Journal of Macromolecular Science, Part A
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597274

Polymerization of α=Aminoisobutyric Acid NCA: Interpretation According to the Hypothesis of a Multiple Mechanism

Michèle Amowal[a]; Bernard Coutin[a]; Hikaru Sekiguchi[a]
[a] Laboratoire de Chimie Macromoléculaire Laboratoire associé au C.N.R.S. Université Pierre-et-Marie-Curie, Paris Cedex 05, France

To cite this Article Amowal, Michèle , Coutin, Bernard and Sekiguchi, Hikaru(1983) 'Polymerization of α=Aminoisobutyric Acid NCA: Interpretation According to the Hypothesis of a Multiple Mechanism', Journal of Macromolecular Science, Part A, 20: 7, 675 — 696
To link to this Article: DOI: 10.1080/00222338308061801
URL: http://dx.doi.org/10.1080/00222338308061801

J. MACROMOL. SCI.–CHEM., A20(7), pp. 675-696 (1983)

Polymerization of α-Aminoisobutyric Acid NCA: Interpretation According to the Hypothesis of a Multiple Mechanism

MICHÈLE AMOUYAL, BERNARD COUTIN, and HIKARU SEKIGUCHI

Laboratoire de Chimie Macromoléculaire
Laboratoire associé au C.N.R.S.
Université Pierre-et-Marie-Curie
75230 Paris Cedex 05, France

ABSTRACT

The basic salt-initiated polymerization of α-aminoisobutyric acid NCA in acetonitrile was studied using various alkaline alcoholates and in the presence or absence of various protic (very weak acid) additives. The cation effect observed was the one expected from either the N-carboxy-α-amino acid anhydride (NCA) anion mechanism (activated monomer mechanism) or the alcoholate anion mechanism (Blout's mechanism). The anion effect appeared to be abnormal for the former mechanism, but did not agree nor disagree substantially with the latter. Furthermore, such additives as methanol (conjugate acid of the initiator), 3-methylhydantoin, 2-oxazolidone, and N-acetylglycine NCA (prototype of the chain growing through the NCA anion mechanism) considerably enhanced the rate of initiation. A still higher rate of initiation could be obtained by the combined use of two additives. IR and DTA analyses of the polymerization products showed the formation of 5,5-dimethylhydantoin-3-isobutyric acid in the sample using the alcohol-free initiator, hence the NCA anion mechanism is operative. This acid was absent in the low DP polymer obtained in the presence of added methanol,

0022-233X/83/2007-0675$3.50/0

and this agrees with the alcoholate anion mechanism without, however, proving it. Thus, while only part of the results could be explained by one or the other of the previous interpretations, all the experimental facts were accounted for, without noticeable contradiction, by the hypothesis of a multiple mechanism which contains both interpretations among its elements.

INTRODUCTION

Unlike the case of amine-initiated polymerizations whose mechanisms seem to have received a fairly wide approbation, authors have never found unanimous consensus for the mechanism of polymerization of N-carboxy-α-amino acid anhydrides (NCAs) by the action of alkaline alcoholate initiators. Indeed, the problem has been the subject of controversies for more than 20 years between the holders of the hypothesis of NCA anion mechanism (activated monomer mechanism) and the supporters of that of the alcoholate-carbamate anion mechanism (Blout's mechanism).

We have recently analyzed this problem and presented a new hypothesis of multiple mechanism [1] which presumes the coexistence with variable significance of reactions of different mechanisms for the NCA polymerizations using any basic initiator. This hypothesis, which unifies under a general composite mechanism all the NCA polymerizations given by basic initiators and considers each of them as a particular case of the mechanism, allowed us to explain without apparent contradiction not only the experimental results of the literature which had been at the center of the controversies, but also many others which had not drawn the attention of authors of either of the two camps.

The proposed hypothesis [1] is characterized by the assumption of a preinitiation stage which involves an acid-basic reaction between the acidic NCA monomer and the basic initiator (amine or alkaline salt). That is, for amines:

$$NCA + B \rightleftharpoons HB^+NCA^- \qquad (1)$$

and for alkaline salts:

$$NCA + Q^+A^- \rightleftharpoons Q^+NCA^- + HA \qquad (2)$$

(where B is an amine and Q^+ an alkaline metal cation or a quaternary ammonium cation), giving rise to an equilibrium in which are implied the NCA monomer and two (the amine initiator and its NCA salt, for an amine initiator) or three (the basic salt initiator, its conjugate acid, and the NCA salt) active species. These active agents (or their anionic parts) separately react with NCA monomer through their nucleophilic attack and initiate the polymerization by their own mechanisms (anion-

oid mechanism, mechanisms by the initiator anion, and by NCA anion). With the appearance of new active species (amino and carbamate endgroups, N-acyl NCA end unit) an equilibrium of cation share sets up between the acidic species present (NCA, carbamic acid, and the conjugate acid of the initiator) according to their acidity and concentration to determine the significance of the reactions of propagation through the various mechanisms, as well as that of the reactions of initiation of the moment.

The classical activated monomer mechanism [2] considers only the NCA anion mechanism (with small differences in the details) operating in the initiation and the propagation, while the ancient Blout's mechanism [3] only took into account the reaction of initiation by the initiator anion and of the reaction of propagation by carbamate anion on the chain thus initiated.

In the cited paper [1] the discussion was limited to the interpretation of the data available in the literature and no new results were added. This should a priori be sufficient, since the hypothesis was proposed for the interpretation of the results of NCA polymerizations as a whole. However, we believe that it will be interesting to verify and to confirm the hypothesis with the help of experiments specially designed for this purpose. This is the reason why we have investigated the polymerization of α-aminoisobutyric acid NCA using alkaline alcoholates and related initiators in the present study.

EXPERIMENTAL PART

Reagents and Solvent

α-Aminoisobutyric Acid NCA

Synthesis of α-aminoisobutyric acid NCA was described in one of our previous papers [4].

Initiators

Alkaline alcoholates were prepared by reacting alkaline metal with alcohols diluted in an inert solvent such as ethyl ether or THF, similar to the preparation of alkaline salts of lactams [5]. Quaternary ammonium salts of lactams were prepared by reacting lactams with the corresponding quaternary ammonium alcoholates according to the method previously described [6, 7].

For the dehydration of alkaline (lithium, sodium, potassium, and cesium) hydroxides, the pure grade commercial products were finely powdered under nitrogen, kept in vacuo in a desiccator over phosphorus pentoxide for one night, and then stored in vacuo over sodium hydride.

Solvent

Acetonitrile was distilled first over fresh calcium hydride and then over phosphorus pentoxide. The middle fraction was collected in

several flasks dried beforehand in an oven at 110°C and was stored with a folding-cap rubber stopper in a desiccator. Water content below 50 ppm (Karl Fisher method), bp 82.0°C. The solvent was taken by a medical syringe and dried 12 h in an oven at 40°C.

Additives

Methanol and ethanol were dried by the technique of preparation of super-dry alcohols, reported in the literature [8]. Isopropanol and t-butanol were first dried over sodium sulfate, then filtered and distilled. They were stored and taken in the same way as acetonitrile.

2-Pyrrolidone, pure grade product, was purified by refluxing over potassium hydroxide and fractionally distilled, bp 94.0°C/0.8 torr. 2-Oxazolidone, commercial product, was purified by recrystallization in ethanol, mp 86-90°C. 3-Methylhydantoin was prepared and purified by the method described by Siemonsen [9]. N-Acetylglycine NCA (3-acetyloxazoline-2,5-dione) was prepared according to the method elaborated by Kricheldorf [10].

Polymerization

All the glassware was dried by flaming and stored in a desiccator over phosphorus pentoxide.

Solid NCA monomer, weighed with precision, was dissolved in one part of solvent in a small, elbow-form vessel, which was then fixed upright on the side-neck of a two-necked Erlenmeyer flask containing the required amount of dry initiator in suspension in the remaining part of the solvent and magnetically stirred.

Polymerization was followed by gasometry under constant pressure at 20.0 ± 0.5°C. Gas volume was read every 30 s for the initial 3 min, every minute until 10 min, every 3 min until 30 min, and every 10 to 15 min for the rest. This method always gives smooth and continuous curves, for which it is useless to indicate the individual experimental points. Relative errors in repeated experiments are estimated to be of the order of 5%.

The apparatus and the technique used in gasometric measurements were described in one of our previous papers [4]. The only modification was the use of decaline instead of mercury in order to improve the precision of the level reading.

Composition of Polymers

The composition of the polymerization products was studied as follows.

2.5 g (0.02 mol) of α-aminoisobutyric acid NCA was polymerized for 1 week at room temperature in 10.0 cc acetonitrile by the action of 3.0 mol% sodium methoxide without any addition of alcohol. The

resulting polymer was crushed in an additional amount of acetonitrile and separated by filtration. Yield 1.53 g (90%). It was then extracted with 200 cc boiling 95% ethanol to give 1.20 g insoluble high polymer (Product I in Fig. 7) and 0.24 g soluble low molecular weight fraction. The latter was recrystallized in 10 cc boiling ethanol, and after separation of the cold insoluble fraction, the remainder was evaporated and treated again with 50 cc ethyl ether containing 1 cc ethanol. The recovered product (Product II in Fig. 7), 10 mg, rich in low molecular weight by-products but nonetheless presenting essentially the same IR spectrum as the ethanol-extracted fraction, was used in the characterization study.

1.26 g (yield 75%) polymer from another polymerization, carried out under the same conditions but in the presence of added methanol (10 mol%), was extracted thrice by 20 cc boiling 95% ethanol to give a trace amount (≃ 100 mg) of insoluble polymer (Product III in Fig. 7) and filtrate. A low molecular weight fraction (Product IV in Fig. 7) was recovered from the latter on evaporating the solvent. This fraction, soluble in THF at room temperature, presented an IR absorption spectrum similar to the insoluble polymer and seemed to be mainly constituted by low polymeric compounds. The amino endgroup titration conducted with 1/20 N HCl on this product after another purification gave $\overline{DP} = 8.7$.

IR absorption spectra were obtained on a Perkin-Elmer Infracord using potassium bromide pellets with a medium rate. The sample concentration was 0.9 mg (I), 1.3 mg (II), 1.0 mg (III), and 1.2 mg (IV) in 220 mg KBr.

DTA analysis was carried out on a Du Pont 990 apparatus, using 3 to 5 mg polymer deposed in a pan. The sample was heated at 20°C/min under a nitrogen flow of 50 cm^3/min. Temperature calibration of the instrument was achieved by melting an indium standard.

RESULTS

1. Effect of Ionic Species

The polymerization of α-aminoisobutyric acid NCA was carried out in acetonitrile (monomer concentration 2.0 mol%) with various basic salt initiators (initiator concentration 3.0 mol%, if not otherwise specified, with respect to monomer). These initiators, generally insoluble in the polymerization solvent, dissolved upon the addition of NCA monomer and the polymerization started immediately after. In general, the polymerization mixture was clear and homogeneous for the initial several hours and then gradually turned to a heterogeneous phase, yielding a swollen but crystalline polymer. In the present paper we only take into account the initial period of homogeneous phase polymerization.

In Fig. 1 are registered the results of the polymerization using alkaline hydroxide initiators. Initiator activity increases with the cation

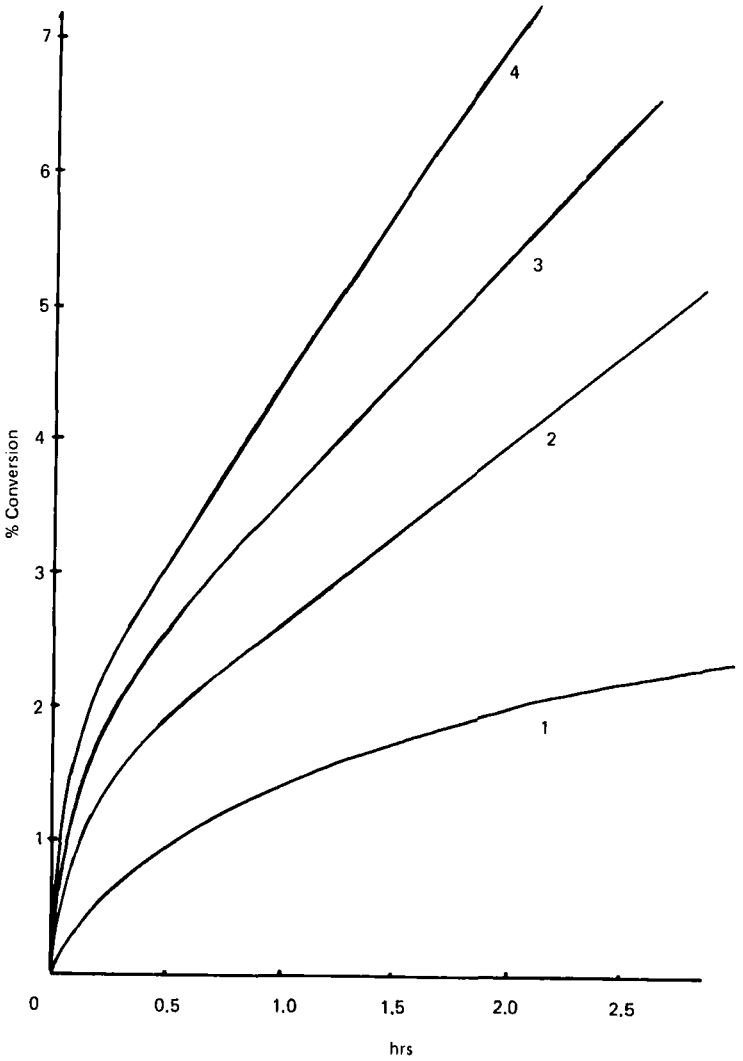


FIG. 1. Cation effect in the alkaline hydroxide-initiated polymerization of α-aminoisobutyric acid NCA in dry acetonitrile at 20.0 ± 0.5°C. Monomer concentration 2.0 mol/L; initiator concentration with respect to monomer 3.0 mol%. Curve 1: lithium hydroxide. Curve 2: sodium hydroxide. Curve 3: potassium hydroxide. Curve 4: cesium hydroxide.

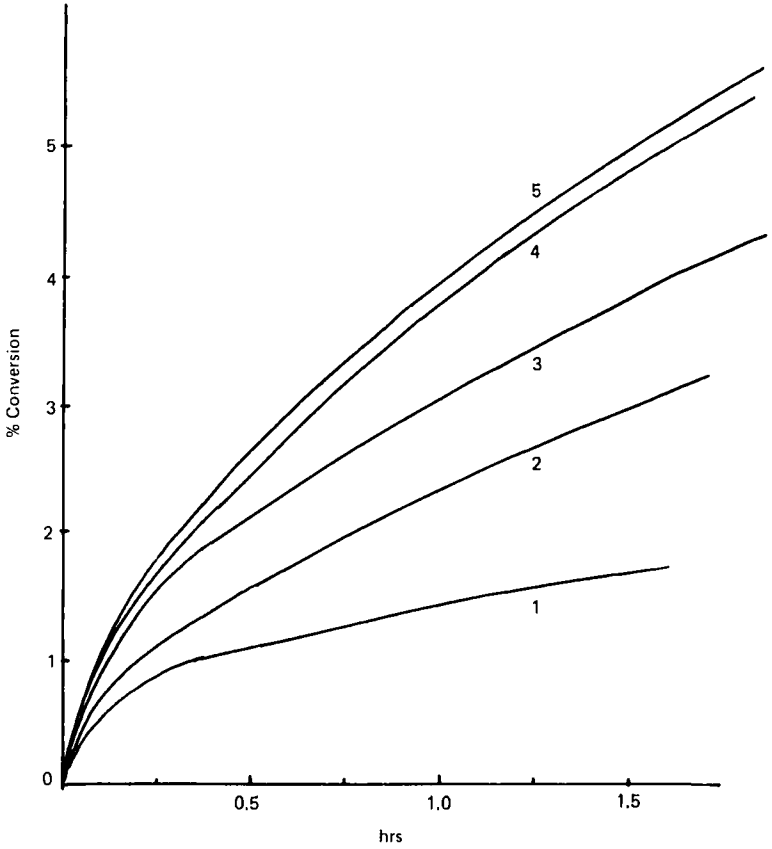


FIG. 2. Cation effect in the alkaline lactam salt-initiated polymerization of α-aminoisobutyric acid NCA in dry acetonitrile at 20.0 ± 0.5°C. Initiators: alkaline salts of 2-pyrrolidone; monomer concentration 2.0 mol/L; initiator concentration is given in mol% with respect to monomer. Curve 1: lithium salt, 4.0%. Curve 2: sodium salt, 3.0%. Curve 3: potassium salt, 3.0%. Curve 4: tetramethylammonium salt, 3.5%. Curve 5: tetrabutylammonium salt, 3.5%.

size. The results confirm those reported by Idelson and Blout [3] for γ-benzyl-L-glutamate NCA. Similar results were obtained with alkaline and quaternary ammonium salts of lactam as initiators (Fig. 2). Alkaline alkoxides behave similarly [3]. In all the cases studied we obtained for a given anion the following order:

$$Li^+ < Na^+ < K^+ < NMe_4^+ < NBu_4^+ \qquad (3)$$

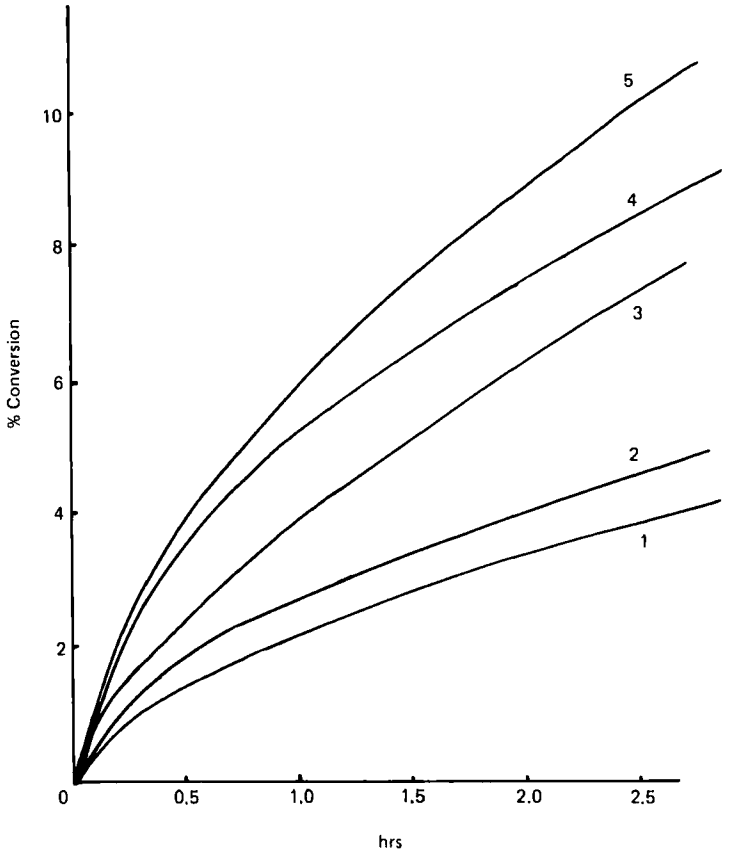


FIG. 3. Anion effect in the strong base-initiated polymerization of α-aminoisobutyric acid NCA in dry acetonitrile at 20.0 ± 0.5°C. Initiators: sodium derivatives of various very weak acids; monomer concentration 2.0 mol/L; initiator concentration with respect to monomer 3.0 mol%. Curve 1: sodium salt of 2-pyrrolidone. Curve 2: sodium hydroxide. Curve 3: sodium t-butoxide. Curve 4: sodium ethoxide. Curve 5: sodium methoxide.

Thus, the results of Fig. 1 and Fig. 2 can be ascribed to the dissociation of the basic, active species in the reaction mixture, whether these are the basic salts introduced or the NCA salts formed in situ. These results are normal as well from the standpoint of Blout's mechanism as the activated monomer mechanism.

Figure 3 reproduces the results of our study of the anion effect. They show that the initiator activity increases for a given cation in the following order:

$$\text{Lactam}^- < HO^- < \text{t-BuO}^- < EtO^- < MeO^- \quad (4)$$

Except for the case of hydroxide anion whose position is somewhat unusual, the observed order is the inverse of the basicity order. If the activated monomer mechanism operated alone, the basic initiator would ionize, viz., "activate," the NCA monomer, and the higher its basicity, the higher its ionizing power, and hence the higher its reactivity would be, which is the opposite of the above results.

These results could be explained, on the contrary, by Blout's mechanism if it could be assumed that basicity and nucleophilicity orders of the initiator anions are inversed. However, this mechanism assumes that NCAs are not acidic and that there is no acido-basic reaction between them and the basic initiators. This question is discussed in the next section.

The particular position of the hydroxide anion can be better understood when Blout's mechanism is assumed. According to this mechanism, the attack of a hydroxide anion yields a chain possessing a carboxylate group on one end and a carbamate group on the other one, which immobilizes two alkaline cations instead of one for the alkoxide-initiated chain, and reduces as much the effective concentration of carbamate anion in the propagation phase. This is supposed to be the reason why the activity of a hydroxide anion is apparently lower than that of alcoholates.

2. Effect of Additives

We show in Fig. 4 the kinetic curves of the sodium methoxide-initiated polymerization of NCA in the presence of added methanol, with a reference curve corresponding to methanol initiation without sodium methoxide (Curve 0). In this figure the more the added alcohol, the greater the reaction rate. This essentially agrees with the results of Idelson and Blout [3], who reported an increase, though relatively weak, of the apparent rate of polymerization k_p of γ-benzyl-L-glutamate NCA with the amount of methanol added as a solvent of the initiator, without explaining this phenomenon.

The increase of the concentration of added alcohol in Fig. 4 gives rise to an effect similar to that given by the acidity of conjugate acids in Fig. 3. The results of Fig. 4 cannot be explained by the cumulative activity of basic salt initiator and alcohol, as shown by Curves 2 and 4 for the addition of 3 mol% methanol (the synthesized Curve 4 sums up the polymerization due to 3 mol% sodium methoxide initiator, Curve 4, and that given by 3 mol% methanol, Curve 0, without taking account of dilution effect arising from the addition of alcohol, which is negligible).

Without being a complete contradiction, the results cannot be interpreted with the help of Blout's mechanism, whose initiation and propagation should be indifferent to additives such as alcohols [3], nor in terms of the changes, found to be slight, in physical properties of the

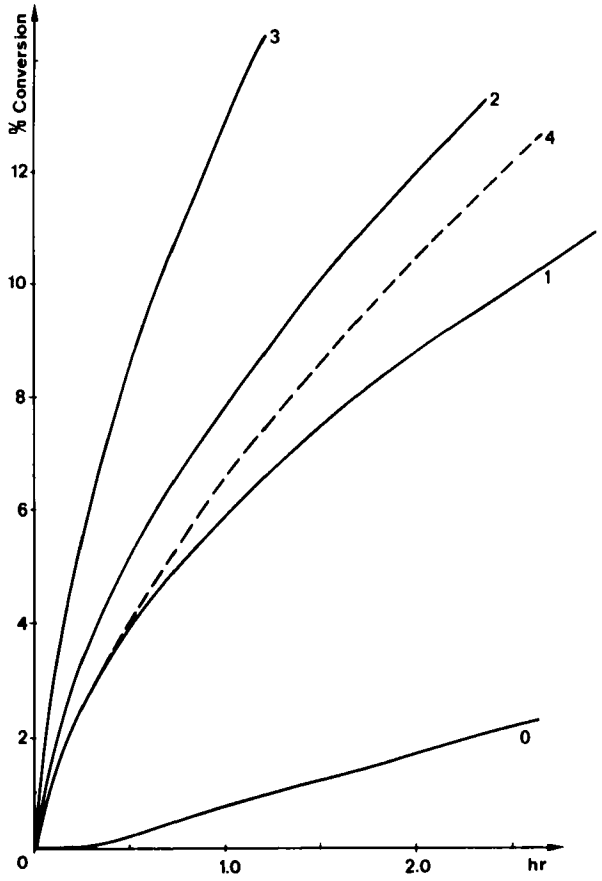


FIG. 4. Effect of methanol addition on the rate of sodium methoxide-initiated polymerization of α-aminoisobutyric acid NCA in dry acetonitrile at 20.0 ± 0.5°C. Monomer concentration 2.0 mol/L; initiator concentration with respect to monomer 3.0 mol%; methanol concentration is given in mol% with respect to monomer. Curve 0: 3.0% methanol without sodium methoxide (reference curve). Curve 1: 0% (no methanol added). Curve 2: 3.0%. Curve 3: 10.0%. Curve 4: curve synthesized from Curves 0 and 1 (0 + 1).

reaction mixture (3 mol% of methanol with respect to NCA corresponds to 0.33 mol% or 0.245 wt% of methanol, pK_a 15.5, dipole moment μ = 2.87, dielectric constant ϵ = 32.70 [11], in acetonitrile, μ = 3.44, ϵ = 37.5 [11]). Yet, they are obviously not consistent with the activated monomer mechanism. If, moreover, its growth center, the N-acylated NCA unit, is highly sensitive to alkaline hydrolysis and alcoholysis, it will be still more difficult to explain the results with this mechanism.

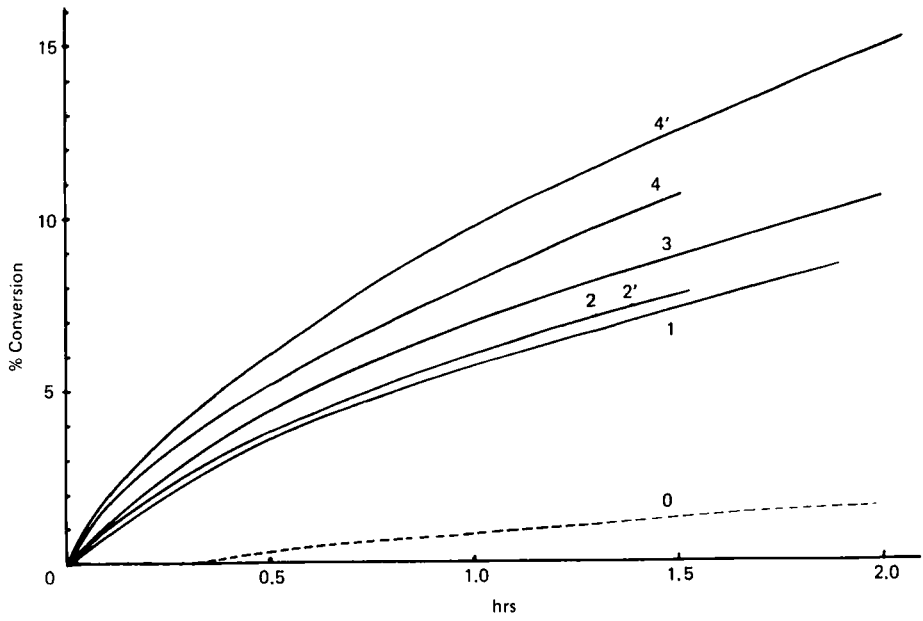


FIG. 5. Effect of cyclic amides on the sodium methoxide-initiated polymerization of α-aminoisobutyric acid NCA in dry acetonitrile at 20.0 ± 0.5°C. Monomer concentration 2.0 mol/L; initiator concentration with respect to monomer 3.0 mol%; additive concentration is given in mol% with respect to monomer and in additive/initiator ratio. Curve 0: methanol 3.0% without sodium methoxide initiator (reference curve). Curve 1: without any additive. Curve 2: 2-pyrrolidone, 1.0% (1.0/3.0). Curve 2': 2-pyrrolidone, 10.0% (10.0/3.0). Curve 3: 2-oxazolidone, 10.0% (10.0/3.0). Curve 4: 3-methylhydantoin, 1.0% (1.0/3.0). Curve 4': 3-methylhydantoin, 10.0% (10.0/3.0).

We register in Fig. 5 the kinetic curves of the sodium methoxide-initiated polymerization of α-aminoisobutyric acid NCA in the presence of cyclic amides as additives: 2-pyrrolidone, 2-oxazolidone, and 3-methylhydantoin. In this figure the addition of 2-pyrrolidone up to 10% of monomer has practically no effect, whereas 2-oxazolidone and 3-methylhydantoin added to 10% considerably enhance the polymerization rate, the effect being sensible for as low as a 1% addition.

It is known that 3-methylhydantoin and 2-oxazolidone possess acidities much closer to NCA than do lactams, the acidity order being [12]:

$$\text{lactams} \ll \text{3-methylhydantoin} < \text{2-oxazolidone} < \text{NCA} \qquad (5)$$

and that they do not polymerize by usual means.

Bamford et al. [13] reported a similar acceleration effect of 3-methylhydantoin for the tributylamine-catalyzed polymerization of proline NCA (a N-substituted NCA) in dimethylformamide and explained it by assuming the formation of 1-prolyl-3-methylhydantoin which would grow thereafter through the aminolytic mechanism. In the same work they pointed out the acceleration effect of water on a similar polymerization, which could be interpreted by initiation through the hydroxyl anion. These results suggest that alcoholate anions can also react with NCAs and initiate the chains, which is an indication in favor of Blout's mechanism, when applied to our results of the alcoholate-initiated polymerization of unsubstituted NCA, contrary to the expectation of the original authors. In other words, the activated monomer mechanism alone cannot account for the acceleration given by cyclic amides.

However, Blout's mechanism alone cannot supply a better explanation of the results for the same reasons as pointed out for the addition of alcohol. Thus the sole explanation would be that the part of polymerization observed without any additives proceeds through the activated monomer mechanism and that the acceleration caused by additives is produced by Blout's mechanism. In fact, such a situation would be difficult to believe.

Figure 6 shows that the addition of N-acetylglycine NCA to the polymerization mixture of α-aminoisobutyric acid NCA and sodium methoxide enhances the polymerization rate remarkably. This effect had been predicted by Kricheldorf who experimentally proved the incorporation of acetyl groups in the resulting polymer [10]. The addition of an equivalent amount of methanol to the reaction mixture containing a strong base initiator and N-acetylglycine NCA, causes additional enhancement of the polymerization.

There is no doubt that the acceleration effect of N-acetylglycine NCA observed in Fig. 6 is consistent with the activated monomer mechanism and is impossible to explain by Blout's mechanism. Besides, it appears to be necessary to admit the activated monomer mechanism even in the presence of added methanol (cf. Fig. 6). However, the part of the acceleration corresponding to the persistent effect of methanol addition would be difficult to understand by this mechanism, which leaves a place for Blout's mechanism.

In Fig. 7 are reproduced the IR spectra determined for the soluble (II, IV) and insoluble (I, III) fractions in 95% boiling ethanol of the polymers we obtained in the absence of additional alcohol (I, II) and in its presence (III, IV) (see Experimental Part). Dimethylhydantoin-isobutyric acid is detected in Fraction II, as confirmed by the reference sample prepared separately and in accordance with the IR spectra (absorption bands at 3120(w) (Ref. 14, 3100), 1770-60(s) (Ref. 14, 1755), 1720-10(s) (Ref. 14, 1700), and 1420(s) (Ref. 14, none) cm^{-1} and the DTA chart (215°C calibrated, heating rate 20°C/min under 50 cm^3/min

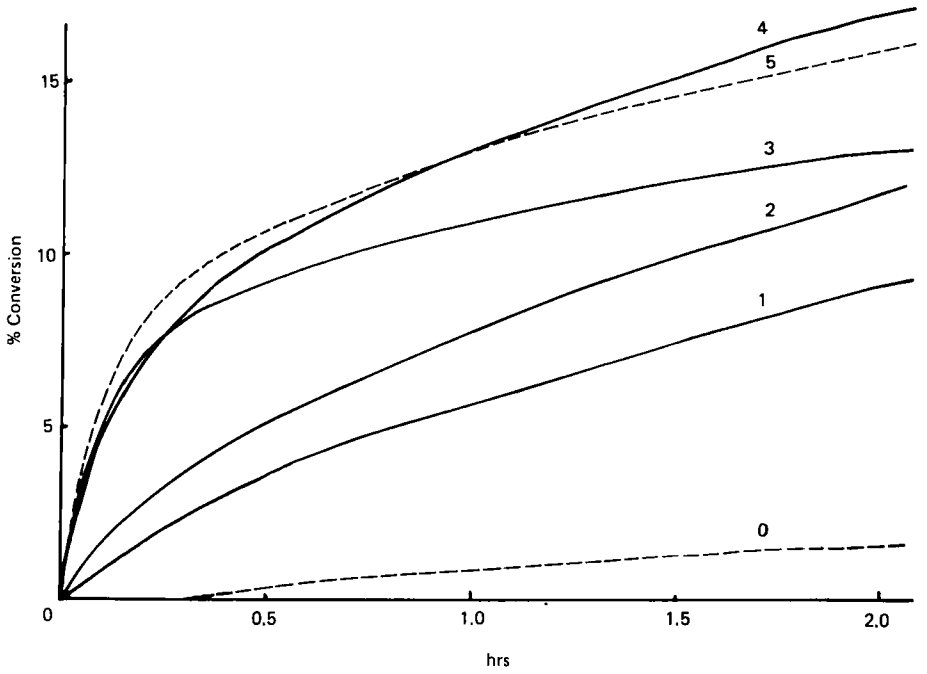


FIG. 6. Acceleration effect of methanol and N-acetylglycine NCA on the sodium methoxide-initiated polymerization of α-aminoisobutyric acid NCA in dry acetonitrile at 20.0 + 0.5°C. Monomer concentration 2.0 mol/L; initiator concentration with respect to monomer 3.0 mol%; additive concentration is given to mol% with respect to monomer and in additive/initiator ratio. Curve 0: methanol 3.0% without sodium methoxide initiator (reference curve). Curve 1: without any additive. Curve 2: methanol 3.0% (3.0/3.0). Curve 3: N-acetylglycine NCA 3.0% (3.0/3.0). Curve 4: the two additives, each 3.0% (3.0 + 3.0/3.0). Curve 5: curve synthesized from Curves 1, 2, and 3 (2 + 3 - 1).

nitrogen flow, (Ref. 14, 215-216). The derivative completely disappeared in Fraction IV, a low molecular weight fraction obtained in the presence of added methanol (10 mol% with respect to monomer) and is absent in boiled Fractions I and III, corresponding to higher polymers. The results obtained in the absence of methanol are consistent with the activated monomer mechanism while those found in its presence do not permit a choice between the two mechanisms.

Table 1 summarizes the mechanistic evaluation we have made by checking the validity or nonvalidity of the two classical mechanisms in the present section.

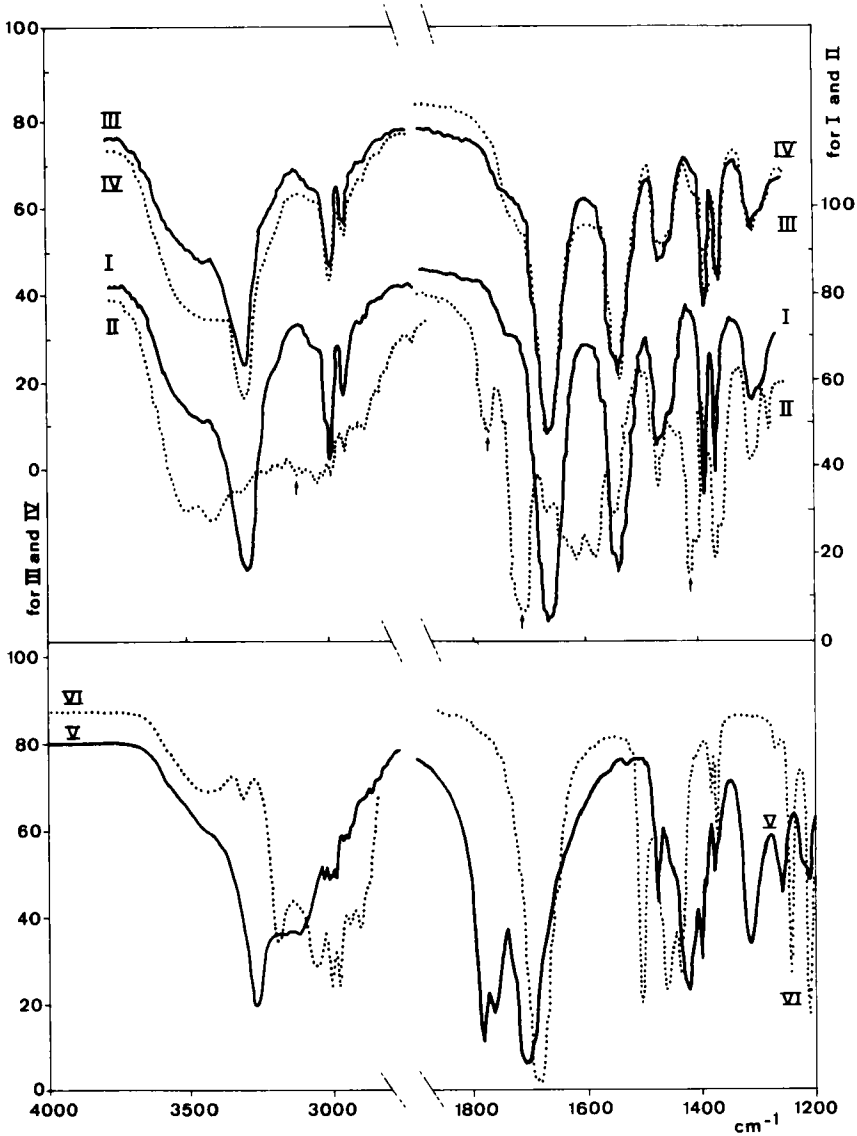


FIG. 7. Infrared spectra of polymers issued from sodium methoxide-initiated polymerization of α-aminoisobutyric acid NCA in dry acetonitrile. Monomer concentration 2.0 mol/L; initiator concentration with respect to monomer 3.0 mol%; methanol added: 0% (Samples I and II) and 3.0 mol% (Samples III and IV) with respect to monomer; temperature 20 ± 1°C; reaction time 1 week. Samples I and III: fractions insoluble in boiling 95% ethanol. Samples II and IV: fractions extracted by boiling 95% ethanol. Arrows indicate the characteristic signals of absorption of 5,5-dimethylhydantoin-3-isobutyric acid. Sample V: 5,5-dimethylhydantoin-3-isobutyric acid. Sample VI: 3,3,6,6-tetramethyl-2,5-piperazinedione.

TABLE 1. Validity or Nonvalidity of the Classical Mechanisms as Shown by the Specific Effects Observed in the Sodium Methoxide-Initiated Polymerization of α-Aminoisobutyric Acid NCA[a]

	Figure	Activated monomer mechanism	Blout's mechanism
Cation effect	1,2	+	+
Anion effect	3	-	+ ?
Methanol addition	4	-	-
Cyclic amide addition	5	-	-
N-Acetylglycine NCA addition	6	++	-
Combined addition of N-acetylglycine NCA and methanol	6	-	-
Analysis of the polymer obtained	7		
In the presence of CH_3OH		+	+
In the absence of CH_3OH		++	-

[a] ++ = supports positively the mechanism considered. + = does not exclude the mechanism considered. - = conflicts with the mechanism considered.

DISCUSSION

1. Merits and Demerits of α-Aminoisobutyric Acid NCA

The choice of α-aminoisobutyric acid NCA as the monomer of the present study was motivated principally by three considerations. First, it is one of the least acidic NCAs and the character of a multiple mechanism would therefore be accentuated in its polymerization, as will be seen in the next section. Second, its rate of polymerization is low, which would enable us to follow the kinetic process of the polymerization, and in particular the effects of the various additives, with a certain accuracy. Third, its low polymerizability in the presence of primary amine-type initiator, as witnessed by several authors [4, 15], would allow us to neglect the aminolytic (so-called "normal") propagation mechanism when discussing the other two classical mechanisms. Other factors, such as the ease of its preparation and purification and its relative stability during storage, were accessory advantages of its choice. The absence of asymmetrical carbon freed us from worry about the racemi-

zation of the monomer in the highly basic reaction mixture, which could have introduced an additional factor into the kinetics [22].

However, these merits are not completely free of some inconveniences. The relatively low reactivity of this NCA forced us to work with high concentrations of monomer, which should normally be avoided in kinetic studies. Another problem was the bending-down of the kinetic curves drawn for the polymerization of this NCA. Authors have apparently been prone to consider that a slow-down of polymerization is an indication of side reactions of termination, and that such a type of reaction does not merit kinetic study. This is true when we want to investigate and to analyze the kinetics, but is not harmless when two polymerizations that are identical except for one condition (the presence or the absence of an additive) are to be compared.

Finally, there is the problem of the low solubility of polyisobutyramide in most solvents. The polymerization mixture, initially homogeneous, becomes heterogeneous at the end of a certain time (cloud point), beyond which it is useless to follow the reaction kinetically. This phenomenon, which is due to the crystallization and the precipitation of the polymer, restricts the choice of the solvents for the polymerization of our monomer.

2. Interpretation on the Basis of the Hypothesis of a Multiple Mechanism [1]

We have seen above, especially in Table 1, that the results obtained for the polymerization of α-aminoisobutyric acid NCA by alkaline alcoholate initiators were sometimes consistent with the activated monomer mechanism, sometimes consistent with Blout's mechanism, and sometimes inconsistent with both. Furthermore, numerous experimental facts have been accumulated in the literature in favor of one or the other mechanism according to the nature of the reactants and the experimental conditions [1]. Thus, we were led to assume that the two mechanisms operate at the same time in the polymerization and that both initiator anion, A^-, and NCA anion, NCA^-, initiate the polymerization [1]. The effective concentration of these two anions will then be governed by the acido-basic equilibrium (2) and the efficiency of the initiation will depend on the nucleophilicity of A^- and NCA^-. The conjugate acid of the initiator, HA, can also initiate the polymerization through the anionoid mechanism with a part corresponding to its nucleophilicity. But as this reaction is very slow in case of α-aminoisobutyric acid NCA [15] (see Fig. 4, Curve 0), we will neglect it when discussing the kinetics in this paper. Thus, for the polymerization of α-aminoisobutyric acid NCA by an alkaline alcoholate initiator, $Q^+ {}^-OR$:

$$\text{NCA} + Q^+OR^- \rightleftharpoons Q^+NCA^- + HOR \qquad (6)$$

Initiation by alcoholate anion mechanism

Initiation by NCA anion mechanism

Initiation by the anionoid mechanism

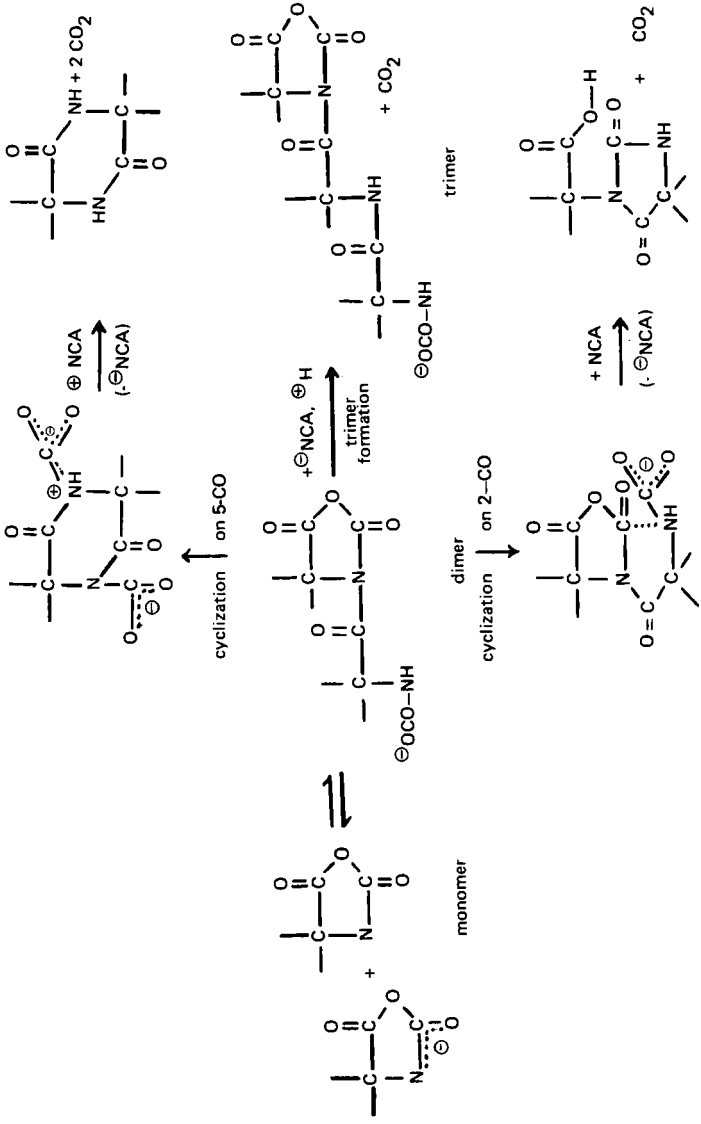
Since α-aminoisobutyric acid NCA is a fairly weak acid (see Section 4 below), it is more sensitive to the acidity of alcohol than the other current NCAs, which means that the alcoholate salt concentration in the mixture cannot be ignored. Thus, the variation in alcohol acidity modifies the significance of the initiations by ^-OR and NCA^-, an increase in acidity increasing the former. The fact that an increase in acidity of alcohol causes acceleration (Fig. 3) suggests that ^-OR has a higher efficiency than NCA^-. Otherwise, acceleration would not be observed. The addition of alcohol influences Equilibrium (6) in the same way but through the concentration of alcohol instead of its acidity (Fig. 4). The other additives (3-methylhydantoin and oxazolidone), which are also weakly acidic compounds, act similarly (Fig. 5). Thus, in this scheme, which involves two mechanisms of initiation, the acceleration caused by these additives can be reasonably considered as being due to an increase in initiation by Blout's mechanism, in contrast to the conclusion of Table 1 which considers one or the other mechanism exclusively.

On the contrary, acceleration due to the addition of N-acetylglycine NCA (Fig. 6, Curve 3) is a clear indication of the presence of NCA anion and of its participation in propagation through a NCA anion mechanism, and strongly supports the assumption of initiation by the same mechanism without, however, proving it. Proof is given by the formation of hydantoin-acetic acid derivatives (see next paragraph). Furthermore, the persistance of the effect of N-acetylglycine NCA, even in the presence of alcohol anion (Fig. 6, Curve 4), shows that the mixed imide anhydride group of the N-acyl NCA end unit is stable and resists the attack of the alcoholate anion to a certain extent, contrary to what would be expected at first sight.

In our preliminary note [23] we reported part of the results of Figs. 3 and 4 and discussed them briefly on a similar basis. Since then we have consolidated our hypothesis of a multiple mechanism, which now allows us to deal more thoroughly with the question.

3. Formation of 5,5-Dimethylhydantoin-3-Isobutyric Acid and Low DP Polymer

The dimer issued from the activated monomer mechanism is involved in three competing reactions (without taking account of the reverse reaction of its formation). (See Scheme 1.) When the rate of



SCHEME 1.

polymerization is relatively low, the slow intramolecular reaction is allowed to take place before the chain becomes a trimer. Cyclization on 5-CO leading to piperazine-2,5-dione is little favored, which was explained by a hypothetical steric factor [19]. The formation of the hydantoin-acetic acid derivative is, therefore, undeniable evidence of the activated monomer mechanism. This compound cannot be formed when Blout's mechanism operates alone.

Their detection was reported for the polymerizations using alkali halides (in dimethylformamide) [16], tertiary amines [16], and weakly basic salts [17], or under constant elimination of carbon dioxide (nitrogen bubbling) [18], but never in the polymerization of current NCAs with the help of basic salt initiators under normal conditions. The absence of such compounds in the latter polymerization embarrassed certain authors who were favorable to the activated monomer mechanism and encouraged others to defend Blout's mechanism. However, it should be borne in mind that their absence is not a proof of the nonoperation of the activated monomer mechanism.

The results of the alcohol-free polymerization in Fig. 7 are the first example of the detection of the hydantoin-acetic acid derivative in the sodium alcoholate-initiated polymerization without nitrogen bubbling (carbon dioxide elimination).

When alcohol is added, the hydantoin-acetic acid derivative disappears (Fig. 7). This result can be interpreted in two ways: either alcohol addition disadvantages the reaction of cyclization for some reason or another within the activated monomer mechanism, or it decreases the part of this mechanism to the profit of Blout's mechanism. The first would mean either that the cyclization is depressed or that the trimerization is accelerated by the added alcohol, which is difficult to conciliate with the activated monomer mechanism. The second interpretation is more plausible; the same interpretation was drawn from kinetic results.

In the same time, a greater proportion of soluble products is obtained in the presence of methanol, which shows that the chains are much shorter and their number is larger. This can arise either from the termination of chain growth by alcohol [20] in the hypothesis of a pure activated monomer mechanism or from the supplementary initiation by alcoholate anion due to the increasing alcoholate anion mechanism. In the former case, this would stop or slow down the polymerization, which is not true because, in Fig. 4, polymerization is actually accelerated to an extent which is superior to the sum of polymerizations by methanol alone and sodium methanolate alone. These results suggest that the NCA anion mechanism operates to a nonnegligible extent in the absence of added methanol, while it becomes less significant when methanol is added, seemingly to the profit of the alcoholate anion mechanism.

4. Significance of Each Elementary Mechanism

Since the hypothesis of a multiple mechanism presumes the coexistence of different mechanisms, it would be valuable to know their significance in polymerization conducted under normal conditions. Unfortunately, it is nearly impossible to separate one mechanism from another experimentally. The data available only allow qualitative information on the preinitiation Equilibrium (6). In the following discussion we take the example of the polymerization of α-aminoisobutyric acid NCA by alcohol-free methanolate in acetonitrile.

α-Aminoisobutyric acid NCA is one of the least acidic NCAs as a consequence of the double substitution by a methyl group on the 4-position of the oxazolidone-2,5-dione ring, a situation somewhat analogous to what t-butanol is to ethanol. Our earlier measurements have given a pK value of 18.9 for this NCA whereby smaller values are expected for current, more reactive NCAs (i.e., 4-monosubstituted oxazoline-2,5-diones) in dimethoxyethane (DME). The cited value would correspond to $\sim pK_a$ 15 in the normal scale since methanol, pK_a 15.5 [12], gives 23.0 in the same solvent [21]. In other words, the acidity of α-aminoisobutyric acid NCA is slightly higher, although still comparable, than that of methanol. It follows that in the reaction mixture containing 3.0 mol% methanol-free sodium methoxide initiator, both acidity and concentration of methanol (formed in situ) are lower than those of NCA monomer. It is expected in these circumstances that Equilibrium (6) sets up to the great advantage of NCA anion even for this rather weakly acidic NCA, and still more for the current, more acidic NCAs such as glycine and γ-benzyl glutamate NCAs. In other words, α-aminoisobutyric acid NCA should be one of the NCAs for which the NCA anion mechanism is relatively less favored to the profit of the alcoholate anion mechanism whose participation is, however, still limited.

However, it is difficult to assert that initiation is due more to NCA anion than alcoholate anion: the efficiency of alcoholate anion in initiation seems to be greater than that of NCA anion (see Paragraph 2) while, on the contrary, a chain growing with the activated anion mechanism might grow faster than one growing by Blout's mechanism. Only the determination of chain endgroups (carbamate anion and N-acyl NCA endgroups) at every moment, and the measurement of the propagation rate at the same time, when it is feasible, can confirm this.

CONCLUSION

As for all the other experimental results of NCA polymerizations reported in the literature, most of our results are found partly consistent with the activated monomer mechanism and in conflict with Blout's mechanism, and partly consistent with the latter and in conflict with the former. They were shown, however, not to conflict with our hypothesis

of a multiple mechanism, presuming an equilibrium between all the active species of these mechanisms.

α-Aminoisobutyric acid NCA is one of the least acidic NCAs, with its acidity only slightly higher than methanol, which allowed us to observe relatively easily the participation of the alcoholate anion in initiation (Blout's mechanism). This is probably one of the NCAs whose polymerization behavior deviates the most from that exactly described by the activated monomer mechanism.

REFERENCES

[1] H. Sekiguchi, Pure Appl. Chem., 53(9), 1689-1714 (1981).
[2] C. H. Bamford and H. Block, J. Chem. Soc., pp. 4989-4991 (1961).
[3] M. Idelson and E. R. Blout, J. Am. Chem. Soc., 80, 2387-2393 (1958).
[4] G. Froyer and H. Sekiguchi, Bull. Soc. Chem. Fr., pp. 2321-2325 (1975).
[5] H. Sekiguchi and B. Coutin, J. Poiym. Sci., Polym. Chem. Ed., 11, 1601-1614 (1973).
[6] H. Sekiguchi and P. Tsourkas-Rapacoulia, Bull. Soc. Chim. Fr., pp. 2585-2588 (1974).
[7] H. Sekiguchi and B. Coutin, Macromol. Synth., 6, 57-61 (1956).
[8] C. S. Marvel and F. D. H. Hager, Org. Synth., 1, 249 (1956).
[9] L. Siemonsen, Justus Liebigs Ann., 333, 101-141 (1904).
[10] H. R. Kricheldorf, Makromol. Chem., 178, 905-939 (1977).
[11] J. H. Riddick and W. B. Bunger, Organic Solvents: Physical Properties and Methods of Purification (Techniques of Chemistry, Vol. II, 3rd ed.), Wiley-Interscience, New York, 1970, p. 145.
[12] A. Caillet, D. Bauer, G. Froyer, and H. Sekiguchi, C. R. Acad. Sci., Ser. C, 277, 1211-1214 (1973).
[13] C. H. Bamford, H. Block, and A. C. P. Pugh, J. Chem. Soc., pp. 2057-2063 (1961).
[14] A. F. McKay, G. Y. Paris, and D. L. Garmaise, J. Am. Chem. Soc., 80, 6276-6280 (1958).
[15] D. G. H. Ballard and C. H. Bamford, J. Chem. Soc., pp. 355-360 (1958).
[16] D. G. H. Ballard, C. H. Bamford, and F. J. Weymouth, Nature, 174, 174-175 (1967).
[17] D. G. H. Ballard and C. H. Bamford, Chem. Soc. (London), Spec. Publ., 2, 25-43 (1955).
[18] C. E. Seeney and H. J. Harwood, J. Macromol. Sci.–Chem., A9(5), 779-795 (1975).
[19] C. H. Bamford and H. Block, "The Polymerization of N-Carboxy-α-amino Acid Anhydrides," in Comprehensive Chemical Kinetics, Vol. 15: Nonradical Polymerization (C. H. Bamford and C. F. H. Tipper, eds.), Elsevier, Amsterdam, 1976, Chap. 8, p. 596.

[20] M. Goodman, E. Peggion, M. Szwarc, and C. H. Bamford, Macromolecules, 10, 1299-1301 (1977).
[21] A. Caillet, Thesis, Univ. Paris VI, C.N.R.S., Register No. A.O. 9666, 1974, p. 100.
[22] M. Amouyal-Ruderman and H. Sekiguchi, Polym. Bull., 6, 69-74 (1981).
[23] H. Sekiguchi and J.-F. Doussin, Biopolymers, 15, 1431-1435 (1976).

Accepted by editor May 23, 1983
Received for publication June 26, 1983