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

Gary E. Martin (1), James C. Turley, Richard F. Miller (2), Karl H. Schram and Louis Williams

Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Houston, Houston, Texas 77004

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As a result of studies dealing with the synthesis of 1-azaphenoxathiins, the synthesis of benzo[1″,2″:5,6:5″,4″:5′,6′]bis[1,4]oxathiino[3,2-*b*:3′,2′-*b*′]dipyridine was examined. Unique evidence of solvent participation in the synthesis of these compounds by the structure elucidation of a novel minor by-product formed during the synthesis of the title compound is also reported.

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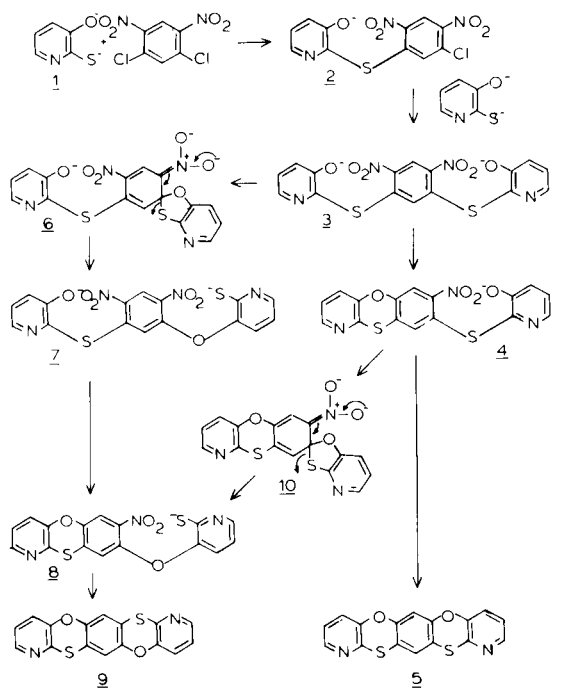
Only one example of a linear benzo[*b*]phenoxathiin has been reported (3), and there have been no reported examples of the related dibenzo[*b*,*i*]phenoxathiins. Similarly, there has also been very little reported on the synthesis or properties of the [1,4]-benzoxathiino[3,2-*b*]-phenoxathiin ring system (4). In terms of aza-substituted phenoxathiins, very little has been reported here in terms of higher systems, with the sole reported example being the synthesis of diquinolino[3,2-*a*:3′,2′-*j*]dibenzo[*c*,*h*]-phenoxathiin (5).

In previous studies, the synthesis of a group of 7-substituted 1-azaphenoxathiins (6) and the subsequent synthesis of the parent 1-azaphenoxathiin ring system were reported (7). As a continuation of this study, we would like to report the synthesis of a novel benzo-[1″,2″:5,6:5″,4″:5′,6′]bis[1,4]oxathiino[3,2-*b*:3′,2′-*b*′]-dipyridine (**5**) as shown in Scheme I.

SCHEME I



Synthesis of **5** was conducted through the condensation of the disodium salt of 2-mercapto-3-pyridinol (**1**) (6) with 1,3-dichloro-4,6-dinitrobenzene which proceeds through **2** to yield the intermediate bis-sulfide **3**. This intermediate, **3**, forms the focal point of the pathways leading to the two pentacyclic systems possible in this synthesis. Although there was a possibility of a Smiles rearrangement (8), on the basis of a previous study (6), this could be largely discounted from the onset. Thus, **5** can be envisioned as forming by a stepwise cyclization proceeding from **3** through **4** to give the desired product. A remaining possibility which would be difficult to discern and which further is also highly unlikely, would be the formation of **5** through a double Smiles Rearrangement, which again can be argued against on the basis of previous work (6). Had a Smiles rearrangement occurred in this synthesis, a somewhat different product, benzo[1″,2″:-5,6:5″,4″:5′,6′]bis[1,4]oxathiino[3,2-*b*:3′,2′-*b*′]dipyridine (**9**) would have resulted. Mechanistically, as shown in Scheme I, **9** could arise by either of two plausible pathways, both originating at **3**. The first, would involve a Smiles rearrangement directly from **3** to give the mixed ether, **7**, which could then go on to cyclize in a step-wise fashion to form **9**. The other possible pathway leading to **9** involves the partial cyclization of **3** to give **4**, which could then undergo rearrangement to give **8** which on completion of the cyclization would give **9**.

Structural discrimination between **5** and **9** was based on the 100 MHz FT-^{1}H nmr spectrum of the product. The observed spectrum showed two clearly separate and distinct signals at δ = 9.64, corresponding to the proton at the 6-position and δ = 9.21 corresponding to the proton at the 13-position. Had a Smiles rearrangement occurred in this reaction resulting in the formation of **9**, because of the inherrently higher order symmetry of the central ring, producing equivalence of the 6 and 13-positions, only a single signal would have been observed. Thus, the structure of the product can unequivocably be assigned to **5**, indicating that a Smiles rearrangement had not occurred.

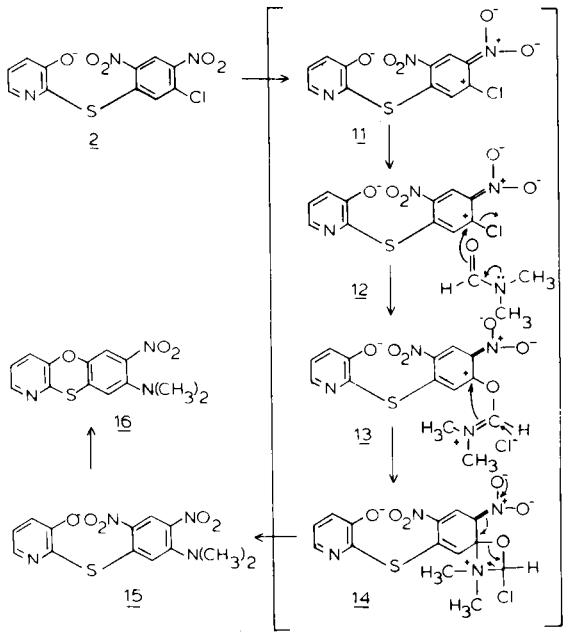
Both high and low resolution mass spectra were

obtained for **5**, with an observed exact mass of 324.0009 which was within 2 mmu of the calculated exact mass of 324.0027 for an elemental composition of $C_{16}H_8N_2O_2S_2$. A field desorption mass spectrum of **5** showed a peak at m/e 323 corresponding to M-1 with no other peaks possessing an intensity greater than 1% observed in the spectrum. The electron impact spectrum of **5** showed an intense molecular ion at m/e 324 which was also the base peak of the spectrum. Complete details of the mass spectral fragmentation will be presented elsewhere.

In addition to the formation of **5**, a novel byproduct of the reaction mixture which has the proposed structure 7-nitro-8-*N*,*N*-dimethylamino-1-azaphenoxathiin (**16**) was observed in samples of the reaction mixture prior to final purification, and appears to have been formed only in minute quantities since it was not possible to isolate the material in pure form by chromatography. The identity of this byproduct was determined from its high resolution and field desorption mass spectra. The high resolution spectrum of **16** showed an observed exact mass of 289.0523 which agreed within 1 mmu of the calculated exact mass of **16** at 289.0521, giving an elemental composition of $C_{13}H_{11}N_3O_3S$. The field desorption spectrum showed a peak at m/e 288 which corresponded to M-1 with no other peaks having an intensity greater than 1% observed, with the sole exception of the m/e 323 peak corresponding to **5** discussed above, which the sample also contained.

The formation of **16** may be envisioned to proceed as illustrated in Scheme II, although other mechanisms may also be possible. The activation of halogen substituents toward SNAr displacement reactions, such as that involved in the formation of **2** and **3** are

SCHEME II



tions, such as that involved in the formation of **2** and **3** are well known (9-12). Further, the nucleophilicity of *N*,*N*-dimethylformamide toward various reactive centers has also been reported (13-15). Thus, the proposed nucleophilic displacement of a highly activated chloro-substituent contained in **2** in this reaction to yield the immonium chloride intermediate **13** is not wholly inexplicable. Subsequent chloride ion attack on various immonium species has also been reported (14,15), although not specifically at the amide derived carbon. The proposed mechanism requires the attack of the chloride ion on the immonium amide carbon, leading to the formation of **14**, containing what should be a highly labile four-member ring moiety which would be expected to undergo a nearly spontaneous collapse, leading to the formation of the *N*,*N*-dimethylamino containing specie **15**. Finally, **15** on cyclization by displacement of the nitro group would give **16**. Similar fragmentation of *N*,*N*-dimethylformamide derived immonium species by nucleophilic attack on the amide carbon, although not specifically by chloride ions, has been previously observed (16).

Due to the highly unusual nature of the byproduct, **16**, observed in this study, further studies will be conducted to investigate the mechanism of its origin as well as the role of the solvent in reactions of this type.

EXPERIMENTAL

Melting points were obtained in open capillary tubes on a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were recorded using a Perkin-Elmer Model 700 spectrophotometer as potassium bromide pellets. Ultraviolet spectra were recorded in absolute ethanol on a Beckmann Model DB-GT spectrophotometer. ^1H nmr spectra were obtained in hexadeuterioacetone on a Varian Model XL-100 spectrometer equipped with a Nicolet TT-100 data system and a Nicolet Model 440 Frequency Synthesizer operating at 100 MHz in the Fourier Transform mode. Low resolution mass spectra were recorded on either a Hewlett-Packard Model 5930 GC/MS system equipped with a Model 5933A data system at an ionizing energy of 70eV and an ion source temperature of 250° or a Varian-Mat Model 112S mass spectrometer with an ionizing energy of 70eV and an ion source temperature of 250°. High resolution mass spectra were recorded on a Varian-Mat Model 731 mass spectrometer using the peak matching method with perfluorokerosene as the reference compound. Resolution was set at 10,000. Field desorption spectra were recorded with a Varian-Mat Model 731 mass spectrometer with the sample being depositied on the emitter using a microsyringe (17). The emitter current was slowly increased until a good signal was obtained and the spectra were then recorded. Microanalyses were performed by Atlantic Microlabs, Atlanta, Georgia.

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

To a solution of 0.9 g. (0.0038 mole) of 1,3-dichloro-4,6-dinitrobenzene in 30 ml. of dry distilled *N*,*N*-dimethylformamide (DMF) at 0° under dry argon purge was added 1.4 g. (0.0076 mole) of the disodium salt of 2-mercapto-3-pyridinol (**1**) (6). The resultant dark colored solution was maintained at 0° with stirring

for 8 hours and was then brought to reflux for 72 hours. Following the completion of the reflux period, the reaction mixture was chromatographed directly on a 1 kg. silica gel column eluted with cyclohexane:ethyl acetate (4:1) to yield 0.114 g. (9% yield) of **5** m.p. 268-269° dec.; ir ν max: 3380, 2900, 2830, 1610, 1550, 1500, 1480, 1440, 1410, 1280, 1260, 1200, 1080, 790 and 710 cm^{-1}; uv ν max (ethanol) (nm) log ϵ: 424, 3.042; 304, 3.692; 243, 4.071; 215, 4.016; FT-^{1}H nmr (hexadeuterioacetone): δ = 10.33, dd $J_{H_2H_3}$ = 4.3 Hz $J_{H_2H_4}$ = 1.4 Hz, 2H; 9.64, s, 1H; 9.47, m, 4H; 9.21, s, 1H; ms: M^+ (% relative intensity) 327 (4.2); 326 (11.9); 325 (22.5); 324 (100); 295 (13); 272 (16); 244 (19); 228 (23);200 (21); high resolution ms: exact mass calculated for $C_{16}H_8N_2O_2S_2$: 324.0027. Found: 324.0009.

Anal. Calcd. for $C_{16}H_8N_2O_2S_2$: C, 59.26; H, 2.46; N, 8.64. Found: C, 59.20; H, 2.62; N, 8.55.

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(1) To whom inquiries should be addressed.

(2) Present address: Dresser Industries, Houston, Texas.

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