The Critical Micelle Concentration of L-*N*-Decyl-*N*-*N*-Dimethylalanine Hydrobromide from Circular Dichroism Measurements

Keyphrases ☐ Critical micelle concentration—L-*N*-decyl-*N*-*N*-dimethylalanine hydrobromide ☐ Circular dichroism measurements—CMC determination

Sir:

In a previous publication by Bonkoski and Perrin (1) it was shown that optical rotatory dispersion (ORD) can be used to determine the critical micelle concentration (CMC) of suitable molecules. We have now confirmed our previously reported CMC of L-*N*-decyl-*N*-*N*-dimethylalanine hydrobromide and shown that circular dichroism can be used for these determinations. All measurements were made in a Cary 6002 circular dichroism accessory for the Cary 60 recording spectropolarimeter. All experimental conditions were identical to those previously described and the solutions were scanned to the limit of the system. The observed ellipticity at 222.5 mμ was plotted against concentration, and a break in the plot occurs at the CMC (0.32%). To emphasise the change in slope on micelle formation, a deviation plot is shown in Fig. 1. Here the slope of the line below the CMC was calculated and the theoretical ellipticity = slope × concentration, and the deviation of the observed ellipticity from this theoretical ellipticity is plotted in the diagram against concentration. Molecular ellipticities of 1966 below the CMC and of 1882 above the CMC at a wavelength of 222.5 mμ can be calculated from an observed ellipticity against concentration plot. This small change of 5.7% in molecular ellipticity on micelle formation can be compared with a change of 10.6% in molecular rotation at 232.5 mμ observed in the previous paper, and the diminished ellipticity on micelle formation should be compared with the effect of acid and base on the ellipticity of the betaine shown in Fig. 2. The diminished ellipticity observed on micelle formation suggests that the betaine becomes more ionized on micelle formation; however, this is in direct conflict with the ORD observations previously reported, where the peak shifts and the diminished rotation on micelle formation suggested a less ionized betaine in the micellar form. Assuming that other environmental factors are secondary to the state of ionization, then CD information is probably more correct in that it measures asymmetric absorption phenomena directly and the absorption observed is due to the carboxylic acid grouping. It is possible that acid and base have a considerable effect on the background curve of the betaine ORD curve and that the correlation with the micelle formation curves was fortuitous in the previous publication.

In the previous report, pH measurements were presented to support the ORD observations; however, it was pointed out that the behavior of the glass electrode is not clearly understood in these systems. It is possible that the glass electrode in the micellar betaine systems only detected the hydrogen ions far from the micelle

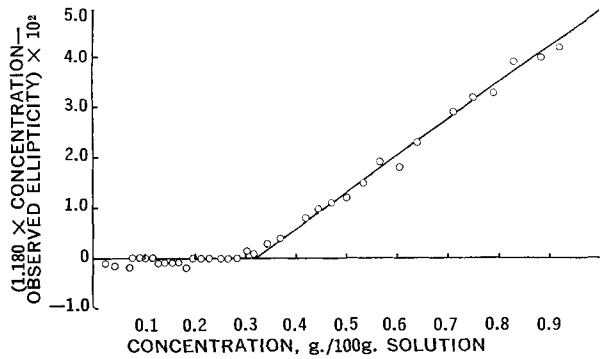

Figure 1—*Deviation plot showing CMC for* L-N-*decyl*-N-N-*dimethylalanine hydrobromide from CD measurements at 222.5 mμ in 2-cm. cells.*

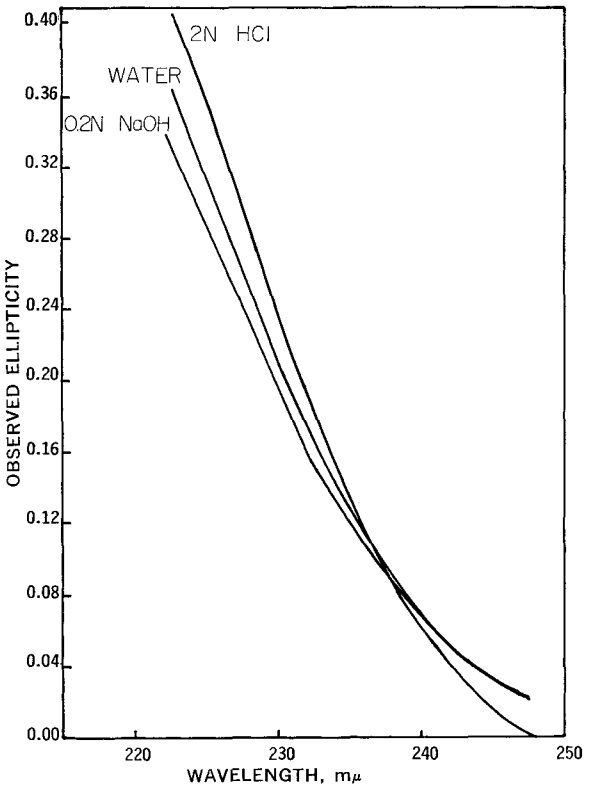

Figure 2—*Effect of pH on CD curve of a 1.84 × 10⁻³ M solution of* L-*decyl betaine hydrobromide. Measurements made in 5-cm. cells.*

surface and not those in close proximity to the micelle surface, so giving a low hydrogen ion determination. These discrepancies between ORD and CD determinations are being further investigated.

(1) S. Bonkoski and J. H. Perrin, *J. Pharm. Pharmacol.*, **20**, 934(1968).

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The Biogenesis of Gramine

Keyphrases ☐ Gramine biogenesis—literature correction ☐ Tryptophan relation—gramine biogenesis

Sir:

Many years ago I demonstrated (1, 2) that *dl*-tryptophan-β-^{14}C fed to sprouting barley, is transformed into the alkaloid gramine in which the ^{14}C is located in one position, corresponding to that in the administered tryptophan, strongly suggesting that it was a precursor of gramine. This was one of the first demonstrations, using a radioactive compound, that an alkaloid could be formed from an amino acid.

In a recent paper (3), Digenis states "Based on other tracer experiments and the fact that tryptophan was formed in *Neurospora* by a condensation reaction between indole and L-serine, Bowden and Marion suggested a reversal of the above-mentioned tryptophan biosynthesis could possibly lead to indole and L-serine in barley. This suggested that the indole could subsequently react in a Mannich-type reaction with formaldehyde and dimethylamine to produce gramine." Later in the paper the author continues, "However, Leete and Marion were able to show that the bond between the 3-position of the indole nucleus and the side chain of tryptophan remained intact during the biosynthesis of gramine in barley, thus disposing of the hypothesis of Bowden and Marion described above."

An examination of the only two papers I have published (1, 2), to which Digenis refers, will show that in them no theory on the biogenesis of gramine from tryptophan is proposed or implied. The only conclusion reached was, I quote, "that tryptophan is a precursor of gramine in barley," a conclusion that has been amply justified by subsequent investigators.

(1) K. Bowden and L. Marion, *Can. J. Chem.*, **29**, 1037(1951).
(2) *Ibid.*, **29**, 1043(1951).
(3) G. A. Digenis, *J. Pharm. Sci.*, **58**, 39(1969).

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Drug Transport I: Effect of Potassium Ion on the *In Vitro* Transfer of Several Drugs Across the Rat Intestine: Preliminary Observations

Keyphrases ☐ Intestinal transport, drug—K^+ effect ☐ K^+ substitution of Na^+—*in vitro* intestinal transport

Sir:

Recent work in our laboratory concerning factors that affect drug transport has resulted in several interesting, preliminary findings as to the effect of replacing Na^+ with K^+ on the transfer of several drugs across the everted rat intestine.

Sprague-Dawley rats,[1] weighing approximately 250 g., were fasted 20–24 hr. prior to the experiment. Water was allowed *ad libitum*. The experimental method for preparing the everted rat intestine preparation has been described previously (1). After severing the intestine at the pyloric junction, the first 15 cm. of intestine are discarded and the following 20 cm. are divided into two 10-cm. segments. The most proximal segment is designated Segment 1, and the distal portion is designated Segment 2. A modified physiologic Kreb's bicarbonate buffer,[2] pH 7.4, was prepared to contain a total cation

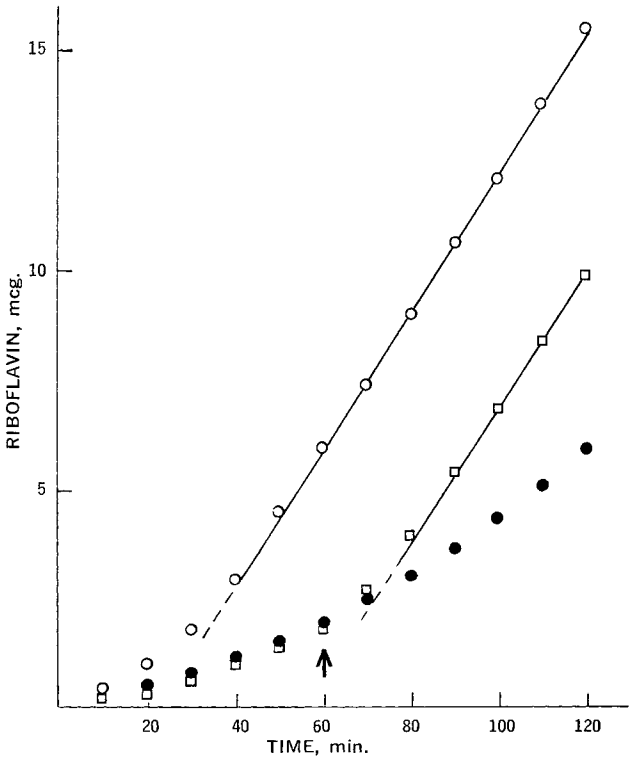

Figure 1—*Cumulative transfer of riboflavin across the everted rat intestine. Mucosal concentration maintained essentially constant at 20 mcg./ml. Key: (○), Na^+-buffer; (●), K^+-buffer; (□), K^+-buffer for 60 min., then placed into Na^+-buffer (arrow). See text for details.*

[1] Blue Spruce Farms, Altamont, N. Y.
[2] KCl, 5 m*M*; KH_2PO_4, 6 m*M*; $NaHCO_3$, 26 m*M*; NaCl *q.s.* 154 m*M* cation ($Na^+ + K^+$).