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One-Pot Synthesis of Benzo[1,4]thiazin-3(4*H*)-ones and a Theoretical Study of the S−N Type Smiles Rearrangement Mechanism

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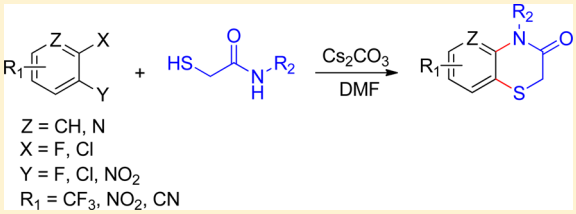
Supporting Information

ABSTRACT: Benzo[1,4]thiazin-3(4*H*)-one derivatives are conveniently prepared in one pot via a Smiles rearrangement (SR) tandem reaction. In order to understand the reaction, we present here a theoretical study on the S−N type SR mechanism.

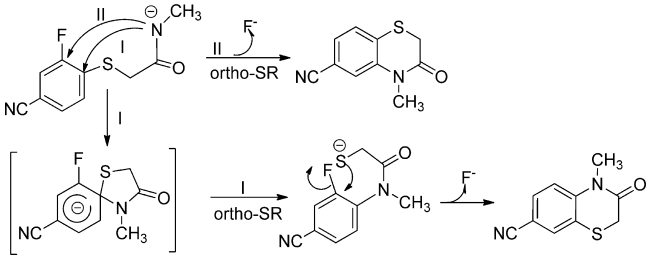


INTRODUCTION

A great number of biologically active molecules and natural products contain the benzo[1,4]thiazin-3(4*H*)-one scaffold.[1] For example, 2*H*-benzo[1,4]thiazin-3(4*H*)-one derivatives act as bacteriostatic,[2] antiarrhythmic,[3] and antidiabetic agents.[4] 4*H*-Benzo[1,4]thiazin-3(4*H*)-ones are used as herbicides.[5] Because of this, some methods for the synthesis of benzo[1,4]thiazin-3(4*H*)-ones have been developed. Most commonly, a multistep reaction,[6] a copper-catalyzed reaction,[7] and a Smiles rearrangement (SR) reaction[8] are taken into consideration. However, there are still some disadvantages of the existing methods, which are limited to synthesizing a substituent diversification of products, such as N-aryl-substituted products. Moreover, the yields of the substituted products are low because of the multistep reaction. Additionally, the reaction conditions are a bit rigorous. Therefore, a new and more effective method, involving mild, environmentally benign, atom-economical, and metal-free conditions, is still in high demand for synthesizing 2*H*-benzo[1,4]thiazin-3(4*H*)-ones.

In a continuation of our studies on the development of economical syntheses of heterocyclic systems,[9] we herein used **1** (**4**) and **2** (**5**) to synthesize a series of compounds **3** (Tables 2 and 3) via a Smiles rearrangement (SR)[10] in a one-pot metal-free reaction which is quite different from the reported procedure.[8] Furthermore, a mechanistic study of this S−N type SR process is essential for designing the desired benzo[1,4]thiazin-3(4*H*)-one derivatives and it is also important for understanding the novel process. Therefore, we performed a theoretical study to rationalize experimental observations. To the best of our knowledge, the mechanism of SR reactions, in particular the SR on the benzene ring, has been rarely studied, although a few relevant theoretical studies have been reported.[11] In the present paper, we turn our attention to a representative SR process with R = CH_3, as shown in Scheme 1. By performing quantum chemistry calculations, we show the molecular mechanism for the S−N type SR. To rationalize the experimental fact that the reaction is substantially predominant via the SR, we also considered the possibility of direct nucleophilic attack by the N atom on the ortho position (path II in Scheme 1) and compared the results with those of the ipso SR.

Scheme 1. Ipso SR vs Direct Nucleophilic Substitution on the Ortho Position



RESULTS AND DISCUSSION

To optimize the reaction conditions, we systematically investigated the reaction parameters using **1a** and **2** (Table 1). First, the effect of bases was investigated (entries 1−4). It was found that the alkali-metal carbonate Cs_2CO_3 afforded **3a** in excellent yields, whereas other bases, such as K_2CO_3, DBU, and NaOH, were less effective. Then we probed the influence of different solvents on the reaction. DMF was found to be an effective solvent for good results. CH_3CN, DMSO, and THF were found to be less effective.

With the optimized reaction conditions in hand, we then explored the scope and generality of the synthesizing benzo[1,4]thiazin-3(4*H*)-ones via Smiles rearrangement (Tables 2 and 3). The desired benzo[1,4]thiazin-3(4*H*)-ones were

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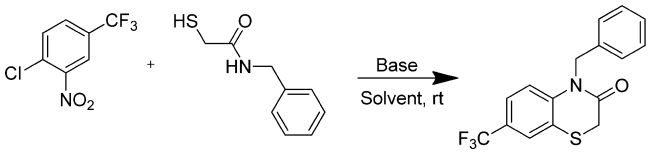
Table 1. Optimization of Conditions[a]

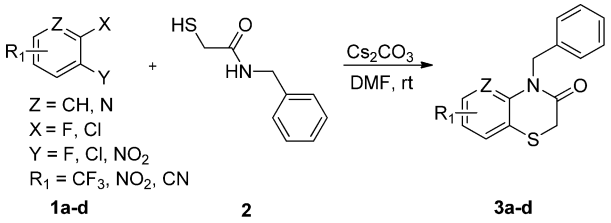


1a 2 3a

entry	base	solvent	time (h)	yield (%)[b]
1	Cs_2CO_3	DMF	7	51
2	NaOH	DMF	8	17
3	K_2CO_3	DMF	10	14
4	DBU	DMF	8	16
5	Cs_2CO_3	CH_3CN	11	30
6	Cs_2CO_3	DMSO	10	36
7	Cs_2CO_3	THF	10	41

[a]Reaction conditions: 1-chloro-2-nitro-4-(trifluoromethyl)benzene **1a** (0.5 mmol), *N*-benzyl-2-mercapto acetamide **2** (0.6 mmol), and base (1.5 mmol) in solvent (15.0 mL) under N_2 at room temperature. [b]Isolated yield.

Table 2. Synthesis of Benzo[1,4]thiazin-3(4*H*)-ones 3[a]



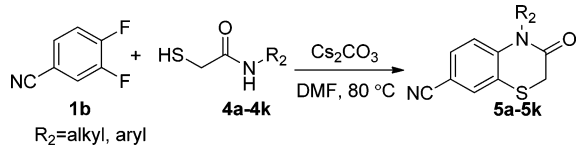
1a-d 2 3a-d

entry	1	product 3	yield (%)[b]
1	 1a	 3a	51
2	 1b	 3b	83
3	 1c	 3c	60
4	 1d	 3d	70

[a]Reaction conditions: 1-chloro-2-nitro-4-(trifluoromethyl)benzene **1a** and analogues **1b–d** (0.5 mmol), *N*-benzyl-2-mercaptoacetamide **2** (0.6 mmol), and base Cs_2CO_3 (1.5 mmol) in DMF (15.0 mL) under N_2 at room temperature for 10 h. [b]Isolated yield.

obtained in 50% to 88% yields (Tables 2 and 3). As shown in Table 2, substrate **1** with stronger electron-withdrawing groups on the aromatic rings gave higher yields. The reaction temperature was increased to 80 °C to shorten the reaction time (Table 3). For the variation of R_2, on comparison of the yield of **5c** with those of **5a,b**, it was obvious that N-alkyl substrates showed a small steric hindrance effect (Table 3, entries 1–6). We also found that the N-aryl substrates with an electron-donating group (Table 3, entries 7–9) provided higher yields than the substrates with electron-withdrawing groups (Table 3, entries 10 and 11). The molecular structure of the representative product **5a** was determined by X-ray crystallography analysis (Figure 1).

Table 3. Synthesis of Benzo[1,4]thiazin-3(4*H*)-ones 5[a]



1b 4a-4k 5a-5k

R_2=alkyl, aryl

entry	4	product 5	yield (%)[b]
1	 4a	 5a	82
2	 4b	5b	88
3	4c	5c	65
4	 4d	5d	83
5	4e	5e	78
6	 4f	5f	50
7	4g	5g	88
8	4h	5h	78
9	 4i	5i	73
10	4j	5j	52
11	4k	5k	53

[a]Reaction conditions: 3,4-difluorobenzonitrile **1b** (0.5 mmol), 2-mercapto-*N*-methylacetamide **4a** and analogues **4b–k** (0.6 mmol), and Cs_2CO_3 (1.5 mmol) in DMF (15.0 mL) under N_2 at 80 °C for 4 h. [b]Isolated yield.

To rationalize the experimental observation that the SR pathway (denoted as pathway I in Scheme 1) is substantially predominant over the direct nucleophilic substitution pathway (denoted as pathway II in Scheme 1), we have performed theoretical calculations on the representative system (Scheme 1) in the framework of density functional theory (DFT), employing the popular B3LYP functional[12,13] with the standard 6-311+g(d,p) basis set,[14] as implemented in the Gaussian 03 software package.[15] This level of theory has been shown to provide reliable accuracy to evaluate structures[16] and energetics[17] and has been successfully applied to the study of heterocyclic systems.[18]

Molecular geometries of minima and transition states were completely optimized by total energy minimization with the use of analytic gradient techniques. Harmonic vibrational frequency calculations have also been conducted to verify all stationary

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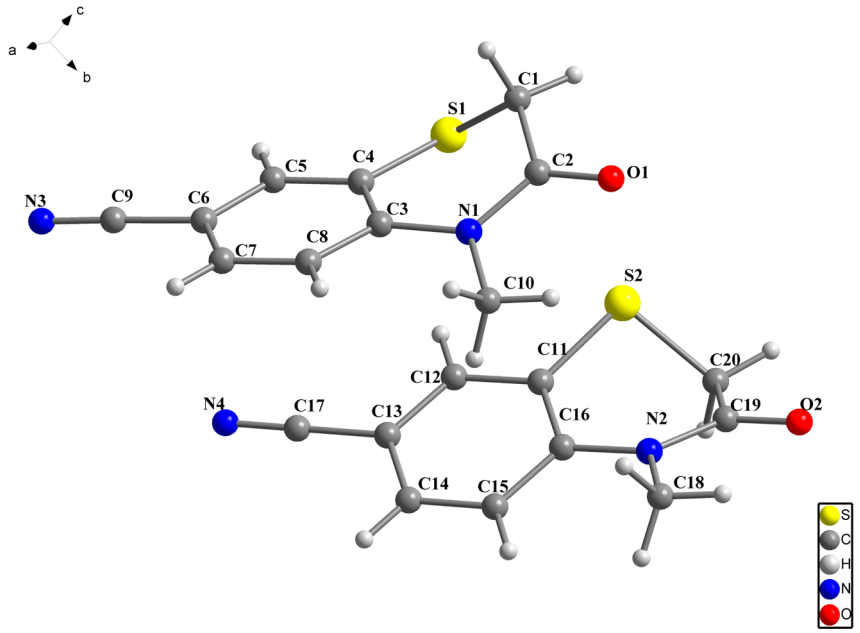

Figure 1. X-ray structure of compound **5a** with the atomic numbering scheme.

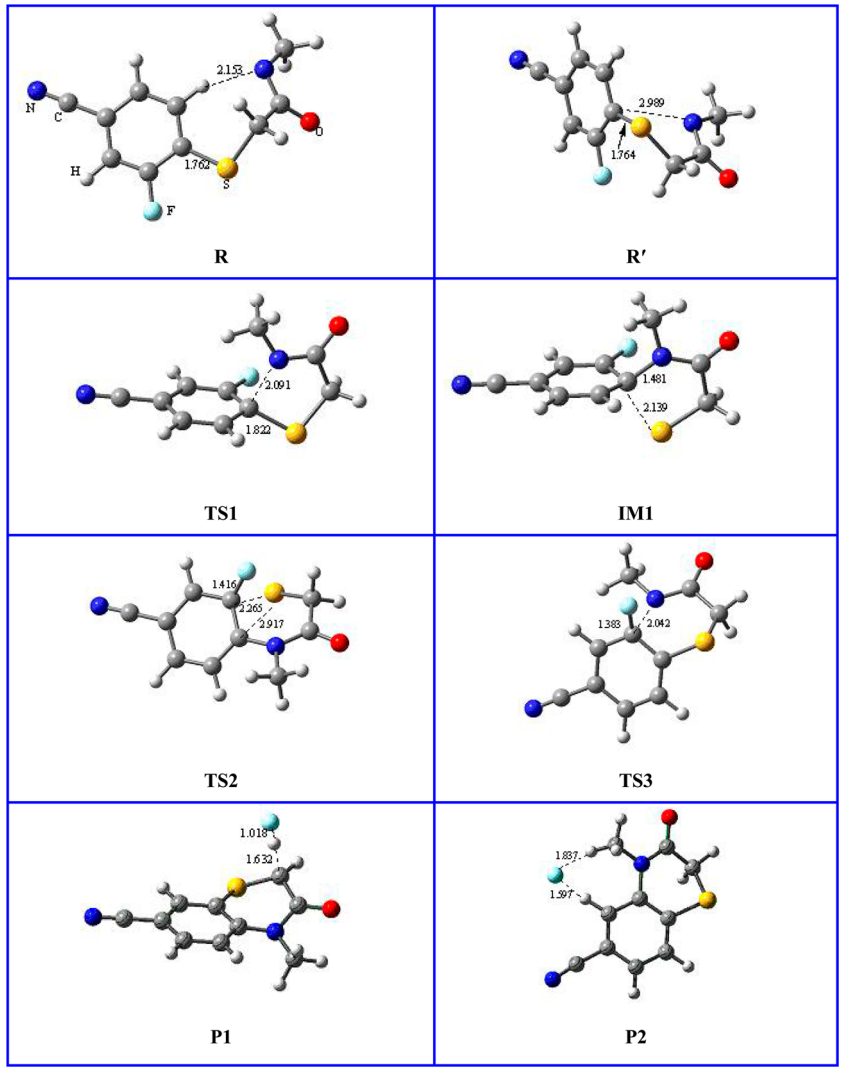

Figure 2. Optimized structures for transition states, intermediate, and products involved along pathways I and II. Distances are in Å.

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points as minima (zero imaginary frequency) or first-order saddle points (one imaginary frequency). Intrinsic reaction coordinates (IRC)[19,20] were calculated for the transition states to verify that such structures indeed connect two relevant minima.

Figure 2 shows the optimized geometries of minimum and transition states along both the two pathways, and Figure 3

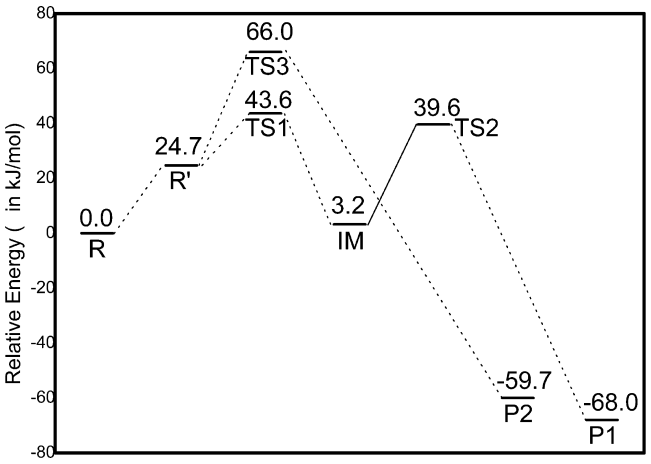

Figure 3. Calculated relative energy profiles along the ipso SR pathway (pathway I) and the direct nucleophilic substitution pathway (pathway II).

gives the calculated relative energy profiles. **R** is the most stable geometry of the anionic reactant, where an intramolecular C−H···N H bond is essential to stabilize the anion. To undergo the Smiles rearrangement, **R** must convert to its conformational isomer, **R′**, which lies above **R** by 24.7 kJ/mol. **TS1** denotes the transition state in which the negatively charged nitrogen is nucleophilically attacking the carbon atom, and its forward product is **IM1**, a metastable intermediate located on the potential energy surface, where the C−N bond has formed and the C−S bond has been remarkably elongated but is not fully broken. The overall barrier from **R** to **IM1** is calculated to be 43.6 kJ/mol. Once formed, **IM1** can be converted to the SR product **P1** via **TS2** with a barrier of 36.4 kJ/mol. In **TS2**, the new C−S bond is forming and the C−F bond becomes longer to cleave from the C atom. Thus, our calculations indicate that the SR pathway consists of two elementary steps, and the first step is the rate-determining step.

Alternatively, if the reaction occurs via the direct nucleophilic substitution pathway, the transition state involved is **TS3**, which lies above the initial reactant by 66.0 kJ/mol. This pathway is energetically less favorable by 22.4 kJ/mol than the SR pathway. Thus, the reactant prefers to undergo the SR to form product **P1** rather than to carry out the direct nucleophilic substitution to form product **P2**. The calculated results not only give good support for the experimental observations but also show the elementary-step mechanism of the reaction.

CONCLUSION

In conclusion, we have developed an operationally simple and economic synthesis of a great number of benzo[1,4]thiazin-3(4*H*)-ones based on the Smiles rearrangement. Furthermore, to get a more in-depth understanding of the reaction mechanism, we carried out quantum chemistry calculations on a representative reaction. The theoretical results show that the Smiles rearrangement pathway is energetically more favorable than the direct nucleophilic substitution pathway. This transition-metal-free process has potential applications in the synthesis of biologically and medicinally relevant compounds.

EXPERIMENTAL SECTION

General Experimental Procedures for the Synthesis of Benzo[1,4]thiazin-3(4*H*)-ones. A 25 mL Schlenk tube equipped with a magnetic stirring bar was charged with 2-mercaptoacetamide substrates (0.6 mmol, 1.2 equiv), aryl halides (0.5 mmol, 1.0 equiv), and Cs_2CO_3 (489 mg, 1.5 mmol, 3.0 equiv), and then 15 mL of DMF was added via syringe at room temperature and the mixture was prestirred for about 15 min. Then the reaction mixture was stirred at room temperature (**3a**−**d**) or 80 °C (**5a**−**k**). After the reaction was complete, the mixture was diluted with brine (40 mL) and extracted with ethyl acetate twice (2 × 30 mL). The combined organic layers were dried with $MgSO_4$, and the solvent was removed in vacuo to afford a residue. The crude product was then purified by column chromatography on silica gel to give the pure product.

*4-Benzyl-7-(trifluoromethyl)-2H-benzo[1,4]thiazin-3(4H)-one (**3a**):* 165 mg (51% yield), yellow liquid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.62 (d, J = 1.8 Hz, 1H), 7.39−7.27 (m, 4H), 7.19 (dd, J = 1.5, 8.1 Hz, 2H), 7.08 (d, J = 8.4 Hz, 1H), 5.26 (s, 2H), 3.56 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.0, 142.2, 136.0, 129.0, 128.0, 127.9, 127.5, 126.2, 125.9, 125.4 (dd, J = 3.8 Hz, 1C), 124.5, 124.2, 124.2, 118.1, 48.4, 31.1; ESI-MS m/z 324.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{16}H_{12}F_3NOS$ $(M + H)^+$ 323.0664, found 323.0668.

*4-Benzyl-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazine-7-carbonitrile (**3b**):* 233 mg (83% yield), white solid; mp 110−112 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64 (d, J = 1.8 Hz, 1H), 7.31 (m, 4H), 7.16 (d, J = 6.9 Hz, 2H) 7.06 (d, J = 8.7 Hz, 1H), 5.25 (s, 2H), 3.56 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 142.9, 135.6, 131.7, 130.9, 129.0, 128.8, 127.9, 127.7, 126.2, 125.1, 118.4, 117.8, 107.1, 48.3, 30.8; ESI-MS m/z 281.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{16}H_{12}N_2OS$ $(M + H)^+$ 281.0743, found 281.0740.

*4-Benzyl-7-nitro-2H-benzo[b][1,4]thiazin-3(4H)-one (**3c**):* 181 mg (60% yield), brown solid; mp 37−39 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.25 (d, J = 1.8 Hz, 1H), 7.95 (dd, J = 2.7 Hz, 9.3, 1H), 8.25 (d, J = 2.7 Hz, 1H), 7.95 (dd, J = 2.7, 9.3 Hz, 1H), 7.31 (m, 3H), 7.20 (dd, J = 13.5, 15.0 Hz, 2H), 7.10 (d, J = 9.0 Hz, 1H), 5.29 (s, 2H), 3.59 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 144.3, 142.9, 135.5, 129.1, 127.7, 126.2, 124.9, 123.7, 122.6, 118.1, 48.4, 30.8; ESI-MS m/z 301.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{15}H_{12}N_2O_3S$ $(M + H)^+$ 301.0641, found 301.0651.

*4-Benzyl-7-(trifluoromethyl)-2H-pyrido[3,2-b][1,4]thiazin-3(4H)-one (**3d**):* 227 mg (70% yield), white solid; mp 61−63 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.48 (dd, J = 0.9 Hz, 2.1, 1H), 7.85 (d, J = 2.1 Hz, 1H), 7.35 (dd, J = 1.8 Hz, 8.4, 2H), 7.25 (m, 1H), 7.19 (m, 2H), 5.47 (s, 2H), 3.56 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.7, 152.5, 142.8, 142.8, 137.1, 133.0, 128.4, 127.9, 127.3, 119.1, 45.7, 30.1, 29.7; ESI-MS m/z 325.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{15}H_{11}F_3N_2OS$ $(M + H)^+$ 325.0617, found 325.0644.

*4-Methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazine-7-carbonitrile (**5a**):* 167 mg (82% yield), white solid; mp 115−116 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69 (m, 1H), 7.55 (m, 1H), 7.15 (d, J = 8.7 Hz, 1H), 3.48 (s, 3H), 3.46 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.0, 143.5, 131.6, 131.0, 124.7, 117.9, 117.7, 106.9, 32.1, 30.6; ESI-MS m/z 205.0 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{10}H_8N_2OS$ $(M + H)^+$ 205.0430, found 205.0460.

*4-Ethyl-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazine-7-carbonitrile (**5b**):* 192 mg (88% yield), white solid; mp 98−99 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.66 (d, J = 1.8 Hz, 1H), 7.53 (dd, J = 2.1, 8.7 Hz, 1H), 7.19 (d, J = 8.7 Hz, 1H), 4.06 (q, J = 7.2, 6.9, 7.2 Hz, 2H), 3.42 (s, 2H), 1.29 (t, J = 7.2, 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1, 142.8, 131.9, 130.9, 125.1, 117.9, 117.5, 106.8, 40.3, 30.8, 12.9; ESI-MS m/z 219.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{11}H_{10}N_2OS$ $(M + H)^+$ 219.0584, found 219.0575.

*4-Isopropyl-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazine-7-carbonitrile (**5c**):* 151 mg (65% yield), white solid; mp 120−123 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70 (m, 1H), 7.51 (m, 1H), 7.28 (d, J = 8.4 Hz,

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1H), 4.65 (m, 1H), 3.33 (s, 2H), 1.54 (s, 3H), 1.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.2, 143.4, 132.2, 130.5, 127.4, 119.3, 117.9, 107.1, 51.8, 32.9, 20.4; ESI-MS m/z 233.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{12}H_{12}N_2OS$ $(M + H)^+$ 233.0743, found 233.0756.

*4-Butyl-3-oxo-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carbonitrile (**5d**):* 204 mg (83% yield), white solid; mp 75−76 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.67 (d, J = 2.1 Hz, 1H), 7.53 (dd, J = 1.8, 8.7 Hz, 1H), 7.18 (d, J = 8.7 Hz, 1H), 4.02 (t, J = 7.5, 7.5 Hz, 2H), 3.42 (s, 2H), 1.60 (m, 2H), 1.35 (m, 2H), 0.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.3, 142.7, 131.9, 130.9, 125.3, 117.9, 117.9, 106.7, 44.6, 30.9, 29.4, 19.9, 13.7; ESI-MS m/z 247.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{13}H_{14}N_2OS$ $(M + H)^+$ 247.0900, found 247.0902.

*3-Oxo-4-phenethyl-3,4-dihydro-2H-benzo[b][1,4]thiazine-7-carbonitrile (**5e**):* 229 mg (78% yield), yellow solid; mp 92−93 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.63 (d, J = 1.8 Hz, 1H), 7.47 (dd, J = 2.1, 8.7 Hz, 1H), 7.30 (m, 1H), 7.22 (m, 4H), 7.09 (d, J = 8.4 Hz, 1H), 4.23 (t, J = 7.5, 1.8 Hz, 2H), 3.41 (s, 2H), 2.63 (t, J = 7.8, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.2, 142.8, 137.7, 131.9, 130.9, 128.8, 128.7, 126.9, 125.4, 117.9, 106.9, 46.6, 33.7, 30.9; ESI-MS m/z 295.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{17}H_{14}N_2OS$ $(M + H)^+$ 295.0900, found 295.0896.

*4-(3,4-Dimethoxyphenethyl)-3-oxo-3,4-dihydro-2H-benzo[1,4]-thiazine-7-carbonitrile (**5f**):* 188 mg (53% yield), white solid; mp 177−179 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64 (d, J = 1.8 Hz, 1H), 7.49 (dd, J = 2.1, 8.7 Hz, 1H), 7.12 (d, J = 8.7 Hz, 1H), 6.77 (d, J = 8.7 Hz, 1H), 6.71 (m, 2H), 4.22 (m, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.407 (s, 2H), 2.89 (t, J = 7.8, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.3, 149.1, 148.0, 142.7, 131.9, 130.9, 130.2, 125.5, 120.8, 117.9, 117.8, 112.1, 111.5, 106.9, 55.9, 46.5, 33.3, 30.9; ESI-MS m/z 355.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{19}H_{18}N_2O_3S$ $(M + H)^+$ 355.1110, found 355.1105.

*3-Oxo-4-phenyl-3,4-dihydro-2H-benzo[1,4]thiazine-7-carbonitrile (**5g**):* 234 mg (88% yield), white solid; mp 158−160 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.68 (d, J = 1.8 Hz, 1H), 7.49 (m, 3H) 7.28 (dd, J = 1.8, 8.4 Hz, 1H), 7.21 (m, 2H), 6.55 (d, J = 8.7 Hz, 1H), 3.58 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.3, 144.4, 138.3, 131.7, 130.5, 130.2, 129.0, 128.6, 124.2, 120.2, 117.9, 107.0, 31.1; ESI-MS m/z 267.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{15}H_{10}N_2OS$ $(M + H)^+$ 267.0587, found 267.0591.

*3-Oxo-4-(p-tolyl)-3,4-dihydro-2H-benzo[1,4]thiazine-7-carbonitrile (**5h**):* 220 mg (78% yield), yellow solid; mp 296−297 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69 (d, J = 1.8 Hz, 1H), 7.30 (m, 3H), 7.08 (m, 2H), 7.02 (d, J = 8.7 Hz, 1H), 3.61 (s, 2H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.4, 144.5, 139.1, 135.5, 131.7, 130.9, 130.4, 128.3, 124.0, 120.2, 117.9, 106.9, 31.1,21.2; ESI-MS m/z 281.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{16}H_{12}N_2OS$ $(M + H)^+$ 281.0743, found 281.0749.

*4-(4-Methoxyphenyl)-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazine-7-carbonitrile (**5i**):* 217 mg (73% yield), brown solid; mp 192−194 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.68 (d, J = 1.8 Hz, 1H) 7.3 (m, 1H), 7.11 (dd, J = 2.1, 9.0 Hz, 2H), 7.02 (d, J = 9.0 Hz, 2H), 6.61 (d, J = 8.4 Hz, 1H), 3.86 (s, 3H), 3.61 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.5, 159.7, 144.6, 131.7, 130.6, 130.5, 129.6, 124.0, 120.1, 117.9, 115.5, 106.9, 55.6, 31.1; ESI-MS m/z 297.1 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{16}H_{12}N_2O_2S$ $(M + H)^+$ 297.0692, found 297.0684.

*4-(4-Fluorophenyl)-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazine-7-carbonitrile (**5j**):* 148 mg (52% yield), yellow solid; mp 267−269 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.70 (d, J = 1.8 Hz, 1H), 7.32 (dd, J = 1.8, 8.7 Hz, 1H), 7.21 (m, 4H), 6.57 (d, J = 8.4 Hz, 1H), 3.61 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.3 (d, J = 22.5 Hz, 1C), 160.8, 144.2, 134.1 (d, J = 1.5 Hz, 1C), 131.8, 130.5 (d, J = 4.5 Hz, 1C), 130.4, 124.3, 120.1, 117.8, 117.5, 117.1, 107.3, 31.1, 29.7; ESI-MS m/z 285.0 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{15}H_9FN_2OS$ $(M + H)^+$ 285.0492, found 285.0482.

*4-(4-Chlorophenyl)-3-oxo-3,4-dihydro-2H-benzo[1,4]thiazine-7-carbonitrile (**5k**):* 159 mg (53% yield), brown solid; mp 312−315 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.71 (d, J = 1.5 Hz, 1H), 7.50 (d, J = 8.4 Hz, 2H), 7.33 (dd, J = 1.5, 8.4 Hz, 1H), 7.15 (d, J = 8.7 Hz, 2H), 6.58 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.3, 144.0, 136.7, 135.0, 131.9, 130.6, 130.5, 130.0, 124.4, 120.1, 117.7, 107.4, 31.2; ESI-MS m/z 301.0 $(M + H)^+$; FT-HRMS (ESI) calcd for $C_{15}H_9ClN_2OS$ $(M + H)^+$ 301.0197, found 301.0188.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures, tables, and a CIF file giving ^{1}H NMR and ^{13}C NMR spectra of all compounds, X-ray datea for **5a**, and the Cartesian coordinates and absolute energies for all structures involved in theoretical calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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