Synthesis of Two Novel Ring Systems *via* Photocyclization: Thieno[2',3':4,5]thieno[2,3-*c*][1,10]Phenanthroline and Thieno[3',2':4,5]thieno[2,3-*c*][1,10]Phenanthroline

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The synthesis of thieno[2',3':4,5]thieno[2,3-*c*][1,10]phenanthroline (**5**) and thieno[3',2':4,5]thieno-[2,3-*c*][1,10]phenanthroline (**10**) are described. Each compound 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.

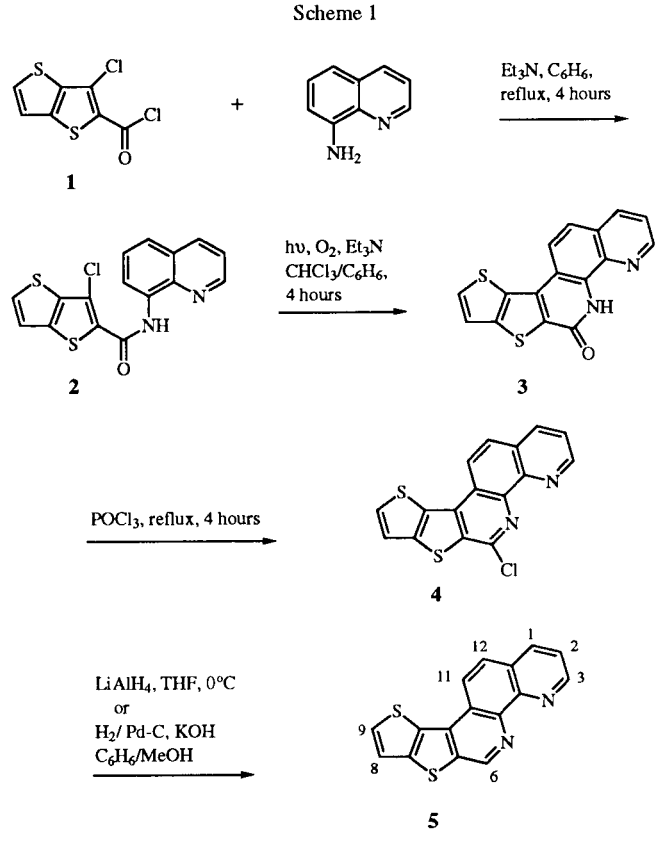
The two new polycyclic heterocycles reported herein, thieno[2',3':4,5]thieno[2,3-*c*][1,10]phenanthroline (**5**) and thieno[3',2':4,5]thieno[2,3-*c*][1,10]phenanthroline (**10**), represent an extension of the series of ring systems reported in references [1a-p]. The novelty of both new ring systems lies in the 1,10-phenanthroline moiety, which could chelate a variety of transition metal ions. We are preparing a series of these ligands with extended pi systems in anticipation of finding metal complexes which possess potentially interesting photochemical properties. The current paper describes the synthesis and characterization of **5** and **10**.

Results and Discussions.

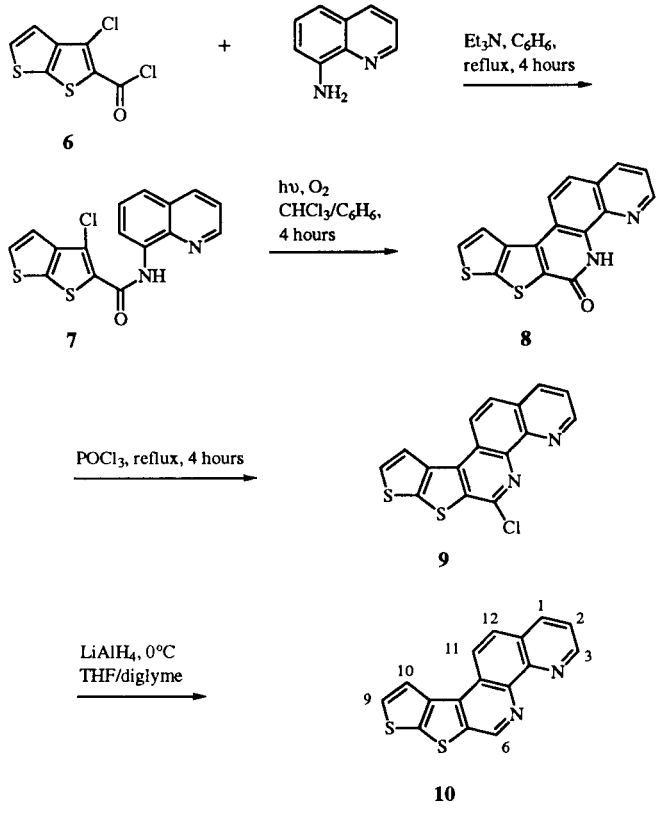
Synthesis.

The requisite starting materials for the synthesis of **5** (Scheme 1) were 8-aminoquinoline and 3-chlorothieno[3,2-*b*]thiophene-2-carbonyl chloride (**1**), the preparation of which had been described by Wright [2]. Condensation of the two reactants afforded a nearly quantitative yield of the amide **2**, which was then photocyclized under ultraviolet light to give **3**. This lactam **3** was aromatized by chlorination with phosphorus oxychloride to give **4**. Dechlorination to give **5** was accomplished under mild conditions with lithium aluminum hydride using a modification of the procedure of Brown and Krishnamurthy [3]. The original procedure called for several hours of reflux in tetrahydrofuran, but we found that **4** decomposed under such conditions. The ^{1}H nmr spectrum of the reaction mixture showed only aliphatic peaks with no identifiable pattern. On the other hand, we obtained acceptable yields when the reagent was added slowly at 0°, and the reaction mixture was allowed to stir at room temperature. Other methods which have been used successfully for dechlorination of similar compounds, namely catalytic hydrogenation [1d] or hydrazinolysis followed by oxidation with cupric sulfate [1g], did not work well in this case. Catalytic hydrogenation gave poor conversion (24%). On the other hand, treatment of **4** with hydrazine afforded the aryl hydrazine in good yield, but subsequent cleavage was problematic because copper(II) was tightly chelated to the 1,10-phenanthroline moiety. The cupric ion could be removed only partially by repeated extraction with excess EDTA.

Scheme 1



Scheme 2



6 7 8 9 10

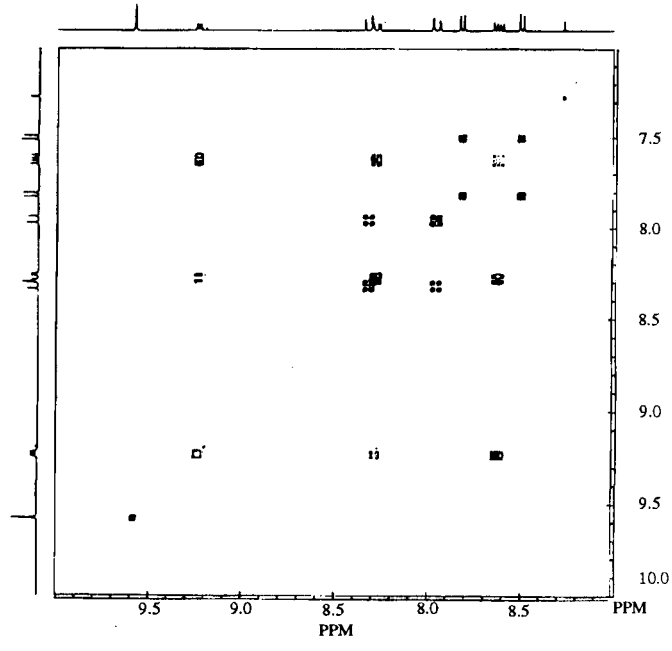


Figure 1. COSY spectrum of **5**.

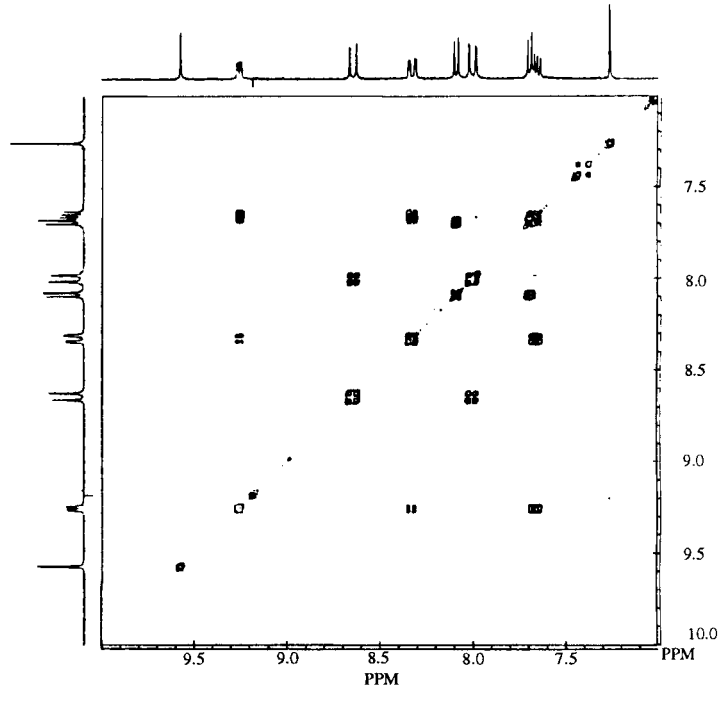


Figure 2. COSY spectrum of **10**.

Compound **10** was prepared by an analogous sequence of steps (Scheme 2) starting with 3-chlorothieno[2,3-*b*]-thiophene-2-carbonyl chloride (**6**) [1a]. Similar yields were obtained in each succeeding step. The only marked difference in reactivity was observed during an attempted dechlorination of **9** by catalytic hydrogenation. The only species observed in the reaction mixture were unreacted starting material and aliphatic decomposition products. This result may be attributable to poisoning of the catalyst due to strong binding between the metal and the two sulfur atoms on the same side of the molecule [4]. Previous attempts to dechlorinate other compounds having the thieno[3',2':4,5]thieno moiety using hydrogen and palladium on carbon were also unsuccessful [1a].

Table 1

^{1}H NMR Assignments for **5** and **10**

Compound **5**			Compound **10**		
Position	δ	Correlated ^{1}H's	Position	δ	Correlated ^{1}H's
H_1	8.30	H_2, H_3	H_1	8.33	H_2, H_3
H_2	7.64	H_1, H_3	H_2	7.66	H_1, H_3
H_3	9.24	H_1, H_2	H_3	9.26	H_1, H_2
H_6	9.59		H_6	9.57	
H_8 [a]	7.98	H_9	H_9	8.01	H_{10}
H_9 [a]	8.36	H_8	H_{10}	8.65	H_9
H_{11}	7.84	H_{12}	H_{11}	8.10	H_{12}
H_{12}	7.52	H_{11}	H_{12}	7.70	H_{11}

[a] May be interchangeable.

NMR.

The assignments of ^{1}H nmr resonances for **5** and **10** are given in Table 1. The COSY spectrum of **5** (Figure 1) clearly shows the three-spin system of H_1-H_2-H_3, and two

two-spin systems: H_8-H_9 and H_{11}-H_{12}. A NOESY spectrum (not shown) revealed a cross peak between the doublet at 7.52 ppm and the doublet-of-doublets at 8.30 ppm, thus allowing the assignment of these peaks to H_{12} and H_1, respectively. Once this was done, H_2, H_3 and H_{11} could also be assigned. However, the two doublets in the remote H_8-H_9 system could not be distinguished by this method. The COSY spectrum of **10** (Figure 2) also shows the expected three-spin and two two-spin systems. As in the case of **5**, a NOESY spectrum (not shown) revealed a cross peak between the doublet at 7.70 ppm and the doublet-of-doublets at 8.33 ppm, which were assigned to H_{12} and H_1, respectively. In addition, there was a second cross peak between the doublets at 8.10 and 8.65 ppm, identifying them as H_{11} and H_{10}, respectively.

EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus and are uncorrected. The nmr spectra were obtained on a Bruker AC 250 spectrometer operating at 250.13 MHz for ^1H 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 ^1H and ^{13}C 90° pulses were calibrated and the values obtained were 8.3 and 5.1 μsec, respectively. The COSY and NOESY spectra were acquired using the standard Bruker microprograms COSY.AU and NOESY.AU [5]. 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.

3-Chloro-*N*-(8-quinolyl)thieno[3,2-*b*]thiophene-2-carboxamide (**2**).

A mixture of **1** (0.174 g, 0.73 mmole), 8-aminoquinoline (0.109 g, 0.76 mmole) and triethylamine (0.1 ml, 0.73 mmole) in 25 ml of benzene was heated under reflux for four hours. Most of the triethylammonium chloride precipitated on cooling to room temperature and was removed by filtration. The filtrate was concentrated and further purified by flash chromatography using chloroform as the eluent. The product was obtained as a yellow solid (0.246 g, 97% yield), mp 173-174.5°; ^1H nmr (deuteriochloroform): δ 7.33 (d, 1H, J = 5 Hz), 7.50 (dd, 1H, J = 3.75, 7.5 Hz), 7.60 (m, 3H), 8.20 (dd, 1H, J = 2.5, 8.75 Hz), 8.91 (m, 2H), 11.42 (br, 1H); ^{13}C nmr (deuteriochloroform): δ 117.2, 117.3, 120.7, 121.7, 122.2, 127.4, 128.0, 131.0(9), 131.1(0), 134.8, 135.0, 136.3, 139.0, 139.6, 148.6, 159.0.

Anal. Calcd. for $C_{16}H_9ClN_2OS_2$: C, 55.73; H, 2.63; N, 8.12. Found: C, 55.55; H, 2.81; N, 8.00.

Thieno[2',3':4,5]thieno[2,3-*c*][1,10]phenanthrolin-6(5*H*)-one (**3**).

A mixture of **2** (0.226 g, 0.66 mmole, dissolved in 50 ml of chloroform), triethylamine (0.1 ml, 0.7 mmole) and 450 ml of benzene was irradiated with a 450 watt Hanovia medium pressure mercury lamp for three hours. A slow stream of air was bubbled through the solution during the reaction. Pure **3** precipitated as a yellow solid and was collected by filtration, washed with water, and air-dried (0.113 g, 56% yield). The ^1H nmr spectrum of the filtrate, after evaporation of the solvent, showed no sign of unreacted starting material. In fact, there was no identifiable pattern in the aromatic region, indicating that decomposition had taken place; ^1H nmr of **3** (deuteriochloroform + a few drops of dimethyl sulfoxide-d_6): δ 7.56 (d, 1H, J = 5 Hz), 7.62 (dd, 1H, J = 3.75, 8.75 Hz), 7.79 (d, 1H, J = 8.75 Hz), 7.87 (d, 1H, J = 5 Hz), 8.19 (d, 1H, J = 8.75 Hz), 8.32 (dd, 1H, J = 1.25, 8.75 Hz), 8.9 (dd, 1H, J = 1.25, 3.75 Hz), 10.90 (br, 1H).

6-Chlorothieno[2',3':4,5]thieno[2,3-*c*][1,10]phenanthroline (**4**).

A mixture of **3** (0.113 g, 0.37 mmole) and 25 ml of phosphorus oxychloride was heated to 110-115° for four hours. After cooling, the mixture was slowly poured over ice then basified (to *p*H 9) with concentrated ammonium hydroxide. The precipitate was filtered, allowed to air-dry and then recrystallized from benzene to give brown needles (0.084 g, 70% yield), mp 291-293°; ^1H nmr (deuteriochloroform): δ 7.50 (d, 1H, J = 5 Hz), 7.62 (dd, 1H, J = 5, 7.5 Hz), 7.83 (d, 1H, J = 5 Hz), 7.95 (d, 1H, J = 10 Hz), 8.25 (m, 2H), 9.24 (m, 1H); ^{13}C nmr (deuteriochloroform): δ 120.3, 120.4, 121.7(6), 121.8(0), 121.9, 122.8, 122.9, 127.3, 127.4, 128.0, 133.0, 136.0(6), 136.1(3), 143.0, 151.0, 151.1.

Anal. Calcd. for $C_{16}H_7ClN_2S_2 \cdot {}^1/_5H_2O$: C, 58.16; H, 2.26; N, 8.48. Found: C, 58.66; H, 2.22; N, 8.05.

Thieno[2',3':4,5]thieno[2,3-*c*][1,10]phenanthroline (**5**).

A. By Catalytic Hydrogenation.

The aryl chloride **4** (0.056 g, 0.172 mmole) was dissolved in 75 ml of a 2:1 benzene-methanol mixture. To this solution were added 0.1 *M* potassium hydroxide in methanol (1.75 ml, 0.175 mmole) and 10% palladium on carbon (0.06 g). The mixture was shaken in a Parr hydrogenator at room temperature for 22 hours, under two atmospheres of hydrogen. Analysis by tlc (silica gel, 2% methanol in chloroform) showed three components with R_f's of 0.31, 0.58 and 1.00. These were separated by flash chromatography using 1% methanol in chloroform as the eluent. The ^1H nmr showed that the components were **5** (0.012 g, 24% yield), unreacted **4** (0.041 g, 73% recovery) and unidentified aliphatic side-products, respectively. (Increasing the reaction time to 48 hours in subsequent experiments did not improve the yield.) Compound **5** was obtained as a white solid, which was recrystallized from benzene; ^1H nmr (deuteriochloroform): δ 7.52 (d, 1H, J = 6 Hz), 7.64 (dd, 1H, J = 9, 4.5 Hz), 7.84 (d, 1H, J = 6 Hz), 7.98 (d, 1H, J = 9 Hz), 8.30 (dd, 1H, J = 9, 1.5 Hz), 8.36 (d, 1H, J = 9 Hz), 9.24 (dd, 1H, J = 4.5, 1.5 Hz), 9.59 (s, 1H); ^{13}C nmr (deuteriochloroform): δ 120.3, 122.3, 122.4(9), 122.5(3), 127.1, 127.7, 132.5, 133.1, 134.7, 136.0, 138.1, 142.1, 142.5, 145.5, 146.3, 150.7.

Anal. Calcd. for $C_{16}H_8N_2S_2 \cdot {}^6/_7H_2O$: C, 62.43; H, 3.18; N, 9.10. Found: C, 61.96; H, 2.70; N, 8.63.

B. By Metal-Hydride Reduction.

The reaction was carried out on a 2:1 mixture of **4** and its 6,9-dichloro analog [6] from an older preparation in the hope that both chloro groups would be displaced. However, dechlorination only took place at the 6-position. A suspension of the mixture (0.056 g, 0.231 milliequivalents of Cl) in 15 ml of anhydrous tetrahydrofuran was cooled in an ice bath under a nitrogen atmosphere. Lithium aluminum hydride (0.8 ml of a

1.0 *M* stock solution in tetrahydrofuran, diluted with 5 ml of tetrahydrofuran) was added dropwise over four to five minutes, during which time the starting material dissolved gradually and the color of the solution slowly changed from light yellow to dark green. The mixture was stirred for ten minutes at 0 to 5°, then at room temperature for half an hour. Excess lithium aluminum hydride was quenched by the successive addition of one ml of water, one pellet of potassium hydroxide and one ml of water. The mixture was allowed to stir at room temperature for one hour, during which time the solution gradually changed color to orange and a white gelatinous precipitate formed. The solution was dried over magnesium sulfate, then all insoluble solids were removed by filtration. The filtrate was concentrated, then purified by flash chromatography using chloroform then 1% methanol in chloroform as the eluent. A yellow oil was obtained, which was dissolved in methanol then triturated with water. A white solid precipitated after a few hours. The ^{1}H nmr spectrum of this solid was consistent with a 2:1 mixture of **5** and its 9-chloro analog (0.026 g, 53% combined yield). The two compounds were not separable on alumina or silica gel; ^{1}H nmr (deuteriochloroform): δ 7.34 (s, $^1/_3$H, $H_{8'}$), 7.50 (d, $^2/_3$H, J = 6.25 Hz, H_8 or H_9), 7.63 (dd, 1H, J = 3.75, 7.5 Hz, $H_{2\&2'}$), 7.82 (d, $^2/_3$H, J = 6.25 Hz, H_8 or H_9), 7.91 (d, $^1/_3$H, J = 8.75 Hz, $H_{12'}$), 7.95 (d, $^2/_3$H, J = 8.75 Hz, H_{12}), 8.04 (d, $^1/_3$H, J = 8.75 Hz, $H_{11'}$), 8.27 (dd, 1H, J = 2.5, 7.5 Hz, $H_{1\&1'}$), 8.31 (d, $^2/_3$H, J = 8.75 Hz, H_{11}), 9.23 (dd, 1H, J = 1.25, 3.75 Hz, $H_{3\&3'}$), 9.54 (s, $^1/_3$H, $H_{6'}$), 9.57 (s, $^2/_3$H, H_6). Note: The primes refer to the 9-chloro compound.

3-Chloro-*N*-(8-quinolyl)thieno[2,3-*b*]thiophene-2-carboxamide (**7**).

The procedure was the same as for the preparation of **2** starting with 0.45 g of **6** (1.9 mmoles) and 0.28 g of 8-aminoquinoline (1.9 mmoles). After chromatography **7** was obtained as a yellow solid (0.61 g, 94% yield), mp 200-202°; ^{1}H nmr (deuteriochloroform): δ 7.30 (d, 1H, J = 5 Hz), 7.46 (d, 1H, J = 5 Hz), 7.49 (dd, 1H, J = 3.75, 7.5 Hz), 7.58 (m, 2H), 8.19 (dd, 1H, J = 1.25, 8.75 Hz), 8.89 (m, 2H), 11.45 (br, 1H); ^{13}C nmr (deuteriochloroform): δ 116.8, 117.2, 119.5, 119.6, 121.7, 122.1, 127.3, 127.9, 129.5, 134.5, 136.2, 138.7, 139.3, 145.4, 148.5, 158.9.

Anal. Calcd. for $C_{16}H_9ClN_2OS_2$: C, 55.73; H, 2.63; N, 8.12; S, 18.59. Found: C, 55.88; H, 2.48; N, 7.92; S, 18.52.

Thieno[3',2':4,5]thieno[2,3-*c*][1,10]phenanthrolin-6(5*H*)-one (**8**).

The procedure was the same as for the preparation of **3** starting with 0.348 g of **7** (1.0 mmole) and 0.14 ml of triethylamine (1.0 mmole). Compound **8** precipitated as a yellow solid and was used in the next step without further purification (0.159 g, 51% yield), mp 295-296° (darkens ~160°); ^{1}H nmr (deuteriochloroform): δ 7.56 (dd, 1H, J = 5, 8.75 Hz), 7.68 (d, 1H, J = 5 Hz), 7.70 (d, 1H, J = 8.75 Hz), 7.93 (d, 1H, J = 5 Hz), 8.25 (dd, 1H, J = 1.25, 8.75 Hz), 8.31 (d, 1H, J = 8.75 Hz), 8.91 (dd, 1H, J = 1.25, 5 Hz), 10.90 (severely broadened).

6-Chlorothieno[3',2':4,5]thieno[2,3-*c*][1,10]phenanthroline (**9**).

The procedure was the same as for the preparation of **4** starting with 0.15 g of **8** (0.49 mmole). After recrystallization, **9** was obtained as brown needles (0.107 g, 67% yield), mp 288.5-290° (gradually darkens ~ 240°); ^{1}H nmr (deuteriochloroform): δ 7.62 (dd, 1H, J = 4.25 Hz), 7.66 (d, 1H, J = 5 Hz), 7.90 (d, 1H, 8.75 Hz), 7.97 (d, 1H, 8.75 Hz), 8.26 (dd, 1H, J = 8.75, 2.5 Hz), 8.46 (d, 1H, J = 8.75 Hz), 9.23 (dd, 1H, J = 5, 2.5 Hz); ^{13}C nmr (deuteriochloroform): δ 121.4, 121.8, 122.9, 123.0, 127.1, 128.0, 130.0, 136.0, 136.6, 138.4, 141.3, 142.6, 144.1, 144.7, 145.4, 151.1. Satisfactory analysis could not be obtained for this compound.

Thieno[3',2':4,5]thieno[2,3-*c*][1,10]phenanthroline (**10**).

The procedure was the same as for the preparation of **5** by lithium aluminum hydride reduction starting with 0.015 g of **9** (0.046 mmole) and 0.55 ml of lithium aluminum hydride (0.5 *M* in diglyme, 6 molar equivalents). The filtrate obtained after removal of the insoluble solids was stripped of solvent *in vacuo*. The yellow oil remaining was triturated with methanol and water, and a yellow solid was collected (0.010 g, 75% yield), which was recrystallized from benzene; ^{1}H nmr (deuteriochloroform): δ 7.66 (dd, 1H, J = 7.5, 4.5 Hz), 7.70 (d, 1H, J = 6 Hz), 8.01 (d, 1H, J = 9 Hz), 8.10 (d, 1H, J = 6 Hz), 8.33 (dd, 1H, J = 7.5, 1.5 Hz), 8.65 (d, 1H, J = 9 Hz), 9.26 (dd, 1H, J = 4.5, 1.5 Hz), 9.57 (s, 1H); hrms: Calcd. for 292.0129: Found: 292.0141. Satisfactory analysis could not be obtained for this compound.

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[6] The synthesis of **1** according to the procedure in reference [2] also produced 3,5-dichlorothieno[3,2-*b*]thiophene-2-carbonyl chloride as a side-product. Instead of separating the two products, both were carried through the sequence in Scheme 1. The penultimate products were **4** and its 6,9-dichloro analog.