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Microwave-Assisted Copper-Catalyzed Four Component Tandem Synthesis of 3-*N*-Sulfonylamidine Coumarins

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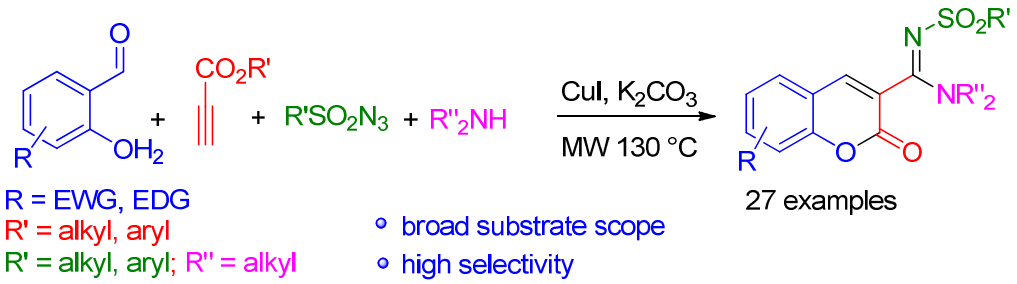


ABSTRACT: Microwave-assisted copper-catalyzed four-component tandem synthesis of 3-*N*-sulfonylamidine coumarins has been described by the coupling of salicylaldehydes, propiolates, sulfonyl azides and secondary amines. This one-pot protocol affords an effective route for the construction of functionalized coumarin structural frameworks in single operation with moderate to high yields.

INTRODUCTION

Coumarins are an important class of heterocyclic scaffolds that exist widely in nature[1] with numerous interesting biological and medicinal properties (Figure 1).[2] Moreover, coumarins serve as an excellent fluorescent probes in biology and medicine,[3] as well as dyes in laser technology.[4] Classically, coumarin core structure is constructed via Knoevenagel condensation (Scheme 1a). However, this traditional approach often suffers due to limited substrate scope and troublesome

chemical processes.[5] Development of effective methods for the construction of functionalized coumarin structural frameworks is thus important in organic synthesis (Scheme 1b).[6]

Multicomponent one-pot tandem reaction affords a powerful tool for the conversion of simple substrates into the diverse complex molecules in a single operation.[7] Furthermore, microwave organic synthesis provides the advantages of greater reactivity, mild reaction conditions and high selectivity.[8] Recently, click chemistry has been considerably explored for the formation of ketenimine and subsequent reaction with nucleophiles for the construction of diverse structural scaffolds.[9] In continuation of our studies on ketenimine reactions,[9q] we here report an efficient microwave-assisted copper(I)-catalyzed four-component synthesis of 3-*N*-sulfonylamidine coumarins by the coupling of salicylaldehydes, propiolates**,** sulfonyl azides and secondary amines (Scheme 1c). This protocol is selective and affords a potential route for the construction of functionalized 3-*N*-sulfonylamidine coumarins in moderate to high yields.[10]

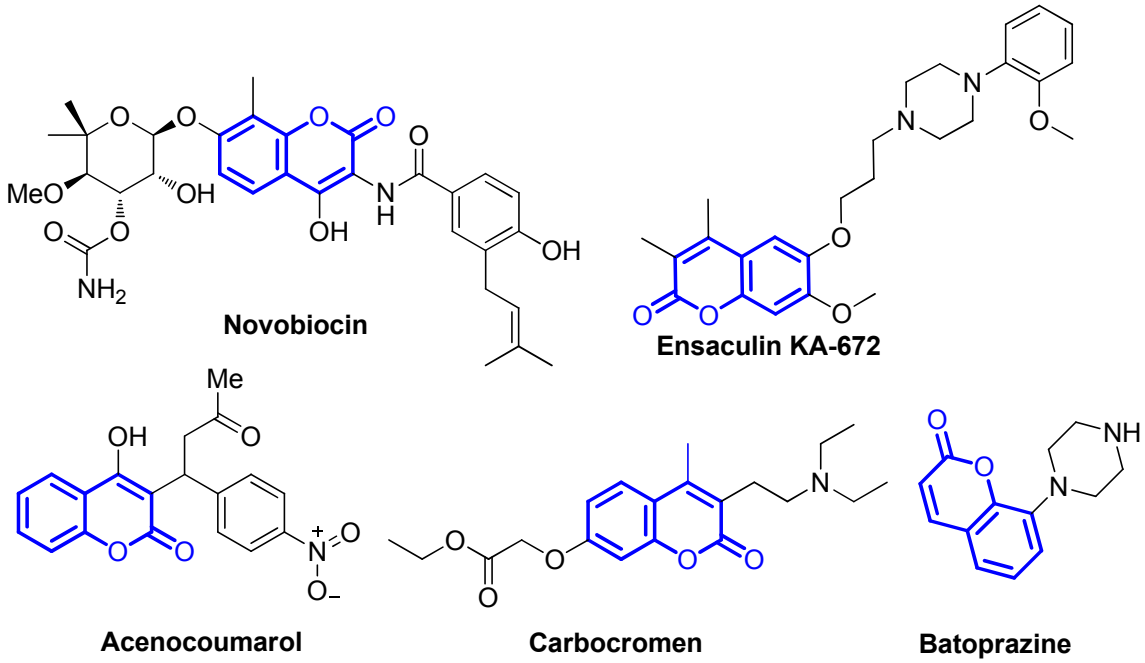
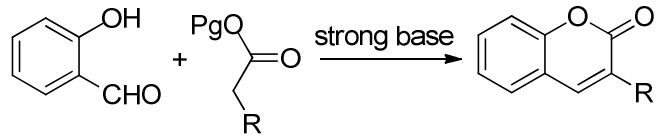


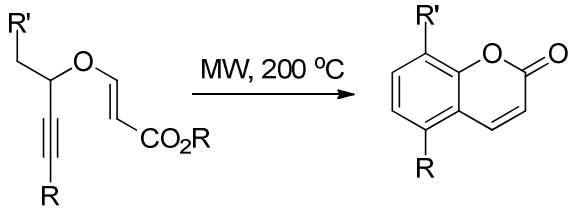
Figure 1. Some examples of biologically important coumarin derivatives

Scheme 1. Methods for Coumarin Syntheses

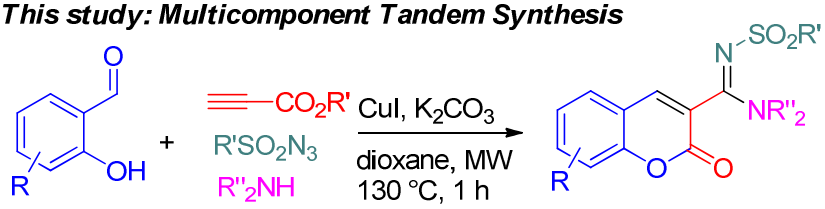
a) ***Classical Approach***



b) ***Microwave-Assisted Domino Process***



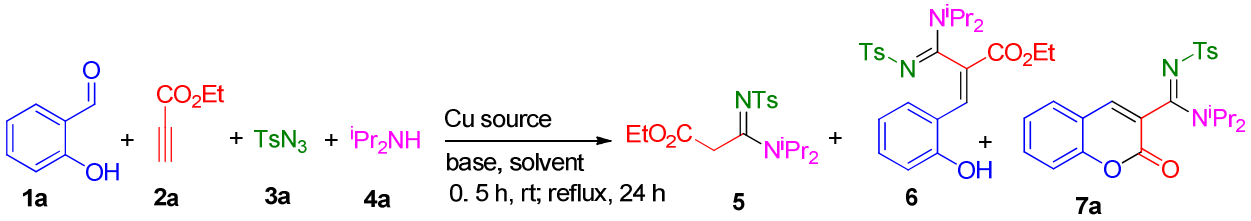
c) ***This study: Multicomponent Tandem Synthesis***



RESULTS AND DISCUSSION

Initially, optimization of the reaction was carried out employing salicylaldehyde **1a**, ethyl propiolate **2a**, tosyl azide **3a** and diisopropylamine **4a** as the model substrates using a series of copper salts in the presence of different bases (Table 1). The coupling of ethyl propiolate **2a**, tosyl azide **3a** and diisopropylamine **4a** readily took place to afford amidine[10a] **5** as the sole product, and the aldehyde **1a** failed to react when the substrates were stirred with 10 mol % CuI and 1.2 equiv K_3PO_4 for 0.5 h in 1,4-dioxane at room temperature (entry 1). However, increasing the reaction temperature to reflux for 24 h led to the coupling of all the substrates to afford ester **6** and coumarin **7a** in 19% and 30%, respectively, along with amidine **5** in 48% (entry 2). Subsequent screening of the base led to an increase in the formation of **7a** to 50% using K_2CO_3, while Cs_2CO_3 exhibited inferior results (entries 3-4). In contrast, Na_2CO_3, and the organic bases

Table 1. Optimization of the Reaction Conditions[a]



entry	[Cu]	base	solvent	yield (%)[b]		
				5	**6**	**7a**
1	CuI	K_3PO_4	1,4-dioxane	<99	n.d.	n.d.[c]
2	CuI	K_3PO_4	1,4-dioxane	48	19	30
3	CuI	K_2CO_3	1,4-dioxane	34	14	50
4	CuI	Cs_2CO_3	1,4-dioxane	38	39	16
5	CuI	Na_2CO_3	1,4-dioxane	83	17	n.d.
6	CuI	Et_3N/lutidine	1,4-dioxane	<99	n.d.	n.d.
7	CuI	DBU	1,4-dioxane	75	25	n.d.
8	CuBr	K_2CO_3	1,4-dioxane	44	12	37
9	CuCl	K_2CO_3	1,4-dioxane	30	25	39
10	$Cu(acac)_2$	K_2CO_3	1,4-dioxane	60	25	9
11	CuI	K_2CO_3	DMSO	71	n.d.	23
12	CuI	K_2CO_3	toluene	50	8	36
13	CuI	K_2CO_3	DMF	64	19	n.d.

[a] Aldehyde **1a** (0.5 mmol), ethyl propiolate **2** (0.5 mmol), tosyl azide **3a** (0.6 mmol), amine **4** (0.6 mmol), Cu source (10 mol %), base (0.6 mmol), solvent (1 mL), 0.5 h, rt; reflux, 24 h. [b] Determined by 400 MHz ^{1}H NMR. [c]0.5 h, rt. n.d.= not detected.

such as DBU, Et_3N and 2,6-lutidine failed to produce the target heterocycle **7a** (entries 5-7). In a set of copper sources screened, CuI, CuCl, CuBr and $Cu(acac)_2$, the former gave the best results

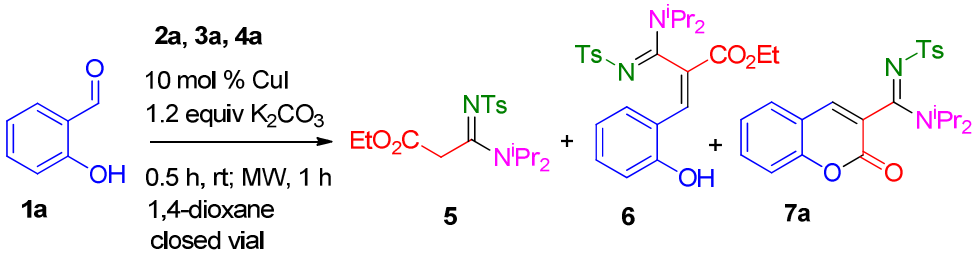
(entries 8-10). Dioxane was found to be the solvent of choice, while the reactions using DMSO, toluene and DMF gave inferior results (entries 11-13). Recrystallization of **6** in MeOH gave single crystal whose structure was confirmed by X-ray analysis (see the Supporting Information).

Next, the reaction was examined using microwave-heating and the results are summarized in table 2. These reactions exhibited greater reactivity and selectivity compared to the conventional heating reactions described in table 1. The best results observed at 130 °C [150 W, closed vial] to afford the target heterocycle **7a** in 1 h with up to 88% along with 7% of **6**. Further increase of the reaction temperature to 140 ^{o}C led to drop in yield to 81% due to decomposition of the product **7a**. Likewise, lowering the catalyst loading (5 mol%) or the reaction temperature (120 °C) or increasing the quantity of the base (2 equiv) led to drop in yield to <70%. A control experiment confirmed that without the copper source the coupling reaction was not observed. Furthermore, the reaction in sealed tube without microwave irradiation afforded **7a** in 34 % yield (entry 7).

Having the optimized reaction conditions, the substrate scope was explored with a series of substituted salicylaldehydes (Scheme 2). The aldehydes **1b-d** having substitution at the 3-position with chloro, methoxy and *tert*-butyl groups underwent reaction to provide the coumarin derivatives **7b-d** in 60-83% yields. The reaction of the aldehydes **1e-g** bearing alkoxy groups at the 4-position furnished **7e-g** in 25-67% yields. Likewise, the aldehydes **1h-j** and **1l-n** having bromo, chloro, fluoro, methoxy and methyl substituents at the 5-position readily reacted to give the coumarin derivatives **7h-j** and **7l-n** in 65-78% yields, while the reaction of the aldehydes **1k** and **1o** with strong electron withdrawing groups 5-CHO and 5-NO_2 was less-successful. Furthermore, the sterically hindered disubstituted aldehydes **1p-q** with 5-iodo-3-*tert*- butyl and 3,5-di-*tert*-butyl groups underwent reaction to produce the heterocycles **7p-q** in 76-80% yields. In addition, 2- naphthaldehyde reacted to furnish **7r** in good yield, which on recrystallization in MeOH-CH_2Cl_2 (1:1) gave single crystals whose structure was confirmed by X-ray analysis (see

the Supporting Information). These results suggest that the reactions can tolerate substantial steric hindrance, and the aldehydes with electron donating groups exhibit superior results compared to that having electron withdrawing groups.

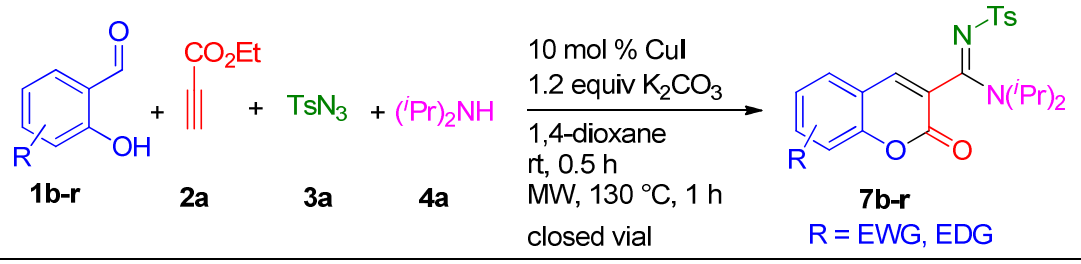
Table 2. Effect of Microwave Heating[a]

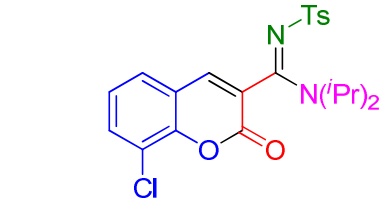


entry	*T* (°C)	yield (%)[b]		
		5	**6**	**7a**
1	130	n.d	7	88
2	130	n.d	3	70[c]
3	130	n.d	25	72[d]
4	120	14	54	30
5	140	n.d.	n.d.	81
6	130	16	18	63[d]
7	130	27	38	34[e]

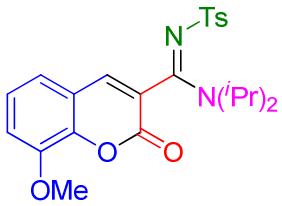
[a] Aldehyde **1a** (0.5 mmol), ethyl propiolate **2** (0.5 mmol), tosyl azide **3a** (0.6 mmol), amine **4a** (0.6 mmol), CuI (10 mol %), K_2CO_3 (0.6 mmol), 1,4-dioxane (1 mL), 0.5 h, rt; MW, 130 °C,1 h. [b] Determined by 400 MHz ^{1}H NMR. [c] 5 mol % CuI. [d] 2 equiv K_2CO_3. [e] Sealed tube without MW, 1 h. n.d.= not detected.

Scheme 2. Reaction of Various Substituted Salicylaldehydes[a]

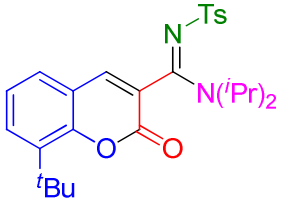




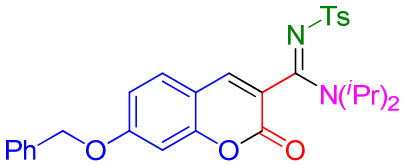
7b (60%)[b]



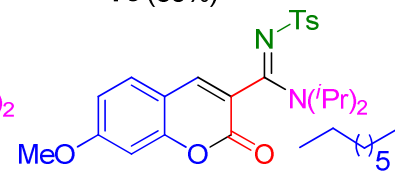
7c (68%)



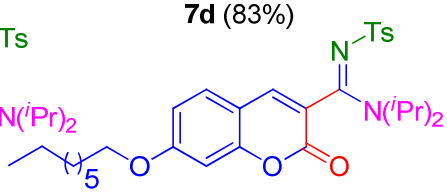
7d (83%)



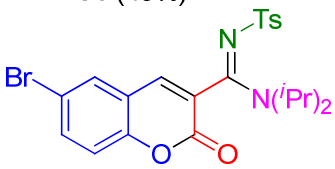
7e (49%)



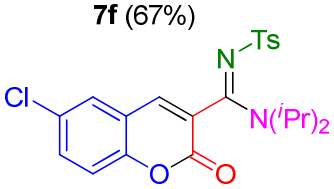
7f (67%)



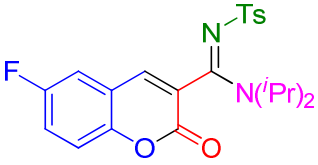
7g(25%)



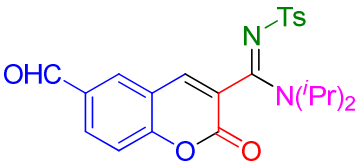
7h (65%)[b]



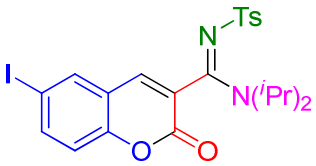
7i (68%)[b]



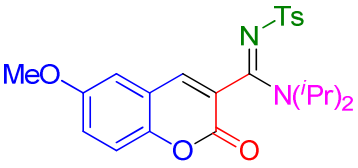
7j (65%)



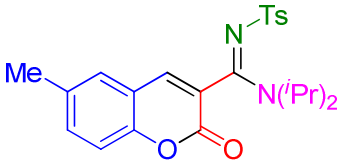
7k(10%)



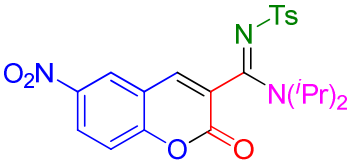
7l (70%)



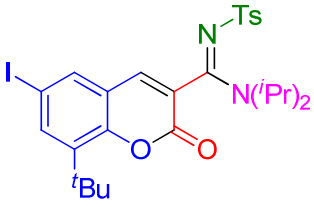
7m (67%)



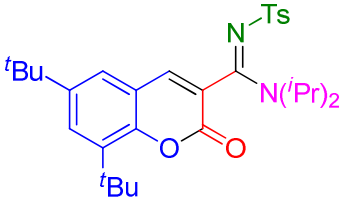
7n (78%)



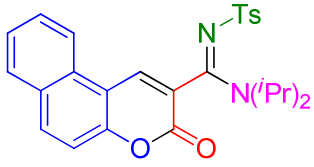
7o (n.d.)



7p (76%)



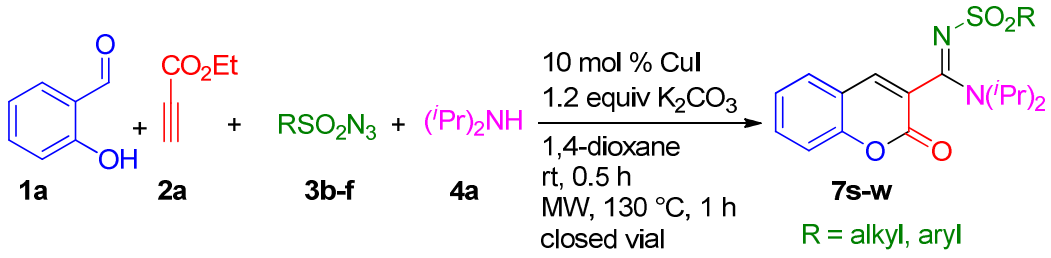
7q (80%)

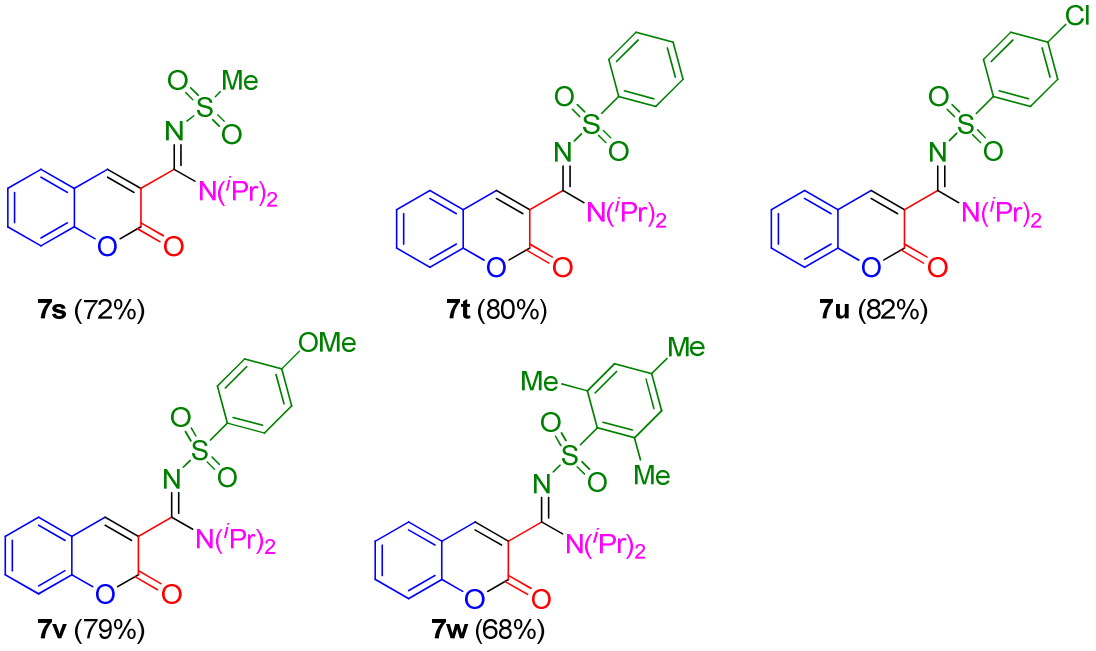


7r (60%)

[a]Aldehyde **1** (0.5 mmol), **2** (0.5 mmol), **3a** (0.6 mmol), **4a** (0.6 mmol), CuI (10 mol %), K_2CO_3 (0.6 mmol), 1,4-dioxane (1 mL), rt, 0.5 h, air; MW, 130 °C, 1 h. [b] Ester (~5%) was obtained as byproduct. n.d. = not detected.

Scheme 3. Reaction of Various Sulfonyl Azides[a]



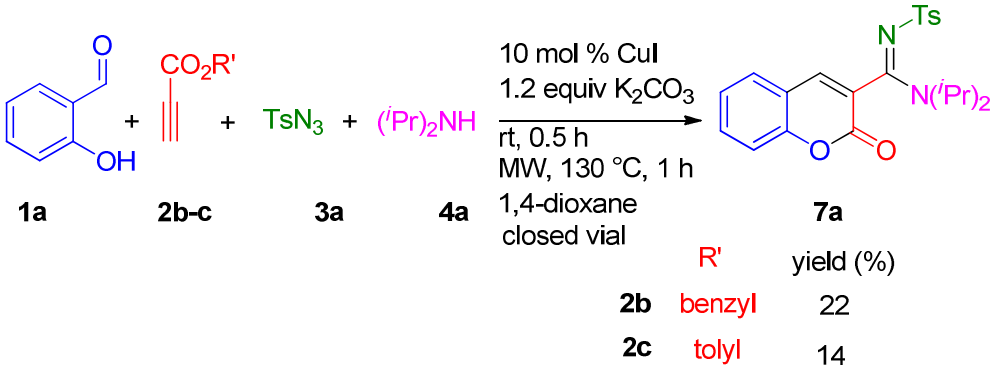


[a]Aldehyde **1a** (0.5 mmol), **2a** (0.5 mmol), **3b-f** (0.6 mmol), **4a** (0.6 mmol), CuI (10 mol %), K_2CO_3 (1.2 equiv), 1,4-dioxane (1 mL), rt, 0.5 h, air; MW, 130 °C, 1 h.

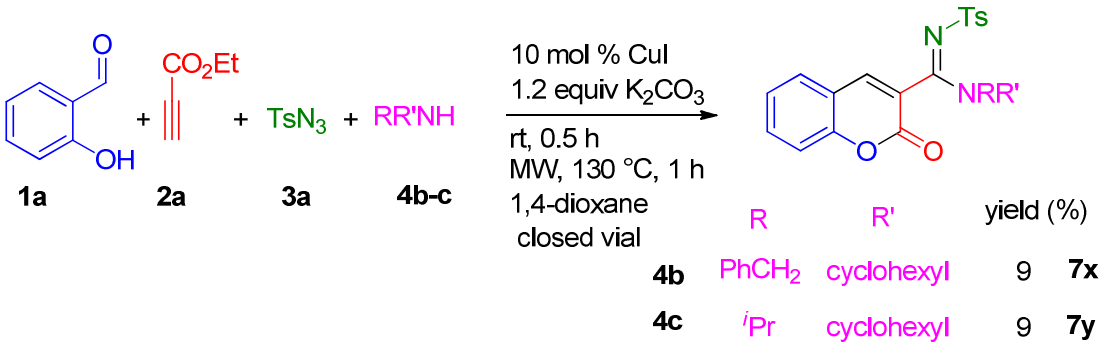
The utility of the protocol was extended to the reaction of various sulfonyl azides (Scheme 3). Methanesufonyl azide **3b** underwent reaction to furnish the coumarin derivative **7s** in 72% yield. The reaction of phenyl sulfonyl azide **3c** occurred to produce **7t** in 80% yield. Likewise,

phenyl sulfonyl azides **3d-f** having 4-chloro, 4-methoxy and 2,4,6-trimethyl groups underwent reaction to afford the corresponding coumarin derivatives **7u-w** in 68-82% yields. These results suggest that the reaction can be compatible with aliphatic as well as aromatic sulfonyl azides with good yields.

Scheme 4. Reactions with Different Propiolates



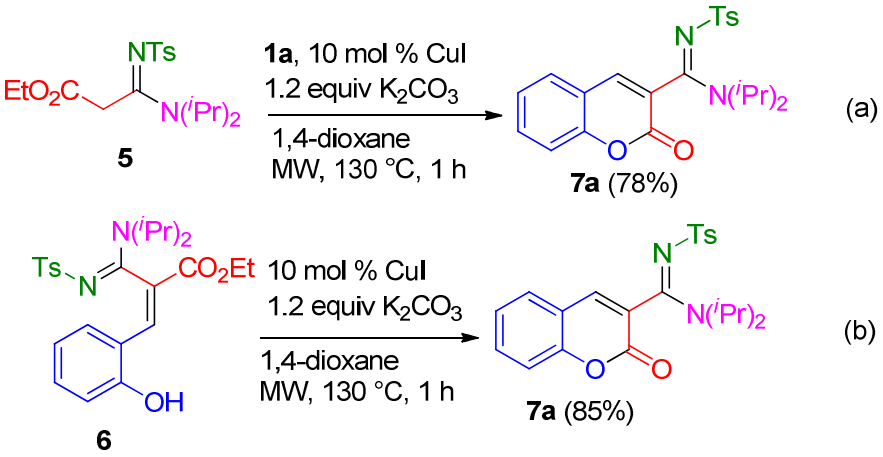
Scheme 5. Reactions with Different Amines



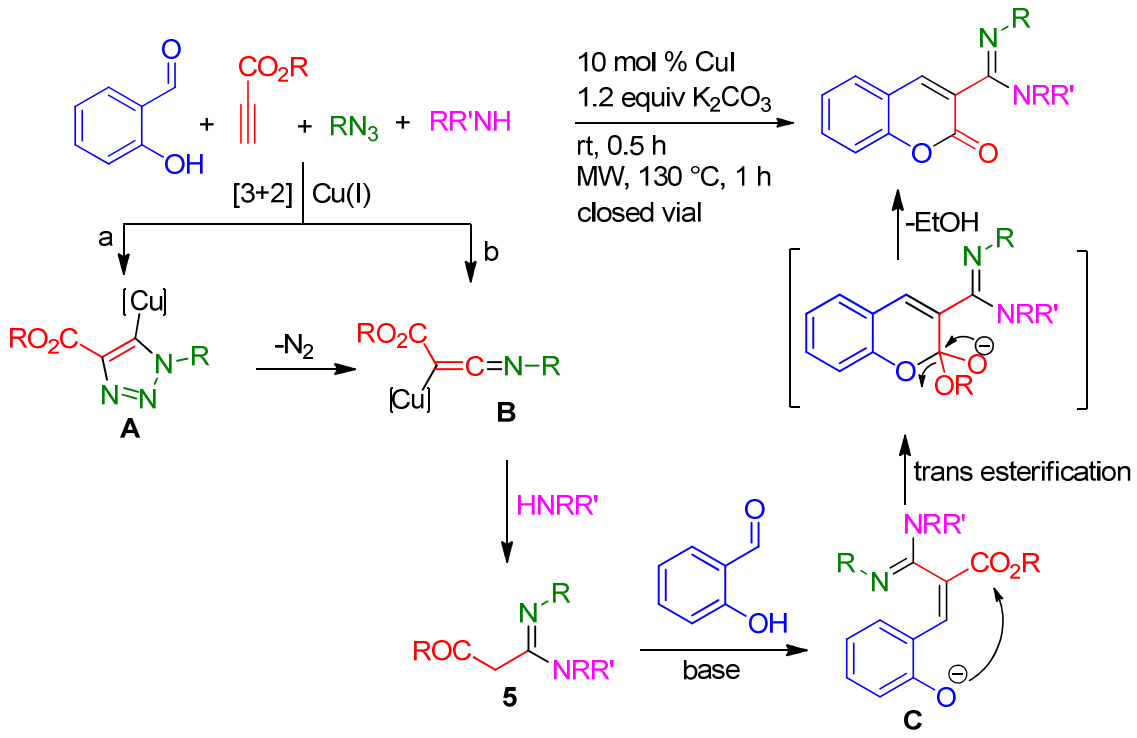
Next, the reactions of different propiolates were examined (Scheme 4). Benzyl propiolate **2b** proceeded reaction with 22% yield, while the reaction of *p*-tolyl propiolate **2c** produced the target heterocycle **7a** in 14% yield. Finally, the reaction of different amines was investigated (Scheme 5). The reactions of cyclohexylamine and morpholine failed to produce the coupled products due to decomposition. However, benzyl cyclohexylamine **4b** underwent reaction to give **7x** as a 3:1 mixture of isomers in 9% yield. Likewise, the reaction of isopropyl cyclohexylamine

4c gave **7y** as a 1:1 mixture of isomers in a 9% yield. These results suggest that the nature of propiolate and secondary amine plays a crucial role in the coupling reaction.

Scheme 6. Mechanistic Studies



Scheme 7. Proposed Catalytic Cycle



To gain insight into the catalytic pathway, the reaction of **1a**, **2**, **3a** and **4a** was stopped at 10 min and the resulting mixture was analyzed using ESI mass analysis, and found three major species **5**, **6** and **7a** (see the Supporting Information). Furthermore, the substrates **2**, **3a** and **4a** readily underwent coupling to provide **5** that could be readily reacted with the aldehyde **1a** to furnish **7a** in 78% yield (Scheme 6a). In addition, the ester **6** readily underwent cyclization to furnish **7a** in 85% yield (Scheme 6b). These results suggest that the reaction may take place via the intermediates **5** and **6** to yield the target heterocycle **7a**. Thus, the cycloaddition of **2** with **3** may produce ketenimine[9] **B** *via* **A**. Nucleophilic addition of the amine to the intermediate **B** may furnish **5** that can react with the aldehyde **1** to give **C**, which may cyclize to produce **7** by trans-esterification (Scheme 7).

In conclusion, copper(I)-catalyzed four-component tandem synthesis of 3-*N*-sulfonylamidine coumarin has been developed via the coupling of salicylaldehydes, propiolates, sulfonyl azides and secondary amines. The reaction using microwave irradiation is found to be superior to the conventional heating processes. The greater reactivity, mild condition and high selectivity constitute the significant practical advantages. This study may open new avenue for the further development of multcomponent studies for the synthesis of highly functionalized coumarin derivatives.

EXPERIMENTAL SECTION

General Information. The reaction was performed in closed vial using *CEM Discover LabMate* microwave reactor equipped with surface sensor for temperature measurement. NMR spectra were recorded on 400 and 600 MHz spectrometers using $CDCl_3$ as a solvent and the data are accounted as follows: chemical shifts (δ ppm) (multiplicity, coupling constant (Hz), integration). The abbreviations for multiplicity are as follows: s = singlet, d = doublet, t = triplet, m =

multiplet and dd = doublet of doublets. Infrared spectra were recorded on FT-IR spectrometer. Melting points were determined with melting point apparatus and are uncorrected. HRMS mass spectra were analyzed using Q-TOF instrument. For single crystal X-ray analysis, the intensity data were collected using CCD diffractometer, equipped with 1.75 kW sealed-tube Mo-Kα irradiation (λ= 0.71073 Å) at 298(2) K and the structures were solved by direct methods using SHELXL-97 (Göttingen, Germany) and refined with full-matrix least squares on F^2 using SHELXL-97. CuI (98%) of Aldrich, CuBr (97%) of Alfa Aesar and CuCl (98%) of Rankem were used as received. 2,6-Lutidine (98%), ethyl propiolate (99%), Cs_2CO_3 (99%), K_3PO_4 (98%), Na_2CO_3 (99%) and DBU (98%) were purchased from commercial suppliers and used as received. Solvents were purchased from commercial source and purified prior to use.[11] Substituted salicylaldehydes[12,13] and sulfonyl azides[14] were prepared according to the literature procedures. The reactions were monitored by analytical TLC on silica gel G/GF 254 plate and the column chromatography was performed with 60-120 mesh silica gel.

Benzyl propiolate 2b.[15] Analytical TLC on silica gel, 1:19 ethyl acetate-hexane R_f = 0.50; colorless liquid; yield 70% (561 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.37 (m, 5H), 5.23 (s, 2H),2.90 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.8, 134.7, 128.93, 128.9, 128.8, 75.3, 74.7, 68.1; FT-IR (neat) 2961, 2924, 2855, 2120, 1716, 1605, 1383, 1223, 1020, 749, 696, 668, 562 cm^{-1}.

***p*-Tolyl propiolate 2c.**[16] Analytical TLC on silica gel, 1:19 ethyl acetate-hexane R_f = 0.30; colorless liquid; yield 53% (424 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 2H), 3.06 (s, 1H), 2.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.4, 147.8, 136.6, 130.3, 121.1, 76.8, 74.5, 21.1; FT-IR (neat) 2962, 2924, 2855, 2125, 1731, 1504, 1384, 1217, 1197, 1018, 909, 807, 744, 607, 502 cm^{-1}.

General Procedure for the Synthesis of Coumarins. To a stirred solution of propiolate **2** (0.5 mmol), sulfonyl azide **3** (0.6 mmol) and CuI (0.05 mmol, 9.5 mg) in 1,4-dioxane (1 mL) was added secondary amine **4** (0.5 mmol), salicylaldehyde **1** (0.5 mmol) and K_2CO_3 (0.6 mmol, 82.9 mg) at room temperature under air. After 0.5 h (arrested N_2 bubbles), the reaction vial was sealed with a cap and stirred at 130 °C [150 W] for 1 h using microwave-irradiation. The solvent was then evaporated under *vacuo* and the residue was diluted with CH_2Cl_2 (30 mL), and washed with saturated NH_4Cl (10 mL) and water (10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using n-hexane/ethyl acetate as eluent.

Compound 5.[10a] Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.40; colorless solid; mp 122-123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 7.6 Hz, 2H), 4.16-4.11 (m, 4H), 3.95-3.88 (m, 1H), 3.61 (br. s, 1H), 2.38 (s, 3H), 1.38 (d, *J* = 6.8 Hz, 6H), 1.27-1.21 (m, 9H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 166.9, 157.9, 141.7, 141.1, 129.0, 126.2, 61.7, 48.4, 37.6, 21.4, 20.2, 19.9, 14.0; FT-IR (KBr) 3015, 2983, 2936, 2907, 1729, 1547, 1484, 1441, 1369, 1325, 1276, 1201, 1135, 1083, 1055, 960, 885, 810, 763, 715, 663, 551, 542 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{29}N_2O_4S$ $[M+H]^+$: 369.1848, found: 369.1875.

Compound 6. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.32; colorless solid; mp 206-207 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.87 (s, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.43 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.11-7.06 (m, 3H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.62 (t, *J* = 8.0 Hz, 1H), 4.30-4.22 (m, 2H), 4.09-4.01 (m, 1H), 3.63-3.55 (m, 1H), 2.28 (s, 3H), 1.57 (d, *J* = 6.8 Hz, 3H), 1.49 (d, *J* = 6.8 Hz, 3H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.11 (d, *J* = 6.4 Hz, 3H), 0.74 (d, *J* = 6.8 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 165.0, 160.9, 156.8, 141.8, 40.5, 136.7, 132.5, 129.0, 129.0, 126.6, 122.9, 119.8, 119.6, 116.7, 61.7, 52.4, 48.4, 21.5, 20.2, 19.7, 19.0, 14.2; FT-

IR (KBr) 3390, 2973, 2924, 2853, 1717, 1700, 1618, 1606, 1536, 1463, 1443, 1367, 1279, 1253, 1219, 1142, 1084, 1036, 1017, 906, 813, 776, 760, 675, 596, 554 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{33}N_2O_5S$ $[M+H]^+$: 473.2110, found: 473.2117.

(*Z*)-*N*,*N*-Diisopropyl-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7a. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.40; colorless solid; yield 75% (160 mg); mp 257-258 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 (s, 1H, H-4), 7.65 (d, *J* =7.8 Hz, 2H, Ar-H (tosyl)), 7.58 (t, *J* = 7.8 Hz, 1H, H-7), 7.54 (d, *J* = 7.8 Hz, 1H, H-5), 7.34-7.30 (m, 2H, H-6 and H-8), 7.16 (d, J = 7.8 Hz, 2H, Ar-H (tosyl)), 3.89-3.85 (m, 1H, -N-CH-), 3.70-3.66 (m, 1H, -N-CH-), 2.36 (s, 3H, -CH_3 (tosyl)), 1.58 (d, *J* = 6.6 Hz, 3H, -CH_3 (isopropyl)), 1.42 (d, *J* =7.2 Hz, 3H, -CH_3 (isopropyl)), 1.26 (d, *J* = 6.6 Hz, 3H, -CH_3 (isopropyl)), 1.14 (d, *J* = 6.6 Hz, 3H, -CH_3 (isopropyl)); ^{13}C {^{1}H}NMR (150 MHz, $CDCl_3$) δ 157.5 (C), 157.4 (C), 154.2 (C), 142.1 (C), 141.6 (CH), 140.8 (C), 132.9 (CH), 129.2 (CH), 129.0 (CH), 126.5 (CH), 125.1 (CH), 123.3 (C), 118.2 (C), 117.1 (CH), 52.8 (CH), 48.6 (CH), 21.6 (CH_3), 20.7 (CH_3), 20.2 (CH_3), 20.1 (CH_3), 19.7 (CH_3); FT-IR (KBr) 3035, 2969, 2932, 1717, 1628, 1608, 1547, 1445, 1371, 1279, 1251, 1210, 1142, 1087, 1013, 901, 812, 780, 759, 676, 595, 553 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{27}N_2O_4S$ $[M+H]^+$: 427.1692, found: 427.1692.

(*Z*)-8-Chloro-*N*,*N*-diisopropyl-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7b. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.37; colorless solid; 60% (138 mg); mp 285-286 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.66-7.62 (m, 3H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 2H), 3.86-3.81 (m, 1H), 3.72-3.66 (m, 1H), 2.38 (s, 3H), 1.60 (d, *J* = 6.8 Hz, 3H), 1.43 (d, *J* = 7.2 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.16 (d, *J* = 6.4 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 156.8, 156.3, 149.9, 142.3, 141.2, 140.6, 133.2, 129.2, 127.5, 126.6, 125.2, 124.0, 122.1, 119.5, 52.9, 48.7, 21.6, 20.7, 20.2, 20.1,

19.7; FT-IR (KBr) 3079, 2998, 2973, 2927, 1727, 1623, 1600, 1547, 1476, 1442, 1367, 1270, 1208, 1138, 1087, 1055, 1014, 903, 838, 787, 756, 682, 593, 551 cm^{-1}; HRMS (APCI) *m/z* calcd for $C_{23}H_{26}ClN_2O_4S$ $[M+H]^+$: 461.1302, found: 461.1301.

(*Z*)-*N*,*N*-Diisopropyl-8-methoxy-2-oxo-*N*'-tosyl-2*H*-chromene-3-carboximidamide 7c. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.50; colorless solid; yield 68% (155 mg); mp 294-295 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 10.0 Hz, 1H), 7.17-7.11 (m, 4H), 3.97 (s, 3H), 3.88-3.84 (m, 1H), 3.69-3.65 (m, 1H), 2.37 (s, 3H), 1.59 (d, *J* = 6.8 Hz, 3H), 1.41 (d, *J* = 6.8 Hz, 3H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 157.3, 156.9, 147.4, 143.9, 142.0, 141.7, 140.8, 129.1, 126.6, 124.9, 123.5, 120.3, 118.8, 114.8, 56.5, 52.7, 48.5, 21.6, 20.6, 20.2, 20.1, 19.7; FT-IR (KBr) 3080, 3032, 2995, 2967, 2936, 2844, 1723, 1623, 1610, 1578, 1543, 1489, 1453, 1369, 1267, 1213, 1175, 1135, 1104, 1085, 1059, 1016, 975, 950, 904, 839, 809, 787, 752, 677, 595, 551 cm^{-1}; HRMS (APCI) *m/z* calcd for $C_{24}H_{29}N_2O_5S$ $[M+H]^+$: 457.1797, found: 457.1797.

(*Z*)-8-(*tert*-Butyl)-*N*,*N*-diisopropyl-2-oxo-*N'*-tosyl-2*H*-chromene-3-carboximidamide 7d. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.53; colorless solid; yield 83% (200 mg); mp 249-250 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 3H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 3.87-3.84 (m, 1H), 3.71-3.68 (m, 1H), 2.33 (s, 3H), 1.61 (d, *J* = 7.2 Hz, 3H), 1.48 (s, 12H), 1.27 (d, *J* = 6.0 Hz, 3H), 1.15 (d, *J* = 6.4 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 157.7, 156.6, 152.8, 143.2, 141.9, 140.7, 138.1, 130.6, 129.1, 127.5, 126.5, 124.6, 121.4, 118.4, 52.7, 48.5, 35.1, 30.0, 21.5, 20.6, 20.2, 20.0, 19.6; FT-IR (KBr) 2996, 2973, 2936, 2881, 1727, 1626, 1593, 1542, 1449, 1432, 1370, 1278, 1213, 1172, 1142, 1122, 1085, 1059, 1016, 941, 909, 819, 801, 754, 678, 592, 549 cm^{-1}; HRMS (APCI) *m/z* calcd for $C_{27}H_{35}N_2O_4S$ $[M+H]^+$: 483.2318, found: 483.2318.

(*Z*)-7-(Benzyloxy)-*N,N*-diisopropyl-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7e. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.30; yellow solid; yield 49% (131 mg); mp 222-223 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 2H), 7.42-7.41 (m, 5H), 7.36 (d, *J* = 6.0 Hz, 1H), 7.14 (d, *J* = 7.2 Hz, 2H), 6.96 (d, *J* = 7.8 Hz, 1H), 6.86 (s, 1H), 5.15 (s, 2H), 3.89-3.87 (m, 1H), 3.66 (s, 1H), 2.35 (s, 3H), 1.58 (d, *J* = 6.6 Hz, 3H), 1.43 (d, *J* = 6.0 Hz, 3H), 1.25 (d, *J* = 6.0 Hz, 3H), 1.13 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.8, 157.9, 157.7, 156.1, 142.0, 141.9, 140.9, 137.8, 130.1, 129.1, 129.0, 128.6, 127.6, 126.5, 119.4, 114.0, 112.0, 102.1, 70.8, 52.7, 48.5, 21.7, 20.7, 20.2, 20.1, 19.7; FT-IR (KBr) 2967, 2923, 2856, 1729, 1616, 1538, 1451, 1373, 1267, 1243, 1122, 1082, 808, 754, 679, 619, 550 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{33}N_2O_5S$ [M+H]: 533.2105, found: 533.2112.

(*Z*)-*N,N*-Diisopropyl-7-methoxy-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7f. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.58; colorless solid; yield 67% (153 mg); mp 265-266 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 2H), 6.90 (dd, *J* = 8.8, 1.2 Hz, 1H), 6.81 (s, 1H), 3.91-3.86 (m, 4H), 3.70-3.64 (m, 1H), 2.37 (s, 3H), 1.58 (d, *J* = 6.8 Hz, 3H), 1.43 (d, *J* = 6.8 Hz, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H); ^{13}C {^{1}H}NMR (150 MHz, $CDCl_3$) δ 163.8, 157.9, 157.7, 156.2, 141.95, 141.91, 140.9, 130.0, 129.1, 126.5, 119.4, 113.3, 111.8, 101.0, 56.1, 52.7, 48.5, 21.6, 20.7, 20.2, 20.1, 19.7; FT-IR (KBr) 3093, 3052, 2972, 2934, 2849, 1730, 1614, 1540, 1512, 1473, 1459, 1444, 1371, 1271, 1244, 1202, 1125, 1080, 1057, 1024, 972, 901, 854. 807, 763, 726, 675, 593, 550 cm^{-1}; HRMS (APCI) *m/z* calcd for $C_{24}H_{29}N_2O_5S$ $[M+H]^+$: 457.1797, found; 457.1798.

(*Z*)-*N,N*-Diisopropyl-7-(octyloxy)-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7g. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.32; pale yellow solid; yield 25% (69

mg); mp 198-199 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 2H), 6.88 (dd, *J* = 9.0, 1.8 Hz, 1H), 6.79 (s, 1H), 4.03 (t, *J* = 6.6 Hz, 2H), 3.91-3.89 (m, 1H), 3.68-3.66 (m, 1H), 2.37 (s, 3H), 1.84-1.80 (m, 2H), 1.58 (d, *J* = 6.6 Hz, 3H), 1.49-1.44 (m, 2H), 1.43 (d, *J* = 7.2 Hz, 3H), 1.37-1.29 (m, 8H), 1.26 (d, *J* = 6.6 Hz, 3H), 1.14 (d, *J* = 6.6 Hz, 3H), 0.90 (t, *J* = 6.6 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 163.4, 158.0, 157.8, 156.2, 142.0, 141.9, 141.0, 130.0, 129.1, 126.6, 119.1, 113.7, 111.6, 101.5, 69.0, 52.7, 48.5, 32.0, 29.5, 29.4, 29.1, 26.1, 22.8, 21.6, 20.7, 20.2, 20.1, 19.7, 14.3; FT-IR (KBr) 2967, 2922, 2855, 1728, 1619, 1539, 1373, 1294, 1272, 1251, 1138, 1081, 806, 789, 682, 552 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{33}N_2O_5S$ [M+H]: 555.2887, found: 555.2895.

(*Z*)-6-Bromo-*N,N*-diisopropyl-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7h. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.70; yellow solid; yield 65% (164 mg); mp 308-309 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 6.4 Hz, 5H), 7.25 (d, *J* = 8.8 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 3.85-3.82 (m, 1H), 3.70-3.66 (m, 1H), 2.38 (s, 3H), 1.57 (d, *J* = 6.4 Hz, 3H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.15 (d, *J* = 6.4 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ 156.9, 156.8, 153.0, 142.1, 140.7, 140.0, 135.5, 131.2, 129.2, 126.5, 124.6, 119.7, 118.8, 117.6, 52.9, 48.6, 21.6, 20.6, 20.1, 19.7; FT-IR (KBr) 3110, 3045, 2980, 2966, 2925, 1726, 1623, 1602, 1542, 1471, 1448, 1372, 1271, 1241, 1207, 1136, 1083, 1016, 941, 904, 828, 809, 761, 683, 621, 549 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{26}BrN_2O_4S$ $[M+H]^+$: 505.0797, found: 505.0800.

(*Z*)-6-Chloro-*N,N*-diisopropyl-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7i. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.58; yellow solid; yield 68% (156 mg); mp 314-315 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 6.0 Hz, 3H), 7.52 (s, 2H), 7.31 (d, *J* = 9.6 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 2H), 3.85-3.80 (m, 1H), 3.69-3.64 (m, 1H), 2.37 (s, 3H),

1.57 (d, *J* = 7.2 Hz, 3H), 1.40 (d, *J* = 6.8 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 157.0, 156.8, 152.6, 142.1, 140.7, 140.1, 132.7, 130.4, 129.2, 128.2, 126.5, 124.6, 119.2, 118.5, 52.9, 48.6, 21.6, 20.7, 20.1, 19.7; FT-IR (KBr) 3044, 2981, 2925, 1727, 1625, 1544, 1473, 1447, 1413, 1373, 1271, 1241, 1208, 1134, 1084, 1058, 1017, 920, 837, 828, 809, 762, 684, 549 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{26}ClN_2O_4S$ $[M+H]^+$: 461.1302, found: 461.1296.

(*Z*)-6-Fluoro-*N,N*-diisopropyl-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7j. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.47; yellow solid; yield 65% (144 mg); mp 303-304 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 3H), 7.33-7.28 (m, 2H), 7.24 (d, *J* = 6.4 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 3.86-3.81 (m, 1H), 3.70-3.65 (m, 1H), 2.38 (s, 3H), 1.58 (d, *J* = 6.8 Hz, 3H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H); ^{13}C {^{1}H}NMR (150 MHz, $CDCl_3$) δ 159.9 (d, J_{C-F} = 244.5 Hz), 157.2, 156.9, 150.4, 142.1, 140.7, 140.3, 129.2, 126.5, 124.7, 120.4 (d, J_{C-F} = 24 Hz), 118.9 (d, J_{C-F} = 13.5 Hz), 118.7 (d, J_{C-F} = 9 Hz), 114.3 (d, J_{C-F} = 24 Hz), 52.8, 48.6, 21.6, 20.7, 20.1, 19.7; ^{19}F NMR (376 MHz, $CDCl_3$, CF_3COOH as internal reference = -76.55) -116.6; FT-IR (KBr) 3045, 2984, 2925, 1725, 1577, 1545, 1490, 1432, 1376, 1267, 1211, 1136, 1085, 1018, 883, 775, 755, 686, 549 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{25}FN_2O_4S$ $[M+H]^+$: 445.1597, found: 445.1589.

(*Z*)-6-Formyl-*N,N*-diisopropyl-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7k. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.33; colorless solid; yield 10% (23 mg); mp 261-262 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.04 (s, 1H), 8.11 (dd, *J* = 8.4, 1.8 Hz, 1H), 8.08 (d, *J* = 1.2 Hz, 1H), 7.82 (s, 1H), 7.69 (d, *J* = 7.8 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.20 (d, *J* = 8.4 Hz, 2H), 3.89-3.85 (m, 1H), 3.72-3.67 (m, 1H), 2.38 (s, 3H), 1.58 (d, *J* = 7.2 Hz, 3H), 1.41 (d, *J* = 7.2 Hz, 3H), 1.28 (d, *J* = 6.6 Hz, 3H), 1.17 (d, *J* = 6.6 Hz, 3H); ^{13}C {^{1}H}NMR

(150 MHz, $CDCl_3$) δ 190.0, 157.8, 156.7, 156.6, 142.3, 140.6, 140.5, 133.3, 133.0, 131.4, 129.3, 126.5, 124.9, 118.6, 118.3, 53.0, 48.7, 21.7, 20.8, 20.2, 20.1, 19.7; FT-IR (KBr) 2981, 2965, 2924, 2852, 1737, 1700, 1623, 1547, 1447, 1373, 1269, 1168, 1136, 1114, 1084, 1056, 103, 947, 907, 644, 810, 762, 684, 549 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{27}N_2O_5S$ $[M+H]^+$: 455.1641, found: 455.1640.

(*Z*)-6-Iodo-*N*,*N*-diisopropyl-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7l. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.66; colorless solid; yield 70% (193 mg); mp 277-278 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86-7.83 (m, 2H), 7.67 (d, *J* = 7.6 Hz, 2H), 7.63 (s, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 1H), 3.85-3.82 (m, 1H), 3.70-3.66 (m, 1H), 2.38 (s, 3H), 1.58 (d, *J* = 6.8 Hz, 3H), 1.41 (d, *J* = 6.8 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.15 (d, *J* = 6.4 Hz, 3H); ^{13}C {^1H}NMR (100 MHz, $CDCl_3$) δ 156.8, 153.8, 142.2, 141.3, 140.7, 139.9, 137.3, 129.2, 126.5, 124.4, 120.2, 119.0, 87.8, 52.9, 48.6, 21.6, 20.7, 20.1, 19.7; FT-IR (KBr) 2981, 2924, 2850, 1727, 1543, 1451, 1371, 1275, 1140, 1083, 1057, 1014, 943, 903, 828, 810, 761, 683, 550 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{26}IN_2O_4S$ $[M+H]^+$: 553.0658, found: 553.0654.

(*Z*)-*N*,*N*-Diisopropyl-6-methoxy-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7m. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.34; colorless solid; yield 67% (153 mg); mp 264-265 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.66 (d, *J* = 7.2 Hz, 2H), 7.28 (s, 1H), 7.17 (d, *J* = 6.8 Hz, 3H), 6.97 (s, 1H), 3.86 (s, 4H), 3.70-3.67 (m, 1H), 2.37 (s, 3H), 1.59 (d, *J* = 6.8 Hz, 3H), 1.43 (d, *J* = 6.4 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.15 (d, *J* = 6.0 Hz, 3H); ^{13}C {^1H}NMR (100 MHz, $CDCl_3$) δ 157.6, 157.5, 156.5, 148.7, 142.0, 141.5, 140.8, 129.2, 126.6, 123.5, 121.0, 118.5, 118.1, 110.7, 56.0, 52.7, 48.5, 21.6, 20.7, 20.2, 20.1, 19.7; FT-IR (KBr) 3035, 2966, 2932, 1713, 1578, 1550, 1497, 1448, 1367, 1280, 1212, 1142, 1089, 1037,

1017, 965, 904, 879, 814, 806, 768, 755, 680, 595, 553 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{29}N_2O_5S$ $[M+H]^+$: 457.1797, found: 457.1805.

(*Z*)-*N*,*N*-Diisopropyl-6-methyl-2-oxo-*N*'-tosyl-2*H*-chromene-3-carboximidamide 7n. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.41; yellow solid; yield 78% (172 mg); mp 295-296 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.33 (s, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 2H), 3.88-3.83 (m, 1H), 3.70-3.64 (m, 1H), 2.42 (s, 3H), 2.37 (s, 3H), 1.59 (d, *J* = 7.2 Hz, 3H), 1.43 (d, *J* = 6.8 Hz, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 157.65, 157.61, 152.3, 141.9, 141.7, 140.8, 134.8, 133.9, 129.1, 128.8, 126.5, 122.9, 117.9, 116.7, 52.7, 48.5, 21.6, 20.8, 20.6, 20.2, 20.0, 19.6; FT-IR (KBr) 3080, 3025, 2982, 2965, 2924, 1718, 1627, 1580, 1542, 1492, 1447, 1373, 1269, 1211, 1175, 1135, 1084, 1061, 1018, 948, 906, 843, 810, 772, 685, 592, 570, 548 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{24}H_{29}N_2O_4S$ $[M+H^+]$: 441.1848, found: 441.1864.

(*Z*)-8-(*tert*-Butyl)-6-iodo-*N*,*N*-diisopropyl-2-oxo-*N'*-tosyl-2*H*-chromene-3-carboximidamide 7p. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.61; yellow solid; yield 76% (231 mg); mp 244-245 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H)), 7.73 (s, 1H), 7.65 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 3.84-3.80 (m, 1H), 3.71-3.68 (m, 1H), 2.35 (s, 3H), 1.60 (d, *J* = 6.8 Hz, 3H), 1.49-1.46 (m, 12H), 1.28 (d, *J* = 6.0 Hz, 3H), 1.15 (d, *J* = 6.4 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) 157.1, 156.1, 152.6, 142.0, 141.5, 140.7, 140.6, 139.2, 135.8, 129.2, 126.5, 122.6, 120.3, 88.2, 52.9, 48.6, 35.3, 29.9, 21.6, 20.7, 20.2, 20.1, 19.6; FT-IR (KBr) 2966, 2924, 1737, 1630, 1541, 1479, 1369, 1282, 1211, 1147, 1086, 1017, 970, 904, 828, 765, 748, 674, 664, 592, 551 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{34}IN_2O_4S$ $[M+H]^+$: 609.1284, found: 609.1288.

(*Z*)-6,8-*tert*-Butyl-*N,N*-diisopropyl-2-oxo-*N′*-tosyl-2*H*-chromene-3-carboximidamide 7q. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.40; colorless solid; yield 80% (215 mg); mp 242-243 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 3H), 7.36 (s, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 3.88-3.85 (m, 1H), 3.71-3.67 (m, 1H), 2.34 (s, 3H), 1.61 (d, *J* = 6.4 Hz, 3H), 1.49-1.47 (m, 12H), 1.36 (s, 9H), 1.26 (d, *J* = 6.4 Hz, 3H), 1.14 (d, *J* = 6.0 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) 158.0, 157.0, 151.0, 147.3, 143.7, 141.9, 140.9, 137.6, 129.2, 128.4, 126.6, 123.7, 121.3, 117.9, 52.7, 48.6, 35.3, 34.9, 31.5, 30.1, 21.6, 20.7, 20.2, 20.1, 19.7; FT-IR (KBr) 2961, 2871, 1731, 1629, 1586, 1543, 1479, 1451, 1371, 1271, 1018, 953, 903, 842, 810, 767, 689, 594, 552 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{31}H_{43}N_2O_4S$ $[M+H]^+$: 539.2944, found: 539.2958.

(*Z*)-*N,N*-Diisopropyl-3-oxo-*N′*-tosyl-3*H*-benzo[*f*]chromene-2-carboximidamide 7r. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.46; colorless solid; yield 60% (143 mg); mp 290-291 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 9.2 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.8 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 3.94-3.91 (m, 1H), 3.74-3.71 (m, 1H), 2.35 (s, 3H), 1.66 (d, *J* = 6.8 Hz, 3H), 1.50 (d, *J* = 6.8 Hz, 3H), 1.30 (d, *J* = 6.8 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H). ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 157.9, 157.5, 154.3, 142.0, 140.9, 137.6, 134.4, 130.5, 129.4, 129.2, 128.7, 126.5, 122.0, 121.9, 116.9, 112.6, 52.8, 48.6, 21.6, 20.7, 20.2, 20.1, 19.7; FT-IR (KBr) 3058, 2991, 2934, 1716, 1573, 1539, 1477, 1440, 1367, 1279, 1213, 1139, 1087, 1015, 955, 901, 849, 817, 669, 552 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{29}N_2O_4S$ $[M+H]^+$: 477.1848, found: 477.1860.

(*Z*)-*N,N*-Diisopropyl-*N′*-(methylsulfonyl)-2-oxo-2*H*-chromene-3-carboximidamide 7s. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.25; colorless solid; yield 72% (126

mg); mp 249-250 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.58-7.53 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.30 (t, *J* = 8.0 Hz, 1H), 3.92-3.89 (m, 1H), 3.75-3.72 (m, 1H), 2.96 (s, 3H), 1.61 (d, *J* = 6.4 Hz, 6H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.17 (d, *J* = 6.4 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 157.8, 157.7, 154.2, 141.4, 132.8, 129.0, 125.0, 123.4, 118.1, 117.1, 52.6, 48.3, 43.1, 20.6, 20.2, 20.1, 19.8; FT-IR (KBr) 2924, 2853, 1719, 1608, 1541, 1449, 1376, 1275, 1214, 1112, 1061, 1018, 961, 908, 816, 756, 726, 518 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{23}N_2O_4S$ $[M+H]^+$: 351.1379, found: 351.1376.

(*Z*)-*N*,*N*-Diisopropyl-2-oxo-*N′*-(phenylsulfonyl)-2*H*-chromene-3-carboximidamide 7t. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.36; colorless solid; yield 80% (165 mg); mp 259-260 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 6.8 Hz, 2H), 7.73 (s, 1H), 7.59-7.53 (m, 2H), 7.44-7.42 (m, 1H), 7.38-7.30 (m, 4H), 3.88-3.85 (m, 1H), 3.69-3.66 (m, 1H), 1.58 (d, *J* = 6.8 Hz, 3H), 1.41 (d, *J* = 6.8 Hz, 3H), 1.26 (d, *J* = 6.0 Hz, 3H), 1.14 (d, *J* = 6.0 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 157.5, 157.4, 154.2, 143.6, 141.6, 132.9, 131.6, 129.0, 128.6, 126.5, 125.1, 123.3, 118.2, 117.1, 52.9, 48.6, 20.7, 20.2, 20.1, 19.7; FT-IR (KBr) 3036, 2969, 2934, 1720, 1628, 1608, 1545, 1482, 1444, 1366, 1278, 1262, 1143, 1088, 1013, 901, 802, 755, 690, 612, 547 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{25}N_2O_4S$ $[M+H]^+$: 413.1535, found: 413.1535.

(*Z*)-*N′*-((4-Chlorophenyl)sulfonyl)-*N*,*N*-diisopropyl-2-oxo-*2H*-chromene-3-carboximidamide 7u. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.40; colorless solid; yield 82% (183 mg); mp 293-294 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.62-7.55 (m, 2H), 7.37-7.32 (m, 4H), 3.92-3.89 (m, 1H), 3.71-3.68 (m, 1H), 1.57 (d, *J* = 6.4 Hz, 3H), 1.39 (d, *J* = 7.2 Hz, 3H), 1.28 (d, *J* = 6.4 Hz, 3H), 1.17 (d, *J* = 6.8 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 157.6, 157.5, 154.2, 142.2, 141.5, 137.8, 133.1, 129.0,

128.8, 128.0, 125.1, 123.4, 118.1, 117.2, 53.0, 48.7, 20.6, 20.1, 19.8; FT-IR (KBr) 3033, 2980, 2928, 1714, 1627, 1609, 1550, 1483, 1444, 1368, 1295, 1271, 1213, 1144, 1088, 1012, 903, 819, 804, 765, 747, 655, 623, 550 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}ClN_2O_4S$ $[M+H]^+$: 447.1145, found: 447.1149.

(*Z*)-*N*,*N*-Diisopropyl-*N′*-((4-methoxyphenyl)sulfonyl)-2-oxo-2*H*-chromene-3-carboximidamide 7v. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.70; colorless solid; yield 79% (175 mg); mp 259-260 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.61-7.54 (m, 2H), 7.35-7.31 (m, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 3.91-3.86 (m, 1H), 3.82 (s, 1H) 3.72-3.67 (m, 1H), 1.59 (d, *J* = 6.8 Hz, 3H), 1.44 (d, *J* = 6.8 Hz, 3H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 6.4 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 162.0, 157.5, 157.3, 154.2, 141.5, 135.8, 132.9, 129.0, 128.5, 125.0, 123.3, 118.2, 117.1, 113.7, 55.6, 52.7, 48.5, 20.7, 20.2, 20.1, 19.7; FT-IR (KBr) 3034, 2975, 2931, 2839, 1718, 1627, 1609, 1597, 1548, 1496, 1445, 1371, 1353, 1314, 1142, 1128, 1087, 1060, 1014, 901, 809, 790, 758, 677, 596, 556 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{27}N_2O_4S$ $[M+H]$: 443.1641, found: 443.1641.

(*Z*)-*N*,*N*-Diisopropyl-*N′*-(mesitylsulfonyl)-2-oxo-2*H*-chromene-3-carboximidamide 7w. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.43; yellow solid; yield 68% (154 mg); mp 289-290 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.32-7.25 (m, 2H), 6.74 (s, 2H), 3.82-3.79 (m, 1H), 3.70-3.66 (m, 1H), 2.48 (s, 6H), 2.24 (s, 3H), 1.60 (d, *J* = 6.8 Hz, 3H), 1.47 (d, *J* = 7.2 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H); ^{13}C {^{1}H}NMR (100 MHz, $CDCl_3$) δ 157.2, 157.1, 154.1, 140.9, 140.8, 138.3, 137.7, 132.8, 131.3, 129.0, 124.9, 123.3, 118.2, 116.9, 52.7, 48.4, 22.8, 21.0, 20.7, 20.4, 20.1, 19.9; FT-IR (KBr) 3037, 2970, 2933, 1721, 1626, 1607, 1540, 1540, 1481, 1445, 1364,

1350, 1281, 1212, 1129, 1061, 1008, 971, 902, 854, 797, 758, 673, 596, 522 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{31}N_2O_4S$ $[M+H]^+$: 455.2005, found: 455.2005.

(*Z*)-*N*-Benzyl-*N*-cyclohexyl-2-oxo-*N'*-tosyl-2*H*-chromene-3-carboximidamide 7x. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.35; colorless solid; yield 9% (22 mg, 3:1 isomers); mp 205-206 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.64 (d, *J* = 8.4 Hz, 0.5H), 7.64-7.60 (m, 2H), 7.52-7.50 (m, 0.6H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.33-7.31 (m, 4H), 7.29-7.26 (m, 3H), 7.25-7.19 (m, 2H), 7.17 (d, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 0.6H), 7.00 (d, *J* = 7.8 Hz, 2H), 5.02 (d, *J* = 15.6 Hz, 1H), 4.67 (s, 0.3H), 4.61 (d, *J* = 15.6 Hz, 1H), 4.56 (d, *J* = 17.4 Hz, 0.3H), 4.40 (d, *J* = 16.8 Hz, 0.3H), 3.58-3.54 (m, 1H), 2.38 (s, 0.9H), 2.32 (s, 3H), 2.02 (d, *J* = 12.6 Hz, 1H), 1.76-1.71 (m, 0.6H), 1.63-1.59 (m, 3.6H), 1.55-1.53 (m, 2H), 1.39-1.33 (m, 3H), 1.14-1.07 (m, 2.4H), 1.00 (t, *J* = 12.6 Hz, 1.3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 160.5, 159.4, 157.6, 157.4, 154.4, 154.1, 143.7, 142.6, 142.4, 142.0, 140.5, 140.3, 137.7, 136.9, 133.2, 133.0, 129.2, 129.1, 129.0, 128.9, 128.6, 127.8, 126.8, 126.7, 126.6, 126.5, 125.2, 125.0, 122.3, 121.9, 118.1, 117.8, 117.3, 116.9, 60.7, 58.4, 49.2, 47.5, 32.1, 31.8, 31.0, 30.32, 30.3, 25.84, 25.8, 25.62, 25.6, 25.1, 21.7, 21.6; FT-IR (KBr) 3033, 3015, 2958, 2936, 2925, 2852, 1714, 1625, 1609, 1574, 1543, 1452, 1420, 1372, 1282, 1185, 1243, 1088, 1065, 997, 980, 907, 686, 555 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{31}N_2O_4S$ [M+H]: 515.1999, found: 515.2005.

(Z)-*N*-Cyclohexyl-*N*-isopropyl-2-oxo-*N'*-tosyl-2*H*-chromene-3-carboximidamide 7y. Analytical TLC on silica gel, 2:3 ethyl acetate-hexane R_f = 0.35; colorless solid; yield 9 % (20 mg, 1:1 isomers); mp 271-272 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.72 (s, 1H), 7.66 (t, *J* = 8.4 Hz, 4H), 7.61-7.56 (m, 4H), 7.37-7.31 (m, 4H), 7.17-7.16 (m, 4H), 3.90-3.87 (m, 1H), 3.74-3.72 (m, 1H), 3.37-3.33 (m, 1H), 3.18 (s, 1H), 2.88-2.87 (m, 1H), 2.47-2.39 (m, 2H), 2.38

(s, 3H), 2.37 (s, 3H), 2.02 (d, *J* = 12.0 Hz, 1H), 1.85 (d, *J* = 12.0 Hz, 1H), 1.77-1.72 (m, 2H), 1.67 (d, *J* = 6.6 Hz, 3H), 1.41 (d, *J* = 7.2 Hz, 3H), 1.25-1.17 (m, 7H), 1.13 (d, *J* = 6.6 Hz, 3H), 1.10-1.00 (m, 9H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 157.6, 157.52, 157.5, 154.3, 142.1, 141.6, 141.5, 140.83, 140.8, 132.9, 129.21, 129.2, 129.1, 129.07, 126.6, 125.1, 123.4, 123.3, 118.24, 118.2, 117.2, 117.1, 61.7, 57.9, 52.9, 49.8, 30.8, 30.3, 29.9, 29.3, 28.6, 26.7, 26.5, 25.62, 25.6, 25.4, 25.1, 21.7, 20.8, 20.2, 19.7; FT-IR (KBr) 2964, 2931, 2849, 1722, 1607, 1540, 1482, 1445, 1383, 1371, 1272, 1143, 1087, 906, 811, 754, 729, 690, 575, 547 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{31}N_2O_4S$ [M+H]: 467.1999, found: 467.2005.

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Notes

The authors declare no competing financial interest.

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ASSOCIATED CONTENT

Supporting Information

Crystal structures and CIF files of **6** and **7r**, mass spectrum of the reaction mixture of **1a**, **2a**, **3a**, and **4a**, and NMR spectra (^{1}H and ^{13}C) of **2b-c**, **5**, **6, 7a-n** and **7o-y**, and 2D (COSY and HSQC) NMR and DEPT of **7a**. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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