Effect of Water of Hydration on the Infrared Spectra of Tertiary Amine Salts

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The presence of water of hydration in a tertiary amine salt, chlorpromazine hydrochloride, has been found to alter the absorption of the R_3NH^+ ion in a unique and characteristic manner. Observance of this alteration makes it possible to establish the presence of a hydrate, a hemihydrate, an anhydrous tertiary amine salt, or free water.

THE PRESENCE or absence of water in the form of a hydrate in tertiary amine salts is a problem frequently encountered by analytical chemists in the pharmaceutical industry. A simple, rapid, and sensitive method which requires only a small amount of sample for determining the presence of a hydrate or hemihydrate is presented.

EXPERIMENTAL

Reagents.—Chlorpromazine hydrochloride[1]; chlorpromazine hydrochloride, hemihydrate; and chlorpromazine hydrochloride, hydrate.

Spectrophotometer.—The infrared spectra were recorded with a Perkin-Elmer model 21 double-beam spectrophotometer with a sodium chloride prism. The amine salts studied were prepared as mineral oil mulls.

RESULTS AND DISCUSSION

Figure 1 shows the infrared spectra obtained for three samples of chlorpromazine hydrochloride in the region 5000 to 2000 cm.$^{-1}$. This is the region which contains absorption bands due to R_3NH^+ ion. All tertiary amine salts exhibit a strong, broad band centered between 2300 and 2500 cm.$^{-1}$. This band is assigned to the hydrogen atom in the ion pair $R_3NH^+X^-$. This band occurs for a large asymmetric tertiary amine ion, R_3NH^+, combined with a small negative ion, X^-. The relatively small negative ion can approach the amine cation from only one direction, forming the ion pair $R_3NH^+X^-$ with the hydrogen strongly bound to the negative ion. This band has been observed in more than 200 tertiary amine salts of hydrochloric, hydrobromic, and sulfuric acids.

Spectrum A is that of anhydrous chlorpromazine hydrochloride. The R_3NH^+ absorption band is strong and broad and centered at 2390 cm.$^{-1}$. Spectrum B is that of the hemihydrate of chlorpromazine hydrochloride. This is indicated by the splitting of the broad band into two peaks located at 2400 and 2550 cm.$^{-1}$. Spectrum C is that of the hydrate chlorpromazine hydrochloride. This shows a weaker R_3NH^+ absorption located at 2600 cm.$^{-1}$. The unusual behavior exhibited by the hydrate and hemihydrate is due to the reduction of hydrogen bonding of H^+ to X^- by the presence of the water.

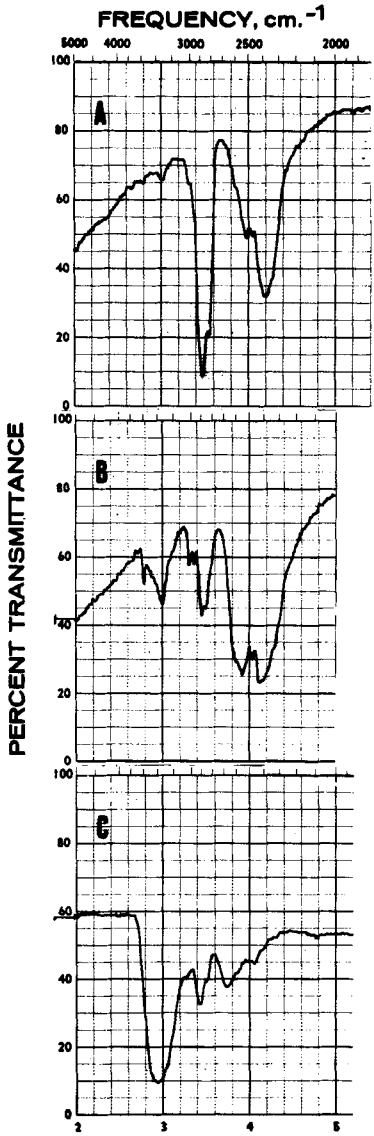

Fig. 1.—Infrared spectra obtained for three samples of chlorpromazine hydrochloride.

SUMMARY

Data are given to show that water of hydration tends to lower the intensity and raise the frequency of the ion pair absorption in the tertiary amine salts, chlorpromazine hydrochloride. This information provides a basis for determining the presence or absence of a hydrate form.

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[1] Marketed as Thorazine by Smith Kline & French Laboratories, Philadelphia, Pa.