JOC The Journal of Organic Chemistry

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Synthesis of 2,3-Dihydrothieno(2,3-*b*)quinolines and Thieno(2,3-*b*)-quinolines via an Unexpected Domino Aza-MBH/Alkylation/Aldol Reaction

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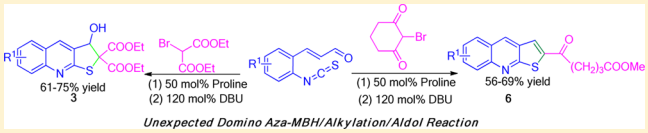
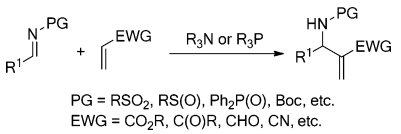
Supporting Information

ABSTRACT: An efficient, mild, and convenient method for the preparation of 2,3-dihydrothieno(2,3-*b*)quinolines and thieno(2,3-*b*)-quinolines via an unexpected domino aza-Morita–Baylis–Hillman/alkylation/aldol reaction has been developed. The plausible mechanisms for the unexpected reaction are also given.



Developing novel synthetic methods that require a minimum number of operations for the construction of new analogues of bioactive heterocyclic compounds represents a major challenge in synthetic organic and medicinal chemistries. Quinoline derivatives are unique nitrogen-containing heterocycles that have attracted particular attention due to their special place as building blocks in natural products, pharmaceutical agents, and materials.[1−3] Quinoline derivatives have also been used as organocatalysts for asymmetric synthesis.[4] Thus, a variety of methods are known in the literature for the synthesis of these interesting scaffolds, which include named reactions such as Friedländer,[5] Combes,[6] and Conrad–Limpach–Knorr syntheses.[7] Quinoline derivatives are often obtained via condensation, Michael addition, or nucleophilic substitution in these named reactions. However, these methods usually lack tolerated functional groups. Recently, many new metal-catalyzed protocols for preparing quinolines have been developed.[8] Among of these quinoline derivatives, dihydrothieno(2,3-*b*)quinolines, which contain both quinoline and thiophene rings, are heterocyclic ring systems of considerable interest due to several biological and pharmaceutical activities that are associated with this scaffold. In addition, some analogues have been found to act as effective pharmaceutical and biological agents.[9,10] As such, we reasoned that the incorporation of a thiophene heterocyclic unit into quinolines in one pot might provide new compounds that have important biological and pharmaceutical activities. In view of the importance of this class of molecules as well as the lack of generality and efficiency to access these important synthetic targets, the development of a novel metal-free and efficient methodology for the synthesis of dihydrothieno(2,3-*b*)-quinolines is still in demand. Being atom-efficient and able to generate functional groups, the aza-Morita–Baylis–Hillman (AMBH) reaction between an α,β-unsaturated carbonyl compound and an imine is recognized as one of the most fruitful carbon–carbon bond-forming processes (Scheme 1).[11] In addition, it affords highly functionalized β-amino carbonyl compounds, which are widely used for the synthesis of biologically active compounds, medicinal reagents, and natural products.[12] The AMBH reaction is often catalyzed by Lewis bases, such as a tertiary amine or tertiary phosphine (Scheme 1), and only a few examples of the use of chiral secondary amines for this reaction have been reported.[13] In this study, we report an unexpected domino AMBH/alkylation/aldol reaction of *o*-isothiocyanato-(*E*)-cinnamaldehydes with α-halocarbonyl compounds, catalyzed by commercially available, low-cost secondary amine L-proline, and demonstrate the direct application of this reaction in the syntheses of 2,3-dihydrothieno(2,3-*b*)quinolines and thieno(2,3-*b*)quinolines.

Scheme 1. Aza-Morita–Baylis–Hillman (AMBH) Reaction



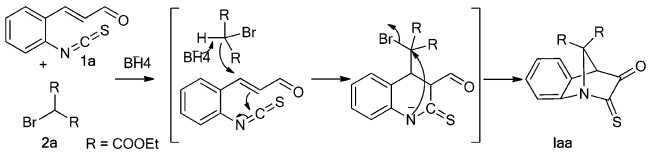
Recently, we demonstrated that α-halocarbonyl and 2-halo-1,3-dicarbonyl compounds are readily available and attractive precursors for the construction of heterocycles via domino reactions.[14] We envisioned that multifunctionalized quinoline derivative **Iaa** would be obtained by the domino reaction of diethyl α-bromomalonate **2a** with *o*-isothiocyanato-(*E*)-cinnamaldehyde **1a**, as outlined in Scheme 2.

To explore the domino reaction, *o*-isothiocyanato-(*E*)-cinnamaldehyde (**1a**) and diethyl α-bromomalonate (**2a**) were first chosen for the initial screening. The model reaction was carried out in the presence of $NaHCO_3$ in THF at room temperature for 24 h (Table 1, entry 1). However, the inorganic base was inert in this reaction. A similar result was obtained in the presence of other inorganic bases, such as Na_2CO_3 (entry 2). Subsequently, a series of organic bases, such

Received: October 13, 2015
Published: January 7, 2016

DOI: 10.1021/acs.joc.5b02369
J. Org. Chem. 2016, 81, 1216–1222

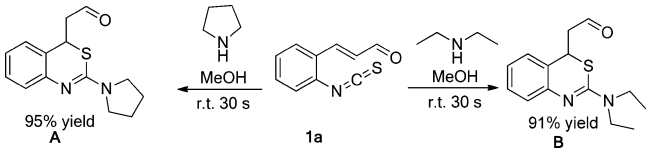
Scheme 2. Potential Strategies for the Domino Reaction of *o*-Isothiocyanato-(*E*)-cinnamaldehyde 1a with α-Bromomalonate 2a



as TEA, DABCO, and DBU, was also screened. To our surprise, no reaction occurred when the reaction was catalyzed by these tertiary amines (entries 3−5). To our delight, the domino reaction proceeded smoothly when the reaction was carried out in the presence of secondary amine L-proline in THF at room temperature for 24 h (Table 1, entry 6). Interestingly, although it was not what we expected, the unexpected functionalized 2,3-dihydrothieno(2,3-*b*)quinoline **3aa** was obtained. Then, we investigated the effect of solvent on the reactivity for this unexpected reaction when L-proline was used as the catalyst. Among the solvents examined, the use of methanol gave the best result (entry 7). Low yields were obtained when DCM or toluene was used as the solvent (entries 8 and 10). Only trace product **3aa** was observed when the reaction was carried out in the presence of L-proline in water at room temperature for 24 h due to the low solubility of **2a** in water (entry 11). Interestingly, clean product **3aa** was obtained in good yield when DBU was added, and the reaction time was decreased (entry 12). It is worthy of note here that product **3aa** (entries 13 and 14) was not isolated but that 4*H*-3,1-benzothiazine derivatives **A** and **B** (Scheme 3) were isolated in high yields within 30 s when L-proline was replaced with other secondary amines, such as pyrrolidine and diethyl amine. Obviously, the secondary amines first attacked the isothiocyanate to yield the corresponding thiourea intermediates, followed by 1,4-conjugate addition to give the corresponding products.[15] On the basis of the above screening results, the optimal reaction conditions were established (entry 12): 0.10 mmol of **1a**, 0.12 mmol of **2a**, and 50 mol % L-proline in methanol for 2 h at room temperaturel then, 120 mol % of DBU was added, and the reactions were stirred for 1 h.

With the optimal reaction conditions in hand, the scope of the domino reaction of 2-halo-1,3-dicarbonyl compounds **2** with *o*-isothiocyanato-(*E*)-cinnamaldehydes **1** was explored; the results are summarized in Table 2. The scope of the domino

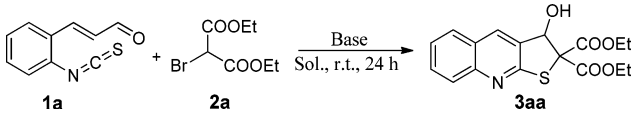
Scheme 3. Preparation of 4*H*-3,1-Benzothiazine Derivatives



reaction was shown to be quite broad with respect to *o*-isothiocyanato-(*E*)-cinnamaldehydes **1**. The novel transformations proceeded smoothly, giving the substituted quinoline derivative in good yields. It appeared that the electronics of the substituents of *o*-isothiocyanato-(*E*)-cinnamaldehydes **1** had a little effect on the efficiency of the domino reactions. Good yields were obtained in the domino reactions of **2a** when there was an electron-donating substituent on the aryl ring of *o*-isothiocyanato-(*E*)-cinnamaldehydes **1** (Table 2, entries 4−7). On the contrary, an electron-withdrawing substituent on the aryl ring of *o*-isothiocyanato-(*E*)-cinnamaldehydes tended to decrease the yield (Table 2, entries 2, 3, 8, and 9). A good yield was also achieved when -OEt (R^2) was replaced with a methyl group, although the diastereoselectivity was poor (entry 10). In addition, only racemic compounds **3** were observed when the reactions were catalyzed by L-proline/DBU in methanol (entry 1). A good result was also obtained when the reaction was scaled up by 30-fold in comparison with the reaction shown in Table 2, entry 1 (cf. entry 11). The structure of products **3** was also established by a single-crystal X-ray diffraction study of compounds **3ca** and **3da** (Figure S1).

To extend the scope of the domino reaction further, other acyclic α-halocarbonyl compounds **2c−2g** were utilized as substrates in the reaction with *o*-isothiocyanato-(*E*)-cinnamaldehydes **1a** in the presence of L-proline/DBU (Table 3). Aside from obtaining the desired product 2,3-dihydrothieno(2,3-*b*)quinoline **3ac** in good yield, thieno[2,3-*b*]quinoline **6ac** was also obtained in 16% yield under the optimal reaction conditions (entry 1). Apparently the expected domino reactions and a further deacecylation occurred to generate the observed thieno[2,3-*b*]quinoline **6ac**. When the loading of the base DBU was increased, only thieno[2,3-*b*]quinoline **6ac** was obtained (entry 2). On the other hand, although low reactivity was observed for other α-halocarbonyl compounds **2d−2g**, the domino reactions also proceeded smoothly under the optimal reaction conditions due to weak steric hindrance effects and the highly reactive aldehyde group (entries 4−7). For example,

Table 1. Reaction of *o*-Isothiocyanato-(*E*)-cinnamaldehyde 1a and α-Bromomalonate 2a under Different Conditions[a]

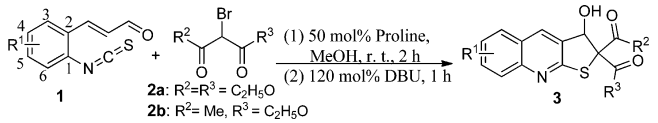


entry	sol.	base	yield (%)[b]	entry	sol.	base	yield (%)[b]
1	THF	$NaHCO_3$		8	DCM	L-proline	21
2	THF	Na_2CO_3		9	acetone	L-proline	trace
3	THF	Et_3N		10	toluene	L-proline	36
4	THF	DABCO		11	H_2O	L-proline	trace
5	THF	DBU		12[c]	Methanol	L-proline/DBU	75
6	THF	L-proline	39	13	methanol	pyrrolidine	
7	methanol	L-proline	73	14	methanol	Et_2NH	

[a]Unless otherwise noted, reactions were performed with 0.10 mmol of **1a**, 0.12 mmol of **2a**, and 50 mol % base in solvent (1.0 mL) at room temperature for 24 h. [b]Isolated yields. [c]The reactions were performed with 0.10 mmol of **1a**, 0.12 mmol of **2a**, and 50 mol % L-proline in methanol for 2 h at room temperature; then, 120 mol % of DBU was added, and the reactions were stirred for 1 h.

DOI: 10.1021/acs.joc.5b02369
J. Org. Chem. 2016, 81, 1216−1222

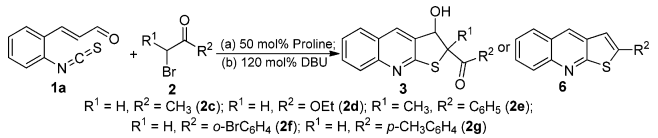
Table 2. Scope of the Domino Reaction of *o*-Isothiocyanato-(*E*)-cinnamaldehydes 1 with 2-Halo-1,3-dicarbonyl Compounds 2[a]



entry	R^1	(1)	2	3/yield (%)[b]	entry	R^1	(1)	2	3/yield (%)[b]
1[c]	H	(**1a**)	**2a**	**3aa**/75	7	4-OCH_3	(**1g**)	**2a**	**3ga**/73
2	3-Br	(**1b**)	**2a**	**3ba**/61	8	3-NO_2	(**1h**)	**2a**	**3ha**/64
3	4-Br	(**1c**)	**2a**	**3ca**/56	9	4-CI	(**1i**)	**2a**	**3ia**/62
4	4-CH_3	(**1d**)	**2a**	**3da**/71	10	H	(**1a**)	**2a**	**3ab**/80
5	5-CH_3	(**1e**)	**2a**	**3ea**/66					(69:31 dr)
6	4-OH	(**1f**)	**2a**	**3fa**/70	11[d]	H	(**1a**)	**2a**	**3aa**/79

[a]Unless otherwise noted, reactions were performed with 0.10 mmol of **1**, 0.12 mmol of **2**, and 50 mol % of L-proline in methanol (1.0 mL) at room temperature for 2 h; then, 120 mol % of DBU was added, and the reactions were stirred for 1 h. [b]Isolated yields. [c]Enantiomeric excess (ee) = 0 (determined by chiral HPLC analysis; see the Supporting Information). [d]The reaction was scaled up by 30-fold.

Table 3. Domino Reaction of *o*-Isothiocyanato-(*E*)-cinnamaldehyde 1a with *α*-Halocarbonyl Compounds[a]



R^1 = H, R^2 = CH_3 (**2c**); R^1 = H, R^2 = OEt (**2d**); R^1 = CH_3, R^2 = C_6H_5 (**2e**); R^1 = H, R^2 = *o*-BrC_6H_4 (**2f**); R^1 = H, R^2 = *p*-$CH_3C_6H_4$ (**2g**)

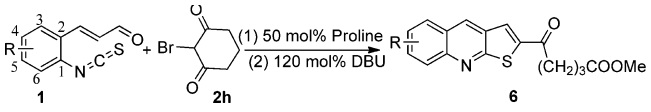
Entry	2	3/Yield (%)[b]	Entry	2	3/Yield (%)[b]
1[c]	**2c**	**3ac** 71	5	**2e**	**3ae** 55 60:40dr
2[d]	**2c**	**6ac** 82	6	**2f**	**6af** 84
3[d]	**2d**	**6ad** 82	7	**2g**	**6ag** 68
4[e]	**2d**	**5ad** 69			

[a]Unless otherwise noted, reactions were performed with 0.10 mmol of **1**, 0.12 mmol of **2**, and 50 mol % of L-proline in methanol (1.0 mL) at room temperature for 2 h; then, 120 mol % of DBU was added, and the reactions were stirred for 1 h. [b]Isolated yields. [c]16% yield of **6ac** was also isolated. [d]200 mol % of DBU was added. [e]18% yield of **6ad** was also isolated.

quinoline derivative **5ad** was obtained as a main product when ethyl bromoacetate reacted with *o*-isothiocyanato-(*E*)-cinnamaldehyde **1a** under the optimal reaction conditions (entry 4). When the loading of DBU was increased, only thieno[2,3-*b*]quinoline **6ad** was observed (entry 3). Interestingly, under the same conditions as above, for acyclic *β*-phenyl *α*-halocarbonyl compounds **2e**–**2g**, 2,3-dihydrothieno(2,3-*b*)-quinoline derivative **3ae** and thieno[2,3-*b*]quinolines derivatives **6af**–**6ag** were isolated, respectively (entries 5–7). However, the diastereoselectivity of **3ae** was poor (entry 5).

What would happen if cyclic *α*-halocarbonyl compounds (e.g., 2-bromocyclohexane-1,3-dione **2h**) were used in this domino reaction? To address this, we next turned our attention to the domino reaction of *o*-isothiocyanato-(*E*)-cinnamaldehyde **1a** with 2-bromocyclohexane-1,3-dione **2h**. To our surprise, unexpected ring-opening products thieno[2,3-*b*]-quinolines **6** were isolated in good yields (Table 4). After the unexpected reactions of 2-bromocyclohexane-1,3-dione **2h** were investigated, more experiments were conducted to test the substrate scope of the domino process and to gain further insight with regard to the possible reaction mechanism. The

Table 4. Scope of the Domino Reaction of *o*-Isothiocyanato-(*E*)-cinnamaldehydes 1 with 2-Bromocyclohexane-1,3-dione 2h[a]



entry	R	(1)	6/yield (%)[b]	entry	R	(1)	6/yield (%)[b]
1	H	(**1a**)	**6ah**/68	4	5-CH_3	(**1e**)	**6eh**/69
2	4-Br	(**1c**)	**6ch**/59	5	4-CI	(**1i**)	**6ih**/56
3	4-CH_3	(**1d**)	**6dh**/61				

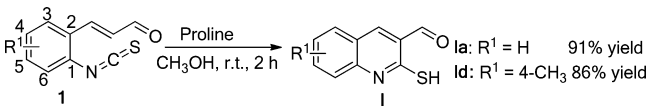
[a]Unless otherwise noted, reactions were performed with 0.10 mmol of **1** and 50 mol % of L-proline in methanol (1.0 mL) at room temperature for 2 h; then, 0.12 mmol of **2** and 100 mol % of DBU were added, and the reactions were stirred at 35 °C for 5 h. [b]Isolated yields.

electronic effect was also very marginal, and good yields were achieved for substrates **1** (Table 4, entries 2–5).

DOI: 10.1021/acs.joc.5b02369
J. Org. Chem. 2016, 81, 1216–1222

A control experiment was conducted to gain some insight into the mechanism of the domino reaction (Scheme 4).

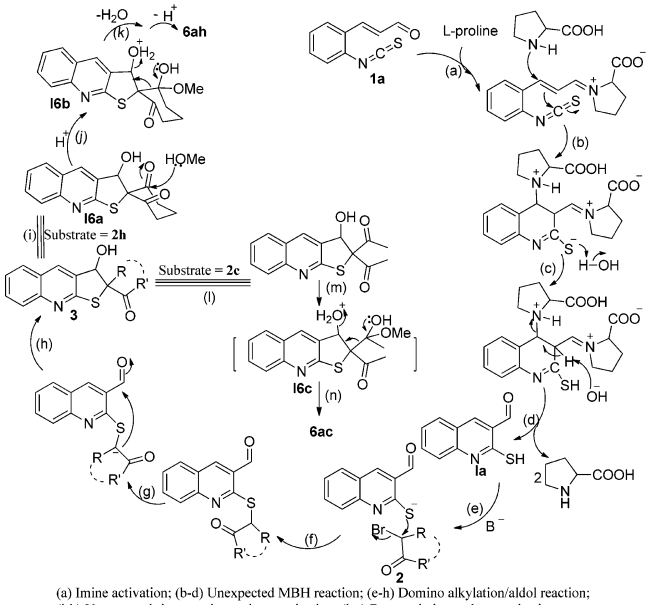
Scheme 4. Control Experiments



Quinoline derivatives **Ia** and **Id** were obtained in high yields when *o*-isothiocyanato-(*E*)-cinnamaldehydes **1** were stirred in the presence of L-proline in methanol at room temperature for 2 h.

On the basis of the experimental observations, a possible mechanism was proposed to explain the domino reaction. As outlined in Scheme 5, an intramolecular AMBH reaction

Scheme 5. Proposed Mechanisms



(a) Imine activation; (b-d) Unexpected MBH reaction; (e-h) Domino alkylation/aldol reaction; (i-k) Unexpected ring opening and aromatization; (l-n) Deacecylation and aromatization

occurred (a–d). L-Proline is an effective catalyst for the formation of iminium **I** with *o*-isothiocyanato-(*E*)-cinnamaldehyde **1a** (a). Following the addition of L-proline to the activated alkene, the in situ generated nucleophile adds to R–N=C=S, and subsequent elimination of L-proline leads to quinoline derivative **Ia** (b–d). After that, a domino alkylation/aldol reaction proceeds to produce 2,3-dihydrothieno(2,3-*b*)-quinoline derivatives **3** (e–h). Intermediate **I6a** was formed when *o*-isothiocyanato-(*E*)-cinnamaldehyde **1a** reacted with 2-bromocyclohexane-1,3-dione **2h** (i), followed by formation of hemiketal **I6b** (j). Unstable hemiketal **I6b** was protonated, and unexpected ring opening, aromatization, and elimination of an H_2O molecule took place to form product **6ah** (k). A similar reaction mechanism provided product **6ac** (l–n). However, the real reaction mechanism still remains to be explored.

In summary, we have developed an unexpected domino AMBH/alkylation/aldol reaction of *o*-isothiocyanato-(*E*)-cinnamaldehydes with α-halocarbonyl compounds, catalyzed by commercially available, low-cost secondary amine L-proline, and demonstrate the direct application of this reaction in the syntheses of 2,3-dihydrothieno(2,3-*b*)quinolines and thieno-(2,3-*b*)quinolines. The scope of the reaction was quite broad, and moderate to good yields were achieved. Notably, when the domino AMBH/alkylation/aldol reaction of *o*-isothiocyanato-(*E*)-cinnamaldehyde **1** with 2-bromocyclohexane-1,3-dione **2h** was performed, an unexpected ring-opening occurred, forming thieno(2,3-*b*)quinolines **6ah–6ih**. A plausible mechanism for this unprecedented domino AMBH/alkylation/aldol/ring-opening reaction is also given.

EXPERIMENTAL SECTION

General Methods. NMR spectra were recorded with tetramethylsilane as the internal standard. TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (150–200 mesh) eluting with ethyl acetate and petroleum ether. All NMR spectra were recorded on a 600 or 400 MHz instrument. Chemical shifts (δ) are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) or DMSO (δ = 2.50 ppm) for ^1H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) or DMSO resonance (δ = 39.5 ppm) for ^{13}C NMR spectroscopy. Coupling constants (*J*) are given in hertz. ESI-HRMS was measured with an ion trap mass spectrometer. *o*-Isothiocyanato-(*E*)-cinnamaldehydes **1** were prepared according to literature procedures.[16]

General Procedure for Synthesis of *o*-Isothiocyanato-(*E*)-cinnamaldehydes. A flask was charged with 6.25 mL (6.84 g, 0.053 mol) of quinoline, 25 mL of dichloromethane, 5.5 g (0.055 mol) of finely powdered calcium carbonate, and 25 mL of water. The mixture was stirred vigorously, cooled to 10 °C, and maintained at 10–15 °C; a solution of 3.75 mL (5.65 g, 0.049 mol) of thiophosgene in 12 mL of dichloromethane was added over 15 min. The cooling bath was removed, and the reaction mixture was stirred vigorously at ambient temperature overnight. The reaction was then filtered. The layers were separated, and the aqueous layer was extracted with 10 mL of dichloromethane. The combined organic layers were washed twice with 15 mL of 2 N hydrochloric acid and then with 15 mL of water and dried over anhydrous magnesium sulfate. Concentration under reduced pressure gave crude products. The crude products were dissolved with heating in 40 mL of cyclohexane, decolorizing carbon was added, and the mixture was filtered. The filtrate was heated under reflux for 1 h and allowed to cool with stirring. The resulting solid was isolated by filtration, washed with cyclohexane, and dried in a vacuum oven at 40 °C to give ~8.1 g (87% yield) of *o*-isothiocyanato-(*E*)-cinnamaldehyde.

*o-Isothiocyanato-(E)-cinnamaldehyde (**1a**).* The spectra are in accord with the literature.[16] ^1H NMR (600 MHz, $CDCl_3$) δ 9.76 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 16.0 Hz, 1H), 7.65 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.44 (td, *J* = 8.1, 1.4 Hz, 1H), 7.39–7.31 (m, 2H), 6.75 (dd, *J* = 16.0, 7.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.4, 146.0, 139.2, 132.1, 131.3, 130.5, 129.6, 128.2, 127.6, 127.5.

*3-(2-Bromo-6-isothiocyanatophenyl)acrylaldehyde (**1b**).* The spectra are in accord with the literature.[16] ^1H NMR (600 MHz, $CDCl_3$) δ 9.77 (d, *J* = 7.5 Hz, 1H), 7.65–7.52 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 6.89 (dd, *J* = 16.3, 7.5 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.5, 146.4, 139.9, 135.0, 132.0, 131.3, 131.3, 129.6, 127.9, 125.5.

*3-(5-Bromo-2-isothiocyanatophenyl)acrylaldehyde (**1c**).* The spectra are in accord with the literature.[16] ^1H NMR (600 MHz, $CDCl_3$) δ 9.77 (d, *J* = 7.5 Hz, 1H), 7.75 (d, *J* = 2.2 Hz, 1H), 7.65 (d, *J* = 16.0 Hz, 1H), 7.53 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.24 (d, *J* = 8.5 Hz, 1H), 6.72 (dd, *J* = 16.0, 7.5 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.9, 144.3, 140.4, 134.8, 131.3, 131.2, 130.3, 130.2, 129.5, 121.0.

*3-(2-Isothiocyanato-5-methylphenyl)acrylaldehyde (**1d**).* The spectra are in accord with the literature.[16] ^1H NMR (600 MHz, $CDCl_3$) δ 9.74 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 16.0 Hz, 1H), 7.43 (s, 1H), 7.24 (d, *J* = 1.1 Hz, 2H), 6.72 (dd, *J* = 16.0, 7.6 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.4, 146.1, 138.4, 137.8, 133.0, 130.3, 129.3, 128.6, 127.9, 127.7, 21.2.

*3-(2-Isothiocyanato-4-methylphenyl)acrylaldehyde (**1e**).* The spectra are in accord with the literature.[16] ^1H NMR (600 MHz, $CDCl_3$) δ 9.63 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.54 (d, *J* = 16.0 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 9.3 Hz, 2H), 6.59 (ddd, *J* = 15.9,

DOI: 10.1021/acs.joc.5b02369
J. Org. Chem. 2016, 81, 1216–1222

7.6, 1.1 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.3, 145.9, 143.2, 138.6, 130.9, 129.5, 128.7, 128.5, 127.2, 126.7, 21.2.

*3-(2-Isothiocyanato-5-methoxyphenyl)acrylaldehyde (**1g**).* The spectra are in accord with the literature.[16] ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.77 (d, J = 7.6 Hz, 1H), 7.71 (d, J = 16.0 Hz, 1H), 7.30 (d, J = 8.8 Hz, 1H), 7.09 (d, J = 2.8 Hz, 1H), 6.98 (dd, J = 8.8, 2.8 Hz, 1H), 6.72 (dd, J = 16.0, 7.6 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.4, 158.4, 145.9, 137.9, 130.7, 130.6, 129.3, 124.0, 118.6, 111.3, 55.7.

*3-(2-Isothiocyanato-6-nitrophenyl)acrylaldehyde (**1h**).* The spectra are in accord with the literature.[16] ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.79 (d, J = 7.3 Hz, 1H), 7.96 (d, J = 7.9 Hz, 1H), 7.77−7.64 (m, 2H), 7.60 (t, J = 7.9 Hz, 1H), 6.63 (dd, J = 16.2, 7.3 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.7, 148.8, 142.7, 141.0, 135.7, 132.5, 131.9, 130.7, 125.8, 122.9.

*3-(5-Chloro-2-isothiocyanatophenyl)acrylaldehyde (**1i**).* The spectra are in accord with the literature.[16] ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.77 (d, J = 7.5 Hz, 1H), 7.67 (d, J = 16.0 Hz, 1H), 7.60 (d, J = 2.3 Hz, 1H), 7.39 (dd, J = 8.6, 2.3 Hz, 1H), 7.32 (d, J = 8.6 Hz, 1H), 6.73 (dd, J = 16.0, 7.5 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.9, 144.4, 140.3, 133.3, 131.9, 131.3, 130.9, 129.9, 129.3, 127.2.

General Procedure for the Preparation of Diethyl 3-hydroxythieno[2,3-b]quinoline-2,2(3*H*)-dicarboxylate. A mixture of *o*-isothiocyanato-(*E*)-cinnamaldehyde **1a** (18.9 mg, 0.1 mmol), L-proline (0.58 mg, 0.05 mol), and diethyl α-bromomalonate **2a** (20 μL, 0.1 mmol) was stirred in methanol (1.0 mL) at room temperature for 2 h; then, DBU (18 μL, 0.05 mol) was added. The reaction mixture was stirred at room temperature for 1 h. Then, flash chromatography on silica gel (20% ethyl acetate/petroleum ether) gave **3aa** as a white solid (26 mg, 75% yield).

*Diethyl 3-Hydroxythieno[2,3-b]quinoline-2,2(3H)-dicarboxylate (**3aa**).* Twenty-six milligrams, 75% yield, white solid, mp 127−128 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 5.89 (s, 1H), 4.39−4.17 (m, 4H), 3.96 (s, 1H), 1.30 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 167.0, 161.8, 148.8, 132.4, 131.8, 130.1, 128.2, 127.8, 126.1, 126.0, 77.9, 69.4, 63.0, 63.0, 13.91, 13.90. ESI-HRMS: calcd for $C_{17}H_{17}NO_5S$ + H, 348.0900; found, 348.0933.

*Diethyl 5-Bromo-3-hydroxythieno[2,3-b]quinoline-2,2(3H)-dicarboxylate (**3ba**).* Twenty-six milligrams, 61% yield, white solid, mp 89−90 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 7.5 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 5.92 (d, J = 6.7 Hz, 1H), 4.39−4.25 (m, 4H), 3.62 (d, J = 7.4 Hz, 1H), 1.33 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 5.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 167.0, 162.9, 149.7, 133.8, 131.1, 130.3, 129.8, 127.8, 125.8, 122.4, 78.0, 69.3, 63.2, 63.1, 13.9, 13.9. ESI-HRMS: calcd for $C_{17}H_{16}BrNO_5S$ + H, 426.0005; found, 426.0010.

*Diethyl 6-Bromo-3-hydroxythieno[2,3-b]quinoline-2,2(3H)-dicarboxylate (**3ca**).* Twenty-four milligrams, 56% yield, white solid, mp 135−137 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, J = 1.5 Hz, 1H), 7.86 (s, 1H), 7.76 (d, J = 8.9 Hz, 1H), 7.70 (dd, J = 8.9, 1.7 Hz, 1H), 5.88 (s, 1H), 4.39−4.21 (m, 4H), 3.88 (s, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 166.9, 162.3, 147.4, 133.44, 133.41, 130.5, 130.1, 129.4, 127.3, 119.6, 77.8, 69.2, 63.18, 63.13, 13.9, 13.9. ESI-HRMS: calcd for $C_{17}H_{16}BrNO_5S$ + H, 426.0011; found, 426.0017.

*Crystal Data for **3ca**.* See the Supporting Information. $C_{17}H_{16}BrNO_5S$ (426.27), triclinic, $P\bar{1}$; a = 9.0005(5) Å, α = 86.350(3)°; b = 9.8533(5) Å, β = 84.591(3)°; c = 10.2837(5) Å, γ = 85.213(3)°. U = 903.35(8) Å^3; Z = 4; T = 296(2) K; absorption coefficient 2.418 mm^{-1}; reflections collected 15 339, unique 4179 [R(int) = 0.0428]; refinement by Full-matrix least-squares on F^2, data/restraints/parameters 4179/0/226, goodness-of-fit on F^2 = 1.043; final R indices [$I > 2\sigma(I)$], $R1$ = 0.0489, w$R2$ = 0.1434; R indices (all data), $R1$ = 0.0743, w$R2$ = 0.1626; largest diff. peak and hole 0.850 and −0.843 Å^{-3}.

*Diethyl 3-Hydroxy-6-methylthieno[2,3-b]quinoline-2,2(3H)-dicarboxylate (**3da**).* Twenty milligrams, 56% yield, white solid, mp 157−159 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.49−7.41 (m, 2H), 5.86 (s, 1H), 4.36−4.21 (m, 4H), 4.09 (s, 1H), 2.47 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 167.0, 160.7, 147.3, 135.8, 132.4, 132.2, 131.3, 127.4, 127.2, 126.1, 77.8, 69.5, 62.97, 62.95, 21.4, 13.9, 13.89. ESI-HRMS: calcd for $C_{18}H_{19}NO_5S$+H 362.1057, found 362.1084.

*Crystal Data for **3da**.* See the Supporting Information. $C_{18}H_{19}NO_5S$ (361.4), monoclinic, $P2_1/c$; a = 16.5377(2) Å, α = 90.00°; b = 7.97520(10) Å, β = 95.102(2) °; c = 13.0814(2) Å, γ = 90.00°; U = 1723.58(4) Å^3; Z = 22; T = 296(2) K; absorption coefficient 0.217 mm^{-1}; reflections collected 14 875, unique 3960 [R(int) = 0.0172]; refinement by Full-matrix least-squares on F^2, data/restraints/parameters 3960/0/227, goodness-of-fit on F^2 = 1.058; final R indices [$I > 2\sigma(I)$] $R1$ = 0.0427, w$R2$ = 0.1263; R indices (all data) $R1$ = 0.0490, w$R2$ = 0.1331; largest diff. peak and hole 0.522 and −0.406 Å^{-3}.

*Diethyl 3-Hydroxy-7-methylthieno[2,3-b]quinoline-2,2(3H)-dicarboxylate (**3ea**).* Twenty-four milligrams, 66% yield, white solid, mp 130−131 °C. ^{1}H NMR (600 MHz, CDCl3) δ 7.93 (s, 1H), 7.69 (s, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.28 (dd, J = 8.2, 1.1 Hz, 1H), 5.86 (s, 1H), 4.36−4.18 (m, 4H), 3.64 (s, 1H), 2.52 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 167.1, 161.6, 149.1, 140.6, 131.5, 1314, 128.1, 127.8, 127.1, 124.1, 77.9, 69.3, 63.0, 63.0, 21.8, 13.9, 13.9. ESI-HRMS: calcd for $C_{18}H_{19}NO_5S$ + H, 362.1057; found, 362.1072.

*Diethyl 3,7-Dihydroxythieno[2,3-b]quinoline-2,2(3H)-dicarboxylate (**3fa**).* Twenty-five milligrams, 70% yield, white solid, mp 168−170 °C. ^{1}H NMR (600 MHz, DMSO) δ 9.98 (s, 1H), 8.04 (s, 1H), 7.70 (d, J = 9.0 Hz, 1H), 7.26 (dd, J = 9.0, 2.7 Hz, 1H), 7.18 (d, J = 2.7 Hz, 1H), 6.66 (d, J = 7.0 Hz, 1H), 5.66 (d, J = 6.5 Hz, 1H), 4.40−4.07 (m, 4H), 1.21 (t, J = 7.1 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, DMSO) δ 168.4, 166.0, 158.9, 155.6, 143.7, 134.4, 131.2, 129.0, 127.7, 122.3, 110.0, 76.2, 70.9, 62.7, 62.6, 14.3, 14.1. ESI-HRMS: calcd for $C_{17}H_{17}NO_6S$ + H, 364.0849; found, 364.0849.

*Diethyl 3-Hydroxy-6-methoxythieno[2,3-b]quinoline-2,2(3H)-dicarboxylate (**3ga**).* Twenty-seven milligrams, 73% yield, white solid, mp 153−155 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.79 (d, J = 9.2 Hz, 1H), 7.28 (dd, J = 9.4, 3.0 Hz, 1H), 7.01 (d, J = 2.8 Hz, 1H), 5.85 (s, 1H), 4.35−4.21 (m, 4H), 3.89 (s, 3H), 3.77 (s, 1H), 1.31 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.9, 167.1, 158.7, 157.3, 144.8, 132.6, 130.8, 129.1, 127.1, 122.0, 106.4, 78.0, 69.4, 62.99, 62.98, 55.5, 13.91, 13.90. ESI-HRMS: calcd for $C_{18}H_{19}NO_6S$ + H, 378.1006; found, 378.1010.

*Diethyl 3-Hydroxy-5-nitrothieno[2,3-b]quinoline-2,2(3H)-dicarboxylate (**3ha**).* Twenty-five milligrams, 64% yield, white solid, mp 169−171 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.25 (dd, J = 7.7, 1.1 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 7.73 (t, J = 8.1 Hz, 1H), 5.95 (d, J = 5.9 Hz, 1H), 4.41−4.25 (m, 4H), 3.67 (d, J = 7.1 Hz, 1H), 1.34 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.5, 166.8, 164.0, 149.0, 146.0, 135.8, 134.6, 128.2, 127.1, 123.6, 119.3, 78.1, 69.3, 63.35, 63.30, 13.92, 13.91. ESI-HRMS: calcd for $C_{17}H_{16}N_2O_7S$ + H, 393.0751; found, 393.0755.

*Diethyl 6-Chloro-3-hydroxythieno[2,3-b]quinoline-2,2(3H)-dicarboxylate (**3ia**).* Twenty-four milligrams, 62% yield, white solid, mp 160−162 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.71 (d, J = 2.2 Hz, 1H), 7.58 (dd, J = 8.9, 2.2 Hz, 1H), 5.88 (s, 1H), 4.39−4.22 (m, 4H), 3.79 (s, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 167.0, 162.1, 147.2, 133.4, 131.6, 130.8, 130.6, 129.3, 126.8, 126.8, 77.9, 69.2, 63.2, 63.1, 13.93, 1392. ESI-HRMS: calcd for $C_{17}H_{16}ClNO_5S$ + H, 382.0510; found, 382.0520.

*Ethyl 2-Acetyl-3-hydroxy-2,3-dihydrothieno[2,3-b]quinoline-2-carboxylate (**3ab**).* Twenty-five milligrams, 80% yield, white solid, mp 142−144 °C, 3:2 dr. ^{1}H NMR (600 MHz, DMSO) δ 8.27 (d, J = 4.1 Hz, 1H), 8.01 (t, J = 7.5 Hz, 1H), 7.89 (dd, J = 8.1, 5.6 Hz, 1H), 7.79−7.72 (m, 1H), 7.56 (dd, J = 11.1, 3.9 Hz, 1H), 6.80 (d, J = 6.8 Hz, 0.61H), 6.67 (d, J = 7.0 Hz, 0.38H), 5.95 (d, J = 6.5 Hz, 0.61H), 5.75 (d, J = 6.7 Hz, 0.38H), 4.31 (dddd, J = 14.3, 10.9, 9.0, 5.5 Hz, 0.80H), 4.27−4.15 (m, 1.29H), 2.37 (s, 1.73H), 2.36 (s, 1.20H), 1.27 (t, J = 7.1 Hz, 1.28H), 1.19 (t, J = 7.1 Hz, 2.01H). ^{13}C NMR (150

DOI: 10.1021/acs.joc.5b02369
J. Org. Chem. 2016, 81, 1216−1222

MHz, DMSO) δ 198.4, 198.1, 168.8, 166.5, 163.2, 162.6, 148.6, 135.1, 134.9, 132.7, 130.6, 129.0, 127.68, 127.66 126.5, 1264, 126.3, 77.4, 77.2, 75.7, 74.9, 63.1, 62.8, 27.6, 26.4, 14.2, 14.1. ESI-HRMS: calcd for $C_{16}H_{15}NO_4S$ + H, 318.0795; found, 318.0800

*1,1′-(3-Hydroxy-2,3-dihydrothieno[2,3-b]quinoline-2,2-diyl)-diethanone (**3ac**).* Thirty-two milligrams, 83% yield, white solid, mp 189−190 °C, ^{1}H NMR (600 MHz, DMSO) δ 8.25 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.75−7.66 (m, 1H), 7.57−7.49 (m, 1H), 6.66 (d, *J* = 6.7 Hz, 1H), 5.93 (d, *J* = 6.6 Hz, 1H), 2.36 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 201.1, 199.7, 162.8, 148.7, 135.3, 132.8, 130.6, 128.9, 127.7, 126.4, 126.3, 83.8, 74.8, 28.4, 27.0. ESI-HRMS: calcd for $C_{15}H_{13}NO_3S$ + H, 288.0689; found, 288.0685.

*1-(Thieno[2,3-b]quinolin-2-yl)ethanone (**6ac**).* Nineteen milligrams, 82% yield, white solid, mp 200−201 °C. ^{1}H NMR (600 MHz, DMSO) δ 9.06 (s, 1H), 8.46 (s, 1H), 8.21 (d, *J* = 8.1 Hz, 1H), 8.09 (d, *J* = 8.6 Hz, 1H), 7.89 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 7.66 (dd, *J* = 11.0, 4.0 Hz, 1H), 2.71 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 193.4, 163.0, 148.0, 144.0, 135.2, 132.2, 131.6, 129.9, 129.7, 128.3, 126.4, 125.9, 26.7. ESI-HRMS: calcd for $C_{13}H_9NOS$ + H, 228.0478; found, 228.0478.

*(2-Bromophenyl)(thieno[2,3-b]quinolin-2-yl)methanone (**6af**).* Thirty-one milligrams, 84% yield, white solid, mp 175−176 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.13 (d, *J* = 8.6 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.80 (t, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.62 (s, 1H), 7.57−7.46 (m, 3H), 7.45−7.40 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.7, 163.7, 148.4, 143.5, 139.3, 134.3, 133.5, 131.8, 131.4, 131.3, 131.2, 129.0, 128.7, 128.4, 127.3, 126.0, 125.7, 119.6. ESI-HRMS: calcd for $C_{18}H_{10}BrNOS$ + H, 367.9739; found, 367.9739.

*Thieno[2,3-b]quinolin-2-yl(p-tolyl)methanone (**6ag**).* Twenty-one milligrams, 68% yield, white solid, mp 207−209 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.17 (d, *J* = 8.6 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.91−7.78 (m, 4H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 2H), 2.50 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.2, 163.4, 148.2, 144.0, 143.8, 134.4, 133.7, 131.5, 130.8, 129.5, 129.5, 129.4, 129.4, 129.2, 128.7, 128.5, 1259, 125.8, 21.7. ESI-HRMS: calcd for $C_{19}H_{13}NOS$ + H, 304.0791; found, 304.0819.

*Methyl Thieno[2,3-b]quinoline-2-carboxylate (**6ad**).* Eighteen milligrams, 82% yield, white solid, mp 160−161 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.12 (d, *J* = 8.2 Hz, 1H), 8.05 (s, 1H), 7.94 (d, *J* = 7.7 Hz, 1H), 7.78 (t, *J* = 6.8 Hz, 1H), 7.55 (t, *J* = 6.8 Hz, 1H), 3.98 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.4, 162.8, 148.1, 134.3, 133.1, 131.0, 130.6, 128.7, 128.4, 128.0, 125.8, 125.7, 52.8. ESI-HRMS: calcd for $C_{13}H_9NO_2S$ + H, 244.0427; found, 224.0432.

*Methyl 2-((3-Formylquinolin-2-yl)thio)acetate (**5ad**).* Twenty-one milligrams, 82% yield, white solid, mp 113−1114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.49 (s, 1H), 7.90 (dd, *J* = 11.8, 8.4 Hz, 2H), 7.84−7.77 (m, 1H), 7.56−7.49 (m, 1H), 4.08 (s, 2H), 3.78 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.9, 170.3, 157.0, 149.1, 143.7, 133.2, 129.1, 128.0, 126.9, 126.5, 124.6, 52.6, 32.5. ESI-HRMS: calcd for $C_{13}H_{11}NO_3S$ + H 262.0532; found, 262.0531.

*(3-Hydroxy-2-methyl-2,3-dihydrothieno[2,3-b]quinolin-2-yl)-(phenyl)methanone (**3ae**).* Eighteen milligrams, 55% yield, mp 162−163 °C, 3:2 dr. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.4 Hz, 1H), 8.05 (s, 1H), 7.95 (t, *J* = 7.3 Hz, 2H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.68−7.41 (m, 5H), 5.96 (s, 0.62H), 5.35 (s, 0.41H), 4.32 (d, *J* = 17.2 Hz, 0.40H), 3.55 (s, 0.65H), 2.11 (s, 1.14H), 1.89 (s, 1.90H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.9, 160.5, 149.0, 134.3, 134.1, 133.3, 132.1, 131.5, 130.3, 129.78, 129.74, 129.6, 129.5, 128.8, 128.4, 128.1, 128.0, 127.88, 127.85, 126.6, 126.5, 126.0, 125.9, 83.7, 78.8, 66.7, 64.6, 23.3, 21.1. ESI-HRMS: calcd for $C_{19}H_{15}NO_2S$ + H, 322.0896; found, 322.0906.

*Methyl 5-Oxo-5-(thieno[2,3-b]quinolin-2-yl)pentanoate (**6ah**).* Twenty-one milligrams, 68% yield, white solid, mp 160−161 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.14 (d, *J* = 8.3 Hz, 1H), 8.06−7.88 (m, 2H), 7.81 (t, *J* = 7.1 Hz, 1H), 7.57 (t, *J* = 7.0 Hz, 1H), 3.72 (s, 3H), 3.13 (t, *J* = 6.7 Hz, 2H), 2.51 (t, *J* = 6.5 Hz, 2H), 2.32−2.07 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.0, 173.6, 163.3, 148.2, 144.0, 133.7, 131.6, 130.8, 128.7, 128.4, 126.5, 125.9, 125.7, 51.7, 37.8, 32.9, 19.4. ESI-HRMS: calcd for $C_{17}H_{15}NO_3S$ + H, 314.0845; found, 314.0870.

*Methyl 5-(6-Bromothieno[2,3-b]quinolin-2-yl)-5-oxopentanoate (**6ch**).* Twenty-three milligrams, 59% yield, white solid, mp 203−205 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.16 (s, 1H), 8.04 (t, *J* = 4.4 Hz, 2H), 7.93−7.83 (m, 1H), 3.74 (s, 3H), 3.18 (t, *J* = 7.2 Hz, 2H), 2.53 (t, *J* = 7.0 Hz, 2H), 2.23−2.06 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.9, 173.5, 163.7, 146.7, 145.0, 134.2, 132.4, 132.2, 130.3, 130.2, 126.7, 126.1, 119.7, 51.7, 37.9, 32.8, 19.4. ESI-HRMS: calcd for $C_{17}H_{14}BrNO_3S$ + H, 391.9951; found, 391.9951.

*Methyl 5-(6-Methylthieno[2,3-b]quinolin-2-yl)-5-oxopentanoate (**6dh**).* Twenty milligrams, 61% yield, white solid, mp 173−174 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.01 (d, *J* = 7.7 Hz, 1H), 7.93 (s, 1H), 7.73−7.56 (m, 2H), 3.72 (s, 3H), 3.10 (d, *J* = 6.4 Hz, 2H), 2.56 (s, 3H), 2.50 (d, *J* = 6.5 Hz, 2H), 2.12 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.9, 173.6, 162.5, 147.1, 143.8, 135.7, 133.4, 132.8, 131.5, 128.0, 127.1, 126.6, 125.8, 51.7, 37.8, 32.9, 21.6, 19.4. ESI-HRMS: calcd for $C_{18}H_{17}NO_3S$ + H, 328.1002; found, 328.1007.

*Methyl 5-(7-Methylthieno[2,3-b]quinolin-2-yl)-5-oxopentanoate (**6eh**).* Twenty-two milligrams, 69% yield, white solid, mp 172−174 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.98 (s, 1H), 7.90 (s, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 3.72 (s, 3H), 3.13 (t, *J* = 7.2 Hz, 2H), 2.62 (s, 3H), 2.51 (t, *J* = 7.0 Hz, 2H), 2.18−2.11 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.9, 173.6, 163.4, 148.6, 143.3, 141.7, 133.4, 130.9, 128.4, 128.2, 127.2, 126.7, 124.0, 51.7, 37.8, 32.9, 22.2, 19.5. ESI-HRMS: calcd for $C_{18}H_{17}NO_3S$ + H, 328.1002; found, 328.1003.

*Methyl 5-(6-Chlorothieno[2,3-b]quinolin-2-yl)-5-oxopentanoate (**6ih**).* Nineteen milligrams, 56% yield, white solid, mp 206−207 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.16 (s, 1H), 8.04 (d, *J* = 7.1 Hz, 2H), 7.87 (d, *J* = 9.1 Hz, 1H), 3.73 (s, 3H), 3.18 (t, *J* = 6.9 Hz, 2H), 2.53 (t, *J* = 6.6 Hz, 2H), 2.20−2.11 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.9, 173.5, 163.7, 146.7, 145.0, 134.2, 132.4, 132.2, 130.3, 130.2, 126.7, 126.1, 119.7, 51.7, 37.9, 32.8, 19.4. ESI-HRMS: calcd for $C_{17}H_{14}ClNO_3S$ + H, 348.0456; found, 348.0465.

*2-Mercaptoquinoline-3-carbaldehyde (**Ia**).* Fourteen milligrams, 73% yield, yellow solid, mp 303−305 °C. ^{1}H NMR (600 MHz, DMSO) δ 13.98 (s, 1H), 10.72 (s, 1H), 8.36 (s, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 192.3, 181.4, 141.4, 137.4, 134.7, 132.3, 131.1, 125.4, 122.1, 116.7. ESI-HRMS: calcd for $C_{10}H_7NOS$+H 190.0321, found 190.0323.

*2-Mercapto-6-methylquinoline-3-carbaldehyde (**Id**).* Seventeen milligrams, 84% yield, yellow solid, mp 281−282 °C. ^{1}H NMR (600 MHz, DMSO) δ 13.94 (s, 1H), 10.72 (s, 1H), 8.25 (s, 1H), 7.77 (s, 1H), 7.58 (dd, *J* = 30.1, 8.5 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 192.3, 180.6, 139.8, 137.0, 136.3, 135.0, 132.2, 130.1, 122.1, 116.6, 21.0. ESI-HRMS: calcd for $C_{11}H_9NOS$+H 204.0478, found 204.0480.

*2-(2-(Pyrrolidin-1-yl)-4H-benzo[d][1,3]thiazin-4-yl)acetaldehyde (**A**).* Twenty-five milligrams, 95% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.69 (s, 1H), 7.23 (td, *J* = 7.7, 1.4 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 7.07 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.97 (td, *J* = 7.4, 1.0 Hz, 1H), 4.50 (dd, *J* = 8.4, 5.9 Hz, 1H), 3.69 (s, 2H), 3.55 (s, 2H), 3.01 (ddd, *J* = 17.7, 8.4, 1.6 Hz, 1H), 2.84 (dd, *J* = 17.7, 5.8 Hz, 1H), 1.95 (dd, *J* = 11.8, 5.8 Hz, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.5, 151.4, 145.4, 128.6, 126.0, 124.9, 122.8, 121.1, 50.2, 47.9, 37.4, 37.4, 25.0, 25.0. ESI-HRMS: calcd for $C_{14}H_{16}N_2OS$ + H, 261.1056; found, 261.1052.

*2-(2-(Diethylamino)-4H-benzo[d][1,3]thiazin-4-yl)acetaldehyde (**B**).* Twenty-four milligrams, 91% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.65 (s, 1H), 7.26−7.19 (m, 1H), 7.12−7.05 (m, 2H), 6.97 (td, *J* = 7.4, 1.1 Hz, 1H), 4.50 (dd, *J* = 8.1, 6.1 Hz, 1H), 3.65 (dq, *J* = 14.0, 7.0 Hz, 2H), 3.55 (dq, *J* = 14.1, 7.0 Hz, 2H), 2.91 (ddd, *J* = 17.6, 8.2, 1.8 Hz, 1H), 2.79 (ddd, *J* = 17.6, 6.0, 0.8 Hz, 1H), 1.20 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.5, 152.1, 145.5, 128.5, 125.8, 124.9, 122.8, 121.4, 49.7, 43.5, 37.5, 37.5, 14.1, 14.1. ESI-HRMS: calcd for $C_{14}H_{18}N_2OS$ + H, 263.1213; found, 263.1211.

DOI: 10.1021/acs.joc.5b02369
J. Org. Chem. 2016, 81, 1216−1222

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02369.

^{1}H and ^{13}C NMR spectra for all new compounds (PDF)

X-ray structural data for **3da** (CIF)

X-ray structural data for **3ca** (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for the financial support from the National Natural Science Foundation, P. R. China (no. 21272214).

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DOI: 10.1021/acs.joc.5b02369
J. Org. Chem. 2016, 81, 1216−1222