Synthesis and Total ^{1}H-NMR Assignment of [1]Benzothieno-[2,3-*c*][1,10]phenanthroline

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Dedicated to the memory of Professor Nicholas Alexandrou

The synthesis of [1]benzothieno[2,3-*c*][1,10]phenanthroline (5) is described. It was obtained in four steps from known starting materials. The basic skeleton of the molecule and of the phenanthroline ring were formed *via* photocyclization. The total assignment of ^{1}H-nmr spectra was accomplished with the aid of two-dimensional nmr methods.

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Introduction.

The new fused aromatic heterocycle reported here, [1]benzothieno[2,3-*c*][1,10]phenanthroline (**5**), represents an extension of the series of ring systems reported in references 1 and 2. These new ring systems incorporate a 1,10-phenanthroline moiety which could chelate a variety of transition metal ions. The appeal of these ligands lies in the potentially interesting photochemical properties of its metal complexes. 1,2,3,4-Tetrahydro[1]benzothieno[2,3-*c*][1,10]phenanthroline (**6**), which is also a new compound, was a minor side product in the preparation of **5**. Preliminary results indicate that it could be obtained as the major product under different reaction conditions. The current paper describes the synthesis and characterization of **5** and **6**.

Results & Discussion.

Synthesis.

3-Chlorobenzo[*b*]thiophene-2-carbonyl chloride (**1**) [2b,3] served as the starting material for the synthesis of **5** (Scheme 1). When **1** was allowed to react with 8-aminoquinoline, 1-chloro-*N*-(8'-quinolyl)benzo[*b*]thiophene-2-carboxamide (**2**) was obtained in 96% yield. Photocyclization of **2** afforded [1]benzothieno[2,3-*c*][1,10]phenanthrolin-6(5*H*)-one (**3**) in 84% yield. Aromatization of **3** was accomplished with phosphorus oxychloride to give 6-chloro[1]benzothieno[2,3-*c*][1,10]phenanthroline (**4**) in 79% yield. Dechlorination of **4** using lithium aluminum hydride [1,4] generated [1]benzothieno[2,3-*c*][1,10]phenanthroline (**5**) in 41% yield and 1,2,3,4-tetrahydro[1]benzothieno[2,3-*c*][1,10]phenanthroline (**6**) as a side product in 20% yield. The overall yield for **5** was 26% based on **1**.

The side product **6** in the dechlorination of **4** with lithium aluminum hydride is of interest because it points to a possible method for selectively reducing certain portions of a fully aromatic molecule. In previous work [1b] we found that the attempted double dechlorination of 6,9-dichlorothieno[2',3':4,5]thieno[2,3-*c*][1,10]phenanthroline with lithium aluminum hydride resulted in facile reaction at the electron-poor site (*i.e.* adjacent to the nitrogen atom), but none at the electron-rich site (*i.e.* adjacent to the sulfur atom). Preliminary observations on the reduction of **4** and on analogous naphthothieno compounds [5] indicate that short reaction times and low temperatures result primarily in dechlorination. On the other hand, longer reaction times lead to greater proportions of the products in which positions one through four, or position

Table 1.

^{1}H NMR Assignments for **5** and **6**

Position	Compound 5 δ	mult	intensity	Position	Compound 6 δ	mult	intensity
H_1	8.36	dd	1H	H_1	3.00	t	2H
H_2	7.68	dd	1H	H_2	2.15	pentet	2H
H_3	9.28	dd	1H	H_3	3.60	br dt	2H
H_6	9.70	s	1H	H_4	6.25	br	1H
H_8	8.13	m	1H	H_6	9.14	s	1H
H_9, H_{10}	7.68-7.74	m	2H	H_8	8.06	m	1H
H_{11}	8.97	m	1H	H_9, H_{10}	7.62	m	2H
H_{12}	9.03	d	1H	H_{11}	8.85	m	1H
H_{13}	8.08	d	1H	H_{12}	8.01	d	1H
				H_{13}	7.37	d	1H

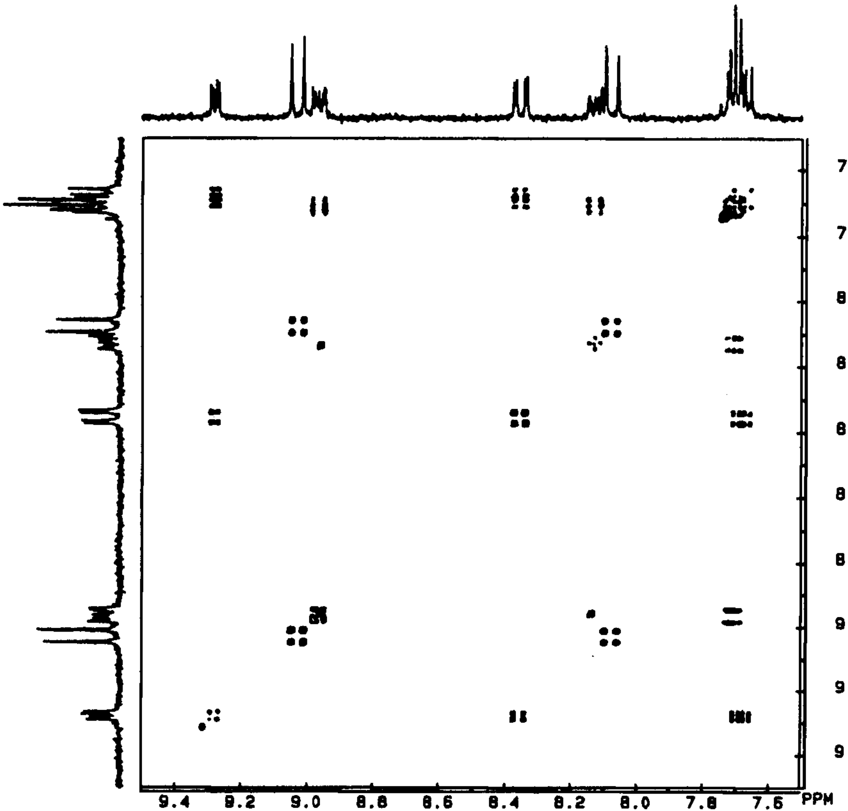


Figure 1.

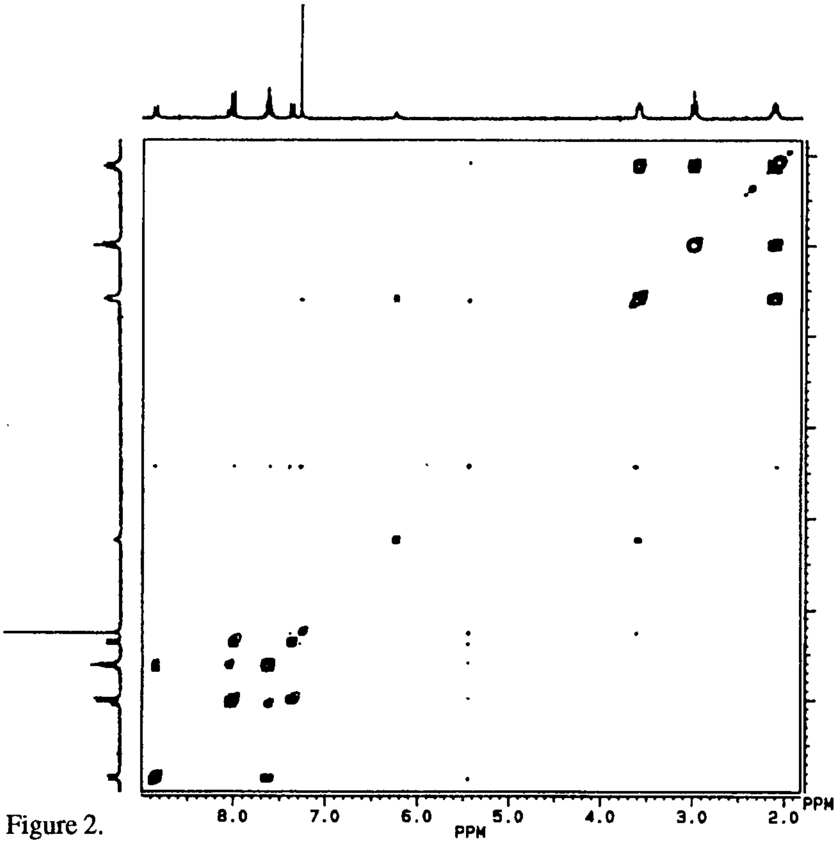
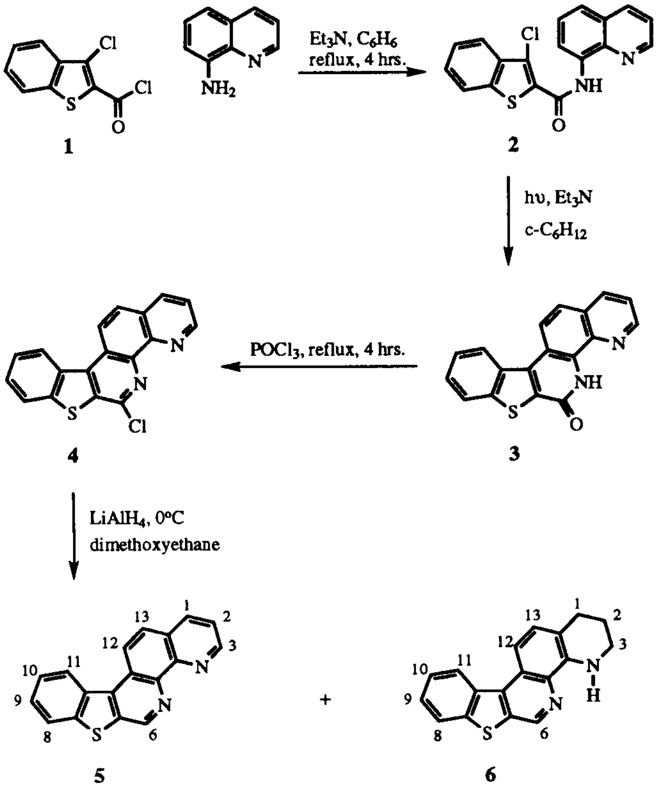
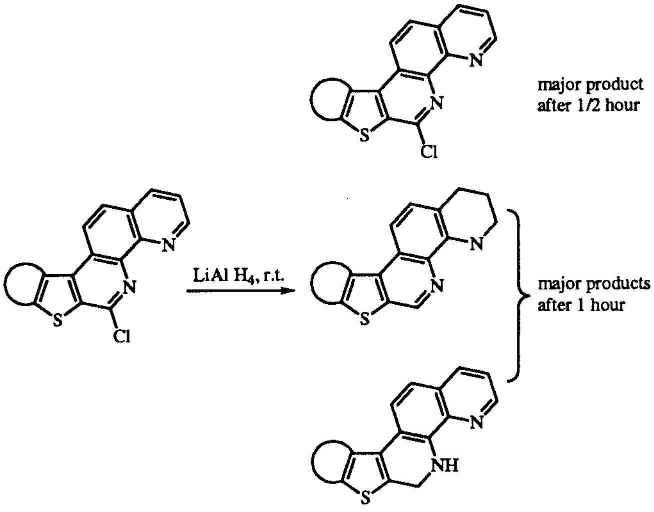


Figure 2.

Scheme 1



Scheme 2



six, have been reduced as well (Scheme 2) [5]. The precise effects of various conditions on the product distribution in this reaction will be the subject of further study in our laboratories.

NMR.

The ^{1}H nmr chemical shift assignments for **5** and **6** were straightforward. The COSY spectrum of **5** (Figure 1) established membership of each resonance in the two-spin, three-spin and four-spin systems which were expected. Further assignment of individual peaks in a spin system (Table 1) were made by comparison of chemical shifts and coupling constants to those of other thienophenanthrolines which we have prepared [1]. H_1 through H_3 were assigned thus. H_{11} and H_{12}, by virtue of their location in the bay region of the molecule, have been assigned to the farthest downfield resonances in their respective spin systems. The resonance at 8.13 ppm is identified as H_8 by the similarity of its splitting pattern with that of H_{11} and by supporting correlations observed in the COSY spectrum. The remaining members of the four-spin system could then be assigned to H_9 and H_{10}. The COSY spectrum of **6** (Figure 2) shows the two-spin and four-spin systems of the aromatic portion of the molecule as well as the spin system of the aliphatic ring. The broad doublet of triplets at 3.60 ppm was assigned to H_3 from a correlation with the NH proton at 6.25 ppm. The identification of H_3 allowed for the assignments of the protons at positions 1 and 2 from correlations observed in the COSY spectrum. The aromatic protons were assigned on the basis of chemical shifts and coupling patterns, as described above. The H_6 proton corresponds to the farthest downfield singlet for both **5** and **6**.

EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus and are uncorrected. The nmr spectra were obtained on a Bruker AC 250 MHz NMR spectrometer operating at 250 13 MHz for ^{1}H and 62.90 MHz for ^{13}C. All nmr experiments were performed using a 5-mm broad band probe. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane as the internal standard. Both the ^{1}H and ^{13}C 90° pulses were calibrated and the values obtained were 8.3 and 5.1 μsec, respectively. The COSY spectra were acquired using the standard Bruker microprogram COSY.AU [6]. Column chromatography was performed using Merck silica gel, grade 9385, 230-400 mesh. Starting materials and reagents were purchased from Aldrich; solvents were obtained from Fisher. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ.

1-Chloro-*N*-(8'-quinolyl)benzo[*b*]thiophene-2-carboxamide (**2**).

3-Chlorobenzo[*b*]thiophene-2-carbonyl chloride (**1**) (1.52 g, 6.56 mmoles), 0.95 g of 8-aminoquinoline (6.56 mmoles) and 0.95 ml of triethylamine (6.8 mmoles) were suspended in 150 ml of cyclohexane and allowed to reflux for four hours. The off-white precipitate which formed was separated by filtration, washed with water and air-dried to give 1.78 g of pure **2** (80% yield), mp 168-169°. The filtrate was washed with water, dried over magnesium sulfate and stripped of solvent *in vacuo*, to give 0.36 g of a yellow solid. Analysis by ^{1}H nmr showed that it consisted of unreacted 8-aminoquinoline (17 mole %, 0.03 g) and **2** (83 mole %, 0.33 g). This gave an overall yield of 96% for **2**;

^{1}H-nmr (deuteriochloroform): δ 7.47-7.58 (m, 3H), 7.58-7.64 (m, 2H), 7.85-7.95 (m, 1H), 7.95-8.03 (m, 1H), 8.21 (dd, 1H), 8.92 (dd, 1H), 8.94-8.98 (m, 1H), 11.60 (br s, 1H).

Anal. Calcd. for $C_{18}H_{11}ClN_2OS$: C, 63.81; H, 3.27; N, 8.27; S, 9.46. Found: C, 63.88; H, 3.50; N, 8.06; S, 9.31.

[1]Benzothieno[2,3-*c*][1,10]phenanthrolin-6(5*H*)-one (**3**).

1-Chloro-*N*-(8'-quinolyl)benzo[*b*]thiophene-2-carboxamide (**2**) (1.51 g, 4.46 mmoles) was dissolved in 100 ml of chloroform and placed in the photocyclization reaction vessel. To this was added 400 ml of cyclohexane and 0.65 ml (4.64 mmoles) of triethylamine. The resulting solution was irradiated for a total of ten hours with a 450 watt Hanovia medium pressure mercury lamp. Every few hours, the precipitated porduct had to be removed by filtration and scraped off the walls of the quart immersion well. The filtrate was returned to the reaction vessel and irradiation was resumed. This procedure was repeated until no more starting material remained in the filtrate. The combined precipitates were washed with water and then dried to yield **3** as a light tan powder (1.13 g, 84% yield). The material was used without further purification; ^{1}H-nmr (deuteriochloroform): δ 7.59 (dd, 1H), 7.61-7.70 (m, 2H), 7.76 (d, 1H), 8.07-8.12 (m, 1H), 8.27 (dd, 1H), 8.75 (d, 1H), 8.78-8.83 (m, 1H), 8.95 (dd, 1H), 11.10 (br s, 1H).

Anal. Calcd. for $C_{18}H_{10}N_2OS \cdot {}^1/_4H_2O$: C, 70.46; H, 3.45; N, 9.13; S 10.45. Found: C, 70.84; H, 3.58; N, 8.95; S, 10.26.

6-Chloro[1]benzothieno[2,3-*c*][1,10]phenanthroline (**4**).

A stirred mixture of 1.02 g (3.38 mmoles) of [1]benzothieno-[2,3-*c*][1,10]phenanthrolin-6(5*H*)-one (**3**) and 100 ml of phosphorus oxychloride was refluxed for four hours. The reaction was allowed to cool to room temperature, poured slowly into ice, then basified to *p*H 9 with concentrated ammonium hydroxide. The brown precipitate that formed was removed by filtration, air-dried overnight then recrystallized from benzene to yield 0.86 g (79%) of **4** as tan needles, mp 220-222°; ^{1}H-nmr (deuteriochloroform): δ 7.63-7.75 (m, 3H), 8.04 (d, 1H), 8.07-8.13 (m, 1H), 8.32 (dd, 1H), 8.84-8.91 (m, 1H), 8.94 (d, 1H), 9.28 (dd, 1H).

Anal. Calcd. for $C_{18}H_9ClN_2S \cdot {}^1/_2H_2O$: C, 65.55; H, 3.06; N, 8.49; S, 9.72. Found: C, 65.61; H, 3.10; N, 8.21; S, 9.60.

[1]Benzothieno[2,3-*c*][1,10]phenanthroline (**5**).

A suspension of **4** (0.312 g, 0.974 mmole) in 20 ml of anhydrous dimethoxyethane was cooled in an ice bath, under a nitrogen atmosphere. Lithium aluminum hydride (11.5 ml of 0.5 *M* stock solution in dimethoxyethane, 6 molar equivalents) was added dropwise over ten minutes, during which time **4** dissolved gradually and the color of the solution slowly changed from light yellow to dark green. The mixture was stirred for 10 minutes at 0 to 5°, then at room temperature for 50 minutes. Excess lithium aluminum hydride was quenched by the successive addition of one ml water, 0.92 g potassium hydroxide and one ml water, while the reaction flask was being cooled in ice. The resulting mixture was allowed to stir at room temperature for one hour, during which time a white gelatinous precipitate formed. This precipitate was removed by filtration and washed with acetone, then the combined filtrate and washings were dried over magnesium sulfate. The dry solution was stripped of solvent *in vacuo*, to yield a red-orange solid. The crude product was purified by flash column chromatography on silica gel with gradient elution. Compound **6** came off the column first with chloroform as the eluent. It was recrystallized from hexane to yield 0.055 g (20%) of yellow crystals, mp 127-128°; ^{1}H-nmr (deuteriochloroform): δ 2.15 (pentet, 2H), 3.00 (t, 2H), 3.60 (br t, 2H), 6.25 (br s, 1H), 7.37 (d, 1H), 7.62 (m, 2H), 8.01 (d, 1H), 8.06 (m, 1H), 8.85 (m, 1H), 9.14 (s, 1H); ^{13}C nmr (deuteriochloroform): δ 21.7, 26.9, 41.4, 108.5, 116.0, 123.5, 124.4, 125.1, 126.3, 127.1, 129.8, 133.1, 134.2, 135.6, 135.7, 141.2, 141.6, 142.1.

Anal. Calcd. for $C_{18}H_{14}N_2S \cdot {}^1/_4H_2O$: C, 73.32; H, 4.96; N, 9.50; S, 10.87. Found: C, 73.74; H, 4.94; N, 9.25; S, 10.70.

Compound **5** eluted from the column with 2% methanol in chloroform as the mobile phase. It was recrystallized from benzene to yield 0.112 g (41%) of red crystals, dec >220°; ^{1}H-nmr (deuteriochloroform): δ 7.66-7.74 (m, 3H), 8.08 (d, 1H), 8.13 (m, 1H), 8.36 (dd, 1H), 8.97 (m, 1H), 9.03 (d, 1H), 9.28 (dd, 1H), 9.70 (s, 1H); ^{13}C nmr (deuteriochloroform): δ 121.7, 122.4, 123.7, 125.2, 125.3, 126.0, 127.1, 127.7, 128.3, 134.7, 135.4, 135.6, 135.9, 141.4, 142.6, 145.0, 146.4, 150.5.

Anal. Calcd. for $C_{18}H_{10}N_2S \cdot {}^1/_4H_2O$: C, 74.33; H, 3.64; N, 9.63; S, 11.02. Found: C, 74.67; H, 3.79; N, 9.37; S, 11.41.

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