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^{13}C-NMR SEQUENCE ANALYSIS—16

SYNTHESIS OF ALTERNATING POLYESTERAMIDES WITH ISOMERIC SEQUENCES OF 4-AMINOBENZOYL, GLYCYL, HYDROXYACETYL AND MERCAPTOACETYL RESIDUES

H. R. KRICHELDORF and J. KASCHIG

Institut für makromolekulare Chemie der Universität, D-7800 Freiburg i.Br., Stefan-Meier Straße 31, W. Germany

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Abstract—Ternary polyesteramides with alternating sequences of 4-aminobenzoyl, glycyl and hydroxyl- or mercaptoacetyl residues were synthesized by thermal condensation polymerization of corresponding isothiocyanatocarboxylic acids. These monomers were prepared in various ways by reaction of 4-isothiocyanatobenzoylchloride with suitable derivatives of glycine and hydroxy- or mercaptoacetic acid. The polymerization conditions must be carefully controlled in order to avoid side-reactions which lead to random sequences. ^{13}C-NMR spectroscopy proved to be suitable for characterization of the sequences.

INTRODUCTION

We have already described the synthesis of polyamides by thermal or base-catalysed condensation polymerization of ω-isothiocyanatocarboxylic acids [1]. This method was especially useful for the synthesis of copolyamides with an alternating sequence of various ω-amino acids [2–5]. Furthermore, alternating copolyamides containing ω-amino acid residues together with ω-amino sulphonic acids were synthesized in this way [6]. Thus, we were interested to test this method for synthesis of polyesteramides or polydepsipeptides with an alternating sequence of ω-amino, ω-hydroxy- and ω-mercapto carboxylic acids. In this paper we report the syntheses of four ternary polyester amides with isomeric sequences. Such copolymers are interesting model compounds for an NMR investigation on sequence (neighbouring residue) effects as well as for studies on the mechanism of thermal degradation. This latter subject will be reported in a later paper.

RESULTS AND DISCUSSION

Synthesis of monomers

Glycine, hydroxyacetic acid and mercaptoacetic acid were chosen as building blocks of the ternary polyesteramides for two reasons:

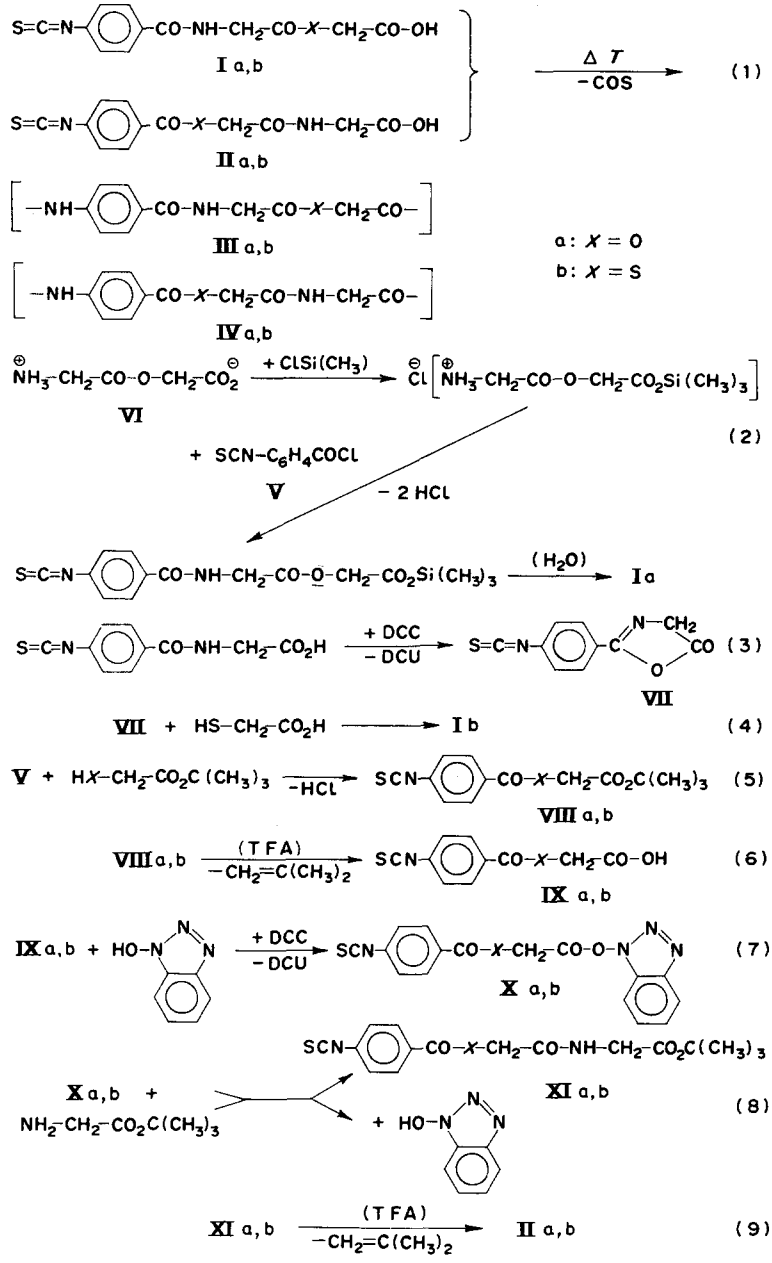
(1) The acids themselves and their precursors (bromoacetic acid and derivatives) are cheap and commercially available; their derivatives, i.e. the tert-butylesters, are easily accessible [7, 8].

(2) Several homo- and copolyesters, -polypeptides and -polyamides containing these building blocks were prepared by us or by other investigators and allow interesting comparisons of properties.

Since isothiocyanatocarboxylic acids and their esters containing more than two monomer units cannot be distilled without decomposition, 4-aminobenzoic acid was chosen as the fourth building block, in order to achieve well crystallizing monomers. Thus, the polyesteramides **III**a,b and **IV**a,b should be prepared by thermal condensation of the monomers **I**a,b and **II**a,b. These monomers must be prepared by various routes, since no simple procedure was found suitable for the synthesis of all four monomers. However, 4-isothiocyanatobenzoyl chloride, easily accessible from 4-aminobenzoic acid, thiophosgene and thionyl chloride, servvved as starting materials for the synthesis of all four monomers.

O-Glycyl hydroxyacetic acid **VI**, first described by Stewart [9], was prepared from benzyloxycarbonyl glycine and bromoacetic acid tert-butylester. The protected depsipeptide was treated with hydrogen bromide in glacial acetic acid to remove both protecting groups and the resulting free depsipeptide **V** was converted to the monomer **I**a in a one flask procedure following our previously described "silylester hydrochloride method" [10] (2). However, this procedure is not useful for the synthesis of monomer **I**b, because S-glycyl mercaptoacetic acid is not easily accessible. In this case first 2-(4-isothiocyanatophenyl-)-oxazolone-5 (**VII**) was prepared from the previously described [2] 4-isothiocyanatohippuric acid and dicyclohexyl carbodiimide (DCC), (3). The oxazolone **VII** reacts smoothly with excess of anhydrous mercaptoacetic acid to the well crystallizing monomer **I**b (4).

The monomers **II**a and b were synthesized by parallel routes. First hydroxy- and mercaptoacetic acid tert-butylester, for which an improved synthetic procedure was described in a previous paper [7], were acylated by 4-isothiocyanatobenzoyl chloride (5). The resulting dimers **VIII**a and b were converted to the corresponding free acids **IX**a and b using anhydrous trifluoroacetic acid. It turned out that the tert-butylester group is the only carboxyl protection besides silylester groups which can be removed without side reactions of the isothiocyanato and the thiolester group. From the free acids **IX**a and the highly reac-



tive 1-hydroxy-1,2,3-benzotriazole, esters **Xa** and b were prepared by means of dicyclohexyl carbodiimide (7). These activated esters proved to be so reactive that their conversion with glycine tert-butylester (8) was not accompanied by the formation of thioureas from the aromatic isothiocyanato group. The trimeric tert-butylesters thus obtained yielded the monomers **IIa** and b by treatment with trifluoroacetic acid (9).

Condensation polymerization

It has been shown that a thermal condensation of aliphatic ω-isothiocyanatocarboxylic acids occurs at temperatures above 150°. Above 180°, on the other hand, side reactions like transamidation can occur. Condensation below 150° is possible if an aprotic strong base like triethylamine is used as catalyst [1]. In this case however, lower polymerization degrees are expected [1, 5]. Since the melting points of the monomers **Ia**,b and **IIa**,b are above 150°, condensation in a homogeneous melt would require temperatures in the range 180–200°. Hence all condensations were carried out in an inert, thermally stable solvent at temperatures $\leq 175°$ in order to avoid disturbing the sequences. Using *N*-methylacetamide which was the best solvent for such condensations in our previous experiments [1, 5], we were able to obtain the polyesteramides **Ia**, **IIa** and **IIb** with the expected alternating sequence (No. 1, 5 and 8, Table 1). Since the reaction temperature of 175° was high enough to allow a fast condensation, no catalyst was added in these experiments. The more basic solvent *N*,*N*-dimethylacetamide allowed a similar fast reaction at lower temperatures (No. 3, 4 and 7, Table 1) however, the resulting polyesteramides did not possess an alternating sequence. The monomer **Ib** proved to be most sensitive to side reactions. Therefore, the reaction

Table 1. Condensation polymerization of the isothiocyanatocarboxylic acids—under various conditions

No.	Monomer	Solvent	Catalyst	Temp (°C)	Time (hr)	$\eta sp/c$* (cm·g^{-1})	Sequence†
1	*N*(4-isothiocyanatohippuryl)-hydroxyacetic acid (**Ia**)	*N*-methyl acetamide	—	175	2	21.6	alternating
2	*N*-(4-isothiocyanatohippuryl)-mercaptoacetic acid (**Ib**)	hexamethyl phosphoric acid triamide	triethylamine	50	18	20.7	alternating
3	*N*-(4-isothiocyanatohippuryl)-mercaptoacetic acid (**Ib**)	*N*,*N*-dimethyl acetamide	—	120	5	—	random
4	*N*-[O-(4-isothiocyanato-benzoyl-)hydroxyacetyl-] glycine (**IIa**)	*N*,*N*-dimethyl acetamide	—	120	1.5	15.7	random
5	*N*-[O-(4-isothiocyanato-benzoyl-)hydroxyacetyl-] glycine (**IIa**)	*N*-methyl-acetamide	—	175	2	14.9	alternating
6	*N*-[O-(4-isothiocyanato-benzoyl-)hydroxyacetyl-] glycine tert-butylester(**XIa**)	1,2-dichloro-benzene	$ZnCl_2$	140	4	—	random
7	*N*-[S-(4-isothiocyanato-benzoyl-)mercaptoacetyl-] glycine (**IIb**)	*N*,*N*-dimethyl-acetamide	—	120	1.5		random
8	*N*-[S-(4-isothiocyanato-benzoyl-)mercaptoacetyl-] glycine (**IIb**)	*N*-methyl-acetamide	—	175	2	—	alternating
9	*N*-[S-(4-isothiocyanato-benzoyl-)mercaptoacetyl-] glycine-tert-butylester (**XIb**)	1,2-dichloro-benzene	$ZnCl_2$	140	4	—	random

* Measured with c = 10 g/l in dichloroacetic acid at 20°.
† Checked by ^{13}C-NMR spectroscopy.
‡ Containing 10% *N*,*N*-dimethylacetamide.

temperature must be lowered to 50° and triethylamine was added as catalyst. In order to prevent a rapid precipitation of oligomers and thereby a marked decrease of the reaction rate, hexamethyl phosphoric triamide was used as solvent for this experiment (No. 2, Table 1).

Besides the isothiocyanatocarboxylic acids **Ia** and b, the corresponding tert-butylesters **IX**a and b were tested as monomers (No. 6 and 9, Table 1). Tert-butylesters of carboxylic acids are known to split off isobutylene at temperatures >200°. In order to lower the condensation temperature an acidic catalyst, viz. zinc chloride was used, since in the case of protic catalysts side-reactions with the isothiocyanato group were expected. Although the reaction temperature was as low as 140°, only random sequences were obtained.

From a comparison of the viscosity measurements given in Table 1 with the viscosity-mole weight relationship reported for the polyester of lactic acid [11] or γ-benzyl glutamate [12], we can estimate the weight average $\bar{M}_w$ of the polyesteramides **III**a,b and **IV**a,b to be in the range 15000–25000. On the other hand, we have measured viscosities of poly-L-leucine, polysarcosine and poly-β-alanine samples for which the polymerization degree was determined by ^{1}H-NMR spectroscopic end-group analysis [13–15]. From a comparison with these values, the number average $\bar{M}_n$ of the polyesteramides may be estimated to be in the range of 4000–8000. It is clear that, under reaction conditions required for alternating sequences, high molecular weight polyesteramides cannot be produced.

^{13}C-NMR spectroscopy

The synthesis of copolymers with a defined sequence requires a suitable analytical tool for characterization of the products if new synthetic methods or monomers of a new class are used. For copolyamides as well as for copolypeptides, ^{13}C-NMR spectra are useful for the characterization and analysis of alternating or random sequences. Thus, alternating binary copolyamides can only show two carbonyl signals, while ^{13}C-NMR spectra of binary random copolyamides may exhibit four signals [16]. A ternary polyesteramide with a random sequence contains nine different ester and amide groups, hence a maximum of nine carbonyl signals is expected in its ^{13}C-NMR spectrum. Since only three carbonyl signals were found in the spectra of Fig. 1(A),(B) and 2(A),(B), our polyesteramides must possess the expected alternating sequence. Figure 1(C) compared with 1(B) demonstrates, on the other hand, that unfavourable reaction conditions lead to transamidation and transesterification, so that the resulting copolymers contain more than three different carbonyl groups.

One reason for the synthesis of the polyesteramides **III**a,b and **IV**a,b was our interest in a spectroscopic comparison of copolymers presenting "sequence isomerism of second order". This expression was previously defined by us for comparison of sequences which are built up from a group of identical monomer

Table 2. Properties of the alternating polyesteramides **IIa–d** obtained from experiment No. 1, 2, 5, 8 Table 1

No.	Polyester amides (IUPAC nomenclature)*	Yield (%)	Softening (DSC-Maximum)	Formula		Analyses C	H	N
1	-oxy-(1-oxoethylene) iminocarbonyl-	69	195–200°	$(C_{11}H_{10}N_2O_4)_n$	Calc	56,41	4,30	11,96
	1,4-phenylene-imino (1-oxoethylene-) **IIIa**		(198°)	$(234,2)_n$	Found	54,28	4,82	11,57
2	thio-(1-oxoethylene) iminocarbonyl-	80	260–267	$C_{11}H_{10}N_2O_3S)_n$	Calc	52,79	4,03	11,19
	1,4-phenylene-imino-(1-oxoethylene-) **IIIb**		(280°)	$(250,3)_n$	Found	50,56	4,73	9,88
3	oxycarbonyl-1,4-phenylene-imino	20	210–260°	$(C_{11}H_{10}N_2O_4)_n$	Calc	56,41	4,30	11,96
	(1-oxoethylene) imino-(1-oxoethylene-) **IVa**		(286°)	$(234,2)_n$	Found	54,30	4,39	11,12
4	thiocarbonyl-1,4-phenylene-imino	34	250–290°	$(C_{11}H_{10}N_2O_3S)_n$	Calc	52,79	4,03	11,19
	(1-oxoethylene) imino-(1-oxoethylene) **IVb**		(301°)	$(250,3)_n$	Found	51,70	4,61	11,85

* $(-X-CO-CH_2-NH-C_6H_4-NH-CO-CH_2)_n$; X = O: **IIIa**, X = S: **IIIb**.
$(-X-CO-C_6H_4-NH-CO-CH_2-NH-CO-CH_2)_n$; X = O: **IVa**, X = S: **IVb**.

† Optically determined.

‡ For reasons of decomposition, the maximum of the DSC curve does not necessarily indicate a correct melting point.

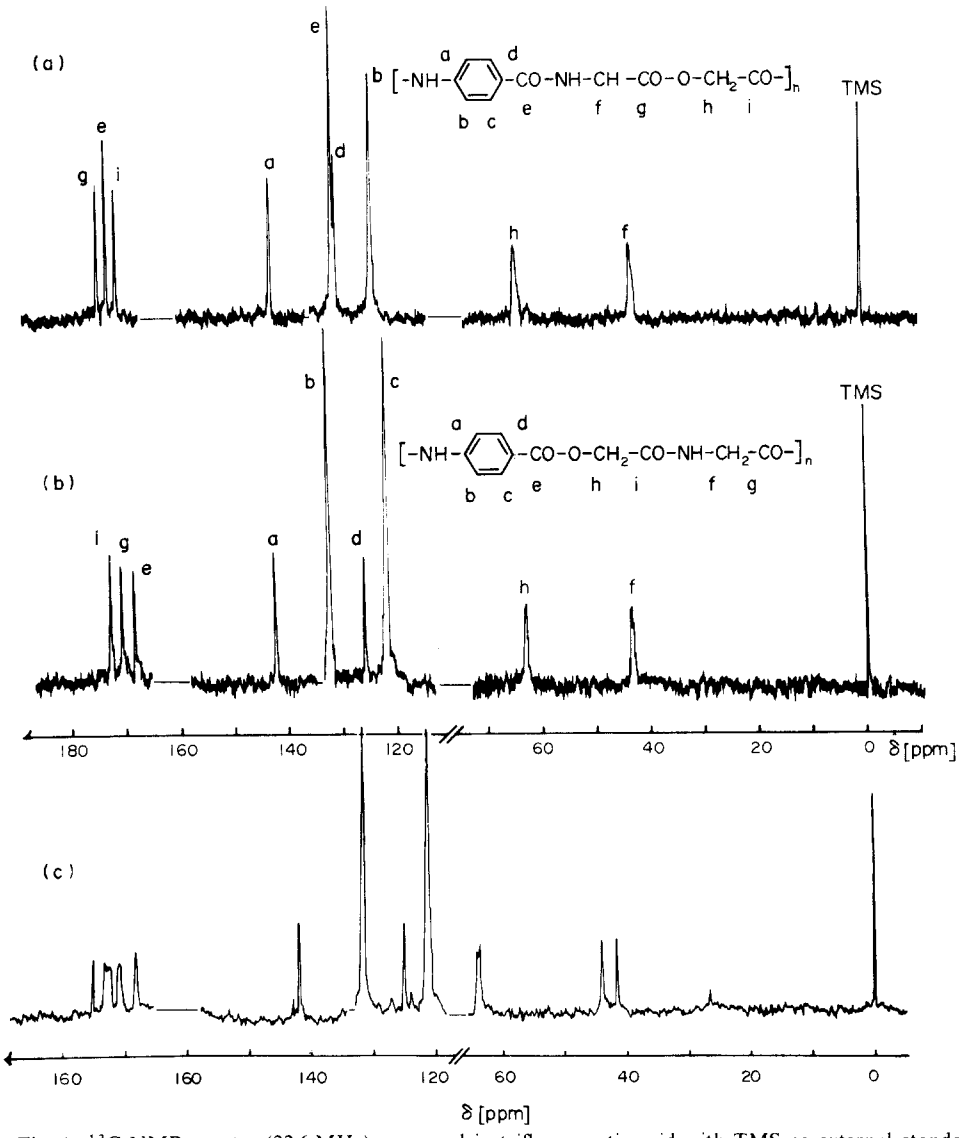


Fig. 1. ^{13}C-NMR spectra (22.6 MHz) measured in trifluoroacetic acid with TMS as external standard (solvent signals are eliminated: (A) Polyesteramide **IIIa** obtained from experiment No. 1 (Table 1), (B) polyestaramide **IVa** obtained from experiment No. 5 (Table 1), (C) polyesteramide (**IVa**) from experiment No. 6 (Table 1).

units having different positions relative to one other in the repeating sequence unit [6]. As shown by Figs. 1(A),(B) and 2(A),(B) (or by Table 3) most signals of the isomeric pairs of polyesteramides possess different shifts, so that the isomeric sequences can easily be distinguished.

In the ^{1}H-NMR spectra, however, the only substantial difference is a shift difference of 0.1–0.2 ppm in the case of the glycine CH_2-protons (Table 4).

The CH_2-protons as well as the α-C-atoms could easily be assigned, since both protons and sp^3 carbons show a substantial downfield shift with increasing electronegativity of the attached hetero atoms. The assignment of the 4-aminobenzoyl residue has already been described for solutions of polyamides in conc. sulphuric acid and is based on a comparison with various para substituted benzoic acid derivatives and anilines [2, 4]. Surprisingly, the quarternary C-1 turned out to be highly sensitive to the nature of the hetero atom attached to the carbonyl group of the aminobenzoyl residue. Contrary to what is expected for sp^3 carbons, the quarternary C-1 shifts upfield with increasing electronegativity of the hetero atoms attached to the carbonyl-group. However, similar inverse relationships are known from other sp^2 and sp carbons. Thus, for example, alkynes linked to an electropositive silicon show a downfield shift of both sp carbons and the CO-signal of trifluoroacetic acid appears highfield from that of trichloroacetic acid which is highfield from that of acetic acid. In agreement with such inverse shift/electronegativity relationships, the carbonyl signals of our polyesteramides show two characteristic shift effects which contribute much to their assignment:

(1) the carbonyl signals of the thiol ester groups are shifted 25–30 ppm downfield of those of the normal ester groups.

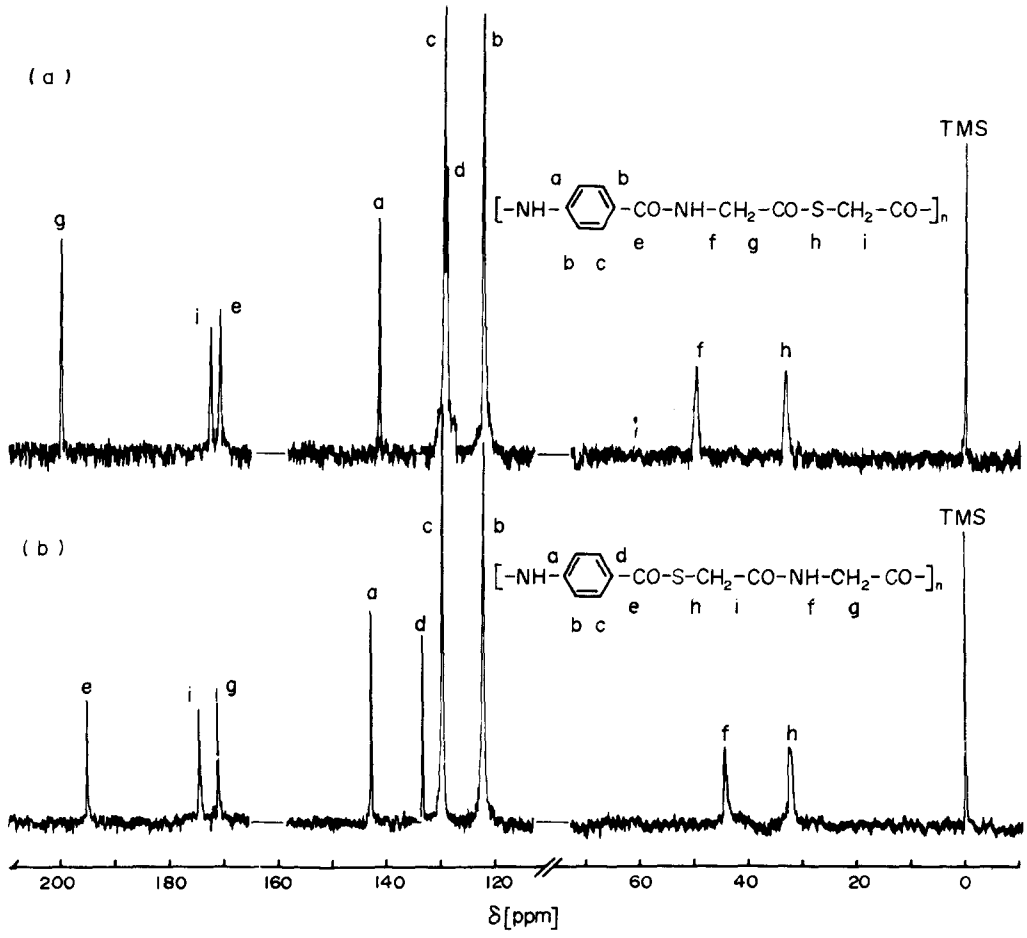


Fig. 2. ^{13}C-NMR spectra (22.6 MHz) measured in trifluoroacetic acid with TMS as external standard (solvent signals are eliminated): (A) polyesteramide **IIIb** from experiment No. 2 (Table 1), (B) polyesteramide **IVb** from experiment No. 8 (Table 1).

(2) The carbonyl signals of mercaptoacetyl residues shift downfield compared with those of hydroxyacetyl residues in an identical environment.

The complete assignment of the carbonyl signals made in Fig. 5. 1(A),(B) and 2(A),(B) is based, furthermore, on the following considerations:

(3) The CO-signals of the 4-aminobenzoyl residues (e) in **IIIa** and **IIIb** should exhibit nearly equal shifts, since their close neighbourhood is identical. The same is true for the glycine CO-signals (g) in **IVa** and **IVb**.

(4) It is known from carboxylic acid amides that an *N*-aryl residue effects a highfield shift of the carbonyl signal compared with an *N*-alkyl substituent. Hence the CO-signal of the hydroxyacetyl residue (i) in **IIIa** should appear highfield from that in **IVa** and the CO-signal of the mercaptoacetyl residue in **IIIb** highfield from that in **IVb**.

All four of these arguments lead to self-consistent assignments. Thus, we conclude that ^{13}C-NMR spectroscopy is useful not only for the characterization of copolyamides but also for polyesteramides and probably copolyesters. Results concerning this latter subject will be presented in succeeding papers.

Table 3. ^{13}C-NMR chemical shifts δ (ppm, relative to external TMS) of the alternating polyesteramides **IIIa,b** and **IVa,b** as well as of polyglycine and polyglycolide in trifluoroacetic acid

Formula No.	—NH-⟨⟩-CO— C-4(a)	C-3,5(b)	C-2,6(c)	C-1(d)	CO(e)	—NH—CH_2—CO— CH_2(f)	CO(g)	—X—CH_2—CO— CH_2(h)	CO(i)
IIIa	140.6	122.0	129.2	128.7	171.0	42.6	172.5	64.0	169.2
IIIb	141.3	121.9	129.2	128.6	170.8	49.9	200.1	33.2	172.6
IVa	142.0	121.9	131.7	125.1	168.1	43.6	170.4	63.6	172.5
IVb	142.3	122.0	129.2	132.8	194.9	44.5	170.8	32.6	174.1
Polyglycine			—			43.6	173.3	—	
Polyglycolide			—			—		61.6	169.1

Table 4. ^{1}H-NMR chemical shifts δ (ppm, relative to internal TMS) of the isothiocyanato carboxylic acids **Ia,b IIa,b** and of the polyesteramides **IIIa,b, IVa,b** in trifluoroacetic acid

Formula No.	NH	H-2.6	H-3.5	—NH—CH_2—CO— NH	α-H	—*X*—CH_2—CO— *X*	α-H
Ia	—	7.89 (d. J = 8.5 Hz)	7.32 (d. J = 8.5 Hz)	7.90	4.47 (d. J = 5.0 Hz)	O	5.00†
Ib	—	7.87 (d. J = 8.5 Hz)	7.30 (d. J = 8.5 Hz)	7.90	4.67 (d. J = 5.5 Hz)	S	3.97†
IIa	—	8.16 (d. J = 8.5 Hz)	7.36 (d. J = 8.5 Hz)	7.78	4.40 (d. J = 5.0 Hz)	O	5.18†
IIb	—	8.00 (d. J = 8.5 Hz)	7.35 (d. J = 8.5 Hz)	8.00	4.34 (d. J = 5.0 Hz)	S	4.08†
IIIa	9.07	7.90*	7.81*	8.07	4.63*	O	5.14*
IIIb	9.14	7.89*	7.80*	8.09	4.66*	S	4.10*
IVa	9.11	8.18*	7.79*	8.18	4.49*	O	5.14*
IVb	9.13	7.98*	7.78*	8.18	4.44*	S	4.09*

* All signals: † broad.

EXPERIMENTAL

Solvents: dioxane, tetrahydrofurane, diethylether and triethylamine were refluxed and distilled over sodium wire. Aromatic solvents and dimethylformamide were refluxed and distilled over P_4O_{10}.

4-Isothiocyanatobenzoyl chloride (**V**)

137 g (1 mole) 4-Amino benzoic acid was dissolved in a mixture of 400 ml conc. HCl and 2 l. warm water. 127 g (1.1 mole) Thiophosgene was added dropwise over a period of 1 hr and the reaction mixture was stirred for an additional 2 hr at room temperature. The precipitated 4-isothiocyanatobenzoic acid was filtered off, washed with 100 ml ice water and dissolved in 2 l. tetrahydrofuran (THF). This solution was dried over sodium sulphate and concentrated *in vacuo*. The crystallization of 4-isothiocyanatobenzoic acid was completed by addition of 400 ml diethylether and 600 ml petrolether. The acid was dried over P_4P_{10} *in vacuo* and refuxed in 500 ml thionylchloride until evolution of gas had almost ceased. The dark solution was concentrated *in vacuo* and the remaining crystalline product was distilled in an apparatus similar to that shown in Fig. 33 of ref. [17], bath temperature 130–150°, pressure 10^{-3} mm, yield 79%, m.p. 68–70°. For C_8H_4ClNOS (185.6): Calc C 45.29 H 2.17 N 7.54; Found C 45.41 H 2.46 N 7.43.

O-(4-Isothiocyanatobenzoyl) hydroxyacetic acid tert-butylester (**VIIIa**)

An icecold solution of 26.4 g (0.2 mole) hydroxyacetic acid tert-butylester and 28 ml (0.2 mole, triethylamine in 100 ml dry THF was added dropwise with stirring to a solution of 23.5 g (0.2 mole) 4-isothiocyanatobenzoyl chloride in 300 ml dry THF at −10°. The reaction mixture was stirred for 4 hr without cooling and then refluxed 15 min. The reaction mixture was then filtered and the filtrate concentrated *in vacuo*. The residue was dissolved in 250 ml ethyl acetate, washed twice with a 5% solution of citric acid in water, dried over sodium sulphate and treated with charcoal. The product crystallized from the concentrated solution after successive addition of ligroin and cooling with ice. Yield 48.7 g (83%), m.p. 62–63°. For $C_{14}H_{15}NO_4S$ (293.35): Calc C 57.32 H 5.15 N 4.78; Found C 57.35 H 5.13 N 4.43.

S-(4-Isothiocyanatobenzoyl) mercapto-acetic acid tert-butylester (**VIIIb**)

This was prepared from mercaptoacetic acid tert-butylester as described above. Yield 53.8 g (87%), m.p. 82–83°. For $C_{14}H_{15}NO_3S_2$ (309.4): Calc C 54.35 H 4.89 N 4.55; Found C 54.61 H 4.93 N 4.84.

O-(4-Isothiocyanatobenzoyl)hydroxy acetic acid (**IXa**)

32.5 g (0.1 mole) O-(4-Isothiocyanatobenzoyl)hydroxy acetic acid tert-butylester was stirred in 60 ml trifluoroacetic acid for 30 min at room temperature and for 20 min at 40–50°. The reaction mixture was diluted with 100 ml carbon tetrachloride, concentrated *in vacuo*, diluted with carbon tetrachloride and concentrated again. The crystallization was completed by cooling with ice and the isolated product was recrystallized from THF/ligroin (including treatment with charcoal) without heating. Yield 23.5 g (99%), m.p. 165–166 (dec.). For $C_{10}H_7NO_4S$ (237.2): Calc C 50.63 H 2.97 N 5.90; Found C 50.73 H 2.79 N 6.01.

S-(4-Isothiocyanatobenzoyl)mercapto acetic acid

This was prepared from the corresponding tert-butylester as described above. Yield 24.8 g (98%), m.p. 150–152 (dec.). For $C_{10}H_7NO_3S_2$ (253.3): Calc C 47.42 H 2.79 N 5.53; Found C 47.68 H 3.00 N 5.81.

N-[O-(4-Isothiocyanatobenzoyl-) hydroxyacetyl-] glycine tert-butylester (**IXa**)

23.7 g (0.1 mole) 4-Isothiocyanatobenzoyl hydroxyacetic acid and 20 g (0.15 mole) 1-hydroxy-1,2,3-benzotriazole were dissolved in 300 ml dry THF and mixed at −10° with a cooled solution of 21.6 g (0.105 mole) dicyclohexyl carbodiimide in 50 ml dry THF. 10 min later a solution of 13.1 g (0.1 mole) glycine tert-butylester [8] in 50 ml dry tetrahydrofurane was added dropwise at −10°. The reaction mixture was stirred for 2 hr without cooling, filtered and concentrated *in vacuo*. The residual oil was diluted with 300 ml ethylacetate washed with a 10% solution of citric acid and with a saturated ammonium sulphate solution. After drying over sodium sulphate, the solution was concentrated *in vacuo* and the product crystallized by successive addition of ligroin under cooling. Recrystallization was achieved from THF/ligroin without heating. Yield 21.2 g (61%), m.p. 164–165°. For $C_{16}H_{18}N_2O_5S$ (350.40): Calc C 54.84 H 5.18 N 8.00; Found C 55.04 H 5.25 N 8.08.

N-[S-(4-Isothiocyanatobenzoyl-) mercaptoacetyl] glycine

Tert-butylester (**IXb**) was prepared similarly from 25.3 g (0.1 mole) S-(4-isothiocyanatobenzoyl)mercaptoacetic acid. Yield 16.8 g (46%), m.p. 154–155°. For $C_{16}H_{18}N_2O_4S_2$ (366.47): Calc C 52.44 H 4.96 N 9.64; Found C 52.56 H 5.03 N 7.83.

N-[-O-(4-Isothiocyanatobenzoyl-)hydroxyacetyl]glycine (**IIa**)

17.5 g (0.05 mole) of the corresponding tert-butylester (**XIa**) was stirred in 60 ml trifluoroacetic acid for 30 min at room temperature and 15 min at 40°C, whereby the product precipitated from the initially clear solution. The reaction mixture was diluted with 100 ml carbon tetrachloride, concentrated *in vacuo*, diluted again and concentrated. The crystalline product was filtered off, washed with carbon tetrachloride and dried over P_4O_{10} at 10^{-3} mm. Yield 13.5 g (92%), m.p. 173–175° (dec.). For $C_{12}H_{10}N_2O_5S$ (294.3): Calc C 48.98 H 3.43 N 9.52; Found C 48.95 H 3.46 N 9.46.

N-[S-(4-Isothiocyanatobenzoyl-)mercaptoacetyl-]glycine (**IIb**)

This was prepared in the same way from 18.3 g (0.05 mole) of its tert-butylester (**XIb**). Yield 14.5 g (94%), m.p. 163–166° (dec.). For $C_{12}H_{10}N_2O_4S_2$ (310.3); Calc C 46.44 H 3.25 N 9.03; Found C 46.56 H 3.30 N 9.03.

2-(4-Isothiocyanatobenzoyl-)oxazol-5-one (**VII**)

71 g (0.3 mole) 4-Isothiocyanato hippuric acid [1] was dissolved in a mixture of 200 ml dry THF and 100 ml dry dimethylsulphoxide, cooled to −10° and mixed with a cold solution of 64 g (0.31 mole) dicyclohexylcarbodiimide in 150 ml dry THF. The reaction mixture was kept 5 hr 0°, 2 h at 20–25° was filtered. The filtercake was washed with ethylacetate and the filtrate concentrated *in vacuo*, until the product began to crystallize. After filtration of the first crop, the filtrate was diluted with 200 ml ethylacetate, washed with ice water, dried over sodium sulphate and concentrated again so that a second crop was obtained. Yield 55.7 g (87%), m.p. 137–139°. For $C_{10}H_6N_2O_2S$ (218.2): Calc C 55.04 H 2.77 N 12.84; Found C 55.06 H 2.60 N 13.03.

S-(4-Isothiocyanatohippuroyl)mercapto acetic acid (**Ib**)

11.0 g (0.05 mole) 2-(4-isothiocyanatophenyl)oxazol-5-one (**VII**) was dissolved in 50 ml mercaptoacetic acid at room temperature. From the initially clear solution, the product begins to precipitate within 10 min. After 45 min the product was filtered off and washed with diethylether. The raw material was dissolved in THF and treated with charcoal. The solution was concentrated *in vacuo* and the product crystallized by addition of carbon tetrachloride with cooling with ice. Yield 6.8 g (42%) m.p. 153–154° (dec.). For $C_{12}H_{10}N_2O_4S_2$ (310.4): Calc C 46.44 H 3.25 N 9.03; Found C 46.61 H 3.36 N 8.96.

O-(4-Isothiocyanatohippuroyl)hydroxy acetic acid (**Ia**)

20.0 g (0.15 mole) (O-glycyl-hydroxy acetic acid (**VI**) was refluxed with stirring in a mixture of 200 ml dry chloroform, 50 ml dry acetonitrile and 20 ml trimethylchlorosilane for 1.5 hr. The reaction mixture was then cooled to −30° 29.7 g (0.15 mole) 4-isothiocyanatobenzoyl chloride dissolved in 60 ml dry chloroform was added at once and 42 ml (0.3 mole) triethylamine were added dropwise. After warming to room temperature, the reaction mixture was washed with 200 ml water containing 5% citric acid and dried over sodium sulphate. After concentration in vacuo, the product crystallized on cooling with ice and addition of carbon tetrachloride. Recrystallization was achieved without warming by successive addition of carbon tetrachloride to a concentrated solution in THF. Yield 33.3 g (75%), m.p. 165–167° (dec.). For $C_{12}H_{10}N_2O_5S$ (294.3): Calc C 48.98 H 3.43 N 9.52; Found C 49.06 H 3.59 N 9.75.

Polycondensation (Table I): 25 mmole of a monomer (**Ia,b** or **IIa,b**) was suspended in 10 ml of dry *N*-methylacetamide or *N,N*-dimethylacetamide in a 50 ml glass flask which was treated before with dimethyl dichlorosilane, in order to avoid catalytic effects of the glass walls. The suspension was heated under a slow stream of nitrogen whereby the monomers went into solution. After cooling, the reaction mixture was poured into 400 ml methanol. Precipitated polymer was filtered off, reprecipitated from 50 ml dichloroacetic acid/500 ml methanol and dried at 70°/0.01 mm. 1 ml triethylamine was used as catalyst in experiment No. 2.

The tert-butylesters **XIa** and b were condensed similarly using a mixture of 9 ml dry 1,2-dichlorobenzene and 1 ml *N,N*-dimethylacetamide as solvent and 100 mg water-free zinc chloride as catalyst.

Measurements

The ^{13}C-NMR spectra were measured on a Bruker WH-90 FT-spectrometer at 30° in 10 mm diameter sample tubes. A coaxial 4 mm capillary containing a 1:1 mixture of dioxane-d_8 and TMS was used for both deuterium lock and chemical shift reference. 500 mg polymer was dissolved in 2 ml trifluoroacetic acid. 8000–10000 Pulses were acquired with 8 K data points on a spectral width of 5000 Hz using a pulse width of 9 μsec (≃60°).

The ^{1}H-NMR spectra were measured on the same spectrometer in 5 mm diameter sample tubes with TMS as internal standard.

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