Intramolecular Diels-Alder Reactions of 1,2,4-Triazines. A Facile Synthesis of Thieno[2,3-*b*]pyridines and 3,4-Dihydro-2*H*-thiopyrano[2,3-*b*]pyridines

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Thieno[2,3-*b*]pyridines and 3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridines have been prepared in high overall yields via intramolecular Diels-Alder reactions of properly substituted 1,2,4-triazine derivatives. A one-pot synthesis of 2,3-dihydrothieno[2,3-*b*]pyridines from thiosemicarbazide is described.

Introduction

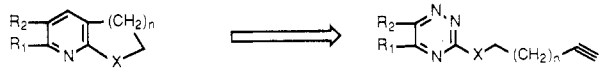
The use of intermolecular inverse electron demand Diels-Alder reactions of 1,2,4-triazines with electron-rich dienophiles to form functionalized pyridine derivatives has been extensively exploited and is well documented.[1] However, extensions of this methodology to the synthesis of fused pyridine derivatives via *intramolecular* Diels-Alder reactions have not been equally utilized.[2] Conceptually, one could view fused [2,3-*b*]pyridine heterocycles **1** as arising from 1,2,4-triazine derivatives **2** with the appropriate dienophile attached to the 3-position of the ring (Scheme I). In this paper we present the results of our study of intramolecular Diels-Alder reactions of 1,2,4-triazines leading to thieno[2,3-*b*]pyridines (**1**, X = S, n = 1) and 3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridines (**1**, X = S, n = 2).[2a,c]

Although not readily found in nature, thienopyridines have found uses as herbicides, as components of antibiotics, and as dyestuffs. Classical syntheses of these compounds involve ring annulation reactions on existing pyridine or thiophene derivatives, and these reactions are usually inflexible, tedious, and low-yielding.[3] Our approach by means of an intramolecular Diels-Alder reaction gives thienopyridines in a single, high-yielding cyclization step, whereby substituents on the final bicyclic system are determined by an appropriate choice of the starting 1,2,4-triazine and the nature of the tethered dienophilic side chain.

Results and Discussion

For our initial study (Scheme II), 5-phenyl-3-(3-butynylthio)-1,2,4-triazine (**4c**) was synthesized by alkylation of 5-phenyl-1,2,4-triazine-3-thione (**3c**) with 4-iodo-1-butyne.[4] Heating **4c** in refluxing dioxane (101 °C) for 24 h

Scheme I



1 **2**

gave 6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (**5c**) in 93% yield. Oxidation of the sulfide **4c** with 1 equiv of *m*-chloroperbenzoic acid (mcpba) yielded the sulfoxide **6c**, *which spontaneously started to cyclize at room temperature.* This reaction was complete after 21 h and gave 1-oxo-6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (**7c**) in 79% yield. Since it is well-known that increasing the electronic deficiency of a 1,2,4-triazine increases the rate with which it undergoes intermolecular Diels-Alder reactions with a given dienophile,[1] this increase in the cyclization rate of the sulfoxide **6c** over the sulfide **4c** was not unexpected. However, we subsequently observed that the even more electron-poor sulfone **8c**, formed via the oxidation of **4c** with 2 equiv of mcpba, cyclized at a significantly slower rate than the sulfoxide **6c**; intramolecular cycloaddition of **8c** to give 1,1-dioxo-6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (**9c**) (78% yield) was complete only after 24 h in refluxing THF. This unexpected spectrum of cyclization rates [sulfoxide ≫ sulfone > sulfide] is, however, explicable if one considers the differing C-S-C bond angles in the dienophilic side chains. The bond angles of dimethyl sulfone, dimethyl sulfoxide, and dimethyl sulfide are 102.6°, 96.6°, and 99.2° respectively.[5] The smaller the C-S-C bond angle in the dienophilic side chains in **4c**, **6c**, and **8c**, the closer the dienophile to the intramolecular diene ("scissoring effect"). Thus, the sulfoxide **6c** has the smallest C-S-C bond angle and the fastest rate of intramolecular cyclization. The positive influence of the high degree of electronic deficiency in the sulfone **8c** is partially negated by its large C-S-C bond angle.

Following the successful completion of these initial studies, we turned our attention to optimization of this methodology. Since it is known that 5-alkyl-1,2,4-triazine-3-thiones readily dimerize,[6] a synthesis of **4** which avoided the intermediacy of the thiones **3** was attractive. Such a method was provided by the work of Paudler and Chen,[7] who described the preparation of a series of 3-

(1) Boger, D. L. *Tetrahedron* **1983**, *39*, 2869.

(2) Only a few papers describing intramolecular Diels-Alder reactions of 1,2,4-triazines have appeared: (a) Seitz, G.; Dietrich, S. *Arch. Pharm.* **1984**, *317*, 379. (b) Seitz, G.; Gorge, L. *Chem. Ztg.* **1984**, *108*, 331. (c) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1985**, *26*, 2419. (d) Taylor, E. C.; Macor, J. E. *Abstracts, 10th International Congress of Heterocyclic Chemistry*, University of Waterloo, Waterloo, Ontario, Canada; Ainsworth: Kitchener, Ontario, Canada, 1985; pp P5-137. (e) Taylor, E. C.; Macor, J. E. *Abstracts, 10th International Congress of Heterocyclic Chemistry*; University of Waterloo, Waterloo, Ontario, Canada; Ainsworth: Kitchener, Ontario, Canada, 1985; pp G4-28. (f) Seitz, G.; Gorge, L.; Dietrich, S. *Tetrahedron Lett.* **1985**, *26*, 4355. (g) Seitz, G.; Dietrich, S. *Arch. Pharm.* **1985**, *318*, 1048, 1051. (h) Seitz, G.; Gorge, L.; Dietrich, S. *Tetrahedron Lett.* **1985**, *26*, 4355. (i) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1986**, *27*, 431. (j) Taylor, E. C.; French, L. G. *Tetrahedron Lett.* **1986**, *27*, 1967. (k) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1986**, *27*, 2107. (l) Seitz, G.; Dietrich, S.; Gorge, L.; Richter, J. *Tetrahedron Lett.* **1986**, *27*, 2747. (m) Taylor, E. C.; Pont, J. L. *Tetrahedron Lett.* **1987**, *28*, 379.

(3) For a review of the syntheses, uses, and chemistry of thienopyridines, see: Barker, J. M. In "The Thienopyridines" *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Boulton, A. J., Eds.; Academic: New York, 1977; Vol. 21, pp 65-119.

(4) Eglinton, G.; Whiting, M. C. *J. Chem. Soc.*, **1950**, 3650.

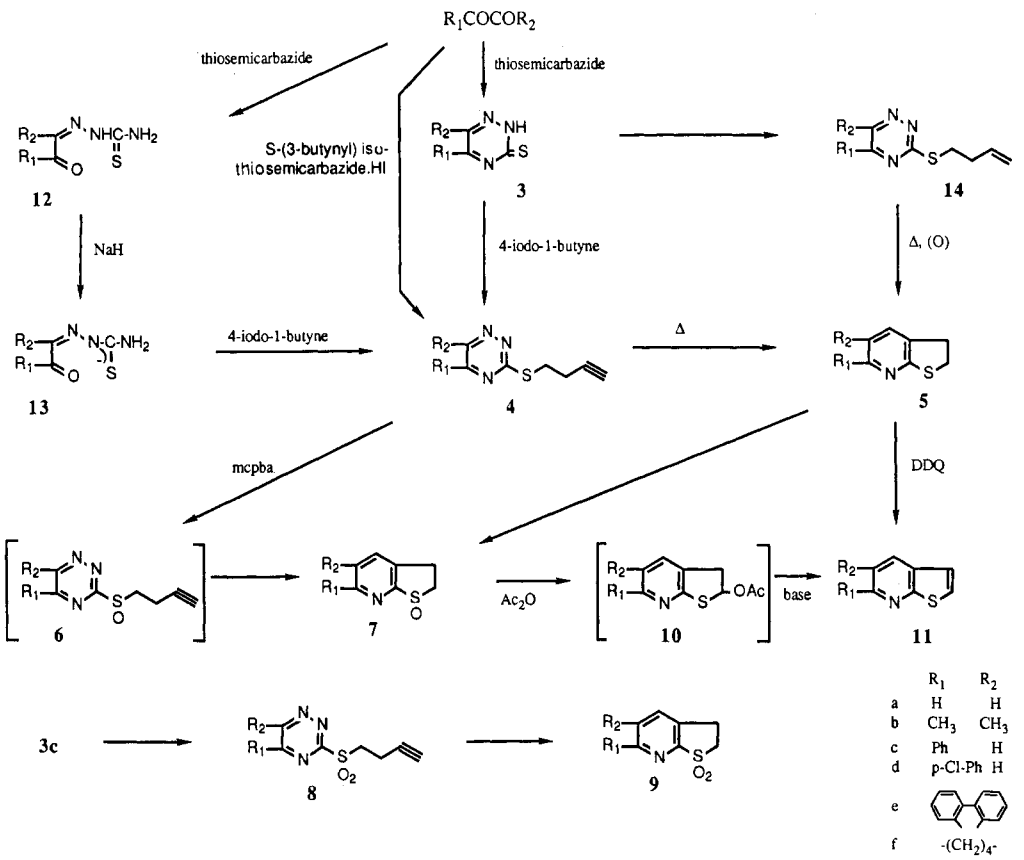
(5) Hargittai, I. In "Sulphone Molecular Structures" *Lecture Notes in Chemistry*; Berthier, G., Dewar, M. J. S., Fischer, H., Fukui, K., Hartmann, H., Jaffe, H. H., Jortner, J., Kutzelwiggs, W., Ruedenberg, K., Scrocco, E., Zeil, W., Ed.; Springer-Verlag: New York, 1978; Vol. 6 p 114.

(6) In fact, only a limited number of 1,2,4-triazine-3-thiones can be synthesized from the reaction of 1,2-dicarbonyl compounds with thiosemicarbazide. 1,2,4-Triazine-3-thiones with C-5 alkyl groups have been shown to dimerize (Neunhoeffer, H. In "1,2,4-Triazines; The Chemistry of 1,2,3-Triazines and 1,2,4-Triazines, Tetrazines, and Pentazines" *The Chemistry of Heterocyclic Compounds*; Weissberger, A., Taylor, E. C., Eds.; Wiley: New York, 1978; Vol. 33.

(7) Paudler, W. W.; Chen, T. K. *J. Heterocycl. Chem.* **1970**, *7*, 767.

0022-3263/87/1952-4280$01.50/0

Scheme II



(methylthio)-1,2,4-triazines from the reaction of *S*-methylisothiosemicarbazide hydrogen iodide with 1,2-dicarbonyl compounds. Modification of this procedure by using *S*-3-butynylisothiosemicarbazide hydrogen iodide (formed from the reaction of thiosemicarbazide and 4-iodo-1-butyne in refluxing ethanol) gave the desired 3-(3-butynylthio)-1,2,4-triazines (**4**) in high yield. Oxidation of **4** with 1 equiv of mcpba at room temperature gave the sulfoxides **6** which readily cyclized to **7**, even at room temperature.

Two methods were then employed to form the fully aromatic thieno[2,3-*b*]pyridines **11**. Dehydration of **7** (which could also be obtained by mcpba oxidation of **5**) with refluxing acetic anhydride (Pummerer reaction) followed by treatment of the intermediates **10** with aqueous base yielded **11** in good yield. Alternatively, dehydrogenation of the sulfides **5** with an excess of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) afforded **11** in moderate to good yields; however, this procedure required long reaction times and did not always go to completion.

Further modifications of this intramolecular Diels–Alder methodology have led to a simple two-pot synthesis of thieno[2,3-*b*]pyridines **11** starting from thiosemicarbazide. Heating a 1,2-dicarbonyl compound with thiosemicarbazide in refluxing ethanol for 15 min formed the thiosemicarbazones **12**. Deprotonation of **12** with 1 equiv of NaH gave the delocalized anions **13**, which upon alkylation with 4-iodo-1-butyne[8] led directly to the triazines **4**. Changing the solvent at this point to chlorobenzene, followed by heating the reaction mixture at reflux, resulted in what amounts to a one-pot formation of 2,3-dihydrothieno[2,3-*b*]pyridines **5**. In the second step, dehydrogenation of **5** with DDQ gave the thieno[2,3-*b*]pyridines **11**. This two-pot sequence represents the most efficient available route to these compounds.

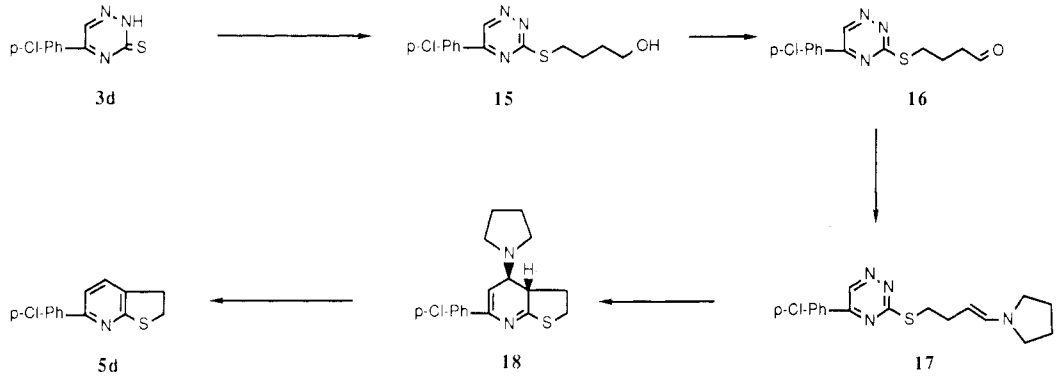
The use of alternative dienophiles in these intramolecular Diels–Alder reactions was also studied. 3-(3-Butenylthio)-1,2,4-triazines (**14**) were synthesized by alkylation of the 1,2,4-triazine-3-thiones **3** with 4-bromo-1-butene. However, the intramolecular cycloaddition reactions of these compounds were accompanied by extensive decomposition, and the dihydrothieno[2,3-*b*]pyridines (**5**) could be isolated only in low yield. Apparently, the dihydropyridines that are formed initially in the Diels–Alder reaction aromatize at the expense of the other components of the reaction mixture. Consequently, the use of alkenes in these intramolecular Diels–Alder reactions was not further investigated.

Although there are numerous examples of intermolecular Diels–Alder reactions of enamines and 1,2,4-triazines, there are no reported *intramolecular* examples of this reaction. Alkylation of the thione **3d** with 4-bromo-1-butanol,[9] followed by oxidation of the resulting alcohol **15** with PCC, led to the aldehyde **16** (Scheme III). When **16** was treated with pyrrolidine, formation of the enamine **17** was clearly confirmed by NMR spectroscopy, but isolation and characterization of the enamine was not possible because of spontaneous albeit gradual cycloaddition which led, over the course of 4 days at room temperature, to the 2,3-dihydrothieno[2,3-*b*]pyridine (**5d**) in 86% yield. From examination of NMR spectra of the reaction mixture taken during the course of this reaction, it appeared that the

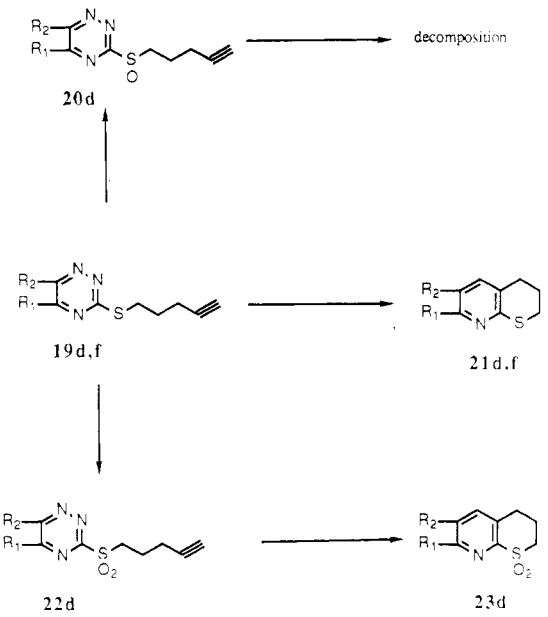
(8) The alkylation of **13** with differently sized alkylating agents was studied. In general, the smaller the alkylating agent, the less S-alkylation (more N-alkylation) occurred. Alkylation with methyl iodide yielded only traces of the expected 3-(methylthio)-1,2,4-triazine, while benzyl bromide led to the desired 3-(benzylthio)-1,2,4-triazine in almost quantitative yield. 4-Iodo-1-butyne reacted primarily on sulfur, but a significant amount of N-alkylation also occurred which lowered the overall yield of this "one-pot" reaction.

(9) Vedjs, E.; Arnost, M. J.; Hagen, J. P. *J. Org. Chem.* **1979**, *44*, 3230.

Scheme III



Scheme IV



rate-limiting step in the overall sequence was cis elimination of pyrrolidine from intermediate **18**. The ease of this cycloaddition reaction contrasts sharply with our failure to effect an analogous cyclization of the enamine formed in situ from 5-methyl-6-[(4-oxobutyl)thio]-1,2,4-triazine and pyrrolidine.[10]

Homologation of the dienophilic side chain of **4** would lead to 3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridine derivatives **21**. Scheme IV outlines the results of such a study. As would be expected (because of decreased entropic assistance[11] due to the greater chain length), the intramolecular Diels–Alder reactions of the sulfides **19** required higher reaction temperatures and longer reaction times than their shorter chain analogues. Additionally, yields of **21** were lower than the corresponding yields of **5**. Alkylation of **3d** with 5-chloro-1-pentyne/NaI/acetone yielded 5-(4-chlorophenyl)-3-(4-pentynylthio)-1,2,4-triazine (**19d**), which cyclized to 7-(4-chlorophenyl)-3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridine (**21d**) in 67% yield after 3 days at 156 °C (bromobenzene reflux). Intramolecular cycloaddition of **19f** yielded 3,4,6,7,8,9-hexahydro-2*H*-thiopyrano[2,3-*b*]quinoline (**21f**) in 44% yield (62% based on returned starting material). Oxidation of **19d** with 1 equiv of mcpba gave the sulfoxide **20d**; however, at the high reaction temperature necessary to effect cyclization (101 °C), this compound decomposed, and no Diels–Alder-derived products were isolated from the reaction. Oxidation of **19d** with 2 equiv of mcpba yielded the sulfone **22d**. When the sulfone was subjected to the high temperature apparently required for cyclization, the major product was 5-(4-chlorophenyl)-1,2,4-triazin-3-one resulting from hydrolysis of the sulfone **22d** by adventitious moisture; 7-(4-chlorophenyl)-1,1-dioxo-3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridine was isolated in only 21% yield from this reaction.

Conclusion

The intramolecular Diels–Alder reaction methodology for the synthesis of fused pyridine heterocycles has been applied to the synthesis of thieno[2,3-*b*]pyridines **11**. Variations of this concept have been developed which constitute general and useful routes to these bicyclic heterocycles. Homologation of the dienophilic side chain leads (under more drastic cycloaddition conditions because of increased flexibility of the tethered dienophilic side chain) to 3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridines.

Experimental Section

Melting points were determined on a Thomas-Hoover open capillary melting point apparatus and are uncorrected. Infrared spectra were obtained on a Perkin Elmer 1320 infrared spectrophotometer, and NMR spectra were determined on either a JEOL FX-90Q (90 MHz) or a Nicolet QE300 (300 MHz) spectrometer. Mass spectra were determined on a AEI MS-9 instrument, and elemental analyses were carried out by Eli Lilly & Co., Indianapolis, IN. Commercial reagents were utilized without further purification.

General Procedure for the Alkylation of 5-Aryl-1,2,4-triazine-3-thiones.[12] To a stirred solution of the 5-aryl-1,2,4-triazine-3-thione (**3c,d**) (10 mmol) and triethylamine (10 mmol) in anhydrous THF (30 mL) at room temperature was added the alkyl halide (10 mmol), and the resulting solution was stirred at room temperature with exclusion of water for 24 h. A saturated solution of sodium bicarbonate (20 mL) was then added to the reaction mixture, which was then extracted with methylene chloride (3 × 30 mL). The methylene chloride extracts were combined, dried (anhydrous $MgSO_4$), and evaporated under reduced pressure. The residual solid or oil was then purified either by ether trituration or silica gel (~50 g) column chromatography.

3-(3-Butynylthio)-5-phenyl-1,2,4-triazine (4c). Method A. The alkyl halide used was 4-iodo-1-butyne; chromatography (eluting with 2:3 ether/petroleum ether) yielded **4c** (97%) as a white, crystalline solid: mp behavior, initial softening at 67.0 °C followed by effervescence and resolidification and then complete melting at 82.0 °C; IR (KBr) 3250, 1595, 1540, 1500, 1430 cm^{-1};

(10) See Macor, J. E., Ph.D. Thesis, Princeton University, 1986, pp 128–131. The coefficients of the triazine LUMO should be larger at C-3 than at C-6, while the HOMO of the enamine should have its largest coefficient at the more electron-rich β-carbon. HOMO–LUMO overlap is thus minimal for a 6-alkynylthio derivative; conversely, it should be maximized in a 3-alkynylthio derivative. This interpretation is in accord with our experimental observations.

(11) Ciganek, E. *Org. React. (N. Y.)* **1984**, *32*, 44, 45.

(12) 5-Phenyl-1,2,4-triazine-3-thione (**4c**) and 5-(4-chlorophenyl)-1,2,4-triazine-3-thione (**4d**) were prepared as described by: Tisler, M. *Croat. Chem. Acta* **1960**, *32*, 123.

^{1}H NMR ($CDCl_3$) δ 9.37 (s, 1 H), 8.18–8.04 (m, 2 H), 7.64–7.40 (m, 3 H), 3.47 (t, J = 7.0 Hz, 2 H), 2.76 (dt, J = 2.6 and 7.0 Hz, 2 H), 2.09 (t, J = 2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 172.7, 154.6, 142.1, 132.9, 132.6, 129.3, 127.5, 82.0, 69.9, 29.5, 19.1.

Anal. Calcd for $C_{13}H_{11}N_3S$: C, 64.70; H, 4.59; N, 17.41; S, 13.29. Found: C, 64.49; H, 4.37; N, 17.25; S, 13.32.

3-(3-Butenylthio)-5-phenyl-1,2,4-triazine (14c). The alkyl halide used was 4-bromo-1-butene; chromatography (eluting with 1:1 ether/petroleum ether) yielded **14c** (88%) as an orange oil at room temperature: IR (neat) 1640, 1600, 1525, 1490, 1435 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.34 (s, 1 H), 8.17–8.06 (m, 2 H), 7.56–7.44 (m, 3 H), 6.15–5.71 (m, 1 H), 5.24–5.04 (m, 2 H), 3.36 (t, J = 7.5 Hz, 2 H), 2.69–2.46 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 173.1, 154.1, 141.7, 135.8, 132.8, 132.4, 129.1, 127.3, 116.4, 33.0, 29.7.

Anal. Calcd for $C_{13}H_{13}N_3S$: C, 64.17; H, 5.39; N, 17.27; S, 13.18. Found: C, 64.22; H, 5.53; N, 16.98; S, 13.01.

3-(3-Butenylthio)-5-(4-chlorophenyl)-1,2,4-triazine (14d). The alkyl halide used was 4-bromo-1-butene; chromatography (eluting with 1:1 ether/petroleum ether) yielded **14d** (87%) as a pale orange solid: mp 51.0–54.0 °C; IR (KBr) 1640, 1595, 1530, 1490, 1440 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.26 (s, 1 H), 8.03–7.98 (m, 2 H), 7.46–7.41 (m, 2 H), 5.90–5.76 (m, 1 H), 5.11–5.00 (m, 2 H), 3.28 (t, J = 7.1 Hz, 2 H), 2.53–2.46 (m 2H); ^{13}C NMR ($CDCl_3$) δ 173.4, 153.3, 141.6, 139.1, 136.0, 131.5, 129.7, 128.8, 116.7, 33.1, 30.0; HRMS calcd for $C_{13}H_{12}ClN_3S$ 277.04624, found 277.04624 ● 0.0005.

5-(4-Chlorophenyl)-3-(4-hydroxybutylthio)-1,2,4-triazine (15). The alkyl haldide used was 4-bromo-1-butanol; chromatography (eluting with 1:1 ethyl acetate/hexanes) yielded **15** (64%) as a white solid: mp 101.0–102.5 °C; IR (KBr) 3350, 1590, 1525, 1490, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.31 (s, 1 H), 8.15–8.00 (m, 2 H), 7.58–7.43 (m, 2 H), 3.84–3.56 (br m, 2 H), 3.34 (t, J = 7.0 Hz, 2 H), 2.17 (br m, 1 H), 2.03–1.64 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 173.7, 153.5, 141.5, 139.2, 131.8, 129.7, 128.8, 62.2, 31.8, 30.5, 25.7.

Anal. Calcd for $C_{13}H_{14}ClN_3OS$: C, 52.79; H, 4.77; Cl, 11.99; N, 14.21; S, 10.84. Found: C, 53.05; H, 4.89; Cl, 12.10; N, 14.23; S, 11.14.

5-(4-Chlorophenyl)-3-(4-pentynylthio)-1,2,4-triazine (19d). The alkyl halide used was 5-chloro-1-pentyne under Finkelstein conditions (1 equiv of NaI), the solvent was acetone (30 mL), and the reaction mixture was heated at reflux (65 °C) with exclusion of water for 16 h; solid purified by ether trituration, followed by chromatography (eluting with methylene chloride) to yield **19d** (71%) as a white solid, mp 112.5–114.0 °C; IR (KBr) 3220, 2110, 1580, 1520, 1485, 1405–1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.35 (s, 1 H), 8.16–8.04 (m, 2 H), 7.60–7.44 (m, 2 H), 3.43 (t, J = 7.0 Hz, 2 H), 2.52–2.34 (m, 2 H), 2.22–1.86 (m, 2 H), 2.02 (t, J = 2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 173.5, 153.5, 141.7, 139.3, 131.9, 129.7, 128.9, 83.1, 69.3, 29.7, 28.1, 17.7.

Anal. Calcd for $C_{14}H_{12}ClN_3S$: C, 58.03; H, 4.17; Cl, 12.23; N, 14.50; S, 11.06. Found: C, 57.75; H, 4.14; Cl, 12.51; N, 14.34; S, 10.81.

***S*-3-Butynylisothiosemicarbazide Hydrogen Iodide.** A mixture of thiosemicarbazide (2.73 g, 29.95 mmol) and 4-iodo-1-butyne (5.40 g, 30.00 mmol) in absolute ethanol (25 mL) was heated at reflux (78 °C) with exclusion of water for 6.0 h. The resulting clear, colorless solution was cooled to −10 °C overnight, and the crystals which had separated were collected by filtration to yield *S*-3-butynylisothiosemicarbazide hydrogen iodide (4.25 g, 15.68 mmol, 52.3%) as a white, crystalline solid: mp, 110.0–112.0 °C; IR (KBr) 3340, 3270–2800, 1645, 1595, 1530 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 8.95 (br s, 5 H), 3.32 (t, J = 6.6 Hz, 2 H), 2.96–2.76 (m, 1 H), 2.66–2.46 (m, 2 H); ^{13}C NMR (Me_2SO-d_6) δ 165.2, 81.0, 72.6, 29.2, 18.8.

Anal. Calcd for $C_5H_{10}IN_3S$: C, 22.15; H, 3.72; N, 15.50; S, 11.83. Found: C, 22.41; H, 3.46; N, 15.36; S, 11.67.

The filtrate was concentrated by evaporation under reduced pressure to yield an additional crop of *S*-3-butynylisothiosemicarbazide hydrogen iodide (3.15 g, 39%, total yield 91%) as an off-white, crystalline sold identical in all respects with the above solid except for a slightly broadened melting point (109–113 °C).

General Procedure for the Condensation of *S*-3-Butynylisothiosemicarbazide with 1,2-Dicarbonyl Compounds. To a stirred mixture of the 1,2-dicarbonyl compound (10.0 mmol) and sodium bicarbonate (10.0 mmol) in absolute ethanol (10 mL) at 0 °C was added dropwise a of *S*-3-butynylisothiosemicarbazide (10.0 mmol) in water (10 mL). The resulting effervescing solution was then stirred at room temperature for 4.0 h. Ethanol was removed from the resulting reaction mixture by evaporation under reduced pressure, and the residual aqueous mixture was extracted with methylene chloride (3 × 20 mL). The methylene chloride extracts were combined, dried (anhydrous $MgSO_4$), and evaporated under reduced pressure. The residual oil or solid was then purified either by silica gel (~50 g) column chromatography or by trituration with ether to yield the desired 3-(3-butynylthio)-1,2,4-triazine (**4**).

3-(3-Butynylthio)-1,2,4-triazine (4a). Aqueous glyoxal (40%) was used. Silica gel chromatography (eluting with 1:2 ether/petroleum ether) yielded **4a** as a pale yellow solid (62%): mp 49.0–51.0 °C; IR (neat) 3280, 2120, 1530, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.97 (d, J = 2.4 Hz, 1 H), 8.41 (d, J = 2.4 Hz, 1 H), 3.43 (t, J = 7.0 Hz, 2 H), 2.72 (dt, J = 2.6 and 7.0 Hz, 2 H), 2.08 (t, J = 2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 173.4, 148.1, 145.4, 81.7, 69.9, 29.4, 18.9.

Anal. Calcd for $C_7H_7N_3S$: C, 50.89; H, 4.27; N, 25.43; S, 19.41. Found: C, 50.79; H, 4.41, N, 25.19; S, 19.68.

3-(3-Butynylthio)-5,6-dimethyl-1,2,4-triazine (4b). Silica gel chromatography (eluting with 1:3 ether/petroleum ether) yielded **4b** as a pale yellow oil (86%): IR 3290, 2120, 1535, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.39 (t, J = 7.0 Hz, 2 H), 2.71 (dt, J = 2.6 and 7.0 Hz, 2 H), 2.61 (s, 3 H), 2.49 (s, 3 H), 2.08 (t, J = 2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.9, 158.6, 153.5, 82.0, 69.9, 29.3, 21.4, 19.0, 18.8; LRMS, m/z (relative intensity) 193 (8, M$^+$), 164 (10), 141 (15), 112 (17), 54 (50), 53 (100); HRMS calcd for $C_9H_{11}N_3S$ 193.0674, found 193.0670 ± 0.0019.

Anal. Calcd for $C_9H_{11}N_3S$: C, 55.93; H, 5.74; N, 21.74; S, 16.59. Found: 55.79; H, 5.45; N, 21.51; S, 16.47.

3-(3-Butynylthio)-5-phenyl-1,2,4-triazine (4c). Method B. Silica gel chromatography (eluting with 1:1 ethyl acetate/petroleum ether) yielded **4c** as a pale yellow solid (95%): ^{1}H NMR ($CDCl_3$) δ 9.36 (s, 1 H), 8.18–8.07 (m, 2 H), 7.57–7.48 (m, 3 H), 3.46 (t, J = 7.0 Hz, 2 H), 2.76 (dt, J = 2.6 and 7.0 Hz, 2 H), 2.09 (t, J = 2.6 Hz, 1 H). The spectral and physical properties of this solid were identical with the spectral and physical properties of 3-(3-butynylthio)-5-phenyl-1,2,4-triazine prepared as described above in method A.

3-(3-Butynylthio)phenanthreno[9,10-*e*]-1,2,4-triazine (4e). Silica gel chromatography (eluting first with 1:1 methylene chloride/hexanes and then with methylene chloride) yielded **4e** as a yellow solid (74%): mp 141.5–143.5 °C; IR (KBr) 3260, 2120, 1605, 1500, 1480, 1445, 1350 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.28–9.08 (m, 1 H), 9.05–8.94 (m, 1 H), 8.46–8.32 (m, 2 H), 7.89–7.55 (m, 4 H), 3.59 (t, J = 7.0 Hz, 2 H), 2.87 (dt, J = 2.6 and 7.0 Hz, 2 H), 2.13 (t, J = 2.6 Hz, 1 H); HRMS (M = $C_{19}H_{11}N_3S$) calcd for ([M$^+$] − [H]) 314.07590, found 314.07590 ± 0.0050.

3-(3-Butynylthio)-5,6-cyclohexeno-1,2,4-triazine (4f). A mixture of thiosemicarbazide (0.91 g, 9.98 mmol) and 1,2-cyclohexanedione (1.12 g, 9.99 mmol) in absolute ethanol (20 mL) was heated at reflux with exclusion of water for 15 min. The resulting solution was cooled in an ice bath, and sodium hydride (60% oil, 0.40 g, 10.00 mmol) was then added, followed by the dropwise addition of 4-iodo-1-butyne (1.00 mL, 10.00 mmol). This mixture was then heated at reflux (78 °C) with exclusion of water for 1 h. A saturated solution of ammonium chloride (20 mL) was added to the reaction mixture, and this aqueous mixture was extracted with methylene chloride (3 × 20 mL). The methylene chloride extracts were combined, dried (anhydrous $MgSO_4$), and evaporated under reduced pressure to yield a yellow oil. Column chromatography of this oil using silica gel (~100 g) and eluting with 1:1 ether/petroleum ether afforded **4f** (1.25 g, 57%) as a clear, colorless oil: IR (neat) 3295, 2120, 1525, 1500 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.38 (t, J = 7.2 Hz, 2 H), 3.07 (t, J = 6.0 Hz, 2 H), 2.87 (t, J = 6.0 Hz, 2 H), 2.71 (dt, J = 2.6 and 7.2 Hz, 2 H), 2.07 (t, J = 2.6 Hz, 1 H), 1.98–1.91 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 169.3, 159.2, 154.4, 82.0, 69.6, 31.2, 29.3, 28.7, 21.8, 21.4, 19.0.

Anal. Calcd for $C_{11}H_{13}N_3S$: C, 60.24; H, 5.98; N, 19.16; S, 14.62. Found: C, 59.96; H, 5.70; N, 19.19; S, 14.53.

General Procedure for One-Pot Formation of 2,3-Dihydrothieno[2,3-*b*]pyridines 5. A mixture of the 1,2-dicarbonyl compound (10 mmol) and thiosemicarbazide (0.91 g, 10.0 mmol) in absolute ethanol (30 mL) was heated at reflux (78 °C) for 20 min. The resulting solution was then cooled in an ice bath, and

sodium hydride (60% oil, 0.40 g, 10.0 mmol) was cautiously added to the mixture, which was then stirred at room temperature with exclusion of water for 15 min. This was followed by the dropwise addition of 4-iodo-1-butyne (1.00 mL, 10.0 mmol), and the resulting reaction mixture was heated at reflux with exclusion of water for 1 h. Ethanol was removed from the reaction mixture by evaporation under reduced pressure, and the residual oily solid was covered with chlorobenzene (10 mL). This mixture was heated at reflux (132 °C) with exclusion of moisture for 6–17 h depending on the substrate. A saturated solution of sodium bicarbonate (20 mL) was added to the resultant reaction solution, and this aqueous mixture was extracted with methylene chloride (3 × 20 mL). The methylene chloride extracts were combined, dried (anhydrous $MgSO_4$), and evaporated under reduced pressure to yield an oil, which was chromatographed over silica gel (~60 g); elution with the appropriate solvent system yielded the desired 2,3-dihydrothieno[2,3-*b*]pyridine **5**.

5,6-Dimethyl-2,3-dihydrothieno[2,3-*b*]pyridine (5b). The reflux time in chlorobenzene was 17 h; chromatography (eluting with 1:2 ether/petroleum ether) yielded **5b** as a pale brown oil which crystallized upon cooling (64% yield based on thiosemicarbazide): mp 50.0–52.0 °C; IR (KBr) 1585, 1550, 1445, 1430, 1400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.11 (s, 1 H), 3.47–3.04 (m, 4 H), 2.39 (s, 3 H), 2.17 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 161.9, 155.4, 132.6, 130.8, 125.8, 33.2, 31.0, 21.7, 18.3.

Anal. Calcd for $C_9H_{11}NS$: C, 65.41; H, 6.71; N, 8.48; S, 19.40. Found: C, 65.67; H, 6.51; N, 8.48; S, 19.30.

6-(4-Chlorophenyl)-2,3-dihydrothieno[2,3-*b*]pyridine (5d). Method A. The reflux time in chlorobenzene was 6 h; chromatography (eluting with 1:1 methylene chloride/hexanes) yielded **5d** as a fluffy white crystalline solid (67% yield based on thiosemicarbazide): mp 166.0–168.0 °C; IR (KBr) 1580–1550, 1485, 1425 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.96–7.81 (m, 2 H), 7.40 (d, J = 7.9 Hz, 1 H), 7.42–7.32 (m, 2 H), 7.25 (d, J = 7.9 Hz, 1 H), 3.52–3.12 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 166.8, 155.4, 137.6, 134.9, 132.5, 131.6, 128.7, 128.1, 115.2, 33.4, 31.0.

Anal. Calcd for $C_{13}H_{10}ClNS$: C, 63.02; H, 4.07; Cl, 14.31; N, 5.65; S, 12.94. Found: C, 63.25; H, 4.17; Cl, 14.32; N, 5.45; S, 12.87.

6-Phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (5c). Method A. A solution of 3-(3-butynylthio)-5-phenyl-1,2,4-triazine (0.74 g, 3.07 mmol) in anhydrous dioxane (5 mL) was heated at reflux under nitrogen for 24 h. Dioxane was removed from the resulting solution by evaporation under reduced pressure, and the residual brown oil was chromatographed over silica gel (~40 g) and eluted with 1:2 ether/petroleum ether to afford 6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (0.61 g, 2.86 mmol, 93%) as a white crystalline solid: mp 82.0–83.0 °C; IR (KBr) 3070, 1575, 1560, 1490, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.98–7.84 (m, 2 H), 7.53–7.20 (m, 5 H), 3.49–3.14 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 166.2, 156.2, 138.8, 132.0, 131.5, 128.5, 128.4, 126.5, 115.4, 33.1, 30.8.

Anal. Calcd for $C_{13}H_{11}NS$: C, 73.20; H, 5.20; N, 6.57; S, 15.03. Found: C, 72.98; H, 5.05; N, 6.69; S, 15.17.

6-(4-Chlorophenyl)-2,3-dihydrothieno[2,3-*b*]pyridine (5d). Method B (via Intramolecular Enamine Cycloaddition). To a stirred mixture of 3-[(4-oxobutyl)thio]-5-(4-chlorophenyl)-1,2,4-triazine (0.29 g, 0.99 mmol) and anhydrous $MgSO_4$ (0.20 g, 1.66 mmol, 1.66 equiv) in a solution of anhydrous ether (10 mL) and anhydrous methylene chloride (5 mL) at room temperature, pyrrolidine (0.17 mL, 2.04 mmol, 2.0 equiv) was added dropwise. The resultant mixture was stirred at room temperature with exclusion of water for 20 h and filtered and the filtrate concentrated to a solid/oil mixture (0.34 g) by evaporation under reduced pressure. An NMR spectrum of this mixture indicated the presence of the intermediate in situ formed enamine [δ 9.21 (s, triazine ring proton), 4.08–3.96 (m, β olefinic enamine proton), 6.22 (d, α olefinic enamine proton)] as well as the desired 2,3-dihydrothieno[2,3-*b*]pyridine. This mixture was redissolved in a solution of anhydrous ether (5 mL) and methylene chloride (5 mL) with anhydrous $MgSO_4$ (0.4 g), and this mixture was stirred at room temperature with exclusion of water for an additional 94 h (114 h total). The resultant reaction mixture was filtered, and the filtrate was passed through a silica gel (~30 g) filter followed by elution with methylene chloride (200 mL). This filtrate was evaporated under reduced pressure to yield 6-(4-chlorophenyl)-2,3-dihydrothieno[2,3-*b*]pyridine (0.21 g, 0.85 mmol, 86%) as a white, crystalline solid: mp 164.0–165.0 °C; ^1H NMR ($CDCl_3$) δ 7.87–7.82 (m, 2 H), 7.41 (d, J = 7.8 Hz, 1 H), 7.38–7.32 (m, 2 H), 7.24 (d, J = 7.7 Hz, 1 H), 3.41–3.36 (m, 2 H), 3.29–3.24 (m, 2 H). The spectral and physical properties of this solid were identical with those of 6-(4-chlorophenyl)-2,3-dihydrothieno-[2,3-*b*]pyridine prepared as described above under method A.

6-Phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (5c). Method B (from 14c). A solution of 3-(3-butenylthio)-5-phenyl-1,2,4-triazine (0.60 g, 2.47 mmol) in anhydrous dioxane (3 mL) was heated at reflux with exclusion of moisture for 10.5 days. The resultant reaction mixture was concentrated by evaporation under reduced pressure, and the residual oil was chromatographed by using silica gel (~40 g) and by eluting with 1:3 ether/petroleum ether to yield 6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (0.21 g, 0.98 mmol, 40%) as a pale yellow solid: mp 81.5–82.5 °C; ^1H NMR ($CDCl_3$) δ 7.99–7.85 (m, 2 H), 7.48–7.23 (m, 5 H), 3.52–3.08 (m, 4 H). The spectral and physical properties of this solid were identical with the spectral and physical properties of 6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine prepared as described above by method A.

6-(4-Chlorophenyl)-2,3-dihydrothieno[2,3-*b*]pyridine (5d). Method C (from 14d). A solution of 3-(3-butenylthio)-5-(4-chlorophenyl)-1,2,4-triazine (0.49 g, 1.76 mmol) in dry Me_2SO (5 mL, stored over 4-Å sieves) was heated at 100–105 °C under nitrogen for 25 h. A saturated solution of sodium bicarbonate (10 mL) was added to the orange-colored reaction solution, and this aqueous mixture was extracted with methylene chloride (25 mL). This extract was then washed with water (15 mL), dried (anhydrous $MgSO_4$), and evaporated under reduced pressure to yield an oil. Column chromatography of this oil using silica gel (~40 g) and elution with methylene chloride afforded 6-(4-chlorophenyl)-2,3-dihydrothieno[2,3-*b*]pyridine (0.15 g, 0.61 mmol, 34%) as a white crystalline solid: mp 163.0–165.0 °C; ^1H NMR ($CDCl_3$) δ 7.94–7.82 (m, 2 H), 7.45–7.25 (m, 4 H), 3.56–3.06 (m, 4 H). The spectral and physical properties of this solid were consistent with the spectral and physical properties of 6-(4-chlorophenyl)-2,3-dihydrothieno[2,3-*b*]pyridine prepared as described above by methods A and B.

General Procedure for the Oxidation of 3-(3-Butynylthio)-1,2,4-triazines with Subsequent Cyclization to 1-Oxo-2,3-dihydrothieno[2,3-*b*]pyridines 7. To a stirred solution of the 3-(3-butynylthio)-1,2,4-triazine (5.00 mmol) in anhydrous methylene chloride (20 mL) at 0 °C was added *m*-chloroperbenzoic acid (80–85% technical solid, 1.05 g, 5.17 mmol maximum, 1.03 equiv maximum) as a solid in small portions over the course of a few minutes. The resultant mixture was warmed to room temperature and stirred at room temperature with exclusion of water for 24 h (6-unsubstituted 1,2,4-triazines) or heated at reflux (39 °C) for 42 h (6-substituted 1,2,4-triazines). The resultant reaction mixture was filtered, and the filtrate was evaporated under reduced pressure. Column chromatography of the residual oil/solid using silica gel (~40 g) and elution with the appropriate solvent system yielded the following 1-oxo-2,3-dihydrothieno-[2,3-*b*]pyridines **7**.

1-Oxo-2,3-dihydrothieno[2,3-*b*]pyridine (7a). Purification by silica gel filtration (eluting first with 1:1 ether/petroleum ether to remove *m*-chlorobenzoic acid, followed by 10% methanol in ethyl acetate) yielded **7a** (88%) as an off-white, crystalline solid; mp 96.0–97.5 °C; IR (KBr) 1570, 1560, 1455, 1410, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.63 (d, J = 4.6 Hz, 1 H), 7.85 (d, J = 7.3 Hz, 1 H), 7.42 (dd, J = 4.6 and 7.7 Hz, 1 H), 4.04–3.49 (m, 1 H), 3.45–3.15 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 164.8, 149.8, 136.5, 134.7, 125.6, 50.5, 28.9.

Anal. Calcd for C_7H_7NOS: C, 54.88; H, 4.61; N, 9.14; S, 20.93. Found: C, 54.63; H, 4.60; N, 8.89; S, 20.73.

5,6-Dimethyl-1-oxo-2,3-dihydrothieno[2,3-*b*]pyridine (7b). Chromatography (eluting with 5% methanol in ethyl acetate) yielded **7b** (57%) as an off-white, crystalline solid: mp 125.0–126.5 °C; IR (KBr) 1585, 1545, 1450, 1415, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (s, 1 H), 4.00–3.56 (m, 1 H), 3.49–3.10 (m, 3 H), 2.56 (s, 3 H), 2.35 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 161.4, 158.5, 135.1, 134.7, 134.3, 50.8, 28.6, 22.2, 19.2.

Anal. Calcd for $C_9H_{11}NOS$: C, 59.64; H, 6.12; N, 7.73; S, 17.69. Found: C, 59.90; H, 5.87; N, 7.68; S, 17.46.

1-Oxo-6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (7c). Purification was accomplished via trituration of the crude evaporation residue with anhydrous ether to yield **7c** (79%) as

a white solid: mp 206.5–208.0 °C; IR (KBr) 1585, 1550, 1500, 1455, 1440, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.13–7.96 (m, 2 H), 7.84 (s, 2 H), 7.54–7.38 (m, 3 H), 4.04–3.59 (m, 1 H), 3.44–3.12 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.2, 158.5, 137.6, 135.4, 134.7, 129.7, 128.8, 127.1, 122.6, 50.8, 28.9.

Anal. Calcd for $C_{13}H_{11}NOS$: C, 68.10; H, 4.84; N, 6.11; S, 13.99. Found: C, 67.88; H, 5.04; N, 6.09; S, 13.80.

1-Oxo-2,3,5,6,7,8-hexahydrothieno[2,3-*b*]quinoline (7f). Chromatography (eluting first with ether and then with 10% methanol in ethyl acetate) yielded **7f** (64%) as a clear, colorless oil: IR (neat) 1590, 1550, 1430, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50 (s, 1 H), 3.81–3.71 (m, 1 H), 3.40–3.23 (m, 3 H), 3.06–2.96 (m, 2 H), 2.92–2.81 (m, 2 H), 1.93–1.78 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 161.5, 158.9, 135.7, 135.0, 133.9, 50.6, 32.1, 28.9, 28.7, 22.5, 22.1; LRMS *m/z* (relative intensity) 208 (12), 207 (M^+, 92), 192 (26), 191 (100), 190 (89), 163 (35), 162 (28), 139 (25); HRMS calcd for $C_{11}H_{13}NOS$ 207.0718, found 207.0721 (mass deviation 1.38 ppm).

1,1-Dioxo-6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (9c). To a stirred solution of 3-(3-butynylthio)-5-phenyl-1,2,4-triazine (0.74 g, 3.07 mmol) in anhydrous methylene chloride (20 mL) at room temperature was added *m*-chloroperbenzoic acid (80–85% technical solid, 1.38 g, 6.79 mmol maximum, 2.21 equiv maximum) as a solid all at once. The resultant reaction mixture was stirred at room temperature with exclusion of water for 21 h. The mixture was filtered, and the filtrate was evaporated under reduced pressure to yield a yellow gum (1.5 g). The NMR spectrum of this gum [^1H NMR ($CDCl_3$) δ 9.87 (s, 1 H), 8.34–8.21 (m, 5 H), 3.93 (t, 2 H), 2.90 (dt, 2 H), 1.98 (t, 1 H)] was consistent with the assigned structure of 3-(3-butynylsulfonyl)-5-phenyl-1,2,4-triazine. This gum was dissolved in anhydrous tetrahydrofuran (20 mL), and this solution was heated at reflux (66 °C) under nitrogen for 24 h. Tetrahydrofuran was removed by evaporation under reduced pressure, and the residual solid was triturated with anhydrous ether (25 mL). The undissolved solid was removed by filtration and washed with ether to yield 1,1-dioxo-6-phenyl-2,3-dihydrothieno[2,3-*b*]pyridine (0.59 g, 2.41 mmol, 78%) as a white crystalline solid: mp 242.5–244.0 °C; IR (KBr) 1595, 1550, 1500, 1460, 1445, 1300, 1120 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 8.33–8.00 (m, 4 H), 7.58–7.44 (m, 3 H), 3.74–3.60 (m, 2 H), 3.45–3.31 (m, 2 H); ^{13}C NMR (Me_2SO-d_6) δ 167.5, 157.3, 138.1, 136.8, 130.8, 129.9, 128.9, 126.7, 124.0, 48.3, 21.6.

Anal. Calcd for $C_{13}H_{11}NO_2S$: C, 63.65; H, 4.52; N, 5.71; S, 13.07. Found: C, 63.39; H, 4.36; N, 5.75; S, 13.07.

Dehydration of 1-Oxo-2,3-dihydrothieno[2,3-*b*]pyridines to Thieno[2,3-*b*]pyridines 11. General Procedure. A solution of the 1-oxo-2,3-dihydrothieno[2,3-*b*]pyridine (5.00 mmol) in acetic anhydride (10 mL) was heated at reflux (140 °C) with exclusion of water for 24 h. Acetic anhydride was then removed by evaporation under reduced pressure, and the residual solid/oil mixture was heated at 40 °C in a 1:1 solution of 1 M sodium carbonate/acetone (10 mL) for 2 h. This solution was then extracted with methylene chloride (3 × 20 mL), and the methylene chloride extracts were combined, dried (anhydrous $MgSO_4$), and evaporated under reduced pressure. The residual solid/oil was purified via column chromatography using silica gel (~40 g); elution with the appropriate solvent system then gave the following thieno[2,3-*b*]pyridines **11**.

Thieno[2,3-*b*]pyridine (11a). Chromatography (eluting with 1:4 ether/petroleum ether) yielded **11a** (64%) as a clear, colorless liquid: IR (neat) 1570, 1550, 1485, 1450, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.54 (dd, *J* = 4.6 and 1.5 Hz, 1 H), 8.00 (dd, *J* = 7.9 and 1.5 Hz, 1 H), 7.47 (d, *J* = 5.9 Hz, 1 H), 7.23 (dd, *J* = 7.9 and 4.6 Hz, 1 H), 7.20 (d, *J* = 5.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 161.6, 146.3, 132.3, 130.7, 126.7, 121.3, 119.1.

Anal. Calcd for C_7H_5NS: C, 62.19; H, 3.73; N, 10.36; S, 23.72. Found: C, 62.44; H, 3.60; N, 10.16; S, 23.44. The spectral and physical properties of this liquid were consistent with the spectral and physical properties previously reported for thieno[2,3-*b*]-pyridine.[13]

5,6-Dimethylthieno[2,3-*b*]pyridine (11b). Method A. Chromatography (eluting with 1:1 ether/petroleum ether) yielded **11b** (89%) as a white, crystalline solid: mp 61.5–63.5 °C; IR (KBr) 1590, 1545, 1475, 1450, 1410, 1385–1365 cm^{-1}; ^1H NMR $CDCl_3$) δ 7.70 (s, 1 H), 7.33 (d, *J* = 5.9 Hz, 1 H), 7.09 (d, *J* = 5.9 Hz, 1 H), 2.57 (s, 3 H), 2.32 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 158.6, 154.7, 131.3, 130.8, 127.4, 125.2, 120.8, 22.6, 19.1.

Anal. Calcd for C_9H_9NS: C, 66.22; H, 5.56; N, 8.58; S, 19.64. Found: C, 66.51; H, 5.27; N, 8.37; S, 19.55.

6-Phenylthieno[2,3-*b*]pyridine (11c). Chromatography (eluting with 1:4 ether/petroleum ether) yielded **11c** (62%) as a white, crystalline solid: mp 78.0–79.0 °C; IR (KBr) 1570, 1555, 1495, 1470, 1450, 1420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10–7.91 (m, 3 H), 7.62 (d, *J* = 8.4 Hz, 1 H), 7.51–7.26 (m, 4 H), 7.13 (d, *J* = 5.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.1, 154.3, 139.0, 131.3, 131.0, 128.8, 128.6, 127.1, 126.7, 121.5, 116.5.

Anal. Calcd for $C_{13}H_9NS$: C, 73.90; H, 4.29; N, 6.63; S, 15.18. Found: C, 73.92; H, 4.55; N, 6.35; S, 15.21.

6-(4-Chlorophenyl)thieno[2,3-*b*]pyridine (11d). Method A. Chromatography (eluting with 1:4 methylene chloride/hexanes) yielded **11d** (68%) as a white, crystalline solid: mp 146.0–148.0 °C; IR (KBr) 1590, 1580, 1570, 1490, 1470, 1435, 1395 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.08 (d, *J* = 8.4 Hz, 1 H), 8.01 (d, *J* = 8.8 Hz, 2 H), 7.67 (d, *J* = 8.3 Hz, 1 H), 7.50 (d, *J* = 5.9 Hz, 1 H), 7.43 (d, *J* = 8.8 Hz, 2 H), 7.24 (d, *J* = 5.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 162.5, 153.3, 137.8, 135.2, 131.4, 131.4, 129.0, 128.5, 127.2, 121.3, 116.4.

Anal. Calcd for $C_{13}H_8ClNS$: C, 63.54; H, 3.28; Cl, 14.43; N, 5.70; S, 13.05. Found: C, 63.79; H, 3.48; Cl, 14.67; N, 5.61; S, 13.05.

5,6,7,8-Tetrahydrothieno[2,3-*b*]quinoline (11f). Chromatography (eluting with 1:1 ether/petroleum ether) yielded **11f** (74%) as a clear, colorless oil, which crystallized below 0 °C; IR (neat) 1590, 1540, 1480, 1425, 1380, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (s, 1 H), 7.32 (d, *J* = 6.0 Hz, 1 H), 7.07 (d, *J* = 6.0 Hz, 1 H), 3.02 (t, *J* = 6.4 Hz, 2 H), 2.83 (t, *J* = 6.3 Hz, 2 H), 1.94–1.86 (m, 2 H), 1.84–1.78 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 158.9, 155.0, 130.9, 130.6, 128.3, 125.3, 120.7 32.7, 28.8, 23.0, 22.7.

Anal. Calcd for $C_{11}H_{11}NS$: C, 69.80; H, 5.86; N, 7.40; S, 16.94. Found: C, 69.88; H, 6.13; N, 7.49; S, 17.10.

Phenanthreno[9,10-*e*]thieno[2,3-*b*]pyridine (11e). To a stirred solution of 3-(3-butynylthio)phenanthreno[9,10-*e*]-1,2,4-triazine (1.00 g, 3.19 mmol) in anhydrous methylene chloride at −10 °C was added *m*-chloroperbenzoic acid (80–85% technical solid, 0.70 g, 3.45 mmol maximum, 1.08 equiv maximum) as a solid all at once. The resultant mixture was stirred at −10 °C with exclusion of water for 1 h and then heated at reflux under nitrogen for 55 h. Methylene chloride was removed from the reaction mixture by evaporation under reduced pressure, and 10 mL of anhydrous tetrahydrofuran was added to the residual solid. This solution was heated at reflux (66 °C) under nitrogen for 16 h to complete the cyclization. The resultant reaction mixture was then evaporated to dryness under reduced pressure, and the residual solid was dissolved in methylene chloride (10 mL). This solution was passed through a silica gel filter (~30 g) by eluting first with methylene chloride (100 mL) and then with 20% methanol in methylene chloride (250 mL). The methanol/methylene chloride filtrate was evaporated under reduced pressure to yield a yellow solid. This solid was dissolved in methylene chloride (10 mL), and the resulting cloudy solution was filtered through Celite. The filtrate was evaporated under reduced pressure to yield crude 1-oxophenanthreno[9,10-*e*]-2,3-dihydrothieno[2,3-*b*]pyridine (0.60 g, 1.98 mmol, 62% yield crude) as a white solid: ^1H NMR ($CDCl_3$) δ 9.38–9.22 (m, 1 H), 8.82 (s, 1 H), 8.65–8.36 (m, 3 H), 7.84–7.52 (m, 4 H), 4.14–3.68 (m, 1 H), 3.60–3.32 (m, 3 H). This compound was not purified further because of its insolubility in organic solvents.

It was dissolved in acetic anhydride (10 mL), the resulting solution was heated at reflux with exclusion of moisture for 24 h and concentrated under reduced pressure, and the residual oil was stirred in a mixture of ethanol (10 mL), methylene chloride (10 mL), and 1 M sodium carbonate (20 mL) for 20 h. This mixture was then extracted with methylene chloride (3 × 20 mL), and the combined extracts were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to yield an oil. Column chromatography of this oil using silica gel (~40 g) and elution with 1:1 methylene chloride/hexanes yielded phenanthreno-[9,10-*e*]thieno[2,3-*b*]pyridine (0.23 g, 0.81 mmol, 41% for the dehydration, 25% overall) as a white, crystalline, fluffy solid: mp 147.0–150.0 °C; IR (KBr) 1590, 1560, 1530, 1495, 1450, 1415 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.37–9.08 (m, 1 H), 8.88 (s, 1 H), 8.49–8.19

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(m, 3 H), 7.73–7.36 (m, 4 H), 7.49 (d, J = 6.2 Hz, 1 H), 7.25 (d, J = 6.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 144.9, 131.7, 131.0, 129.7, 128.8, 127.9, 127.5, 127.4, 127.2, 127.0, 126.9, 126.0, 125.6, 124.9, 123.4, 123.0, 122.5, 122.3, 121.5.

Anal. Calcd for $C_{19}H_{11}NS$: C, 79.97; H, 3.89; N, 4.91; S, 11.27. Found: C, 79.66; H, 4.14; N, 4.62; S, 11.24.

General Procedure for the Dehydrogenation of 2,3-Dihydrothieno[2,3-*b*]pyridines to Thieno[2,3-*b*]pyridines 11. A solution of the 2,3-dihydrothieno[2,3-*b*]pyridine (2.00 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (0.91 g, 4.0 mmol, 2.0 equiv) in anhydrous dioxane (5 mL) was heated at reflux (101 °C) with exclusion of water for 13 h. A saturated solution of sodium bicarbonate (10 mL) was then added to the reaction mixture, which was extracted with methylene chloride (3 × 10 mL). The methylene chloride extracts were combined, dried (anhydrous $MgSO_4$), and evaporated under reduced pressure. Column chromatography of the residual oil using silica gel (~40 g) and elution with the appropriate solvent system yielded the following thieno[2,3-*b*]pyridines 11.

5,6-Dimethylthieno[2,3-*b*]pyridine (11b). Method B. Chromatography (eluting with 1:4 ether/petroleum ether) yielded **11b** (46%, 65% based on recovered starting material) as a white, crystalline solid: mp 61.0–63.0 °C; ^{1}H NMR ($CDCl_3$) δ 7.78 (s, 1 H), 7.38 (d, J = 5.9 Hz, 1 H), 7.14 (d, J = 5.9 Hz, 1 H), 2.60 (s, 3 H), 2.38 (s, 3 H). The spectral and physical properties of this solid were identical with the spectral and physical properties for **11b** prepared as described above under method A.

6-(4-Chlorophenyl)thieno[2,3-*b*]pyridine (11d). Method B. Chromatography (eluting with 1:3 methylene chloride/hexanes) afforded **11d** (85%) as a fluffy, white solid: mp 146.0–148.0 °C; ^{1}H NMR ($CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 1 H), 8.01 (d, J = 8.8 Hz, 2 H), 7.67 (d, J = 8.3 Hz, 1 H), 7.50 (d, J = 5.9 Hz, 1 H), 7.43 (d, J = 8.8 Hz, 2 H), 7.24 (d, J = 5.9 Hz, 1 H). The spectral and physical properties of this solid were consistent with the spectral and physical properties of a sample of **11d** prepared as described above under method A.

3-[(4-Oxobutyl)thio]-5-(4-chlorophenyl)-1,2,4-triazine (16). To a stirred mixture of pyridinium chlorochromate (0.60 g, 2.78 mmol, 1.17 equiv) in anhydrous methylene chloride (20 mL) at room temperature was added dropwise a solution of 3-[(4-hydroxybutyl)thio]-5-(4-chlorophenyl)-1,2,4-triazine (0.70 g, 2.37 mmol) in anhydrous methylene chloride (5 mL). The resultant mixture was stirred at room temperature with exclusion of water for 2.0 h. Anhydrous ether (20 mL) was added to the reaction mixture, which was then filtered through a silica gel filter (~30 g) followed by elution with ethyl acetate (125 mL). The combined filtrates were evaporated under reduced pressure, and the residual oil was chromatographed over silica gel (~40 g) (elution with 1:2 ethyl acetate/hexanes) to afford 3-[(4-oxobutyl)thio]-5-(4-chlorophenyl)-1,2,4-triazine (0.40 g, 1.36 mmol, 57%) as a pale yellow solid: mp 71.5–73.5 °C; IR (KBr) 3100, 3040, 1705, 1590, 1525, 1485 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.74 (t, J = 1.3 Hz, 1 H), 9.28 (s, 1 H), 8.04–8.00 (m, 2 H), 7.47–7.43 (m, 2 H), 3.28 (t, J = 7.1 Hz, 2 H), 2.64–2.60 (m, 2 H), 2.14–2.05 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 201.1, 173.1, 153.6, 141.8, 139.2, 131.4, 129.7, 128.9, 42.5, 29.9, 21.6.

Anal. Calcd for $C_{13}H_{12}ClN_3OS$: 53.15; H, 4.12; Cl, 12.07; N, 14.30; S, 10.91. Found: C, 52.85; H, 4.05; Cl, 12.07; N, 13.98; S, 10.90.

5,6-Cyclohexeno-3-(4-pentynylthio)-1,2,4-triazine (19f). A mixture of thiosemicarbazide (0.91 g, 9.98 mmol) and 1,2-cyclohexanedione (1.12 g, 9.99 mmol) in absolute ethanol (30 mL) was heated at reflux for 15 min. The resulting solution was cooled to 0 °C, and sodium hydride (60% oil, 0.40 g, 10.00 mmol) was added, followed by dropwise addition of 5-iodo-1-pentyne[5] (2.10 g, 10.39 mmol, 1.04 equiv). The resulting mixture was heated at reflux with exclusion of water for 1 h. Ethanol was removed from the resulting reaction mixture by evaporation under reduced pressure, and the residual solid/oil mixture was added to a saturated solution of sodium bicarbonate (20 mL). This aqueous mixture was extracted with methylene chloride (3 × 20 mL), and the combined extracts were dried (anhydrous $MgSO_4$) and evaporated under reduced pressure to yield a brown oil. Column chromatography of this oil over silica gel (~40 g) and elution with 1:1 ether/petroleum ether afforded 5,6-cyclohexeno-3-(4-pentynylthio)-1,2,4-triazine (1.30 g, 5.57 mmol, 56%) as a pale yellow oil; IR (neat) 3300, 2120, 1535, 1505, 1450, 1430 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.34 (t, J = 7.1 Hz, 2 H), 3.07 (t, J = 5.9 Hz, 2 H), 2.87 (t, J = 6.4 Hz, 2 H), 2.38 (dt, J = 7.1 and 2.6 Hz, 2 H), 2.06–1.87 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 169.8, 159.0, 154.3, 83.1, 69.0, 31.3, 29.3, 28.8, 27.7, 21.9, 21.5, 17.4.

Anal. Calcd for $C_{12}H_{15}N_3S$: C, 61.77; H, 6.48; N, 18.01; S, 13.74. Found: C, 61.52; H, 6.23; N, 17.79; S, 14.14.

5-(4-Chlorophenyl)-3-(4-pentynylsulfinyl)-1,2,4-triazine (20d). To a stirred solution of 5-(4-chlorophenyl)-3-(4-pentynylthio)-1,2,4-triazine (0.68 g, 2.35 mmol) in anhydrous methylene chloride (15 mL) at 0 °C was added *m*-chloroperbenzoic acid (80–85% technical solid, 0.50 g, 2.46 mmol maximum, 1.05 equiv maximum) as a solid all at once. The resultant mixture was stirred at 0 °C with exclusion of water for 2 h, concentrated by evaporation under reduced pressure, and the residual solid dissolved in a solution of 1:1 methylene chloride/ether (4 mL). This solution was then passed through a silica gel filter (~30 g), which was then washed first with 1:1 ether/petroleum ether (100 mL) and then with 1:3 ethyl acetate/petroleum ether. The ethyl acetate/petroleum ether filtrate was evaporated under reduced pressure to yield a pale yellow solid, which was stirred in anhydrous ether (10 mL), and the undissolved solid was removed by filtration to yield 5-(4-chlorophenyl)-3-(4-pentynylsulfinyl)-1,2,4-triazine (0.50 g, 1.64 mmol, 70%) as a pale yellow, crystalline solid: mp 101.5–103.5 °C; IR (KBr) 3240, 2110, 1595, 1530, 1480, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.79 (s, 1 H), 8.29 (d, J = 8.6 Hz, 2 H), 7.58 (d, J = 8.6 Hz, 2 H), 3.54–3.20 (m, 2 H), 2.55–1.85 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 173.8, 155.8, 146.0, 140.4, 130.6, 129.9, 129.4, 82.1, 69.8, 52.6, 21.3, 17.6.

Anal. Calcd for $C_{14}H_{12}ClN_3OS$: C, 54.99; H, 3.96; Cl, 11.59; N, 13.74; S, 10.49. Found: C, 54.74; H, 3.96; Cl, 11.63; N, 13.90; S, 10.54.

7-(4-Chlorophenyl)-3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridine (21d). A solution of 5-(4-chlorophenyl)-3-(4-pentynylthio)-1,2,4-triazine (0.58 g, 2.00 mmol) in bromobenzene (3 mL) was heated at reflux (156 °C) under nitrogen for 72.0 h. A saturated solution of sodium bicarboante (10 mL) was added, and this aqueous mixture was extracted with methylene chloride (2 × 20 mL). The combined extracts were dried (anhydrous $MgSO_4$) and evaporated under reduced pressure to yield a brown solution (~3 mL). Column chromatography of this solution using silica gel (~40 g) followed by elution first with hexanes (100 mL, to remove bromobenzene) and then with 1:1 methylene chloride/hexanes afforded 7-(4-chlorophenyl)-3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridine (0.35 g, 1.34 mmol, 67% yield, 78% based on recovered starting material) as an off-white crystalline solid: mp 101.5–103.5 °C; IR (KBr) 1590, 1575, 1545, 1485, 1440, 1400 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.96–7.81 (m, 2 H), 7.43–7.27 (m, 2 H), 7.23 (s, 1 H), 3.19–3.06 (m, 2 H), 2.87–2.74 (m, 2 H), 2.23–1.97 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 156.9, 154.0, 137.3, 137.3, 134.9, 128.8, 128.6, 128.0, 115.4, 29.3, 28.6, 22.5.

Anal. Calcd for $C_{14}H_{12}ClNS$: C, 64.24; H, 4.62; Cl, 13.54; N, 5.35; S, 12.25. Found: C, 64.26; H, 4.64; Cl, 13.74; N, 5.25; S, 12.43.

3,4,6,7,8,9-Hexahydro-2*H*-thiopyrano[2,3-*b*]quinoline (21f). A solution of 5,6-cyclohexeno-3-(4-pentynylthio)-1,2,4-triazine (1.20 g, 5.14 mmol) in bromobenzene (10 mL) was heated at reflux (156 °C) with exclusion of water for 6.0 days. A saturated solution of sodium bicarbonate (20 mL) was then added to the reaction solution, and this aqueous mixture was extracted with methylene chloride (3 × 20 mL). The methylene chloride extracts were combined, dried (anhydrous $MgSO_4$), and evaporated under reduced pressure to yield a brown oil. Column chromatography of this oil over silica gel (~80 g) followed by elution with 1:4 ether/petroleum ether afforded 3,4,6,7,8,9-hexahydro-2*H*-thiopyrano[2,3-*b*]pyridine (0.46 g, 2.24 mmol, 44% yield, 62% based on recovered starting material) as a clear, colorless oil, which crystallized upon cooling: mp 55.0–58.0 °C; IR (neat) 1590, 1550, 1435, 1420 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.91 (s, 1 H), 3.11–3.07 (m, 2 H), 2.79 (t, J = 6.4 Hz, 2 H), 2.74 (t, J = 6.2 Hz, 2 H), 2.63 (t, J = 6.2 Hz, 2 H), 2.11–2.04 (m, 2 H), 1.86–1.69 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 155.1, 152.1, 137.6, 127.4, 126.8, 31.8, 28.8, 28.4, 27.9, 22.9, 22.6, 22.3.

Anal. Calcd for $C_{12}H_{15}NS$: C, 70.20; H, 7.36; N, 6.82; S, 15.62. Found: C, 69.92; H, 7.09; N, 6.79; S, 15.87.

Further elution yielded the starting material, 5,6-cyclohexeno-3-(4-pentynylthio)-1,2,4-triazine (0.35 g, 1.50 mmol, 29%

recovery) as a clear, colorless oil.

5-(4-Chlorophenyl)-3-(4-pentynylsulfonyl)-1,2,4-triazine (22d). To a stirred solution of 5-(4-chlorophenyl)-3-(4-pentynylthio)-1,2,4-triazine (0.69 g, 2.38 mmol) in anhydrous methylene chloride (20 mL) at 0 °C was added, all at once, *m*-chloroperbenzoic acid (80–85% technical solid, 1.03 g, 5.07 mmol maximum, 2.13 equiv maximum). The resultant mixture was stirred at room temperature with exclusion of moisture for 5 h, concentrated by evaporation under reduced pressure, and the residual solid stirred in anhydrous ether (15 mL). The undissolved solid was collected by filtration to yield 5-(4-chlorophenyl)-3-(4-pentynylsulfonyl)-1,2,4-triazine (0.59 g, 1.83 mmol, 77%) as a white powder, mp 116.0–118.0 °C; IR (KBr) 3290, 2120, 1595, 1530, 1475, 1320, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.85 (s, 1 H), 8.34–8.19 (m, 2 H), 7.63–7.53 (m, 2 H), 3.94–3.77 (m, 2 H), 2.55–2.01 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 168.0, 156.4, 147.4, 141.0, 130.1, 129.9, 129.6, 81.7, 70.2, 51.0, 21.5, 17.5; LRMS, *m/z* (relative intensity) 295 (30), 294 (13% of M^+), 293 (M^+, 71), 244 (10), 230 (41), 228 (100), 166 (22).

Anal. Calcd for $C_{14}H_{12}ClN_3O_2S$: C, 52.26; H, 3.76; Cl, 11.02; N, 13.06; S, 9.96. Found: C, 52.09; H, 3.98; Cl, 11.09; N, 12.89; S, 10.06.

7-(4-Chlorophenyl)-1,1-dioxo-3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridine (23d). A solution of 5-(4-chlorophenyl-3-(4-pentynylsulfonyl)-1,2,4-triazine (0.42 g, 1.31 mmol) in bromobenzene (5 mL) was heated at reflux under nitrogen for 14 h. Anhydrous ether (25 mL) was added to the reaction mixture, and the undissolved solid was collected by filtration to give 5-(4-chlorophenyl)-1,2,4-triazin-3-one (0.18 g, 0.87 mmol, 66%) as a gray solid which decomposed over 230 °C: ^1H NMR (Me_2SO-d_6) δ 8.73 (s, 1 H), 8.24 (d, J = 8.6 Hz, 2 H), 7.66 (d, J = 8.6 Hz, 2 H), 3.62 (br s, 1 H).[14] The above filtrate was passed through a silica gel filter (~30 g), which was then washed first with ether (100 mL) and then with ethyl acetate (150 mL). The ethyl acetate filtrate was evaporated under reduced pressure to yield 7-(4-chlorophenyl)-1,1-dioxo-3,4-dihydro-2*H*-thiopyrano[2,3-*b*]pyridine (0.08 g, 0.27 mmol, 21%) as a pale yellow solid: mp 191.0–194.0 °C; IR (KBr) 1590, 1535, 1490, 1455, 1425, 1310-1290, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.02 (d, J = 8.6 Hz, 2 H), 7.80 (d, J = 8.1 Hz, 1 H), 7.63 (d, J = 8.3 Hz, 1 H), 7.42 (d, J = 8.6 Hz, 2 H), 3.56–3.43 (m, 2 H), 3.05 (t, J = 5.7 Hz, 2 H), 2.65–2.36 (m, 2 H); LRMS, *m/z* (relative intensity) 294 (13% of M^+), 293 (M^+, 71), 230 (41), 228 (100), 166 (22); HRMS calcd for $C_{14}H_{12}ClNO_2S$ 293.0267, found 293.0267 ± 0.0050.

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Registry No. **3c**, 15969-28-5; **3d**, 98592-50-8; **4a**, 103020-26-4; **4b**, 109216-70-8; **4c**, 100037-88-5; **4e**, 59851-26-2; **4f**, 109216-71-9; **5b**, 109216-72-0; **5c**, 100037-77-2; **5d**, 109216-73-1; **7a**, 109216-74-2; **7b**, 109216-75-3; **7c**, 100037-78-3; **7f**, 109216-76-4; **9c**, 100037-79-4; **11a**, 272-23-1; **11b**, 109216-77-5; **11c**, 100037-80-7; **11d**, 109216-78-6; **11e**, 109216-79-7; **11f**, 18425-96-2; **14c**, 109216-65-1; **14d**, 109216-66-2; **15**, 109216-67-3; **16**, 109216-81-1; **19d**, 109216-68-4; **19f**, 109216-82-2; **20d**, 109216-83-3; **21d**, 109216-84-4; **21f**, 109216-85-5; **22d**, 109216-86-6; **23d**, 109216-87-7; $I(CH_2)_2C{\equiv}CH$, 43001-25-8; $H_2C{=}CH(CH_2)_2Br$, 5162-44-7; $HO(CH_2)_4Br$, 33036-62-3; $HC{\equiv}C(CH_2)_3Cl$, 14267-92-6; $H_2NN{=}C(NH_2)S(CH_2)_2C{\equiv}CH{\cdot}HI$, 109216-69-5; $H_2NC(S)NHNH_2$, 79-19-6; OHCCHO, 107-22-2; AcAc, 765-87-7; PhCOCHO, 1074-12-0; $4\text{-}ClC_6H_4COCHO$, 4998-15-6; $I(CH_2)_3C{\equiv}CH$, 2468-55-5; 1,2-cyclohexanedione, 765-87-7; phenanthrene-9,10-dione, 84-11-7; 1-oxophenanthreno[9,10-*e*]-2,3-dihydrothieno[2,3-*b*]pyridine, 109216-80-0; 5-(4-chlorophenyl)-1,2,4-triazin-3-one, 109216-88-8.

Intramolecular Diels–Alder Reactions of 1,2,4-Triazines. Synthesis of Condensed Pyrimidines

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1,2,4-Triazines with C5 tethered dienophilic side chains are sterically constrained to undergo intramolecular Diels–Alder reactions across the N2/C5 triazine positions; elimination of a nitrile from the intermediate adduct (N1 and C6 of the starting 1,2,4-triazine) leads to condensed pyrimidines. The reactivity of 5-(alkynyl-substituted)-1,2,4-triazines in the intramolecular Diels–Alder process is highly dependent on the steric and electronic disposition of the dienophilic side chain; cycloaddition is hindered when an electron-donating atom (O, N) is used to link the dienophilic side chain to the triazine nucleus, while the introduction of bulky groups into the side chain facilitates the process via the Thorpe–Ingold effect.

Introduction

Diels–Alder reactions of 1,2,4-triazines have been the subject of extensive investigations of scope and applications.[1] As electron-deficient heterocyclic azadienes, 1,2,4-triazines generally participate in inverse electron demand [4 + 2] cycloadditions with electron-rich dienophiles across C3/C6 of the 1,2,4-triazine nucleus with subsequent extrusion of molecular nitrogen. Such reactions have provided access to a host of novel pyridine systems.[2] Conversely, 1,2,4-triazines with simple dienophilic side chains tethered to C3 or C6 of the 1,2,4-triazine nucleus have been shown by our group[3a-d] and others[4] to afford fused pyridine species, often under extremely mild conditions. The "entropic assistance" inherent in the latter reaction eliminates the need for an electron-rich dienophile.

The mode of cycloaddition in these reactions involves addition across C3 and C6 of the 1,2,4-triazine nucleus; the

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