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Micelle Formation and Its Significance in Interpretation of NMR Spectra of Phenothiazine Derivatives

Keyphrases □ Phenothiazine derivatives—micelle formation □ Micelle formation, phenothiazine derivatives—effect on NMR spectra □ NMR spectroscopy—micelle formation effect

Sir:

On occasion, we have observed some unusual behavior when evaluating NMR spectra of the salts of phenothiazine derivatives. The spectra of the compounds run in D_2O consisted of a series of broad peaks with little or no resolution and fine structure, which made it impossible to determine J constants. The broadening effect suggested the possibility of a ferromagnetic impurity in the compounds. Accordingly, the phenothiazines were purified as described by Craig *et al.* (1). The spectra were rerun, but the broadening effect previously observed persisted. This effect is illustrated in Fig. 1, using chlorpromazine hydrochloride as the model compound. At this point, the possibility of micelle formation was considered. Micelle formation was reported previously for phenothiazine derivatives (2).

In the previous study, it was noted that a compound in the micellar state showed broad resolution bands; however, when the temperature was raised the micelle was disrupted and the NMR bands became sharper and more distinguishable (3). We obtained similar results when chlorpromazine HCl was run in D_2O at 95° . Figure 1 shows this behavior. The spectrum at the elevated temperature showed increased resolution and sharp absorption peaks, which permitted the determination of J constants. Evidently, the strong association in the micellar state completely masked the NMR spectrum of the compound. A series of phenothiazine derivatives, including promazine HCl, prochlorperazine HCl, trifluoperazine HCl, trifluoromeprazine HCl, and

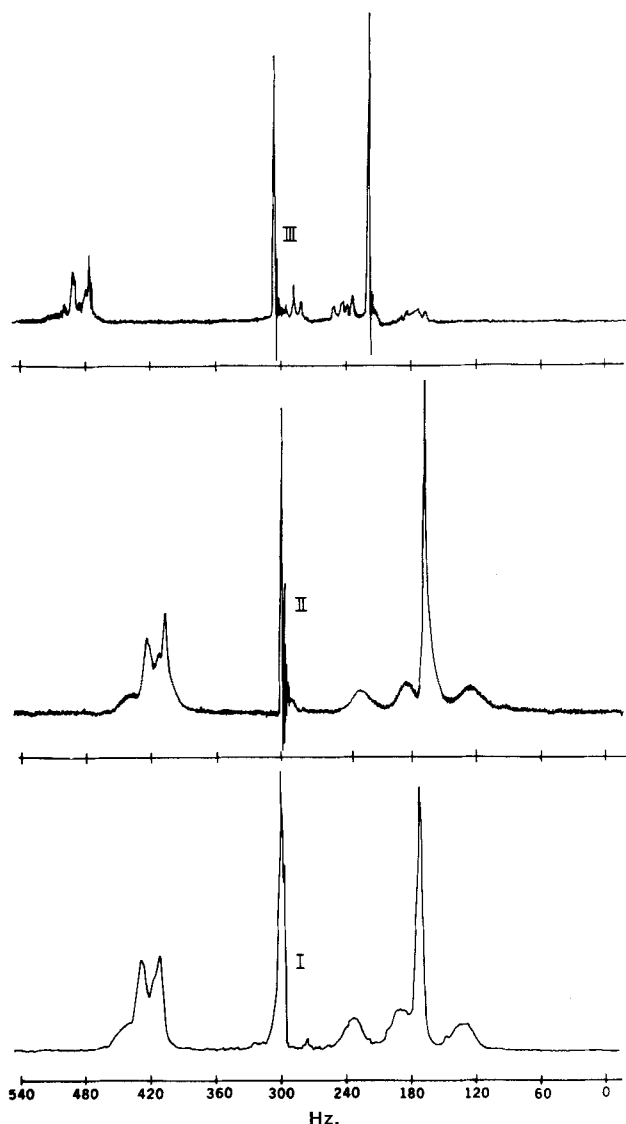


Figure 1—NMR spectra for 10% solutions of chlorpromazine HCl in D_2O . Key: I, solution containing added amount of known ferromagnetic impurity; II, solution prepared with purified chemical; and III, solution from II run at 95° .

vespazine HCl, were run in the same manner, and all exhibited similar behavior. These studies suggest that the broadening effect observed in the NMR spectra of the compounds in D_2O may be attributable to the formation of micelles, rather than to the presence of ferromagnetic impurities. We feel that this observation should be of general interest to other investigators and should save considerable time and effort when NMR studies of a similar or related nature are involved.

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