five for ethanol. In the liquid–solid equilibria, the rule of the number of layers being the larger the larger the dielectric constant is even more predominant than in vapor–solid equilibria.

The number of sites calculated from the three optimum curves, as well as the value of the slope, corresponds very closely with those obtained in different circumstances using conventional techniques (6). In the cited references, the ratio of adsorption to desorption rate (k_+/k_-) was related to the dielectric constant by a log reciprocal relationship; *i.e.*, log $[k_+/k_-] = \alpha \cdot (1/\epsilon) + \beta$. Comparison of log $[k_+/k_-]$ calculated by inserting the dielectric constants for ethanol, methanol, and acetonitrile into the equation of *Reference 6* with values obtained in this study gives good correlation, as shown in the last two columns of Table I. The number of sites obtained in *Reference 6* also agrees with those found in this study to within an order of magnitude (10^{19}–$6 \cdot 10^{19}$ sites/g. vis-a-vis $7 \cdot 10^{19}$ sites/g.).

The value of the described approach is not only that of establishing the number of layers of solvent in the montmorillonite but, from an experimental point of view, also of pointing out the necessity of volume adjustment in establishing adsorption isotherms in solutions where solvent intercalation into the adsorbing species is a possibility.

SUMMARY

The effect of solvent intercalation in adsorption isotherms of montmorillonite from solvents with a high dielectric constant was described, and it was shown that the number of solvent layers in the interlaminar spacing is higher than when montmorillonite is equilibrated with the vapor. The utility of this point in establishing isotherms was described.

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New Compounds: Convenient Preparation of Nicotinoyl Glycine Derivatives

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Abstract □ A simple preparation of nicotinoyl glycine derivatives by the anhydride method is reported.

Keyphrases □ Nicotinoyl glycine derivatives—convenient preparation, anhydride method □ Nicotinic anhydride and methyl glycinate—convenient preparation of nicotinoyl glycine derivatives

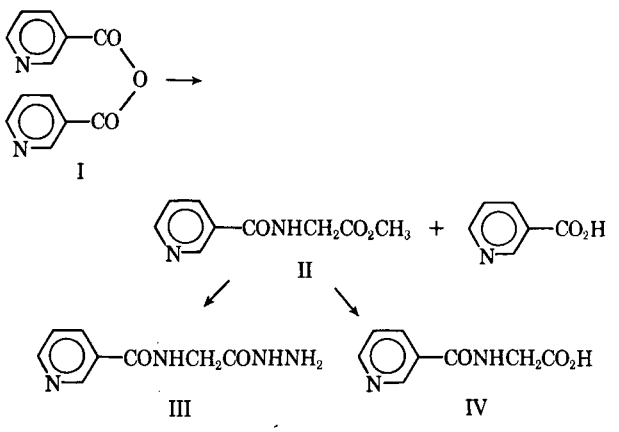
A new convenient preparation of nicotinoyl glycine derivatives, consisting of treatment of nicotinic anhydride (I) (1) with methyl glycinate, was developed. Since I and the amino acid esters are soluble in nonpolar solvents while the nicotinic acid formed in the reaction is insoluble, the product can be isolated conveniently.

Nicotinoyl glycine methyl ester (II) was obtained in good yield by treatment of I with equivalent amounts of methyl glycinate in chloroform and dioxane at room temperature. The by-product, nicotinic acid, was removed by filtration. Compound II was then treated with hydrazine hydrate in ethanol to give nicotinoyl glycine hydrazide (III) (2) in 81% yield (Scheme I).

Saponification of II with aqueous sodium hydroxide, followed by acidification, yielded nicotinoyl glycine (IV) (3) in 75% yield. The IR spectrum was identical with an authentic sample of IV and a mixed melting point gave no depression.

EXPERIMENTAL

Nicotinoyl Glycine Hydrazide (III)—Compound I (1.14 g., 0.005 mole) was dissolved in 30 ml. of chloroform with the aid of 20 ml. of dioxane. The solution was added with stirring to a solution prepared from methyl glycinate hydrochloride (0.63 g., 0.005 mole) and triethylamine (0.75 ml.) in chloroform (20 ml.). After 1 hr., the nicotinic acid was removed by filtration, and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in 10 ml. of ethanol containing 1 ml. of 85% hydrazine hydrate and



Scheme I

heated under reflux for 1 hr. The solvent was then removed under reduced pressure, and the solid was recrystallized from ethanol to give 0.84 g. (81% from I) of nicotinoyl glycine hydrazide, m.p. 177–180°. Recrystallization gave an analytical sample from ethanol, m.p. 179–180° [lit. (2) m.p. 178.5°]; $\nu_{max.}^{mineral\ oil}$ 3300, 1640, 1600, and 1550 cm.$^{-1}$.

Anal.—Calc. for $C_8H_{10}N_4O_2$: C, 49.50; H, 5.14. Found: C, 49.69; H, 5.39.

Nicotinoyl Glycine (IV)—Compound I (1.14 g., 0.005 mole) and methyl glycinate hydrochloride (0.63 g., 0.005 mole) were suspended in 50 ml. of dry benzene, the mixture was heated under reflux for 20 hr., and any undissolved material was separated from the hot solution. The filtrate was evaporated under reduced pressure, and the residue was treated with 6 ml. of 1 *N* NaOH. After acidification to pH 2 with 2 *N* HCl, followed by evaporation to dryness under reduced pressure, the residual solid was recrystallized from water to give 0.69 g. of IV, m.p. 245–246° (3). This weight represented a yield of 75% from I.

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COMMUNICATIONS

A New Antibacterial Mode of Action for Sulfonamides

Keyphrases ☐ Sulfonamides—antibacterial mechanism ☐ Antibacterial agents—sulfonamides, mode of action ☐ Streptococci, oral—mechanism of antibacterial sulfonamides ☐ Sulfadiazine-containing agar medium—growth of oral streptococci

Sir:

The several species of common human oral streptococci differ in their use of the sucrose molecule. *Streptococcus salivarius* forms a levan-type extracellular polysaccharide from the fructose portion of sucrose, *Streptococcus mutans* forms a dextran-type extracellular polysaccharide from the glucose portion of sucrose, and *Streptococcus mitis* is incapable of forming any extracellular polysaccharide from sucrose. Of these streptococci, only *Strep. mutans* is resistant to the inhibitory effect of sulfonamides. *Streptococcus faecalis*, which is found transitorily in the mouth, is also resistant to sulfonamides but is incapable of forming any extracellular polysaccharide from sucrose.

During a study on the metabolic relationships of the oral streptococci, we grew the organisms on an agar medium composed of: 1.5% trypticase peptone[1], 0.5% NaCl, 0.2% sulfadiazine[2], 1% total sugar(s), 0.002% phenol red, and 0.8% Oxoid Ionagar No. 2[3]. The sugars used as energy sources were: sucrose alone, glucose alone, fructose alone, and an equimolar mixture of glucose and fructose. The inoculated plates were observed after 24 hr. of incubation at 37°. The results are shown in Table I.

Surprisingly, the sulfadiazine-sensitive streptococci *Strep. salivarius* and *Strep. mitis*, were able to grow on the sulfadiazine-containing agar medium supplemented with fructose. Subsequently, a wider variety of bacteria was inoculated into liquid media containing: 1.5% trypticase peptone, 0.5% NaCl, 0.2% sulfadiazine, 1% methionine, either 1% glucose or 1% fructose, and 0.002% phenol red. The inoculated tubes were observed after 24 hr. of incubation at 37° (or at room temperature for *Leuconostoc*). The results are shown in Table II.

From the data in Tables I and II, two basic observations were made concerning the growth of the organisms on the sulfadiazine-containing media: (*a*) all the sulfadiazine-resistant bacteria typically grew and formed acid from fructose and from glucose; and (*b*) with the exception of two species, all the sulfadiazine-sensitive bacteria typically grew and formed acid from fructose but did not grow in the presence of glucose. Each of the typical organisms, whether resistant or sensitive to

Table I—Growth of *Strep. faecalis* and Common Human Oral Streptococci on Sulfadiazine-Containing Agar Medium Supplemented with Sucrose or Glucose and/or Fructose

	Energy Source			
Organism[a]	Sucrose	Glucose	Fructose	Glucose and Fructose
Strep. faecalis F24	+[b]	+	+	+
Strep. mutans BHT	+	+	+	+
Strep. salivarius HHT[c]	+	−	+	+
Strep. mitis 903[c]	−	−	+	+

[a] Obtained from Dr. Allan L. Delisle, Department of Microbiology, School of Dentistry, University of Maryland. [b] + = growth *with acidity*; − = no growth. [c] Sensitive to sulfonamides.

[1] BBL (Baltimore Biological Laboratories), Cockeysville, Md.
[2] Eli Lilly and Co., Indianapolis, Ind.
[3] Colab Laboratories, Inc., Glenwood, Ill.