compounds and no evidence was found for Fe-$(OR)_6$---. It is possible that other maxima might be observed at different concentrations and wave lengths. For ethyl acetoacetate, the ferric chloride is believed to react with the cis enol form.[5] Letellier[6] has reported that the maximum of color exists at the ratio of 1 ferric chloride:2 ester in water. The existence of other complex ions has been demonstrated.[7]

The concentration of OR ions may be an important factor in determining which particular complex is formed.[1] It is of interest, therefore, to compare the ionization constants of the organic compounds used. The classical dissociation constants in water at 25° for salicylaldehyde and m-cresol are 1.53×10^{-5} [8] and 0.98×10^{-10},[9] respectively. Using the relationship[10]

$$K_a = K_g (1 + K_E)/K_E \qquad (1)$$

where K_a is the classical dissociation constant of the enol form, K_g is the classical dissociation constant, and K_E is the enol–keto equilibrium constant results in a value of 2.9×10^{-10} for K_a for ethyl acetoacetate in water at 25°. Values of 2.09 $\times 10^{-11}$ [10] for K_g and 0.078[5] for K_E were used. Thus it is the more acidic compound, salicylaldehyde, which forms the 1:1 complex. This may be due to steric influences between the ortho CHO group and the hydrated ferric ion.

In regard to electrolysis experiments, Wesp and Brode[1] reported that the phenol complex migrates toward the cathode, while Bent and French[2] claim the color migrates toward the anode. Our results show that the complexes for m-cresol and ethyl acetoacetate are neutral: the salicylaldehyde complex should migrate toward the cathode. The observed disappearance of color may be due to the instability of the complex. Due to the neutral nature of the m-cresol and ethyl acetoacetate complexes it is essential to establish the existence of the RO⁻ complex rather than a possible ROH complex. A determination of the pH of the solutions as the complexes are formed may prove fruitful in establishing this fact.

Acknowledgment.—The authors are indebted to Mr. Joseph M. Rizzo for technical assistance.

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(6) L. Letellier, *Bull. Sci. Pharmacol.*, **38**, 145–217 (1931).

(7) B. Emmert and W. Seebode, *Ber.*, **71B**, 242 (1938).

(8) "International Critical Tables," McGraw–Hill Book Co., Inc., New York, N. Y., Vol. 6, 1929, p. 279.

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DEPARTMENT OF CHEMISTRY
UTICA COLLEGE OF SYRACUSE UNIVERSITY
UTICA, NEW YORK   RECEIVED JULY 9, 1951

Cevine, a Correction

By LÉO MARION, D. A. RAMSAY AND R. NORMAN JONES

In a previous study of the infrared absorption spectra of a number of alkaloids[1] we reported the presence of a carbonyl absorption band in the infrared spectrum of cevine and concluded that this alkaloid contained a carbonyl group. At the

(1) L. Marion, D. A. Ramsay and R. N. Jones. THIS JOURNAL, **73**, 305 (1951).

suggestion of Dr. H. L. Holmes we re-examined the base on which our observation had been made and found that it consisted not of cevine but of one of the minor alkaloids occurring with it. This alkaloid which is obtained like cevine by saponification of crude veratrine, crystallizes in short prismatic needles melting at 266–270.5° whereas cevine melts at 164–174°. The infrared absorption spectrum of an authentic sample of cevine *does not* contain a carbonyl absorption band.

CHEMISTRY DIVISION
NATIONAL RESEARCH COUNCIL
OTTAWA, CANADA   RECEIVED SEPTEMBER 28, 1951

Additional Studies on the Intramolecular Hydrogen Bonding in Acetylglycine N-Methylamide

By SAN-ICHIRO MIZUSHIMA, TAKEHIKO SHIMANOUCHI, MASAMICHI TSUBOI AND REISUKE SOUDA

In a previous paper[1] we reported our experimental results of near infrared absorption observed for $CH_3CONHCHRCONHCH_3$ and $CH_3CONHCHRCONHC_6H_5$ (R = H or C_4H_9) in dilute carbon tetrachloride solutions. All these compounds show two NH bands at about 2.9 μ and 3.0 μ of which the former is assigned to the vibrations of the NH group in the free state and the latter to that involved in the *intramolecular* hydrogen bonding of the structure
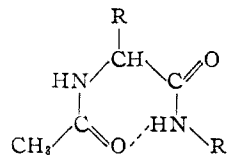
which corresponds to "B form" (one of the two unit structures of a polypeptide chain) proposed by us in 1947.[2] In view of the importance of proving the existence of B form in the structural chemistry of proteins we have recently made additional measurements of the near infrared absorption, the results of which will be reported in the present note.

In order to obtain further information concerning the relation between molar absorption coefficient κ and concentration c for these two NH bands measurements were made at 60° on carbon tetrachloride solutions of acetylglycine N-methylamide $CH_3CONHCH_2CONHCH_3$ of different concentrations c and absorption path-lengths l, keeping the product $c \times l$ constant. The results are shown in Fig. 1. If these two NH bands arise solely from single molecules and not from associated molecules (*intermolecular* hydrogen bonding), all the curves (1), (2) and (3) of Fig. 1 must be of the same form. Actually they are found almost of the same form, but differ slightly from one another.

Let us now consider to what extent these three absorption curves should differ from one another, if the 2.98 μ band were to be assigned solely to the *intermolecularly* hydrogen-bonded NH vibration (*i.e.*, solely to the NH association band). Since

(1) S. Mizushima, T. Shimanouchi, M. Tsuboi, T. Sugita, E. Kato and E. Kondo. THIS JOURNAL, **73**, 1330 (1951).

(2) T. Shimanouchi and S. Mizushima. *Kagaku*, **17**, 24, 52 (1947); *Bull. Chem. Soc. Japan*, **21**, 1 (1948), see C. A., **43**, 8843 (1949).
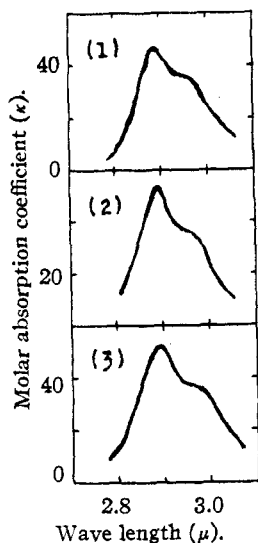
Fig. 1.—Near infrared absorption curves of acetylglycine N-methylamide in dilute carbon tetrachloride solutions at 60°. Concentrations and absorption path-lengths are: (1) 0.0006 mole/1. 5 cm.; (2) 0.0003 mole/1. 10 cm.; (3) 0.00015 mole/1. 20 cm.
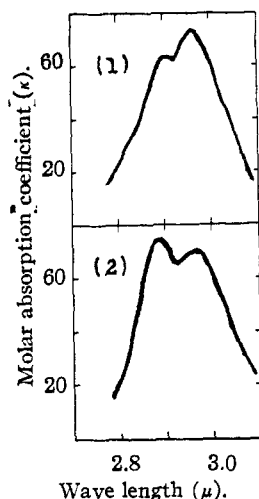

Fig. 3.—Near infrared absorption curves of acetylglycine N-methylamide in dilute carbon tetrachloride solutions at 30°. Concentrations and absorption path-lengths are: (1) 0.0003 mole/1. 5 cm.; (2) 0.00015 mole/1. 10 cm.

Fig. 2.—Relations between concentration c and degree of association α for different values of equilibrium constant K.

the first step of molecular association would be the formation of a dimer, only the monomer–dimer equilibrium is taken into consideration. Figure 2 shows the relation between concentration c and degree of association α calculated for the different values of equilibrium constant K from the law of mass action. (κ of the dimer band is proportional to α, and κ of the monomer band to $1 - \alpha$.) An inspection of this figure reveals that the effect of dilution upon the decrease of α is remarkable. Thus the dilution of a solution from 0.0006 mole/1. to 0.00015 mole/1. results in the decrease of α by one-third for $K = 55$, and by one-half for $K = 1097$.[3] (There is no need of taking the value of K greater than 1097, because κ corresponding to the 2.8 μ band for the 0.0006 mole/1. solution at 60° (Fig. 1) is about one-half of that for the 0.0003 mole/1. solution at 30° (Fig. 3) and, therefore, α cannot be greater than 50% for 0.0006 mole/1. solution at 60°.) For the smaller values of K the decrease in α is more pronounced.

On the other hand the changes in κ for the NH bands of acetylglycine N-methylamide actually observed on dilution from 0.0006 mole/1. to 0.00015 mole/1. at 60° are very small. This fact shows that the 2.98 μ band observed by us in dilute solutions at 60° arises almost solely from the intramolecularly hydrogen-bonded NH group.

We have made similar absorption measurements on dilute solutions of the same compound at 30°, again keeping $c \times l$ constant. On dilution of a solution from 0.0003 mole/1. to 0.00015 mole/1.

an appreciable increase of κ for the 2.90 μ band and an appreciable decrease of κ for the 2.98 μ band have been observed (see Fig. 3). This shows that at 30° even in a solution as dilute as 0.0003 mole/1. there is an appreciable molecular association in this compound and that the 2.98 μ band must be considered to arise partly from the NH group involved in the abnormally strong intermolecular hydrogen bonding. However, as the actually observed changes in κ are far smaller than those for the case in which the 2.98 μ band would solely arise from the intermolecularly hydrogen-bonded NH group, we can surely consider that even at 30° the 2.98 μ band arises for the most part from the NH group involved in the intramolecular hydrogen bonding.

According to what we have stated above we can confirm our previous conclusion that in dilute carbon tetrachloride solutions of acetylglycine N-methylamide the molecules take partly the "B form."

HONGO, TOKYO, JAPAN　　　　RECEIVED AUGUST 14, 1951

Camoquin Relatives[1]

BY H. J. NICHOLAS[2] AND J. H. BURCKHALTER[2]

Camoquin (I) and O-methyl Camoquin (II) are known to possess high antimalarial activity in birds, and the former is now marketed for the treatment of human malaria. Many close analogs of these compounds have already been described,[3] but none apparently possesses an advantage over Camoquin. We have been interested in making somewhat wider variations in structure in order to observe the effect upon antimalarial potency. Two such products, V and VIII, have now been prepared, but they also are inferior to Camoquin.

V was prepared by starting with 2-methoxy-5-nitrophenylacetonitrile (III), which was made from the corresponding benzyl chloride. III was reduced catalytically to the desired intermediate

(3) For δ-valerolactam which forms a dimer with the double intermolecular hydrogen bond in its carbon tetrachloride solution K was found to be 45 at 60.7° (Tsuboi, Bull. Chem. Soc. Japan, 24, 75 (1951).

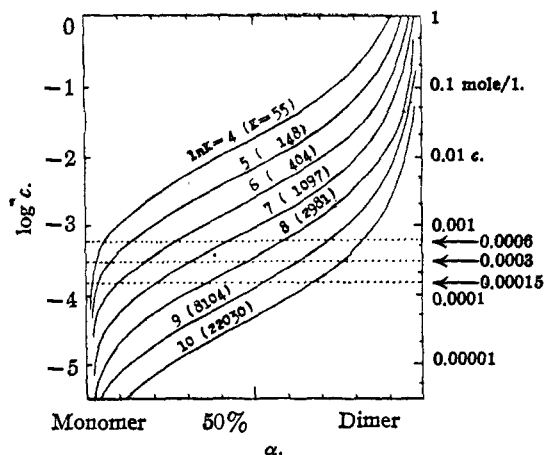(1) Camoquin is a registered trademark name of Parke, Davis and Co., Detroit.

(2) University of Kansas, Lawrence, Kansas.

(3) (a) J. H. Burckhalter, F. H. Tendick, E. M. Jones, P. A. Jones, W. F. Holcomb and A. L. Rawlins, THIS JOURNAL, 70, 1363 (1948); (b) J. H. Burckhalter, J. Am. Pharm. Assoc., 38, 658 (1949).