Chemistry of the Phenoxathiins VIII. Synthesis of 7-chlorobenzo[1″,2″:5,6:3″,4″:5′,6′]*bis*[1,4]oxathiino[3,2-*b*:3′,2′-*b*′]dipyridine

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As a continuation of recent study on the synthesis of a *bis*[1,4]oxathiinodipyridine ring system, we would now like to report the preparation of 7-chlorobenzo[1″,2″:5,6:3″,4″:5′,6′]-*bis*[1,4]oxathiino[3,2-*b*:3′,2′-*b*′]dipyridine. Although a potentially complex reaction with several products possible, the title compound was formed exclusively, suggesting considerable mechanistic selectivity. The characterization of the product by FT-^{1}H-nmr as well as its mass spectral fragmentation pathways are also reported.

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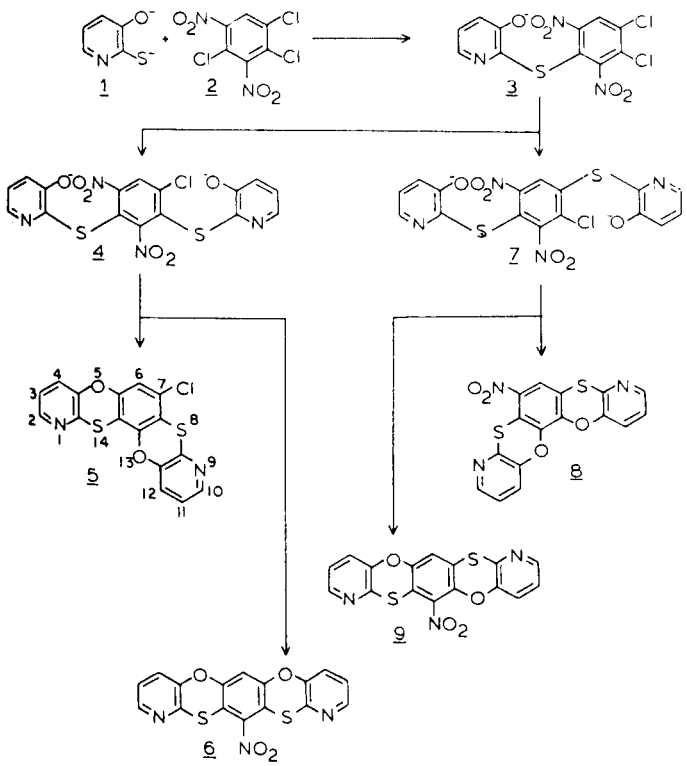
The synthesis of several 7-substituted-1-azaphenoxathiins (2) and the parent 1-azaphenoxathiin (3) ring system have recently been reported. In an extension of these earlier studies, the synthesis of the linear pentacyclic system, benzo[1″,2″:5,6:5″,4″:5′,6′]*bis*[1,4]oxathiino[3,2-*b*:3′,-2′-b]dipyridine has also recently been reported (4). As a further continuation of our studies in this series of compounds, we would now like to report the first synthesis of an analog of the non-linear benzo[1″,2″:5,6:3″,4″:-5′,6′]*bis*[1,4]oxathiino[3,2-*b*:3′,2′-*b*′]dipyridine ring system (**5**), as shown in Scheme I.

The synthesis of **5** was carried out through the condensation of the disodium salt of 2-mercapto-3-pyridinol (**1**) (2) with 3,5-dinitro-1,2,4-trichlorobenzene (**2**) (5),

SCHEME I



which should proceed in a stepwise fashion through **3** to yield the isomeric phenylene bispyridylsulfides, **4**, which is synthetically the favored product, and **7**, which is not favored due to the positioning of the nitro substituent of **2** (6). An additional possibility, although there is no evidence to support its existence, would involve the displacement of the 1- and 2-chloro substituents of **2** to give a third phenylene bispyridylsulfide. This latter possibility, which is not shown in Scheme I, would not be synthetically favored because of considerable steric hinderance.

Thus, from the outset of the synthesis, it was anticipated that the formation of **4** would represent the major intermediate pathway of the reaction based on prior mechanistic studies (6). In contrast, the formation of **7** could not be totally ruled out, since recent studies (7,8) have shown that even in cases of unfavorable substituent placement, such as leading to the formation of **7**, the reaction can occur and thus might represent a minor product of the reaction. Further, from **4**, there are two possible cyclization products, 7-chlorobenzo[1″,2″:5,6:-3″,4″:5′,6′]*bis*[1,4]oxathiino[3,2-*b*:3′,2′-*b*]dipyridine (**5**), representing displacement of the nitro group and the corresponding linear benzo 13-nitrobenzo[1″,2″:5,6:3″,-4″:5′,6′]*bis*[1,4]oxathiino[3,2-*b*:3′,2′-*b*′]dipyridine (**6**), arising through the displacement of the chloro substituent.

Examination of the crude reaction mixture by mass spectrometry showed the formation of **5** (to the virtual exclusion of the other products) to be the major pathway in Scheme I. Evidence for this conclusion is the presence of a single chlorine atom and an exact mass corresponding to an elemental composition consistant with structure **5** (*vida infra*). The material which did form with m/e 369 seen in the mass spectrum of crude reaction materials was most likely **6** based on the anticipated mechanism (6), although it could not be discriminated from **8** and **9**, which could form through cyclization of **7**, on the basis of the mass spectral data.

The electron impact mass spectrum of **5** is dominated by the molecular ion (100% relative intensity) and

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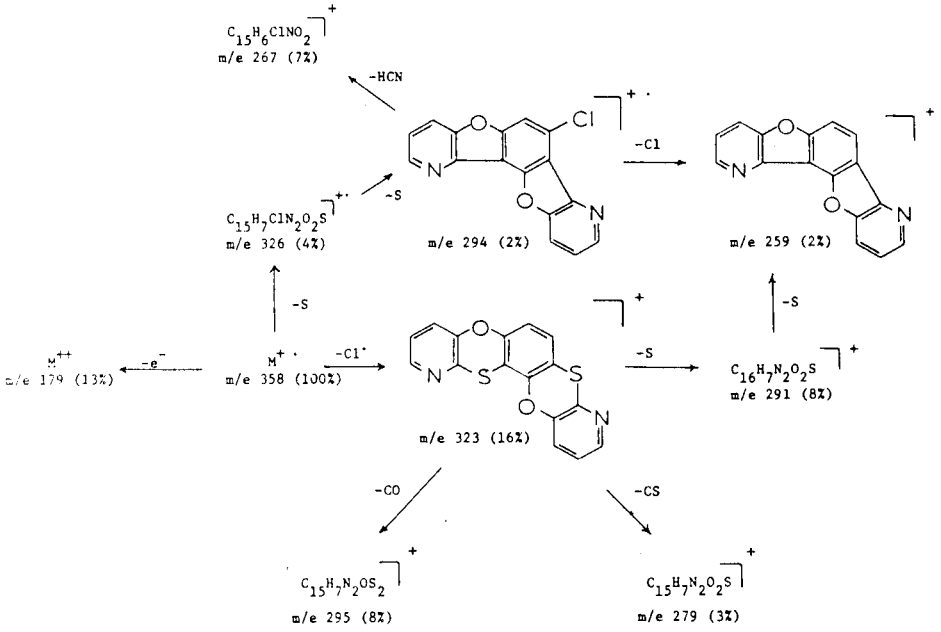

SCHEME II

fragment ions are few and of low relative intensity. The lack of extensive fragmentation is to be expected due to the highly aromatic character of **5**. An ion at m/e 179 is due to a doubly charged molecular ion which is also characteristic of highly aromatic systems (9,10).

The fragmentations which are observed appear to arise by two routes. The first pathway is initial loss of chlorine from the molecular ion to give an ion at m/e 323 (See Scheme II). Loss of one or two sulfur atoms gives rise to ions at m/e 291 and m/e 259, respectively. Which sulfur atom is lost first is not, at present, known. The ion at m/e 323 can also loose CO or CS to give ions at m/e 295 and m e 279, respectively. This sequence is similar to the fragmentation of phenoxathiin (11) and other sulfur containing heterocycles (12). The identity of the specific sulfur, oxygen and carbon atoms being lost is not known and will require some rather difficult labeling experiments to assign exact structures to some of these ions. For this reason, the elemental compositions are given to avoid ambiguous or incorrect structures. Structures are drawn where no ambiguity exists. The compositions of the ions are valid as shown by high resolution mass measurements.

The other decomposition pathway involves initial loss of sulfur from the molecular ion to give the ion at m/e 326. Loss of the other sulfur atom gives rise to the ion at m/e 294, which can loose chlorine giving m/e 259 by a second route or expell hydrogen cyanide, a common fragmentation of pyridine compounds (13), to give the ion at m/e 267. In the second case, the identity of which nitrogen is lost is, again, unknown. Further fragmentations are of low intensity (< 1%) and will require labeling to assign structures. The high resolution data supporting the proposed elemental compositions is presented in Table 1.

Table 1

Exact Mass of Some Selected Ions of **5**

m/e	Elemental Composition	Observed Mass	Calculated Mass	Δ (millimass Units)
358	$C_{16}H_7ClN_2O_2S_2$	357.9617	357.9638	2.1
326	$C_{16}H_7ClN_2O_2S$	325.9882	325.9917	2.5
323	$C_{16}H_7N_2O_2S_2$	322.9935	322.9949	1.4
295	$C_{15}H_7N_2OS_2$	295.0034	295.0000	3.4
294	$C_{16}H_7ClN_2O_2$	294.0197	294.0196	0.1
291	$C_{16}H_7N_2O_2S$	291.0269	291.0228	4.1
279	$C_{15}H_7N_2O_2S$	279.0205	279.0028	2.3
267	$C_{15}H_6ClNO_2$	266.9942	267.0075	3.3
259	$C_{16}H_7N_2O_2$	259.0493	259.0507	1.4
179	$C_{16}H_7ClN_2O_2S_2^{++}$	178.9828	178.9808	2.0

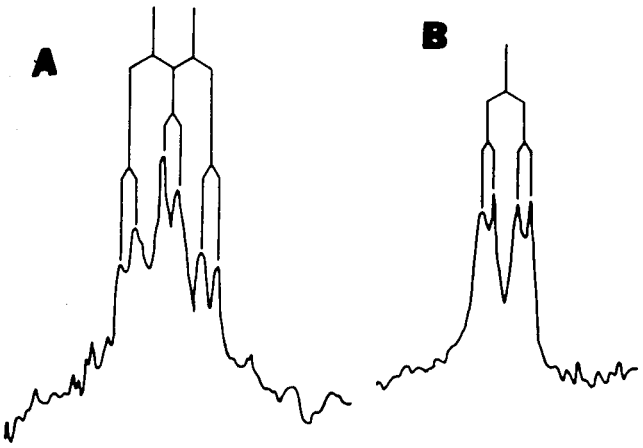

Figure 1. Expansion of the Pyridino-*alpha* Proton Region of: A. 7-Chlorobenzo[1″,2″:5,6:3″,4″:5′,6′]*bis*[1,4]-oxathiino[3,2-*b*:3′,2′-*b*]dipyridine, **5**; B. Benzo[1″,2″:-5,6:5″,4″:5′,6′]*bis*[1,4]oxathiino[3,2*b*:3′,2′*b*′]dipyridine (4).

Table II

100 MHz FT-^{1}H-nmr Line Positions of **5** from Figure 2

Frequency (Hz)	Ppm	Frequency (Hz)	Ppm
829.35	8.286	743.797	7.433
826.595	8.261	740.516	7.400
825.847	8.253	737.859	7.374
824.106	8.236	736.450	7.360
821.330	8.208	735.725	7.353
819.259	8.190	734.713	7.323
753.366	7.529	733.264	7.328
751.893	7.514	728.845	7.284

Examination of the 100 MHz fouier transform ^{1}H-nmr spectrum of **5** readily showed the nonequivalence of the two protons *alpha* to the pyridine derived nitrogen atoms at C-2 and C-10 which appeared as a pair of overlapping doublet of doublets (Figure 1A). Had the molecule assumed a symmetric, linear configuration, as for example **6** or the previously reported linear benzo[1″,2″:5,6:-5″,6″:3″,4″:5′,6′]oxathiino[3,2-*b*:3′,2′-*b*′]dipyridine (4) (see Figure 1B), a simple doublet of doublets would be expected to result from the equivalent *alpha* protons. The remainder of the proton spectrum was largely overlapped and essentially unassignable, with the exception of the sharp singlet at δ = 7.40 assigned to the proton at the 6-position, *ortho* to the chloro substituent (See Figure 2).

Thus, although initially anticipated to be a complex reaction resulting in the formation of a number of closely related products as shown by Scheme I, the reaction unexpectedly showed a great deal of selectivity. On this basis with proper functionalization, this reaction should provide the means of access to a variety of analogs of the benzo[1″,2″:5,6:3″,4″:5′,6′]*bis*[1,4]oxathiino[3,2-*b*:3′,-2′-*b*′]dipyridine ring system.

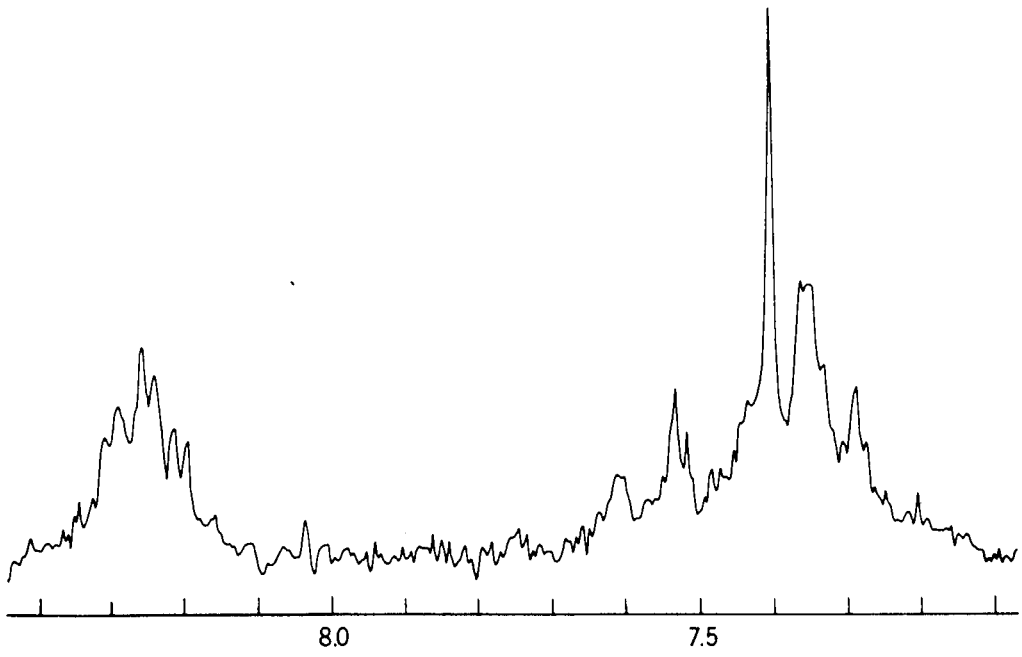

Figure 2. 100 MHz FT-^{1}H-nmr Spectrum of 7-Chloro-benzo[1″,2″:5,6:3″,4″:5′,6′]*bis*[1,4]oxathiino[3,2-*b*:3′,-2′-*b*′]dipyridine (**5**).

EXPERIMENTAL

Melting points were obtained in open capillary tubes in a ThomasHoover melting point apparatus and are reported uncorrected. Infrared spectra were recorded on a Perkin-Elmer model 283 spectrophotometer as potassium bromide pellets. ^{1}H-nmr spectra were recorded in hexadeuterioacetone on a Varian XL-100 spectrometer equipped with a Nicolet Technology TT-100 data system and a NT-440 frequency synthesizer and operating at 100 MHz in the fourier transform mode with the following fixed operating parameters: pulse wideth, 10 μsec; pulse delay, 1.000 sec; sweep width, 1500 Hz; acquisition time, 2.7279 sec; data size 16 K. Low resolution mass spectra were obtained using a Hewlett-Packard Model 5930 GC-MS system with a Model 5933A data system at an ionizing energy of 70 eV and an ion source temperature of 250°. Samples were introduced using a direct probe.

7-Chlorobenzo[1″,2″:5,6:3″,4″:5′,6′]bis[1,4]oxathiino[3.2-*b*:3′,2′-*b*]dipyridine (**5**).

To a stirred solution of 1,2,4-trichloro-3,5-dinitrobenzene (2.00 g., 0.0074 mole) in 30 ml. of dry distilled dimethylsulfoxide under dry argon purge at room temperature was added 2.531 g. (0.0148 mole) of 2-mercapto-3-pyridinol (**1**) (2). The reaction mixture, which immediately darkened, was stirred at room temperature for 24 hours and then brought to reflux temperature for an additional 48 hours. Following the completion of the reflux, the solution was allowed to cool and then poured over 50 g. of ice and the resultant cold, aqueous solution extracted with four 100 ml. portions of ethyl acetate. The ethyl acetate extracts were combined, extracted with four 200 ml. portions of distilled water and then dried over anhydrous sodium sulfate. The pale yellow extract was concentrated to an oil which was chromatographed over a silica gel column eluted with cyclohexane/ethyl acetate (4:1) and subsequently recrystallized from absolute ethanol to yield 0.070 g. of **5** (2.7% yield) as fine brownish crystals, m.p. 105-110° (darkening). The balance of the reaction mixture appears to have been polymeric by-products which would not move on the chromatography column; ir: max 3410, 3060, 2920, 2850, 1605, 1570, 1545, 1445, 1410, 1380, 1265, 1085, 790, 720 cm^{-1}; FT1H-nmr (deuterioacetone): see Figure 2 and Table II; ms: m/e (% relative intensity) 358 (100), 326 (4), 323 (16), 291 (8), 179 (13); high resolution ms: exact mass calculated for $C_{16}H_7ClN_2O_2S_2$: 357.9638. Found: 357.9617. See also Table I.

Anal. Calcd. for $C_{17}H_7ClN_2O_2S_2$: C, 53.63; H, 1.95; N, 7.82. Found: C, 53.79; H, 2.07; N, 8.22.

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