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[Chem. Pharm. Bull. 14(4) 433~435 (1966)] UDC 547.864.4.03 : 543.422.25

Yutaka Morita : Studies on Phenazines. XXVIII.*1 Nuclear Magnetic Resonance Studies. II. Ring Protons of Halogenophenazines and Methyl, Methoxylprotons of Substituted Phenazines.

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In the preceding paper, the analyses of ring protons on simple and substituated phenazines especially on dimethoxyphenazine derivatives were reported.[1)]

In the present paper, at first, ring proton analyses of halogenophenazine will be demonstrated. As is well known, chlorine atom has been denoting little anisotropic effect on the ring protons in substituted benzenes.[2)] Comparing with a methoxyl function, chlorine has shown a small paramagnetic effect to ring protons.[3)]

On these reasons, it would be appropriate to analyze ring protons of chlorophenazine derivatives for obtaining fundamental data.

Secondly, methyl and methoxyl protons will be examined. It could be reasonably understood, in phenazine derivatives, that alpha and beta substituents have shown marked differences in their chemical reactivity. Although the NMR (nuclear magnetic resonance) analysis is a useful tool for the static study, still there could be some possibilities in it to indicate, parallel with the above mentioned chemical reactivity, differences between alpha and beta positions.

For the sake of these purposes, the following compounds were prepared to take NMR spectra : 1,6-dichloro-, 1,9-dichloro-, 2,8-dichloro-, 1-methyl-, 2-methyl-, 1-methoxy-, 2-methoxy-, 1,3-dimethoxy-, 2,3-dimethoxy-, 1,4-dimethoxy-, 1,6-dimethoxy-, 2,8-dimethoxy-, 1,9-dimethoxy-, 1,6-dimethyl-4-methoxy-, 1,6-dimethyl-4-acetoxy-, and 1,6-dimethyl-4,9-dimethoxy-phenazines.

Results and Discussion

A) 1,6-Dichlorophenazine and 1,9-Dichlorophenazine

These compounds have two chlorines each one at alpha position on both sides of benzene rings in phenazine, therefore their proton signals are expected to be ABC type as observed in the corresponding dimethoxyphenazines.[1)] In Fig. 1, the NMR spectrum of 1,6-dichlorophenazine is presented. As were shown in dimethoxyphenazines, 1,6- and 1,9-dichlorophenazines give entirely same patterns (chemical shifts and various J-values). On comparison with dimethoxyphenazines, however, the signal pattern differs severely from the dimethoxy derivatives, owing to the distinct anisotropy between chlorine and methoxyl function.

Judging from the pattern, A and B proton signals look to overlap each other with a mode as demonstrated in Fig. 2. On the basis of this interpretation the spectrum of 1,6-dichlorophenazine was assigned as shown in Fig. 1. The figure presents at the

*1 This is one of series of Studies on Phenazines (I. Yosioka). Part XXVII : This Bulletin, **14**, 419 (1966).

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1) Y. Morita : Part XXVII, This Bulletin, **14**, 419 (1966).

2) J. A. Pople, W. G. Schneider and H. J. Bernstein : "High Resolution Nuclear Magnetic Resonance," 263 (1959). MacGraw-Hill, New York.

3) Ref. 2) p. 269.

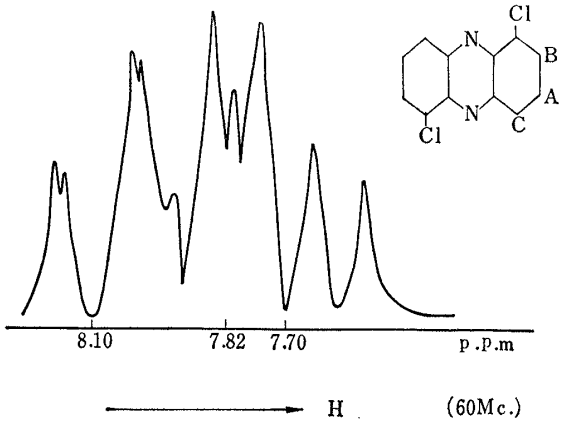

Fig. 1. Nuclear Magnetic Resonance Spectrum of 1,6-Dichlorophenazine

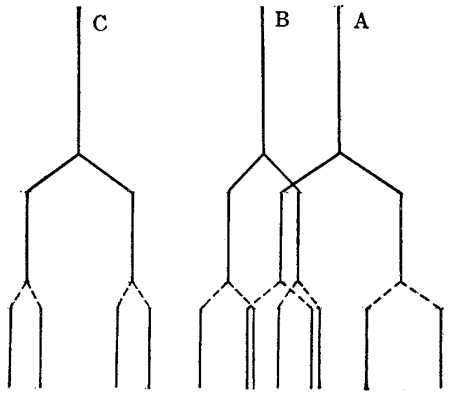

Fig. 2. Coupling Mode of ABC Protons

bottom of base line the chemical shifts of ring protons, giving following values as constants; $\delta_A=7.70$ p.p.m., $\delta_B=7.82$ p.p.m., and $\delta_C=8.10$ p.p.m. (cf. Fig. 2).

The anisotropic effect of chlorine atom on ring protons in phenazine is now disclosed to be entirely small one with the amount of -0.15 p.p.m. for ortho locating proton.

B) 2,8-Dichlorophenazine

In Fig. 3, the NMR spectrum of 2,8-dichlorophenazine is reproduced. This compound contains two chlorine atoms at the beta positions. As shown in the case of 2,8-dimethoxyphenazine,[1] the distribution of the proton of this compoud is also ABC type and can be analyzed easily. The twin peaks at the higher field are assigned to proton 3 (also 7), since the distance of two peaks (J=9 c/s) and their somewhat splitting features (J=*ca.* 2 c/s) would agree with the assumption. The left hand signals are now considered to be overlapped ones of proton 1 and 4 (also 6 and 9). The assignment obtained by the above bases is presented in Fig. 3, which is comparable to the anisotropic abnormality of beta-substituted dimethoxyphenazine[1]: the value for shielding effect to proton

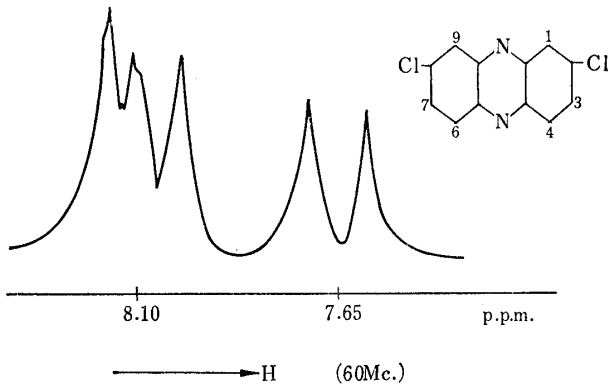

Fig. 3. Spectrum of 2,8-Dichlorophenazine

Table I. CH_3 and OCH_3 Proton Shifts in Phenazines

Compound	CH_3 (p.p.m.)	OCH_3 (p.p.m.)
1-CH_3	2.75	
2-CH_3	2.55	
1-OCH_3		4.01
2-OCH_3		3.94
1,3-di-OCH_3		3.92
2,3-di-OCH_3		3.96
1,4-di-OCH_3		4.00
1,6-di-OCH_3		4.02
2,8-di-OCH_3		3.94
1,9-di-OCH_3		4.02
1,6-di-CH_3-4-OCH_3	2.70, 2.80	4.00
1,6-di-CH_3-4-AcO	2.78	
1,6-di-CH_3-4,9-di-OCH_3	2.70	4.02

3 of the methoxyl function in 2,8-dimethoxyphenazine was as small as 0.37 p.p.m., comparing with the shielding effect (0.67 p.p.m.) to proton 2 in 1,6-dimethoxyphenazine. The chemical shifts of 7.65 p.p.m. for proton 3, and 8.10 p.p.m. for proton 1 and 4 are found to be entirely same values for the corresponding protons of phenazine itself, indicating almost negligible effect of beta chlorine atom to adjacent protons (alpha chlorine showed −0.15 p.p.m. deshielding effect, see above).

C) Methyl and Methoxyl Proton Shifts in Phenazines

In Table I, the chemical shifts for methyl and methoxyl protons of various substituted phenazines are given. Among the methyl protons, signals of 1-methyl, *i.e.* in alpha position, are observed in the down field below 2.70 p.p.m. and 2-methyl's, *i.e.* in beta, is at 2.55 p.p.m. Similarly to the methyl protons, the signals of alpha methoxyl functions appear at slightly lower field than beta ones. Thus, 1-methoxyl function had signals below 4.00 p.p.m., comparing with around 3.95 p.p.m. for 2-methoxyl's. These data seem to be quite useful criteria for the elucidation of synthesized methyl- or methoxy-phenazines whose substituent is uncertain of its location whether it is in alpha or in beta of phenazine ring (Fig. 4).

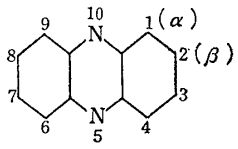

Fig. 4. Numbering of Phenazine

Experimental

Samples——All samples were synthesized by the known methods previously reported in the series of Studies on Phenazines (I. Yosioka, *et al.*).[4]

Measurement of NMR Spectra——NMR spectra of all samples were measured with HITACHI H-60 at 60 Mc. in CCl_4 solution at about $M/200$ concentration. Chemical shifts were presented in p.p.m. value from the signal of tetramethylsilane.

The author's thanks are heartfully expressed to Prof. I. Yosioka, Osaka University, for his kind guidance. Also his thanks are due to Miss M. Suzuki, Osaka University, for measurement of nuclear magnetic resonance spectra.

Summary

The NMR spectra of chlorophenazines were measured and analyzed as the one of representative examples of substituted phenazines.

Comparing with previously reported methoxyphenazines, ring protons of chlorophenazines showed weakly influenced signal patterns in which the anisotropic effects of chlorine atoms were observed in opposite sign to the methoxyl's.

The significant abnormality in its shielding power of beta substituent on phenazine ring is conceivable to propose an additional interest for clarification of the reactivity and the polarizability of beta substituent.

Concerning to the reactivity of substituent, methyl and methoxyl proton shifts of alpha and beta substituted phenazines were examined giving explicit descrimination in their absorption region as were seen in ring protons.

(Received December 13, 1965)

4) I. Yosioka : Pharm. Bull. (Tokyo), **2**, 25 (1954); I. Yosioka, H. Otomasu : *Ibid.*, **2**, 53 (1954).