# Synthesis of Thieno[3,4-*b*]quinoxaline and Derivatives

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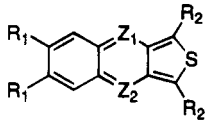
The highly reactive *o*-quinonoid heterocycles thieno[3,4-*b*]quinoxaline (**1a**) and its 6,7-dimethyl derivative (**1b**) have been synthesized by a base-catalyzed Pummerer reaction and isolated in crystalline form. In contrast, the 1,3-dibromothieno[3,4-*b*]quinoxaline (**8**) could be characterized in solution but not isolated in pure form. The readily prepared 1,3-dihydrothieno[3,4-*b*]quinoxaline (**5a**) underwent a direct Knoevenagel condensation with thiophene-2-carboxaldehyde to give the stilbenoid **14a**. Sulfide **5a** was also converted in a two-step process to the stable 1,3-diformylthieno-[3,4-*b*]quinoxaline **11a**.

Almost 20 years ago, Roland and Anderson[1] reported the generation and attempted isolation of thieno[3,4-*b*]-quinoxaline (**1a**). Dehydration of 1,3-dihydrothieno[3,4-*b*]quinoxaline 2-oxide (**2**) under acid conditions ($CF_3$-$COOH/Ac_2O$) as well as thermal conditions ($Al_2O_3$/150 °C/ 0.5 mm) did not afford **1a**. However, the transient formation of **1a** was shown by trapping experiments with *N*-phenylmaleimide. Similar results were reported earlier[2] for the analogous thieno[3,4-*b*]quinoline (**1d**). Indeed, the only derivatives of thieno[3,4-*b*]quinoxaline and thieno[3,4-*b*]quinoline isolated to date are the sterically stabilized 1,3-diphenyl-substituted compounds **1c** and **1e**.[3] In this paper, we report the synthesis and isolation of thieno[3,4-*b*]quinoxaline (**1a**) and 6,7-dimethylthieno-[3,4-*b*]quinoxaline (**1b**), as well as some further chemistry of the thienoquinoxaline system.

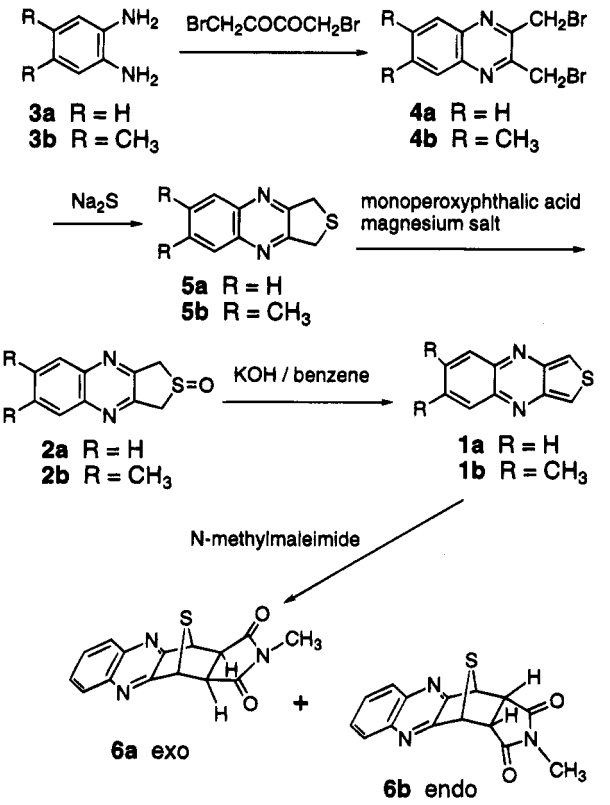


**1a** $Z_1 = Z_2 = N$; $R_1 = R_2 = H$
**1b** $Z_1 = Z_2 = N$; $R_1 = CH_3$; $R_2 = H$
**1c** $Z_1 = Z_2 = N$; $R_1 = H$; $R_2 = C_6H_6$
**1d** $Z_1 = N$; $Z_2 = CH$; $R_1 = R_2 = H$
**1e** $Z_1 = N$; $Z_2 = CH$; $R_1 = H$; $R_2 = C_6H_6$

## Results and Discussion

The synthesis of **1a** and **1b** was accomplished as outlined in Scheme 1. Reaction of the appropriate *o*-diamino-substituted benzene **3** with 1,4-dibromo-2,3-butanedione gave the known 2,3-bis(bromomethyl)quinoxaline (**4a**)[1] and its 6,7-dimethyl-substituted analog **4b**. The conversion of **4** to 1,3-dihydrothieno[3,4-*b*]quinoxaline (**5a**) and 6,7-dimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline (**5b**), respectively, was greatly improved using technical anhydrous sodium sulfide instead of sodium sulfide nonahydrate. In this way, yields improved from 40% to 77%. Oxidation of **5** to the corresponding sulfoxides **2** was best carried out in high yield (**5a**: 90%, **5b**: 73%), using monoperoxyphthalic acid magnesium salt hexahydrate. The desired aromatic heterocycles **1** were obtained by a base (KOH)-catalyzed Pummerer dehydration of **2** in moderate yields (**2a**: 26%, **2b**: 40%). Similar base Pummerer reactions have been reported by us earlier[4] as a route to benzo[*c*]thiophene and naphtho[1,2-*c*]thiophene. Thieno[3,4-*b*]quinoxaline (**1a**) and 6,7-dimethylthieno[3,4-*b*]quinoxaline (**1b**) were obtained as acid-sensitive orange crystals which, protected from light and oxygen, are stable for at least several days. Both compounds were characterized spectroscopically and by analysis. Compound **1a** was further characterized by conversion to its Diels–Alder adducts with *N*-methylmaleimide. The ratio of exo and endo adduct varies a little with reaction time and temperature, but the formation of the exo isomer is generally favored. The structures of **6a** (exo) and **6b** (endo) were assigned on the basis of their $^1$H-NMR spectra by analogy with the corresponding *N*-phenyl adducts of benzo[*c*]thiophene.[5] Thus, **6a**

**Scheme 1**

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(1) Roland, M. M.; Anderson, R. C. *J. Heterocycl. Chem.* **1977**, *14*, 541.

(2) MacDowell, D. W. H.; Jeffries, A. T.; Meyers, M. B. *J. Org. Chem.* **1971**, *36*, 1416.

(3) Haddadin, M. J.; Chelhot, N. C.; Pieridou M. *J. Org. Chem.* **1974**, *39*, 3278.

(4) Horner, C. J.; Saris, L. E.; Lakshmikantham, M. V.; Cava, M. P. *Tetrahedron Lett.* **1976**, *30*, 2581.

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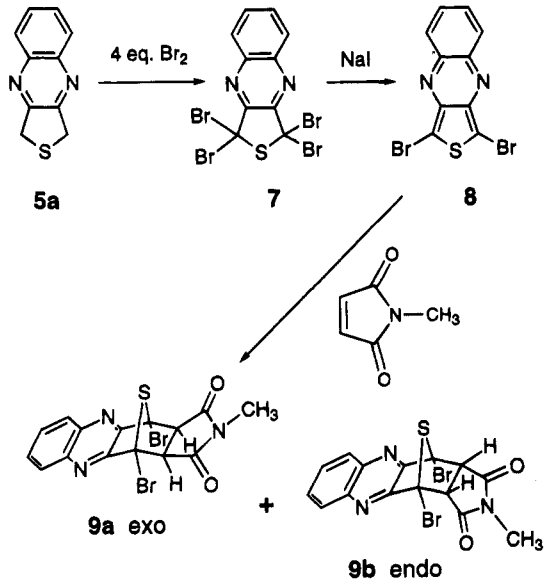
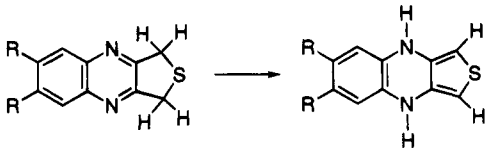
**Scheme 2**




shows two singlets at 3.53 ppm (protons α to the imido carbonyls) and at 5.05 ppm (bridgehead protons), while the corresponding signals for **6b** appear as doublets of doublets at 4.27 ppm (2.0 and 2.7 Hz, protons α to the imido carbonyls) and at 5.06 ppm (2.0 and 2.7 Hz, bridgehead protons). The resonances for the methyl goups are found at 3.10 ppm for **6a** and at 2.38 ppm for **6b**, respectively. These data are also in very close agreement with those reported by Roland and Anderson[1] for the *N*-phenylmaleimide adducts of **1a**.

Bromination of sulfide **5a** in dry benzene with 4 equiv of bromine leads to 1,3-dihydro-1,1,3,3-tetrabromothieno-[3,4-*b*]quinoxaline (**7**) in quantitative yield (Scheme 2). Reaction of **7** with sodium iodide in acetone affords, after iodine removal by sodium sulfite, a dark red-purple solution ($\lambda_{max}$ = 524, 350, 290 nm) containing 1,3-dibromothienoquinoxaline (**8**). Attempts to isolate **8** by evaporation of the solvent yielded only a dark solid containing traces of **8**, detected spectroscopically (HRMS calcd for $C_{10}H_4Br_2S$ 343.844 146, found 343.844 619; $^1H$ NMR ($CDCl_3$) 7.63 (m, 2H), 8.00 ppm (m, 2 H)). Dibromide **8** was much more stable in solution, as shown by trapping experiments with *N*-methylmaleimide, which led to a mixture of the exo and endo isomers **9a** and **9b** in a combined yield of 33% (based on **7**). The $^1H$ NMR spectra again allowed the assignment of the two isomers (**9a**: 3.20 (*N*-methyl protons) and 3.55 ppm (protons α to the imido carbonyls); **9b**: 2.37 (*N*-methyl protons) and 4.54 ppm (protons α to the imido carbonyls)).

The sulfides **5** have been treated under Vilsmeier conditions (DMF and $POCl_3$ in 1,2-dichloroethane (Scheme 3), affording an inseparable mixture of the diformyl compounds **10** and the corresponding monoformyl compounds. The formation of these products implies that the tautomeric form **5'** of **5**, in which the thiophene ring is aromatic, must be produced to some extent under the reaction conditions, since only this tautomer can react in a Vilsmeier reaction. Related behavior has been observed in the case of 2,3-dimethylquinoxaline, which reacts in its tautomeric form in an Diels–Alder reaction with maleic anhydride and *p*-benzoquinone.[6]




The same dialdehydes **10** were obtained when the sulfides **5** were treated with butyllithium, followed by quenching with DMF. This method is superior in comparison to the Vilsmeier reaction in that it furnishes only the dialdehydes in reasonable yields (**10a**: 50%; **10b**: 28%). The poor solubility of these compounds in organic solvents made their purification difficult and probably decreased their isolated yields. The aldehydes **10** were oxidized smoothly with iodobenzene diacetate to the corresponding fully aromatic dialdehydes **11**, which form stable orange-red crystals. Best results were obtained when the crude aldehydes **10** were transformed directly to **11** without further purification (**11a**: 54%; **11b**: 27%). The aldehydes **11** are the first examples in the thieno-[3,4-*b*]quinoxaline series in which the stability is due exclusively to electronic effects.

The dihydro aldehydes **10** show absorptions at higher wavelengths (**10a**: $\lambda_{max}$ = 559.5 and 521.8 nm, **10b**: $\lambda_{max}$ = 578.0 and 536.8 nm) than the fully aromatic aldehydes (**11a**: $\lambda_{max}$ = 507.6 and 479.8 nm, **11b**: $\lambda_{max}$ = 515.2 and 487.3 nm). As a result, solutions of **10** in organic solvents show a dark purple color while solutions of **11** have an orange color. This phenomenon may be attributed to the strong donor–acceptor nature of aldehydes **10**, which contain a highly polarizable vinylogous amide system. In accord with this interpretation, the proton resonance of the aldehyde function of **11a** (11.04 ppm) is shifted strongly downfield in comparison to the corresponding resonance of **10a** (9.39 ppm).

Dihydrothieno[3,4-*b*]quinoxalines (**5**) react with aromatic aldehydes (**13**) in a Knoevenagel reaction with the formation of the unsaturated condensation products **14** (Scheme 4). Several different procedures were studied, but the best results (40–50%) were obtained under basic conditions (potassium *tert*-butoxide) in diethyl ether. The same products **14** were obtained when the reactions were carried out under Lewis acid catalysis ($ZnCl_2$) in ethanol as well as under mineral acid conditions (HCl). In the case of Lewis acids, the reaction time requires 1 week and the Knoevenagel monoproducts are found as byproducts. In addition, the yields are lower (≈25%) and the separation of the bis and mono products is tedious. If HCl is employed as catalyst, only about 15% of **14** is formed along with various byproducts. The reason is the instability of **5** toward acids.

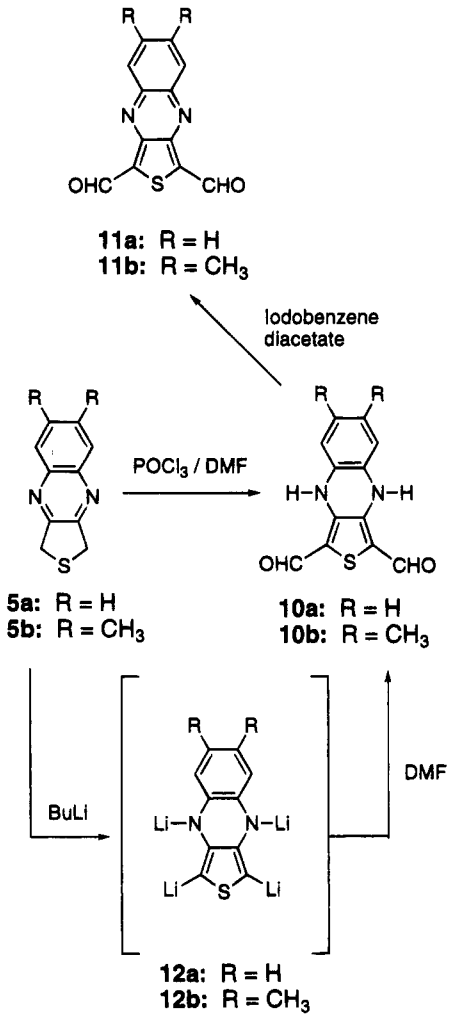
Hanack et al.[7] have prepared several compounds analogous to **14** in which the thienoquinoxaline unit is replaced by a thiophene,[7a] benzo[*c*]thiophene,[7a] naphtho-[*c*]thiophene,[7c] or thieno[3,4-*c*]thiophene,[7b] but the corresponding dihydrosulfides could not be used in the condensation reaction, since the protons in the α-positions to the S-atom are not sufficiently acidic. Only when

(5) (a) Cava, M. P.; Pollack, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 4112. (b) Cava, M. P.; Pollack, N. M.; Mamer, O. A.; Mitchell, M. J. *J. Org. Chem.* **1971**, *36*, 3932.

(6) Schönberg, A.; Mostafa, A. *J. Chem. Soc.* **1943**, 654.

(7) (a) Hieber, G.; Hanack, M.; Wurst, K; Strähle, J. *Chem. Ber.* **1991**, *124*, 1597. (b) Hanack, M.; Schmid, U.; Röhrig, U.; Toussaint, J.-M.; Adant, C.; Brédas, J.-L. *Chem. Ber.* **1993**, *126*, 1487. (c) Hanack, M.; Schmid, U.; Echinger, S.; Teichert, F.; Hieber, J. *Synthesis* **1993**, *6*, 634. (d) Hanack, M.; Mangold, K.-M.; Röhrig, U.; Maichle-Mössmer, C. *Synth. Met.* **1993**, *60*, 199.

**Scheme 3**



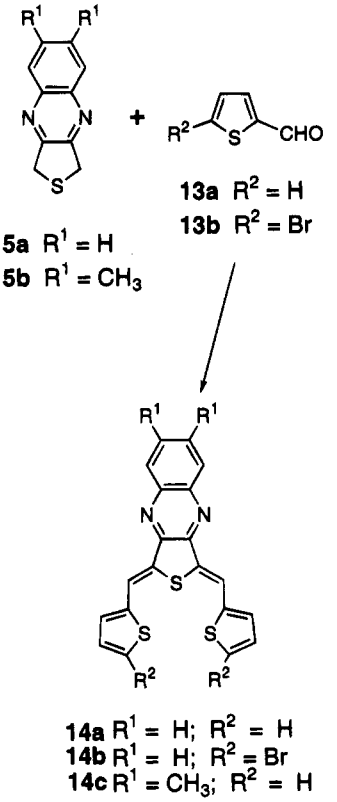

these sulfides were oxidized to the corresponding sulfoxides would the Knoevenagel reaction take place. The resulting products then had to be reduced selectively to give compounds analogous to **14**. The special reactivity of **5** is therefore due to the electron-withdrawing effect of the pyrazine ring condensed to the 3 and 4 positions of the thiophene ring. In support of this interpretation, 2,3-dimethylquinoxaline is known to be deprotonated with the strong base potassium amide, as shown by subsequent alkylation to give 2,3-dipropylquinoxaline.[8] The *Z,Z*-configuration for the condensation products **14** is based on NMR spectroscopy as described for analogous products.[7]

If a solution of dihydrothieno[3,4-*b*]quinoxaline (**5a**) is treated with acids, a dark color forms immediately. Upon workup, a dimer assigned the structure **15** can be isolated. The best results were obtained when **5a** was dissolved in trifluoroacetic acid, and the solution was stirred for 40 min in an open vessel, leading to the formation of **15** in a yield of 41% (Scheme 5). Most likely, this dimerization involves radicals which are formed by the oxidation of the protonated tautomer of **5a**.

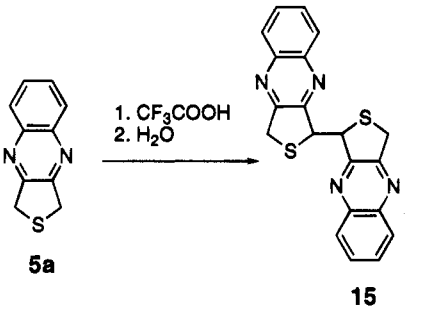
## Experimental Section

**General.** Melting points were taken on a MEL TEMP II capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra ($\delta$) were recorded on a Bruker 360 MHz spectrometer. Chemical shifts are reported using the residual solvent proton resonance as the internal reference. Ultraviolet–visible absorption spectra were recorded on a Perkin-Elmer Lambda 4B spectrophotometer. Electron impact mass spectra and high-resolution mass spectra were obtained on a VG Auto Spec instrument. Microanalyses were determined by Atlantic Microlab, Norcross, GA.

**Scheme 4**




**Scheme 5**




**1,3-Dihydrothieno[3,4-*b*]quinoxaline (5a).** 2,3-Bis(bromomethyl)quinoxaline (**4a**) (10.0 g, 31.6 mmol) was added in one portion to a stirred solution of sodium sulfide flakes (4.60 g, anhydrous, ≈60%) in a mixture of 95% ethanol (200 mL) and water (50 mL). The mixture was stirred at room temperature for 40 min and filtered using suction. The filtrate was diluted with water (100 mL) and extracted four times with toluene (100 mL). The combined organic phase was dried over sodium sulfate and evaporated to yield a crude product (5.34 g). Crystallization from hexanes afforded light orange crystals (4.61 g, 77%): mp 113–114 °C (lit.[1] mp 111–112 °C); $^1$H NMR ($CDCl_3$) 4.39 (s, 4 H), 7.76 (m, 2 H), 8.05 (m, 2H); $^{13}$C NMR ($CDCl_3$) 34.8, 128.8, 129.9, 140.5, 155.4; MS *m/e* 188.0 ($M^+$, 100), 187.0 (92), 186.0 (10), 143.1 (12), 142.1 (10), 129.0 (15). Anal. Calcd for $C_{10}H_8N_2S$: C, 63.80; H, 4.28; N, 14.88; S, 17.03. Found: C, 63.91; H, 4.27; N, 14.84; S, 16.96.

**2,3-Bis(bromomethyl)-6,7-dimethylquinoxaline (4b).** 1,4-Dibromo-2,3-butanedione (17.9 g, 73.4 mmol) and 1,2-diamino-4,5-dimethylbenzene (**3b**) (10.0 g, 73.4 mmol) were

(8) Ogg, R. A., Jr.; Bergstrom, F. W. *J. Am. Chem. Soc.* **1931**, *53*, 1846.

dissolved in ethanol in separate flasks. The solutions were cooled to 0 °C and poured together. After 30 min, the precipitate was collected and washed with cold ethanol. After drying (air), pure product (19.8 g, 78%) was obtained. An analytical sample was prepared by column chromatography ($SiO_2$/$CHCl_3$): mp 159–160 °C; $^1H$ NMR ($CDCl_3$) 2.49 (s, 6 H), 4.89 (s, 4 H), 7.80 (s, 2H); $^{13}C$ NMR ($CDCl_3$) 20.4, 30.8, 128.0, 140.6, 141.8, 149.7; MS *m/e* 342.0/344.0/346.0 ($M^+$, 20/34/20), 263.0/265.0 (100/99), 186.1 (35), 185.1 (66), 184.1 (67), 170.1 (26), 169.1 (38), 145.1 (24), 142.1 (11), 141.1 (16), 128.1 (11), 116.1 (19), 115.1 (19), 104.1 (27), 103.1 (39). Anal. Calcd for $C_{12}H_{12}N_2Br_2$: C, 41.89; H, 3.52; N, 8.14; Br, 46.45. Found: C, 41.91; H, 3.55; N, 8.19; Br, 46.36.

**6,7-Dimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline (5b).** 2,3-Bis(bromomethyl)-6,7-dimethylquinoxaline (**4b**) (10.0 g, 29.1 mmol) was added in one portion to a stirred solution of sodium sulfide flakes (4.20 g, anhydrous, ≈60%) in a mixture of 95% ethanol (200 mL) and water (50 mL). The mixture was stirred at room temperature for 40 min and filtered using suction. The filtrate was diluted with water (100 mL) and extracted four times with toluene (100 mL). The combined organic phase was dried over sodium sulfate and evaporated to yield 5.37 g of crude product. Crystallization from hexanes afforded light orange crystals (4.58 g, 73%): mp 160–162 °C; $^1H$ NMR ($CDCl_3$) 2.45 (s, 6 H), 4.31 (s, 4 H), 7.72 (s, 2 H); $^{13}C$ NMR ($CDCl_3$) 20.3, 34.8, 127.8, 139.4, 140.3, 154.1; MS *m/e* 216.1 ($M^+$, 100), 215.1 (88), 214.1 (12), 201.1 (6), 171.1 (6), 103.1 (11). Anal. Calcd for $C_{12}H_{12}N_2S$: C, 66.63; H, 5.59; N, 12.95; S, 14.82. Found: C, 66.72; H, 5.69; N, 13.02; S, 14.57.

**1,3-Dihydrothieno[3,4-*b*]quinoxaline 2-Oxide (2a).** A 1% aqueous solution of monoperoxyphthalic acid magnesium salt (≈85%, ≈800 mg) was added dropwise to a stirred solution of 1,3-dihydrothieno[3,4-*b*]quinoxaline (**5a**) (500 mg, 2.70 mmol) in methanol (50 mL). The end point for the addition of oxidizing agent was controlled by TLC ($SiO_2$/$CHCl_3$). The mixture was extracted several times with dichloromethane. The combined organic phase was washed with a saturated sodium hydrogen carbonate solution, dried over sodium sulfate, and finally evaporated to yield gray white crystals (486 mg, 90%). An analytical sample was obtained by crystallization from hexanes: mp 157–158 °C dec (lit.[1] mp 157–158 °C); $^1H$ NMR ($CDCl_3$) 4.37 (d, $J_{AB}$ = 17.7 Hz, 2 H), 4.48 (d, $J_{AB}$ = 17.6 Hz, 2 H), 7.76 (m, 2 H), 8.06 (m, 2 H); $^{13}C$ NMR ($CDCl_3$) 57.9, 129.0, 130.3, 141.8, 151.5.; MS *m/e* 204.0 ($M^+$, 14), 186.0 (100), 159.0 (18), 156.0 (19), 153.0 (9), 142.0 (18), 129.0 (14), 115.0 (8), 103.0 (9). Anal. Calcd for $C_{10}H_8N_2OS$: C, 58.80; H, 3.95; N, 13.72; S, 15.70. Found: C, 59.01; H, 3.85; N, 13.81; S, 15.66.

**6,7-Dimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline 2-Oxide (2b).** A 1% aqueous solution of monoperoxyphthalic acid magnesium salt (≈85%, 1.35 g) was added dropwise to a stirred solution of 6,7-dimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline (**5b**) (1.00 g, 4.60 mmol) in methanol (200 mL) and benzene (50 mL). The mixture was diluted by addition of water (100 mL). The phases were separated, and the water phase was extracted several times with dichloromethane. The combined organic phase was washed with a saturated sodium hydrogen carbonate solution, dried over sodium sulfate, and finally evaporated to yield beige crystals (0.780 g, 73%). An analytical sample was obtained by crystallization from hexanes: dec > 160 °C; $^1H$ NMR ($CDCl_3$) 2.51 (s, 6 H), 4.37 (d, $J_{AB}$ = 17.4 Hz, 2 H), 4.50 (d, $J_{AB}$ = 17.5 Hz, 2 H), 7.83 (s, 2 H); $^{13}C$ NMR ($CDCl_3$) 20.4, 58.0, 128.0, 140.8, 141.2, 150.2; MS *m/e* 232.1 ($M^+$, 11), 214.1 (100), 199.1 (24), 184.1 (20), 169.1 (9), 103.1 (10). Anal. Calcd for $C_{12}H_{12}N_2OS$: C, 62.04; H, 5.21; N, 12.06; S, 13.80. Found: C, 62.14; H, 5.15; N, 12.02; S, 13.90.

**Thieno[3,4-*b*]quinoxaline (1a).** 1,3-Dihydrothieno[3,4-*b*]-quinoxaline 2-oxide (**2a**) (240 mg, 1.2 mmol) and finely ground potassium hydroxide (80 mg) were added to dry benzene (15 mL) under nitrogen and sonicated in an ultrasonic bath for 3 h. The mixture was filtered through Celite. The filtrate was evaporated to afford the crude product (85.0 mg). Further purification was done by extraction of crude material with hexanes followed by filtration. The filtrate was evaporated to yield orange crystals (56.0 mg, 26%): dec > 80 °C; $^1H$ NMR ($C_6D_6$) 7.05 (m, 2 H), 7.81 (s, 2 H), 7.96 (m, 2 H); $^{13}C$ NMR ($C_6D_6$) 115.7, 130.1, 130.8, 144.4, 144.7; MS *m/e* 186.1 ($M^+$, 100), 159.0 (15), 142.1 (18), 129.1 (17), 103.0 (13); HRMS calcd for $C_{10}H_6N_2S$ 186.0252, found 186.0259. Anal. Calcd for $C_{10}H_6N_2S$: C, 64.49; H, 3.25; N, 15.04; S, 17.22. Found: C, 63.81; H, 3.33; N, 14.78; S, 16.98.

**6,7-Dimethylthieno[3,4-*b*]quinoxaline (1b).** 6,7-Dimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline 2-oxide (**2b**) (250 mg, 1.10 mmol) and well ground potassium hydroxide (four pellets) were added to dry benzene (50 mL) under nitrogen and treated in an ultrasonic bath for 5 h. The mixture was filtered through Celite. The filtrate was evaporated, and the remaining solid was purified by extraction with hexanes followed by filtration. The filtrate was evaporated to yield orange crystals (92.0 mg, 40%): dec > 130 °C; $^1H$ NMR ($C_6D_6$) 1.93 (s, 6 H), 7.80 (s, 2 H), 7.86 (s, 2 H); $^{13}C$ NMR ($C_6D_6$) 20.1, 115.3, 128.8, 141.5, 144.39, 144.45; UV (EtOH) 468.6, 371.4, 250.5. MS *m/e* 214.0 ($M^+$, 100), 199.0 (15), 77.0 (7). Anal. Calcd for $C_{12}H_{10}N_2S$: C, 67.26; H, 4.70; N, 13.07; S, 14.96. Found: C, 67.33; H, 4.69; N, 13.00; S, 14.86.

***N*-Methylmaleimide Adducts of Thieno[3,4-*b*]quinoxaline (6a and 6b).** 1,3-Dihydrothieno[3,4-*b*]quinoxaline 2-oxide (**2a**) (250 mg, 1.20 mmol) and powdered potassium hydroxide (150 mg) were suspended in dry benzene (120 mL) under nitrogen and refluxed for 30 min. The KOH was filtered off. *N*-Methylmaleimide (180 mg, 1.6 mmol) was added to the filtrate. This mixture was first stirred for 2 h at room temperature under nitrogen and in the absence of light and later refluxed for 30 min. The benzene was removed by use of the rotavapor to afford crude product (241 mg), which was purified by chromatography ($SiO_2$/ethyl acetate–hexanes 1:1): yield 136 mg of the exo-isomer and 21.0 mg of the endo-isomer (43% combined).

***exo*-Isomer (6a):** mp 258–260 °C; $^1H$ NMR ($CDCl_3$) 3.10 (s, 3 H), 3.53 (s, 2 H), 5.05 (s, 2 H), 7.72 (m, 2 H), 7.96 (m, 2 H); $^{13}C$ NMR ($CDCl_3$) 25.5, 49.2, 55.0, 129.1, 130.0, 139.5, 159.0, 174.3; MS *m/e* 297.1 ($M^+$, 44), 263.1 (4), 212.1 (10), 186.1 (100), 180.1 (28), 168.1 (13), 153.1 (6), 129.1 (6), 106.1 (7), 103.1 (6). Anal. Calcd for $C_{15}H_{11}N_3O_2S$: C, 60.59; H, 3.73; N, 14.13; S, 10.78. Found: C, 60.77; H, 3.74; N, 13.95; S, 10.55.

***endo*-Isomer (6b):** mp 210–214 °C; $^1H$ NMR ($CDCl_3$) 2.38 (s, 3 H), 4.27 (dd, 2.0 and 2.7 Hz, 2 H), 5.06 (dd, 2.0 and 2.9 Hz, 2 H), 7.70 (m, 2 H), 7.99 (m, 2 H); $^{13}C$ NMR ($CDCl_3$) 24.4, 52.1, 54.1, 129.4, 130.0, 139.8, 156.8, 172.6; MS *m/e* 297.0 ($M^+$, 33), 212.0 (26), 186.0 (100), 180.0 (11), 168.0 (33), 158.0 (8), 142.0 (8), 129.0 (15), 102.7 (11); HRMS calcd for $C_{15}H_{11}N_3O_2S$ 297.0572, found 297.0569.

**1,3-Dihydro-1,1,3,3-tetrabromothieno[3,4-*b*]quinoxaline (7).** A solution of 1,3-dihydrothieno[3,4-*b*]quinoxaline (**5a**) (1.86 g, 9.90 mmol) in dry benzene (200 mL) and bromine (4.5 mL) was refluxed overnight. The benzene was distilled under reduced pressure, whereby white gray crystals (4.97 g, 100%) were obtained, which were pure by elemental analysis and spectroscopic methods: dec > 90 °C; $^1H$ NMR ($CDCl_3$) 7.99 (m, 2 H), 8.35 (s, 2 H); $^{13}C$ NMR ($CDCl_3$) 50.2, 129.8, 132.8, 141.9, 149.9; MS *m/e* 504 ($M^+$, < 1), 424 (< 1), 341.9/343.9/345.9 (44/83/58), 264.0/266.0 (9/8), 263.0/265.0 (6/8), 184.0 (100), 171.9 (7), 160.9 (10), 140.0 (12), 124.9 (8), 114.0 (8), 102.1 (41), 79.9 (30). Anal. Calcd for $C_{10}H_4N_2Br_4S$: C, 23.84; H, 0.80; N, 5.56; Br, 63.44; S, 6.36. Found: C, 23.97; H, 0.92; N, 5.42; Br, 63.25; S, 6.22.

***N*-Methylmaleimide Adducts of 1,3-Dibromothieno-[3,4-*b*]quinoxaline (9a and 9b).** 1,1,3,3-Tetrabromo-1,3-dihydrothieno[3,4-*b*]quinoxaline (**7**) (250 mg, 0.5 mmol) was dissolved in acetone (100 mL). A saturated solution of sodium iodide in acetone (3 mL) was added. The solution turned red immediately. It was stirred for 10 min. Water (100 mL) and a saturated solution of sodium bisulfite (5 mL) was added. This mixture was extracted with benzene (100 mL). *N*-Methylmaleimide (250 mg, 2.3 mmol) was added to the purple benzene phase, and the mixture was refluxed for 12 h. After being cooled to room temperature it was filtered. The filtrate was evaporated, and the residue was purified by chromatography ($SiO_2$/$CHCl_3$) to yield a mixture of exo and endo adduct (≈2:1, 77.0 mg, 33%). The isomers could be separated by chromatography ($SiO_2$/$CH_2Cl_2$) and crystallized from ethanol.

***exo*-Isomer (9a):** dec > 140 °C; $^1H$ NMR ($CDCl_3$) 3.20 (s, 3 H), 3.55 (s, 2 H), 7.85 (m, 2H), 8.19 (m, 2 H); $^{13}C$ NMR ($CDCl_3$)

26.1, 55.7, 63.7, 129.5, 131.3, 140.0, 154.4, 169.7; MS *m/e* 453.0/455.0/457.0 ($M^+$, 14/27/14), 374.0/376.0 (29/32), 341.9/343.9/345.9 (27/50/28), 317.0/319.0 (59/61), 289.0/291.0 (80/80), 264.0/266.0 (31/32), 245.0/247.0 (22/22), 210.1 (100), 186.1 (48), 184.0 (37), 102.1 (62), 84.0 (96), 76.1 (46), 62.0 (28); HRMS calcd for $C_{15}H_9N_3{}^{79}Br^{81}BrO_2S$ 454.8762, found 454.8751; calcd for $C_{15}H_9N_3{}^{81}Br_2O_2S$ 456.8741, found 456.8740. Anal. Calcd for $C_{15}H_9N_3Br_2O_2S$: C, 39.58; H, 1.99; N, 9.23; Br, 35.11; S, 7.05. Found: C, 39.69; H, 1.97; N, 9.15; Br, 35.01; S, 7.16.

***endo*-Isomer (9b):** dec > 100 °C; $^1$H NMR ($CDCl_3$) 2.37 (s, 3 H), 4.54 (s, 2 H), 7.82 (m, 2H), 8.19 (m, 2 H); $^{13}$C NMR ($CDCl_3$) 24.7, 60.6, 62.6, 129.7, 131.3, 140.2, 151.7, 169.0; MS *m/e* 453.0/455.0/457.0 ($M^+$, 10/21/12), 374.0/376.0 (16/16), 341.9/343.9/345.9 (27/54/27), 317.0/319.0 (40/42), 289.0/291.0 (58/62), 264.0/266.0 (10/10), 245.0/247.0 (15/15), 210.1 (78), 186.1 (14), 184.0 (23), 166.1 (12), 149.1 (21), 129.1 (14), 105.0 (24), 102.1 (37), 76.1 (28), 69.1 (37), 62.0 (100); HRMS calcd for $C_{15}H_9N_3{}^{79}Br_2O_2S$ 452.8782, found 452.8776; calcd for $C_{15}H_9N_3{}^{79}Br^{81}BrO_2S$ 454.876175, found 454.8761; calcd for $C_{15}H_9N_3{}^{81}Br_2O_2S$ 456.874128, found 456.8751. Anal. Calcd for $C_{15}H_9N_3Br_2O_2S$: C, 39.58; H, 1.99; N, 9.23; Br, 35.11; S, 7.05. Found: C, 39.51; H, 1.97; N, 9.16; Br, 35.03; S, 7.12.

**1,3-Diformyl-4,9-dihydrothieno[3,4-*b*]quinoxaline (10a).** Both TMEDA (1.2 mL, 8.00 mmol) and *n*-BuLi (4.0 mL of 2.5 M solution in hexanes) were added to dry hexanes (30 mL). 1,3-Dihydrothieno[3,4-*b*]quinoxaline (**5a**) (250 mg, 1.3 mmol), dissolved in anhydrous THF (5 mL), was added dropwise using a syringe, whereby a bright yellow suspension was formed. The mixture was stirred for 1 h at room temperature and then cooled in an acetone–dry ice bath. Dry DMF (4.0 mL, 52 mmol) was added within 15 min. The mixture was allowed to come to room temperature overnight and was then poured onto crushed ice (300 mL). The organic phase (almost colorless) was removed. The water phase was slightly acidified by addition of a diluted HCl solution under cooling. A precipitate formed which was collected by filtration and dried in air (246 mg). Chromatography ($SiO_2$/$CHCl_3$) of a part of the crude product (100 mg) led to purple crystals (66.0 mg, 50%). An analytical sample was obtained by crystallization from ethanol: mp > 300 °C; $^1$H NMR ($CDCl_3$) 6.47 (m, 2 H), 6.74 (m, 2 H), 8.66 (s, 2 H), 9.39 (s, 2 H); $^{13}$C NMR (DMSO-$d_6$) 112.3, 114.3, 122.8, 128.8, 140.8, 181.6; UV ($CH_2Cl_2$) 559.5, 521.8, 486.5 sh, 390.0 sh, 342.0, 272.9; MS *m/e* 244.0 ($M^+$, 100), 214.0 (37), 186.0 (36); HRMS calcd for $C_{12}H_8N_2O_2S$ 244.0306, found 244.0301. Anal. Calcd for $C_{12}H_8N_2O_2S$: C, 59.00; H, 3.30; N, 11.47; S, 13.13. Found: C, 59.11; H, 3.27; N, 11.56; S, 13.07.

**1,3-Diformylthieno[3,4-*b*]quinoxaline (11a).** Iodobenzene diacetate (185 mg, 0.60 mmol) was added to a stirred solution of crude 1,3-diformyl-4,9-dihydrothieno[3,4-*b*]quinoxaline (140 mg) in dichloromethane (100 mL). The mixture was stirred for 3 h. The volume was reduced to about 10 mL and passed through a column ($SiO_2$/$CH_2Cl_2$). The orange fraction was collected and evaporated to give orange-red crystals (98.0 mg, 54% based on 1,3-dihydrothieno[3,4-*b*]quinoxaline (**5a**)): mp 213–214.5 °C; $^1$H NMR ($CDCl_3$) 7.86 (m, 2 H), 8.12 (m, 2 H), 11.04 (s, 2 H); $^{13}$C NMR ($CDCl_3$) 130.4, 133.1, 137.1, 145.9, 146.0, 182.5; UV ($CH_2Cl_2$) 507.6 sh, 479.8, 454.1, 393.3, 375.8, 328.8, 315.6; MS *m/e* (%) 242.0 ($M^+$, 80), 214.0 (96), 186.0 (100), 159.0 (19), 153.0 (12), 142.1 (55), 129.0 (10), 114.0 (17), 103.0 (10); HRMS calcd for $C_{12}H_6N_2O_2S$ 242.0150, found 242.0146. Anal. Calcd for $C_{12}H_6N_2O_2S$: C, 59.50; H, 2.50; N, 11.56; S, 13.24. Found: C, 59.41; H, 2.48; N, 11.50; S, 13.19.

**1,3-Diformyl-6,7-dimethyl-4,9-dihydrothieno[3,4-*b*]quinoxaline (10b).** Both TMEDA (1.0 mL, 6.6 mmol) and n-BuLi (3.0 mL of 2.5M solution in hexanes) were added to hexanes (50 mL). 6,7-Dimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline (**5b**) (0.57 g, 2.6 mmol), dissolved in anhydrous THF (20 mL), was added dropwise using a syringe, whereby a bright yellow suspension was formed. The mixture was stirred for 1 h at room temperature and then cooled in an acetone–dry ice bath. Dry DMF (3.0 mL, 39 mmol) was added within 15 min. The mixture was allowed to come to room temperature overnight and was then poured onto crushed ice (300 mL). The organic phase (almost colorless) was removed. The water phase was slightly acidified by addition of a diluted HCl solution with cooling. A precipitate was formed, which was collected by filtration and dried in air (0.75 g). Chromatography ($SiO_2$/$CH_2Cl_2$) of a part of the crude product (300 mg) led to purple crystals (80.0 mg, 28%): mp > 300 °C; $^1$H NMR (DMSO-$d_6$) 2.03 (s, 6 H), 6.48 (s, 2 H), 9.77 (s, 2 H), 10.03 (s, 2 H); $^{13}$C NMR (DMSO-$d_6$) 18.8, 111.7, 115.5, 126.3, 130.4, 141.0, 181.3; UV ($CH_2Cl_2$) 578.0, 536.8, 500.7 sh, 407.0, 361.2 sh, 345.5, 273.4; MS *m/e* 272.0 ($M^+$, 79), 270.0 (77), 242.0 (100), 214.0 (80), 199.0 (49), 170.0 (36), 155.0 (23), 103.0 (36), 81.0 (31), 77.0 (55). Anal. Calcd for $C_{14}H_{12}N_2O_2S$: C, 61.75; H, 4.44; N, 10.29; S, 11.77. Found: C, 61.81; H, 4.43; N, 10.19; S, 11.88.

**1,3-Diformyl-6,7-dimethylthieno[3,4-*b*]quinoxaline (11b).** Iodobenzene diacetate (500 mg, 1.60 mmol) was added to a stirred solution of crude 1,3-dicarboxy-6,7-dimethyl-4,9-dihydrothieno[3,4-*b*]quinoxaline (300 mg) in chloroform (150 mL). The mixture was stirred for 1 h. The volume was reduced to about 15 mL and then passed through a column ($SiO_2$/$CH_2Cl_3$). The orange fraction was collected and evaporated to give orange-red crystals (77.0 mg, 27% based on 6,7-dimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline (**5b**)): mp 264–266 °C dec; $^1$H NMR ($CDCl_3$) 2.57 (s, 6 H), 7.84 (s, 2 H), 11.00 (s, 2 H); $^{13}$C NMR ($CDCl_3$) 20.8, 128.4, 136.8, 145.3, 145.7, 146.2, 182.5; UV ($CH_2Cl_2$) 515.2 sh, 487.3, 408.3, 372.0, 341.0, 320.4, 263.7, 256.2; MS *m/e* 270.0 ($M^+$, 70), 242.0 (100), 214.0 (67), 199.0 (31), 170.0 (19), 103.0 (23), 77.0 (31). Anal. Calcd for $C_{14}H_{10}N_2O_2S$: C, 62.21; H, 3.73; N, 10.36; S, 11.86. Found: C, 61.43; H, 3.91; N, 10.02; S, 11.59.

**1,3-Bis(2-thienylmethylene)-1,3-dihydrothieno[3,4-*b*]-quinoxaline (14a).** 1,3-Dihydrothieno[3,4-*b*]quinoxaline (**5a**) (100 mg, 0.50 mmol), 2-thiophenecarboxaldehyde (**13a**) (0.50 mL, 5.3 mmol), and potassium *tert*-butoxide (120 mg, 1.1 mmol) were added to dry diethyl ether (15 mL) and stirred overnight. The solution was neutralized by addition of a 10% HCl solution. The solvent was evaporated, and the residue was purified by column chromatography ($SiO_2$/toluene–hexanes 90:10), followed by recrystallization (acetone), to give dark red crystals (85.0 mg, 43%): mp 311–313 °C; $^1$H NMR ($CDCl_3$) 7.21 (dd, $J$ = 4.9 + 3.9 Hz, 2 H), 7.48 (d, $J$ = 3.6 Hz, 2 H), 7.56 (d, $J$ = 5.0 Hz, 2 H), 7.75 (m, 2 H), 8.10 (m, 2 H), 8.32 (s, 2 H); $^{13}$C NMR ($CDCl_3$) 116.4, 128.06, 128.12, 128.4, 129.2, 129.8, 130.1, 140.1, 142.2, 150.3; MS *m/e* 375.9 ($M^+$, 100), 374.9 (76), 342.9 (15), 280.9 (48), 186.9 (17), 149.0 (18), 129.0 (18), 119.0 (13), 115.0 (11), 111.1 (14), 108.0 (11), 105.0 (12). Anal. Calcd for $C_{20}H_{12}N_2S_3$: C, 63.80; H, 3.21; N, 7.44; S, 25.55. Found: C, 63.93; H, 3.15; N, 7.35; S, 25.41.

**1,3-Bis(2-bromo-5-thienylmethylene)-1,3-dihydrothieno-[3,4-*b*]quinoxaline (14b).** 1,3-Dihydrothieno[3,4-*b*]quinoxaline (**5a**) (100 mg, 0.50 mmol), 5-bromo-2-thiophenecarboxaldehyde (**13b**) (0.20 mL, 1.70 mmol), and potassium *tert*-butoxide (120 mg, 1.10 mmol) were added to dry diethyl ether (15 mL) and stirred for 2 d. The solution was neutralized by addition of a 10% HCl solution. The precipitate was filtered and purified by column chromatography ($SiO_2$/$CHCl_3$), giving red-brown crystals (138 mg, 49%): mp 284–288 °C; $^1$H NMR ($CDCl_3$) 7.17 (m, 4 H), 7.75 (m, 2 H), 8.08 (m, 2 H), 8.16 (s, 2 H); MS *m/e* 533.9 ($M^+$, 100), 455.9 (52), 454.9 (52), 376.0 (38), 375.0 (48), 374.0 (16), 373.0 (39), 341.0 (18), 329.0 (21), 297.1 (12), 285.1 (10), 281.0 (13), 187.0 (18), 186.0 (10). Anal. Calcd for $C_{20}H_{10}N_2Br_2S_3$: C, 44.96; H, 1.89; N, 5.24; Br, 29.91; S, 18.00. Found: C, 45.05; H, 1.91; N, 5.14; Br, 29.88; S, 18.06.

**1,3-Bis(2-thienylmethylene)-6,7-dimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline (14c).** 6,7-Dimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline (**5b**) (200 mg, 0.90 mmol), 2-thiophenecarboxaldehyde (**15a**) (0.30 mL, 3.20 mmol), and potassium *tert*-butoxide (208 mg, 1.90 mmol) were added to dry diethyl ether (15 mL) and stirred for 2 d. The solution was neutralized by addition of a 10% HCl solution. The precipitate was filtered and purified by column chromatography ($SiO_2$/$CHCl_3$), giving dark red crystals (142 mg, 38%); an analytical sample was prepared by crystallization from acetone: mp 262–264 °C; $^1$H NMR ($CDCl_3$) 2.51 (s, 6 H), 7.20 (dd, $J$ = 3.6 + 5.0 Hz, 2 H), 7.45 (d, $J$ = 3.7 Hz, 2 H), 7.53 (d, $J$ = 5.0 Hz, 2 H), 7.84 (s, 2 H), 8.25 (s, 2 H); $^{13}$C NMR ($CDCl_3$) 20.4, 115.5, 128.0, 128.2, 128.5, 129.4, 140.2, 141.0, 141.2, 149.3; MS *m/e* 404.1 ($M^+$, 100), 403.1 (64), 371.1 (13), 324.1 (11), 323.0 (10), 202.0 (18), 201.0 (23), 108.0 (10), 103.0 (9).

Anal. Calcd for $C_{22}H_{16}N_2S_3$: C, 65.31; H, 3.99; N, 6.92; S, 23.78. Found: C, 65.08; H, 3.92; N, 6.90; S, 23.63.

**1,1'-Bi(1,3-dihydrothieno[3,4-*b*]quinoxaline) (15).** 1,3-Dihydrothieno[3,4-*b*]quinoxaline (**5a**) (250 mg, 1.30 mmol) was dissolved in trifluoroacetic acid (20 mL) and stirred for 40 min. Water (80 mL) was then added. The resulting precipitate was collected by filtration, washed with water, and dried (air). Starting material was removed by suspending the solid material in hot hexanes followed by filtration. Light pink to purple crystals (60.0 mg) remained. A second crop was obtained when the filtrate of the reaction was diluted further with water (100 mL). Purification in the same way led to a pure sample (41.0 mg). Total yield: 101 mg (41%); mp > 300 °C; $^1$H NMR ($CDCl_3$) 4.27 (d, $J_{AB}$ = 15.6 Hz, 2 H), 4.63 (d, $J_{AB}$ = 15.6 Hz, 2 H), 5.73 (s, 2 H), 7.79 (m, 4 H), 8.12 (m, 4 H); $^{13}$C NMR ($CDCl_3$) 35.4, 57.5, 128.7, 128.8, 129.3, 130.0, 130.3, 130.4, 140.9, 141.1, 155.9; UV ($CHCl_3$) 517.1, 326.0, 240.4, 224.3; MS *m/e* 372.0 ($M^+$ − 2 H, 82), 342.1 (20), 339.0 (30), 327.0 (25), 309.1 (17), 307.1 (17), 229.0 (12), 188.0 (85), 187.0 (100), 153.0 (8), 143.0 (30), 129.0 (16), 115.0 (8), 103.0 (11). Anal. Calcd for $C_{20}H_{14}N_4S_2$: C, 64.15; H, 3.77; N, 14.96; S, 17.13. Found: C, 64.19; H, 3.80; N, 14.87; S, 17.03.

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