be very similar to fibrinogen molecules in size and shape. But when the urea concentration is reduced to 2.35 *M*, two peaks appear in the sedimentation diagram, with constants of 9 and 25 *S*.

The presence of the fast peak, both in partly polymerized fibrinogen inhibited by glycol or urea, and in depolymerized fibrin in urea, is always accompanied by a high viscosity which depends markedly on the rate of shear. The reduced specific viscosity falls rapidly with dilution of the protein, however, approaching that characteristic of the original fibrinogen, indicating dissociation of long linear aggregates.

The behavior of the intermediate represented by the fast peak is thus the same whether it is formed from fibrinogen by the action of thrombin or from urea-depolymerized fibrin by decreasing the concentration of urea.[4]

We are much indebted to Professor J. W. Williams for use of the Svedberg oil turbine ultracentrifuge.

(4) In general agreement with the experience of Mihályi,[5] there was no evidence, under the conditions of our experiments, of the denaturation which is observed[5] at somewhat higher urea concentrations or temperatures (or lower *p*H). Fibrinogen in 2.35 *M* urea had the same intrinsic viscosity as in the absence of urea; and the solubility of fibrinogen was not impaired by contact for 18 hours with 3.5 *M* urea, at *p*H 7.5, room temperature, and subsequent removal of the urea by dialysis. These criteria are of course not applicable to fibrin, but the susceptibilities of fibrinogen and fibrin to denaturation should be similar. Also, the viscosity of a fibrin solution in 3.5 *M* urea at *p*H 6.3 showed no change with time for two days, indicating that no progressive changes were taking place.

(5) E. Mihályi, *Acta Chem. Scand.*, **4**, 317 (1950).

DEPARTMENT OF CHEMISTRY SIDNEY SHULMAN
UNIVERSITY OF WISCONSIN PAUL EHRLICH
MADISON, WISCONSIN JOHN D. FERRY

RECEIVED FEBRUARY 12, 1951

DIETHYL CHLOROARSENITE AS A REAGENT FOR THE PREPARATION OF PEPTIDES

Sir:

In the course of an investigation in these Laboratories of methods of peptide synthesis, new reagents for forming the peptide linkage at either the amino or carboxylic function of an aminoacid or peptide chain have been found. The use of diethyl chlorophosphite has been reported recently.[1] Similarly, diethyl chloroarsenite[2] reacts readily with aminoacid esters and with N-substituted aminoacids to give highly reactive amides and anhydrides, respectively. The new reagent has advantages over the phosphite analog in being stable and readily prepared. Comparable yields are obtained with either reagent.

Both the amides, $(C_2H_5O)_2AsNHCH(R)COOR'$, and the anhydrides, $R'NHCH(R)COOAs(OC_2H_5)_2$, are non-distillable oils which are conveniently prepared and reacted without isolation. The reactions are accomplished in an inert solvent in the presence of an equivalent of triethylamine as the acid acceptor. After removal of the precipitated triethylamine hydrochloride, the solution of the intermediate diethylarsenite amide or anhydride is refluxed one hour with an equivalent of a second N-substituted aminoacid or aminoacid ester, respectively. The by-product, presumably diethyl arsenite in both cases, is precipitated quantitatively as arsenic trioxide by addition of water.

The N-substituted peptide ester prepared by either of these procedures is obtained crystalline by first extracting the reaction solution successively with dilute sodium bicarbonate and dilute hydrochloric acid and then concentrating in an air stream. One crystallization from ethanol–water or ethyl acetate–petroleum ether generally has given pure products.

Prepared by the intermediate amide method were carbobenzoxyglycine anilide[3] (79%), m.p. 144–145°; carbobenzoxyglycine morpholide[4] (70%), m.p. 144–145°; ethyl carbobenzoxyglycyl-DL-phenylalanate[5] (59%), m.p. 91–92°; ethyl phthalyl-DL-alanyl-DL-valinate[4] (71%), m.p. 121–123°; and ethyl carbobenzoxyglycyl-L-tyrosinate (74%), m.p. 125–126° (a mixed m.p. with an authentic sample[6] was not depressed).

Prepared by the anhydride method were carbobenzoxyglycine anilide[3] (63%), m.p. 146–147°; ethyl carbobenzoxyglycyl-DL-phenylalanate[5] (52%), m.p. 92–93°; ethyl carbobenzoxy-DL-alanyl-DL-phenylalanate[4] (60%), m.p. 104–106°; ethyl carbobenzoxy-L-leucyl-DL-phenylalanate[4] (74%), m.p. *ca.* 90° $[\alpha]^{24}D$ −9.2° (*c* = 5, 95% ethanol) and ethyl carbobenzoxyglycylglycyl-DL-phenylalanate monohydrate[4] (30%), m.p. 80–82° (from ethyl phenylalanate and the diethyl arsenite anhydride from carbobenzoxyglycylglycine).

(1) Anderson, Welcher and Young, THIS JOURNAL, **72**, 501 (1951).
(2) McKenzie and Wood, *J. Chem. Soc.*, **117**, 406 (1920).
(3) Wieland and Sehring, *Ann.*, **569**, 122 (1950).
(4) Carbon, hydrogen and nitrogen analyses were satisfactory.
(5) Neurath, *et al.*, *J. Biol. Chem.*, **170**, 222 (1947).
(6) Bergmann and Fruton, *ibid.*, **118**, 412 (1937).

CHEMOTHERAPY DIVISION
STAMFORD RESEARCH LABORATORIES
AMERICAN CYANAMID COMPANY JAMES R. VAUGHAN, JR.
STAMFORD, CONNECTICUT

RECEIVED FEBRUARY 7, 1951

CRYSTALLINE XYLOBIOSE AND XYLOTRIOSE

Sir:

Charcoal chromatography of partially hydrolyzed xylan permits the separation and isolation of a considerable amount of crystalline xylobiose and xylotriose. This is the first isolation of crystalline di- and trisaccharides composed only of pentose sugar units.

In one instance a 2% solution of xylan in 42% hydrochloric acid was hydrolyzed at 0° until the reaction was 66% complete as indicated by reducing value and by optical rotation. The hydrolyzate was neutralized with sodium bicarbonate and chromatographically separated on charcoal columns following the method of Whistler and Durso.[1] After washing the column with water, xylobiose was removed with 5% ethanol. The sirupy concentrate from this extraction was dissolved in a small amount of warm water and hot methanol added. On cooling, crystallization occurred. The yield was 4.8% of the xylan used, m.p. 186–187°; $[\alpha]D^{25}$ −32.0→−25.5 (1 hour) (*c*, 1 in water).

(1) Roy L. Whistler and Donald F. Durso, THIS JOURNAL, **72**, 677 (1950).