Synthesis and Polymerization of Substituted β-Propiolactams[1]

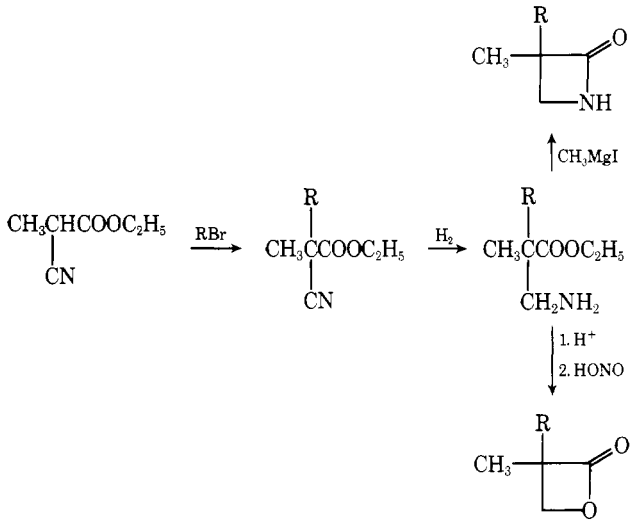
Claus D. Eisenbach and Robert W. Lenz*

Polymer Science and Engineering Program, Chemical Engineering Department, University of Massachusetts, Amherst, Massachusetts 01002. *Received August 15, 1975*

ABSTRACT: Several new 3-methyl-3-alkyl-2-azetidinones (β-propiolactams) were synthesized and polymerized with potassium pyrrolidone as initiator and *N*-acetylpyrrolidone as coinitiator in dimethyl sulfoxide as solvent. Kinetic studies showed that the rate of propagation increased with increasing length of the alkyl substituent.

β-Lactams (azetidin-2-ones) were first prepared by Staudinger in 1907,[2a] but the polymerization of this type of monomer to a polyamide was not investigated in detail until 1962 when Graf and coworkers developed a convenient monomer synthesis based upon the reaction of olefins with *N*-carbonylsulfamoyl chloride.[2b] This synthetic route, however, yields only β-lactams with substituents on the 4 position as determined by the structure of the olefin used.

In this laboratory investigations are in progress on the preparation and polymerization of α,α-disubstituted-β-propiolactones,[3] and it is of interest to compare these monomers with the behavior of equivalent β-lactams both in reactivity and structure–property relationships of the resulting polymers. It is particularly convenient to do this in our case because the principal synthetic route we have chosen for the synthesis of the β-lactone monomers proceeds through an aminoester, from which the analagous β-lactam can readily be obtained as follows:[4–7]

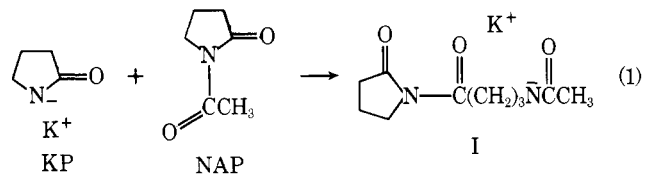


Using this procedure a series of new 3-methyl-3-alkyl-2-azetidinones were prepared, and the yields, physical constants, and elemental analyses for the respective intermediates and β-lactam monomers are collected in Tables II–IV. The parent monomer of this series is β-pivalolactam (the α,α-dimethyl monomer), and the others investigated contained a larger alkyl group (either ethyl, propyl, or butyl) in place of one of the methyl groups. These monomers and polymers, therefore, had asymmetric centers, and it was of interest to determine the effect of the alkyl group on both the rate of polymerization and the properties of the resulting polymers. The latter will be described in a subsequent publication.

Rate of Polymerization

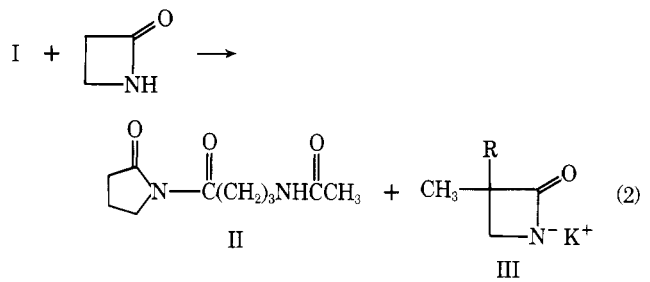
Rate determinations were carried out with strong-base anionic initiators, which could be used on these monomers without side reactions because of the absence of α-hydrogen atoms. Hence these reactions are believed to be "living polymer" systems.[8] It is well known that the anionic polymerization reactions of lactams in general are greatly facilitated by the addition of coinitiators based upon *N*-acylated lactams,[9] and these were used in the present system with amide anion initiators.

The specific initiator–coinitiator combination chosen was potassium pyrrolidone, KP, and *N*-acetylpyrrolidone, NAP, respectively, because the former can be readily prepared in pure form and easily proportioned into the reaction mixture.[10] All reactions were run in dimethyl sulfoxide,[2b] DMSO, which is a poor solvent for KP alone at room temperature but readily dissolves KP in the presence of NAP, indicating that the true initiating species, I, is formed in a rapid reaction between KP and NAP[11] as follows:



(1)

That is, in the presence of the monomer, this reaction is followed by a rapid proton exchange to form the stable lactam adduct, II, and the amide anion form of the monomer, III:[9,12]



(2)

Initiation is then completed in the rate-determining step,[12] reaction 3, by the reaction of the pyrrolidone end of II with III, followed by rapid proton exchange to reform III, reaction 4. Propagation, reaction 5, then ensues by successive anion addition reactions of the reactive monomer, III, with the lactam end of the growing polymer molecule, V, and rapid proton exchange of the latter with another monomer.

If this mechanism applies to the present case, it should be possible to determine the rate of propagation directly by following the disappearance of monomer or the formation of polymer when the lactam is added to the preformed initiator–coinitiator adduct, I, although possible differences in the rates of reactions 3 and 5 must be taken into account. The reaction was followed successfully by use of infrared spectroscopy after early attempts to follow the reaction by either NMR or uv spectroscopy proved unsuitable.

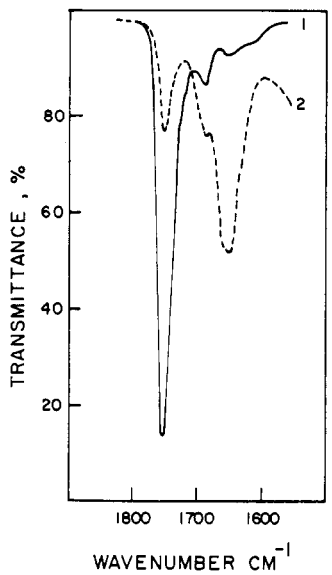
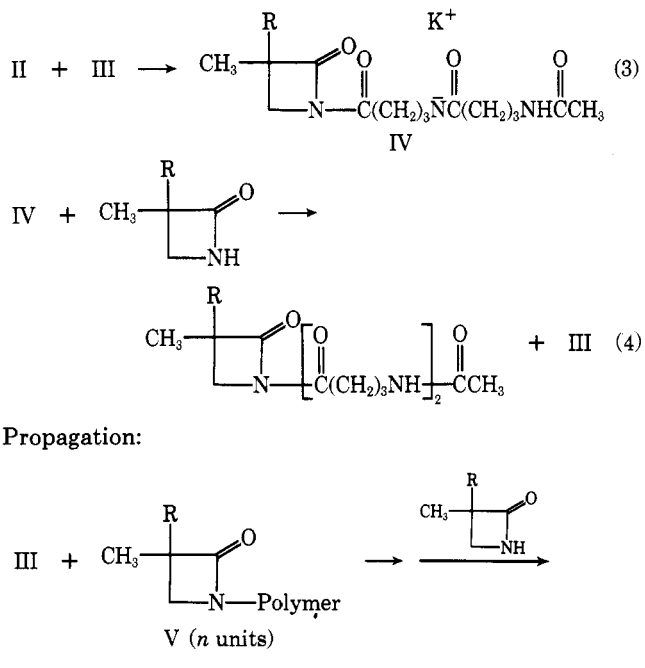


Figure 1. Ir spectra of the polymerization reaction solution for α-methyl-α-ethyl-β-propiolactam: (1) after 1 min, (2) after 293 min reaction time (row 5 of Table I).



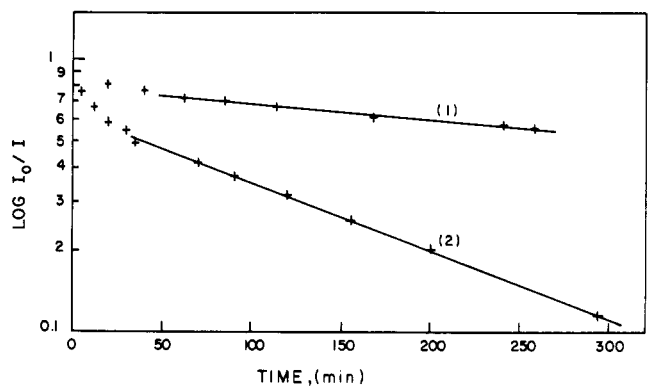


Figure 2. First-order rate plot for the polymerization of α-methyl-α-ethyl-β-propiolactam: (1) and (2) are for the reactions in rows 4 and 5, respectively, of Table I.

Attempts to use NMR analysis were unsuccessful because of the overlap of the fairly sharp methylene proton peak of the lactam monomer (δ = 2.9 ppm) with the rather broad peak of the polyamide (δ = 3.2 ppm) in deuterated DMSO solutions. Sufficient difference existed in the chemical shifts of the amide proton peaks of the monomer (δ = 7.5 ppm) and polymer (δ = 7.1 ppm) to prevent overlap, but both were too broad for accurate analysis by integration.

Uv spectroscopy seemed at first to be a practical method for following reaction conversion because the absorption peaks of the amide carbonyl function at 280 nm were approximately 12 times as intense in the polymer as in the monomer. However, this difference was masked when using the coinitiator, NAP, which increased the absorption to such an extent at this wavelength that essentially no change was observed during the polymerization. On the other hand, this technique could be satisfactorily used for studying the polymerization in the absence of the coinitiator, and it served in that case to demonstrate the very poor initiating ability of KP alone as expected.[11-13]

Ir spectroscopy[14] was readily applicable to obtaining rate data by a quantitative comparison of the carbonyl stretching frequencies of the monomer at 1751 cm^{-1} and polymer at 1653 cm^{-1} as shown in Figure 1 for a typical analysis. When this method was applied by adding monomer to a prereacted mixture of KP and NAP, as described above, and the intensity of the monomer peak was observed as a function of time, the propagation rate constant, k_p, could be determined quite simply by the kinetic analysis[15] described below.

Assuming that the disappearance of monomer is entirely

Table I
Kinetic Data for the Polymerization of α-Methyl-α-alkyl-β-propiolactams[a]

Alkyl group	$[M]_o$, M	$[KP]_o$,[b] M	$[NAP]_o$,[b] M	$k_a \times 10^3$, min^{-1}	k_p, M^{-1} min^{-1}	k_i, M^{-1} min^{-1}
Methyl	0.22[c]	0.008 7	0.008 25	4.06	0.49	
	0.205	0.017 6	0.015 9	7.82	0.49	4.1
Ethyl	0.123	0.012	0.008 9	6.42	0.72	
	0.200	0.002 33	0.002 22	1.30	0.59	4.3
	0.16	0.010 1	0.007 7	5.75	0.75	4.3
Propyl	0.105	0.010 8	0.008 0	6.58	0.82	5.3
	0.128	0.013 6	0.008 8	5.85	0.67	
	0.147	0.014 7	0.012 5	10.9	0.87	
Butyl	0.138	0.012 3	0.009 3	11.6	1.24	
	0.227[d]	0.015 6	0.012 9	15.3	1.19	
	0.112	0.017 1	0.012 7	14.0	1.11	7.1

[a] In DMSO at 22 °C. [b] Abbreviations: KP = potassium pyrrolidone; NAP = *N*-acetylpyrrolidone. [c] $\bar{M}_n$ (VPO) = 2100 (Calcd $\bar{M}_n$ = 2600). [d] $\bar{M}_n$ (VPO) = 2000 (Calcd $\bar{M}_n$ = 2500).

Table II
Preparation of Ethyl 2-Cyano-2-alkylpropionates

Alkyl group	Yield, %	Bp, °C (mm)
CH_3	76	40 (1.0)
C_2H_5	88	56 (1.7)
C_3H_7	80	50 (0.4)
C_4H_9	84	52 (0.2)

attributable to propagation reactions (i.e., that initiation, termination, and transfer are absent and the polymerization is carried out far below its ceiling temperature) the rate of consumption of monomer, M, can be described by the following equation:

$$\frac{-d[M]}{dt} = k_p C_0[M] = k_a[M]$$

where C_0 is the initial concentration of the KP–NAP adduct, I, and k_a is an apparent or pseudo-first-order rate constant.[16-18] On integration this equation becomes:

$$\ln [M] = \ln [M]_0 - k_a t$$

where [M] is the concentration of monomer at time t and $[M]_0$ is the initial monomer concentration. Hence a plot of ln [M] vs. time should be linear with a slope equal to k_a, and such a plot is shown in effect in Figure 2 for the polymerization reaction of α-methyl-α-ethyl-β-propiolactam at two different levels of initiator adduct concentration.

The rate plots in Figure 2 are seen to have initial steep slopes, but after approximately 30% conversion, the following linear portions prevailed throughout the remainder of the reaction time. The reactions could be followed over the linear regions with good accuracies up to conversions of about 90%. The concentration and rate constant data for these investigations on the four monomers are collected in Table I. The apparent propagation rate constants, k_a, were obtained from the linear portions of plots of the type shown in Figure 2 in which the actual monomer concentration [M] is expressed by its extinction: $E = \log (I_0/I)$. This rate constant was then converted to k_p by dividing by initiator adduct concentration. It was assumed in this calculation that no transfer or termination reactions occurred to significantly effect the rate, and this assumption appears justified from the good agreement between calculated (based upon monomer-to-initiator ratios) and observed molecular weights shown in the footnotes of Table I.

The initial portion of the plot in Figure 2 can be attributed to a faster reaction of the monomer anion with the pyrrolidone end group of the initiator adduct, reaction 3, than with subsequent β-lactam end groups in propagation, reaction 5 (see columns 6 and 7 of Table I). This explanation is also in agreement with the significantly higher rate constants for the anionic polymerization of pyrrolidone previously observed[11,13] than those of the β-lactams obtained in the present investigations. The rate constants for the initiation reaction, eq 3, were obtained from the initial slopes in the same manner as that used for calculating the k_p values.[15]

In the preparation of the adduct, KP was always used in excess of NAP, and the concentration of the latter was taken for the adduct. If the salt of the lactam monomer itself had been used instead of KP for forming the initiating species of eq 1, the differences in the rates of initiation and propagation would have been eliminated. Unfortunately, however, the usual procedures employed for the preparation of KP were not successful when applied to the present β-lactam monomers. Furthermore, attempts were made to calculate the initiation and propagation rates by a mathematical treatment derived by Beste and Hall,[15] but this approach was also unsuccessful (as it has been for other anionic polymerizations) indicating that the initiation reaction in the present lactam polymerization is basically dif-

Table III
Preparation of 2-Amino-2-alkylpropionates

Alkyl group	Yield, %	Bp, °C (mm)	Formula (mol wt)	Elemental Anal. C Calcd	C Found	H Calcd	H Found	N Calcd	N Found
CH_3	84	47 (3.5)	$C_7H_{15}NO_2$ (145.19)	57.90	57.93	10.41	10.13	9.64	9.75
C_2H_5	81	47 (1.1)	$C_8H_{17}NO_2$ (159.21)	60.35	60.42	10.76	10.46	8.79	8.62
C_3H_7	86	73 (4.2)	$C_9H_{19}NO_2$ (173.24)	62.39	62.23	11.06	10.72	8.08	8.23
C_4H_9	82	80 (3.1)	$C_{10}H_{21}NO_2$ (187.21)	64.14	64.10	11.30	11.30	7.47	7.29

Table IV
Preparation of 3-Methyl-3-alkyl-2-azetidinones (β-Lactams)

Alkyl group	Yield, %	Bp, °C (mm)	Formula (mol wt)	Elemental Anal. C Calcd	C Found	H Calcd	H Found	N Calcd	N Found
CH_3	48	68[a] (1.8)	C_5H_9NO (99.12)	60.58	60.76	9.15	9.07	14.13	14.06
C_2H_5	43	80 (1.6)	$C_6H_{11}NO$ (113.15)	63.69	63.44	9.80	9.71	12.37	12.33
C_3H_7	49	87 (1.4)	$C_7H_{13}NO$ (127.17)	66.11	66.39	10.30	10.24	11.01	11.13
C_4H_9	51	101 (1.6)	$C_8H_{15}NO$ (141.20)	68.05	67.84	10.71	10.57	9.91	10.17

[a] Mp 28 °C.

ferent than that of the lactones, for which the treatment was successfully applied.

These present results indicate that the rates of propagation of α,α-disubstituted-β-propiolactams are surprisingly low in comparison with that for the anionic polymerization of β,β-dimethyl-β-propiolactam (4,4-dimethyl-2-azetidinone), with essentially the same initiator in DMSO at 20 °C,[2b] for which we calculated a k_p value of approximately 135 M^{-1} min^{-1} from the plot given in ref 2b. In comparison, the value of k_p for the bulk polymerization of pyrrolidone was reported to be still greater at 480 M^{-1} min^{-1}.[13]

Also unexpected was the increase in k_p with increasing size of the alkyl group as seen in Table I. This observation contrasts to the more reasonable opposite effect observed in lactones[19] and other lactams.[12,20] To account for this trend, consideration must be given of the expected substituent effect on the reactivities of both the monomer amide anion and the lactam imide end group as well as on the ion pair structure of the monomer anion in the highly polar solvent used. It might have been expected that the role of the alkyl groups would be primarily a steric effect, with little contribution to inductive effects, and the larger groups would be expected to sterically hinder the reaction,[21] but such is apparently not the controlling influence on rate. Perhaps the increase in k_p can be attributed to a change in the ion pair character of the monomer anion, III, in which the alkyl group enhances the reaction rate by inhibiting contact or intimate ion pair formation between the large potassium cation and the amide nitrogen anion.

Experimental Section

Monomer Synthesis. The β-lactam monomers (3-methyl-3-alkyl-2-azetidinones) were synthesized from ethyl 2-cyanopropionate, VI (Aldrich). The second alkyl group was inserted by the following procedure: 500 ml of a 2 M sodium hydroxide solution in ethanol was added to a mixture of 1 mol of VI and 1.1 mol of the appropriate alkyl bromide and refluxed for from 3 to 8 h, depending on the size of the alkyl group, until the reaction mixture was essentially neutral. The product was obtained pure by distillation[22] as analyzed by gas chromatography, GC (>99%), with the results shown in Table II.

Selective catalytic hydrogenation[23] of the cyano group in the pure products of Table II over an alkaline Raney nickel catalyst prepared in a highly reactive form from nickel–aluminum alloy (PCR Inc.)[24] gave the aminoester of Table III. This reaction was carried out in a 1-l. Parr Autoclave on a suspension of 20 g of Raney nickel in 200 ml of absolute ethanol with 0.3–0.7 mol of the cyanoester at 80–100 °C with 1500–1700 psi initial hydrogen pressure. Reaction times of 2 h gave the yields indicated in Table III, and the products were again purified by distillation and analyzed by GC (>98%).

Ring closure of the aminoesters to the lactams of Table IV was carried out with methylmagnesium iodide by the procedure of Testa and coworkers,[6] and the monomers were twice distilled before use (GC > 99.8%).

Initiator and Coinitiator. Potassium pyrrolidone, KP, was prepared as described in the literature[10] and stored under dry argon. *N*-Acetylpyrrolidone, NAP, was prepared by adding 14.1 g (0.18 m) of acetyl chloride to a suspension of 23.8 g (0.19 mol) of KP in 80 ml of toluene at room temperature (see ref 25). NAP was distilled in 48% yield with 99.9% purity by GC analysis; boiling point 75 °C (1.7 mm) (99 °C (4 mm)[26]).

Polymerization. Dimethyl sulfoxide, DMSO (Aldrich spectrophotometric grade), was refluxed in the dark over calcium hydride for 1 day and distilled under argon before use.[27] All polymerization reactions were run under argon in a 50-ml round-bottom flask equipped with a magnetic stirrer and a 3-way stopcock containing a serum cap for addition of monomer from a syringe. DMSO was distilled into the reaction flask containing a weighed amount of KP under an argon atmosphere; NAP was added with a syringe followed by the monomer. Samples were removed periodically with a syringe and analyzed on a Perkin-Elmer Model 257 Infrared Spectrometer in a 0.0025-cm solution cell balanced against pure DMSO (medium scan speed, *N* slit width).

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