO_2+H]^+$: 322.1807, Found: 322.1801.

N-(tert-butyl)-3-(4-nitrophenyl)-1*H*-isochromene-1-carboxamide (7c). Yellow solid (yield 0.305 g, 87%), mp 167-168 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.26 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.89 (d, *J* = 9.0 Hz, 2H, Ar-H), 7.43-7.27 (m, 3H, Ar-H), 7.18 (d, *J* = 6.6 Hz, 1H, Ar-H), 6.70 (s, 1H, =CH), 6.23 (s, 1H, NH), 5.55 (s, 1H, CH), 1.36 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.3, 148.7, 147.5, 139.5, 129.3, 129.0, 128.4, 126.9, 125.1, 125.0, 124.9, 128.8, 123.9, 123.8, 105.7, 77.9, 51.4, 28.6. HRMS Calculated for $[C_{20}H_{20}N_2O_2+H]^+$: 353.1501, Found: 353.1492.

N-(tert-butyl)-3-(4-chlorophenyl)-1*H*-isochromene-1-carboxamide (7d). White solid (yield 0.304 g, 89%), mp 126-127 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.66 (d, *J* = 9.0 Hz, 2H, Ar-H), 7.40-7.23 (m, 5H, Ar-H), 7.11 (d, *J* = 7.2 Hz, 1H, Ar-H), 6.48 (s, 1H, =CH), 6.28 (s, 1H, NH), 5.49 (s, 1H, CH), 1.33 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.7, 149.9, 134.9, 132.0, 129.9, 128.8, 128.7, 128.6, 127.4, 126.6, 125.9, 125.1, 124.0, 102.5, 77.9, 51.3, 28.6. HRMS Calculated for $[C_{20}H_{20}ClNO_2+H]^+$: 342.1261, Found: 342.1253.

N-(tert-butyl)-3-(o-tolyl)-1*H*-isochromene-1-carboxamide (7e). Light yellow oil (yield 0.243 g, 76%); ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.45 (t, *J* = 7.8 Hz, 2H, Ar-H), 7.31-7.26 (m, 5H, Ar-H), 7.10 (d, *J* = 5.4 Hz, 1H, Ar-H), 6.34 (s, 1H, NH), 6.12 (s, 1H, =CH), 5.49 (s, 1H, CH), 2.47 (s, 3H, CH_3), 1.36 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.7, 153.5, 136.7, 134.5, 130.9, 130.7, 128.9, 128.8, 127.2, 126.3, 125.9, 125.8, 124.5, 123.9, 106.3, 78.0, 51.3, 28.7, 20.9. HRMS Calculated for $[C_{21}H_{23}NO_2+H]^+$: 322.1807, Found: 322.1796.

N-(tert-butyl)-3-(2-fluorophenyl)-1*H*-isochromene-1-carboxamide (7f). Light yellow solid (yield 0.253 g, 78%), mp 87-88 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.72 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.41 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.33-7.12 (m, 6H, Ar-H), 6.64 (s, 1H, =CH), 6.46 (s, 1H, NH), 5.51 (s, 1H, CH), 1.35 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.8, 160.9, 159.3, 146.3, 130.2, 129.9, 128.7, 127.9, 127.5, 126.6, 125.1, 124.5, 124.4, 121.9, 116.3, 107.4, 77.7, 51.3, 28.6. HRMS Calculated for $[C_{20}H_{20}FNO_2+H]^+$: 326.1556, Found: 326.1548.

N-(tert-butyl)-3-(2-iodophenyl)-1*H*-isochromene-1-carboxamide (7g). White solid (yield 0.316 g, 73%), mp 73-75 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.94 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.53-7.08 (m, 7H, Ar-H), 6.47 (s, 1H, NH), 6.17 (s, 1H, =CH), 5.64 (s, 1H, CH), 1.41 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 167.3, 153.6, 140.1, 139.7, 130.5, 130.4, 130.3, 128.5, 128.1, 127.7, 126.4, 124.1, 124.0, 107.1, 96.4, 78.0, 51.4, 28.7. HRMS Calculated for $[C_{20}H_{20}INO_2+H]^+$: 434.0617, Found: 434.0601.

N-(tert-butyl)-3-methyl-1*H*-isochromene-1-carboxamide (7h). Light yellow oil (yield 0.187 g, 76%); ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.32 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.23-7.14 (m, 2H, Ar-H), 6.92 (d, *J* = 7.8 Hz, 1H, Ar-H), 6.29 (s, 1H, NH), 5.70 (s, 1H, =CH), 5.32 (s, 1H, CH), 1.99 (s, 3H, CH_3), 1.39 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 168.1, 151.9, 130.4, 128.6, 126.3, 125.4, 124.9, 122.6, 102.7, 77.7, 51.2, 28.6, 19.6. HRMS Calculated for $[C_{15}H_{19}NO_2+H]^+$: 246.1494, Found: 246.1485.

N-(tert-butyl)-1*H*-isochromene-1-carboxamide (7i). Light yellow solid (yield 0.163 g, 71%), mp 58-60 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.36 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.24-7.18 (m, 2H, Ar-H), 6.96 (d, *J* = 7.2 Hz, 1H, Ar-H), 6.56 (d, *J* = 6.0 Hz, 1H, =CH), 6.31 (s, 1H, NH), 5.86 (d, *J* = 6.0 Hz, 1H, =CH), 5.34 (s, 1H, CH), 1.38 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.6, 142.9, 128.7, 128.4, 127.1, 126.4, 124.9, 123.2, 106.5, 76.9, 51.1, 28.5. HRMS Calculated for $[C_{14}H_{17}NO_2+H]^+$: 232.1338, Found: 232.1329.

N-(tert-butyl)-3-(chloromethyl)-1*H*-isochromene-1-carboxamide (7j). White solid (yield 0.216 g, 77%), mp 124-125 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.36 (d, *J* = 6.0 Hz, 1H, Ar-H), 7.24-6.95 (m, 3H, Ar-H), 6.85 (s, 1H, NH), 5.91 (s, 1H, =CH), 5.53 (s, 1H, CH), 4.24 (d, *J* = 12.0 Hz, 1H, 1/2$ClCH_2$), 4.14 (d, *J* = 12.0 Hz, 1H, 1/2$ClCH_2$), 1.36 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.9, 147.8, 128.7, 127.8, 127.7, 126.9, 126.0, 123.9, 105.0, 77.6, 51.8, 44.3, 28.7. HRMS Calculated for $[C_{15}H_{18}ClNO_2+H]^+$: 280.1104, Found: 280.1093.

N-cyclohexyl-3-phenyl-1*H*-isochromene-1-carboxamide (7k). White solid (yield 0.273 g, 82%), mp 144-146 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.74 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.43-7.21 (m, 6H, Ar-H), 7.11 (d, *J* = 7.2 Hz, 1H, Ar-H), 6.50 (s, 1H, =CH), 6.41 (d, *J* = 7.2 Hz, 1H, NH), 5.60 (s, 1H, CH), 3.88-3.84 (m, 1H, NCH), 1.93-1.05 (m, 10H, $5CH_2$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.7, 151.0, 133.4, 130.3, 129.1, 128.6, 128.5, 127.1, 126.4, 125.0, 124.7, 124.1, 102.0, 77.8, 47.8, 32.7, 25.3, 24.4. HRMS Calculated for $[C_{22}H_{23}NO_2+H]^+$: 334.1807, Found: 334.1800.

3-(4-chlorophenyl)-N-cyclohexyl-1*H*-isochromene-1-carboxamide (7l). White solid (yield 0.312 g, 85%), mp 196-197 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.66 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.41-7.23 (m, 5H, Ar-H), 7.11 (d, *J* = 7.2 Hz, 1H, Ar-H), 6.48 (s, 1H, =CH), 6.30 (d, *J* = 7.2 Hz, 1H, NH), 5.59 (s, 1H, CH), 3.88-3.83 (m, 1H, NCH), 1.92-1.06 (m, 10H, $5CH_2$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.5, 150.1, 134.9, 131.9, 130.0, 128.9, 128.7, 127.4, 126.4, 126.0, 124.9, 124.0, 102.4, 77.7, 47.8, 32.7, 25.3, 24.5. HRMS Calculated for $[C_{22}H_{22}ClNO_2+H]^+$: 368.1417, Found: 368.1406.

N-cyclohexyl-3-(p-tolyl)-1*H*-isochromene-1-carboxamide (7m). White solid (yield 0.281 g, 81%), mp 168-169 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.63 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.41 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.29-7.21 (m, 4H, Ar-H), 7.10 (d, *J* = 7.8 Hz, 1H, Ar-H), 6.46 (s, 1H, =CH), 6.41 (d, *J* = 7.2 Hz, 1H, NH), 5.59 (s, 1H, CH), 3.88-3.83 (m, 1H, NCH), 2.40 (s, 3H, CH_3), 1.94-1.06 (m, 10H, $2CH_2$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.9, 151.2, 139.4, 130.7, 130.5, 129.3, 128.7, 127.0, 126.4, 125.0, 124.7, 123.9, 101.2, 77.8, 47.9, 32.7, 25.4, 24.5, 21.4. HRMS Calculated for $[C_{23}H_{25}NO_2+H]^+$: 348.1964, Found: 348.1957.

N-cyclohexyl-3-(4-nitrophenyl)-1*H*-isochromene-1-carboxamide (7n). White solid (yield 0.318 g, 84%), mp 207-208 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.29 (t, *J* = 8.4 Hz, 2H, Ar-H), 7.91 (q, *J* = 8.4 Hz, 2H, Ar-H), 7.46-7.18 (m, 4H, Ar-H), 6.70 (t, *J* = 7.8 Hz, 1H, =CH), 6.24 (t, *J* = 9.0 Hz, 1H, NH), 5.67 (t, *J* = 7.8 Hz, 1H, CH), 3.89-3.85 (m, 1H, NCH), 1.96-1.07 (m, 10H, $5CH_2$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.2, 148.9, 147.6, 139.5, 129.4, 129.0, 128.5, 126.7, 125.2, 125.0, 124.8, 123.9, 105.7, 77.9, 48.1, 32.8, 25.3, 24.5. HRMS Calculated for $[C_{22}H_{22}N_2O_4+H]^+$: 379.1658, Found: 379.1648.

N-(tert-butyl)-6-chloro-3-phenyl-1*H*-isochromene-1-carboxamide (7o)

White solid (yield 0.281 g, 82%), mp 113-115 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.73 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.43-7.11 (m, 6H, Ar-H), 6.51 (s, 1H, =CH), 6.37 (s, 1H, NH), 5.50 (s, 1H, CH), 1.33 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.9, 150.9, 133.5, 130.2, 129.2, 128.6, 128.5,

126.7, 125.1, 124.7, 124.6, 124.1, 102.1, 77.9, 51.3, 28.6. HRMS Calculated for $[C_{20}H_{20}ClNO_2+H]^+$: 342.1255, Found: 342.1261.

N-(tert-butyl)-3-(furan-2-yl)-1*H*-isochromene-1-carboxamide (7p)

White solid (yield 0.202 g, 68%), mp 98-99 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.47-7.09 (m, 5H, Ar-H), 6.66-6.49 (m, 2H, Ar-H), 6.45 (s, 1H, NH), 6.42 (s, 1H, =CH), 5.46 (s, 1H, CH), 1.33 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.7, 148.6, 143.3, 143.1, 129.3, 128.7, 127.1, 126.7, 125.9, 124.1, 111.5, 108.0, 101.3, 77.5, 51.3, 28.5. HRMS Calculated for $[C_{18}H_{19}NO_3+H]^+$: 298.1438, Found: 298.1438.

N-(tert-butyl)-3-(thiophen-2-yl)-1*H*-isochromene-1-carboxamide (7q)

White solid (yield 0.220 g, 70%), mp 107-108 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.39-7.07 (m, 7H, Ar-H), 6.45 (s, 1H, NH), 6.37 (s, 1H, =CH), 5.48 (s, 1H, CH), 1.33 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 167.6, 146.4, 137.8, 129.6, 128.7, 127.8, 126.9, 126.4, 126.0, 125.7, 124.2, 123.8, 101.1, 77.8, 51.3, 28.5. HRMS Calculated for $[C_{18}H_{19}NO_2S+H]^+$: 314.1209, Found: 314.1209.

General Procedure for the Preparation of 1,2-dihydroisoquinolines 9

A mixture of phosphonium salt **5b-c** (1 mmol), amine (1 mmol), acid (1 mmol) and isocyanide (1 mmol) was stirred in methanol (5 mL) at room temperature for 48 h, and then the solvent was evaporated under reduced pressure. The residue was washed with ether/petroleum ether (10 mL, V/V = 1:1). The solid K_2CO_3 (0.27 g, 2 mmol) with toluene (5 mL) was added to the reaction system and the reaction mixture was stirred at 110 °C for 2-4 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (ether/petroleum ether = 1 : 2, V/V) to give **9**.

N-(tert-butyl)-2,3-diphenyl-1,2-dihydroisoquinoline-1-carboxamide (9a). Light yellow solid (yield 0.214 g, 56%), mp 189-191 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.55 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.31-6.88 (m, 12H, Ar-H), 6.57 (s, 1H, =CH), 6.42 (s, 1H, NH), 5.33 (s, 1H, CH), 1.26 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.3, 146.9, 140.4, 136.5, 131.2, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 127.1, 127.0, 124.2, 122.6, 122.4, 111.6, 69.0, 51.3, 28.6; HRMS Calculated for $[C_{26}H_{26}N_2O+H]^+$: 383.2123, Found: 383.2118.

N-(tert-butyl)-2-(4-chlorophenyl)-3-phenyl-1,2-dihydroisoquinoline-1-carboxamide (9b). White solid (yield 0.237 g, 57%), mp 188-190 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.53 (d, *J* = 7.8 Hz,

2H, Ar-H), 7.33-7.23 (m, 7H, Ar-H), 7.06 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.93 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.54 (s, 1H, =CH), 6.14 (s, 1H, NH), 5.27 (s, 1H, CH), 1.23 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.0, 145.5, 140.4, 136.2, 131.3, 128.7, 128.5, 128.4, 127.8, 127.6, 127.4, 127.2, 127.1, 124.4, 123.8, 123.6, 111.5, 68.8, 51.3, 28.4; HRMS Calculated for $[C_{26}H_{25}ClN_2O+H]^+$: 417.1734, Found: 417.1716.

N-(tert-butyl)-3-phenyl-2-(p-tolyl)-1,2-dihydroisoquinoline-1-carboxamide (9c). White solid (yield 0.212 g, 51%), mp 141-143 °C; ^1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.55 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.29-7.21 (m, 7H, Ar-H), 6.91 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.86 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.55 (s, 1H, =CH), 6.51 (s, 1H, NH), 5.27 (s, 1H, CH), 2.18 (s, 3H, CH_3), 1.26 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.4, 144.6, 140.5, 136.7, 132.4, 131.2, 129.4, 129.2, 128.4, 127.9, 127.8, 127.1, 127.0, 124.1, 122.6, 122.5, 111.1, 69.3, 51.2, 28.5, 20.6; HRMS Calculated for $[C_{27}H_{28}N_2O+Na]^+$: 419.2099, Found: 419.2091.

N-(tert-butyl)-2-(4-chlorophenyl)-3-(p-tolyl)-1,2-dihydroisoquinoline-1-carboxamide (9d). White solid (yield 0.243 g, 54%), mp 213-215 °C; ^1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.41 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.32-7.20 (m, 4H, Ar-H), 7.09 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.06 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.92 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.51 (s, 1H, =CH), 6.20 (s, 1H, NH), 5.26 (s, 1H, CH), 2.30 (s, 3H, CH_3), 1.23 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.1, 145.6, 140.3, 138.3, 133.4, 131.3, 129.4, 129.2, 128.7, 128.5, 127.7, 127.6, 127.1, 127.0, 123.8, 123.6, 111.0, 68.9, 51.3, 28.6, 21.1; HRMS Calculated for $[C_{27}H_{27}ClN_2O+Na]^+$: 453.1710, Found: 453.1706.

N-(tert-butyl)-3-phenyl-2-(o-tolyl)-1,2-dihydroisoquinoline-1-carboxamide (9e). White solid (yield 0.178 g, 45%), mp 207-209 °C; ^1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.78-6.61 (m, 14H, Ar-H and =CH), 6.60 (s, 0.30H, NH), 6.21 (s, 0.70H, NH), 5.08 (s, 0.30H, CH), 4.87 (s, 0.70H, CH), 2.65 (s, 2H, CH_3), 1.76 (s, 1H, CH_3), 1.27 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 169.6, 145.5, 141.9, 136.5, 132.3, 131.7, 131.0, 128.7, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 126.2, 126.1, 113.2, 68.0, 51.2, 28.6, 18.9; HRMS Calculated for $[C_{27}H_{28}N_2O+H]^+$: 397.2280, Found: 397.2276.

N-(tert-butyl)-2-(3-chlorophenyl)-3-phenyl-1,2-dihydroisoquinoline-1-carboxamide (9f). Light yellow solid (yield 0.195 g, 47%), mp 56-58 °C; ^1H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.55 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.32-7.24 (m, 7H, Ar-H), 7.05 (s, 1H, Ar-H), 6.99-6.81 (m, 3H, Ar-H), 6.58 (s, 1H, =CH), 6.12 (s, 1H, NH), 5.30 (s, 1H, CH), 1.23 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 169.8, 148.1, 140.3, 136.1, 134.3, 131.2, 128.7, 128.5, 128.3, 127.9, 127.7, 127.4, 127.2, 127.1, 124.7,

122.6, 122.2, 120.7, 112.1, 68.8, 51.4, 28.4; HRMS Calculated for $[C_{26}H_{25}ClN_2O+H]^+$: 417.1734, Found: 417.1722.

N-(tert-butyl)-2-(4-chlorophenyl)-3-(4-nitrophenyl)-1,2-dihydroisoquinoline-1-carboxamide (9g). Yellow solid (yield 0.241 g, 50%), mp 271-273 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.13 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.74 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.40-7.22 (m, 4H, Ar-H), 7.08 (d, *J* = 9.0 Hz, 2H, Ar-H), 6.95 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.61 (s, 1H, =CH), 5.61 (s, 1H, NH), 5.30 (s, 1H, CH), 1.21 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 169.7, 147.2, 144.8, 143.1, 139.1, 131.0, 129.0, 128.8, 128.3, 128.1, 127.6, 125.2, 123.9, 123.8, 123.7, 123.5, 113.6, 68.2, 51.5, 28.6; HRMS Calculated for $[C_{26}H_{24}ClN_3O_3+Na]^+$: 484.1404, Found: 484.1400.

N-(tert-butyl)-2,3-bis(4-chlorophenyl)-1,2-dihydroisoquinoline-1-carboxamide (9h). White solid (yield 0.248 g, 55%), mp 179-181 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.49 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.33-7.20 (m, 6H, Ar-H), 7.06 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.93 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.49 (s, 1H, =CH), 5.86 (s, 1H, NH), 5.27 (s, 1H, CH), 1.21 (s, 1H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 169.9, 145.1, 139.7, 134.9, 134.0, 131.3, 128.8, 128.7, 128.6, 128.0, 127.5, 127.2, 124.6, 123.8, 123.7, 111.5, 68.6, 51.4, 28.5; HRMS Calculated for $[C_{26}H_{24}Cl_2N_2O+H]^+$: 451.1344, Found: 451.1336.

N-(tert-butyl)-2-(4-chlorophenyl)-3-(4-(trifluoromethyl)phenyl)-1,2-dihydroisoquinoline-1-carboxamide (9i). Light yellow solid (yield 0.232 g, 48%), mp 108-110 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.67 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.53 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.35-7.22 (m, 4H, Ar-H), 7.08 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.94 (d, *J* = 7.2 Hz, 2H, Ar-H), 6.56 (s, 1H, =CH), 5.79 (s, 1H, NH), 5.29 (s, 1H, CH), 1.22 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 169.9, 145.0, 140.0, 139.6, 131.1, 130.1, 129.9, 128.9, 128.7, 128.6, 128.2, 127.6, 127.4, 127.2, 125.5, 125.0, 124.8, 123.8, 123.6, 123.0, 112.5, 68.6, 51.5, 28.4; HRMS Calculated for $[C_{27}H_{24}ClF_3N_2O+H]^+$: 485.1608, Found: 485.1597.

N-(tert-butyl)-2-(4-chlorophenyl)-3-(p-tolyl)-1,2-dihydroisoquinoline-1-carboxamide (9j). Light yellow solid (yield 0.223 g, 50%), mp 139-141 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.46 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.31-7.20 (m, 4H, Ar-H), 7.06 (d, *J* = 9.0 Hz, 2H, Ar-H), 6.92 (d, *J* = 9.0 Hz, 2H, Ar-H), 6.81 (d, *J* = 9.0 Hz, 2H, Ar-H), 6.46 (s, 1H, =CH), 6.13 (s, 1H, NH), 5.25 (s, 1H, CH), 3.77 (s, 3H, OCH_3), 1.23 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.1, 159.6, 145.6, 140.2, 131.6, 128.7, 128.6, 128.5, 127.7, 127.6, 127.4, 124.2, 123.9, 123.7, 114.0, 113.9, 110.2, 68.9, 55.3, 51.3; 28.5. HRMS Calculated for $[C_{27}H_{27}ClN_2O_2+H]^+$: 447.1839, Found: 447.1833.

N-(tert-butyl)-2-(4-chlorophenyl)-3-(3-nitrophenyl)-1,2-dihydroisoquinoline-1-carboxamide (9k).

Yellow solid (yield 0.236 g, 51%), mp 139-141 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 8.48 (s, 1H, Ar-H), 8.09 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.86 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.43-7.22 (m, 5H, Ar-H), 7.08 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.96 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.61 (s, 1H, =CH), 5.72 (s, 1H, NH), 5.29 (s, 1H, CH), 1.22 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 169.7, 148.4, 144.7, 138.9, 138.4, 133.7, 131.0, 129.6, 128.9, 128.8, 128.4, 127.6, 127.5, 127.2, 125.1, 123.9, 123.0, 121.7, 112.8, 68.5, 51.5, 28.5; HRMS Calculated for $[C_{26}H_{24}ClN_3O_3+H]^+$: 462.1584, Found: 462.1574.

N-(tert-butyl)-2-(4-ethoxyphenyl)-3-phenyl-1,2-dihydroisoquinoline-1-carboxamide (9l). Light yellow solid (yield 0.231 g, 54%), mp 139-141 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.55 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.30-7.20 (m, 7H, Ar-H), 6.90 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.64 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.53 (s, 1H, NH), 6.52 (s, 1H, =CH), 5.21 (s, 1H, CH), 3.88 (q, *J* = 6.6 Hz, 2H, OCH_2), 1.32 (t, *J* = 6.6 Hz, 3H, CH_3), 1.26 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.5, 154.9, 140.8, 140.5, 136.7, 131.3, 128.3, 128.0, 127.8, 127.5, 127.2, 127.1, 124.2, 124.1, 114.6, 114.5, 110.6, 69.7, 63.5, 51.2, 28.7, 14.8; HRMS Calculated for $[C_{28}H_{30}N_2O_2+H]^+$: 427.2386, Found: 427.2388.

N-(tert-butyl)-2-(4-chlorophenyl)-1,2-dihydroisoquinoline-1-carboxamide (9m). Light yellow solid (yield 0.191 g, 53%), mp 155-157 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.31-6.99 (m, 8H, Ar-H), 6.66 (d, *J* = 7.2 Hz, 1H, =CH), 5.97 (s, 1H, NH), 5.85 (d, *J* = 7.8 Hz, 1H, =CH), 5.24 (s, 1H, CH), 1.22 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.0, 143.7, 130.1, 129.4, 129.2, 128.0, 127.2, 126.7, 126.6, 126.5, 124.1, 117.8, 117.6, 105.1, 65.3, 51.4, 28.4; HRMS Calculated for $[C_{20}H_{21}ClN_2O+Na]^+$: 363.1240, Found: 363.1249.

2-(4-chlorophenyl)-N-cyclohexyl-3-phenyl-1,2-dihydroisoquinoline-1-carboxamide (9n). Light yellow solid (yield 0.200 g, 45%), mp 174-176 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.54 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.32-7.23 (m, 7H, Ar-H), 7.05 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.93 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.48 (s, 1H, =CH), 5.98 (d, *J* = 6.6 Hz, 1H, NH), 5.35 (s, 1H, CH), 3.74-3.72 (m, 1H, NCH), 1.77-0.95 (m, 10H, $5CH_2$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.0, 145.4, 140.9, 136.3, 131.6, 128.7, 128.6, 128.5, 127.8, 127.5, 127.4, 127.3, 124.6, 123.9, 123.8, 111.1, 68.3, 48.2, 32.8, 25.3, 24.3; HRMS Calculated for $[C_{28}H_{27}ClN_2O+H]^+$: 443.1890, Found: 443.1884.

2,3-bis(4-chlorophenyl)-N-(tert-butyl)-6-chloro-1,2-dihydroisoquinoline-1-carboxamide (9o)

White solid (yield 0.237 g, 49%), mp 165-167 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ (ppm) 7.40 (d, *J* = 7.8 Hz, 2H, Ar-H), 7.19-6.83 (m, 9H, Ar-H), 6.40 (s, 1H, =CH), 5.77 (s, 1H, NH), 5.18 (s, 1H, CH), 1.13 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 169.9, 145.1, 139.8, 134.9, 134.0, 131.3, 128.8,

128.7, 128.6, 128.5, 128.0, 127.5, 127.4, 124.7, 123.8, 123.7, 111.3, 68.6, 51.4, 28.5; HRMS Calculated for $[C_{26}H_{23}Cl_3N_2O+H]^+$: 485.0949, Found: 485.0947.

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One-Pot Synthesis of 1*H*-Isochromenes and 1,2-Dihydroisoquinolines by a Sequential Isocyanide-based Multicomponent/Wittig Reaction

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A new sequential isocyanide-based multicomponent/Wittig reaction was developed to construct 1*H*-isochromene and 1,2-dihydroisoquinoline derivatives.