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MICELLAR EFFECT ON THE PREPARATION OF POLY-β-ALANINE FROM β-ALANINE-S-ALKYL ESTERS

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S-Dodecyl, S-decyl, and S-octyl esters of β-alanine were reacted in water in the presence of a base at 100°C for 40 hours to give poly-β-alanine. The yields and the degrees of polycondensation for dodecyl, decyl, and octyl esters were 44, 24, and 2 % and 13, 12, and 20, respectively. Poly-β-alanine was not obtained from S-hexyl and S-ethyl esters. The specific acceleration of polycondensation reaction for the higher alkyl esters was explained by micellar effect.

Hydrochloride of alanine-S-dodecyl ester gave cyclic dimer of alanine, 3,6-dimethyl-2,5-piperazinedione (Ala-Anh) in good yields through the neutralization with base, although hydrochloride of alanine-S-ethyl ester gave no Ala-Anh but alanine. The acceleration of aminolysis for higher alkyl thioester was explained by a matrix reaction on micellar surface.$^{1)}$

S-Dodecyl, S-decyl, S-octyl, S-hexyl, and S-ethyl esters of β-alanine were prepared from β-alanyl chloride and alkyl mercaptans and were reacted in water in the presence of pyridine, NaOH or imidazole at 100°C for 5~80 hours. The results of polycondensation reaction were listed in Table. When the polycondensates were reprecipitated three times from formic acid solution by pouring into methanol, they contained thioalkyl groups at carboxyl chain ends, which could be removed by the treatment with hydroxylamine. In the cases of lower alkyl thioesters the formation of β-alanine was detected. Cyclic dimer of β-alanine was not obtained.

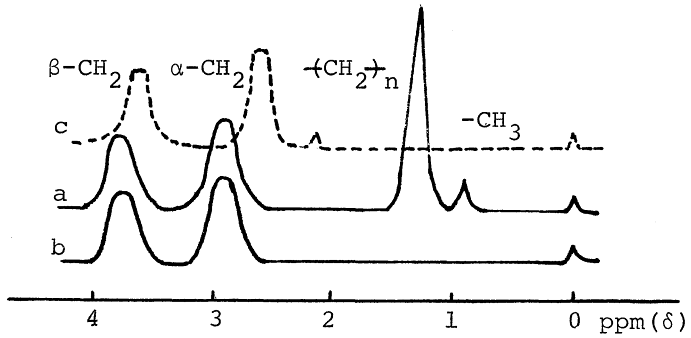

Figure Typical NMR spectra of poly-β-alanine
a —— before dealkylation (in CF_3COOH)
b —— after dealkylation (in CF_3COOH)
c --- poly-β-alanine in Lit.$^{4)}$ (in H_2O)

The degree of polycondensation(DP) was calculated from the integral curve of NMR spectra for α- and β-methylene of β-alanine unit (δ 2.8, δ 3.7) based on that for polyalkyl-methylene (δ 1.3) of thioalkyl chain end. Elementary analyses, mp (footnote of Table), and IR spectra support the calculated DP values. With the increase of reaction time the resulting polyamide deposited out from the reaction mixture and the degree of polycondensation attained to a limiting value. Polycon-

Table Polycondensation reactions of β-alanine-S-alkyl esters

No	Alkyl Group of β-Alanine-S-alkyl Ester	Reaction Time(hr)	Degree of Polycondensation	Yield* (%)
1	dodecyl	40	13	44 e)
2	dodecyl a)	40	13	28
3	dodecyl b)	40	9	31
4	dodecyl c)	40	13	42
5	dodecyl d)	40	-	0
6	dodecyl	5	11	27
7	dodecyl	10	10	35
8	dodecyl	20	12	33
9	dodecyl	80	17	42
10	decyl	40	12	24
11	octyl	40	20	2
12	hexyl	40	-	0
13	dodecyl + SDS**	40	9	50
14	decyl + SDS	40	15	30
15	octyl + SDS	40	19	27
16	hexyl + SDS	40	-	0

β-Alanine-S-alkyl ester 0.03 mole; Solvent, Water 320 ml; Pyridine 8 ml; Reaction temperature 100°C. a) 30 ml of 1 N NaOH instead of pyridine + water 290 ml. b) Imidazole 2.1 g instead of pyridine. c) Water 1920 ml (320 ml x 6). d) Solvent, Water 160 ml + 1,4-dioxane 160 ml. e) mp 304~7°C; 311~20°C after dealkylation; Anal. before dealkylation, Calcd. for $C_{12}H_{25}S(COCH_2CH_2NH)_{11}COCH_2CH_2NH_2\cdot HCl$, C 52.24 H 7.89 N 15.24, Found C 52.63 H 7.97 N 14.40, after dealkylation, Calcd. for $HO(COCH_2CH_2NH)_{11}CO$-$CH_2CH_2NH_2\cdot HCl$, C 47.66 H 6.95 N 18.53, Found C 47.69 H 7.04 N 18.03

* Yield of methanol insoluble polycondensate; mole % based on β-alanine unit.

** SDS: Sodium dodecylbenzenesulfonate 0.7 g

densates obtained at the early stage of the reaction contained a fairly amount of low molecular weight analogs (No 6, ca. 60 wt % was soluble in methanol).

The reaction did not proceed in a dioxane-water (50:50) mixed solvent which retards the formation of micelle. The yield and the degree of polycondensation did not change by dilution of six times (No 4). The yields of polyamides (44, 24, 2, 0, and 0 %) were related to the length of S-alkyl groups (S-dodecyl, S-decyl, S-octyl, S-hexyl, and S-ethyl), and the degrees of polycondensation were independent of alkyl chain length.

The addition of anionic surfactant (SDS) resulted in the increase of the yield of polyamide.

The enhanced reactivity of -CO-S- bond to the attack of $-NH_2$ is a basic factor in this polycondensation reaction, because O-dodecyl and O-ethyl esters of β-alanine gave no condensation product.

From these results the reaction path of the preparation of poly-β-alanine on micellar surface is paralleled to the scheme of biosynthesis of such antibiotic oligopeptides as gramicidin S and tyrocidine.[2,3]

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