Synthesis, Dimerization, and Polymerization of 5-Oxazolones

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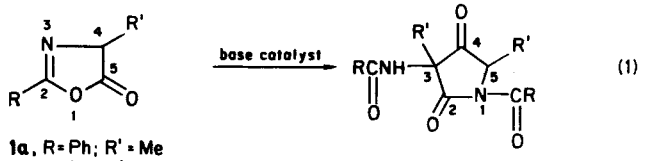
ABSTRACT: Six 2,4-disubstituted 5-oxazolones (**1**) and two 2-unsubstituted 5-oxazolones (**2**) were prepared. The isolation of **2** has been accomplished for the first time, albeit in a solution of high concentration. **1** and **2a** underwent a selective dimerization with a basic catalyst to give cyclic ketoimide dimers (**3a–g**). 2-Unsubstituted monomers (**2**) were found to polymerize via ring-opening isomerization at room temperature with a cationic initiator, giving rise to poly(*N*-formyl-α-peptides) (**4**). This result provides a new single-step method for preparing polymer **4**, which has not been synthesized previously. By the use of this method, optically active poly(*N*-formyl-L-alanine) (**4a′**) was obtained for the first time.

2-Oxazolines constitute a family of cyclic 1,3-oxaza monomers, whose ring-opening polymerization is an important research field within polymer science.[1,2] For the extension of our studies on 2-oxazoline polymerizations,[1] we have examined the ring-opening polymerization of 5-oxazolones (2-oxazolin-5-ones **1** and **2**), in which the methylene group at the 5 position of 2-oxazoline has been replaced by a carbonyl group.

5-Oxazolones have been known since the last century.[3] The structures were first termed "azlactones" by Erlenmeyer.[3c] 5-Oxazolones can be viewed as dehydration products, anhydrides of *N*-acyl-α-amino acids that are prepared by ring closure of the acids. In the hydrolysis of activated *N*-acyl-α-amino acid esters, 5-oxazolones are involved as intermediates and have been extensively investigated for their relevance to enzymatic acylation and deacylation reactions.[4] 5-Oxazolones have been employed as intermediates for various organic syntheses,[5] especially in peptide synthesis.[6] Furthermore, several addition/ring-opening polymerizations of 5-oxazolones have been reported.[2] In spite of this wide variety of investigations the ring-opening polymerization of 5-oxazolones has not yet been described.

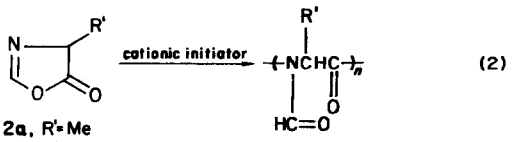
The present paper deals with synthesis of 5-oxazolones, including the first isolation of 2-unsubstituted 5-oxazolones (**2**) in the form of a concentrated solution, dimerization of 5-oxazolones (**1** and **2a**) with a basic catalyst to **3** (reaction 1), and the cationic ring-opening polymerization of **2** to poly(*N*-formyl-α-peptides) **4** (reaction 2). The dimer



1a, R = Ph; R′ = Me
b, R = Ph; R′ = *i*-Pr
c, R = R′ = Ph
d, R = Me; R′ = *i*-Pr
e, R = Me; R′ = *i*-Bu
f, R = Me; R′ = PhCH$_2$
2a, R = H; R′ = Me

3a, R = Ph; R′ = Me
b, R = Ph; R′ = *i*-Pr
c, R = R′ = Ph
d, R = Me; R′ = *i*-Pr
e, R = Me; R′ = *i*-Bu
f, R = Me; R′ = PhCH$_2$
g, R = H; R′ = Me

(1)



2a, R′ = Me
b, R′ = H

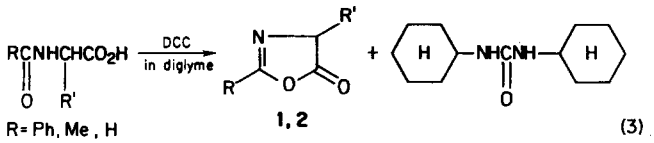
4a, R′ = Me
b, R′ = H

(2)

formation described in the present study was first observed by Rügheimer, and the dimer's structure was established by Cornforth and Huang.[7] A further dimerization study was reported by Taylor et al.,[8] who obtained a dimer and reconfirmed its structure. To our knowledge, the present work is the first preparation of poly(*N*-formyl-α-peptides).

Results and Discussion

Monomer Synthesis. Monomers **1** and **2** were prepared by the dehydrating cyclization of an *N*-acyl- or *N*-formyl-α-amino acid with an equimolar amount of *N,N′*-dicyclohexylcarbodiimide (DCC) (reaction 3).[4a] Six



R = Ph, Me, H

1, 2

(3)

2,4-disubstituted monomers **1a–f** were prepared from the corresponding DL-α-amino acids and were stable enough to be isolated by a purification procedure of distillation or sublimation.

2-Unsubstituted monomers **2** proved less stable. Siemion and Nowak[9] reported reactions of several *N*-formyl-α-amino acids with DCC and claimed the isolation of 2-unsubstituted 5-oxazolones, including **2a**. We followed a similar procedure with a variety of solvents but failed to isolate either type of **2**. Other investigators have also experienced difficulty in the isolation of these compounds.[4a,b] In the present study, therefore, the isolation of **2** was achieved by removal of *N,N′*-dicyclohexylurea by filtration of the reaction mixture followed by codistillation at reduced pressure with a carrier solvent of diglyme, by which the stability problem of **2** was overcome.[10] Thus, **2** was obtained as a diglyme solution of conveniently high concentration (up to 0.86 mol/L). The spectral data of 2-unsubstituted 5-oxazolones in diglyme are as follows. **2a** from DL-alanine: IR 1810 (C=O) and 1625 cm^{-1} (C=N); ^{1}H NMR δ 1.42 (d, 3 H, CH$_3$), 4.05 (m, 1 H, CHCH$_3$), 7.46 (d, 1 H, N=CH). **2b**: IR 1815 (C=O) and 1620 cm^{-1} (C=N); ^{1}H NMR δ 4.14 (d, 2 H, NCH$_2$), 7.60 (d, 1 H, N=CH).

Base-Catalyzed Dimerization of 5-Oxazolones. To start our work on the ring-opening polymerization of 5-oxazolones, 2,4-disubstituted 5-oxazolines **1** were employed for their ease of preparation and isolation. All the base-catalyzed reactions of **1a–f** with a typical anionic polymerization initiator in CH$_2$Cl$_2$ or THF did not cause the ring-opening polymerization but yielded dimers **3** of a cyclic 1,3-diketo imide structure in moderate to good yields (Table I, entries 1–23). The product dimers **3** were isolated in all cases by thin layer chromatography (TLC) on silica plates developed in chloroform. Taylor et al. previously reported the dimerization of **1a** to **3a** in refluxing chloroform catalyzed by triethylamine.[8] It can be seen in Table I that triethylamine is not a general catalyst for the se-

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Table I
Base-Catalyzed Dimerizations of 5-Oxazolones under Various Reaction Conditions

		reaction conditions				dimer	
entry	5-oxazolone	catalyst, (mol %)	solv	temp, °C	time, h	isolated yield, %	struct
1	**1a**	BuLi (5)	CH_2Cl_2	−78	72	40	**3a**
2	**1a**	BuLi (5)	THF	−78	120	10	**3a**
3	**1a**	BuLi (5)	THF	−10	24	33	**3a**
4	**1a**	BuLi (5)	THF	rt	20	70	**3a**
5	**1a**	Et_3N (5)	THF	60	96	87	**3a**
6	**1a**	NaOMe (5)	THF	rt	96	85	**3a**
7	**1a**	NaOMe (5)	THF	60	1	69	**3a**
8	**1b**	BuLi (5)	THF	rt	72	68	**3b**
9	**1b**	Et_3N (5)	THF	60	144	0	**3b**
10	**1b**	pyridine (5)	THF	60	144	0	**3b**
11	**1b**	NaOMe (5)	THF	60	120	36	**3b**
12	**1c**	BuLi (5)	THF	rt	120	80	**3c**
13	**1c**	Et_3N (5)	THF	rt	144	55	**3c**
14	**1c**	NaOMe (5)	THF	rt	144	38	**3c**
15	**1d**	BuLi (5)	THF	rt	144	9	**3d**
16	**1d**	BuLi (15)	THF	rt	48	40	**3d**
17	**1d**	Et_3N (5)	THF	rt	288	0	**3d**
18	**1e**	BuLi (10)	THF	rt	48	52	**3e**
19	**1e**	BuLi (10)	CH_2Cl_2	rt	48	30	**3e**
20	**1e**	Et_3N (5)	THF	rt	288	0	**3e**
21	**1f**	Et_3N (10)	THF	rt	96	43	**3f**
22	**1f**	Et_3N (10)	CH_2Cl_2	rt	72	39	**3f**
23	**1f**	Et_3N (5)	THF	rt	288	0	**3f**
24	**2a**	LDA[a] (5)	diglyme	rt	96	43	**3g**
25	**2a**	NaOMe (5)	diglyme	rt	96	42	**3g**

[a] Lithium diisopropylamide.

Table II
Cationic Ring-Opening Polymerization of 2-Unsubstituted 5-Oxazolones 2a and 2b at Room Temperature

		reaction conditions			polymer		
entry	5-oxazolone	init (mol %)	solv	time, h	yield, %	MW	struct
26	**2a**	MeOTf (0.5)	diglyme	48	70	5100	**4a**
27	**2a**	MeOTf (1.0)	diglyme	48	78	4000	**4a**
28	**2a**	MeOTf (1.0)	diglyme (75%)/CH_3CN (25%)	72	60	2900	**4a**
29	**2a**	$TiCl_4$ (1.0)	diglyme	36	62		**4a**
30	**2a**	$BF_3{\cdot}OEt_2$ (1.6)	diglyme	144	21		**4a**
31	**2a**	MeI (5.0)	diglyme	336	34	1200	**4a**
32	**2a**	none	diglyme	120[a]	28	700	**4a**
33	**2a′**[b]	MeOTf (0.5)	diglyme	6	100	1450	**4a′**[b]
34	**2b**	MeOTf (1.0)	diglyme (75%)/CH_3CN (25%)	72	38	2400	**4b**
35	**2b**	MeOTf (1.0)	diglyme	72	45		**4b**
36	**2b**	$BF_3{\cdot}OEt_2$ (1.0)	diglyme	36	50		**4b**

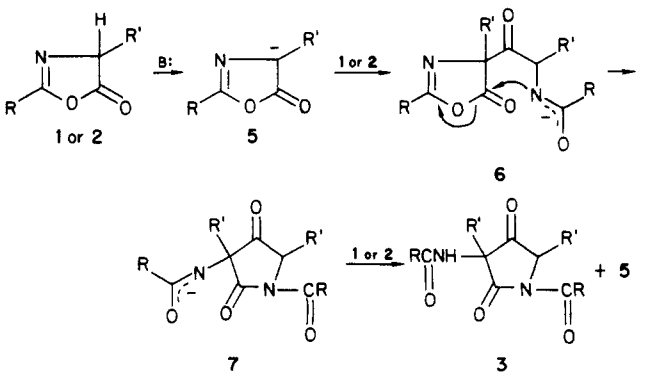
[a] Reaction at 60 °C. [b] Starting amino acid was L-alanine.

lective dimerization and that *n*-butyllithium or sodium methoxide is an even more active catalyst; triethylamine and pyridine are sometimes inactive (entries 9, 17, 20, 23, and 10). The dimerization occurred at as low a temperature as −78 °C.

Dimer **3** was the main product in every run. From the TLC analysis other oligomers such as the trimer, tetramer, etc., are byproducts that were present in much smaller amounts. Polymeric materials were not produced. Thus, the dimerization is a selective reaction. The structures of **3** were determined by IR and ^1H NMR spectroscopy as well as elemental analysis (see Experimental Section). The data for the structural determination of **3a** coincided with those previously reported.[8] The precise stereochemistry of dimers **3**, however, has not been elucidated yet. It is to be noted that a cationic or radical initiator did not induce the oligomerization of 2,4-disubstituted 5-oxazolones **1**.

2-Unsubstituted 4-methyl-5-oxazolone (**2a**) was found also to undergo a selective dimerization by base catalysis, giving rise to dimer **3g** of cyclic 1,3-diketo imide structure (Table I, entries 24 and 25). Dimer **3g** could be isolated by a preparative TLC technique in 43% yield from the products of reaction with lithium diisopropylamide catalyst. No polymeric product was formed from **2a** with a basic catalyst. A radical initiator did not cause any change of **2a**.

A mechanistic route leading to dimers **3** is reasonably explained in the following way. Hydrogen at the C-4 position of the monomer is acidic and abstracted by a basic catalyst to give a carbanion **5**, which attacks the carbonyl carbon of a second monomer molecule producing the ring-opened, dimeric anion **6**. Since the carbonyl group

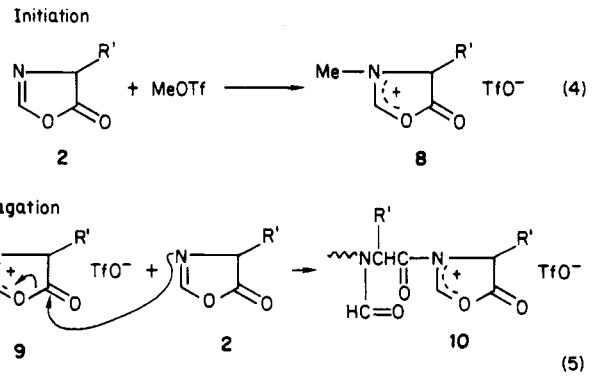


in the ring of **6** is still reactive, a nucleophilic cyclization takes place, giving rise to 1,3-diketo ring structure **7**, whose hydrogen abstraction from the monomer gives the product dimers **3** and **5**.

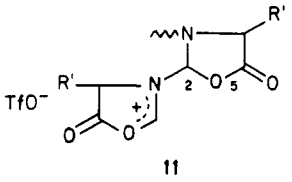
Cationic Ring-Opening Polymerization of 2-Unsubstituted 5-Oxazolones. Solutions of monomers, **2a** from DL-alanine and **2b** from glycine, were obtained by codistillation with a carrier solvent of diglyme as discussed above. Treatment of the solution with a cationic initiator $MeOSO_2CF_3$ (MeOTf) at room temperature resulted in a smooth polymerization to give white powdery polymeric materials (entries 26–28, 34, and 35 in Table II). Other catalysts, such as $TiCl_4$ and $BF_3{\cdot}OEt_2$ seem less effective. MeI also induced the polymerization of monomer **2a** to produce polymeric materials of relatively lower molecular weights (entry 31). With MeOTf initiator, the polymerization of **2a** seems to be complete within several hours, as seen in a run with optically active monomer **2a'** (entry 33), although other runs were carried out for longer reaction times.

All the polymeric materials are hygroscopic and soluble in highly polar organic solvents such as Me_2SO, DMF, pyridine, and triethyl phosphate but insoluble in water, ethanol, benzene, and diethyl ether. The structure of the polymer obtained by MeI initiator was determined as poly(*N*-formyl-α-alanine) (**4a**) on the basis of the following spectroscopic data: IR (KBr) 1680 cm^{-1} (vs, two imide C=O); ^1H NMR (Me_2SO-d_6) δ 1.0–1.8 (br, 3 H, CH_3), 4.1–5.1 (vbr, 1 H, $CHCH_3$), 8.5 (vbr, 1 H, NCHO); ^{13}C NMR (Me_2SO-d_6 with Me_4Si) δ 17 (CH_3), 51 ($CHCH_3$), 163 and 171 (2 C=O). For a polymer sample prepared by MeOTf initiator (entry 26), a weak band at 1810 cm^{-1} in IR and a weak signal at δ 93 in the ^{13}C NMR were additionally observed. Analytical data supported structure **4a**. Anal. Calcd for $[C_4H_5NO_2(H_2O)_{0.3}]_n$: C, 45.98; H, 5.40; N, 13.40. Found: C, 46.13; H, 4.96; N, 13.41. Polymer **4b** (entry 34): IR (KBr) 1810 cm^{-1} (w), 1680 (vs, two imide C=O); ^1H NMR (Me_2SO-d_6) δ 4.56 (br, 2 H, CH_2), 8.51 (br, 1 H, NCHO); ^{13}C NMR (Me_2SO-d_6 with Me_4Si) δ 168 and 162 (2 C=O); signals due to CH_2 seem to overlap with those of Me_2SO around δ 40. Anal. Calcd for $[C_3H_3NO_2(H_2O)_{0.4}]_n$: C, 39.05; H, 4.15; N, 15.18. Found: C, 39.31; H, 4.42; N, 14.38. Poly(*N*-formyl-α-peptides) had been unknown, and the present cationic ring-opening polymerization of 2-unsubstituted 5-oxazolones **2** represents the first single-step synthesis of such polymers.

The polymerization course of **2** with methyl triflate (MeOTf) initiator is best presented in the following way. Initiation involves methylation at the nitrogen atom of **2** to form 5-oxazolonium ion **8**. Propagation is represented by reaction 5, in which the carbonyl carbon of the propagating cyclic 5-oxazolonium ion **9** is nucleophilically attacked by monomer **2** to give an *N*-formyl-α-peptide unit **10** via ring opening as well as isomerization of **9**. The onium propagating species, **8** and **9**, are less stable due to an inductive effect of the carbonyl group compared with those of 2-oxazolinium ion species, and hence the ring-opening polymerizability of **2** is enhanced. In fact, **2** polymerized very readily at room temperature as seen in Table II, but 2-oxazolines require higher temperatures to induce their polymerization.[1,2]

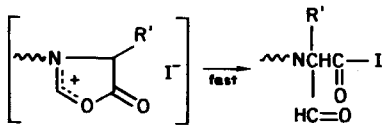


Polymers **4** produced by MeOTf initiator, however, showed an IR band at 1810 cm^{-1} and ^{13}C NMR signals at around δ 93, which were absent in the polymer **4a** by MeI. These observations suggest side reaction(s) to form a repeat unit other than an *N*-formyl-α-peptide structure. It is assumed that a side reaction takes place in the propagating step; the C-2 atom of the propagating species **9** may be attacked by monomer **2** to produce a ring-preserved unit **11**. Then, the carbonyl group of **11** accounts for the IR band at 1810 cm^{-1} and the C-2 carbon of **11** bonded to two nitrogen atoms and one oxygen atom gives rise to ^{13}C NMR signals around δ 93.



11

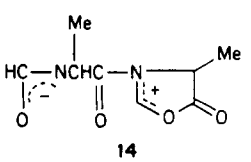
With MeI initiator, on the other hand, it is highly likely that an onium type propagating species **12** is rather unstable, and so, a covalent acid iodide type propagating end **13** is involved as a more stable species. Since the intramolecular reaction in **12** to open the ring is probably very fast and selective, this process will not produce a unit like **11** due to a side reaction.



12 **13**

Thermal Polymerization of Monomer 2a. It is striking that **2a** gave polymer **4a** without added initiator at a higher temperature (entry 32). The IR and ^1H and ^{13}C NMR spectral data are almost identical with those of a polymer sample obtained by MeI initiation (entry 31). Therefore, this "thermal" polymerization is a clean reaction to give poly(*N*-formyl-α-alanine) **4a**, although the molecular weight is not high.

The mechanism of the polymerization may be explained as follows. The "azlactone" monomer **2** contains a nucleophilic group of a cyclic imino ether and an electrophilic group of a lactone within the same molecule and, therefore, is expected to be "amphiphilic". At a higher reaction temperature, one molecule of **2a** acts as a nucleophile and the other molecule of **2a** behaves as an electrophile to produce a zwitterion **14**, which is a key intermediate. Once



14

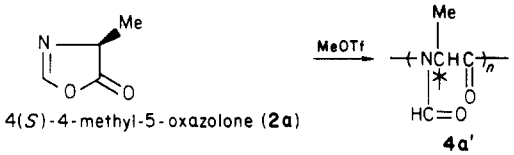
14 is formed, reactions between molecules of **14**, between **14** and macrozwitterions, and/or between monomer **2a** and these zwitterions lead to the formation of polymer **4a**. This kind of thermal polymerization has already been observed with a cyclic phosphorus monomer of 2-phenyl-1,2-thiaphospholane.[11]

Actually, **2a** and **2b** have been found to be reactive nucleophilic monomers (M_N) toward an electrophilic monomer (M_E) such as acrylamide or 2-hydroxyethyl acrylate. Copolymerization between M_N and M_E took place without added initiator, giving rise to an alternating copolymer, probably via zwitterionic intermediates.[12]

In all of the above polymerizations, the most important prerequisite was the isolation of the 2-unsubstituted monomer **2** as a solution. If the concentration and purity of the monomer were higher, polymers **4** of higher molecular weight might possibly be obtained and the side reaction with MeOTf initiator might be dimenished or eliminated.

In polymerization reactions, 2-unsubstituted **2** showed a higher ring-opening reactivity than 2-substituted monomers, e.g., 2-methyl-5-oxazolone. The polymerization of the latter monomer is induced by MeI initiator to give oligomeric products containing the *N*-acetylglycine unit after a relatively long reaction time at room temperature. The ring-opening polymerizations of the 2-substituted 5-oxazolones are currently under way.

Preparation of Poly(*N*-formyl-L-alanine). In both reactions 4 and 5, the carbon at the C-4 position is not involved, the configuration of the carbon being preserved during the polymerization. Taking advantage of this fact, an attempt was made to prepare optically active poly(*N*-formyl-L-alanine) (**4a'**). L-Alanine was N-formylated to give *N*-formyl-L-alanine[13] ($[\alpha]^{22}_D$ −79.1°; H_2O solution c = 0.445) followed by dehydrating ring closure with DCC, producing 4(*S*)-4-methyl-5-oxazolone (**2a'**). Codistillation



4(*S*)-4-methyl-5-oxazolone (**2a**) **4a'**

with diglyme gave its solution of **2a'** ($[\alpha]^{22}_D$ −18°; diglyme solution c = 0.60). The cationic ring-opening polymerization of **2a'** with MeOTf quantitatively produced polymer **4a'** (entry 33). Polymer **4a'** is a white solid decomposing above 190 °C, which is a much higher temperature than that for **4a**, prepared from recemic monomer **2a** (decomposition at 143–150 °C). The specific rotation of **4a'** was $[\alpha]^{22}_D$ −3.60° (trimethyl phosphate solution c = 0.49). As observed with polymer **4a** by MeOTf initiator, polymer **4a'** showed a band at 1810 cm^{-1} (IR) and signals around δ 93 (^{13}C NMR). Therefore, **4a'** also contains a unit like **11** due to a side reaction.

Experimental Section

Materials. Solvents diglyme, CH_2Cl_2, $CHCl_3$, THF, ethyl acetate, diethyl ether, and acetonitrile were purified by distillation under nitrogen. *N,N'*-Dicyclohexylcarbodiimide (DCC) and an *n*-hexane solution of *n*-butyllithium (1.65 mol/L) were obtained commercially and used without purification. Commercial reagents of benzoyl chloride, acetyl chloride, $TiCl_4$, and $BF_3{\cdot}OEt_2$ were purified by distillation under nitrogen. MeOTf was prepared from Me_2SO_4 and TfOH, bp 95–98 °C. Starting amino acids glycine, DL-alanine, L-alanine, DL-valine, DL-*C*-phenylglycine, DL-leucine, and DL-phenylalanine were commercial reagents and used without further purification.

Monomers. 4-Methyl-2-phenyl-5-oxazolone (**1a**) was prepared by the dehydration of *N*-benzoyl-DL-alanine according to well-established procedures[8,14] and purified by sublimation in vacuo: mp 41 °C (lit. 41 °C,[8] 38.4–39.6 °C[15]); IR (KBr) 1810 (C=O), 1660 cm^{-1} (C=N); ^1H NMR ($CDCl_3$ with Me_4Si) δ 1.56 (d, J = 8 Hz, 3 H, CH_3), 4.40 (q, J = 8 Hz, 1 H, CH), 7.3–7.6 (m, 3 H, phenyl protons), 7.8–8.1 (m, 2 H, phenyl protons). 4-Isopropyl-2-phenyl-5-oxazolone (**1b**)[16] was obtained from *N*-benzoyl-DL-valine: bp 63–65 °C (4.5 mmHg); IR (neat) 1820 (C=O), 1655 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 0.95 (d, J = 7 Hz, 3 H, CH_3), 1.08 (d, J = 7 Hz, 3 H, CH_3), 2.23 (m, 1 H, $CHMe_2$), 4.12 (d, J = 5 Hz, 1 H, CHN), 7.2–7.6 (m, 3 H, phenyl protons), 7.7–8.0 (m, 2 H, phenyl protons); ^{13}C NMR ($CDCl_3$ with Me_4Si) δ 17.4, 18.6 (2 CH_3), 31.1 (CMe_2), 70.3 (CN=), 125.5, 127.6, 128.5, 132.4 (phenyl carbons), 161.3 (C=N), 177.4 (C=O). 2,4-Diphenyl-5-oxazolone (**1c**) was prepared from DL-*C*-phenylglycine according to the literature:[15] mp 104 °C (lit.[15] 103.5–105.5 °C); IR (KBr) 1813 (C=O), 1640 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 5.47 (s, 1 H, CH), 7.2–8.2 (m, 10 H, phenyl protons). 4-Isopropyl-2-methyl-5-oxazolone (**1d**) was obtained from DL-leucine: bp 42 °C (7 mmHg) (lit.[17] 60 °C (10 mmHg)); IR (neat) 1810 (C=O) 1680 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 0.90, 1.03 (2 d, 6 H, $(CH_3)_2$), 2.10 (d, 3 H, N=CCH_3), 3.88 (m, 1 H, CHN). 4-Isobutyl-2-methyl-5-oxazolone (**1e**)[6a] was prepared from DL-valine: bp 54–55 °C (10 mmHg); IR (neat) 1820 (C=O), 1680 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 0.93 (d, J = 6 Hz, $C(CH_3)_2$), 1.3–2.0 (m, 3 H, CH_2CHMe_2), 2.16 (d, 3 H, N=CCH_3), 4.0–4.3 (m, 1 H, NCH); ^{13}C NMR ($CDCl_3$) δ 15.0, 21.5, 22.5 (3 CH_3), 25.0 (CH_2), 40.3 ($CHMe_2$), 63.1 (NCH), 162.5 (N=C), 179.0 (C=O). DL-Phenylalanine was N-acetylated and the resulting product was dehydrated to give 4-benzyl-2-methyl-5-oxazolone (**1f**):[6a] bp 52–54 °C (7 mmHg); IR (neat) 1820 (C=N), 1685 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 2.01 (d, 3 H, CH_3), 3.09 (t-like, 2 H, CH_2), 4.32 (m, 1 H, NCH), 7.20 (br.s, 5 H, phenyl protons).

For 2-unsubstituted 5-oxazolones (**2**) the cyclization of *N*-formylglycine[18] or *N*-formyl-DL-alanine[18] was carried out with an equimolar amount of DCC in a dry carrier solvent, e.g., diglyme. After filtration of insoluble *N,N'*-dicyclohexylurea, **2** was codistilled with the carrier at reduced pressure. Since the head temperature of the codistillation was important for obtaining solutions of 5-oxazolone of the proper concentration, a needle valve was used to control precisely the pressure of the distillation. This needle valve was placed between the dry ice trap and the oil pump. A head temperature of 37–40 °C (4–5 mmHg) was found to give a diglyme solution of **2b** ranging in concentration from 0.45 to 0.86 mol/L (a lower head temperature gave lower concentrations and a higher head temperature resulted in extensive decomposition of the ring). An oil bath at approximately 50 °C was employed for codistillation of **2b**. Similarly for 4-methyl-5-oxazolone (**2a**), a head temperature of 60–74 °C (15–28 mmHg) and an oil bath temperature of about 100 °C were used. The concentration of the 5-oxazolones was determined easily by ^1H NMR using an internal standard of DMF. The spectral data of **2** are given in the text.

A procedure for the preparation of 4(*S*)-4-methyl-5-oxazolone (**2a'**) is given as a typical example. A mixture of *N*-formyl-L-alanine (2.28 g, 1.95 mmol) and DCC (4.47 g, 2.15 mmol) in a mixed solvent of diglyme (12.5 mL) and CH_2Cl_2 (30 mL in this case as a lower boiling solvent) was stirred at room temperature for 48 h. During the reaction the formation of solids (*N,N'*-dicyclohexylurea) was observed. The urea was removed by filtration from the reaction mixture and washed twice with 5 mL of diethyl ether, which was combined with the filtrate. Then, lower boiling solvents of CH_2Cl_2 and diethyl ether in the combined filtrate were gently evaporated at reduced pressure with an aspirator. After the evaporation of the solvents, monomer **2a'** was codistilled with a carrier of diglyme at a pressure of 15 mmHg with a head temperature of 60–65 °C, the oil bath temperature being 90–100 °C. A diglyme solution of **2a'** (10 mL) was obtained, whose concentration was determined by ^1H NMR as 0.60 mol/L (31% yield). Based on this concentration of **2a'** a value of $[\alpha]^{22}_D$ −18° (diglyme solution) was obtained.

Base-Catalyzed Dimerization. The following general procedure is described by taking entry 24 as a typical example. A lithium diisopropylamide (LDA) solution was prepared by adding an *n*-hexane solution of butyllithium into diisopropylamine (equimolar) in diethyl ether. Into 10 mL of a diglyme solution of 4-methyl-5-oxazolone (**2a**) (0.4 mol/l) was added 5 mol % of the LDA solution at room temperature. The reaction mixture was allowed to stir for 4 days at the same temperature under nitrogen. The reaction was stopped with the addition of 10 mL of water, and the product dimer was extracted with 20 mL of $CHCl_3$ from the mixture. The extracts were combined, dried over Na_2SO_4, and concentrated in vacuo to give white solids (0.17 g, 43% yield). The solid was determined as 1-formyl-3-(formylamino)-3,5-dimethylpyrrolidine-2,4-dione (**3g**): TLC R_f = 0.66 (silica gel, 1:9 MeOH–$CHCl_3$); mp 139–142 °C; IR (KBr) 1780,

1750, 1705, 1670 cm^{-1}; ^1H NMR ($CDCl_3$ with Me_4Si) δ 1.5 (s, 3 H), 1.6 (d, 3 H, J = 7.2 Hz), 4.6 (q, 1 H, J = 7.2 Hz), 8.0 (s, 1 H), 8.0–8.4 (br, 1 H), 9.3 (s, 1 H); mass spectrum, m/e 198 (parent peak). Anal. Calcd for $C_8H_{10}N_2O_4$: C, 48.49; H, 5.09; N, 14.14. Found: C, 48.56; H, 5.29; N, 14.05.

Analogously, base-catalyzed dimerizations of **1a–f** and **2a** were carried out under reaction conditions given in Table I using 3–5 mmol of monomer in ca. 10 mL of solvent under nitrogen. The product dimers were isolated by a preparative TLC technique. Data for structural determinations of dimers **3a–g** are given as follows, in which the stereochemistry of these dimers is not clarified.

1-Benzoyl-3-(benzoylamino)-3,5-dimethylpyrrolidine-2,4-dione (3a): TLC R_f = 0.68 (silica gel, diethyl ether); mp 236 °C (lit.[8] 234 °C); IR (KBr) 1780, 1740, 1680, 1623 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.49 (d, 3 H, J = 7 Hz), 1.60 (s, 3 H), 4.78 (q, 1 H, J = 7 Hz), 7.1–7.9 (m, 10 H), 9.51 (s, 1 H); mass spectrum, m/e 350 (parent peak). Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.12; H, 5.33; N, 7.88.

1-Benzoyl-3-(benzoylamino)-3,5-diisopropylpyrrolidine-2,4-dione (3b): TLC R_f = 0.25 (silica gel, $CHCl_3$); mp 199–200 °C; IR (KBr) 1770, 1720, 1690, 1650 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.04–1.15 (overlapping d, 12 H), 2.36 (m, 2 H), 4.64 (d, 1 H), 7.42–7.74 (br m, 10 H), 8.79 (br, 1 H).

1-Benzoyl-3-(benzoylamino)-3,5-diphenylpyrrolidine-2,4-dione (3c: TLC R_f = 0.40 (silica gel, $CHCl_3$); mp 65 °C; IR (KBr) 1780, 1740, 1690, 1640 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 6.12 (s, 1 H), 7.25–8.08 (br m, 21 H). Anal. Calcd for $C_{30}H_{22}N_2O_4$: N, 5.93. Found N, 5.73.

1-Acetyl-3-(acetylamino)-3,5-diisopropylpyrrolidine-2,4-dione (3d): TLC R_f = 0.50 (silica gel, diethyl ether); an oily material; IR (neat) 1775, 1738, 1710, 1650 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 0.96 (q of d, 12 H), 1.90 (s, 3 H), 2.25 (m, 2 H), 2.50 (s, 3 H), 4.47 (d, 1 H), 6.11 (s, 1 H).

1-Acetyl-3-(acetylamino)-3,5-diisobutylpyrrolidine-2,4-dione (3e): TLC R_f = 0.60 (silica gel, diethyl ether); an oily material; IR (neat) 1770, 1738, 1710, 1660 cm^{-1}.

1-Acetyl-3-(acetylamino)-3,5-dibenzylpyrrolidine-2,4-dione (3f): TLC R_f = 0.47 (silica gel, diethyl ether); an oily material; IR (neat) 1775, 1740, 1700, 1650 cm^{-1}.

Cationic Polymerization of 2-Unsubstituted 5-Oxazolones (2). A typical polymerization procedure is shown by taking the polymerization system of **2a′** (entry 33) as an example. Into 4.5 mL of a diglyme solution of **2a′** (0.6 mol/L), obtained by codistillation, in a tube, was added 1.35×10^{-2} mmol (0.5 mol % for **2a′**) of MeOTf with stirring at room temperature under nitrogen. Several minutes later precipitation of white solids was observed. The tube was sealed. The mixture was allowed to react further for 6 h with stirring at the same temperature. The tube was opened and 0.02 mL of methanol was added to the mixture for quenching the reaction. The stirring was continued for 1 h at room temperature. Then, the mixture was poured into 100 mL of diethyl ether. The resulted white solids were collected and dried in vacuo. The solids were dissolved in 1.6 mL of dry DMF and the DMF solution was poured into 250 mL of diethyl ether to precipitate polymeric materials, which were collected by filtration and dried in vacuo to give 270 mg of white solid polymer (**4a′**): molecular weight 1450 by vapor pressure osmometry in DMF at 55 °C; $[\alpha]^{22}_D$ = −3.60° (trimethyl phosphate solution c = 4.17); IR (KBr) 1680 (vs) and 1810 cm^{-1} (vw); ^{13}C NMR (Me_2SO-d_6) δ 17 (CH_3), 51 ($CHCH_3$), 163 and 171 (2 C=O) plus 93.

Data for structural determinations of polymers **4a** and **4b** are given in the text.

Measurements. ^1H and ^{13}C NMR spectra were recorded on a Hitachi 60-MHz R-20B NMR spectrometer and a Hitachi 22.6-MHz R-900 Fourier transform NMR spectrometer, respectively. The IR measurements were performed on a Hitachi 260-50 infrared spectrophotometer. The molecular weights of the polymers were measured by vapor pressure osmometry in DMF with a Corona 117 instrument at 55 °C. Low-resolution mass spectra were recorded on a JEOL JMS-D300 (24 eV) mass spectrometer. The specific rotations were obtained with a Perkin-Elmer 243 Polarimeter.

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References and Notes

(1) For our recent studies see: (a) Kobayashi, S.; Miyamoto, M.; Seagusa, T. *Macromolecules* **1981**, *14*, 1582. (b) Kobayashi, S.; Isobe, M.; Saegusa, T. *Ibid.* **1982**, *15*, 703. (c) Kobayashi, S.; Tokuzawa, T.; Saegusa, T. *Ibid.* **1982**, *15*, 707. (d) Kobayashi, S.; Kaku, M.; Mizutani, T.; Saegusa, T. *Polym. Bull. (Berlin)* **1983**, *9*, 169. (e) Kobayashi, S.; Mizutani, T.; Saegusa, T. *Makromol. Chem.* **1984**, *185*, 441. (f) Kobayashi, S.; Morikawa, K.; Shimizu, N.; Saegusa, T. *Polym. Bull. (Berlin)* **1984**, *11*, 253. (g) Kobayashi, S.; Saegusa, T. *Makromol. Chem., Suppl.* **1985**, *12*, 11.

(2) For a recent comprehensive review see: Kobayashi, S.; Saegusa, T. *Ring-Opening Polymerization*; Elsevier Applied Science: Essex, England, 1984; Vol. 2, pp 761–807.

(3) (a) Plöchl, J. *Chem. Ber.* **1883**, *16*, 2813. (b) Erlenmeyer, E. *Justus liebigs Ann. Chem.* **1893**, *275*, 1. (c) Erlenmeyer, E. *Ibid.* **1904**, *337*, 265. (d) Mohr, E.; Geis, T. *Chem. Ber.* **1908**, *41*, 798.

(4) (a) de Jersey, J.; Willadsen, P.; Zermer, B. *Biochemistry* **1969**, *8*, 1959. (b) de Jersey, J.; Zermer, B. *Ibid.* **1969**, *8*, 1967. (c) Curran, T. C.; Farrar, C. R.; Niazy, O.; Williams, A. *J. Am. Chem. Soc.* **1980**, *102*, 6828.

(5) Carter, H. E. *Organic Reactions*; Wiley: New York, 1946; Vol. 3, pp 198–239.

(6) (a) Bergmann, M.; Stern, F.; Witte, C. *Justus Liebigs Ann. Chem.* **1926**, *449*, 277. (b) Leplawy, M. T.; Jones, D. S.; Kenner, G. W.; Sheppard, R. C. *Tetrahedron* **1960**, *11*, 39.

(7) Cornforth, J. W.; Huang, H. T. *J. Chem. Soc.* **1948**, 1958.

(8) Taylor, L. D.; Platt, T. E.; Mach, M. H. *Polym. Lett.* **1970**, *8*, 537.

(9) Siemion, I. Z.; Nowak, K. *Rocz. Chem.* **1961**, *35*, 979; *Chem. Abstr.* **1962**, *56*, 6084C.

(10) We thank Professor H. K. Hall, Jr., University of Arizona, for suggesting the codistillation method using a carrier solvent.

(11) Kobayashi, S.; Suzuki, M.; Saegusa, T. *Macromolecules* **1986**, *19*, 462.

(12) Bryant, L. L., Jr.; Kinstle, J. F.; Saegusa, T.; Kobayashi, S. *Polym. Bull. (Berlin)* **1986**, *15*, 227.

(13) Sheehan, J. C.; Yang, D. D. H. *J. Am. Chem. Soc.* **1958**, *80*, 1154.

(14) Mohr, E. *J. Prakt. Chem.* **1910**, *81*, 473.

(15) Gotthardt, H.; Huisgen, R.; Bayer, H. O. *J. Am. Chem. Soc.* **1970**, *92*, 4340.

(16) Bello, C. D.; Filira, F.; D'Angeli, F. *J. Org. Chem.* **1971**, *36*, 1818.

(17) Cornforth, J. W. *The Chemistry of Penicillin*; Princeton University: Princeton, NJ 1949; pp 688–848.

(18) Muramatsu, I.; Murakami, M.; Yoneda, T.; Hagitani, A. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 244.