

active. Only the compounds given in Table II showed significant cytotoxic activity.

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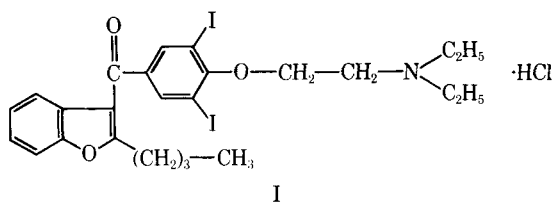
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Observations on the Micelle Formation of 2-Butyl-3-benzofuranyl-4-[2-(diethylamino)ethoxy]-3,5-diiodophenyl Ketone Hydrochloride (SK&F 33134-A) by NMR Spectroscopy

Keyphrases □ 2-Butyl-3-benzofuranyl-4-[2-(diethylamino)ethoxy]-3,5-diiodophenyl ketone hydrochloride (SK&F 33134-A)—micelle formation □ Critical micelle concentration—SK&F 33134-A □ NMR spectroscopy—micelle formation determination

Sir:

In recent years, several papers (1-3) have dealt with the use of high-resolution NMR for the determination of CMC. In our laboratories, we have used NMR to show the existence of micelles in a 5% aqueous solution of SK & F 33134-A(I).¹ Micelle formation has not previously been reported for this system.



All measurements were carried out with a Jealco C60H NMR spectrometer equipped with a variable

¹ Marketed as Cordarone by Labaz Laboratories in several European countries.

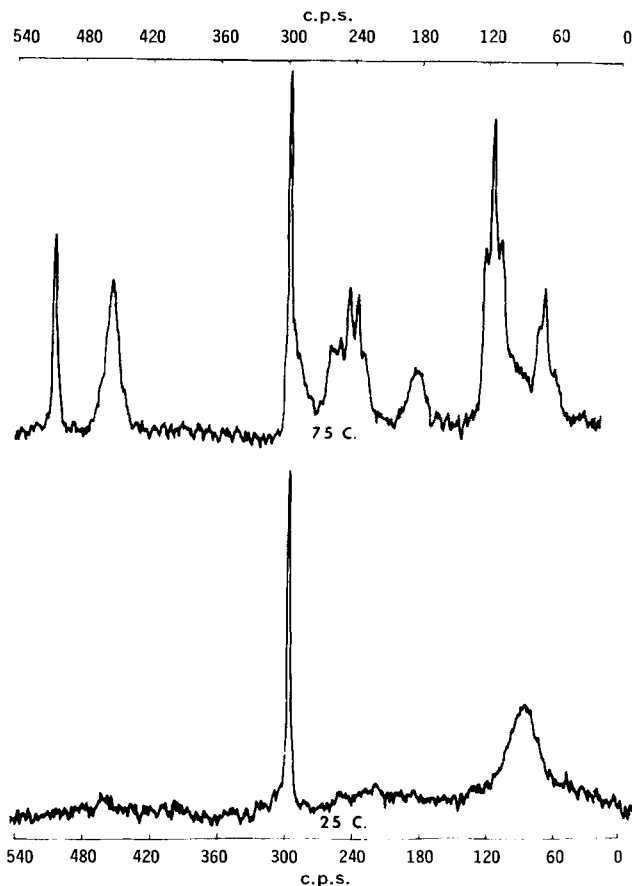


Figure 1—NMR spectra for a 5% solution of SK&F 33134-A in D_2O at 25 and 75°, respectively.

temperature probe. Spectra were recorded at temperatures ranging from 25 to 95°. Figure 1 illustrates the NMR spectrum for a 5% solution of SK&F 33134-A in D_2O at 25°. There are no sharp resonance lines as one would expect under normal conditions. Instead, there is a large broadening effect of all resonance lines. We attribute this broadening to dipolar interaction in the micellar structure where molecular motion is se-

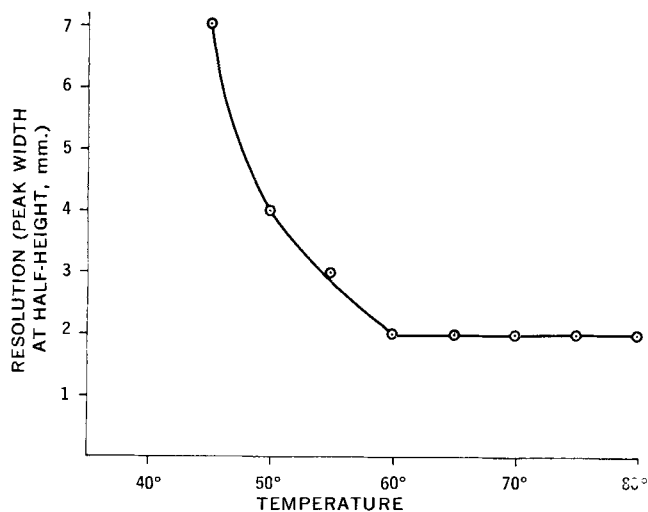


Figure 2—A plot showing the effect of temperature on the resolution (peak width at half-height) at 504 c.p.s. for a 5% solution of SK&F 33134-A in D_2O .

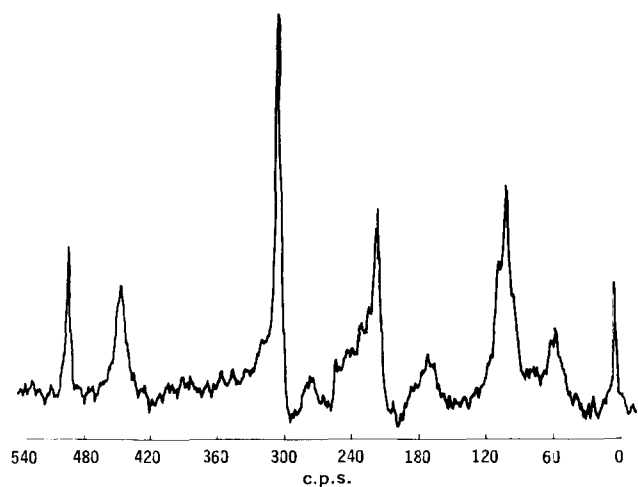


Figure 3—NMR spectrum for SK&F 33134-A solution diluted with methanol- d_4 .

verely inhibited. Raising the temperature of this solution in small increments and recording the NMR spectra at selected temperature intervals resulted in spectra having increasing resolutions, with corresponding increases in signal intensities. The spectrum for SK & F 33134-A at 75° is also shown in Fig. 1. The sharpening of the spectrum with an increase in signal intensity suggests the gradual breakdown of the micellar structure as the temperature increases. The resolution reaches its maximum at approximately 60°. We assume that the micellar structure is completely disrupted at this temperature. The effect is further illustrated in Fig. 2, which contains a plot of band width at half-height of the aromatic protons on the iodinated benzene ring at 504 c.p.s. (resolution) versus temperature. The fact that band width at half-height reaches a minimum constant value at approximately 60° again illustrates the apparent breakdown of the micellar structure at this temperature.

Water-miscible organic solvents have been shown to have some effect on micelle formation (4). Figure 3 illustrates the effect of the addition of methanol- d_4 to the micellar solution of SK & F 33134-A at 25°. The NMR spectrum becomes highly resolved, indicating that the micelle has been disrupted.

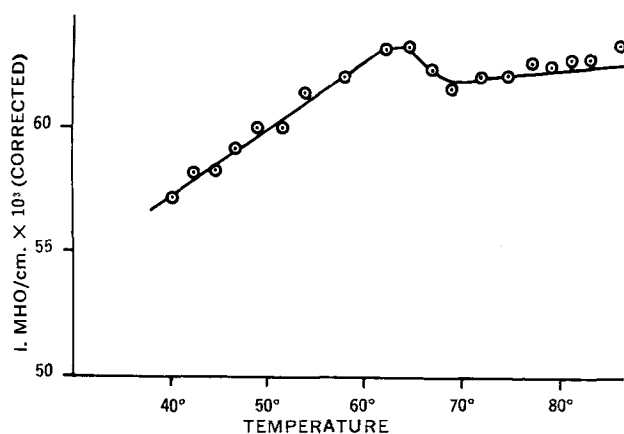


Figure 4—Plot showing the effect of temperature on the specific conductance of a 5% aqueous solution of SK&F 33134-A.

To substantiate the effect of temperature on the micellar state of SK & F 33134-A, conductivity studies were done over the same temperature range. A Serfass conductivity bridge, model RCM15B1, and a Beckman K 1.00/cm. conductivity cell were used. An aqueous solution of SK & F 33134-A was poured into two small jacketed glass vessels connected to each other and to a constant-temperature bath. The conductivity cell was immersed into one vessel and a thermometer into the other vessel. The temperature of the water bath was increased slowly. The temperature and the conductivity of the test solution were recorded. The results are shown in Fig. 4. The conductivity increases gradually to 60° and then becomes relatively constant. These conductivity data are in good agreement with the NMR data, indicating the presence of micelles at 25° and the subsequent complete destruction of the micelles as the temperature is increased. In both cases the temperature effect is reversible.

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Imidazole and Pyrazole Bis(2-fluoroethyl)triazenes

Keyphrases Bis(2-fluoroethyl)triazene derivatives—synthesis
 Antileukemic activity—triazenoimidazoles

Sir:

Among a considerable number of 5-(disubstituted-triazeno) and 5-(monosubstituted-triazeno) derivatives of imidazole-4-carboxamide and of imidazole-4-carboxylic acid esters tested against lymphoid leukemia L-1210, 5-[3,3-bis(2-chloroethyl)-1-triazeno]imidazole-4-carboxamide (I, NSC-82196) has proved to be the most effective. In certain of the standard L-1210 tests, a majority of the afflicted mice treated with NSC-82196