# Cyclopolymerization and Cyclocopolymerization

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Early in the history of modern polymer science, a general principle was established by Staudinger[1] that polymerization of nonconjugated dienes leads to cross-linked, and therefore nonsoluble, nonlinear polymers or copolymers. An exception to this widely accepted principle was observed by Butler and coworkers,[2-9] who found that a variety of diallyl quaternary ammonium salts polymerized to yield soluble, and hence linear, polymers containing little or no residual unsaturation. To account for these results, Butler and Angelo[9] suggested a polymerization mechanism that involves an alternating intramolecular–intermolecular chain propagation.

In efforts to substantiate the proposed structures, representative polymers were degraded to show conclusively the presence of cyclic structures in the polymer chain.[10] However, these degradative studies did not unequivocably establish the size of the ring formed during the intramolecular step. The six-membered structure proposed for radical-initiated cyclopolymerization of 1,6-dienes was based upon the generally accepted hypothesis advanced by Flory[11] regarding the predominance of the more stable radical in controlling the course of vinyl polymerization. Intervening studies have shown that in numerous cases cyclopolymerizations do not adhere to this hypothesis but lead to cyclic structures derived via propagation through the less stable intermediate; i.e., the reactions are proceeding under kinetic rather than thermodynamic control. An extensive discussion of these results, including supporting evidence, has been published in an earlier review.[12] Further discussion of these aspects of the problem is included in the following sections.

Since the initial investigations, it has been demonstrated that by use of appropriate initiators, 1,6-dienes can be polymerized to yield soluble, saturated polymers containing rings along the linear chain (eq 1). The



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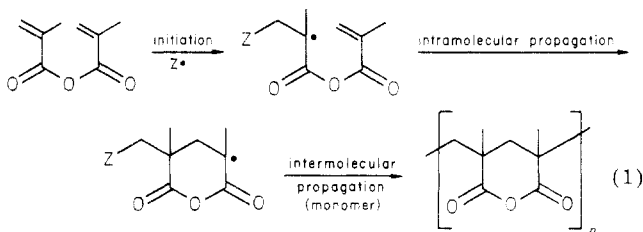
general course of the reaction is illustrated by use of methacrylic anhydride, a typical 1,6-diene. Cyclopolymerization is thus any type of chain-growth addi-

tion polymerization that leads to introduction of cyclic structures into the main chain of the polymer. Its scope is broad, including, at least conceptually, not only symmetrical diene counterparts of all known monomers capable of undergoing addition polymerization but the unsymmetrical ones as well. Many of the latter have not been investigated.

It has been shown that suitable monomers undergo cyclopolymerization via all of the well-known methods of initiation of polymerization. For example, 1,2-divinylbenzene[13-15] undergoes initiation by free radical, cationic, and anionic methods to yield the same cyclopolymer (eq 2). However, the polymerization of *o*-



$$(2)$$



$$(3)$$
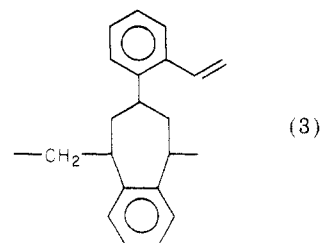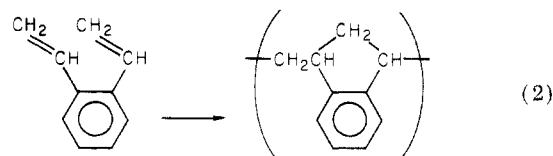
divinylbenzene has been reinvestigated,[16] and the authors have concluded on the basis of kinetic studies and the energetics of the process that the polymers are mainly comprised of seven-membered rather than the originally proposed five-membered rings (eq 3). Furthermore, 2,6-diphenyl-1,6-heptadiene undergoes initiation by all of the above-mentioned methods, as well as by thermal means and Ziegler–Natta methods, to

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yield essentially the same cyclopolymer in each case[17]

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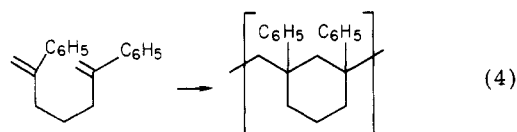
Other types of monomers that have been shown to undergo cyclopolymerization[18] are unsymmetrical dienes, diynes, dialdehydes, diisocyanates, diepoxides, and dinitriles, as well as unsymmetrical monomers with respect to the functional groups referred to here. In addition, a variety of monomers are reported to lead to bicyclic structures.

Methyl allyl maleate and methyl allyl fumarate were perhaps the earliest examples of unsymmetrical dienes to be studied,[19] but numerous other unsymmetrical dienes have been studied and discussed in detail.[18] Polycyclic systems have been synthesized via cyclopolymerization in a number of ways. For example, it has been shown[20] that *cis,cis*-1,5-cyclooctadiene can be converted to the bicyclic structure via use of a Ziegler–Natta catalyst (eq 5).

$$(5)$$
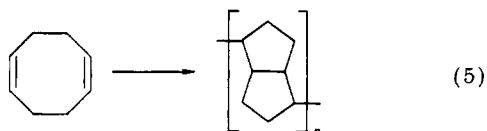
A variety of dialdehydes have been studied with regard to polymerization and polymer structure; *o*-phthalaldehyde has perhaps been studied most extensively.[21,22] This compound led to cyclopolymer via $\gamma$ irradiation and cationic, anionic, and coordination initiation (eq 6).

$$(6)$$
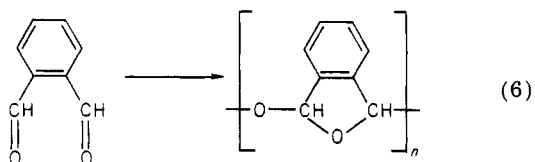
1,2:5,6-Diepoxyhexane has been reported[23] to undergo cyclopolymerization via a variety of initiators to yield polymers for which tetrahydropyran recurring units were proposed (eq 7).

$$(7)$$
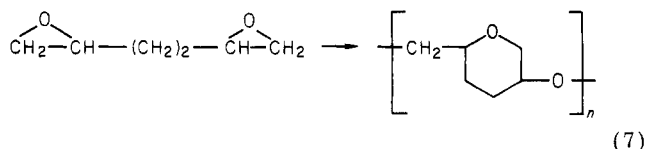
Cyclopolymerization of 1,1-divinylferrocene has been reported to form soluble polymers[24,25] via both radical and cationic initiation with formation of three-carbon bridged ferrocene units in the chain (eq 8). Recent

$$(8)$$
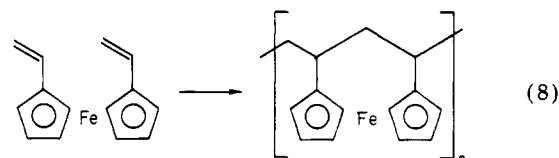
investigation of these polymers by Mössbauer spectroscopy[26] has shown that these polymers have significantly different structures. By use of model compounds, it was shown that radical initiation does yield the three-carbon bridged cyclopolymer but that polymers produced by cationic initiation do not have this structure.

## Copolymerization of Nonconjugated Dienes with Vinyl Monomers

A variety of copolymerizations of 1,6-dienes with conventional vinyl monomers have been studied. For example, copolymerization of methacrylic anhydride with a variety of vinyl monomers has been studied.[27] It was concluded that, in general, higher conversion to soluble copolymers was realized (a) the less reactive the comonomer in radical-initiated copolymerizations, (b) the greater the dilution, (c) the greater the difference in the molar concentration of the two monomers, and (d) the lower the conversion.

A type of copolymerization distinctly different from that described above[27] now constitutes a significant portion of the cyclopolymerization literature.[28,29] This process, referred to as cyclocopolymerization, incorporates both comonomers into the developing cyclic structure. Perhaps the most extensively studied example of this unusual type of copolymerization is the cyclocopolymer of divinyl ether and maleic anhydride (eq 9). This copolymer has been extensively studied for its biological properties; it exhibits a broad spectrum of biological activities,[30] including antitumor, antiviral, antibacterial, anticoagulant, and antiarthritic properties, as well as being capable of generating interferon, inhibiting inverse transcriptase, activating macrophages, and eliminating plutonium.

## Cyclopolymerization of Monomers Containing Different Functional Groups

A number of monomers having two kinds of functional groups have been studied in cyclopolymerization. For example, *o*-vinylbenzaldehyde[31] has been cyclopolymerized via cationic initiation to yield polymer containing both of the predicted cyclized structures shown (eq 10). However, evidence was presented for

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$$\text{CH}_2\text{=CH} \quad \text{O—CH} \quad \text{CH}_2 + \text{Z} \cdot \xrightarrow[\;(1)\;]{\text{initiation}} \text{ZCH}_2\text{—CH} \quad \text{O—CH} \quad \text{CH}_2 \xrightarrow[\substack{\text{intermolecular}\\\text{propagation}}]{(2)\;\text{selective}} \cdots \xrightarrow[\substack{\text{intramolecular}\\\text{propagation}}]{(3)\;\text{selective}} \cdots$$

$$\tag{9}$$

(eq 9 scheme with selective intermolecular propagation (4) and alternate repetition of (1–4))
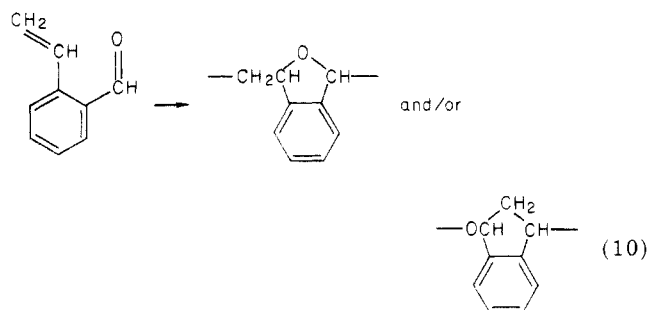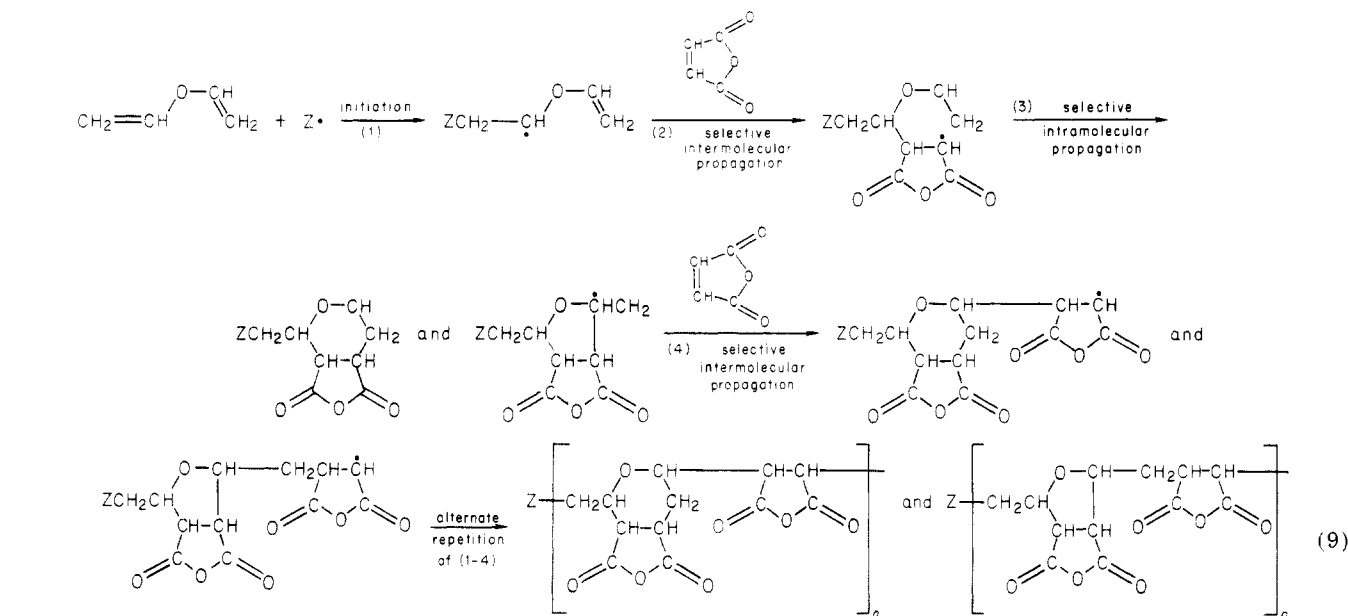
the predominance of the latter cyclic structure since the aldehyde group is more reactive toward the cationic initiator than the vinyl group. The cyclopolymer also contained 20% of pendant vinyl group and 5% of pendant aldehyde group. Glycidyl acrylate and methacrylate have been reported to cyclopolymerize, using $BF_3O(C_2H_5)_2$ as initiator.[32]

$$\tag{10}$$

## Cyclopolymerization of Diene Monomers Leading to Larger Ring Sizes

Poly(diallyl phthalate) has been commercially important for many years. The monomer is functionally capable of undergoing cyclopolymerization, and early studies[33,34] led to the conclusion that soluble polymers could be obtained prior to gelation that contained 31–41% of a cyclic structure presumed to consist of 11 or 13 members.

Polymerization of the hydrocarbons $CH_2$=CH-$(CH_2)_n$CH=$CH_2$, in which $n$ is equal to 4–9, 11, 12, 14, and 18, were studied by use of coordination initiation.[35] In all cases, both cyclic and acyclic recurring units were formed, the largest extent of cyclization (25%) occurring at calculated ring size = 7; however, the extent of cyclization among the larger calculated ring sizes varied only from a low of 4% to a high of 15%. The extents of cyclization observed corresponded roughly to those

that have been obtained in other cyclization reactions.[36]

Recent work on cyclopolymerization reactions leading to larger ring sizes (eq 11) has dealt with conforma-

R = H or CH$_3$

$$\tag{11}$$

R = H or CH$_3$
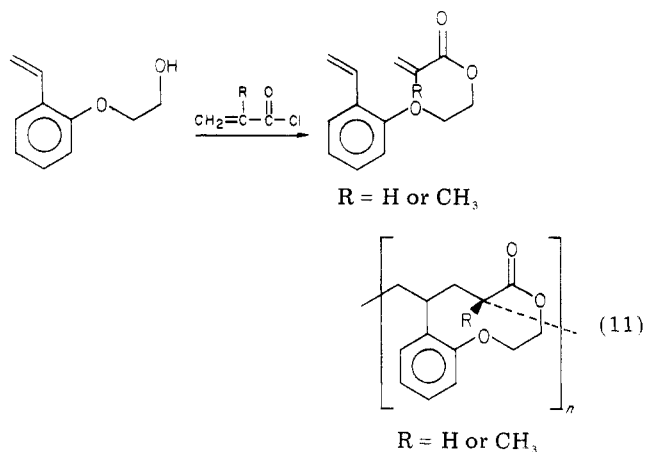
tionally controlled unsymmetrical dienes such as 2-(*o*-vinylphenoxy)ethyl acrylate and methacrylate[37] and their cyclopolymerization, utilizing both radical-initiated and photoinitiated polymerization. The polymers obtained were essentially completely cyclized.

Large rings have also been synthesized from a variety of other monomers. Cyclopolymers having [3.3]para-cyclophane repeating units (eq 12) are obtained by

$$\tag{12}$$

1,3-bis(4-vinylphenyl)propane

cationic initiation[38] but not by other initiators. Tetraethylene glycol divinyl ether has been reported to yield a polymer containing 16-crown-5 units that is

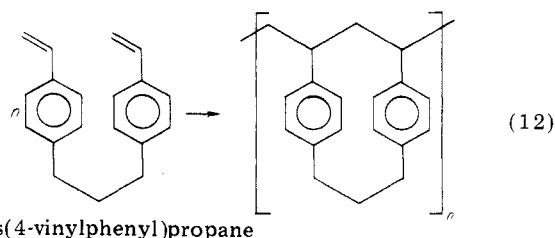(32) I. A. Arbuzova and V. N. Efremova, *Vysokomolek. Soedin.*, 1, 455 (1959).

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effective as a phase-transfer catalyst[39] (eq 13).



(13)
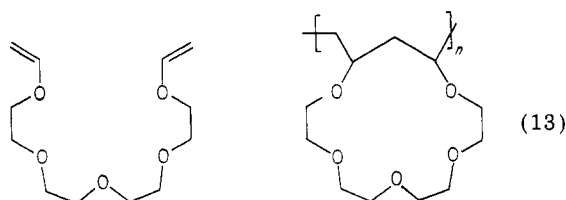
## Mechanism of Cyclopolymerization

Mechanistic studies dealing with various aspects of the cyclopolymerization process are extensive and cannot be presented in det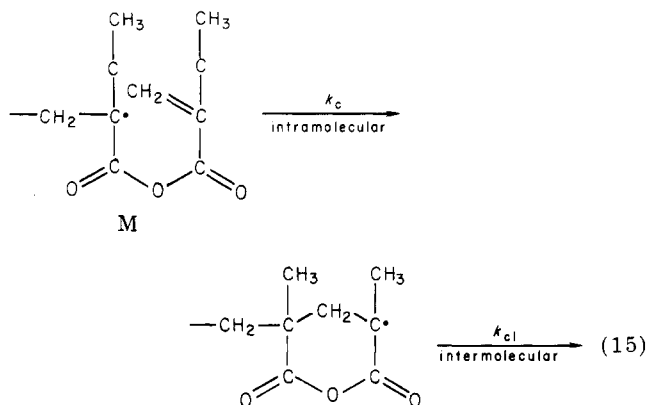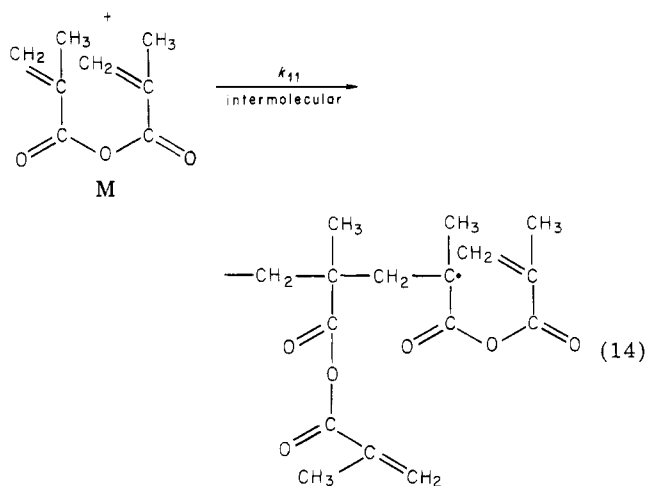ail here. However, important aspects of the process are embodied in a kinetic study carried out on methacrylic anhydride.[40] The kinetic relationship between intramolecular and intermolecular propagation was derived from the reaction schemes 14 and 15. This study showed that the energy of activation for the intramolecular cyclization step is higher



(14)



(15)

than that for the intermolecular step by about 2.6 kcal/mol. The rate of cyclization, however, was found to be considerably faster than the intermolecular propagation step, in support of a very high steric factor favoring cyclization. The value $k_c/k_{11}$ was found to be 2.4 mol/L, and the Arrhenius frequency factor ratio was found to be 256 mol/L in favor of the cyclization step. Also, it was shown that increasing steric factors, higher temperature, lower monomer concentration, poorer solvent, and higher conversion favor cyclization.

Numerous other kinetic studies have reported $k_c/k_{11}$

values to vary from 2.8 for radical-initiated polymerization of o-divinylbenzene in benzene at 50 °C to 200 for radical-initiated polymerizatin of divinylformal in benzene at 50 °C. Arrhenius frequency factor ratios have been reported to vary from 50 mol/L for radical-initiated polymerization of o-divinylbenzene in benzene at 50 °C up to $2.2 \times 10^4$ for cationic-initiated polymerization of o-divinylbenzene in toluene. The values for $E_c-E_{11}$ have been reported to vary from approximately zero for radical-initiated polymerization of vinyl *trans*-cinnamate at 70 °C in benzene to 5.3 kcal/mol for cationic-initiated polymerization of o-divinylbenzene in toluene.[41]

It was recognized quite early that less-favored ring sizes may be formed in cyclopolymerization and that the less-stable radical may predominate in the cyclization.[42] It was shown that the less-stable radical predominated in the cyclization step during polymerization of allyl and methallyl crotonates (eq 16). Although



R′ = H, CH$_3$

(16)
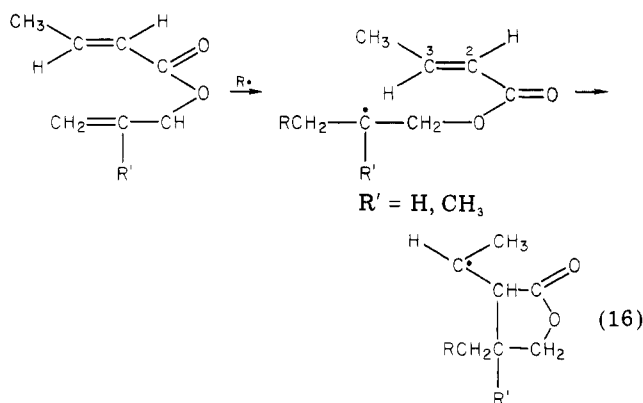
attack at C2 may be somewhat more favored sterically than at C3, it was reasoned that attack at C3 should be favored because of the resonance-stabilized radical formed at C2. Further evidence for formation of the less-favored ring structure and/or predominance of the less energetically favored intermediate radical in controlling the course of the cyclopolymerization process has been obtained. These results have bveen summarized in a recent review.[43]

Justification of this preference for five-membered ring formation has been based on both electronic[44] and steric[45,46] factors. A suggestion that there may be an electronic interaction[44] between the initially formed radical and the neighboring double bond of the diene has received considerable attention.[41] The formation of methylcyclopentane from the reaction of 5-hexenyl mercaptan with triethyl phosphite was explained[45] as arising from the attack of the radical at the more accessible end of the double bond, the process being irreversible. It has been noted that, for approach of the radical to the double bond with the p orbitals in a common plane, formation of five-membered rings would be less sterically hindered.[46] One of the terminal hy-

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drogens lies in the nodal plane directly between the radical carbon and the carbon on the terminal end of the double bond, thus hindering six-membered ring formation. No such steric interference exists for approach of the radical to the other end of the double bond, leading to five-membered rings.

Considerable work dealing with small molecule cyclizations has been done, and much of this work has been summarized in a review article by Julia.[47] In a study of cyclization of 1-substituted 4-hexenyl radicals, it was shown that as substitution in the 1-position by radical stabilizing groups (one or two CN or C(O)OEt groups) was increased, the mixture of cyclized products changed from nearly pure cyclopentane to nearly pure cyclohexane derivatives. Higher temperatures favored cyclohexane formation. Also, it was shown that the cyclization reactions were reversible when C1 was disubstituted, although it had been shown[48] earlier that in the case of the primary hexenyl radical, the cyclization step is irreversible. On this basis, it was proposed that the cyclopentane product is the kinetically preferred product while the cyclohexane product is preferred via thermodynamic control, with the energy of activation for cyclization being higher for the cyclohexane derivatives.

The majority of the radical cyclizations reported have been accomplished by permitting alkyl radicals to react with an unsubstituted double bond, thus producing the intermediate, non-resonance-stabilized primary or secondary radical.[49] As stabilization of the generated radical increased, the ratio of six-membered ring increased. A more recent study[50] has shown that when the radical generated after cyclization of the six-membered ring can be stabilized by resonance, the ratio of six-membered to five-membered ring is markedly increased (eq 17). The results of this study strongly indicate that radical stabilization results in greater selectivity and thus an increase in the more thermodynamically stable six-membered ring. The cyclization
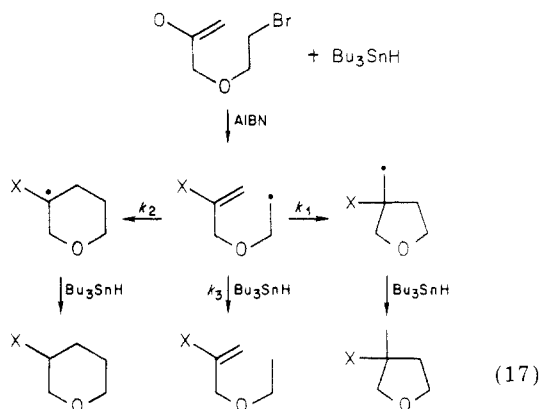


rate constant ratios at 40 °C and the derived Arrhenius parameters showed that the radical-stabilizing effect of the methyl group was not sufficient to prevent the predominance of the tetrahydrofuran ring. The $k_1/k_2$ ratio at this temperature was 43; however, the corre-

sponding ratio for the phenyl case was only 0.55. The Arrhenius parameter ratios, $A_2/A_1$, were $0.35 \pm 0.08$ for the methyl case and $2.8 \pm 0.2$ for the phenyl case.

An analogy can be drawn between five-membered ring formation in cyclopolymerization of 1,6-dienes and head-to-head polymerization in an ordinary vinyl monomer.

By means of IR, $^1$H NMR, and $^{13}$C NMR spectroscopy, it has been shown[51] that the ratio of five- to six-membered ring formation in cyclopolymerization of acrylic anhydride at 50 °C varies with the dipole moment ($\mu$) of the solvent from 5% five-membered ring at $\mu = 0$ to 30% at $\mu = 4$. A pronounced temperature effect was also observed. At 90 °C, the five-membered ring content was 20% at $\mu = 0$ and increased to 75% at $\mu = 4$. Cyclopolymerization in $\gamma$-butyrolactone at 120 °C resulted in 90% five-membered ring. Under all conditions described, methacrylic anhydride led only to six-membered ring structures.

The five-membered ring content of poly(acrylic anhydride) has also been shown[52] to vary with both conversion at constant monomer concentration and with monomer concentration at constant conversion. For example, in benzene, the five-membered ring content increased from 5% at 40% conversion to 10% at 90% conversion; however, in $\gamma$-butyrolactone, the five-membered ring content increased from 28% at 15% conversion to 75% at 50% conversion, a much greater change than in the nonpolar medium.

On the basis of the previously described studies on acrylic anhydride, it was postulated[53] that, if methacrylic anhydride were polymerized above the ceiling temperature of its monoene counterpart, methacrylic isobutyric anhydride, the poly(methacrylic anhydride) should consist largely of five-membered-ring anhydride structures. The ceiling temperature of methyl methacrylate is 164 °C in bulk and decreases with dilution. Previous studies[51] had shown that cyclic poly(methacrylic anhydride) consisted exclusively of six-membered rings under the lower temperature conditions. As postulated, polymerization of methacrylic anhydride at 160 °C in benzonitrile was found to consist of 53% five-membered rings, and polymerization at 180 °C gave almost exclusively the five-membered ring structure. Furthermore, in accord with the postulate, five-membered ring formation was found to increase with increasing temperature and dilution.

Radiation-induced cyclopolymerization of N-substituted dimethacrylamides has been studied extensively in the liquid, supercooled-liquid, glassy, and crystalline states.[54-56] In most of these cases, cyclopolymerization occurred exclusively, predominantly to five-membered rings, except in the glassy state, where no polymerization was observed. The ratio of six-membered rings was higher in the crystalline state than in the liquid states.

A recently published single-crystal X-ray diffraction and solid-state polymerization study[57] of N-(p-bromo-

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phenyl)dimethylacrylamide led to the conclusion that
the monomer crystallizes in a conformation that favors
the intramolecular over the intermolecular polymeri-
zation reaction. The polymer consisted of exclusively
cyclopolymer having 60% five-membered and 40%
six-membered rings. The ratio of five- to six-membered
ring could not be predicted from the atomic positions
in the crystal, however. Radical-initiated solution po-
lymerization of the monomer at 58 °C yielded cyclo-
polymer containing 80% five-membered and 20% six-
membered ring. At 114 °C, the cyclopolymer contained
only 42% five-membered ring.

Evidence has also been obtained that certain of the
diallyamines and quaternary ammonium salts also yield
cyclopolymer consisting largely of five-membered rings.
On the basis of a ^{13}C NMR study of poly(*N*,*N*-diallyl-
*N*-methylamine),[58] it was concluded that five-membered
rings were formed; however, when the allyl groups were
substituted in the 2-position, mixtures of both five- and
six-membered rings were formed. Also, it has now been
shown by ^{13}C NMR and model compound studies that
poly(diallyldimethylammonium chloride)[59] consists
predominantly of five-membered rings linked mainly
in a 3,4-cis configuration.

A fundamental study of cyclocopolymerization[60] has
been carried out. A series of copolymer composition
equations were derived that are consistent with the
addition of monoolefin to diene radicals by a concerted
bimolecular step proceeding through a cyclic transition
state to produce the cyclic repeating unit. It was rec-
ognized quite early[61] that the above requirements could
be satisfied if the monomer pair formed a charge-
transfer complex that participated in the co-
polymerization. Considerable evidence has now been
presented for charge-transfer complex participation in
a variety of highly alternating cycloco-
polymerizations.[60–63]

A recent review has summarized much of the pub-
lished literature dealing with ring size in cycloco-
polymerization.[42] The early work[64] had led to the
suggestion that the more thermodynamically stable
six-membered ring was formed. However, it is apparent
that cyclocopolymerization could lead to the thermo-
dynamically favored six-membered ring via the more
stable radical, to the five-membered ring via the less
stable radical, or to a mixture of both.

It has been suggested[65] that the tetrahydrofuran
(THF) structure for the divinyl ether–maleic anhydride
copolymer is more in accord with experimental data
from polymer solution measurements on the copolymer
and its methyl ester than the originally proposed tet-

rahydropyran (THP) structure. However, potentio-
metric titration[66] has shown that at pH 7, only ap-
proximately three of the four carboxyl groups are neu-
tralized. These results have been interpreted to mean
that one of the carboxyl groups in the hydrolyzed form
of the copolymer is different from the other three, a
structural feature that is not consistent with the THF
structure but is consistent with the THP structure.

Recent studies,[67–69] which included model compound
and deuterated monomer syntheses, ^{1}H and ^{13}C NMR
investigations of the resulting copolymers, and solvent
effects, have led to the tentative conclusion that the
copolymer includes both THF and THP structures.
The ratio of the two appears to vary in favor of the
THF ring with increasing polarity of the medium. A
copolymer prepared in benzene was reported to contain
THF–THP structures in a ratio of 0.8:1.0.[69] The ster-
eochemistry of the chiral centers in the copolymer is
uncertain, although evidence has been presented for
trans junctures at the bridgeheads in the THP struc-
ture[67] and cis junctures for the corresponding centers
in the THF structure.[68]

Some large-ring-containing cyclocopolymers have
recently been reported. Cyclocopolymerization of the
divinyl monomer 1,2-bis(2-(ethenyloxy)ethoxy)benzene
with maleic anhydride via radical initiation has been
shown[70] to produce the 1:2 alternating cyclocopolymer
shown in eq 18. The monomer pair was shown by UV



$$(18)$$
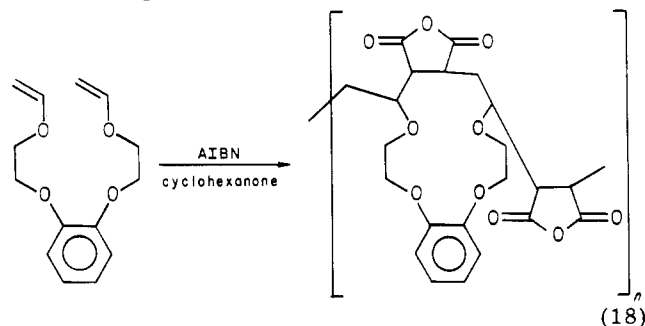
spectroscopy to form a charge-transfer complex having
an equilibrium constant (*K*) of 0.280, suggesting par-
ticipation of the complex in the copolymerization. Also
consistent with this proposal was the observation that
the maximum rate of copolymerization occurred at the
monomer molar ratio of 1:2.

## Interpretations of Mechanistic Proposals

A satisfactory theory for cyclopolymerization must
adequately account for the following observations: (a)
almost all nonconjugated dienes and other similar po-
lymerizable structures studied to date undergo cyclo-
polymerization in preference to cross-linking or other
modes of propagation; (b) such dienes invariably un-
dergo polymerization at a higher rate than their re-
spective monoene counterparts; (c) the cyclization step
has invariably been shown to be of higher activation

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energy than propagation without cyclization; (d) the cyclization step often leads to propagation via the less thermodynamically stable reaction intermediate, leading to the less thermodynamically stable ring structure.

Numerous examples where the rates of cyclopolymerization have been shown to be significantly greater than those for homopolymerization of their corresponding monoolefinic counterparts have been published.[46] Relative rates up to 590 have been reported.[71]

It was suggested quite early that an electronic interaction may occur between the nonconjugated double bonds of 1,6-dienes or between the intramolecular double bond and the reactive center after initiation.[29] Such an interaction would provide an energetically favorable pathway from monomer to cyclic product and may be the major driving force for cyclopolymerization. This theory has been investigated extensively, with conflicting results. Further spectroscopic studies[72-74] have failed to produce evidence for interspecial interactions in monomers that cyclopolymerize. However, kinetic evidence has been obtained[75] which shows that the reactivity of each double bond in the 3-allyl-5-hexenyl radical, a model for cyclopolymerization, is about 5 times greater than the double bond in the 5-hexenyl radical under similar conditions. Presently, no satisfactory explanation for this enhanced reactivity is available. It cannot be attributed solely to homoconjugation.

Stabilization of a reactive center would be expected to occur in the case of cationic initiation. 1,3-Bis(4-vinylphenyl)propane can be polymerized, by use of cationic initiators, to a cyclopolymer having [3.3]paracyclophane units in the chain.[38] An interaction was proposed between the styryl cation and the intramolecular styryl group that stabilizes the transition state
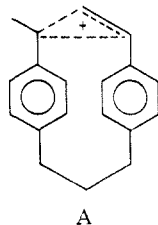


A

leading to cyclopolymer.

Studies have invariably shown that the intramolecular step leading to cyclization has a higher activation energy than the intramolecular step. Many of these studies point toward a thermodynamic explanation for cyclopolymerization. Although the differences in activation energies between the intramolecular and intermolecular propagation reactions suggest that the former is a slightly less favorable reaction,[40] the high tendency for cyclization has been explained[76] as due to a smaller decrease in entropy for such a reaction com-

pared to intermolecular addition. Thus, the Gibbs free energy of activation will be smaller for cyclopolymerization than for intermolecular propagation.

This hypothesis has been extended, leading to the proposal that highly cyclized polymers may be obtained from monomers whose monofunctional counterparts do not homopolymerize. This has been successfully applied to a number of systems, including N-substituted dimethacrylamides.[54-56] Thus, N-isobutyryl-N-propylmethacrylamide did not homopolymerize. However, complete cyclization occurred on homopolymerization or copolymerization of N-propyldimethacrylamide. It was proposed that the loss of internal rotation degrees of freedom is less effective in decreasing entropy than a loss of translational and rotational degrees of freedom and the activation entropies favoring cyclization.

The present understanding of the mechanistic aspects of the cyclocopolymerization has been summarized in a recent review.[77] Although cyclopolymerization and cyclocopolymerization are certainly related mechanistically, the unusual nature of the latter reaction, in which bimolecular ring closure is highly favored, requires further explanation. The early kinetic treatment,[60] which suggested that the bimolecular ring closure step is concerted, led to the proposal that the propagating species is a charge-transfer complex.[61] This proposal was supported by evidence for the existence of complexes in several comonomer pairs. Solvent effects on the cyclocopolymerization of maleic anhydride and divinyl ester have provided further evidence to support a charge-transfer complex as the active species.[78] However, it has been concluded[79] from kinetic data that the mechanism can be explained without invoking a charge-transfer complex.

Many attempts have been made to account for the otherwise unpredictable ring size or preference for head-to-head propagation in cyclopolymerization and other radical cyclizations.[42] It has been suggested that I strain[41] in the cyclic structures being formed during cyclopolymerization may shed some light on the competition between five- and six-membered ring systems and their relative ease of formation. In five-membered ring systems, when hybridization at any one carbon is changed from $sp^3$ to $sp^2$, I strain is decreased. The transition from cyclopentane to cyclopentanone would reduce I strain. In the six-membered ring, change of hybridization from $sp^3$ to $sp^2$ increases I strain. Indicative of these internal strains are the relative rates of reduction of the two cyclic ketones with sodium borohydride and the relative values of the equilibrium constants for cyanohydrin formation. The relative rate for $NaBH_4$ reduction is 23 for cyclohexanone, and the relative $K_e$ for cyanohydrin formation in cyclohexanone is 21, both reactions being indicative of the much higher driving force for relief of I strain in cyclohexanone.

Consideration of the fact that five-membered ring formation in the dimethacrylamides requires introduction of $sp^2$ hybridization at two carbons, which should reduce I strain relative to cyclopentane, whereas

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$sp^2$ hybridization at two carbons in the six-membered ring should increase I strain relative to cyclohexane, may offer a partial explanation for the five-membered ring preference in these cases. Similar comparisons have been referred to earlier.[71] These observations are consistent with the fact that the six-membered ring is favored with increasing temperatures in cyclopolymerization of the *N*-substituted dimethacrylamides.[57]

On the other hand, the relative differences in the calculated heats of formation[41] of the cyclic anhydrides and their open-chain dicarboxylic acids indicate that the six-membered ring should be favored over the five-membered ring from these considerations. The differences between the heats of formation of the acids and their corresponding anhydrides are, respectively: propionic, 82.6; maleic, 76.2; succinic, 80.9; and glutaric, 71.7 kcal/mol. However, these observations are consistent with the fact that the five-membered anhydride ring is favored at higher temperatures in cyclopolymerization of both acrylic and methacrylic anhydrides.[51-53]

It is now well established that the ring size formed in free-radical cyclization reactions of 5-hexenyl radicals is influenced according to whether the reaction is rate or equilibrium controlled.[80] With many alkenyl radicals, the formation of a five-membered ring is kinetically favored over formation of a six-membered ring.[81] However, with 5-substituted 5-hexenyl radicals, the formation of a six-membered ring can be increased due to either the steric effect of the substituent causing a retardation in the rate of 1,5 cyclization[82] or a resonance-stabilizing effect that favors 1,6 cyclization.[50] 1,5-Ring closures of substituted 5-hexenyl and related radicals are stereoselective: 1- or 3-substituted systems afford mainly cis-disubstituted products, whereas 2- or 4-substituted systems give mainly transproducts.[81]

Studies of the cyclopolymerization of variously substituted diallylamines suggest that these monomers also exhibit the characteristics of kinetic vs. thermodynamic control.[83] Consistent with kinetic control, cyclopolymerization of *N*,*N*-diallylmethylamine gave five-membered rings with a cis configuration. Steric or conjugative factors, introduced by 2-substitution of one or both allyl groups, influence the initial attack on the monomer and the cyclization reaction, where, with bulky or resonance stabilizing groups at the point of attack, six-membered rings predominate. The six-membered ring content of cyclopolymers from *N*,*N*-dimethallylmethylamine increases with an increase in the temperature of the reaction as the higher energy pathway becomes possible.

The stereoelectronic requirements of the transition state for radical addition reactions have been proposed to explain the kinetic preference for the formation of five-membered ring products.[84] This concept demands maximum overlap of the half-filled p orbital with the vacant $\pi^*$ orbital of the double bond. Approach of the radical must be along a vertical line from one of the carbon atoms of the double bond with the orbitals holding the three electrons being in the same plane throughout the reaction. Such conditions can be met by 1,5 cyclization of 5-hexenyl radicals but not by 1,6 cyclization. It has also been suggested that the predominance of cis addition in some cyclopolymerizations may be the result of hyperconjugative maxima of the p orbital with the alkyl CH $\sigma^*$ orbitals, leading to a delocalized orbital of similar symmetry to the $\pi^*$ orbital, which results in an attractive interaction between the alkyl substituent and the double bond (B, C). This



B          C
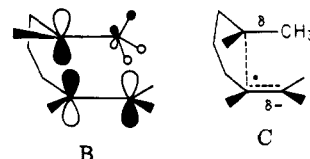
model for the cyclization reaction can explain the increasing preference for cyclopolymers with six-membered rings as bulky 2-substituents are introduced to one or both allyl groups of diallylamines.

Other workers have provided support for this hypothesis to explain the cyclization mechanism by examinations of molecular models,[85,86] calculations of geometrical probability factors,[85,87] and molecular orbital evaluations.[88-90] The ring size in cyclopolymers will be influenced by the nature of the cyclization reaction; it is therefore important to understand the energetics and kinetics of model reactions. However, there are indications that correlation between models and polymers is unsatisfactory.[83] For example, the cyclization of *N*,*N*-bis(2-ethylallyl)methylamine produced a six-membered ring low molecular weight product exclusively, but the cyclopolymer contained 40% of a five-membered ring structure.[57] These results may reflect the relative abilities of the intermediate radicals to undergo propagation and/or termination reactions. In addition, the factors controlling the cyclization reactions may be influenced by the growing chain, such that polymer microstructure is related to molecular weight. However, further studies are needed along these lines.

The present understanding of cyclopolymerization would indicate that the structures of cyclopolymers and cyclocopolymers are highly dependent on the nature of the monomers and the reaction conditions. Predictions of structures based upon thermodynamic control of the cyclization reaction can be misleading since kinetic products are often found. An important driving force for the cyclization reaction may be an intramolecular interaction, particularly in some cases, where a charge-transfer interaction can occur, or is induced, and in cationic-initiated reactions. However, the predominance of cyclization over intermolecular propagation

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can be ascribed to a smaller decrease in activation entropy, which compensates for the unfavorable difference in activation energies. Further studies on the kinetics and energetics of the cyclization reaction during polymerization are necessary before a completely acceptable mechanistic explanation is forthcoming.

## Practical Significance of Cyclopolymerization

A variety of commercial products have been developed utilizing cyclopolymerization. The first cyclopolymer to be manufactured in commercial quantities apparently was poly(dimethyldiallylammonium chloride).[91] This polymer, now manufactured by a number of suppliers, has been shown to possess optimum functional properties for application to electrographic paper reproduction processes.[92]

A review and use analysis of cyclopolymerization of dialkyldiallylammonium halides has recently been published.[93] In addition to the above referenced use of these materials, other uses as paper additives include antistatic agents, fluorescent whiteners, paperboard reinforcement, and retention aids. In the water treatment field, the polymer is used as a flocculant and/or as a primary coagulant or coagulant aid in potable water, wastewater, coal flotation, foam flotation of metal sulfides, etc. It is also reported to be used in the zinc, tin, and lead electroplating industries, as well as in the cosmetic field, as a biocide in water, as a demulsifier of dispersed oils, and as a detergent additive.

The copolymers of dialkyldiallylammonium salts with sulfur dioxide first reported by Harada and Katayama[94] are manufactured commercially in Japan and have similar industrial uses and properties to the homopolymers reported above.

Although anion-exchange materials containing the quaternary ammonium cation in the polymeric network were synthesized as early as 1949,[2] a reinvestigation in this area[95] has shown that $N,N,N',N'$-tetraallyl-$N,N'$-dimethylethylenediammonium dichloride could yield ion exchangers of both superior rate and capacity for use in extraction of uranium.

Polytriallylamine[96] is reported to be superior to other weak-base amine polymers for use in the "Sirotherm" demineralization process. This process, described in several publications,[97] is reported to be a thermally regenerated ion-exchange process for the cheap removal of salinity from brackish waters.

In a recent paper[98] it was shown that an amine exchanger prepared by copolymerizing diallylamine hydrochloride with a suitable crosslinker gave superior thermally regenerable capacity in the 20–80 °C range to other amine exchangers evaluated.

The use of synthetic polymers as biologically active materials is increasing. Among those polymers receiving most attention by investigators is the alternating cyclocopolymer of divinyl ether and maleic anhydride (eq 9), commonly known as "pyran" copolymer or DIVEMA. This copolymer has been investigated extensively for a variety of biological effects since the initial observation by scientists at the National Cancer Institute that the hydrolyzed and neutralized copolymer had considerable antitumor activity along with a much reduced toxicity in comparison with other polyanions investigated. As pointed out by Breslow,[99] DIVEMA has also been shown to be an interferon inducer, to possess antiviral, antibacterial, antifungal, anticoagulant, and antiarthritic activity, to aid in removing polymeric plutonium from the liver, to inhibit viral RNA-dependent DNA polymerase (reverse transcriptase), and to activate macrophages in effecting the immune response of test animals.

In a recent review on mechanistic aspects of synthesis of this copolymer,[43] the importance of molecular weight and molecular weight distribution was discussed. A biphasic response of the reticuloendothelial system to the copolymer drug had been observed, which led to the postulate that the copolymer may consist of a toxic molecular weight fraction and another fraction of lower toxicity. Other evidence for molecular weight dependence is based upon the observation that antiviral activity of the copolymer requires a higher molecular weight than antitumor activity. The latter was optimum with low molecular weight samples of narrow molecular weight distribution.

These results led to development of a method for synthesizing a copolymer of narrow molecular weight distribution by photochemically initiating a solution polymerization in acetone, using tetrahydrofuran as a chain transfer agent. This method gave samples having molecular weight distribution ranging from 1.6 to 2.6, in contrast to 3.7–7.7 for earlier prepared samples.

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