cooling. The salt which formed in 80–90% yield consisted of colorless, deliquescent crystals which could be recrystallized from absolute alcohol. However, only the urea ethyl sulfate could be thus recrystallized to a constant melting point. Their neutralization equivalents were as given in Table I.

Anal. Calculated for $C_3H_{10}O_5N_2S$: C, 19.3; H, 5.59; N, 14.8. Found: C, 19.4; H, 5.38; N, 15.0.

When the urea ethyl sulfate was prepared from chlorosulfonic acid, using the same procedure as for sulfuryl chloride except that equal moles of alcohol and chlorosulfonic acid were employed, almost the theoretical yield of sulfate was obtained m. p. 126.5°, which gave no depression of the melting point when mixed with some of the same salt prepared from the sulfuryl chloride.

These alkyl urea sulfates form urea nitrate (slowly) and urea picrate, and give the biuret and furfuryl alcohol tests for urea. In aqueous solution they are strongly acid and their neutralization equivalents correspond to the expected formulas. When treated with barium chloride they give no appreciable precipitate unless they have been previously boiled with concentrated mineral acid, such as hydrochloric or nitric acids. Their property of deliquescence tends to give indefinite melting points.

Summary.—(1) The hitherto unknown urea alkyl sulfates are described. (2) It has been shown that the main reaction products of alcohols with sulfuryl chloride are alkyl hydrogen sulfates. (3) The isolation of ethyl hydrogen sulfate as the urea salt is far superior to its isolation as a metallic salt.

DUNEDIN, N 1, NEW ZEALAND

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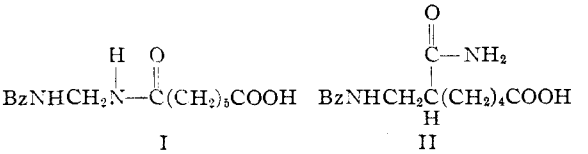
The Preparation of N-(Benzamidomethyl)-pimelamic Acid: A Correction

BY JACKSON P. ENGLISH AND RICHARD C. CLAPP

We have previously reported the synthesis of a compound which was assumed to be 7-benzoylamino-6-carbamylheptylic acid.[1] This compound was thought to result as the product of a synthesis which began with the condensation of N-methylolbenzamide and a substituted cyanoacetic ester. We are indebted to Dr. S. R. Buc, who permitted us to see his manuscript before publication, for pointing out that the initial reaction has taken another and isomeric course. The work which led him to this conclusion is published concurrently.[2] With his demonstration of the course of the reaction we have now been enabled to show that the product of the series of reactions described in the previous note is N-(benzamidomethyl)-pimelamic acid, I, and not the heptylic acid derivative, II (compound IV of the earlier publication). This was shown by its conversion into formaldehyde, benzoic acid, and pimelic acid by acid hydrolysis. These products are not possible with the earlier formulation.



(1) J. P. English and R. C. Clapp, THIS JOURNAL, **67**, 2262 (1945).
(2) S. R. Buc, *ibid.*, **69**, 254 (1947).

Experimental

Hydrolysis of N-(benzamidomethyl)-pimelamic Acid (I).—A solution of 302 mg. of N-(benzamidomethyl)-pimelamic acid in 10 cc. of water and 5 cc. of concentrated hydrochloric acid was refluxed for six hours. The flask was swept out with nitrogen throughout the period of refluxing, and the emergent gas was bubbled through alcoholic dimedone solution. A total of 123 mg. of a crude precipitate melting from 170 to 180° was obtained. This product melted at 188 to 190° after recrystallization and did not depress the melting point of a sample of the dimedone derivative of formaldehyde.[3] Considerable solid collected in the condenser during the refluxing, and removal by washing with ether yielded 78 mg. of a product melting from 116 to 120° that was proved to be benzoic acid (62%) by a mixed melting point.

Approximately 20 cc. of water was added to the solution from the hydrolysis, and it was concentrated to a small volume. Treatment of the distillate with dimedone solution gave an additional 27 mg. of the dimedone derivative of formaldehyde (total of 50% of theoretical yield). Steam distillation of the remaining solution yielded no additional benzoic acid, and concentration to dryness gave 112 mg. of a solid melting from 95 to 100°. This product melted at 103–105° on recrystallization and was identical with an authentic sample of pimelic acid (68% of theoretical quantity).

(3) "Organic Reagents for Organic Analysis," Chemical Publishing Co., Inc., Brooklyn, N. Y., 1946, p. 44.

STAMFORD RESEARCH LABORATORIES
AMERICAN CYANAMID COMPANY
STAMFORD, CONNECTICUT RECEIVED SEPTEMBER 28, 1946

Tryptophan as a Competitive Growth Inhibiting Analog of Phenylalanine

BY ERNEST BEERSTECHER, JR., AND WILLIAM SHIVE

Burrows and Neymann[1] pointed out nearly thirty years ago that pure α-amino acids inhibit the growth of living cells. Wyon and McLeod[2] shortly thereafter showed that tryptophan in concentrations of 30 millimoles per liter was toxic to the growth of certain bacteria. Gordon and McLeod[3] later showed that serum reversed this tryptophan toxicity. More recently Sullivan, *et al.*,[4] have pointed out that high tryptophan diets are injurious to rats. Most early workers attributed the toxicity of tryptophan to the formation of decomposition products in the medium. Modern studies have considered the toxicity of some other amino acids from the stand-point of competition with another metabolite for some enzyme system essential to the growth of the organism.[5] In the light of our present understanding of analog inhibition, it therefore seems strange that some of the β-substituted alanines, particularly those substituted with aromatic groups, have not been demonstrated to be mutual antagonists.

We have recently had occasion to study the effect of *dl*-phenylalanine on bacterial growth in the presence of large concentrations of trypto-

(1) M. T. Burrows and C. A. Neymann, *J. Exp. Med.*, **25**, 93 (1917).
(2) G. A. Wyon and J. W. McLeod, *J. Hyg.*, **21**, 376 (1923).
(3) J. Gordon and J. W. McLeod, *J. Path. Bact.*, **29**, 13 (1926).
(4) M. X. Sullivan, W. C. Hess and W. H. Sebrell, *U. S. Pub. Health Repts.*, **47**, 75 (1932).
(5) R. O. Roblin, Jr., *Chem. Rev.*, **38**, 255 (1946).

phan.[6] The medium of Stokes, *et al.*,[7] was employed with *Streptococcus faecalis* R which was incubated for thirty-seven hours at 31°. The tests were conducted at a number of levels of tryptophan, and the results obtained are shown in Fig. 1.

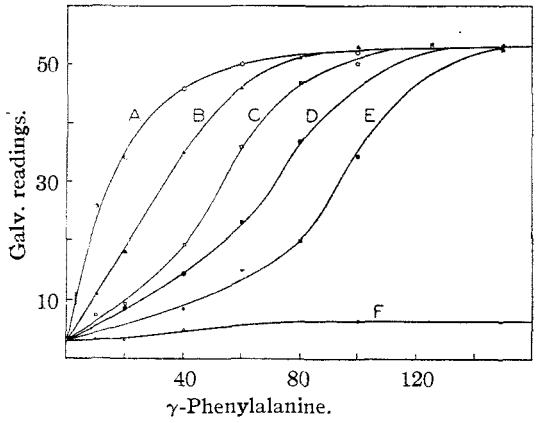


Fig. 1.—Prevention of the toxicity of *dl*-tryptophan for *Streptococcus faecalis* R by *dl*-phenylalanine: Curve A, 2000 γ *dl*-tryptophan per 10 cc. of culture medium; Curve B, 4000 γ; Curve C, 6000 γ; Curve D, 8000 γ; Curve E, 10,000 γ; Curve F, 0 γ. Galvanometer readings, a measure of culture turbidity; distilled water reads zero, an opaque object 100. γ-Phenylalanine, quantity of phenylalanine per 10 cc. of culture medium.

As shown, *dl*-tryptophan prevented growth of *Streptococcus faecalis* R when relatively low concentrations of phenylalanine are present, and the inhibition was competitive in nature; *i. e.*, it became apparent only when the *ratio* of tryptophan to phenylalanine exceeded a certain value and was independent of the absolute amount of inhibitor over the range of concentrations of the tests. Over this range of concentrations, a ratio of *dl*-tryptophan to *dl*-phenylalanine of about 100:1 was sufficient to cause a 50% inhibition of growth as measured turbidimetrically. Such an effect indicates that tryptophan competes with phenylalanine for an enzyme, the functioning of which is essential for growth of the organism. Similar effects may be observed with *l*-tryptophan in place of the racemic form and with *Lactobacillus casei* and *Staphylococcus aureus* as well as with *Streptococcus faecalis* R.

While it is admittedly improbable that ratios of tryptophan to phenylalanine of the magnitude of 100:1 would ever actually exist in nature, it is of importance to realize that such natural analog–metabolite pairs do exist, and that they may by cumulative effects constitute a complex system of biological balances and controls.

(6) E. Beerstecher, Jr., and W. Shive, *J. Biol. Chem.*, **164**, 53 (1946).

(7) J. L. Stokes, M. Gunness, I. M. Dwyer and M. C. Caswell, *ibid.*, **160**, 35 (1945).

THE CLAYTON BIOCHEMICAL INSTITUTE
AND THE DEPARTMENT OF CHEMISTRY
THE UNIVERSITY OF TEXAS
AUSTIN, TEXAS RECEIVED SEPTEMBER 30, 1946

Surface Area of Chrome-Plated Nickel

BY CALLAWAY BROWN AND HERBERT H. UHLIG*

In studies of reaction rates on apparently plane metal strips, the area available for reaction is an important undetermined factor. Bowden and Rideal,[1] from studies of electrolytic hydrogen deposition on metal electrodes, conclude that the interfacial area may be very much higher than the apparent or projected area even on apparently smooth surfaces such as polished silver, and annealed, electroplated or rolled nickel. Although these results appear entirely consistent, the method is indirect and the significance of the "accessible" areas obtained has not been clarified by independent measurements.

Quantitative determination of the area of a gas–solid interface by low-temperature adsorption of inert gas[2] has been applied largely to powdered materials because of the large ratio of surface to volume available. However, by use of an adsorption reagent at very low temperature and pressure, surface areas smaller than 100 sq. cm. may be measured.[3] We have applied this low-pressure adsorption technique to strips of chrome-plated nickel and find a large ratio of accessible to apparent area, sensitive to the previous history of the sample. This result confirms a similar conclusion[4] based on studies of the quantity of passive iron adsorbed on electrodeposited chromium.

Preliminary tests with ethylene showed that large quantities of this gas were sorbed by chrome-plated nickel at room temperature and at low pressure. The sorption was irreversible and increased slowly for many hours, typical of activated adsorption. This complication made ethylene unsuitable for surface area determination by physical adsorption at low temperature, but it is of interest that the quantity of ethylene ultimately sorbed at room temperature and at very low pressure was sufficient to cover in a unimolecular layer an area about 20 times the apparent area. Sample 3 in Table I, taken from the same lot of chrome plate, was later found to have a ratio of accessible to apparent area of 49, so that the ethylene sorbed actually covered less than one half the accessible area.

Ethane at −183° was chosen for the low temperature work as it was practically unadsorbed at room temperature and equilibrated rapidly and reversibly at −183°. Nickel strips 5 cm. wide, 15 cm. long, and approximately 0.6 cm. thick were chrome-plated by standard commercial practice. A single strip was usually cut in half, cleaned with fine silica sand, washed with

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(1) F. Bowden and E. Rideal, *Proc. Roy. Soc.* (London), **A120**, 59, 80 (1928).

(2) S. Brunauer, P. H. Emmett and E. Teller, THIS JOURNAL, **60**, 309 (1938).

(3) L. A. Wooten and C. Brown, *ibid.*, **65**, 113 (1943).

(4) H. H. Uhlig, unpublished data.