Tetrahedron 65 (2009) 1287–1293

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Application of *ortho*-chloro-β-aroylthioamides in synthesis(II): an efficient one-pot, three-component synthesis of tricyclic thiochromeno[2,3-*b*] pyridine derivatives

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ARTICLE INFO

Article history:
Received 16 June 2008
Received in revised form 15 December 2008
Accepted 16 December 2008
Available online 24 December 2008

Keywords:
ortho-Halo-β-aroylthioamides
Meldrum's acid
Multicomponent reactions
Thiochromeno[2,3-*b*]pyridine derivatives

ABSTRACT

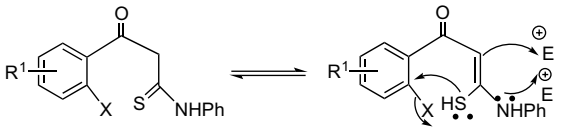
Tricyclic thiochromeno[2,3-*b*]pyridine derivatives have been successfully synthesized in an unusual one-pot multicomponent cascade reaction from *ortho*-halo-β-aroylthioamides, Meldrum's acid, and aromatic aldehydes. The reaction presumably proceeds via Knoevenagel condensation–Michael addition–cyclocondensation–decarboxylation–rearrangement–intramolecular S_NAr reaction sequence. High bond forming efficiency of this reaction makes it attractive for the synthesis of thiochromeno[2,3-*b*]pyridine derivatives in a single step operation.

1. Introduction

Multicomponent reactions (MCRs), an important sub-class of tandem reaction,[1] are one-pot processes in which several easily accessible components react to form a single product.[2] They offer significant advantages over conventional linear-step syntheses due to their flexible, convergent, and atom efficient nature.[3] Devising such types of MCRs that achieve the formation of multiple bonds in a single operation is one of the major challenges in modern organic synthesis.[4]

Functionalized thiochromones and their fused analogues[5] are of interest because they represent an important class of heterocycles, many of which exhibit useful biological activities and have been tested and applied as drugs.[6] However, little attention has been paid toward the synthesis and biological evaluation of pyridine-fused to thiochromones (thiochromeno[2,3-*b*]pyridines). It is still a challenge to explore new and efficient synthetic routes for this class of compounds, particularly those with wide applicability to achieve more flexible substitution pattern.

A rapidly increasing recognition of the thioamide as a useful functional group in organic synthesis has been brought out in the last decades.[7] In fact, thioamides, referred as ketene-(*N*,*S*)-acetals,[8] are known to readily react with both electrophilic and nucleophilic reagents to yield a wide variety of interesting compounds.[9] *ortho*-Halo-β-aroylthioamides[10] were studied as a versatile reagent offering considerable opportunities for the construction of thiochromeno[2,3-*b*]pyridine derivatives in which four reactive centers are presented (Scheme 1). Owing to the conjugation effect of the electron-donating secondary amino group and the electron-withdrawing carbonyl group, the C=C bond is highly polarized and the electron density on the α-carbon is increased. Both the α-carbon and the secondary amino group can be employed in the reaction with electrophiles to form fused heterocyclic structures by nucleophilic addition or substitution and cyclocondensation sequences. In the meantime, a good leaving chloro group on the aromatic ring can be replaced by mercapto via intramolecular S_NAr reactions.



Scheme 1. The tautomer of *ortho*-halo-β-aroylthioamides.

Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione),[11] a class of acylal, was discovered in 1908 by Meldrum.[12] It is very acidic (pK_a 7.3 in DMSO at 25 °C) as compared to the related dicarbonyl

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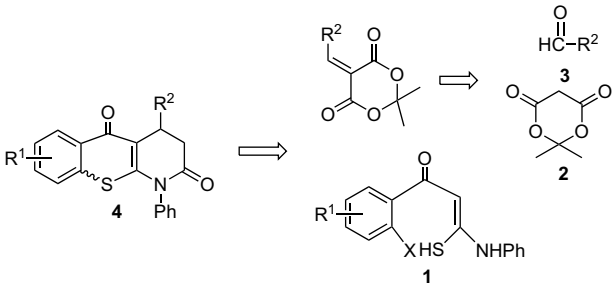
0040-4020/$ – see front matter © 2008 Published by Elsevier Ltd.
doi:10.1016/j.tet.2008.12.057



Scheme 2. Retrosynthetic analysis for the thiochromeno[2,3-*b*]pyridines.

Table 1
The effects of various catalysts and solvents on three-component reaction

Entry	Catalyst (equiv)	Solvent	Time (h)	**4a** Yield[a] (%)
1	None	EtOH	7[b]	0
2	Et_3N (0.2)	EtOH	7[b]	55
3	Et_3N (0.3)	EtOH	7[b]	65
4	Et_3N (0.3)	EtOH	10[c]	0
5	Et_3N (0.5)	EtOH	7[b]	63
6	Et_3N (0.6)	EtOH	7[b]	61
7	Piperidine (0.3)	EtOH	7[b]	53
8	NaH (0.3)	EtOH	7[b]	26
9	K_2CO_3 (0.3)	EtOH	7[b]	20
10	Et_3N (0.3)	CH_3CN	7[b]	51
11	Et_3N (0.3)	CH_2Cl_2	10[b]	43
12	Et_3N (0.3)	CH_3OH	7[b]	63

[a] Isolated yields.
[b] Solvent (10 mL), reflux.
[c] EtOH (10 mL), room temperature.

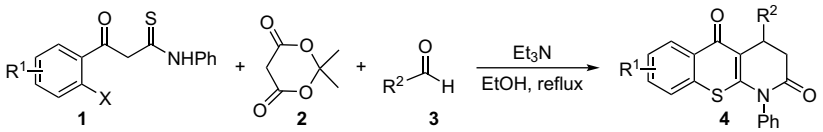
compounds.[13] This unusual C–H acidity has made it an important building block in organic synthesis.[14] For example, Meldrum's acid can undergo facile condensation with aldehydes to afford the alkylidene Meldrum's acids,[15] which are highly reactive 1,1-diactivated alkenes. They have been used extensively as acceptors in Michael addition.[16] We designed a strategy that *ortho*-halo-β-aroylthioamides should react with alkylidene Meldrum's acid to undergo new annulations based on a condensation–Michael addition–domino carbonyl formation–nucleophilic substitution sequence.

In our earlier papers, we described the application of *ortho*-halo-β-aroylthioamides.[10] To the best of our knowledge, very few molecules of this sort have been synthesized and there is no general strategy to prepare them. Continuing our studies on the synthesis of thiochromeno[2,3-*b*]pyridine derivatives, we have focused on the thiochromeno[2,3-*b*]pyridine core as a model to construct two carbon–carbon bonds, two carbon–heteroatom bonds, and two new rings in a single synthetic operation (Scheme 2). This model requires nucleophilic addition of the NH group of **1** to one of the carbonyl center in **2** to form C–N bond, and subsequently the C–S bond formation via intramolecular S_NAr reaction between the *ortho*-halo group and the mercapto group in **1**. The retrosynthetic analysis of the target motif **4** leads to the precursors *ortho*-halo-β-aroylthioamides **1**, Meldrum's acid **2**, and aldehydes **3**.

2. Results and discussion

Simple reagents and conditions were used in this three-component domino reaction. Initially, the reaction of 3-(2,4-dichlorophenyl)-3-oxo-*N*-phenyl-propanethioanide **1a**, Meldrum's acid **2**, and 2,5-dichlorobenzaldehyde **3a** was carried

Table 2
Synthesis of products **4**



Entry	X	R^1	R^2	Time (h)	Yield[a] (%)
1	Cl	4-Cl	2,5-$Cl_2C_6H_3$	7	**4a** (65)
2	Cl	4-Cl	4-ClC_6H_4	6	**4b** (63)
3	Cl	4-Cl	2,4-$Cl_2C_6H_3$	7	**4c** (66)
4	Cl	4-Cl	3-$NO_2C_6H_4$	7	**4d** (64)
5	Cl	4-Cl	C_6H_5	7	**4e** (62)
6	Cl	4-Cl	3,4-$(OCH_3)_2C_6H_3$	9	**4f** (57)
7	Cl	4-Cl	4-$OCH_3C_6H_4$	9	**4g** (55)
8	Cl	4-Cl	4-$CH_3C_6H_4$	9	**4h** (55)
9	Cl	5-Cl	2,5-$Cl_2C_6H_3$	8	**4i** (61)
10	Cl	5-Cl	4-ClC_6H_4	8	**4j** (60)
11	Cl	5-Cl	2,4-$Cl_2C_6H_3$	8	**4k** (61)
12	Cl	5-Cl	3-$NO_2C_6H_4$	8	**4l** (59)
13	Cl	5-Cl	C_6H_5	9	**4m** (58)
14	Cl	5-Cl	3,4-$(OCH_3)_2C_6H_3$	11	**4n** (52)
15	Cl	5-Cl	4-$OCH_3C_6H_4$	11	**4o** (50)
16	Cl	5-Cl	4-$CH_3C_6H_4$	11	**4p** (51)
17	Cl	4-Cl, 5-F	4-FC_6H_4	6	**4q** (70)
18	Cl	4-Cl, 5-F	3-FC_6H_4	7	**4r** (65)
19	Cl	4-Cl, 5-F	2-FC_6H_4	6	**4s** (68)
20	Cl	4-Cl, 5-F	C_6H_5	7	**4t** (66)
21	Cl	4-Cl, 5-F	4-$OCH_3C_6H_4$	9	**4u** (60)
22	F	H	2,5-$Cl_2C_6H_3$	12	**4v** (53)
23	F	H	4-$OCH_3C_6H_4$	14	**4w** (47)
24	F	4-F	2,5-$Cl_2C_6H_3$	6	**4x** (70)
25	F	4-F	4-ClC_6H_4	6	**4y** (69)
26	F	4-F	3,4-$(OCH_3)_2C_6H_3$	9	**4z** (61)

[a] Isolated yields.

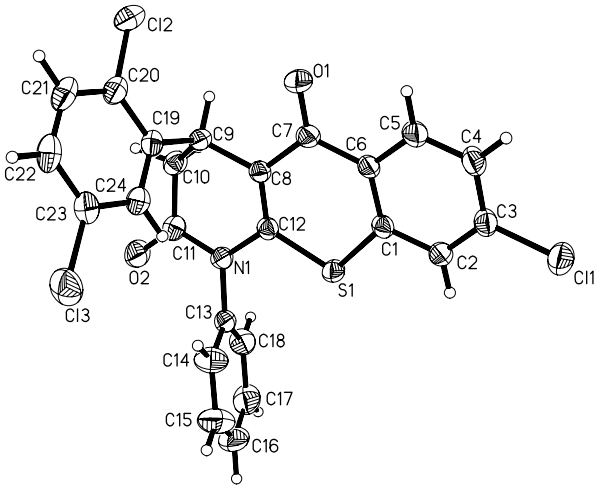


Figure 1. Molecular structure of **4a**.

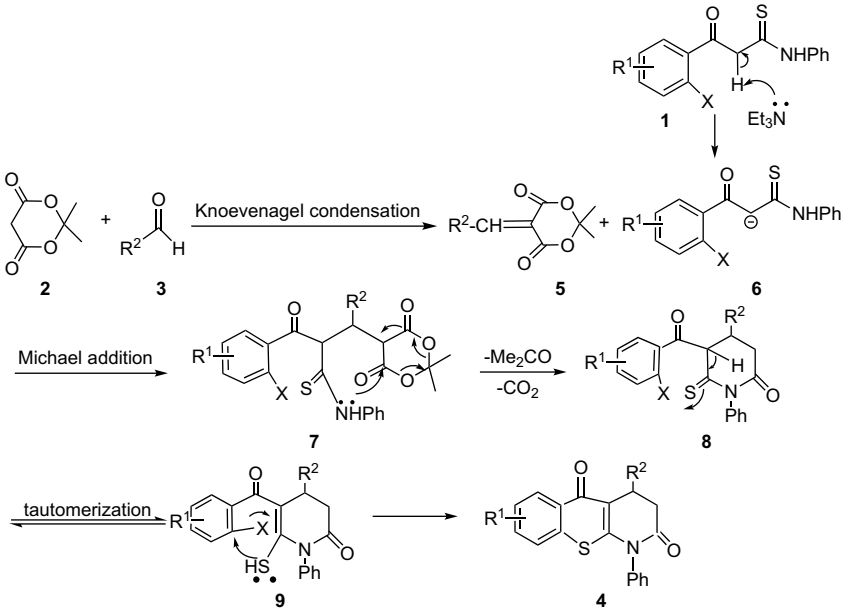
out with different catalysts and solvents. The reaction conditions were then optimized and the results are listed in Table 1. No reaction occurred without addition of any catalyst (Table 1, entry 1) or with Et_3N (0.3 equiv) as catalyst in EtOH but at room temperature (Table 1, entry 4). It was found that, with Et_3N (0.3 equiv) as the catalyst, **4a** was produced in 65% yield for 7 h at reflux in EtOH (Table 1, entry 3). However, the yield of **4a** was not further improved with increased amount of the catalyst (Table 1, entries 5 and 6). In the presence of piperidine, NaH or K_2CO_3, the reaction was sluggish and the yield of the corresponding product was lower than that of Et_3N (Table 1, entries 7–9). Among the solvents tested, CH_3CN, CH_2Cl_2, and CH_3OH gave lower product yields (Table 1, entries 10–12) than EtOH. Thus, it was clear from the experimental results that employing Et_3N as catalyst and EtOH as solvent at reflux was optimal reaction condition (Table 1, entry 3).

In this domino reaction, the substituents of the thioamides and the aldehydes had obvious influence on its reactivity and yield (Table 2).

Firstly, aromatic aldehydes were generally the better substrates. Under the optimized reaction conditions, reactions involving aromatic aldehydes usually went smoothly and gave the corresponding products **4** in good yields. Reactions involving simple aliphatic aldehydes were also investigated. Unfortunately, when acetaldehyde and butyraldehyde were used as the carbonyl reactants, the reactions were usually very slow and resulted in a complicated mixture of products. Secondly, reactions with aromatic aldehydes carrying electron-withdrawing groups (Table 2, entries 1–4) normally resulted in good yields, whereas the substrates with electron-rich groups (Table 2, entries 6–8) had lower reactivity and required longer reaction times. Under similar conditions, the aromatic aldehydes of different substituted sites (Table 2, entries 17–19) reacted with thioamides and Meldrum's acid to afford the corresponding products **4q**–**4s** in good yields. In addition, substituents on thioamides **1** had the influence on the efficiency of the domino reaction, which might be attributed to the inductive effect. In this reaction, two C–C bonds, one C–S bond, one C–N bond, and two new rings are constructed with all reactants efficiently utilized. Therefore, it is an excellent method for the synthesis of thiochromeno[2,3-*b*]pyridine derivatives.

All products **4a**–**z** were characterized by their analytical and spectral data. The structure of **4a** was confirmed by X-ray single-crystal diffraction analysis[17] (Fig. 1).

Based on the experimental results, we proposed a plausible mechanism for this cascade reaction to form thiochromeno[2,3-*b*]pyridine derivatives as shown in Scheme 3. Initially, Knoevenagel condensation of aromatic aldehydes **3** with the α-carbon atom of Meldrum's acid **2** could lead to the formation of intermediate **5** (**2**+**3**→**5**). Then, Michael addition between **5** and **6** would give **7** (**5**+**6**→**7**). Next, the intermediate **8** would be formed by cyclocondensation and decarboxylation (**7**→**8**), in which the unusual collapse of the Meldrum's acid ring could lead to the generation of reactive ketene intermediates and the formation of a pyridine ring. Finally, the product would be produced by the intramolecular cyclization of the mercapto group attacking carbon atom linked to *ortho*-halo in phenyl ring of the intermediate **9** (the tautomer of **8**) to form a thiopyran ring (Scheme 3).



Scheme 3. A plausible mechanism of the synthesis of **4**.

3. Conclusion

In summary, we have developed an efficient and novel synthetic route to tricyclic thiochromeno[2,3-*b*]pyridine derivatives based on the three-component reaction of *ortho*-halo-β-aroylthioamides with Meldrum's acid and aromatic aldehydes. High bond forming efficiency of this reaction makes it attractive for the synthesis of thiochromeno[2,3-*b*]pyridine derivatives in a single step operation. Further investigations to expand the scope of the of *ortho*-chloro-β-aroylthioamides as versatile building blocks by the combined use of MCRs are in progress, and will be reported in due course.

4. Experimental

4.1. General

The ^{1}H and ^{13}C NMR spectra were recorded by using a Bruker AV-500 spectrometer. Chemical shifts were reported in parts per million (δ) relative to tetramethylsilane (TMS), or the residual proton resonances in the deuterated solvent: dimethylsulfoxide (DMSO) or ($CDCl_3$). IR spectra were recorded on a Nicolet 510P FT-IR spectrometer. Mass spectra were performed on a Bruker Esquire Hct or Ultima Global spectrometer with an ESI source. Elemental analyses were carried out on a Vario EL-III analyzer. The X-ray single-crystal diffraction was performed on Bruker APEX area-detector. The melting point was determined on a RY-1 microscopic melting apparatus and uncorrected. TLC analysis was performed on 0.25 mm Silica gel GF_{254} plates. All chemicals were purchased and used without further purification. *ortho*-Chloro-β-aroylthioamides were synthesized according to a previously reported procedure.[18]

4.2. General procedure for the three-component reaction

The *ortho*-halo-β-aroylthioamides (1 mmol), aromatic aldehydes (1 mmol), Meldrum's acid (1 mmol), and Et_3N (0.3 mmol) were successively added into the anhydrous ethanol (10 mL). The mixture was refluxed for the appropriate time. After completion of the reaction as indicated by TLC (petroleum ether–ethyl acetate, 4:1, v/v), the reaction mixture was cooled to room temperature. The solid product was filtered, washed with anhydrous ethanol (3×10 mL), and subsequently recrystallized from THF to give the pure products **4**.

*4.2.1. 8-Chloro-4-(2,5-dichlorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4a**)*

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 5:1); mp 247–248 °C. δ_H (500 MHz; DMSO-d_6) 2.79 (1H, d, *J*=16.0 Hz), 3.57 (1H, dd, *J*=8.0, 15.5 Hz), 5.11 (1H, d, *J*=6.5 Hz), 7.27 (1H, d, *J*=2.5 Hz, ArH), 7.33 (1H, s, ArH), 7.42 (1H, dd, *J*=3.5, 8.5 Hz, ArH), 7.55–7.65 (6H, m, ArH), 8.07 (1H, d, *J*=25.0 Hz, ArH), 8.22 (1H, d, *J*=8.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 33.7, 36.5, 115.1, 126.4, 126.8, 126.9, 128.4, 128.8, 129.1, 129.7, 129.9, 130.2, 130.4, 131.4, 132.0, 132.4, 135.3, 135.8, 137.0, 139.6, 152.9, 167.4, 176.5; IR (KBr, cm^{-1}) 1711, 1607, 1578, 1538, 1462, 1388, 1267, 1129, 821, 780, 689. Anal. Calcd for $C_{24}H_{14}Cl_3NO_2S$: C, 59.22; H, 2.90; N, 2.88. Found: C, 59.39; H, 2.91; N, 2.85. MS (ESI) *m*/*z*: 508.1 $[M+Na]^+$.

*4.2.2. 8-Chloro-4-(4-chlorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4b**)*

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 5:1); mp 231–232 °C. δ_H (500 MHz; DMSO-d_6) 2.88 (1H, d, *J*=15.0 Hz), 3.43 (1H, dd, *J*=7.5, 16.0 Hz), 4.83 (1H, d, *J*=7.0 Hz), 7.26 (1H, s, ArH), 7.35 (4H, q, *J*=8.5, 18.5 Hz, ArH), 7.47 (1H, s, ArH), 7.54–7.59 (4H, m, ArH), 7.99 (1H, d, *J*=2.0 Hz, ArH), 8.22 (1H, d, *J*=8.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 31.3, 34.5, 113.1, 122.7, 123.2, 124.7, 125.0, 125.2, 125.6, 126.2, 126.5, 126.7, 128.0, 131.4, 132.2, 133.3, 136.2, 148.0, 164.5, 172.9; IR (KBr, cm^{-1}) 1710, 1611, 1572, 1537, 1490, 1387, 1268, 1219, 1128, 829, 779, 692. Anal. Calcd for $C_{24}H_{15}Cl_2NO_2S$: C, 63.73; H, 3.34; N, 3.10. Found: C, 63.87; H, 3.30; N, 3.12.

*4.2.3. 8-Chloro-4-(2,4-dichlorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4c**)*

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 5:1); mp 243–244 °C. δ_H (500 MHz; DMSO-d_6) 2.79 (1H, d, *J*=15.0 Hz), 3.56 (1H, dd, *J*=3.0, 16.0 Hz), 5.09 (1H, d, *J*=6.5 Hz), 7.30 (1H, d, *J*=8.0 Hz, ArH), 7.39 (1H, dd, *J*=2.0, 8.5 Hz, ArH), 7.52 (2H, d, *J*=6.5 Hz, ArH), 7.59–7.64 (4H, m, ArH), 7.73 (1H, d, *J*=2.0 Hz, ArH), 8.08 (1H, d, *J*=2.0 Hz, ArH), 8.22 (1H, d, *J*=9.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 33.8, 36.8, 115.7, 126.8, 127.2, 128.5, 128.9, 129.2, 130.0, 130.1, 130.2, 130.5, 130.6, 130.7, 133.1, 134.2, 135.6, 136.2, 137.5, 153.1, 167.9, 176.8; IR (KBr, cm^{-1}) 1709, 1614, 1576, 1539, 1388, 1215, 1130, 818, 735, 692. Anal. Calcd for $C_{24}H_{14}Cl_3NO_2S$: C, 59.22; H, 2.90; N, 2.88. Found: C, 59.11; H, 2.87; N, 2.90. MS (ESI) *m*/*z*: 486.3 $[M+H]^+$.

*4.2.4. 8-Chloro-4-(3-nitrophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4d**)*

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 5:1); mp 235–236 °C. δ_H (500 MHz; DMSO-d_6) 3.00 (1H, dd, *J*=1.5, 16.5 Hz), 3.54 (1H, dd, *J*=7.5, 16.5 Hz), 5.03 (1H, d, *J*=7.0 Hz), 7.33 (1H, s, ArH), 7.54 (1H, s, ArH), 7.58–7.63 (4H, m, ArH), 7.67 (1H, t, *J*=8.0 Hz, ArH), 7.84 (1H, d, *J*=8.0 Hz, ArH), 8.06 (1H, d, *J*=2.0 Hz, ArH), 8.13 (1H, dd, *J*=2.0, 8.0 Hz, ArH), 8.21 (1H, s, ArH), 8.26 (1H, d, *J*=8.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.7, 38.4, 116.6, 121.9, 122.6, 126.9, 127.3, 128.9, 130.3, 130.6, 131.0, 134.1, 135.5, 136.2, 137.4, 143.7, 148.6, 152.5, 168.4, 177.0; IR (KBr, cm^{-1}) 1709, 1604, 1580, 1528, 1393, 1349, 1224, 833, 781, 697. Anal. Calcd for $C_{24}H_{15}ClN_2O_4S$: C, 62.27; H, 3.27; N, 6.05. Found: C, 62.13; H, 3.25; N, 6.11. MS (ESI) *m*/*z*: 463.3 $[M+H]^+$.

*4.2.5. 8-Chloro-1,4-diphenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4e**)*

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 5:1); mp 179–181 °C. δ_H (500 MHz; DMSO-d_6) 2.90 (1H, dd, *J*=1.5, 16.0 Hz), 3.40 (1H, dd, *J*=2.0, 16.0 Hz), 4.79 (1H, d, *J*=6.5 Hz), 5.98 (2H, d, *J*=5.0 Hz, ArH), 6.75 (1H, dd, *J*=1.5, 8.0 Hz, ArH), 6.85 (1H, d, *J*=8.0 Hz, ArH), 6.95 (1H, d, *J*=1.5 Hz, ArH), 7.24 (1H, s, ArH), 7.49 (1H, s, ArH), 7.55–7.62 (4H, m, ArH), 8.01 (1H, d, *J*=1.5 Hz, ArH), 8.26 (1H, d, *J*=8.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.6, 39.0, 101.5, 108.1, 108.9, 117.9, 119.7, 126.8, 127.5, 128.8, 130.4, 130.5, 135.1, 135.6, 136.5, 137.4, 146.7, 148.2, 151.8, 168.8, 177.1; IR (KBr, cm^{-1}) 1710, 1610, 1580, 1536, 1393, 1256, 1120, 833, 781, 694. Anal. Calcd for $C_{24}H_{16}ClNO_2S$: C, 68.98; H, 3.86; N, 3.35. Found: C, 69.06; H, 3.85; N, 3.37. MS (ESI) *m*/*z*: 418.2 $[M+H]^+$.

*4.2.6. 8-Chloro-4-(3,4-dimethoxyphenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4f**)*

Primrose yellow solid, R_f=0.30 (petroleum ether–ethyl acetate, 4:1); mp 226–227 °C. δ_H (500 MHz; DMSO-d_6) 2.89 (1H, d, *J*=16.0 Hz), 3.38 (1H, dd, *J*=7.5, 16.0 Hz), 3.67 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 4.78 (1H, d, *J*=6.5 Hz), 6.73 (1H, d, *J*=8.0 Hz, ArH), 6.85 (1H, d, *J*=8.5 Hz, ArH), 6.96 (1H, s, ArH), 7.23 (1H, s, ArH), 7.47 (1H, s, ArH), 7.52–7.57 (4H, m, ArH), 7.98 (1H, s, ArH), 8.22 (1H, s, ArH); δ_C (125 MHz; DMSO-d_6) 35.6, 39.0, 55.9, 56.0, 111.6, 112.3, 117.9, 118.3, 126.8, 127.4, 128.8, 129.6, 130.3, 130.5, 130.7, 131.0, 133.6, 135.6, 136.5, 137.3, 148.4, 149.5, 151.6, 169.0, 177.1; IR (KBr, cm^{-1}) 1717, 1603, 1582, 1534, 1515, 1392, 1269, 1128, 833, 782, 694. Anal. Calcd for $C_{26}H_{20}ClNO_4S$: C, 65.34; H, 4.22; N, 2.93. Found: C, 65.49; H, 4.24; N, 2.97.

*4.2.7. 8-Chloro-4-(4-methoxyphenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4g**)*

Primrose yellow solid, R_f=0.30 (petroleum ether–ethyl acetate, 4:1); mp 210–211 °C. δ_H (500 MHz; DMSO-d_6) 2.88 (1H, d,

J=16.0 Hz), 3.41 (1H, dd, J=7.0, 16.0 Hz), 3.71 (3H, s, OCH_3), 4.81 (1H, d, J=6.5 Hz), 6.90 (2H, d, J=8.5 Hz, ArH), 7.25 (3H, d, J=8.5 Hz, ArH), 7.50 (1H, s, ArH), 7.58–7.62 (4H, m, ArH), 8.02 (1H, d, J=1.5 Hz, ArH), 8.26 (1H, d, J=8.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.1, 38.9, 55.5, 114.6, 118.0, 126.8, 127.3, 128.2, 128.8, 129.6, 130.2, 130.3, 130.4, 130.6, 130.9, 133.0, 135.5, 136.4, 137.3, 151.5, 158.6, 168.8, 177.0; IR (KBr, cm^{-1}) 1712, 1608, 1582, 1539, 1391, 1269, 1120, 830, 778, 692. Anal. Calcd for $C_{25}H_{18}ClNO_3S$: C, 67.04; H, 4.05; N, 3.13. Found: C, 67.09; H, 4.04; N, 3.14. MS (ESI) m/z: 448.2 $[M+H]^+$.

4.2.8. 8-Chloro-1-phenyl-4-p-tolyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4h**)

Primrose yellow solid, R_f=0.30 (petroleum ether–ethyl acetate, 4:1); mp 223–225 °C. δ_H (500 MHz; DMSO-d_6) 2.24 (3H, s, CH_3), 2.90 (1H, d, J=16.0 Hz), 3.41 (1H, dd, J=2.0, 16.0 Hz), 4.83 (1H, d, J=7.0 Hz), 7.15 (2H, d, J=8.0 Hz, ArH), 7.22 (3H, d, J=8.0 Hz, ArH), 7.51 (1H, s, ArH), 7.58 (4H, d, J=9.5 Hz, ArH), 8.00 (1H, s, ArH), 8.24 (1H, d, J=9.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 21.0, 35.5, 38.9, 117.8, 126.7, 127.0, 127.3, 128.7, 129.6, 129.8, 130.2, 130.4, 130.6, 130.8, 135.5, 136.4, 136.5, 137.3, 138.2, 151.5, 168.7, 177.0; IR (KBr, cm^{-1}) 1713, 1607, 1571, 1536, 1269, 1218, 1129, 832, 778, 691. Anal. Calcd for $C_{25}H_{18}ClNO_2S$: C, 69.52; H, 4.20; N, 3.24. Found: C, 69.43; H, 4.16; N, 3.21.

4.2.9. 7-Chloro-4-(2,5-dichlorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4i**)

Primrose yellow solid, R_f=0.40 (petroleum ether–ethyl acetate, 4:1); mp 225–226 °C. δ_H (500 MHz; DMSO-d_6) 2.80 (1H, dd, J=1.0, 15.5 Hz), 3.58 (1H, dd, J=8.0, 16.5 Hz), 5.12 (1H, d, J=6.5 Hz), 7.20 (1H, d, J=2.5 Hz, ArH), 7.33 (1H, s, ArH), 7.43 (1H, dd, J=2.5, 8.5 Hz, ArH), 7.59–7.65 (5H, m, ArH), 7.76 (1H, dd, J=2.5, 8.5 Hz, ArH), 7.91 (1H, d, J=8.5 Hz, ArH), 8.19 (1H, d, J=2.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 33.8, 36.4, 114.9, 126.8, 126.9, 128.8, 129.1, 129.4, 129.6, 129.9, 130.2, 130.3, 131.4, 131.9, 132.0, 132.3, 132.4, 133.0, 135.8, 139.5, 153.4, 167.4, 176.1; IR (KBr, cm^{-1}) 1714, 1614, 1588, 1548, 1359, 1270, 1127, 745, 693, 616. Anal. Calcd for $C_{24}H_{14}Cl_3NO_2S$: C, 59.22; H, 2.90; N, 2.88. Found: C, 59.41; H, 2.93; N, 2.83.

4.2.10. 7-Chloro-4-(4-chlorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4j**)

Primrose yellow solid, R_f=0.30 (petroleum ether–ethyl acetate, 5:1); mp 221–222 °C. δ_H (500 MHz; $CDCl_3$) 3.15 (1H, dd, J=2.0, 16.5 Hz), 3.24 (1H, dd, J=7.0, 16.5 Hz), 5.04 (1H, d, J=6.0 Hz), 7.09 (1H, s, ArH), 7.24–7.34 (6H, m, ArH), 7.47 (1H, dd, J=2.0, 8.5 Hz, ArH), 7.54 (3H, d, J=1.5 Hz, ArH), 8.44 (1H, d, J=2.5 Hz, ArH); δ_C (125 MHz; $CDCl_3$) 35.0, 37.6, 117.9, 127.7, 128.1, 128.6, 129.1, 129.7, 130.2, 130.3, 131.8, 131.9, 133.1, 134.3, 135.8, 139.1, 151.7, 168.3, 177.3; IR (KBr, cm^{-1}) 1713, 1311, 1571, 1537, 1409, 1268, 1217, 832, 731, 694, 538. Anal. Calcd for $C_{24}H_{15}Cl_2NO_2S$: C, 63.73; H, 3.34; N, 3.10. Found: C, 63.87; H, 3.37; N, 3.12. MS (ESI) m/z: 452.4 $[M+H]^+$.

4.2.11. 7-Chloro-4-(2,4-dichlorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4k**)

Primrose yellow solid, R_f=0.32 (petroleum ether–ethyl acetate, 5:1); mp 246–247 °C. δ_H (500 MHz; DMSO-d_6) 2.80 (1H, d, J=16.0 Hz), 3.56 (1H, dd, J=2.5, 15.5 Hz), 5.11 (1H, d, J=7.0 Hz), 7.30 (1H, d, J=8.0 Hz, ArH), 7.38 (1H, d, J=7.5 Hz, ArH), 7.52 (2H, s, ArH), 7.61 (3H, s, ArH), 7.74 (2H, d, J=12.0 Hz, ArH), 7.88 (1H, d, J=8.5 Hz, ArH), 8.18 (1H, s, ArH); δ_C (125 MHz; DMSO-d_6) 33.9, 36.9, 115.6, 127.3, 128.6, 129.3, 129.8, 129.9, 130.0, 130.1, 130.3, 130.6, 130.7, 130.8, 132.5, 132.6, 133.2, 133.6, 134.2, 136.3, 137.0, 153.8, 168.0, 176.4; IR (KBr, cm^{-1}) 1719, 1608, 1539, 1537, 1405, 1264, 1211, 1129, 818, 733, 691. Anal. Calcd for $C_{24}H_{14}Cl_3NO_2S$: C, 59.22; H, 2.90; N, 2.88. Found: C, 59.07; H, 2.89; N, 2.92.

4.2.12. 7-Chloro-4-(3-nitrophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4l**)

Primrose yellow solid, R_f=0.30 (petroleum ether–ethyl acetate, 5:1); mp 234–235 °C. δ_H (500 MHz; DMSO-d_6) 3.00 (1H, dd, J=2.0, 16.5 Hz), 3.54 (1H, dd, J=7.5, 16.5 Hz), 5.04 (1H, d, J=6.5 Hz), 7.33 (1H, s, ArH), 7.54 (1H, s, ArH), 7.59 (3H, d, J=5.0 Hz, ArH), 7.67 (1H, t, J=8.0 Hz, ArH), 7.75 (1H, dd, J=2.5, 9.0 Hz, ArH), 7.84 (1H, d, J=8.0 Hz, ArH), 7.88 (1H, d, J=8.5 Hz, ArH), 8.13 (1H, d, J=8.0 Hz, ArH), 8.22 (2H, t, J=2.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.7, 38.3, 116.5, 121.9, 122.6, 127.3, 129.8, 130.0, 130.6, 130.8, 131.0, 132.4, 132.5, 133.5, 134.1, 136.3, 143.6, 148.6, 153.1, 168.4, 176.6; IR (KBr, cm^{-1}) 1713, 1610, 1580, 1538, 1393, 1359, 1224, 833, 732, 693. Anal. Calcd for $C_{24}H_{15}ClN_2O_4S$: C, 62.27; H, 3.27; N, 6.05. Found: C, 62.45; H, 3.29; N, 6.09.

4.2.13. 7-Chloro-1,4-diphenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4m**)

Primrose yellow solid, R_f=0.27 (petroleum ether–ethyl acetate, 5:1); mp 243–244 °C. δ_H (500 MHz; DMSO-d_6) 2.90 (1H, d, J=16.0 Hz), 3.43 (1H, dd, J=7.0, 16.5 Hz), 4.85 (1H, d, J=7.0 Hz), 7.20–7.23 (2H, m, ArH), 7.31 (4H, d, J=4.0 Hz, ArH), 7.48 (1H, s, ArH), 7.54 (3H, s, ArH), 7.69 (1H, dd, J=2.0, 8.5 Hz, ArH), 7.81 (1H, d, J=9.0 Hz, ArH), 8.18 (1H, d, J=2.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 36.0, 38.8, 117.5, 127.2, 127.4, 127.5, 129.4, 129.6, 129.8, 130.1, 130.2, 130.5, 130.6, 130.8, 132.3, 132.5, 133.5, 136.5, 141.3, 152.4, 168.8, 176.7; IR (KBr, cm^{-1}) 1705, 1616, 1574, 1539, 1406, 1359, 1266, 1208, 823, 718, 692, 555. Anal. Calcd for $C_{24}H_{16}ClNO_2S$: C, 68.98; H, 3.86; N, 3.35. Found: C, 68.80; H, 3.88; N, 3.39. MS (ESI) m/z: 418.2 $[M+H]^+$.

4.2.14. 7-Chloro-4-(3,4-dimethoxyphenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4n**)

Primrose yellow solid, R_f=0.25 (petroleum ether–ethyl acetate, 4:1); mp 227–228 °C. δ_H (500 MHz; DMSO-d_6) 2.94 (1H, d, J=16.0 Hz), 3.42 (1H, dd, J=7.5, 16.0 Hz), 3.71 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 4.83 (1H, d, J=6.5 Hz), 6.76 (1H, dd, J=2.0, 8.5 Hz, ArH), 6.88 (1H, d, J=8.0 Hz, ArH), 7.00 (1H, d, J=2.0 Hz, ArH), 7.27 (1H, s, ArH), 7.51 (1H, s, ArH), 7.58 (3H, d, J=5.5 Hz, ArH), 7.74 (1H, dd, J=2.0, 8.5 Hz, ArH), 7.86 (1H, d, J=9.0 Hz, ArH), 8.23 (1H, d, J=2.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 34.9, 38.4, 55.4, 55.5, 111.0, 111.7, 117.2, 117.8, 126.9, 128.8, 129.3, 129.6, 130.0, 130.3, 131.8, 132.0, 133.1, 136.0, 147.8, 148.9, 151.6, 168.5, 176.2; IR (KBr, cm^{-1}) 1711, 1605, 1535, 1517, 1405, 1267, 1217, 1135, 1028, 813, 730, 695. Anal. Calcd for $C_{26}H_{20}ClNO_4S$: C, 65.34; H, 4.22; N, 2.93. Found: C, 65.22; H, 4.20; N, 2.89. MS (ESI) m/z: 500.1 $[M+Na]^+$.

4.2.15. 7-Chloro-4-(4-methoxyphenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4o**)

Primrose yellow solid, R_f=0.20 (petroleum ether–ethyl acetate, 4:1); mp 202–203 °C. δ_H (500 MHz; DMSO-d_6) 2.90 (1H, dd, J=1.5, 16.0 Hz), 3.41 (1H, dd, J=7.0, 16.0 Hz), 3.71 (3H, s, OCH_3), 4.82 (1H, d, J=6.0 Hz), 6.91 (2H, d, J=8.5 Hz, ArH), 7.25 (3H, d, J=8.5 Hz, ArH), 7.51 (1H, s, ArH), 7.58 (3H, s, ArH), 7.72 (1H, dd, J=2.5, 8.5 Hz, ArH), 7.83 (1H, d, J=8.5 Hz, ArH), 8.21 (1H, d, J=2.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.1, 38.9, 55.5, 117.8, 127.4, 128.2, 129.6, 129.8, 130.0, 130.1, 130.5, 130.7, 130.8, 132.2, 132.5, 133.0, 133.4, 136.5, 152.1, 158.7, 168.8, 176.6; IR (KBr, cm^{-1}) 1705, 1605, 1537, 1511, 1247, 1222, 1134, 1034, 849, 735, 695. Anal. Calcd for $C_{25}H_{18}ClNO_3S$: C, 67.04; H, 4.05; N, 3.13. Found: C, 67.23; H, 4.01; N, 3.11. MS (ESI) m/z: 448.2 $[M+H]^+$.

4.2.16. 7-Chloro-1-phenyl-4-p-tolyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4p**)

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 4:1); mp 223–224 °C. δ_H (500 MHz; DMSO-d_6) 2.26 (3H, s, CH_3), 2.90 (1H, dd, J=1.5, 16.0 Hz), 3.43 (1H, dd, J=7.0, 16.0 Hz), 4.84 (1H, d, J=7.0 Hz), 7.15 (2H, d, J=8.0 Hz, ArH), 7.22 (3H, t, J=8.5 Hz, ArH),

7.50 (1H, d, J=6.0 Hz, ArH), 7.57 (3H, s, ArH), 7.74 (1H, dd, J=2.0, 8.5 Hz, ArH), 7.86 (1H, d, J=8.5 Hz, ArH), 8.22 (1H, d, J=2.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 21.0, 35.5, 117.6, 127.0, 127.4, 129.8, 130.0, 130.2, 130.5, 130.6, 130.8, 132.3, 132.5, 132.6, 133.4, 136.4, 136.5, 138.1, 152.2, 168.8, 176.6; IR (KBr, cm^{-1}) 1712, 1608, 1536, 1513, 1269, 1217, 1130, 832, 735, 695. Anal. Calcd for $C_{25}H_{18}ClNO_2S$: C, 69.52; H, 4.20; N, 3.24. Found: C, 69.37; H, 4.19; N, 3.25. MS (ESI) m/z: 432.2 $[M+H]^+$.

4.2.17. 8-Chloro-7-fluoro-4-(4-fluorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4q**)

Primrose yellow solid, R_f=0.40 (petroleum ether–ethyl acetate, 4:1); mp 219–220 °C. δ_H (500 MHz; DMSO-d_6) 2.93 (1H, d, J=16.0 Hz), 3.46 (1H, dd, J=7.5, 16.0 Hz), 4.87 (1H, d, J=7.0 Hz), 7.17 (2H, t, J=9.0 Hz, ArH), 7.28 (1H, s, ArH), 7.37–7.40 (2H, m, ArH), 7.51 (1H, s, ArH), 7.59 (3H, s, ArH), 8.12 (1H, d, J=9.5 Hz, ArH), 8.29 (1H, d, J=6.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.3, 38.8, 115.0, 115.2, 116.0, 116.2, 117.0, 125.3, 125.4, 129.1, 129.2, 129.5, 130.0, 130.6, 136.4, 137.3, 152.7, 156.0, 158.0, 160.7, 162.6, 168.7, 176.4; IR (KBr, cm^{-1}) 1712, 1611, 1593, 1540, 1404, 1221, 1143, 833, 621, 535. Anal. Calcd for $C_{24}H_{14}ClF_2NO_2S$: C, 63.51; H, 3.11; N, 3.09. Found: C, 63.41; H, 3.15; N, 3.07.

4.2.18. 8-Chloro-7-fluoro-4-(3-fluorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4r**)

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 4:1); mp 191–192 °C. δ_H (500 MHz; DMSO-d_6) 2.98 (1H, d, J=16.0 Hz), 3.47 (1H, dd, J=7.0, 16.0 Hz), 4.89 (1H, d, J=7.0 Hz), 7.09 (1H, t, J=8.5 Hz, ArH), 7.16–7.25 (3H, m, ArH), 7.40 (1H, q, J=7.5, 14.5 Hz, ArH), 7.51 (1H, s, ArH), 7.59 (3H, s, ArH), 8.10 (1H, d, J=10.0 Hz, ArH), 8.27 (1H, d, J=6.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.7, 38.5, 114.4, 115.0, 115.2, 116.5, 123.0, 125.3, 125.4, 129.4, 129.9, 130.3, 130.7, 131.4, 136.3, 144.2, 152.9, 156.0, 158.0, 162.0, 163.9, 168.6, 176.4; IR (KBr, cm^{-1}) 1723, 1610, 1590, 1537, 1407, 1247, 1204, 739, 693. Anal. Calcd for $C_{24}H_{14}ClF_2NO_2S$: C, 63.51; H, 3.11; N, 3.09. Found: C, 63.70; H, 3.15; N, 3.13.

4.2.19. 8-Chloro-7-fluoro-4-(2-fluorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4s**)

Primrose yellow solid, R_f=0.40 (petroleum ether–ethyl acetate, 4:1); mp 217–218 °C. δ_H (500 MHz; DMSO-d_6) 2.78 (1H, dd, J=1.0, 16.0 Hz), 3.54 (1H, dd, J=8.0, 16.0 Hz), 5.06 (1H, d, J=7.0 Hz), 7.17 (1H, t, J=7.5 Hz, ArH), 7.24–7.29 (2H, m, ArH), 7.31–7.36 (1H, m, ArH), 7.42 (1H, d, J=4.5 Hz, ArH), 7.53 (1H, s, ArH), 7.57–7.63 (3H, m, ArH), 8.07 (1H, d, J=10.0 Hz, ArH), 8.30 (1H, d, J=6.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 31.0, 37.7, 115.0, 116.3, 116.5, 125.5, 127.7, 127.8, 128.5, 129.2, 129.3, 129.8, 129.9, 130.6, 130.7, 136.4, 153.4, 156.0, 158.0, 159.8, 161.8, 168.2, 176.2; IR (KBr, cm^{-1}) 1714, 1612, 1541, 1403, 1223, 1147, 750, 728, 691, 542. Anal. Calcd for $C_{24}H_{14}ClF_2NO_2S$: C, 63.51; H, 3.11; N, 3.09. Found: C, 63.35; H, 3.07; N, 3.12.

4.2.20. 8-Chloro-7-fluoro-1,4-diphenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4t**)

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 4:1); mp 203–204 °C. δ_H (500 MHz; DMSO-d_6) 2.93 (1H, dd, J=2.0, 16.0 Hz), 3.47 (1H, dd, J=7.0, 16.0 Hz), 4.88 (1H, d, J=5.5 Hz), 7.24–7.27 (2H, m, ArH), 7.35 (4H, t, J=3.0 Hz, ArH), 7.51 (1H, s, ArH), 7.59 (3H, s, ArH), 8.10 (1H, d, J=10.0 Hz, ArH), 8.28 (1H, d, J=6.5 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.9, 38.8, 115.0, 115.2, 117.0, 125.2, 125.4, 127.2, 127.5, 129.4, 129.6, 129.7, 130.0, 130.2, 130.6, 136.4, 141.2, 152.5, 156.0, 158.0, 168.7, 176.4; IR (KBr, cm^{-1}) 1716, 1614, 1593, 1539, 1406, 1219, 1143, 728, 694. Anal. Calcd for $C_{24}H_{15}ClFNO_2S$: C, 66.13; H, 3.47; N, 3.21. Found: C, 66.37; H, 3.52; N, 3.17.

4.2.21. 8-Chloro-7-fluoro-4-(4-methoxyphenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4u**)

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 4:1); mp 252–253 °C. δ_H (500 MHz; DMSO-d_6) 2.89 (1H, dd, J=1.5, 16.0 Hz), 3.42 (1H, dd, J=7.5, 16.5 Hz), 3.72 (3H, s, OCH_3), 4.82 (1H, d, J=6.0 Hz), 6.91 (2H, d, J=8.5 Hz, ArH), 7.25 (3H, d, J=8.5 Hz, ArH), 7.51 (1H, s, ArH), 7.51–7.64 (3H, m, ArH), 8.11 (1H, d, J=9.5 Hz, ArH), 8.28 (1H, d, J=7.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.1, 38.9, 55.5, 114.6, 115.0, 115.1, 117.3, 125.1, 125.3, 128.2, 129.3, 129.9, 130.1, 130.5, 130.8, 132.9, 136.4, 152.2, 156.0, 158.0, 158.6, 168.8, 176.3; IR (KBr, cm^{-1}) 1713, 1608, 1592, 1540, 1406, 1247, 1217, 831, 729, 692. Anal. Calcd for $C_{25}H_{17}ClFNO_3S$: C, 64.45; H, 3.68; N, 3.01. Found: C, 64.18; H, 3.65; N, 2.96.

4.2.22. 4-(2,5-Dichlorophenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4v**)

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 4:1); mp 249–250 °C. δ_H (500 MHz; DMSO-d_6) 2.79 (1H, dd, J=1.5, 16.0 Hz), 3.57 (1H, dd, J=7.5, 16.0 Hz), 5.13 (1H, d, J=6.0 Hz), 7.24 (1H, d, J=2.5 Hz, ArH), 7.32 (1H, s, ArH), 7.42 (1H, dd, J=2.5, 9.0 Hz, ArH), 7.58–7.69 (7H, m, ArH), 7.79 (1H, d, J=8.0 Hz, ArH), 8.26 (1H, dd, J=1.0, 8.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 34.2, 36.9, 115.4, 127.3, 127.6, 128.2, 128.5, 128.6, 129.2, 129.5, 130.3, 130.6, 130.8, 131.9, 132.5, 132.8, 133.9, 136.3, 140.2, 153.3, 167.9, 177.6; IR (KBr, cm^{-1}) 1716, 1613, 1588, 1543, 1365, 1270, 1208, 818, 748, 692. Anal. Calcd for $C_{24}H_{15}Cl_2NO_2S$: C, 63.72; H, 3.34; N, 3.10. Found: C, 63.51; H, 3.37; N, 3.08.

4.2.23. 4-(4-Methoxyphenyl)-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4w**)

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 4:1); mp 179–181 °C. δ_H (500 MHz; DMSO-d_6) 2.89 (1H, d, J=15.5 Hz), 3.42 (1H, dd, J=7.5, 16.5 Hz), 3.71 (3H, s, OCH_3), 4.85 (1H, d, J=7.0 Hz), 6.91 (2H, d, J=8.5 Hz, ArH), 7.27 (3H, d, J=8.5 Hz, ArH), 7.51–7.65 (6H, m, ArH), 7.72 (d, 1H, J=8.0 Hz, ArH), 8.30 (d, 1H, J=8.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.2, 39.1, 55.5, 114.7, 118.0, 127.5, 128.2, 128.3, 128.4, 128.7, 129.7, 130.1, 130.4, 130.6, 130.9, 132.3, 133.3, 133.8, 136.7, 151.5, 158.7, 168.9, 177.7; IR (KBr, cm^{-1}) 1707, 1609, 1590, 1543, 1361, 1247, 1224, 745, 692, 546. Anal. Calcd for $C_{25}H_{19}NO_3S$: C, 72.62; H, 4.63; N, 3.39. Found: C, 72.83; H, 4.67; N, 3.25.

4.2.24. 4-(2,5-Dichlorophenyl)-8-fluoro-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4x**)

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 4:1); mp 224–225 °C. δ_H (500 MHz; DMSO-d_6) 2.78 (1H, dd, J=1.5, 16.5 Hz), 3.56 (1H, dd, J=7.5, 16.0 Hz), 5.11 (1H, d, J=6.5 Hz), 7.27 (1H, d, J=2.5 Hz, ArH), 7.34 (1H, s, ArH), 7.41–7.47 (2H, m, ArH), 7.55 (1H, s, ArH), 7.58–7.86 (4H, m, ArH), 7.85 (1H, dd, J=2.5, 9.5 Hz, ArH), 830 (1H, dd, J=6.0, 9.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 34.2, 37.0, 113.6, 115.4, 116.8, 125.6, 127.4, 129.3, 129.5, 130.4, 130.7, 131.5, 131.6, 131.9, 132.5, 132.8, 136.2, 136.4, 140.1, 153.1, 162.8, 164.6, 167.6, 176.6; IR (KBr, cm^{-1}) 1717, 1614, 1588, 1544, 1270, 1203, 781, 744, 693. Anal. Calcd for $C_{24}H_{14}Cl_2FNO_2S$: C, 61.29; H, 3.00; N, 2.98. Found: C, 61.58; H, 3.02; N, 3.00.

4.2.25. 4-(4-Chlorophenyl)-8-fluoro-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4y**)

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 4:1); mp 190–191 °C. δ_H (500 MHz; DMSO-d_6) 2.92 (1H, d, J=15.0 Hz), 3.45 (1H, dd, J=7.5, 16.5 Hz), 4.87 (1H, d, J=6.5 Hz), 7.29 (1H, s, ArH), 7.36–7.43 (5H, m, ArH), 7.50 (1H, s, ArH), 7.57 (3H, s, ArH), 7.78 (1H, dd, J=2.0, 9.0 Hz, ArH), 8.33 (1H, q, J=6.0, 9.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.3, 38.6, 113.5, 113.7, 116.7, 117.0, 125.5, 129.1, 129.2, 129.7, 130.1, 130.5, 130.8, 131.6, 132.0, 136.0, 136.1, 136.3, 140.3, 151.8, 162.7, 164.7, 168.5, 176.9; IR (KBr, cm^{-1}) 1719,

1616, 1592, 1543, 1365, 1217, 1124, 740, 694, 610. Anal. Calcd for $C_{24}H_{15}ClFNO_2S$: C, 66.13; H, 3.47; N, 3.21. Found: C, 66.56; H, 3.43; N, 3.14.

*4.2.26. 4-(3,4-Dimethoxyphenyl)-8-fluoro-1-phenyl-3,4-dihydro-1H-thiochromeno[2,3-b]pyridine-2,5-dione (**4z**)*

Primrose yellow solid, R_f=0.35 (petroleum ether–ethyl acetate, 4:1); mp 187–188 °C. δ_H (500 MHz; DMSO-d_6) 2.93 (1H, dd, J=1.5, 16.0 Hz), 3.40 (1H, dd, J=7.5, 16.0 Hz), 3.70 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 4.82 (1H, d, J=6.5 Hz), 6.77 (1H, dd, J=2.5, 8.0 Hz, ArH), 6.88 (1H, d, J=8.5 Hz, ArH), 7.00 (1H, d, J=2.0 Hz, ArH), 7.41 (1H, d, J=2.5 Hz, ArH), 7.43 (1H, d, J=2.5 Hz, ArH), 7.44 (1H, d, J=2.0 Hz), 7.55–7.60 (3H, m, ArH), 7.80 (1H, dd, J=2.0, 9.5 Hz, ArH), 8.34 (1H, dd, J=6.0, 9.0 Hz, ArH); δ_C (125 MHz; DMSO-d_6) 35.5, 38.3, 55.9, 56.0, 111.6, 112.4, 113.7, 116.7, 117.7, 118.3, 125.7, 129.6, 130.4, 131.6, 133.7, 136.1, 136.5, 148.3, 149.5, 151.3, 162.7, 164.7, 168.9, 176.9; IR (KBr, cm^{-1}) 1715, 1614, 1591, 1545, 1369, 1252, 1204, 1026, 931, 744, 695, 609. Anal. Calcd for $C_{26}H_{20}FNO_4S$: C, 67.67; H, 4.37; N, 3.04. Found: C, 67.85; H, 4.34; N, 2.98.

Acknowledgements

This investigation has enjoyed financial support from the National Natural Science Foundation of China (No. 20572057 and 20872074), Natural Science Foundation of Shandong Province (No. Y2006B11), and the Doctoral Foundation of Qingdao University of Science and Technology.

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