assumes that, for example, the rate at which the number of molecules in the second layer increases is proportional to the number of "uncovered" first layer molecules (in agreement with B.E.T.) and the rate at which this number decreases is proportional to the *total* number of molecules in the second layer (in disagreement with the B.E.T. theory which uses instead the number of *uncovered* second layer molecules). These two rates are equated at equilibrium. Otherwise the two theories have identical assumptions. Ross[3] and Fergusson and Barrer[4] have examined and extended the Hüttig theory in some detail.

The Hüttig equation may be useful as an empirical equation but in the writer's opinion the derivations[2,4] on which the equation is based are fallacious[5]:

(1) The Hüttig kinetic derivation violates the principle of microscopic reversibility because the equilibrium condition (for example, for the second layer) is obtained by equating the rates of two molecular processes which are *not* the reverse of each other.[6]

(2) In the statistical derivation of Fergusson and Barrer different layers are treated as different "phases" in equilibrium. The equilibrium condition is taken as $\mu_1 = \mu_2 = \mu_3 = \ldots$, where the μ_i are chemical potentials. However, it is easy to show by the standard method of minimizing the total free energy of the combined "phases" that this is *not* the correct equilibrium condition here, since the free energy of the i-th layer ("phase") depends not only on the number of molecules in the i-th layer but *also* on the number of molecules in the $(i - 1)$-th layer.[4] That the Hüttig free energy is not the correct minimum (B.E.T.) free energy is the essential reason why, for the same value of the B.E.T. constant c, the Hüttig isotherm is always below the B.E.T. isotherm and hence accounts for the accidental better agreement of the Hüttig isotherm with experiment for $p/p_0 < 0.8$ (*i. e.*, for *other* reasons, the B.E.T. model has too low a free energy).

Actually, those assumptions which the B.E.T. and Hüttig theories have in common are sufficient to lead uniquely to the B.E.T. equation, as is clear from a statistical argument[7] which makes no assumption about kinetic mechanism.

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(3) Ross, *J. Phys. and Colloid Chem.*, **53**, 383 (1949).

(4) Fergusson and Barrer, *Trans. Faraday Soc.*, **46**, 400 (1950).

(5) However, in fairness to Fergusson and Barrer it should be emphasized that they intentionally set out to find the statistical treatment which would lead to Hüttig's kinetic result. To accomplish this the assumption $\mu_1 = \mu_2 = \mu_3 = \ldots$ in (2), below, had to be used. The fact that this assumption does not lead to the minimum free energy for the system of adsorbed molecules is of course just a reflection of the violation of the principle of microscopic reversibility already present in the original kinetic derivation (see (1) below).

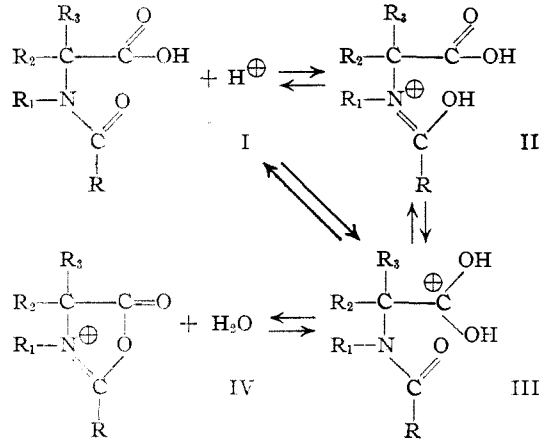
(6) Tolman, "Principles of Statistical Mechanics," Oxford Univ. Press, New York, N. Y., 1938, p. 163.

(7) Hill, *J. Chem. Physics*, **14**, 263 (1946); see also THIS JOURNAL, **68**, 535 (1946).

THE ACID CATALYZED CYCLIZATION OF α-ACYLAMINO ACIDS

Sir:

In the course of an investigation of the ionization of certain polyfunctional compounds in absolute sulfuric acid solutions the following van't Hoff "i" factors[1-3] were observed: glycine, 2.2; acetylglycine, 2.5; benzoylglycine, 3.6; and benzoylsarcosine, 3.8. These data suggested that in sulfuric acid solutions α-acylamino acids are cyclized, at least in part, to the corresponding oxazolonium ions via the following reaction mechanism:



The above conclusion was confirmed when it was found that an intense red-violet color, characteristic of basic solutions of azlactones derived from the *p*-nitrobenzoylamino acids,[4,5] was formed when a sulfuric acid solution of *p*-nitrobenzoylalanine was quickly poured into an excess of cold aqueous potassium hydroxide, and when a sulfuric acid solution of α-acetamidocinnamic acid, which had been allowed to stand overnight at room temperature, was poured into cold water to give 2-methyl-4-benzal-5-oxazolone, m. p. 150–152°,[6] either alone or when mixed with an authentic sample.

The influence of the R, R_1, R_2 and R_3 groups in determining the "i" factor can only be evaluated by consideration of their respective influences in the several equilibrium reactions noted above. The limited cyclization of acetylglycine in sulfuric acid solutions is in accord with the reported ease of hydrolysis of 2-methyl-5-oxazolones,[7] the equilibrium in this case favoring the noncyclic structures II and III. In contrast the "i" values indicate that the cyclization of benzoyl-

(1) L. P. Hammett and A. J. Deyrup, THIS JOURNAL, **55**, 1900 (1935).

(2) H. P. Treffers and L. P. Hammett, *ibid.*, **59**, 1708 (1937).

(3) M. S. Newman, H. G. Kuivila and A. B. Garrett, *ibid.*, **67**, 704 (1945).

(4) E. Waser and E. Brauchli, *Helv. Chim. Acta*, **7**, 757 (1924).

(5) P. Karrer and R. Keller, *ibid.*, **26**, 50 (1943).

(6) M. Bergmann and F. Stern, *Ann.*, **448**, 20 (1926).

(7) H. E. Carter, "Organic Reactions," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 198.

glycine and benzoylsarcosine is essentially complete, *i. e.*

$$C_6H_5CONR_1CH_2CO_2H + 2H_2SO_4 \rightleftharpoons \left[C_6H_5C(=O)=NR_1CH_2CO\right]^+ + H_3O^+ + 2HSO_4^-$$

(R_1 = H, CH_3; i = 4)

The similarity in the behavior of the latter two solutes is not disconcerting for there is no feature of any one of the reaction steps which would render the N-methyl compound incapable of cyclization. Indeed this situation may not be unique, for we regard as inconclusive the evidence[8,9] upon which is based the repeated claim[7,8,10] that acylsarcosines cannot cyclize in acetic anhydride.

It has been observed that the acid catalyzed cyclization of α-acylamino acids can also be conducted in the solvent acetic anhydride. Further observations on the cyclization of acylsarcosines and some preparative applications of the above observations will be reported in a subsequent communication.

(8) R. Heard, *Biochem. J.*, **27**, 54 (1933).
(9) V. Deulofeu, *Ber.*, **67**, 1542 (1934).
(10) R. H. Wiley and O. H. Borum, THIS JOURNAL, **72**, 1626 (1950).

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RECEIVED AUGUST 28, 1950

TWO HYDROGEN-BONDED SPIRAL CONFIGURATIONS OF THE POLYPEPTIDE CHAIN

Sir:

During the past fifteen years we have been carrying on a program of determination of the detailed atomic arrangements of crystals of amino acids, peptides, and other simple substances related to proteins, in order to obtain structural information that would permit the precise prediction of reasonable configurations of proteins. We have now used this information to construct two hydrogen-bonded spiral configurations of the polypeptide chain, with the residues all equivalent, except for variation in the side chain.

We have attempted to find all configurations for which the residues have the interatomic distances and bond angles found in the simpler substances and are equivalent, and for which also each CO group and NH group is involved in the formation of a hydrogen bond. The plane layer of extended polypeptide chains is a structure of this type, the hydrogen bonds being formed between adjacent chains. In addition there are two spiral structures, in which the plane of the conjugated system C–CO–NH–C is nearly parallel to the spiral axis, and hydrogen bonds are formed between each carbonyl and imino group and an imino or carbonyl group of a residue nearly one turn forward or back along the spiral.

One of these spirals is the three-residue spiral, in which there are about 3.7 residues per turn and each residue is hydrogen-bonded to the third residue from it in each direction along the chain. The unit translation per residue is 1.47 Å. There is evidence that indicates strongly that this configuration is present in α-keratin, contracted myosin, and some other fibrous proteins and also in hemoglobin and other globular proteins.[1]

The second hydrogen-bonded spiral is the five-residue spiral, in which there are about 5.1 residues per turn and each residue is hydrogen-bonded to the fifth residue from it in each direction. The unit translation is 0.96 Å. We believe that this spiral is present in supercontracted keratin, which is formed from α-keratin with a shrinkage of about 35% in the fiber direction.

We are indebted to Drs. H. R. Branson and S. Weinbaum for assistance. Our work has been aided by grants from the Rockefeller Foundation and the National Foundation for Infantile Paralysis. A detailed account of the work will be published soon.

(1) A three-residue spiral described by Huggins (*Chem. Rev.*, **32**, 211 (1943)) is similar to ours, but differs from it in essential structural details.

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RECEIVED OCTOBER 16, 1950

CHEMICAL NATURE AND SYNTHESIS OF THE *LACTOBACILLUS BULGARICUS* FACTOR[1]

Sir:

The presence of 65–75% of bound pantothenic acid in concentrates of the *Lactobacillus bulgaricus* factor (LBF)[2] indicated that the unidentified portion(s) of the molecule must be relatively small in size. Hydrolysates of such preparations[2] had an unpleasant odor reminiscent of sulfur compounds. Application of the iodine-azide reagent[3] to paper chromatograms of LBF confirmed the presence of sulfur. In acid hydrolysates, a sulfur-containing fragment that also gave a color with ninhydrin and with nitroprusside–cyanide reagent appeared on papergrams. Since LBF is essentially neutral and is not destroyed by nitrous acid[4] it contains no free amino or carboxyl groups. An amide linkage between pantothenic acid and a mercaptoamine (or the corresponding disulfide) is thus indicated. Biogenetic and analytical considerations pointed to β-mercaptoethylamine as a possible fragment. Pure β-mercaptoethylamine[5] showed the same R_F value on papergrams (0.43;

(1) Supported in part by grants from Parke, Davis and Co., and the National Institutes of Health.
(2) G. M. Brown, J. A. Craig and E. E. Snell, *Arch. Biochem.*, **27**, 473 (1950).
(3) E. Chargaff, C. Levine and C. Green, *J. Biol. Chem.*, **175**, 67 (1948).
(4) W. L. Williams, E. Hoff-Jorgensen and E. E. Snell, *ibid.*, **177**, 933 (1949).
(5) E. J. Mills and M. T. Bogert, THIS JOURNAL, **62**, 1173 (1940).