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Efficient synthesis of 2-imino-1,2-dihydroquinolines and 2-imino-thiochromenes via copper-catalyzed domino reaction

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Abstract

A domino approach to 2-imino-1,2-dihydroquinolines and 2-imino-thiochromenes from sulfonyl azides, alkynes, and 2-acyl anilines or the potassium salt of 2-mercapto-benzaldehyde has been developed. This one-pot method is efficient and versatile.

Keywords: Domino reaction; 2-Imino-1,2-dihydroquinolines; 2-Imino-thiochromenes; Sulfonyl azides; Alkynes

1. Introduction

Dihydroquinolines are an important class of scaffolds found in numerous naturally occurring and synthetic molecules possessing a broad spectrum of biological activities.[1,2] Additionally, functionalized 1,2-dihydroquinolines are versatile synthons for the preparation of structurally complex alkaloids.[3] Accordingly, the development of efficient synthetic strategies for the construction of this molecular architecture is of considerable importance from the standpoint of the medicinal and organic chemistry. Skraup and Bischler–Napieralski reactions have been commonly utilized in the synthesis of dihydroquinolines, which involve the use of aniline and a ketone or an intramolecular condensation of an aromatic amide.[4] The reaction of lithium anilides and phenyl acetylene with a stoichiometric amount of tin(IV) chloride could yield 2,4-diphenyl-2-methyl-1,2-dihydroquinolines.[5] More recently, Li and co-workers developed a methodology for the synthesis of 1,2-dihydroquinolines via a transition metal catalyzed domino reaction between anilines and alkynes.[6] Wang and co-workers reported an enantioselective synthesis of 1,2-dihydroquinolines via an organocatalyzed conjugate addition–aldol–dehydration reaction of α,β-unsaturated aldehydes with *N*-protected 2-aminobenzaldehydes.[7] Herein, we wish to present the synthesis of a new class of dihydroquinoline derivatives, 2-imino-1,2-dihydroquinolines, from sulfonyl azides, alkynes, and 2-acyl anilines.

2. Results and discussion

Previously, we developed an efficient synthesis of iminocoumarins via a domino reaction of sulfonyl azides, alkynes, and salicaldehydes, involving a ketenimine intermediate in situ generated from copper-catalyzed cycloaddition of azides and alkynes.[8] We anticipated that using 2-aminobenzaldehyde instead of salicaldehydes to perform the reaction would give 2-imino-1,2-dihydroquinoline. However, when treating 2-aminobenzaldehyde with tolylsulfonyl azide (**1a**) and phenyl acetylene (**2a**) in the presence of CuI and triethylamine (TEA), we found that the reaction did not take place under various conditions (Scheme 1). We then turned our attention to examine the scope utilizing 2-acetyl aniline (**3a**), and found that the three-component reaction of **1a** with **2a** and **3a** could smoothly proceed at room temperature to afford 2-imino-1,2-dihydroquinoline **4a** (Scheme 1). The reaction conditions were examined and CH_3CN was screened as the most effective solvent. The structure of **4a** was unambiguously confirmed by X-ray analysis (Fig. 1), which is in accordance with ^1H NMR, ^{13}C NMR, MS, and HRMS spectra.

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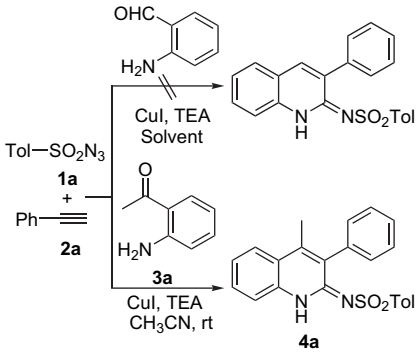


Scheme 1. Reaction of tolylsulfonyl azide with phenyl acetylene and 2-amino-benzaldehyde or 2-acetyl aniline.

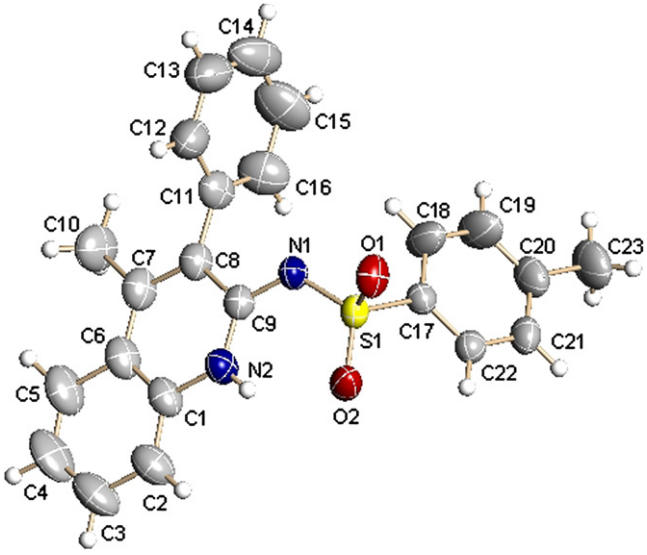


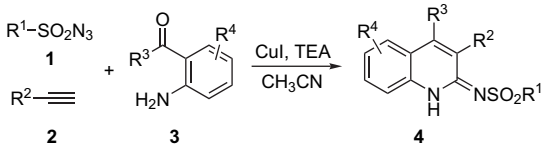
Figure 1. Crystal structure of compound **4a**.

With the suitable reaction conditions in hand, we next tested the feasibility of the protocol using various sulfonyl azides, alkynes, and 2-acyl anilines (Table 1). As shown in Table 1, we obtained the corresponding substituted 2-imino-1,2-dihydroquinolines **4a**–**4m** with good to excellent yields (63–93%). It is noteworthy that the resulting 2-imino-1,2-dihydroquinolines are highly stable under both acidic and basic conditions while their tautomerization to 2-aminoquinolines has not been observed.

We also examined alkyl acetylenes such as hex-1-yne (**2f**), but the reaction gave *N*-sulfonylamidine **5a** rather than the cyclized 2-imino-1,2-dihydroquinoline **4n** either at room temperature or under reflux presumably due to the relative poor reactivity of its ketenimine intermediate (Scheme 2).

Recently, the interest in the sulfur-containing heterocycles has been significantly surged since a wide range of biological activities associated with the scaffold have been identified.[9] For example, 1-benthiopyrans exhibit anti-inflammatory,[10] anti-bacteria,[11] anti-hyperplasia,[12] anti-psychiatric,[13] analgesic, and anti-cancer activities.[14] Thiochromenes constitute an important class of sulfur-containing heterocyclic scaffolds, but methods for their preparation are limited.[14] With the development of the substituted dihydroquinolines in hands, we

Table 1
Synthesis of 2-imino-1,2-dihydroquinolines



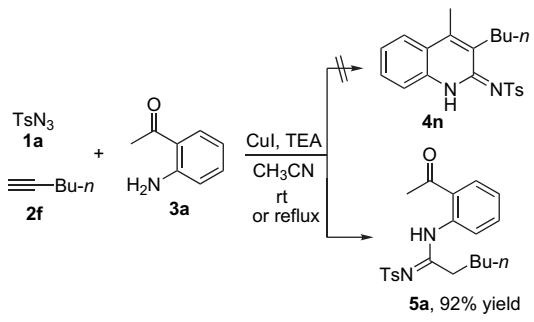
Entry	R^1	R^2	R^3	R^4	Product	Yield[a] (%)
1	4-MeC_6H_4 (**1a**)	Ph (**2a**)	Me (**3a**)	H (**3a**)	**4a**	91
2	(**1a**)	4-$MeOC_6H_4$ (**2b**)	**3a**	**3a**	**4b**	93
3	4-ClC_6H_4 (**1b**)	4-MeC_6H_4 (**2c**)	**3a**	**3a**	**4c**	87
4	Ph (**1c**)	4-FC_6H_4 (**2d**)	**3a**	**3a**	**4d**	85
5	**1c**	**2b**	**3a**	**3a**	**4e**	78
6	**1b**	Pyridine-2-yl (**2e**)	**3a**	**3a**	**4f**	75
7	**1b**	**2a**	**3a**	**3a**	**4g**	78
8	**1c**	**2a**	**3a**	**3a**	**4h**	82
9	**1c**	**2c**	**3a**	**3a**	**4i**	88
10	**1a**	**2a**	Ph (**3b**)	H (**3b**)	**4j**	89
11	**1b**	**2c**	**3b**	**3b**	**4k**	63
12	Me (**1d**)	**2a**	**3a**	**3a**	**4l**	88[b]
13	**1c**	**2a**	Ph (**3c**)	4-Cl (**3c**)	**4m**	91

[a] Isolated yields refer to 2-acyl aniline.
[b] The reaction mixture must be heated immediately to reflux after addition of TEA, otherwise it afforded acyclic amidine rather than the cyclized product.

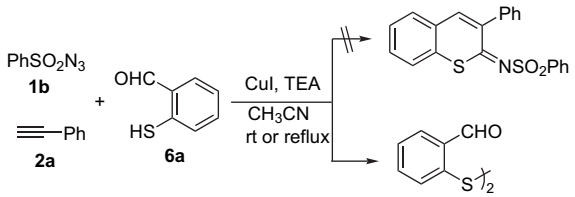
envisioned that the present domino protocol might be applied for the preparation of 2-imino-thiochromenes when 2-mercapto-benzaldehyde or 2-acyl-benzenethiol instead of 2-acyl-aniline is used as one of the components.

As a preliminary study, we found that the reaction of phenylsulfonyl azide (**1b**) with phenyl acetylene (**2a**) and 2-mercapto-benzaldehyde (**6a**) gave 2,2′-disulfanediyldibenzaldehyde in quantitative yield and released N_2 vigorously (Scheme 3). We believed that sulfonyl azide was rapidly reduced to sulfonyl amide and N_2 by mercaptan in the presence of TEA, while mercaptan was converted to disulfide in our reaction system.[15]

Therefore, we directed our effort to alternate strategy. We performed the reaction using potassium salt of 2-mercaptobenzaldehyde **6b**, which could be easily prepared from **6a** and the potassium carbonate. It was found that the reaction could be



Scheme 2. Reaction of hex-1-yne with azide and 2-acetylaniline.

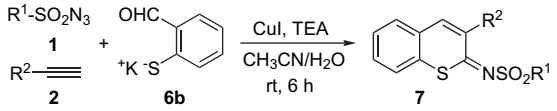


Scheme 3. Reaction of phenylsulfonyl azide with phenyl acetylene and 2-mercaptobenzaldehyde.

carried out in CH_3CN-H_2O (8:1) to furnish 2-imino-thiochromenes in excellent yields (Table 2). Furthermore, an enhancement of reaction rate was observed when an aqueous cosolvent system was employed.

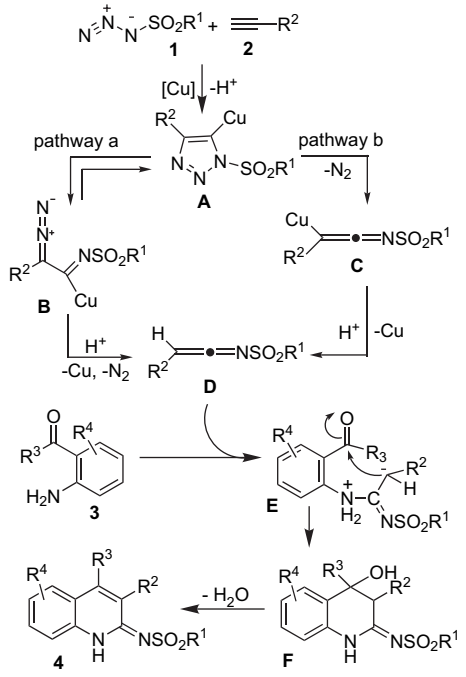
A proposed reaction mechanism is shown in Scheme 4. The formation of the heterocyclic rings can be rationalized as being initiated by the copper-mediated cycloaddition of azides **1** and alkynes **2**, followed by the release of N_2 (pathway a or pathway b) to form intermediate ketenimine **D**.[16] Then an addition of amines **3** to **D** and a subsequent cyclization–dehydration sequence lead to the construction of 2-imino-1,2-dihydroquinolines **4**. The way of formation of 2-imino-thiochromenes **7** follows the same pathway.

Table 2
Synthesis of 2-imino-thiochromenes



Entry	R^1	R^2	Product	Yield (%)
1	**1a**	**2a**	**7a**	95
2	**1a**	**2f**	**7b**	91
3	**1c**	$THPOCH_2$ (**2g**)	**7c**	93

Isolated yields refer to alkyne.



Scheme 4. Possible mechanistic routes to 2-imino-1,2-dihydroquinolines.

3. Conclusion

In conclusion, we have developed a copper-catalyzed domino reaction for the preparation of synthetically and biologically useful 2-imino-1,2-dihydroquinolines and 2-imino-thiochromenes. The present one-pot procedure is efficient, general, and versatile. Further application of the methodology to synthesize heterocyclic compound libraries and natural products is in progress in our laboratory.

4. Experimental

4.1. General

Infrared spectra were obtained on a FTIR spectrometer. NMR spectra were recorded for ^1H NMR at 400 MHz otherwise noted and ^{13}C NMR at 100 MHz at 293 K. Chemical shifts are reported relative to residue peaks of $CDCl_3$ (7.27 ppm for ^1H and 77.0 ppm for ^{13}C). The following abbreviations are used to describe peak patterns where appropriate: br=broad, s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet. Coupling constants are reported in hertz (Hz). Low-resolution MS and HRMS were obtained using ESI ionization. Melting points were measured with micro melting point apparatus.

4.2. General procedure for synthesis of 2-imino-1,2-dihydroquinolines *4*

To a solution of sulfonyl azide (1.0 mmol), alkynes (1.0 mmol), 2-acyl anilines (1.0 mmol), and CuI (0.1 mmol) in CH_3CN (5 mL) was added slowly triethylamine (2 mmol) through a syringe. The reaction solution was stirred at room temperature under N_2 for 8 h. After concentrated in vacuum, the solution was diluted with CH_2Cl_2 (30 mL), washed with water (10 mL) and brine (10 mL), and dried over sodium sulfate. The solvent was removed in vacuum and the residue was purified by column chromatography on silica gel with hexane–ethyl acetate (2:1) to give *N*-sulfonyl-1,2-dihydroquinoline-2-imines. The products were further recrystallized from ethyl acetate.

4.2.1. 4-Methyl-N-(4-methyl-3-phenylquinolin-2(1H)-ylidene)benzenesulfonamide (*4a*)

White crystal; mp 196–197 °C; ^1H NMR ($CDCl_3$): δ 11.66 (br, 1H), 7.83 (d, J=8.0 Hz, 1H), 7.75 (d, J=8.4 Hz, 2H), 7.62–7.58 (m, 1H), 7.44–7.38 (m, 5H), 7.21–7.15 (m, 4H), 2.36 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 152.6, 146.0, 142.1, 140.2, 135.3, 130.8, 130.0, 128.9, 128.1, 127.7, 126.0, 124.9, 124.4, 122.2, 117.7, 21.3, 17.0 ppm; IR (KBr) 3265, 1624, 1595, 1375, 1080, 869, 668, 561 cm^{-1}; MS (ESI) *m/z* 411.1 ($[M+Na]^+$); HRMS (ESI) calcd for $C_{23}H_{20}N_2O_2S$ ($[M+Na]^+$) 411.1136, found 411.1131.

*4.2.2. N-(3-(4-Methoxyphenyl)-4-methylquinolin-2(1H)-ylidene)-4-methylbenzenesulfonamide (**4b**)*

White crystal; mp 186–188 °C; ^{1}H NMR ($CDCl_3$): δ 12.12 (br, 1H), 7.82–7.78 (m, 3H), 7.60–7.56 (m, 1H), 7.38–7.36 (m, 2H), 7.20 (d, J=8.0 Hz, 2H), 7.08 (d, J=8.8 Hz, 2H), 6.95 (d, J=8.0 Hz, 2H), 3.84 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 159.1, 152.7, 146.0, 142.2, 140.2, 135.7, 131.3, 130.6, 129.0, 127.3, 126.1, 124.9, 124.4, 122.3, 117.8, 113.6, 55.2, 21.3, 17.0 ppm; IR (KBr) 3274, 2957, 1624, 1598, 1250, 1080, 872, 668, 563 cm^{-1}; MS (ESI) *m/z* 441.1 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{24}H_{22}N_2O_3S$ ([M+Na]$^+$) 441.1244, found 441.1238.

*4.2.3. 4-Chloro-N-(4-methyl-3-p-tolylquinolin-2(1H)-ylidene)benzenesulfonamide (**4c**)*

White crystal; mp 242–244 °C; ^{1}H NMR ($CDCl_3$): δ 12.06 (br, 1H), 7.85 (d, J=8.0 Hz, 1H), 7.78 (d, J=8.0 Hz, 2H), 7.64–7.60 (m, 1H), 7.43–7.36 (m, 4H), 7.23 (d, J=7.2 Hz, 2H), 7.03 (d, J=8.0 Hz, 2H), 2.42 (s, 3H), 2.36 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 152.9, 146.6, 141.8, 137.8, 137.5, 135.3, 132.1, 130.9, 129.8, 129.0, 128.6, 125.0, 124.6, 122.3, 117.7, 21.2, 17.1 ppm; IR (KBr) 3280, 3207, 1627, 1599, 1377, 1137, 876, 750, 555 cm^{-1}; MS (ESI) *m/z* 445.1 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{23}H_{19}ClN_2O_2S$ ([M+Na]$^+$) 445.0747, found 445.0741.

*4.2.4. N-(3-(4-Fluorophenyl)-4-methylquinolin-2(1H)-ylidene)benzenesulfonamide (**4d**)*

White crystal; mp 185–187 °C; ^{1}H NMR ($CDCl_3$): δ 12.00 (br, 1H), 7.84–7.81 (m, 3H), 7.62–7.58 (m, 1H), 7.45–7.37 (m, 5H), 7.11–7.08 (m, 4H), 2.33 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 162.2 (d, J_{C-F}=245.3 Hz), 152.8, 146.7, 143.1, 135.2, 131.8 (d, J_{C-F}=8.2 Hz), 131.6, 131.1, 131.0, 130.7, 128.4, 125.7, 125.0, 124.5, 121.9, 117.3, 115.1 (d, J_{C-F}= 20.5 Hz), 17.1 ppm; DEPT-135 ($CDCl_3$): δ 131.8, 131.7, 131.5, 131.1, 128.3, 125.7, 125.0, 124.5, 115.1, 114.9, 17.1 ppm; IR (KBr) 3274, 3067, 1624, 1597, 1134, 873, 759, 555 cm^{-1}; MS (ESI) *m/z* 415.1 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{22}H_{17}FN_2O_2S$ ([M+Na]$^+$) 415.0890, found 415.0882.

*4.2.5. N-(3-(4-Methoxyphenyl)-4-methylquinolin-2(1H)-ylidene)benzenesulfonamide (**4e**)*

White crystal; mp 182–183 °C; ^{1}H NMR ($CDCl_3$): δ 12.13 (br, 1H), 7.87 (d, J=7.0 Hz, 2H), 7.81 (d, J=8.4 Hz, 1H), 7.60–7.56 (m, 1H), 7.44–7.36 (m, 5H), 7.07 (d, J=8.4 Hz, 2H), 6.94 (d, J=8.8 Hz, 2H), 3.83 (s, 3H), 2.35 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 159.0, 153.1, 146.3, 143.1, 134.8, 131.5, 131.2, 130.7, 128.3, 127.2, 125.9, 124.9, 124.4, 122.2, 116.9, 113.5, 55.1, 17.1 ppm; IR (KBr) 3279, 1625, 1599, 1509, 1246, 1080, 874, 557 cm^{-1}; MS (ESI) *m/z* 427.1 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{23}H_{20}N_2O_3S$ ([M+Na]$^+$) 427.1088, found 427.1085.

*4.2.6. 4-Chloro-N-(4-methyl-3-(pyridin-2-yl)quinolin-2(1H)-ylidene)benzenesulfonamide (**4f**)*

White crystal; mp 203–204 °C; ^{1}H NMR ($CDCl_3$): δ 12.11 (br, 1H), 8.69–8.68 (m, 1H), 7.85 (d, J=8.4 Hz, 1H), 7.78–7.72 (m, 3H), 7.65–7.61 (m, 1H), 7.42–7.27 (m, 6H), 2.34 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 154.4, 153.0, 149.4, 148.34, 141.9, 137.8, 136.2, 135.0, 131.6, 130.9, 128.6, 127.3, 126.0, 125.2, 124.8, 122.7, 122.0, 117.1, 16.7 ppm; IR (KBr) 3281, 3093, 1628, 1603, 1137, 1083, 875, 751, 557 cm^{-1}; MS (ESI) *m/z* 432.0 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{21}H_{16}ClN_3O_2S$ ([M+Na]$^+$) 432.0544, found 432.0540.

*4.2.7. 4-Chloro-N-(4-methyl-3-phenylquinolin-2(1H)-ylidene)benzenesulfonamide (**4g**)*

Pale yellow crystal; mp 221–225 °C; ^{1}H NMR ($CDCl_3$): δ 11.97 (br, 1H), 7.86 (d, J=8.4 Hz, 1H), 7.75 (d, J=8.4 Hz, 2H), 7.66–7.62 (m, 1H), 7.45–7.41 (m, 5H), 7.36 (d, J=8.8 Hz, 2H), 7.14 (d, J=6.8 Hz, 2H), 2.36 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 152.7, 146.7, 141.8, 137.8, 135.4, 135.2, 131.7, 131.1, 130.0, 128.6, 128.2, 127.8, 127.5, 125.1, 124.7, 122.2, 117.7, 17.1 ppm; IR (KBr) 3283, 3079, 1627, 1595, 1136, 1083, 874, 749, 556 cm^{-1}; MS (ESI) *m/z* 430.8 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{22}H_{17}ClN_2O_2S$ ([M+Na]$^+$) 431.0591, found 431.0590.

*4.2.8. N-(4-Methyl-3-phenylquinolin-2(1H)-ylidene)-benzenesulfonamide (**4h**)*

White crystal; mp 198–202 °C; ^{1}H NMR ($CDCl_3$): δ 12.13 (br, 1H), 7.85–7.83 (m, 3H), 7.64–7.60 (m, 1H), 7.46–7.38 (m, 8H), 7.17–7.15 (m, 2H), 2.35 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 153.2, 146.5, 143.5, 135.3, 134.9, 132.3, 131.5, 131.0, 130.0, 128.4, 128.1, 127.7, 125.8, 125.1, 124.5, 122.0, 117.0, 17.2 ppm; IR (KBr) 3265, 2923, 1624, 1596, 1133, 870, 558 cm^{-1}; MS (ESI) *m/z* 396.9 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{22}H_{18}N_2O_2S$ ([M+Na]$^+$) 397.0985, found 397.0980.

*4.2.9. N-(4-Methyl-3-p-tolylquinolin-2(1H)-ylidene)-benzenesulfonamide (**4i**)*

White crystal; mp 193–194 °C; ^{1}H NMR ($CDCl_3$): δ 12.15 (br, 1H), 7.89–7.82 (m, 3H), 7.62–7.58 (m, 1H), 7.46–7.39 (m, 5H), 7.23 (d, J=7.6 Hz, 2H), 7.04 (d, J=8.0 Hz, 2H), 2.41 (s, 3H), 2.35 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 153.3, 146.3, 143.3, 137.4, 134.9, 132.2, 131.6, 130.8, 129.9, 128.9, 128.4, 125.9, 125.0, 124.5, 122.2, 116.9, 21.2, 17.1 ppm; IR (KBr) 3274, 3064, 1624, 1599, 1134, 872, 555 cm^{-1}; MS (ESI) *m/z* 410.8 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{23}H_{20}N_2O_2S$ ([M+Na]$^+$) 411.1136, found 411.1136.

*4.2.10. N-(3,4-Diphenylquinolin-2(1H)-ylidene)-4-methyl-benzenesulfonamide (**4j**)*

White crystal; mp 202–205 °C; ^{1}H NMR ($CDCl_3$): δ 12.27 (br, 1H), 7.74 (d, J=8.0 Hz, 2H), 7.57–7.55 (m, 1H), 7.44–7.41 (m, 1H), 7.30–6.97 (m, 14H), 2.38 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 153.3, 150.7, 142.1, 140.4, 135.45, 135.40, 134.5, 132.2, 131.1, 130.7, 129.4, 129.0, 127.9, 127.8, 127.7, 127.2, 127.0, 125.8, 124.2, 121.9, 116.6, 21.4 ppm; IR (KBr) 3388, 1620, 1592, 1364, 1136, 1083, 785, 545 cm^{-1}; MS (ESI) *m/z* 473.0 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{28}H_{22}N_2O_2S$ ([M+Na]$^+$) 473.1295, found 473.1290.

*4.2.11. 4-Chloro-N-(4-phenyl-3-p-tolylquinolin-2(1H)-ylidene)benzenesulfonamide (**4k**)*

White crystal; mp 204–205 °C; ^{1}H NMR ($CDCl_3$): δ 12.21 (br, 1H), 7.77 (d, J=7.6 Hz, 2H), 7.59–7.55 (m, 1H), 7.44–7.20 (m, 8H), 7.05–7.03 (m, 2H), 6.91 (d, J=6.8 Hz, 2H), 6.85 (d, J=6.8 Hz, 2H), 2.22 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 153.5, 151.0, 141.9, 137.7, 136.7, 135.5, 135.2, 132.1, 131.3, 131.1, 130.5, 129.4, 128.6, 128.0, 127.8, 127.7, 127.4, 124.4, 122.1, 116.7, 21.1 ppm; IR (KBr) 3249, 1619, 1599, 1138, 1086, 817, 782, 562 cm^{-1}; MS (ESI) *m/z* 506.9 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{28}H_{21}ClN_2O_2S$ ([M+Na]$^+$) 507.0906, found 507.0903.

*4.2.12. N-(4-Methyl-3-phenylquinolin-2(1H)-ylidene)-methanesulfonamide (**4l**)*

Pale yellow crystal; mp 163–164 °C; ^{1}H NMR ($CDCl_3$): δ 11.87 (br, 1H), 7.84 (d, J=6.8 Hz, 1H), 7.60–7.56 (m, 1H), 7.44–7.38 (m, 5H), 7.22 (d, J=7.2 Hz, 2H), 2.93 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 145.8, 140.4, 135.2, 132.3, 130.7, 130.0, 128.5, 127.9, 124.9, 124.5, 122.4, 117.9, 17.0 ppm; IR (KBr) 3297, 3019, 1622, 1595, 1265, 1109, 868, 527 cm^{-1}; MS (ESI) *m/z* 335.1 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{17}H_{16}N_2O_2S$ ([M+Na]$^+$) 335.0825, found 335.0821.

*4.2.13. N-(6-Chloro-3,4-diphenylquinolin-2(1H)-ylidene)-benzenesulfonamide (**4m**)*

Pale yellow crystal; mp 222–224 °C; ^{1}H NMR ($CDCl_3$): δ 8.02 (d, J=7.2 Hz, 2H), 7.60–7.53 (m, 3H), 7.51–7.45 (m, 2H), 7.30 (d, J=2.0 Hz, 1H), 7.27–7.26 (m, 3H), 7.20–7.18 (m, 3H), 7.03–7.00 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$): δ 151.0, 149.1, 141.8, 135.0, 133.9, 132.3, 131.1, 130.4, 130.2, 129.5, 128.5, 128.14, 128.10, 128.1, 127.8, 127.1, 126.3, 124.1, 122.5 ppm; IR (KBr) 3292, 3064, 1619, 1592, 1447, 1084, 548 cm^{-1}; MS (ESI) *m/z* 493.0 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{27}H_{19}ClN_2O_2S$ ([M+Na]$^+$) 493.0750, found 493.0746.

*4.3. Procedure for synthesis of amidine **5a***

To a solution of phenylsulfonyl azide (1.0 mmol), alkynes (1.0 mmol), 2-acyl anilines (1.0 mmol), and CuI (0.1 mmol) in CH_3CN (5 mL) was added slowly triethylamine (2 mmol) through a syringe. The reaction solution was stirred at room temperature under N_2 for 8 h. After concentrated in vacuum, the solution was diluted with CH_2Cl_2 (30 mL), washed with water (10 mL) and brine (10 mL), and dried over sodium sulfate. The solvent was removed in vacuum and the residue was purified by column chromatography on silica gel with hexane–ethyl acetate (6:1) to *N*-(2-acetylphenyl)-*N*′-tosylhexanimidamide **5a**. White crystal; mp 89–90 °C; ^{1}H NMR ($CDCl_3$): δ 11.88 (br, 1H), 8.63 (d, J=8.4 Hz, 1H), 7.91–7.86 (m, 3H), 7.48–7.44 (m, 1H), 7.28 (d, J=7.6 Hz, 2H), 7.16–7.15 (m, 1H), 3.03 (t, J=8.0 Hz, 2H), 2.66 (s, 3H), 2.41(s, 3H), 1.89–1.85 (m, 2H), 1.45–1.38 (m, 4H), 0.92 (t, J=6.8 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 203.1, 166.7, 142.3, 140.4, 140.0, 134.8, 131.7, 129.2, 126.3, 123.4, 122.9, 122.2, 35.8, 31.3, 28.5, 26.9, 22.1, 21.4, 13.7 ppm; IR (KBr) 3117, 2953, 1659, 1512, 1246, 1091, 700, 598 cm^{-1}; MS (ESI) *m/z* 409.1 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{21}H_{26}N_2O_3S$ ([M+Na]$^+$) 409.1558, found 409.1555.

*4.4. General procedure for synthesis of 2-imino-chromenes **7***

To a solution of 2-mercaptobenzaldehyde (1 mmol) in CH_3CN (3 mL) was added saturated aqueous potassium carbonate (1 mL). Through two dropping funnels, the resulting potassium salt solution and TEA (2 mmol) in CH_3CN (2 mL) were added dropwise simultaneously to the mixture of sulfonyl azide (1 mmol), alkyne (1 mmol), and CuI (0.1 mmol) in CH_3CN (3 mL) in a three-necked flask under N_2 for about 30 min. The reaction mixture was stirred at room temperature for 6 h. After diluted with CH_2Cl_2 (30 mL), the aqueous solution was extracted with CH_2Cl_2 (15×2 mL) and the combined organic phase was washed with water (10 mL) and brine (10 mL), and dried over sodium sulfate. The solvent was removed in vacuum and the crude product was purified by column chromatography on silica gel with hexane–ethyl acetate (4:1). The products were further recrystallized from ethyl acetate–hexane.

*4.4.1. 4-Methyl-N-(3-phenyl-2H-thiochromen-2-ylidene)-benzenesulfonamide (**7a**)*

Yellow crystal; mp 168–169 °C; ^{1}H NMR ($CDCl_3$): δ 7.80 (d, J=8.0 Hz, 2H), 7.74 (s, 1H), 7.63 (d, J_1=6.8 Hz, J_2=8.0 Hz, 2H), 7.55–7.51 (m, 1H), 7.48–7.41 (m, 3H), 7.37–7.35 (m, 3H), 7.24 (d, J=8.4 Hz, 2H), 2.40 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 167.1, 143.1, 142.0, 138.1, 137.2, 136.6, 134.5, 131.4, 129.9, 129.5 129.2, 128.3, 127.9, 127.6, 126.9, 125.4, 21.5 ppm; IR (KBr) 3034, 1606, 1487, 1459, 1447, 1286, 1147, 1083, 682, 563 cm^{-1}; MS (ESI) *m/z* 414.1 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{22}H_{17}NO_2S_2$ ([M+Na]$^+$) 414.0595, found 414.5091.

*4.4.2. N-(3-Butyl-2H-thiochromen-2-ylidene)-4-methyl-benzenesulfonamide (**7b**)*

Yellow crystal; mp 128–130 °C; ^{1}H NMR ($CDCl_3$): δ 7.95 (d, J=8.0 Hz, 2H), 7.60–7.56 (m, 3H), 7.47–7.43 (m, 2H), 7.31 (d, J=8.0 Hz, 2H), 2.66 (t, J=5.6 Hz, 2H), 2.42 (s, 3H), 1.56–1.52 (m, 2H), 1.36–1.32 (m, 2H), 0.88 (t, J=7.6 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$): δ 168.0, 143.3, 139.7, 137.9, 137.1, 133.9, 130.6, 129.2, 129.1, 127.4, 127.1, 126.8, 125.3, 33.0, 30.6, 22.4, 21.5, 13.8 ppm; IR (KBr) 2956, 2925, 2856, 1608, 1488, 1459, 1431, 1301, 1150, 1086, 859, 681, 587 cm^{-1}; MS (ESI) *m/z* 394.1 ([M+Na]$^+$); HRMS (ESI) calcd for $C_{20}H_{21}NO_2S_2$ ([M+Na]$^+$) 394.0910, found 394.0905.

*4.4.3. N-(3-((Tetrahydro-2H-pyran-2-yloxy)methyl)-2H-thiochromen-2-ylidene)benzenesulfonamide (**7c**)*

Yellow crystal; mp 146–148 °C; ^{1}H NMR ($CDCl_3$): δ 8.06 (d, J=7.2 Hz, 2H), 8.00 (s, 1H), 7.69 (d, J=7.2 Hz, 1H), 7.62 (d, J=7.6 Hz, 1H), 7.57 (d, J=7.2 Hz, 1H), 7.53–7.45 (m, 4H), 4.75–4.71 (m, 2H), 4.52–4.48 (m, 1H), 3.86–3.85 (m, 1H), 3.53–3.50 (m, 1H), 1.90–1.55 (m, 6H) ppm; ^{13}C NMR

($CDCl_3$): δ 166.9, 140.6, 138.6, 133.9, 132.8, 132.7, 131.4, 129.6, 128.7, 127.6, 127.1, 126.5, 125.4, 99.1, 65.4, 62.6, 30.6, 25.3, 19.6 ppm; IR (KBr) 2956, 2925, 2856, 1608, 1488, 1459, 1431, 1301, 1150, 1086, 859, 681, 587 cm^{-1}; MS (ESI) *m/z* 438.1 ($[M+Na]^+$); HRMS (ESI) calcd for $C_{21}H_{21}NO_4S_2$ ($[M+Na]^+$) 438.0875, found 438.0870.

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Supplementary data

Crystallographic data (CCDC-659198 for **4a**) have been deposited at the Cambridge Crystallographic Database Center. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.11.025.

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