Chemistry of the Phenoxathiins and Isosterically Related Heterocycles. XXIV (1). Synthesis of Characterization by ^{13}C-NMR Spectroscopy of Isomeric Benzoxathiinopyridazinones: 1-Oxo-1,2-dihydro-2,3-diazaphenoxathiin and 4-Oxo-3,4-dihydro-diazaphenoxathiin. The First Observation of a Smiles Rearrangement Involving Divalent Sulfur During the Synthesis of an Azaphenoxathiin

Charles H. Womack, Linda M. Martin and Gary E. Martin* (2)

Department of Medicinal Chemistry, College of Pharmacy, University of Houston, Houston, Texas 77004, USA

Keith Smith

Department of Chemistry, University College of Swansea, Singleton Park, Swansea SA2 8PP, UK

Received June 28, 1982

Condensation of the disodium salt of *o*-mercaptophenol with 4,5-dichloro-6(1*H*)-pyridazinone in *N,N*-dimethylformamide has been observed to lead to the formation of both possible isomeric benzoxathiinopyridazinones. The separation of these isomers, 1-oxo-1,2-dihydro-2,3-diazaphenoxathiin and 4-oxo-3,4-dihydro-2,3-diazaphenoxathiin and their characterization by ^{13}C-nmr spectroscopy is described. Mechanisms to account for the formation of both isomers are discussed, the most probable mechanism involving a Smiles rearrangement of the phenolate sulfide intermediate formed by the initial displacement of the 4-chloro substituent, providing a specie analogous to a β-halovinylogous ketone.

J. Heterocyclic Chem., **19**, 1447 (1982).

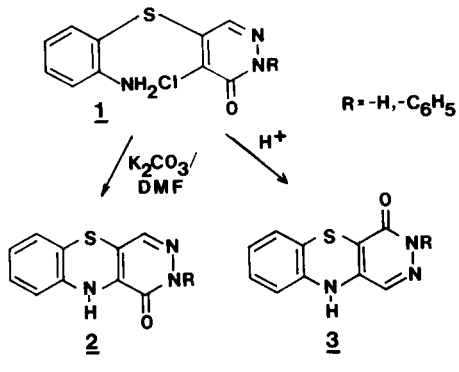
Introduction.

As part of our ongoing investigation into the effects of annular azasubstitution on the molecular geometry of sulfur containing tricyclic compounds (3-9), we were interested in synthesizing examples of the 2,3-diazaphenoxathiin ring system. A convenient access to this system could be provided by the reaction of the disodium salt of *o*-mercaptophenol (**4**) with the readily prepared 4,5-dichloro-6(1*H*)pyridazinone (**5**) (10), the oxo-moiety providing a convenient starting point for further chemical manipulations.

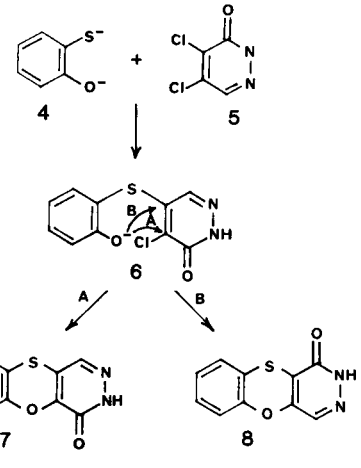
Various phenothiazine analogs have been prepared from 4,5-dihalogeno-6-(1*H*)-pyridazinones (11-16). A unifying feature of the synthesis of these compounds in the intermediacy of a diaryl sulfide, such as **1** (Scheme I), formed by the displacement of the 4-halo substituent, this being the more reactive of the two halgen substitutents, this accounted for by the behavior of β-halovinyl ketones (17). The intermediate, **1**, cyclizes under basic conditions (12-14) to give **2** *via* direct cyclization, or under acidic conditions (16) to give **3** *via* a Smiles rearrangement. Indeed, Smiles rearrangements are quite common during phenothiazine syntheses.

In contrast, in so far as we are aware, there have been no reported examples of the occurrence of a Smiles rearrangement during the synthesis of an azaphenoxathiin in which sulfur was present in its divalent form (4-9, 18-22). It was therefore of particular interest to discover whether the use of a β-chlorovinyl ketone analog, more specifically

SCHEME I



SCHEME II



4,5-dichloro-6(1*H*)-pyridazinone (**5**), in which the carbonyl group could act as an electron sink would facilitate such a rearrangement. We now report that two isomeric benzoxathiino pyridazinones, **7** and **8**, are formed from the reaction of **4** and **5**. Although we have not at this stage investigated the mechanism, the most plausible means of accounting for the formation of **8** would appear to be *via* a Smiles rearrangment (Scheme II).

Results and Discussion.

An equimolar mixture of **4** and **5** was stirred in *N,N*-dimethylformamide (DMF) for 18 hours at room temperature under an argon atmosphere and then heated for 1 hour at reflux. The crude product, after removal of the sodium chloride and DMF, consisted primarily of two isomeric materials which were separated by gradient elution on a silica gel column using a mixture of cyclohexane and ethyl acetate.

Each compound exhibited an intense ion (base peak) at m/z = 218, which corresponds to the relative molecular mass of the expected benzoxathiinopyridazinone system, and each analyzed for the formula $C_{10}H_6N_2O_2S$. The chromatographically more mobile compound melted at 295-296°, while its less mobile counterpart had a melting point of 264-265°.

Distinction between the two isomers was made on the basis of ^{13}C-nmr spectroscopy. Chemical shifts of the parent 2,3-diazaphenoxathiin system were calculated (7) by incrementation of the assigned chemical shifts of 2-azaphenoxathiin (5) for the insertion of a second nitrogen atom at the 3-position. The calculated shifts are shown in Figure 1.

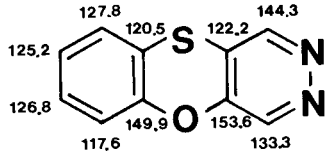


Figure 1. Calculated ^{13}C-nmr chemical shifts for the 2,3-diazaphenoxathiin ring system obtained by incrementing the observed chemical shifts of th 2-azaphenoxathiin ring system (5) for the insertion of a second annular nitrogen at the 3-position (7).

Calculated chemical shifts for **7** and **8** were obtained using chemical shift additivities of 2-hydroxyl subsitiuent on a pyridine ring (23), which gave chemical shifts shown in Figure 2.

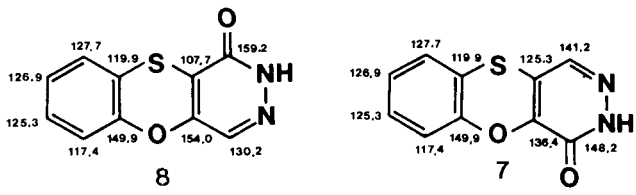
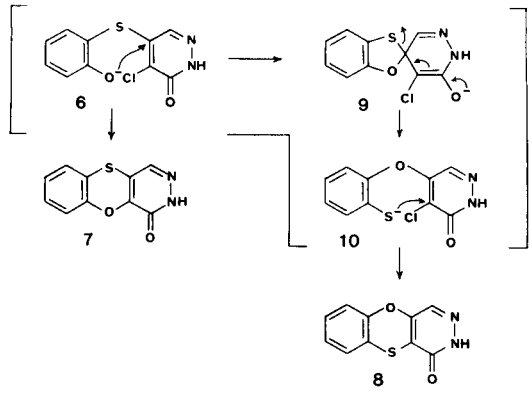


Figure 2. Calculated ^{13}C-nmr chemical shifts of 1-oxo-1,2-dihydro-2,3-diazaphenoxathiin (**8**) and 4-oxo-3,4-dihydro-2,3-diazaphenoxathiin (**7**) obtained by incrementation of the calculated 2,3-diazaphenoxathiin chemical shifts for the inclusion of a pyridine 2-hydroxyl substituent (23) at the 1- and 4-positions respectively.

Discrimination between **7** and **8** depends particularly on the assignment of the easily distinguished C1 and C4 resonances in the pyridazinone portion of the molecule (See Figure 3). The key features employed in the assignment of the structures from the ^{13}C-nmr spectral data are the calculated chemical shifts of the "carbonyl" carbon atoms, C4 and C1, for **7** and **8**, respectively.

SCHEME III



Thus, the chemical shift of the resonance observed at δ = 158.3 for the more mobile isomer agrees well with the calculated chemical shift of δ = 159.2, calculated for the C1 resonance of **8**, but is in very poor agreement with the value of δ = 148.2 calculated for the C4 resonance of **7**. In contrast, the observed chemical shift for C4 in the less mobile isomer is δ = 153.5, which is in better although not close agreement. Similarly, the observed resonance at δ = 130.5 in the spectrum of the more mobile isomer is in good agreement with the shift of δ = 130.2 calculated for the C4 resonance of **8**, but in very poor agreement with the value of δ = 141.2 which is calculated for the C1 resonance of **7**. In contrast, once again, the observed resonance at δ = 135.0 is a more reasonable fit for the chemical shift calculated for **7**. On this basis, we assign the structure **8**, 1-oxo-1,2-dihydro-2,3-diazaphenoxathiin, to the chromatographically more mobile isomer and the

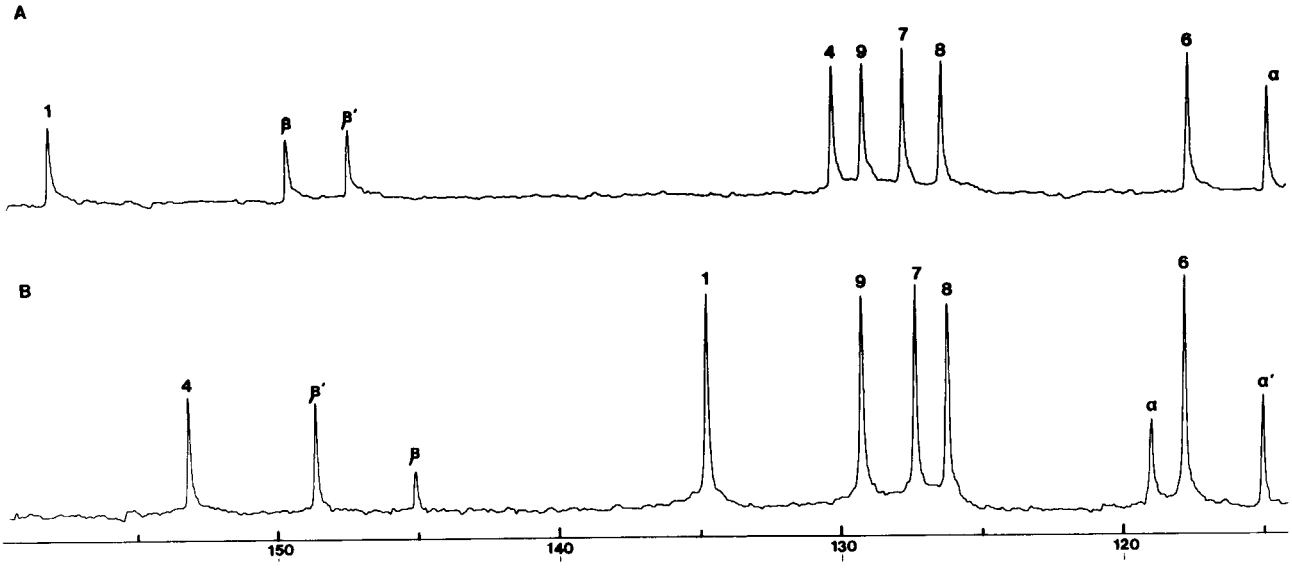
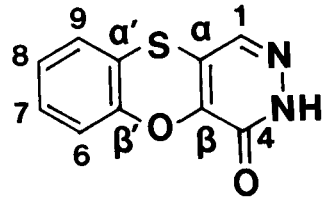


Figure 3. ^{1}H-Decoupled 25.158 MHz ^{13}C-nmr spectra of the aromatic region of : A) 1-oxo-1,2-dihydro-2,3-diazaphenoxathiin (**8**); B) 4-oxo-3,4-dihydro-2,3-diazaphenoxathiin (**7**). Both spectra were obtained in hexadeuteriodimethylsulfoxide.

Table I

Calculated *vs.* Observed ^{13}C-NMR Chemical Shifts and ^{1}H-^{13}C Spin Coupling Constants for 3,4-dihydro-4-oxo-2,3-diazaphenoxathiin (**7**) in Hexadeuteriodimethylsulfoxide at 33°



	$\delta^{13}C_{ca}$	$\delta^{13}C_{obs}$	$\Delta\delta$	$^1J_{CH}$	$^2J_{CH}$	$^3J_{CH}$
α	125.3	119.27	−6.0	—	$^2J_{C_\alpha H_1}$ = 7.3	—
α′	119.9	115.29	−4.6	—	—	$^3J_{C_{\alpha'}H_6}$ = $^3J_{C_{\alpha'}H_8}$ = 8.45
β	136.4	145.40	+9.0	—	—	$^3J_{C_\beta H_1}$ = 7.4
β′	149.9	148.96	−1.0	—	—	(a)
1	141.2	134.99	−6.2	$^1J_{C_1H_1}$ = 192.8 (b)	—	—
4	148.2	153.47	+5.3	—	—	—
6	117.6	118.10	+0.5	$^1J_{C_6H_6}$ = 164.3	—	$^3J_{C_6H_8}$ = 7.2
7	126.9	127.61	+0.7	$^1J_{C_7H_7}$ = 164.2	—	$^3J_{C_7H_9}$ = 6.0
8	125.3	126.48	+1.2	$^1J_{C_8H_8}$ = 164.9	—	$^3J_{C_8H_6}$ = 7.9
9	127.7	129.49	+1.8	$^1J_{C_9H_9}$ = 165.4	—	$^3J_{C_9H_7}$ = 6.8

(a) Was not clearly resolved. (b) Verified by selective excitation.

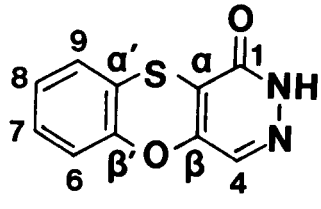
structure **7**, 4-oxo-3,4-dihydro-2,3-diazaphenoxathiin, to the less mobile isomer. As final confirmation of this structural assignment, and X-ray crystal structure determination has been carried out on the less mobile isomer (24) which has confirmed its structure as assigned on the basis of the ^{13}C-nmr spectral analysis presented above.

The agreement between observed and calculated ^{13}C-nmr chemical shifts for **8** is reasonable across the entire spectrum (maximum $\Delta\delta$ = 4.7 − See Table I), whereas the agreement for **7** is generally much poorer (See Table II). A possible explanation for this is that in solution **7** may exist in equilibrium with a significant proportion of its enol tautomer, which can be stabilized by hydrogen bonding to the ether bridge. In the crystalline state, however, **7** was found to exist exclusively in its "carbonyl" form (24) and further studies will be required to confirm this contention.

Although we have not, at this stage, attempted a rigorous mechanistic investigation of this reaction, the probable mechanism can be deduced from previous studies. Our previous phenoxathiin and thianthrene syntheses (3-9, 18-22, 25) have invariably occurred *via* direct cyclization uncomplicated by rearrangement processes. For direct cyclization, the formation of **8** would require the initial attack of the thiolate anion at the 5-position of the pyridazinone system, which is unlikely on the basis of previous work (11-17), or the initial attack by the phenolate anion at the 4-position of **5**. Significantly, it has shown that intial attack of mercaptonaniline invariably occurs at the 4-position of **5** (11-16), and it is furthermore well known that thiolate anions are much more powerfully nucleophilic than the phenolate anion (26). Thus, the formation of both **7** and **8** by direct cyclization pathways would seem to be unlikely. Rather, the anticipated primary intermediate would be **6** which would result in the formation of **7** by a direct cyclization pathway. In contrast, the initial formation of **6** would require that a Smiles rearrangement occur to account for the formation of **8** (Scheme III). Support for this contention is provided by the results obtained when 5-chloro-4-thiobenzyl-6(1*H*)-pyridazinone (**11**) is treated with hydroxide anion (See Equation 1) (27). One product of this reaction, 4-hydroxy-5-thiobenzyl-6(1*H*)-pyridazinone (**12**), is presumably formed by the initial attack of the hydroxide on the 4-position

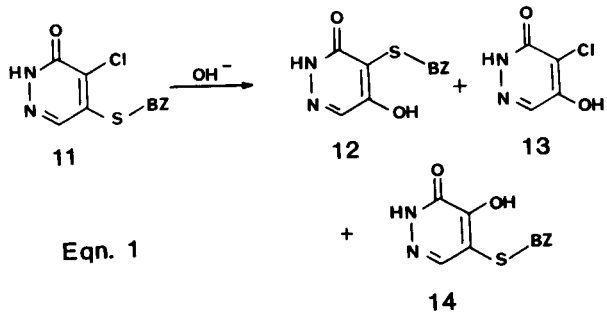
Table II

Calculated *vs.* Observed ^{13}C-NMR Chemical Shifts and ^{1}H-^{13}C Spin Coupling Constants for 1,2-dihydro-4-oxo-2,3-diazaphenoxathiin (**8**) in Hexadeuteriodimethylsulfoxide at 33°



	$\delta^{13}C_c$	$\delta^{13}C_o$	$\Delta\delta$	$^{1}J_{CH}$	$^{2}J_{CH}$	$^{3}J_{CH}$
α	107.7	—	—	—	—	—
α'	119.9	115.19	−4.7	—	—	—
β	154.0	149.83	+4.2	—	$^{2}J_{C_\beta H_4}$ = 3.8	—
β'	149.9	147.64	−2.3	—	—	—
1	159.2	158.32	−0.9	—	—	—
4	130.2	130.52	+0.3	$^{1}J_{C_4H_4}$ = 192.8 (a)	—	—
6	117.4	118.01	+0.6	$^{1}J_{C_6H_6}$ = 171.2	—	$^{3}J_{C_6H_8}$ = 5.2
7	126.9	128.05	+1.2	$^{1}J_{C_7H_7}$ = 161.6	—	$^{3}J_{C_7H_9}$ = 7.2
8	125.3	126.20	+0.9	$^{1}J_{C_8H_8}$ = 164.7	—	$^{3}J_{C_8H_6}$ = 8.2
9	127.7	129.45	+1.8	$^{1}J_{C_9H_9}$ = 164.3	—	$^{3}J_{C_9H_7}$ = 8.7

(a) Verified by selective excitation.

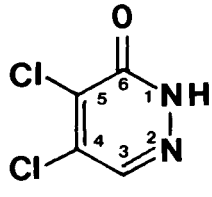


to displace the thiobenzyl anion, this pathway supported by the observed formation of 5-chloro-4-hydroxy-6(1*H*)-pyridazinone (**13**). Subsequent reaction of **13** with the liberated thiobenzyl anion would then result in the formation of **12**, an overall process which is analogous to the proposed Smiles rearrangement in the present report, and which further would account for the formation of **8**. The other product formed in Equation 1, 5-hydroxy-4-thiobenzyl-6(1*H*)-pyridazinone (**14**), is analogous to the formation of **7** *via* a direct cyclization route.

In summary, we are inclined to the belief that **8** is obtained by a Smiles rearrangement of **6**. If this contention is ultimately supported by a rigorous mechanistic study, the formation of **8** would represent the first example of a Smiles rearrangement during the synthesis of a phenoxathiin in which the sulfur is in its divalent state. It is presumed that this reaction is facilitated by the electron withdrawing properties of the carbonyl and its ability to serve as an electron sink which presumably stabilizes **9** (Scheme III) thus allowing the rearrangement to occur *via* the collapse of this intermediate to form **10**. Further studies in this area are at present underway an aim to use this observation to facilitate induced Smiles rearrangements to provide synthetic means of access to otherwise difficultly accessable ring systems.

Table III

Observed ^{13}C-NMR Chemical Shifts and ^{1}H-^{13}C Spin Coupling Constants for 4,5-dichloro-6(1*H*)-pyridazinone (**5**) in Hexadeuteriodimethylsulfoxide at 33°



Position	δ^{13}C	$^{1}J_{CH}$	$^{2}J_{CH}$	$^{3}J_{CH}$
		^{1}H-^{13}C Spin Coupling Constants (Hz)		
3	136.65	$^{1}J_{C_3H_3}$ =199.0	—	—
4	136.79	—	$^{2}J_{C_4H_3}$ = 5.0	—
5	133.42	—	—	$^{3}J_{C_5H_3}$ = 7.7
6	157.02	—	—	—

EXPERIMENTAL

All melting points were obtained in open capillaries using a Thomas-Hoover melting point apparatus and are reported uncorrected. All solvents were reagent grade or better and were freshly distilled prior to use. The *N,N*-dimethylformamide employed as the cyclization solvent was freshly distilled from calcium hydride and stored over 3Å Linde molecular sieves prior to use.

Infrared spectra were obtained as potassium bromide pellets on a Perkin-Elmer Model 283 spectrophotometer. Mass spectra were obtained on a Hewlett-Packard Model 5930 GC/MC system equipped with a Model 5933A data system. Spectra were obtained by direct probe insertion at a source temperature of 250° and an ionizing energy of 70eV. The ^{13}C-nmr spectra were obtained on a Varian XL-100-15 spectrometer operating at 25.158 MHz in the Fourier transform mode. The spectrometer was equipped with a Nicolet TT-100 data system, an NT-440 frequency synthesizer and a TT-760 decoupler operating at a power of 20 watts, with irradiation centered at δ = 7.0 in the ^{1}H-spectral window and $\gamma H_2/2\pi$ = 2.9 KHz. The ^{1}H-decoupled spectra were obtained using the following instrument parameters: pulse width 6μs (30° tip angle); interpulse delay = 4s; spectral width 5KHz digitized with 8K data points at an acquisition time = 0.82s, providing 4K data points after Fourier transformation. The ^{1}H-^{13}C spin-coupled spectra were obtained using the gated decoupling technique, the parameters employed differing only in that 16K data points were employed for an acquisition time = 1.64s. Selective excitation experiments were employed using the modifications previously reported (28), with excitation generated by the application of a train of 50 × 4 μs pulses (attenuated 15dB using a Kay Variable Attenuator) applied to the sample at the precession time of the resonance to be excited. All spectra were obtained in hexadeuteriodimethylsulfoxide, the spectrometer internally locked to the deuterium resonance of the solvent. All chemical shifts are reported in ppm (δ) downfield of tetramethylsilane, which was taken as 36.9 ppm upfield of the residual center line of the solvent resonance.

Synthesis and separation of 4-oxo-3,4-dihydro-2,3-diazaphenoxathiin (**7**) and 1-Oxo-1,2-dihydro-2,3-diazaphenoxathiin (**8**).

To 20 ml of freshly distilled DMF in a 100 ml flame dried three neck flask was added 0.50 g (0.02 mole) of sodium hydride (99% dry powder). The resultant suspension was stirred under an argon atmosphere for one hour after which was added 1.26 g (0.01 mole) of *o*-mercaptophenol in an additional 25 ml of DMF, the addition conducted over a period of 25 minutes, to provide the dianion as in the previously reported procedure of Elliott and co-workers (29). After five hours stirring at room temperature, the solution was cooled to -15°, after which was added 1.65 g (0.01 mole) of 4,5-dichloro-6(1*H*)-pyridazinone which was prepared according to the procedure of Mowry (10) (^{13}C-nmr chemical shift assignments are shown in Table III), the material added in 10 ml of DMF over a period of 15 minutes. The stirred reaction mixture was then allowed to return to room temperature at which it was maintained for eighteen hours. The reaction mixture was then brought to reflux for one hour, during which it rapidly darkened to a reddish brown color. The reaction was then allowed to cool to room temperature and monitored by tlc (silica; developed by cyclohexane:ethyl acetate (2:1)) which separated two highly fluorescent spots (R_f 0.19 and 0.10) visible under long wave length uv light. The precipitated sodium chloride was removed by Buchner filtration after which the DMF was removed *in vacuo* to give the product mixture as a crude yellow solid.

After drying at 45° in a vacuum oven overnight, the isomers were separated by gradient elution on a silica gel column. The solvent was varied from pure cyclohexane to a final composition of 1:1 cyclohexane:ethyl

acetate, after which all remaining traces of the second isomer were collected with pure ethyl acetate.

The first isomer eluted from the column, 0.588 g (26% yield), mp 295-296°, gave a mass spectrum containing the following ions, m/z (% relative intensity): 220 (5), 219 (12), 218 (100), 189 (8), 176 (3), 162 (3), 161 (11). The infrared spectrum contained the following prominent absorbances, ν (cm^{-1}): 3450 (broad), 1645, 1600, 1550, 1465, 1245, 1195, 800, 750.

Anal Calcd. for $C_{10}H_6N_2O_2S$: C, 55.03; H, 2.77; N, 12.84. Found: C, 54.98; H, 2.82; N, 12.79.

The ^{13}C-nmr assignment showed the structure of this isomer to be 1-oxo-1,2-dihydro-2,3-diazaphenoxathiin (**8**). (The ^1H-decoupled ^{13}C-nmr spectrum is shown in Figure 3A; calculated *vs.* observed ^{13}C-nmr chemical shifts and ^1H-^{13}C spin-coupling constants are shown in Table II.)

The second isomer eluted from the column, 0.472 g (21.6% yield), mp 264.5-266°, gave a mass spectrum containing the following ions, m/z (% relative intensity): 220 (5), 219 (12), 218 (100), 176 (1), 162 (5), 161 (14). The infrared spectrum contained the following prominent absorbances, ν (cm^{-1}): 3450 (broad), 1655, 1615, 1585, 1550, 1475, 1470, 1440, 1295, 1275, 1250, 1200, 975, 875, 755.

Anal. Calcd. for $C_{10}H_6N_2O_2S$: C, 55.03; H, 2.77; N, 12.84. Found: C, 54.95; H, 2.82; N, 12.82.

The ^{13}C-nmr assignment showed the structure of this isomer to be 4-oxo-3,4-dihydro-2,3-diazaphenoxathiin (**7**). (^1H-decoupled ^{13}C-nmr spectrum is shown in Figure 3B; calculated *vs.* observed ^{13}C-nmr chemical shifts and ^1H-^{13}C spin-coupling constants are shown in Table I.) Confirmation of the assignment of the structure of **7** was independently provided by a single crystal X-ray diffraction study which was in agreement with the spectroscopically determined structure (24).

Acknowledgements.

One of the authors, G. E. M., would like to express his appreciation to the Merck, Sharp and Dohme University Grants Program for the partial support of the synthetic phase of this work and also to the Robert A. Welch Foundation which supported the spectroscopic portion of this work and which also provided a pre-doctoral fellowship for C. H. W. through Grant No. E-792. We would also like to acknowledge the support of the National Science Foundation, which provided funds for the acquisition of the XL-100 spectrometer system utilized in this work through Grant No. CHE-7506162. Finally, the support of the North Atlantic Treaty Organization in the form of Grant No. 019.81 which facilitated a visit to Swansea in the summer of 1981 by G. E. M. is also gratefully acknowledged.

REFERENCES AND NOTES

(1) This paper represents Part 12 in the series "Novel Heterocyclic Systems." For the previous paper in this series, see: "Chemistry of the Phenoxathiins and Isosterically Related Heterocycles. XXIII. 1-Azathianthrene: First Reported Synthesis of a Monoazathianthrene and the Investigation of the ^{13}C-NMR Spectrum Using Two-Dimensional NMR Techniques." S. Puig-Torres, G. E. Martin, J. J. Ford, M. R. Willcott, III, and K. Smith, *J. Heterocyclic Chem.*, **19**, **1441 (1982).**

(2) To whom inquiries should be addressed.

(3) S. R. Caldwell and J. C. Turley and G. E. Martin, *J. Heterocyclic Chem.*, **17**, 1145, (1980).

(4) G. E. Martin, J. C. Turley and L. Williams, *ibid.*, **14**, 1249 (1977).

(5) S. R. Caldwell and G. E. Martin, *ibid.*, **17**, 989 (1980).

(6) S. R. Caldwell, G. E. Martin, S. H. Simonsen, R. R. Inners and M. R. Willcott, III, *ibid.*, **18**, 469 (1981).

(7) C. H. Womack and G. E. Martin, *ibid.*, **18**, 1165 (1981).

(8) C. H. Womack, J. C. Turley, G. E. Martin, M. Kmura and S. H. Simonsen, *ibid.*, **18**, 1173 (1981).

(9) S. Puig-Torres, G. E. Martin, K. Smith, P. Cacioli and J. A. Reiss, *ibid.*, **19**, 688 (1982).

(10) D. T. Mowry, *J. Am. Chem. Soc.*, **75**, 1909 (1953).

(11) J. Druey, K. Meier and A. Staehelin, Swiss Patent, 382,749 (1964); *Chem. Abstr.*, **62**, 16264a (1965).

(12) F. Yoneda, T. Ohtaka and Y. Nitta, *Chem. Pharm. Bull.*, **13**, 580 (1965).

(13) F. Yoneda, T. Ohtaka and Y. Nitta, *Yakugaku Zasshi*, **86**, 887 (1966).

(14) G. Scapini, F. Duro and G. Pappalardo, *Ann. Chim. (Rome)*, **58**, 718 (1968).

(15) P. Condorelli, G. Pappalardo and M. Raspagliesi, *Boll. Sedute Accad. Gioenia Sci. Nat. (Catania)*, **9**, 242 (1967); *Chem. Abstr.*, **71**, 70556a (1969).

(16) Y. Maki, M. Suzuki, O. Toyota and M. Takaya, *Chem. Pharm. Bull.*, **21**, 241 (1973).

(17) W. R. Benson and A. E. Pohland, *J. Org. Chem.*, **29**, 385 (1964).

(18) G. E. Martin, J. C. Turley, L. Williams, M. L. Steenberg and J. P. Buckley, *J. Heterocyclic Chem.*, **14**, 1067 (1977).

(19) G. E. Martin and J. C. Turley, *ibid.*, **15**, 209 (1978).

(20) G. E. Martin, J. D. Korp, J. C. Turley and I. Bernal, *ibid.*, **15** 721 (1978).

(21) J. C. Turley and G. E. Martin, *Spec. Letters*, **1**, 681 (1978).

(22) G. E. Martin, *J. Heterocyclic Chem.*, **17**, 429 (1979).

(23) F. W. Wehrli and T. Wirthlin, "Interpretation of Carbon-13 NMR Spectra," Heyden and Sons, Inc., NY, 1976, p 49.

(24) C. H. Womack, G. E. Martin, A. F. Hoffschwele, S. H. Simonsen and K. Smith, manuscript in preparation.

(25) J. S. Davies, K. Smith, J. R. Turner and G. Gymer, *Tetrahedron Letters*, 5035 (1979).

(26) A. J. Parker, "Organic Sulfur Compounds", Vol. 1, N. Kharsch, ed, Pergamon Press, NY, 1966, p 103.

(27) K. Kaji, Japanese Patent 69 12,421 (1966); *Chem. Abstr.*, **71**, 101875k (1969).

(28) G. E. Martin, *J. Heterocyclic Chem.*, **15**, 1539 (1978).

(29) A. J. Elliott, N. Eisenstein and L. C. Iorio, *J. Med. Chem.*, **23**, 333 (1980).