zene light petroleum ether mixture, m.p. 129°; identified as IIa.

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Syntheses of Poly-β-aspartyl Dipeptides

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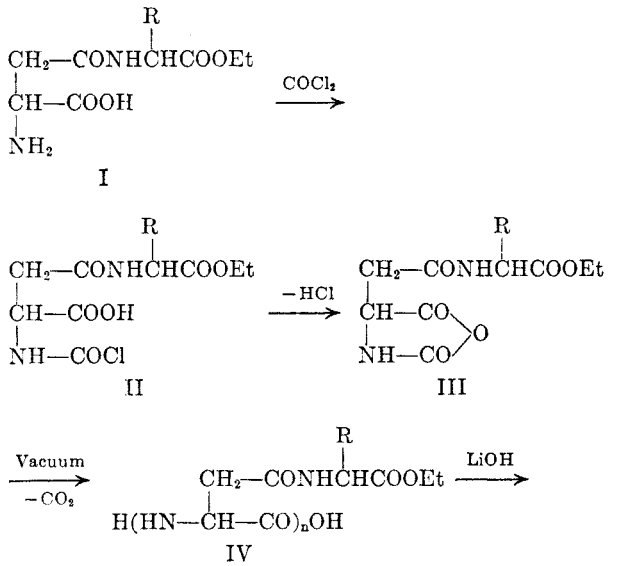
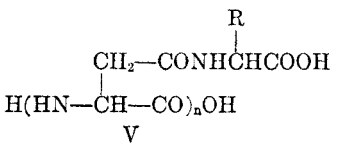
In continuation of previous work[1] on the polymerization of trifunctional amino acids, polyaspartic acids having their β-carboxyl group linked to other amino acids in a peptide linkage were prepared. These polymers are interesting in that they have a dipeptide linked to the backbone of a polymeric amino acid.

These polymers were prepared according to the accompanying scheme starting with DL-β-aspartyl-dipeptide ethyl esters (I) prepared by the maleic anhydride method[2] previously described. Passing phosgene into a suspension of these compounds in dioxane yielded their *N*-carboxy anhydride (III) probably through the intermediate *N*-chloroformyl derivatives (II), which were polymerized by heating *in vacuo*. The resulting poly-DL-β-aspartyl dipeptide



esters (IV) yielded the poly free dipeptides (V) on mild hydrolysis with lithium hydroxide (1*N*).



The polymers thus prepared included poly-DL-β-aspartylglycine, poly-DL-β-aspartyl-DL-alanine, poly-DL-β-aspartyl-DL-valine, poly-DL-β-aspartyl-DL-phenylalanine.

The poly dipeptides differed from the poly dipeptide esters in having much higher melting points and being more soluble in water and less in ethanol and other organic solvents. Their R_f-values were also much lower. They gave positive biuret reaction and positive ninhydrine after prolonged boiling.

Total hydrolysis of poly-DL-β-aspartylglycine ethyl ester was accomplished by refluxing the polymer in hydrochloric acid (5*N*) for 20 hr. This was confirmed by α-amino nitrogen determinations on the hydrolysate and paper partition chromatography whereby the characteristic spots of aspartic acid and glycine were obtained.

EXPERIMENTAL

Micro analyses are by Drs. Weiler and Strauss.

In the following a general description is given for the preparation of the *N*-carboxy anhydrides, poly-β-aspartyl dipeptide esters, and poly-β-aspartyl dipeptides, the specific polymers and their properties being tabulated in the accompanying table.

Preparation of N-carboxy anhydrides of DL-β-*aspartyl dipeptide ethyl esters.* To a suspension of 2 g. DL-β-aspartyl dipeptide ethyl ester, previously dried in a vacuum desiccator, in 100 ml. dry dioxane placed in a three-necked flask fitted with a mechanical stirrer, gas leading tube, and reflux condenser protected with a calcium chloride tube, phosgene dried over concentrated sulfuric acid was passed for 1 hr. at 60°. The substance dissolved during reaction. The solution was evaporated *in vacuo* at 40°, and the *N*-carboxy anhydride remained as a viscous oil which refused to crystallize.

*Poly-*DL-β-*aspartyl-dipeptide ethyl esters.* The *N*-carboxy anhydride was heated in a high vacuum system. At 60° there was gas evolution which stopped and started once more at about 80°. The heating was continued and the temperature allowed to reach 110–120°, after 2 hr. On cooling the polymer solidified.

*Poly-*DL-β-*aspartyl-dipeptides.* Poly-DL-β-aspartyl dipeptide ester (0.2 g.) was dissolved in 3 ml. lithium hydroxide (1*N*) and left for 2–3 hr. at room temperature. Where the polymer was insoluble in water, ethanol was added to effect solution. The solution was acidified with hydrochloric acid and evaporated to dryness *in vacuo*, leaving, sometimes, an oily residue which crystallized on addition of absolute ethanol. The polymer was filtered and washed with absolute ethanol to remove lithium chloride; water insoluble polymers were washed with this solvent. Only slight hydrolysis of the peptide linkages occurred under these conditions.

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TABLE I

POLY-DL-β-ASPARTYL DIPEPTIDE ETHYL ESTERS AND POLY-DL-β-ASPARTYL DIPEPTIDES

Poly-DL-Aspartyl-	Chain Length	Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Van-Slyke Nitrogen, %		Remarks (Solubility, yield, etc.)
			Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	
Glycine ethyl ester	8	$C_{64}H_{98}N_{16}O_{33}$	47.4	47.2	6.0	6.0	13.8	13.6	0.87	0.9	Soluble with difficulty in water, easily in ethanol, acetone, ethyl acetate, acetic acid, and chloroform, insoluble ether. M.p. 130°. R_f (80% phenol) = 0.9
Alanine ethyl ester	7	$C_{67}H_{100}N_{14}O_{29}$	49.9	47.7	6.6	6.4	12.9	12.0	0.93	1.0	Soluble with difficulty in water, easily in ethanol
Valine ethyl ester	7	$C_{77}H_{128}N_{14}O_{29}$	54.0	52.2	7.5	7.4	11.4	10.6	0.82	0.8	Soluble ethanol, glacial acetic acid, insoluble water and dilute alkali
Phenyl alanine ethyl ester	10	$C_{150}H_{182}N_{20}O_{41}$	61.3	59.4	6.2	6.3	9.6	9.0	0.48	0.5	Soluble glacial acetic acid, insoluble water and dilute alkali
Glycine	6	$C_{36}H_{60}N_{12}O_{25}$					16.0	14.7	1.3	1.4	Slightly soluble ethanol. Very soluble water. Yield from ester (70%). M.p. 250°. R_f (80% phenol) = 0.2
Valine	6–7	$C_{58.5}H_{93}N_{13}O_{27}$	49.8	49.5	6.6	6.6	12.9	12.2	1.0	1.0	Insoluble water, yield from ester (60%)
Phenylalanine	9	$C_{117}H_{128}N_{18}O_{37}$	59.0	57.5	5.4	5.5	10.6	10.0	0.6	0.6	Insoluble water, yield 80% from ester