

XIII. ^{13}C -NMR Spectroscopy of 1-Azaphenoxathiin 10,10-Dioxide.An Unusual Perturbation of ^1H - ^{13}C Coupling Constants

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The total assignment of the ^{13}C -nmr spectrum of 1-azaphenoxathiin 10,10-dioxide is reported based on the utilization of additivity correlations for the conversion of sulfide to sulfone linkages. Although the benzenoid portion of the molecule obeyed standard additivity correlations, substantial deviation in additivity behavior was observed in the pyridyl portion of the molecule. Examination of the ^1H - ^{13}C spin-coupling constants showed a perturbation of the primary one bond ($^1J_{\text{CH}}$) couplings of the C-2 and C-4 carbons.

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Empirical additivity correlations provide what is perhaps one of the most useful aspects of ^{13}C -nmr spectroscopy which ultimately can be expected to make ^{13}C -nmr and exceedingly versatile structure elucidation technique. As an adjunct, it is also frequently convenient to have at hand simple procedures for derivatization which affect chemical shift additivities in a predictable manner thereby simplifying signal assignments. In this sense, several papers have appeared in the recent literature describing the affects of *N*-oxidation on the ^{13}C -nmr chemical shifts (3-5) and coupling constants (3-5) of a variety of heterocycles. Although several papers have also dealt with the effects of *S*-oxidation on ^{13}C -nmr chemical shifts in thiochromanone (6) and benzo[*b*]thiophene analogs (7), there have been no similar reports dealing with heterocyclic systems containing annular nitrogen substitutions. Following the recently reported synthesis of a variety of 1-azaphenoxathiin 10,10-dioxide analogs (8) (1) we now report the effects of conversion of the sulfur linkage of this system to the corresponding sulfone and the consequent effects displayed in the ^{13}C -nmr chemical shifts and coupling constants of this system.

Prior to beginning the assignment of the eleven well resolved resonances of 1, shown in Figure 1, chemical shift

additivities were calculated for the conversion of the sulfide linkage to its corresponding sulfone linkage. The additivities were calculated from the changes observed in the chemical shifts on conversion of diphenylsulfide to diphenylsulfone (6). Additivities with a positive value indicated a downfield shift on oxidation, while those with a negative value indicate an upfield shift relative to the sulfide. For comparison, additivities are included for oxidation of the sulfide linkage to the corresponding sulfoxide. (Table I).

Table I
Calculated Additivities for the Conversion of Diphenylsulfide to the Corresponding Sulfoxide and Sulfone

	C-1	additivities (ppm)		
		<i>ortho</i>	<i>meta</i>	<i>para</i>
diphenylsulfide	+ 7.2	+2.4	+0.5	-1.6
diphenylsulfoxide	+17.1	-3.9	+0.6	+2.4
diphenylsulfone	+13.0	-1.0	+0.7	+4.6
S → SO	+ 9.9	-6.3	+0.1	+4.0
S → SO ₂	+ 5.8	-3.4	+0.2	+6.2

Anticipated chemical shifts for the eleven resonances of 1 were calculated from the reported ^{13}C -nmr chemical shifts of 1-azaphenoxathiin (9) utilizing the calculated

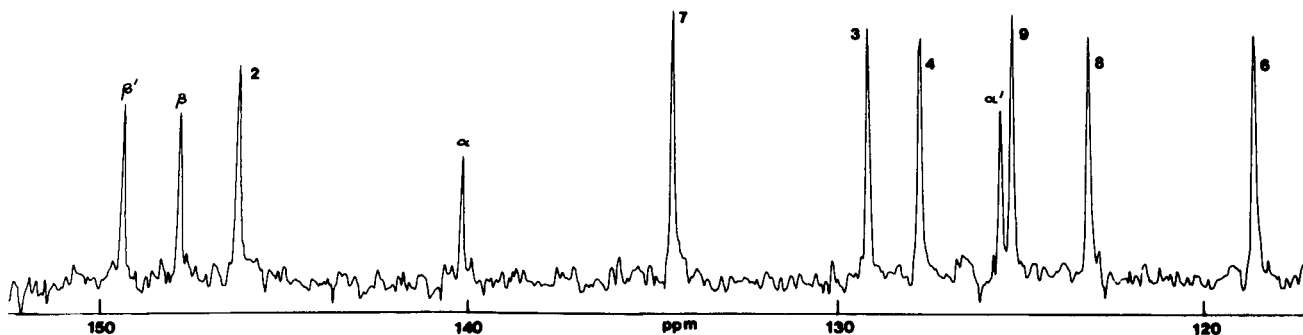
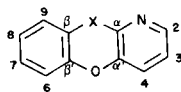


Figure 1. Decoupled 25.2 MHz ^{13}C -nmr spectrum of 1-azaphenoxathiin 10,10-dioxide in hexadeuteriodimethylsulfoxide.

Table II

Calculated *vs.* Observed ^{13}C -NMR Chemical Shifts and Additivity Constants of 1-Azaphenoxathiin 10,10-Dioxide (I) in Hexadeuteriodimethylsulfoxide

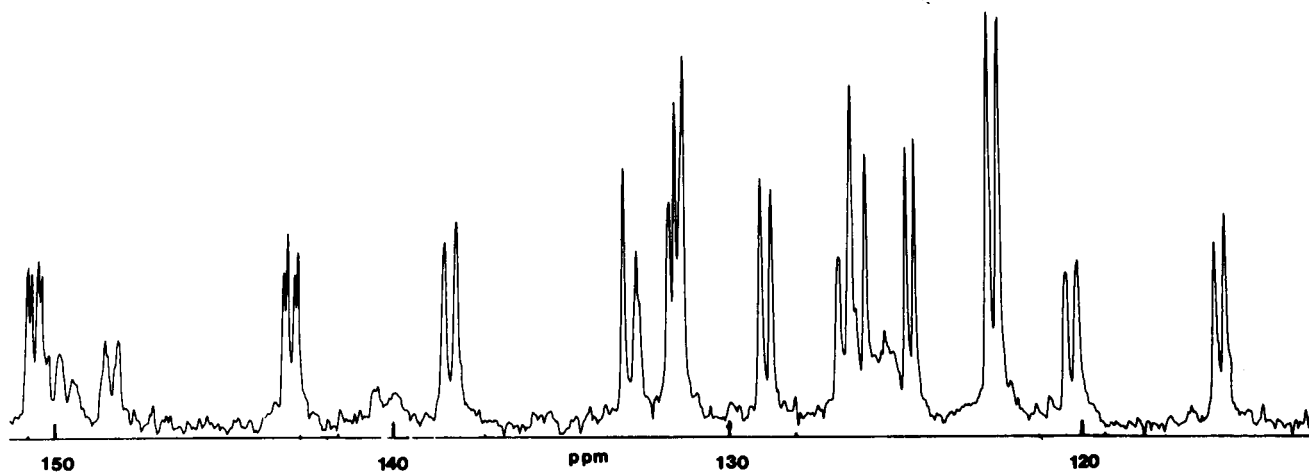
$$\text{X} = \text{SO}_2$$

	X = S	Calcd. add. S-SO ₂ ^a	Calcd. $\delta^{13}\text{C}$	Obs. $\delta^{13}\text{C}$	$\Delta\delta^{13}\text{C}$	S - SO ₂ additivities
α	143.5	+5.8	149.3	140.25	-9.1	-3.2
β	147.9	-3.4	144.5	147.90	+3.4	0.0
α'	119.0	+5.8	124.8	125.58	+0.8	+6.6
β'	150.0	-3.4	146.6	149.42	+2.8	-0.6
2	144.7	+0.2	144.9	146.31	+1.4	+1.6
3	122.2	+6.2	128.4	129.22	+0.8	+7.0
4	124.7	+0.2	124.9	127.80	+2.9	+3.1
6	117.4	+0.2	117.6	118.64	+1.0	+1.2
7	126.9	+6.2	133.1	134.52	+1.4	+7.6
8	123.6	+0.2	123.8	123.20	-0.6	-0.4
9	127.7	-3.4	124.3	125.52	+1.0	-2.4

Table III

 ^1H - ^{13}C Spin Coupling Constants for the Protonated Resonances of 1-Azaphenoxathiin 10,10-Dioxide in Hexadeuteriodimethylsulfoxide

Resonance	$^1\text{J}_{\text{CH}}$	$^2\text{J}_{\text{CH}}$	$^3\text{J}_{\text{CH}}$
2	$^1\text{J}_{\text{C}_2\text{H}_2} = 187.40$	$^2\text{J}_{\text{C}_2\text{H}_3} = 3.03$	$^3\text{J}_{\text{C}_2\text{H}_4} = 7.40$
3	$^1\text{J}_{\text{C}_3\text{H}_3} = 168.48$	$^2\text{J}_{\text{C}_3\text{H}_2} = 10.93$	-----
4	$^1\text{J}_{\text{C}_4\text{H}_4} = 171.39$	-----	$^3\text{J}_{\text{C}_4\text{H}_2} = 6.50$
6	$^1\text{J}_{\text{C}_6\text{H}_6} = 167.86$	-----	$^3\text{J}_{\text{C}_6\text{H}_8} = 7.40$
7	$^1\text{J}_{\text{C}_7\text{H}_7} = 166.10$	-----	$^3\text{J}_{\text{C}_7\text{H}_9} = 8.58$
8	$^1\text{J}_{\text{C}_8\text{H}_8} = 167.84$	-----	$^3\text{J}_{\text{C}_8\text{H}_6} = 7.99$
9	$^1\text{J}_{\text{C}_9\text{H}_9} = 168.55$	-----	$^3\text{J}_{\text{C}_9\text{H}_7} = 7.48$

Figure 2. ^1H - ^{13}C spin coupled spectrum of 1-azaphenoxathiin 10,10-dioxide in hexadeuteriodimethylsulfoxide.

additivities contained in Table I. On this basis, the predicted chemical shifts for **1** were obtained, as shown in Table II. Assignment of the observed ^{13}C -nmr chemical shifts was then begun using the predicted chemical shift data as a starting point for the assignment.

Relaxation considerations (10) initially allowed the discrimination of the non-protonated quaternary carbon resonances from their counterpart protonated resonances. Thus, the resonances attributable to C- β and C- β' were observed at $\delta = 149.42$ and 147.90 , although no specific assignments were unequivocally possible because of the observed discrepancies between the calculated chemical shifts which were $\delta = 144.5$ and 146.6 . The resonances for C- α and C- α' were, in contrast, unequivocally assignable solely on the basis of the chemical shift data since these resonances exhibit markedly dissimilar chemical shifts. Therefore, C- α was assigned to the resonance observed at $\delta = 140.25$ while C- α' was assignable to the resonance observed at $\delta = 125.58$. Interestingly, the chemical shift of C- α' was accurately predicted by calculation to be $\delta = 124.8$, in direct contrast to the predicted shift of C- α which, $\delta = 149.3$ ($\Delta\delta^{13}\text{C} = -9.1$), sharply disagreed with the observed resonance.

Several of the protonated resonances in the spectrum of **1** were also assignable on the basis of chemical shift information. Thus, C-2, which is the only protonated resonance downfield as a result of the annular nitrogen, was clearly assignable to the resonance observed at $\delta = 146.31$. Similarly, the resonance for C-6 was assignable as the extreme upfield resonance of the spectrum, which was observed at $\delta = 118.64$. In both of these cases, the observed chemical shift was in reasonable accord with the chemical shift predicted on the basis of additivity. The resonance for C-7, which is subject to the largest additivity perturbation, was likewise assignable since it was predicted to be the furthest downfield of the remaining resonances. Based on this premise, C-7 was assigned to the resonance observed at $\delta = 134.52$, in good agreement with the predicted chemical shift of $\delta = 133.1$. The remaining protonated ^{13}C -resonances, although potentially assignable on the basis of chemical shift, were not assigned solely on this basis but rather were assigned in conjunction with ^1H - ^{13}C spin-coupling constant behavior.

The ^1H - ^{13}C spin-coupled spectrum of **1** is shown in Figure 2. Examination of the coupling behavior of the resonance corresponding to C-2, which is the most easily and unequivocally considered because of its chemical shift, showed a perturbation in the magnitude of the primary one bond ($^1J_{\text{CH}}$) coupling which was observed to be $^1J_{\text{CH}} = 187.40$ Hz. (See Table III.) Based on this observation, to avoid any potential ambiguities in the spin-coupling constant extraction from the coupled spectrum, the spin-coupling constants of all of the protonated

resonances of **1** were determined using selective excitation (11-13) with gated decoupling (14). The resultant selectively excited spin-coupled sub-spectra are shown in Figure 3 while all of the coupling constants are contained in Table III.

Based on the selectively excited spin-coupled sub-spectra, perturbations were observed in the one-bond coupling constants of the resonances which were assigned to C-2 and C-4 (15). Curiously, no perturbation of any of the coupling constants were observed for the resonances contained in the benzenoid portion of the molecule (16). In addition, the two bond coupling of C3, $^2J_{\text{CH}} = 10.93$ Hz, was also somewhat larger than the observed coupling of 8.6 Hz observed for 1-azaphenoxathiin (9) or the 7.89 Hz coupling observed in 1-azaphenoxathiin 1-oxide (5). From the observed changes, it is concluded that the conversion of the sulfide to the corresponding sulfone elicits changes in spin coupling constants which are a result of altered electronic properties of the annular nitrogen. These effects, both in magnitude of changes in the coupling constants and the positions at which they are observed, are analogous to those observed for 1-azaphenoxathiin 1-oxide (5). Indeed, it is also probable that the observed discrepancy of the C- α chemical shift can be attributed to enhanced electron density at this position from the annular azasubstitution. This would also account for the accurately predicted chemical shift of the C- α' resonance which, in contrast, cannot receive a similar increase in electron density. This same factor can also account for the relative accuracy of the remaining chemical shifts in the benzenoid portion of the molecule which were thus assigned based on chemical shift calculation as shown in Table II.

Further studies are at present underway in these laboratories to investigate the effects of sulfur oxidation in other azaphenoxathiin analogs on both the alteration of chemical shift additivities and spin-coupling constants. Results of these studies are expected to provide a more uniform concept of the interaction of annular nitrogen substituents with substituents external to the pyridyl derived ring and will be reported.

EXPERIMENTAL

Melting points were obtained in open capillary tubes using a Thomas-Hoover melting point apparatus and are uncorrected. Infra red spectra were obtained as potassium bromide pellets using a Perkin-Elmer Model 283 spectrophotometer. All nmr experiments were conducted on a Varian Associates Model XL-100-15 spectrometer system operating at 25.158 MHz in the Fourier transform mode for ^{13}C -nmr. The spectrometer was equipped with a Nicolet Model TT-100 data system, a Model NT-440 MONA and a Model TT-760 decoupler operating at 15 watts ($\gamma\text{H}_2/2\pi = 2.9$ KHz). Modifications previously described were utilized in the conduct of the selective excitation experiments (13). Typical instrument operating parameters were: pulse width = 10.0 μsec (45°); pulse delay = 0.500 sec; sweep width = 5 KHz; data size = 4K(decoupled)/8K(coupled); acquisition time = 0.8192 sec; apodization = 1.00 sec;

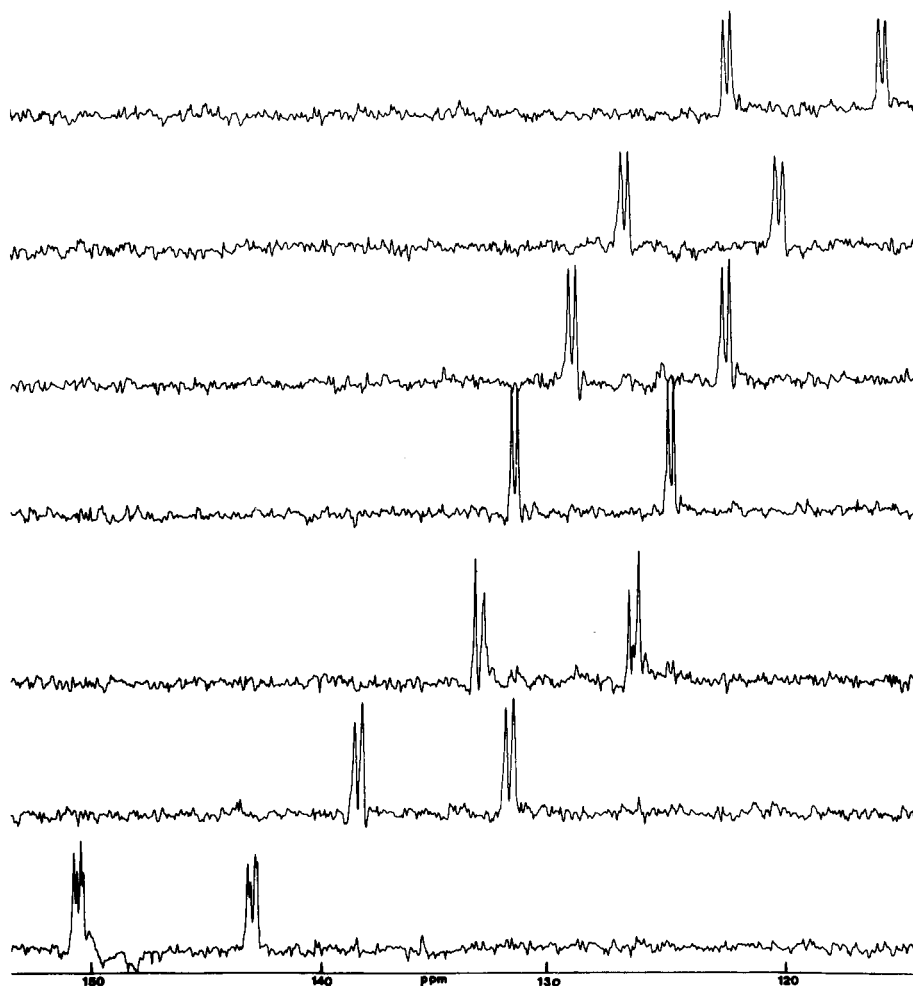


Figure 3. ^1H - ^{13}C Spin-coupled sub-spectra of 1-azaphenoxathiin 10,10-dioxide proton bearing resonances in hexa-deuteriodimethylsulfoxide obtained by selective excitation.

decoupler frequency = 100.061200 MHz. Selective excitation experiments were performed using 100 pulses in the excitation sequence with a pulse delay = 2.00 sec.

Synthesis of 1-Azaphenoxathiin 10,10-Dioxide.

The synthesis of 1-azaphenoxathiin 10,10-dioxide was conducted according to the procedure of Elliott (8). All proton and ir data were consistent with that previously reported.

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- (15) Signal assignments for the C-3 and C-4 resonances were confirmed by coherent single-frequency on resonance decoupling.
- (16) This observation is particularly interesting especially since a downfield shift of H-9 was noted on S-oxidation by Elliott and co-workers (*cf. ref. 6*).