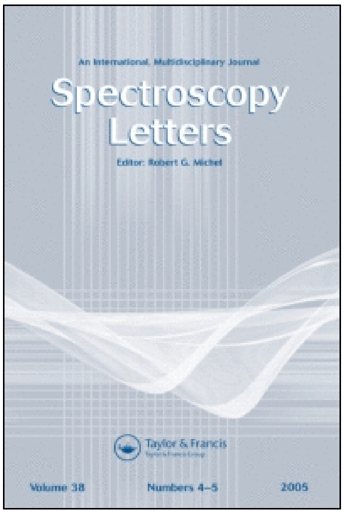


Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Chemistry of the Phenoxathiins VII. A Re-Examination of the Mauthner Systhesis of 1,3-Dinitrophenoxathiin for the Possible Occurrence of a Smiles Rearrangement

J. C. Turley[a]; G. E. Martin[a]
[a] Department of Medicinal Chemistry and Pharmacognosy College of Pharmacy, University of Houston, Houston, Texas

To cite this Article Turley, J. C. and Martin, G. E.(1978) 'Chemistry of the Phenoxathiins VII. A Re-Examination of the Mauthner Systhesis of 1,3-Dinitrophenoxathiin for the Possible Occurrence of a Smiles Rearrangement', Spectroscopy Letters, 11: 9, 681 — 692

To link to this Article: DOI: 10.1080/00387017808063440
URL: http://dx.doi.org/10.1080/00387017808063440

SPECTROSCOPY LETTERS, 11(9), 681-692 (1978)

CHEMISTRY OF THE PHENOXATHIINS VII.
A RE-EXAMINATION OF THE MAUTHNER SYSTHESIS OF 1,3-DINITROPHENOXATHIIN FOR THE POSSIBLE OCCURRENCE OF A SMILES REARRANGEMENT.

Key words: phenoxathiin, Smiles Rearrangement, carbon-13 nmr, selective excitation

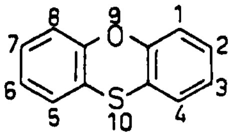
J. C. Turley and G. E. Martin*

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

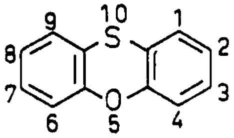
ABSTRACT

The preparation of 1,3-dinitrophenoxathiin represents the first reported synthesis of the phenoxathiin ring system. Based on known relative nucleophilicities either an unprecedented reversal of nucleophilicities or the occurrence of a Smiles Rearrangement would be required to account for the reported substituent locations. The re-examination of this synthesis with confirmation of actual substituent locations by ^{13}C-nmr and the correction of the original literature is described.

The first synthesis of an analog of the phenoxathiin ring system was reported by Mauthner[1]. His procedure utilized the condensation of picryl chloride with the disodium salt of *o*-mercaptophenol to yield the corresponding dinitrophenoxathiin product. The compound he reported was the 1,3-dinitrophenoxathiin, using the numbering scheme shown by 1. This numbering system was also employed by Beilstein but was later changed with the fourth decennial index of Chemical Abstracts to conform to the numbering of Patterson[2,3] shown by 2. Thus, by modern nomenclature, the compound reported by Mauthner should be named the 2,4-dinitrophenoxathiin.



1



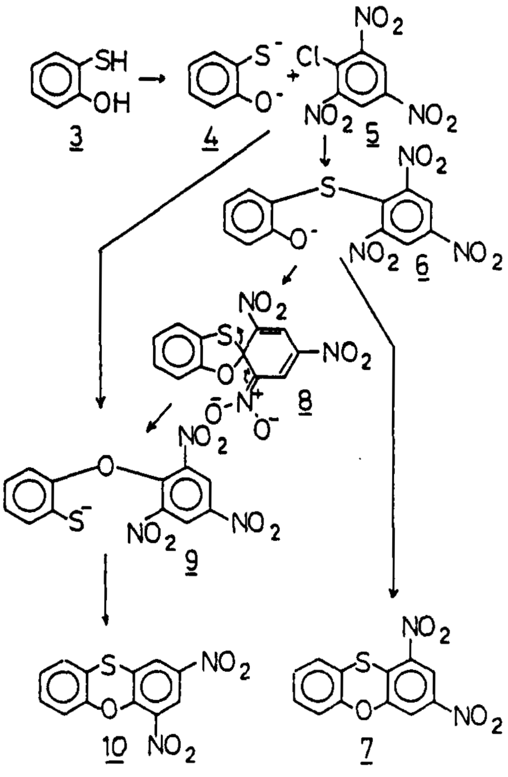
2

Based on the known relative nucleophilicities of the phenolate and thiophenolate anions[4], to obtain the substitution reported by Mauthner[1] in a direct cyclization, an unprecedented reversal of relative nucleophilicities would be required. Another alternative, however, which would lead to the reported substitution requires the occurrence of a Smiles Rearrangement[5] which is shown in Scheme I.

Recent work on the synthesis of [1,4]benzoxathiino[3,2-*b*] pyridine[6] and a variety of analogs[7-9] has shown that Smiles Rearrangements have not occured in this closely related synthesis. In addition, the synthesis of the [1,4]benzoxathiino[2,3-*c*] pyridine ring system[10], which employed a pathway virtually idential to that used by Mauthner[1], also did not exhibit any sign of a Smiles Rearranged product. These results have thus prompted the re-examination of the Mauthner synthesis.

As shown in Scheme I, the disodium salt of *o*-mercaptophenol was prepared by the general procedure of Martin[7]. Isolation of this salt followed by reaction with a molar equivalent of picryl chloride in ethanol was observed to yield a reddish-orange crystalline material, exactly as was reported by Mauthner. Preliminary examination of the isolated product by 100 MHz FT-^{1}H-nmr in hexadeuteriodimethylsulfoxide gave results which were consistent with either isomeric product, but which could not unequivocally be assigned to either isomer.

The unequivocal establishment of the nitro-substitution positions was however achieved by ^{13}C-nmr. The assignment of the resonances shown in Figure 1 to the 1,3-dinitrophenoxathiin (7) isomer was based on the correlation of the calculated chemical shifts of both possible isomers with the observed spectral data, as shown in Table 1.



Scheme I

Calculation of the ^{13}C-nmr chemical shifts was based the available shift data for phenoxathiin[11] to which were then added the appropriate additivity parameters for both nitro-substitution patterns[12]. Preliminary assignment of the carbon resonances shown in Figure 1 and Table 1 were confirmed by gated decoupling techniques[13], the spectrum shown in Figure 2. With the distinct

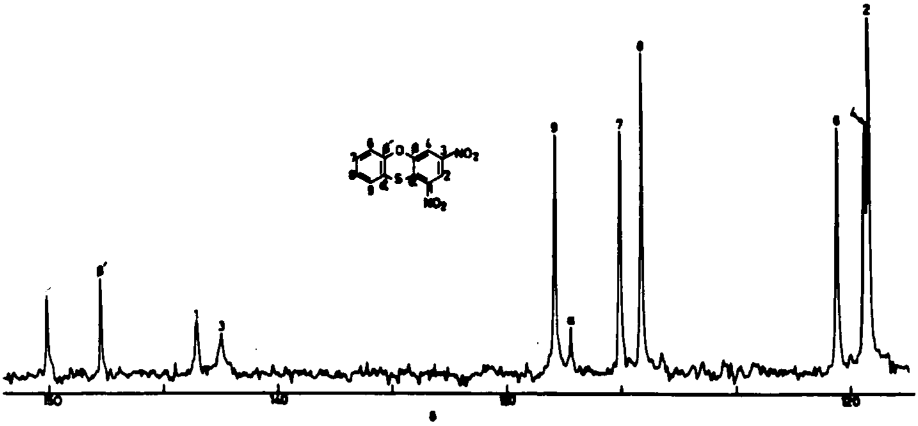


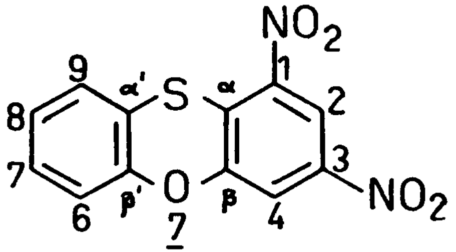
Fig. 1. 25.158 MHz decoupled ^{13}C-nmr spectrum of the aromatic region of 1,3-dinitrophenoxathiin (7).

exception of the α-carbon resonance, relatively good agreement was obtained between calculated and observed chemical shifts associated with 7[14].

The sizeable deviation between the calculated and observed chemical shifts for the α-carbon merits further explanation. The location of the sulfur atom *ortho* to the nitro-group at the 1-position facilitates the occurrence of an interaction between these structural components which was first observed in X-ray crystallographic studies[15-17]. When the 9-nitro[1,4]benzoxathiino[3,2-*b*]pyridine system, which contains an analogous placement of the sulfur and nitro components, was examined by ^{13}C-nmr, a pronounced downfield shift of 7.0 ppm was observed

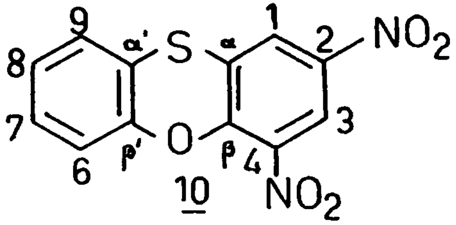
TABLE 1.

Calculated vs. Observed 25.158 MHz ^{13}C-Chemical Shift Data for 1,3-Dinitrophenoxathiin (7) and 2,4-Dinitrophenoxathiin (10).



7

	α	β	α'	β'	1	2	3	4	6	7	8	9
CALC.	120.9	153.7	119.9	151.9	148.3	114.6	147.4	118.5	117.5	126.5	124.2	129.4
OBS.	129.4	152.1	116.4	149.8	145.4	116.1	144.5	116.5	117.6	127.2	126.2	130.0
$\Delta\delta^{13}C$	+8.5	-1.6	-3.5	-1.9	-2.9	+1.5	-2.9	-2.0	+0.1	+0.7	+2.0	+0.6



10

	α	β	α'	β'	1	2	3	4	6	7	8	9
CALC.	121.7	152.9	119.9	151.9	128.4	145.1	116.9	138.4	117.5	126.5	124.2	129.4

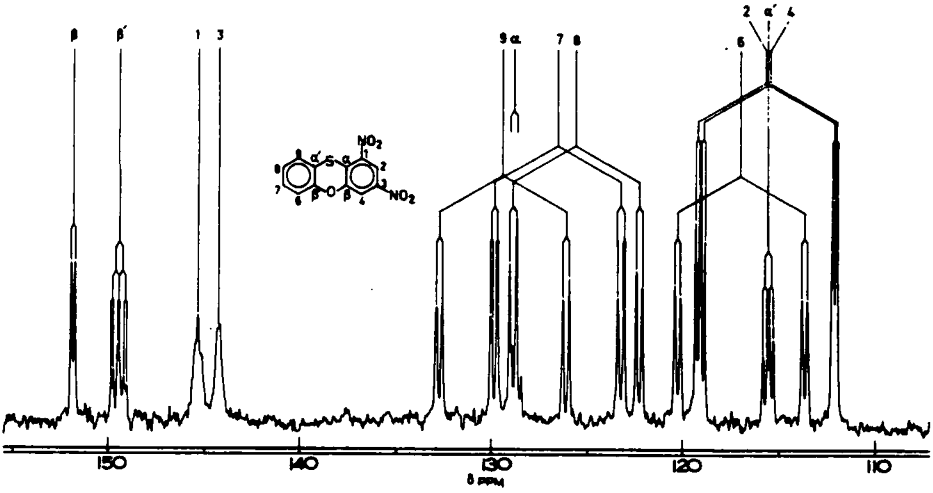


Fig. 2. Gated decoupled ^{13}C-nmr spectrum of the aromatic region of 1,3-dinitrophenoxathiin (7).

for the α-carbon resonance[8]. This behavior, which is consistant with that observed for the substitution of 7, thus provides a valuable means of discriminating between the two isomers.

The gated decoupled spectrum shown in Figure 2 was essentially first order and nearly all coupling constants could be directly obtained from this spectrum. The overlap of the spin multiplets associated with resonances for carbons 2 and 4 did however preclude direct measurement of the coupling constants for these two carbons. This problem was however conveniently solved by the utilization of the selective excitation procedure of Bodenhausen, Freeman and Morris[18]. In this fashion, the set of spectra for the individual resonances involved, shown in Figure 3 was obtained, allowing the coupling constants for both of these resonances to also be accurately measured. (See Table 2).

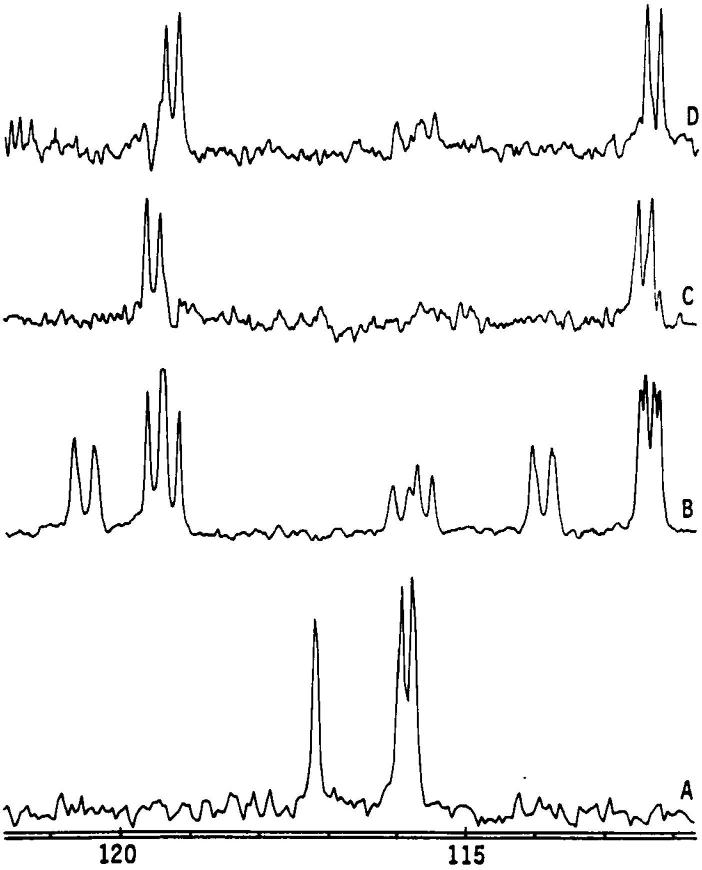


Fig. 3. Selectively excited resonances of 1,3-dinitrophenoxathiin (7): A. normal decoupled spectral segment; B. gated decoupled spectral segment; C. selectively excited spectrum of the resonance assigned to C-4; D. selectively excited spectrum of the resonance assigned to C-2 - note also the simultaneous excitation of the α-carbon resonance.

TABLE 2.

Observed $^{13}C-^{1}H$ Coupling Constants for 1,3-Dinitrophenoxathiin (7).

Carbon	$^{1}J_{CH}$	$^{2}J_{CH}$	$^{3}J_{CH}$
α	—	—	$J_{C_{\alpha}H_4} = 11.74$
β	—	$J_{C_{\beta}H_4} = 4.79$	—
α'	—	—	$J_{C_{\alpha}'H_6} = 8.66^{a}$ $J_{C_{\alpha}'H_8} = 5.66^{a}$
β'	—	$J_{C_{\beta}'H_6} = 2.39$	$J_{C_{\beta}'H_7} = 6.08^{a}$ $J_{C_{\beta}'H_9} = 8.02^{a}$
1	—	—	—
2	$J_{C_2H_2} = 177.75$	—	$J_{C_2H_4} = 4.85$
3	—	—	—
4	$J_{C_4H_4} = 173.30$	—	$J_{C_4H_2} = 4.89$
6	$J_{C_6H_6} = 165.01$	—	$J_{C_6H_8} = 6.91$
7	$J_{C_7H_7} = 165.84$	$J_{C_7H_6} = 2.39$	$J_{C_7H_9} = 8.32$
8	$J_{C_8H_8} = 165.40$	—	$J_{C_8H_6} = 8.36$
9	$J_{C_9H_9} = 163.80$	—	$J_{C_9H_7} = 7.39$

a. may be permuted.

By the application of ^{13}C-nmr spectroscopy, it has thus been shown that the initial reported synthesis of the phenoxathiins was in error, so far as nitro-substituent location is concerned. Further, the generality of the interaction between the sulfur and an ortho-nitro group and its utility for purposes of isomer discrimination in selected cases has also been demonstrated. Finally, the need to closely examine the nature of the product(s) reported in the early literature, where various isomers are possible, is clearly demonstrated.

All ^{13}C-nmr spectra were obtained on a Varian XL-100 specttometer operating at 25.158 MHz in the fourier transform mode. The spectrometer was equipped with a Nicolet TT-100 data system and a Nicolet NT-440 Multi-nuclei frequency synthesizer. Typically, a 8K spectrum covering 200 ppm was acquired with a pulse width of 4 microseconds (20° flip), 10 second delay and an acquisition time of 1.6384 seconds. All samples were prepared as saturated solutions in d_6-DMSO at 90°, with adequate signal to noise generally obtained in 1000 acquisitions for decoupled spectra and 10,000 acquisitions for gated decoupled spectra.

ACKNOWLEDGEMENTS

We would like to express our appreciation to the University of Houston Student Research Program for the partial support of this project through Grant K-94 to JCT. We would also like to express our sincere thanks to Mrs. Deborah Jones for the preparation of this manuscript.

REFERENCES

1. F. Mauthner, Ber., 38, 1411 (1905)

2. A.M. Patterson, L.T. Capell and D.F. Walker, "The Ring Index," 2nd. ed., American Chemical Society, Washington, 1960, p. 441.

3. D.S. Breslow and H. Skolnik, "Multi-Sulfur and Sulfur and and Oxygen Five- and Six-Membered Heterocycles," Part II, Interscience, New York, 1966, p. 864.

4. A.J. Parker, "Organic Sulfur Compounds," Vol. 1, N. Kharsach, ed., Pergamon Press, New York, 1961, p. 107.

5. W.E. Truce, E.M. Kreider and W.W. Brand, Org. Reactions, 18, 99, (1970)

6. G.E. Martin, J.C. Turley and L. Williams, J. Heterocyclic Chem., 14, 1249 (1977)

7. G.E. Martin, J.C. Turley, L. Williams, M.L. Steenberg and J.P. Buckley, ibid., 14, 1067 (1977)

8. G.E. Martin and J.C. Turley, ibid., 15, in press (1978)

9. G.E. Martin, J.D. Korp, J.C. Turley and I. Bernal, ibid., 15, in press (1978)

10. S.R. Caldwell, G.E. Martin, R. Inners and M.R. Willcott, III, Org. Mag. Res., submitted

11. L.R. Isenbrandt, R.K. Jensen and L. Petrakis, J. Mag. Res., 12, 143 (1973)

12. F.W. Wehrli and T. Wirthlin, "Interpretation of Carbon-13 NMR Spectra," Heyden, London, 1976, p. 47.

13. R. Freeman and H.D.W. Hill, J. Mag. Res., 5, 278 (1971)

14. Calculated chemical shift data were based on available data from the literature which were obtained at ambient temperature, while all spectra obtained in this study were acquired at 90°.

15. J.S. Ricci and I. Bernal, J. Chem. Soc., 806 (1970)

16. R. Eriksen and S. Hauge, Acta Chem. Scand., 26, 3152 (1972)

17. R. Eriksen, ibid., A29, 517 (1975)

18. G. Bodenhausen, R. Freeman and G.A. Morris, J. Mag. Res., 23, 171 (1976)

Received 6-14-78
Accepted 7- 6-78