Inclusion Reactions and Polymerization

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INTRODUCTION

A variety of monomers can be trapped in the inclusion spaces at the molecular level and polymerized under suitable conditions. Such a reaction is called inclusion polymerization. The study of inclusion polymerization started soon after the discovery of a honeycomb structure of urea inclusion compounds. The early study aimed to obtain highly stereoregular and asymmetric polymers in the spaces. Further studies brought about a profound understanding of the space effects from various viewpoints. Now, inclusion polymerization is classified between bulk or solution polymerization and solid state polymerization. In other words, it may be situated in low-dimensional and space-dependent polymerizations. Such a polymerization closely relates to supra-molecular chemistry from a viewpoint of molecular information and expression.

GENERAL FEATURES

In Fig. 1, a cyclic process for inclusion polymerization is shown. The process consists of four steps: 1) hybridization of a host assembly with a solvent; 2) complexation of the host with a guest monomer; 3) polymerization of the monomer; and 4) separation of the resulting polymer from the host. This cycle is based on spontaneous and non-covalent phenomena, such as intermolecular association and dissociation among host–host, host–guest, and guest–guest components.

The host components (Fig. 1a) are first recrystallized from usual solvents for isolation and purification. This operation produces host assemblies with or without the separated host components assemble together by recrystallization to give original inclusion compounds with guest components. A macroscopic flask (Fig. 2a) in a chemical laboratory practically has an infinite space as compared with a monomeric molecule, enabling us to neglect any effects of the space. Monomer molecules freely move in the space at moderate temperatures. In contrast, a molecular flask at a nanometer level (Fig. 2b, c) has spaces nearly equal to guest molecules in size. Because electromagnetic forces work among the host and guest molecules, monomer molecules are constrained in the spaces, even at relatively high temperatures, leading to the observation of various space effects. On the other hand, assemblies composed of the monomers only (Fig. 2d) have no inclusion spaces in the solid state, meaning that the space effects may be ignored. In this case, the monomer molecules can move slightly below their melting temperatures.

A comparison among the polymerizations in the different states is summarized in Table 1. The monomer molecules form low-dimensional and anisotropic assemblies in the inclusion and solid states, although they form three-dimensional and isotropic assemblies in the solution.

Effects of the Inclusion Spaces

Inclusion polymerization may be reasonably distinguished from other polymerizations by various effects of the inclusion spaces, as mentioned below. Shown in Fig. 2 is a general relation in size between the inclusion spaces and guest molecules. A macroscopic flask (Fig. 2a) in a chemical laboratory practically has an infinite space as compared with a monomeric molecule, enabling us to neglect any effects of the space. Monomer molecules freely move in the space at moderate temperatures. In contrast, a molecular flask at a nanometer level (Fig. 2b, c) has spaces nearly equal to guest molecules in size. Because electromagnetic forces work among the host and guest molecules, monomer molecules are constrained in the spaces, even at relatively high temperatures, leading to the observation of various space effects. On the other hand, assemblies composed of the monomers only (Fig. 2d) have no inclusion spaces in the solid state, meaning that the space effects may be ignored. In this case, the monomer molecules can move slightly below their melting temperatures.

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or bulk state. One- or two-dimensional assemblies are formed in a channel (canal) or an interlayer, where corresponding one- or two-dimensional inclusion polymerization may take place, respectively. The inclusion spaces vary in size, shape, polarity, and chirality. The use of a set of the different spaces enables us to observe different inclusion polymerizations, leading to interpretation of the space effects.

**ONE-DIMENSIONAL INCLUSION POLYMERIZATION**

**Hosts and Monomers**

Inclusion polymerization is now recognized as a general polymerization that is useful for over 100 different monomers. Shown in Figs. 3 and 4 are some hosts and monomers employed so far for one-dimensional inclusion polymerization, respectively. First, a pair of hosts, urea (Fig. 3a) and thiourea (Fig. 3b), were used for the polymerization of 1,3-butadiene and 2,3-dimethyl-1,3-butadiene, respectively. Perhydrotriphenylene (Fig. 3c) was applied to many methyl-substituted butadiene derivatives, yielding the corresponding polymers with 1,4-trans units. Pioneering work was accomplished for optical resolution of the racemic host, leading to the first asymmetric inclusion polymerization of 1,3-pentadiene. A chiral host could readily be available from a naturally occurring compound. The use of steroidal acid, deoxycholic acid (Fig. 3d), yielded comprehensive polymers, particularly, optically active polymers from prochiral monomers. Many derivatives of deoxycholic acid have the corresponding characteristic inclusion abilities. For example, use of apocholic acid (Fig. 3e), cholic acid (Fig. 3f), and chenodeoxycholic acid (Fig. 3g) enabled us to perform one-dimensional inclusion polymerization of various diene and vinyl monomers. Other effective hosts are cyclophosphazenes, such as tris(o-phenylenedioxy)cyclotriphosphazene (Fig. 3h) and

**Table 1** Space effects among the polymerizations in different states

<table>
<thead>
<tr>
<th>T1.1 Polymerization</th>
<th>T1.2 Space size</th>
<th>T1.3 Solution or bulk</th>
<th>T1.4 Assembly</th>
<th>T1.5 Space effect Dimensionality</th>
<th>T1.6 Solid state</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Macroscopic</td>
<td>Molecular-level</td>
<td>Isotropic</td>
<td>Negligible</td>
<td>Anisotropic</td>
</tr>
<tr>
<td>T1.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1.4</td>
<td></td>
<td></td>
<td>Isotropic</td>
<td>Negligible</td>
<td>Anisotropic</td>
</tr>
<tr>
<td>T1.5</td>
<td>Negligible</td>
<td>Anisotropic</td>
<td>Low-dimensional</td>
<td>Low-dimensional</td>
<td></td>
</tr>
<tr>
<td>T1.6</td>
<td>Three-dimensional</td>
<td>Low-dimensional</td>
<td></td>
<td></td>
<td>Anisotropic</td>
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<td></td>
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</table>
Fig. 3 Organic hosts used for one-dimensional inclusion polymerization: (a) urea; (b) thiourea; (c) perhydrotriphenylene; (d) deoxycholic acid; (e) apocholeic acid; (f) cholic acid; (g) chenodeoxycholic acid; (h) tris(o-phenylenedioxy)cyclotriphosphazene; and (i) tris(2,3-naphthalenedioxy)cyclotriphosphazene.

Vinyl

Diene

Triene

Others

Fig. 4 Various monomers used for one-dimensional inclusion polymerization.
they were utilized for inclusion polymerization of many diene and vinyl monomers. Cyclodextrins were used for addition polymerization as well as polycondensation.

Some kinds of inorganic polymers were used for one-dimensional polymerization. For example, a novel zeolite ZSM-5 was employed for the polymerization of vinyl monomers, such as propylene and 1-hexene.

It can be seen from Fig. 4 that many diene monomers were polymerized using various hosts. It might be possible to polymerize multicongjugated monomers, such as trienes and tetraenes, in one-dimensional spaces. Diacetylene spontaneously polymerized in channels of three hosts: perhydrotriphenylene, deoxycholic acid, and apocholic acid. On the other hand, there are not so many studies of the polymerization of vinyl monomers, because highly stereoregular polymers are not obtained.

### Reaction Mechanism

Direct evidence for polymerization in the channels is given by crystal structure analysis. We can compare crystal structures before the polymerization and after the polymerization. Computed tomography works well in simulating whether or not inclusion polymerization will take place. Comparison of cross sections of channels with those of polymers enables us to consider whether or not the resulting polymers can be accommodated in the channels.

Radical species during inclusion polymerization can readily be detected by ESR spectroscopy, indicating that the radicals are thermally stable in the channels. The reason is that the radicals in the channels do not meet with each other due to the host walls. γ-Irradiation produces radicals of the host component as well as the monomers. Monomeric and propagating radicals were observed in the case of urea, while only the propagating radicals were observed in the case of perhydrotriphenylene, deoxycholic acid, and apocholic acid. Simulation of the spectra clarified that the propagating radicals do not rotate freely, indicating that mobilities of the radicals are constrained in the channels.

Molecular motions are much smaller in channels than in solution at the same temperature. This indicates that the polymerization may proceed slowly. But the neighboring monomers are located very near, suggesting that the reaction may proceed rapidly. This is how the reversed effects work during the propagation reaction. It is known that inclusion polymerization smoothly occurs at low temperatures in the channels of urea, thiourea, and perhydrotetrapienylene. However, in the case of steroidal hosts, we observed a decrease in polymerization rates. For example, in one case, the polymerization reached a saturated state after 1 month.

### Steric Control

There are many possible schemes for addition reactions of diene monomers from electronic and steric viewpoints. Because the monomer molecules arrange along the direction of the channels, α,ω-addition may selectively take place in one-dimensional inclusion polymerization. Therefore, conjugated polyenes, such as dienes and trienes, may selectively polymerize by 1,4- and 1,6-addition, respectively. 1,3-Butadiene polymerized via 1,4-addition exclusively in the channels of urea and perhydrotetraphiynylene, while the same monomer polymerized via both 1,2- and 1,4-additions in the channels of deoxycholic acid and apocholic acid. Moreover, we have to evaluate head-to-tail or head-to-head (tail-to-tail) additions in the case of disymmetric conjugated diene monomers such as isoprene and 1,3-pentadiene.

Tacticities of the polymers were estimated. For example, poly(1,3-pentadiene) was highly isotactic in the channels of perhydrotetraphiynylene, while it was preferentially isotactic (meso:racemic = 2:1) in the channels of deoxycholic acid. A completely isotactic polymer was utilized to prepare a unique polymer, hemitactic polypropylene, by hydrogenation of a completely 1,4-trans isotactic poly(2-methyl-1,3-pentadiene).

Chiral hosts provide chiral molecular-level spaces, where asymmetric inclusion polymerization may occur. A requirement is that the polymerization proceed via head-

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**Table 2 Parameters for the inclusion and solution polymerizations**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Inclusion</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_p$</td>
<td>$10^{-3}$ kg mol$^{-1}$ s$^{-1}$</td>
<td>$10^0$–$10^3$ L mol$^{-1}$ s$^{-1}$</td>
</tr>
<tr>
<td>$k_t$</td>
<td>$10^{-9}$ kg mol$^{-1}$ s$^{-1}$</td>
<td>$10^{-10}$–$10^0$ L mol$^{-1}$ s$^{-1}$</td>
</tr>
<tr>
<td>$k_M$</td>
<td>$10^{-3}$ mol kg$^{-1}$</td>
<td>$10^{-7}$–$10^{-8}$ mol L$^{-1}$</td>
</tr>
<tr>
<td>$T_2$ Lifetime of M</td>
<td>$&gt;10^5$ s</td>
<td>0.1–1 s</td>
</tr>
</tbody>
</table>
to-tail and isotactic addition along a one-dimensional array in a chiral channel. So far, many optically active polymers were prepared from prochiral diene monomers by using chiral hosts. For example, optically resolved perhydrotriphenylene gave asymmetric polymers from trans-1,3-pentadiene, while deoxycholic acid gave those from cis-1,3-pentadiene. These polymers were ozonolyzed to give optical yields over 10% e.e. and about 20%, respectively.

Space-Size Effects

It is considered that the motion of guest molecules depends on the space sizes even at the same temperature. That is, the molecules can move more freely in a larger space than in a smaller space. Such a difference would affect polymerization behaviors. Such space effects can be observed on the basis of subtle changes of polymerization behaviors by using a suitable set of hosts. Use of a set of the hosts, deoxycholic acid, apocholic acid, cholic acid, and chenodeoxycholic acid, enables us to observe the space effects of one-dimensional polymerization in detail. On the other hand, a pair composed of urea and thiourea is not suitable for such an aim, because the pair does not include identical monomers at the same temperatures. The following three points were ascertained: 1) polymerizabilities of the monomers; 2) motion of polymer chains around the ends of the propagating radicals; and 3) microstructures of the resultant polymers. These space effects are summarized in Table 3.

The radicals can move depending on space sizes and shapes. So, it is considered that the propagating radicals are tightly included in the smaller channels and loosely in the larger channels. This means that an identical monomer exhibits different ESR spectra in various channels. A set of steroidal hosts enabled us to detect a large amount of such slightly different ESR spectra of the propagating radicals from various vinyl and diene monomers having alkyl and polar substituents. Simulation studies showed that such spectra may be explained by different conformations of the polymer chain ends.

Stereoregularities of the resulting polymers depend on the sizes of the host channels. Moreover, the space effect in chirality was observed in asymmetric inclusion polymerization of trans- or cis-2-methyl-1,3-pentadiene by using a pair of hosts, deoxycholic acid and apocholic acid. We obtained optically active polymers with predominant absolute configurations (R). Optical yields varied with the polymerization conditions and the hosts. A maximum optical yield of the trans monomer was 36% in the channel of apocholic acid.

<table>
<thead>
<tr>
<th>Inclusion space</th>
<th>Polymerizability</th>
<th>Propagating radicals</th>
<th>Selectivity of reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large space</td>
<td>Large scope</td>
<td>Large motion</td>
<td>Low selectivity</td>
</tr>
<tr>
<td>Small space</td>
<td>Small scope</td>
<td>Small motion</td>
<td>High selectivity</td>
</tr>
</tbody>
</table>

Table 3  Space-size effects on one-dimensional inclusion polymerization
TWO-DIMENSIONAL INCLUSION POLYMERIZATION

Some two-dimensional inclusion polymerizations are known. For example, montmorillonite and graphite were used for the polymerization of vinyl monomers such as methyl methacrylate and styrene, respectively. Polymerization of salts of 6-amino-2,4-trans,trans-hexadienoic acid was performed using perovskite-type layered compounds on UV or γ-ray irradiation, resulting in stereoregular polymers with a high head-to-tail, 1,4-trans structure. Many organic long-chain compounds form bilayered membranes to form a matrix for the two-dimensional polymerization. For example, photopolymerization was carried out using cast films composed of double-chain ammonium amphiphile involving a cross-linked acrylate polymer. Extraction of the amphiphile with methanol left a multilayered film. Recently, it was found that crystalline organic salts of unsaturated carboxylic acids with aromatic amines were polymerized by UV irradiation to yield highly stereoregular polymers.11,12 The bilayered polymeric aggregates were ascertained to replace amine components through intercalation. So, the polymerization is considered to correspond to one of the two-dimensional inclusion polymerizations. In this assembly, the aromatic part of the amines corresponds to the host component, while the alkyl part of the acids corresponds to the guest component. The amines employed are benzylamine, 1-naphthylmethylamine, long-alkylamines and their derivatives, and so on. The polymerization of sorbic acid was found to proceed highly selectively to give a 1,4-trans, erythro-di-isotactic structure, because $^{13}$C-NMR spectrum of the polymer exhibits simple and sharp absorptions. Although the resulting polymers showed no optical rotation, crystal structural analysis tells us the following interesting feature of the polymerization. The molecules in one array polymerize to give a chiral polymer with (R,R) absolute configuration, while that in the neighboring array do so with (S,S). This means that we obtained a racemate of chiral polymers.

INCLUSION POLYMERIZATION BASED ON MOLECULAR INFORMATION

The study on inclusion polymerization by using steroidal hosts led us to the concept of molecular information and expression, as follows. It is theoretically considered that molecular information at a nanometer level may originate from sequential and chiral carbon chains, like proteins and steroidal molecules. As shown in Fig. 6a, the proteins express their molecular information through noncovalent bonds by the following processes: molecular architecture (Fig. 6A), host–guest compounds (Fig. 6B), and reactions of the included guest components (Fig. 6C). Similarly, the steroidal molecules express their information through the noncovalent processes (Fig. 6b). Therefore, inclusion polymerization corresponds to one step of the expression process of molecular information that the sequential and chiral carbon-chains store.

CONCLUSION

Starting from the synthesis of stereoregular and optically active polymers, we reached the idea that inclusion polymerization constitutes one of supramolecular chemistry from a viewpoint of the space effects. Now such a study might be connected to nanotechnology, because the polymerization can produce molecular composite materials, such as molecular wires, layers, and so on. The bottom-up technology would be constructed through various noncovalent processes that are based on the principle of molecular information and expression.

![Fig. 6](https://example.com/fig6.png)  
Fig. 6 Conceptual comparison of the processes for enzymatic reaction of proteins (a) and inclusion polymerization (b). The chiral and sequential carbon chains express their information through their architectures (A), host–guest compounds (B), and reactions of the guests (C).
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349 CROSS-REFERENCES

350 Channel Inclusion Compounds; Chirality Induction; Crystal Engineering; Deoxycholic, Cholic, and Apocholic Acids; EPR Spectroscopy; Layered Solids; Nanotechnology; Solid-State Reactivity.

354 REFERENCES
