only small pressures or vacua are developed is shown in Plate 1.

Pieces of tubing, mouths of flasks, etc., are simply flared and given a flat lip, and then this lip is grounded in the usual manner by emery on a flat glass surface. The customary small glass arms for anchorage of rubber bands for holding pieces together can be easily fused to the main element.

The writer has built "T's," "L's," and straight lengths of tubing of varying lengths which are all

SPECIAL ARTICLES

A SYNTHETIC PEPTIDE AS SUBSTRATE FOR TRYPTIC PROTEINASE

LITTLE is known regarding the mechanism and the specificity of those enzymes which split true proteins — the proteinases. This is due to the fact that until recently it was not possible to obtain a proteinase substrate of known structure.

By means of the carbobenzoxy method¹ a peptidelike substrate for tryptic proteinase was synthesized. It is a derivative of the tripeptide glycyl glutamyl glycine (I). The amino group at one end of the molecule was blocked with the carbobenzoxy group, and the glycine carboxyl on the other end was esterified with ethyl alcohol (II). Thus the only free reactive group was the γ -carboxyl of the glutamic acid.

$$\begin{array}{c} \text{COOH} \\ (\text{CH}_2)_2 \\ \text{NH}_2 \cdot \text{CH}_2 \cdot \text{CO} - \text{NH} \cdot \text{CH} \cdot \text{CO} - \text{NH} \cdot \text{CH}_2 \cdot \text{COOH} \\ \text{I} \\ \text{C}_{\theta}\text{H}_{\theta} \cdot \text{CH}_2 \cdot \text{O} \cdot \text{CO} \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{CO} - \begin{array}{c} (\text{CH}_2)_2 \\ \text{O} \cdot \text{CO} + \text{O} \cdot \text{CO} - \text{O} + \text{O} \cdot \text{CO} - \text{O} + \text{O} \cdot \text{CH}_2 \cdot \text{COOC}_2 \text{H} \\ \text{II} \\ \text{C}_{\theta}\text{H}_{\theta} \cdot \text{CH}_2 \cdot \text{O} \cdot \text{CO} \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{COOH} \\ \text{III} \\ \text{COOH} \\ (\text{CH}_2)_2 \\ \text{NH}_2 \cdot \text{CH} \cdot \text{CO} - \text{NH} \cdot \text{CH}_2 \cdot \text{COOC}_2 \text{H}_5 \\ \text{IV} \end{array}$$

Substance II was split quite rapidly by pancreatin Merck as well as by a preparation of crystalline trypsin (tryptic proteinase) kindly placed at our disposal by Dr. John H. Northrop. The products of the splitting were carbobenzoxy glycine (III) and glutamyl glycine ester (IV). The latter product is rapidly transformed to a diketopiperazine under the conditions of the experiment.

¹ M. Bergmann, SCIENCE, 79: 439, 1934.

surprisingly interchangeable. Figs. 1 and 2 give a simple method for reducing the diameter of a tube *i.e.*, by the insertion of a ground glass disk with a hole in it. The ground glass disk idea is also satisfactory where it is desired to have two tubes connect with one vessel or another tube. Fig. 3 shows a straight connection involving the same size tubing.

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This experiment shows that tryptic proteinase does not require for its action linkages of unknown nature, but is able to split ordinary peptide linkages if the rest of the molecule fulfils certain structural requirements. In II one of these requirements is the presence of the free γ -carboxyl, which combines with the tryptic proteinase and thus enables it to split the peptide.

It is probable that the other amino dicarboxylic and diamino carboxylic constituents of the proteins play a rôle similar to that of glutamic acid in combining with proteinases by means of their extra acid or basic groups. From the work of Gurin and Clarke² it is to be expected that the ε -amino group of lysine in a protein combines with pepsin. By means of the carbobenzoxy method we are preparing peptides of lysine and aspartic acid and shall report on their behavior towards proteinases in the near future. The theoretical significance of these results as well as the interesting experiments of Matsui,³ Ishiyama⁴ and Shibata⁵ on the splitting of diketopiperazines will be discussed in a future publication.

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THE ELECTRICAL RESPONSE OF THE VES-TIBULAR NERVE DURING ADEQUATE STIMULATION

A STRIKING characteristic of the vestibular nystagmus which is produced in virtually all vertebrate species by the angular retardation incident to the termination of a prolonged period of uniform bodily rotation (also by the acceleration incident to the onset of such a period of rotation) is that this response ordinarily persists for a considerable time often 20 or 30 seconds—after the cessation of its

³J. Matsui, Jour. Biochem., 17: 163, 253, 1933.

⁵ K. Shibata, Acta Phytochimica, 8: 173, 1934.

² S. Gurin and H. T. Clarke, Jour. Biol. Chem., 107: 395, 1934.

⁴ T. Ishiyama, Jour. Biochem., 17: 285, 1933.