Synthesis and Degradabilities of Polyesters from 1,4:3,6-Dianhydrohexitols and Aliphatic Dicarboxylic Acids

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SYNOPSIS
Six different polyesters (6a–6c and 7a–7c) were prepared by the bulk polycondensations of the respective combinations of 1,4:3,6-dianhydro-D-glucitol (3) and 1,4:3,6-dianhydro-D-mannitol (4) with succinyl dichloride (5a), glutaryl dichloride (5b), and adipoyl dichloride (5c) at 140–180°C. Polyesters having number average molecular weights up to \(2.6 \times 10^4\) were obtained in high yields. Only polyester 7a based on 4 and 5a was partially crystalline, whereas all the other polyesters were amorphous. Thin films of these polyesters except that of 7a were spontaneously hydrolyzed in a neutral phosphate buffer solution at 50°C, whereas they were reluctant to be hydrolyzed at 27°C. The polyesters were more or less degraded at 27°C by treatment with an activated sludge or by prolonged burial in soil. © 1995 John Wiley & Sons, Inc.

Keywords: polyester • polycondensation • anhydroglucitol • anhydromannitol • spontaneous hydrolysis • biodegradability • aliphatic dicarboxylic acid

INTRODUCTION
Except biodegradable polymers based on naturally occurring polysaccharides such as cellulose and starch, commercially available biodegradable polymers are mostly confined to aliphatic polyesters such as poly(3-hydroxyalkanoates), poly(ε-caprolactone), poly(L-lactide), and poly(butylene succinate).1-8 Aliphatic polyesters including copolymers can cover a wide range from flexible elastomers to stiff plastics, but they do not always meet the diverse and specific needs for polymeric materials used for practical application. Therefore, it is highly desirable to develop different types of biodegradable polyesters so that we can broaden the scope of the utilization of biodegradable polymeric materials.

We have recently found that polyesters (1 and 2) having tetrahydropyran rings in their backbones undergo biodegradation in soil or in activated sludge as well as spontaneous hydrolytic degradation in a neutral phosphate buffer solution.6-8 These polyesters were prepared by cationic ring-opening polymerization of bicyclic lactones, 6,8-dioxabicyclo[3.2.1]octan-7-one and 2,6-dioxabicyclo[2.2.2]octan-3-one, respectively.

This finding stimulated us to continue basic researches on the molecular design of biodegradable polyesters containing cyclic ether structure in their backbones. The present article is concerned with the synthesis of polyesters having fused tetrahydrofuran rings in the main chains by polycondensation of 1,4:3,6-dianhydro-D-glucitol (3) and 1,4:3,6-dianhydro-D-mannitol (4) with succinyl dichloride (5a), glutaryl dichloride (5b), and
adipoyl dichloride (5c) and their hydrolytic and biological degradabilities.

\[
\begin{align*}
\text{HO} & \quad \text{H} \quad \text{O} \\
\text{OH} & \quad \text{H} \quad \text{O} \\
\text{5a: } n = 2 & \quad \text{5b: } n = 3 \\
\text{5c: } n = 4 &
\end{align*}
\]

A number of attempts have been undertaken to utilize carbohydrates as monomers for polymer synthesis by polycondensation and polyaddition. However, because of their polyfunctionality, the control of polymerization is generally difficult, without tedious regiospecific protection of the hydroxyl groups prior to polymerization. 1,4:3,6-Dianhydro-D-glucitol (3) is cheaply obtained from D-glucose by reduction followed by dehydration.\(^9\) 1,4:3,6-Dianhydro-D-mannitol (4) is also readily prepared from mannitol by dehydration. These compounds can be used as bifunctional monomers suitable for polycondensation and polyaddition. Thiem et al.\(^{10}\) were the first that used 3 and 4 as monomers in polyester syntheses; they synthesized aromatic polyesters by melt polycondensation of 3, 4, and their stereoisomer, 1,4:3,6-dianhydro-L-iditol as well, with terephthaloyl chloride. More recently, Ballauff et al.\(^{11}\) obtained the same polyesters of higher molecular weights by the solution polycondensation in toluene or sulfolane at lower temperatures. Reinecke and Ritter\(^{12}\) reported the synthesis and crosslinking of an unsaturated oligoester from 3 and maleic anhydride. However, to the best of our knowledge, there has been no article dealing with degradability of polyesters containing 3 or 4 as the diol components.

Succinyl dichloride (5a), glutaryl dichloride (5b), and adipoyl dichloride (5c) were employed as the diacid components. Succinic acid is found not only in a wide range of plants but also in animals and microorganisms, and it is a component in the well-known tricarboxylic acid cycle (TCA cycle or Krebs cycle).\(^{13}\) Glutaric acid occurs in green sugar beets. It is also found in water extracts of crude wool. In addition, glutaryl-CoA is one of the metabolic intermediates of lysin and triptophan, and via acetyl-CoA, it is also oxidized in the TCA cycle. Adipic acid is found in beet juice in nature. Because both the diols as well as the diacid components originate from naturally occurring compounds, polyesters derived from them are expected to be potentially biodegradable. Moreover, the fused tetrahydrofuran rings in the backbones of the polyesters might impart desirable thermal and mechanical properties to the polyesters.

**EXPERIMENTAL**

**Materials**

Commercially available 1,4:3,6-dianhydrohexitols 3 and 4 were purified by repeated recrystallization from chloroform for 3 and chloroform-hexane (2:1, v/v) for 4. The aliphatic diacid chlorides 5a, 5b, and 5c were prepared by the reactions of the respective diacids and thionyl chloride in the presence of a small amount of N,N-dimethylformamide, and purified by distillation under nitrogen.

**Polycondensation**

Polycondensation was carried out in bulk without catalyst at 140–160°C, first at normal pressure, then under reduced pressure by an aspirator, and finally under vacuum. Polymers were purified by repeated reprecipitation using chloroform and methanol as a pair of solvent and precipitant, and dried under reduced pressure to a constant weight. Polycondensation of 3 and 5a was attempted in the presence of titanium isopropoxide (0.5–4 mol %) at 180°C. Solution polycondensation of 3 and 5a was attempted in a mixed solvent of pyridine and sulfolane (1:1, v/v) at 40°C. However, black polymers of number average molecular weights of less than five thousands were obtained in 60–70% yield.

**Characterization**

Molecular weights of polyesters were determined by gel permeation chromatography using chloroform as eluent. Standard polystyrene was used as a reference. \(^1\)H and \(^13\)C NMR spectra were taken by a JEOL FX-270 spectrometer operating at 270 MHz (\(^1\)H) and
67.8 MHz ($^{13}$C), respectively, on solutions in deuteriochloroform. X-Ray powder diffraction diagrams were recorded with a Rigaku Denki No.2030/P Geigerflex diffractometer using Ni-filtered Cu-K$_{\alpha}$ radiation. Surfaces of the films after soil burial tests were observed by a JEOL JSM-F7 scanning electron microscope.

Degradation Tests

Spontaneous Hydrolysis in Phosphate Buffer Solution

A sample of polyester (25 mg) was taken in each of several test tubes. A small amount of chloroform was added to dissolve the sample. By rotating the test tube and slowly evaporating the solvent, the bottom part (height, about 2 cm) of the inner wall of the test tube was coated with a thin film of the polyester. A phosphate buffer solution (5 mL, pH 7.5) was added to each test tube. The test tubes were allowed to stand in a room thermostated at 27°C. At specified intervals, the remaining insoluble polymer was separated from the aqueous solution by decantation. The water insoluble polymer was washed with water, dried under reduced pressure, and weighed.

Degradation in Activated Sludge

Degradation in an activated sludge was carried out in a manner similar to the procedure described above by using an activated sludge instead of the buffer solution. The activated sludge (pH 7.2) was obtained from a sewage treatment plant in Meito-ku, Nagoya. Carbon dioxide evolved during the degradation was quantitatively determined by the method described previously.$^{8}$

Soil Burial Degradation

Soil burial test was undertaken on thin films or disks, the diameter and thickness of the latter being 10 and 0.6 mm, respectively. The films and disks were buried in soil in a desiccator, in which the relative humidity was adjusted to ca. 80% by a saturated solution of ammonium nitrate. The desiccator was placed in a room thermostated at 27°C. After several months, the films or disks were taken out and dissolved in chloroform to remove soil by filtration. After the evaporation of the solvent from the filtrate, the residue was dried to a constant weight under reduced pressure. The weights and molecular weights of the recovered samples were determined.

RESULTS AND DISCUSSION

Synthesis of Polyesters

Polycondensations of 1,4:3,6-dianhydrohexitols 3 and 4 with aliphatic diacid chlorides 5a, 5b, and 5c were carried out in bulk at different temperatures ranging from 140 to 180°C, first at normal pressure, then under reduced pressure (40 mmHg), and finally under vacuum (1 mmHg). Some of the results on the polycondensations are presented in Table I. Polyesters with molecular weights up to $2.6 \times 10^4$ were obtained in high yields. The molecular weights of these polyesters were estimated by gel permeation chromatography (polystyrene standard). Solution polycondensation of 3 and 5a was attempted in a mixed solvent of pyridine and sulfolane (1:1, vol/vol) at 40°C. However, highly colored polymers of number average molecular weights up to five thousands were formed. Polycondensation of 3 and dimethyl succinate was also carried out in bulk in the presence of titanium isopropoxide (0.5-4.0 mol %) as a catalyst at 180°C. The polycondensation proceeded considerably slowly compared with the polycondensation of 3 and 5a. Therefore, a higher concentration of the catalyst and a prolonged reaction time were needed to obtain polyester 6a having a molecular weight comparable to that of the same polyester obtained by polycondensation of 3 and 5a in bulk.

Polyesters 6a–6c and 7a–7c were characterized by $^1$H and $^{13}$C NMR, IR, GPC, x-ray diffraction, DSC, and elemental analysis. Figure 1 shows the $^{13}$C NMR spectrum of polyester 6b derived from 3 and 5b. The assignments of the signals are given in the figure.

The signal a due to the ester carbonyl carbon appeared as a set of four peaks of nearly equal intensities ($\delta$, 172.2, 172.1, 171.9, and 171.8 ppm). The signal h due to the methylene carbon adjacent to the ester–carbonyl group appeared as a pair of peaks of nearly equal intensities ($\delta$, 32.9 and 32.8 ppm), and the signal i due to the central methylene carbon appeared as a set of three peaks with the relative intensities of approximately 1:2:1. These characteristic splittings of the signals originates from the endo- and exo-orientations of the C–O bonds at the 2 and 5 positions, respectively, in the 1,4:3,6-dianhydro-D-glucitol moieties. The observed relative intensities clearly indicate the random placement of the 1,4:3,6-dianhydro-D-glucitol units in the polymer chain, that is, there are almost equal fractions of 2→5 (head to tail), 5→2 (tail to head), 2→2 (head
Table I. Polycondensation of 1,4:3,6-Dianhydro-D-hexitols (3 and 4) with Diacid Chlorides (5a–5c)*

<table>
<thead>
<tr>
<th>Diol, g</th>
<th>Diacid chloride, g</th>
<th>Temp., °C</th>
<th>Time, h</th>
<th>Polyester</th>
<th>Yield, %</th>
<th>$M_w$</th>
<th>$M_n$</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>1.19 5a 1.27</td>
<td>160</td>
<td>20</td>
<td>6a</td>
<td>97</td>
<td>0.74</td>
<td>1.8</td>
</tr>
<tr>
<td>3</td>
<td>4.98 5b 5.76</td>
<td>160</td>
<td>20</td>
<td>6b</td>
<td>93</td>
<td>1.6</td>
<td>1.7</td>
</tr>
<tr>
<td>3</td>
<td>1.44 5c 1.80</td>
<td>140</td>
<td>10</td>
<td>6c</td>
<td>92</td>
<td>1.7</td>
<td>1.5</td>
</tr>
<tr>
<td>3</td>
<td>1.25 5c 1.57</td>
<td>160</td>
<td>10</td>
<td>6c</td>
<td>94</td>
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<tr>
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<td>180</td>
<td>10</td>
<td>6c</td>
<td>96</td>
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<td>1.7</td>
</tr>
<tr>
<td>3</td>
<td>5.77 5c 7.23</td>
<td>160</td>
<td>20</td>
<td>6c</td>
<td>92</td>
<td>2.6</td>
<td>1.5</td>
</tr>
<tr>
<td>4</td>
<td>1.19 5a 1.26</td>
<td>160</td>
<td>10</td>
<td>7a</td>
<td>91</td>
<td>1.0</td>
<td>1.7</td>
</tr>
<tr>
<td>4</td>
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<td>140</td>
<td>10</td>
<td>7b</td>
<td>97</td>
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<tr>
<td>4</td>
<td>1.12 5b 1.29</td>
<td>160</td>
<td>10</td>
<td>7b</td>
<td>98</td>
<td>1.1</td>
<td>1.6</td>
</tr>
<tr>
<td>4</td>
<td>1.15 5b 1.33</td>
<td>180</td>
<td>10</td>
<td>7b</td>
<td>95</td>
<td>1.0</td>
<td>1.8</td>
</tr>
<tr>
<td>4</td>
<td>1.07 5c 1.35</td>
<td>140</td>
<td>10</td>
<td>7c</td>
<td>90</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td>4</td>
<td>1.41 5c 1.77</td>
<td>160</td>
<td>10</td>
<td>7e</td>
<td>91</td>
<td>1.6</td>
<td>1.7</td>
</tr>
<tr>
<td>4</td>
<td>2.42 5c 3.03</td>
<td>160</td>
<td>20</td>
<td>7e</td>
<td>95</td>
<td>2.0</td>
<td>1.5</td>
</tr>
</tbody>
</table>

* In bulk.

** Total heating time (6 h/760 mmHg, 2 h/40 mmHg, and 2 or 12 h/1 mmHg).

* Determined by GPC in chloroform (polystyrene standard).

* Anal. (%): Calcd. for (C₁₂H₁₆O₆)ₓ: C, 56.24; H, 6.30. Found: C, 56.20; H, 6.16.


Figure 1. $^1$H NMR spectrum of polyester 6b. Solvent, CDCl₃; conc., 10%; internal reference, tetramethylsilane; 67.8 MHz.
the spectra of these polyesters, some peaks cannot be resolved because of the very slight differences in chemical shifts.

In contrast to polyesters 6a–6c, polyesters 7a–7c containing 1,4:3,6-dianhydro-D-mannitol moieties gave simple 13C NMR spectra without any splitting of the signals. This is reasonable, because both of the C—O bonds at the 2 and 5 positions in the 1,4:3,6-dianhydro-D-mannitol moieties are endo-oriented, giving rise to the symmetrical polymer structure.

X-Ray diffraction measurements of these polyesters demonstrated that only polyester 7a derived from 4 and 5a was semicrystalline, whereas the other five polyesters were amorphous. As illustrated in Scheme 1, the unsymmetrical 1,4:3,6-dianhydro-D-glucitol units 3 in 6b are statistically randomly incorporated in the polymer chain, forming head to tail, head to head, and tail to tail linkages. In contrast, polyesters 7a–7c are regular because of the symmetrical 1,4:3,6-dianhydro-D-mannitol units 4. The x-ray diffraction data suggest that only polyester 7a with two methylene carbons between the 1,4:3,6-dianhydro-D-mannitol units can be crystallized.

The thermal transition temperatures of these polyesters were determined by DSC. Only 7a has the melting point of about 175°C. Its glass transition temperature is 75°C, which is higher than the glass transition temperatures of the other polyesters (Tg; 6a, 36°C; 6b, 28°C; 6c, 40°C; 7b, 37°C; 7c, 28°C). All these polyesters do not decompose up to 300°C. Polyesters 6a–6c based on 3 are soluble in a variety of organic solvents such as dichloromethane, chloroform, 1,4-dioxane, acetonitrile, dimethylformamide, dimethyl sulfoxide, pyridine, sulfolane, m-cresol, and trifluoroacetic acid. Polyesters 6b and 6c are soluble in tetrahydrofuran too. Polyester 7a derived from 4 and 5a is of the lowest solubility; it is soluble in dichloromethane, chloroform, sulfolane, m-cresol, and trifluoroacetic acid. The solubilities of polyesters 7b and 7c are similar to those of 6b and 6c, except that 7b and 7c are partially soluble in tetrahydrofuran and acetonitrile. The lower solubility of 7a is clearly ascribable to its crystallinity described above.

Thin films of these polyesters could be formed by casting their solutions in chloroform or dichloromethane. They were, however, brittle because of the relatively low molecular weights.

Degradabilities

Spontaneous Hydrolysis in Phosphate Buffer

In order to evaluate the spontaneous hydrolytic degradability, thin films of polyesters were coated on the inner wall surface of test tubes and they were allowed to contact with a phosphate buffer solution (pH 7.5). Figure 2 shows the recovery of water-insoluble polyesters 6a, 6b, and 6c as functions of time. At 27°C, only slight decrease in the polymer recovery was observed with increasing immersion time, and there was not any significant difference between these three polyesters. At 50°C, however, polyesters 6b and 6c were hydrolyzed nearly com-
Figure 2. Recovery of water-insoluble polymer in spontaneous hydrolysis of polyesters 6a–6c in a phosphate buffer solution (pH 7.5). ■, 6a; ●, 6b; ▲, 6c at 27°C. □, 6a; ○, 6b; Δ, 6c at 50°C.

Figure 3. Recovery of water-insoluble polymer in spontaneous hydrolysis of polyesters 7a–7c in a phosphate buffer solution (pH 7.5). ■, 7a; ●, 7b; ▲, 7c at 27°C. □, 7a; ○, 7b; Δ, 7c at 50°C.

Figure 4. Recovery of water-insoluble polymer in the degradation of polyesters 6a–6c in an activated sludge. Temp., 27°C; pH 7.4. ■, 6a; ●, 6b; ▲, 6c.

Figure 5. Recovery of water-insoluble polymer in the degradation of polyesters 7a–7c in an activated sludge. Temp., 27°C; pH 7.4. ■, 7a; ●, 7b; ▲, 7c.

completely after the immersion in the phosphate buffer for 20 days, whereas for polyester 6a, about 20 wt % of the original sample still remained water-insoluble even after 40 days.

Figure 3 illustrates the recovery of polyesters 7a, 7b, and 7c when their thin films were contacted with the same buffer solution. Although spontaneous hydrolysis took place very slowly at 27°C, polyesters 7b and 7c were nearly completely hydrolyzed at 50°C after 30 days. In contrast, for polyester 7a, approximately 60 wt % of the original sample remained water-insoluble even after 40 days. The enhanced stability of 7a against spontaneous hydrolysis in neutral phosphate buffer solution among these six polyesters is, again, ascribable to its partial crystallinity.

Degradation in Activated Sludge

Figures 4 and 5 present the results on the degradation of polyesters 6a–6c and 7a–7c, respectively, in an activated sludge at 27°C. In comparison with the spontaneous hydrolytic degradation in the phosphate buffer solution, these polyesters except 7a were more rapidly degraded in the activated sludge. The recovery of the water-insoluble polymers after the treatment in the activated sludge for 40 days was in the range of 60–77%, whereas the recovery of the water-insoluble polymers was higher than 90% in the buffer solution under similar conditions. In contrast, the degradation rate of polyester 7a in the activated sludge was only slightly faster than that in the phosphate buffer.

Table II summarizes the changes in the molecular weight and molecular weight distribution after the treatment of polyesters 6a–6c and 7b–7c in the activated sludge at 27°C for 40 days. The recovery of the water-insoluble polymers was in the range of 61–77%, in other words, 23–39% of the original samples became water-soluble, low molecular weight compounds. Nevertheless, the molecular weights and polydispersity indices of the remaining water-insoluble polymers did not significantly differ from the corresponding values of the original samples. The relatively small changes in the molecular weights...
POLYESTERS FROM DIANHYDROHEXITOLS

and polydispersity indices during the degradation in the activated sludge are in contrast to those observed during the hydrolysis of the same polyesters in the buffer solution at 50°C where the molecular weights of the remaining water-insoluble polymers decreased, and the polydispersity indices increased, appreciably.

When we design biodegradable polymers, it is important to know what potential degradation products may be released and whether they are safely catabolized or not. In the present case, the final hydrolysis products are 1,4:3,6-dianhydrohexitos 3 and 4 along with the dicarboxylic acids corresponding to 5a–5c. In order to check whether 3 and 4 are catabolized by microorganisms, these diols were treated in an activated sludge, and the carbon dioxide evolved was quantitatively determined in a manner similar to that described previously.\(^8\) The results are graphically shown in Figure 6.

The ordinate of the figure represents the percent of the cumulative amount of carbon dioxide to the theoretical amount of carbon dioxide calculated on the assumption that all the carbons in the samples are converted to carbon dioxide. For both 3 and 4, the total amount of carbon dioxide increased gradually after an induction period of several days and exceeded 50% after about 2 weeks. Because the evolution of carbon dioxide was still continuing, although slowly, after 3 weeks, it appears that most of the samples would be converted to carbon dioxide and water during prolonged treatment in the activated sludge.

**Soil Burial Degradation**

Figure 7 shows the results of soil burial test on 6a, 6b, 7a, and 7b. The soil used for the burial test had been composted for more than 10 years in the farm of Nagoya University (pH 6.8). As clearly seen in Figure 7, polyester 7b was degraded fastest among the four polyesters. After 6 months, it was nearly completely degraded. In contrast, polyester 7a was scarcely degraded. The relative degradabilities of 6a and 6b in soil lie in between those of 7a and 7b. The unusually high stability of 7a must arise from its crystallinity. Scanning electron microscopy detected the presence of some unidentified microorganisms on the surface of the films of 7b after soil burial for four months.

These observations described above strongly suggest that most of the polyesters derived from the 1,4:3,6-dianhydrohexitos 3 and 4 and aliphatic dicarboxylic chlorides 5a–5c are biodegradable.

In summary, six polyesters 6a–6c and 7a–7c were prepared by the bulk polycondensation of the combinations of the two 1,4:3,6-dianhydrohexitos 3 and 4 with three aliphatic diacid chlorides 5a–5c. These polyesters, except 7a which is partially crystalline, are amorphous and dissolve in a wide variety of organic solvents. They are spontaneously hydrolyzed in neutral phosphate buffer solution at

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**Table II. Degradation of Polyesters in an Activated Sludge**\(^a\)

<table>
<thead>
<tr>
<th>Polyester</th>
<th>(M_n^b \times 10^{-3})</th>
<th>(M_w/M_n^b)</th>
<th>Recovery, (%)</th>
<th>(M_n^c \times 10^{-3})</th>
<th>(M_w/M_n^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>7.4</td>
<td>1.8</td>
<td>69</td>
<td>9.0</td>
<td>1.6</td>
</tr>
<tr>
<td>6b</td>
<td>20</td>
<td>1.7</td>
<td>71</td>
<td>19</td>
<td>1.7</td>
</tr>
<tr>
<td>6c</td>
<td>26</td>
<td>1.5</td>
<td>77</td>
<td>20</td>
<td>1.8</td>
</tr>
<tr>
<td>7b</td>
<td>11</td>
<td>1.6</td>
<td>67</td>
<td>10</td>
<td>1.0</td>
</tr>
<tr>
<td>7c</td>
<td>20</td>
<td>1.5</td>
<td>61</td>
<td>17</td>
<td>1.6</td>
</tr>
</tbody>
</table>

\(^a\) At 27°C.

\(^b\) Determined by GPC in chloroform (polystyrene standard).

\(^c\) Recovery of water-insoluble polymer.
Figure 7. Recovery of polymer in the soil burial degradation of polyesters 6a, 6b, 7a, and 7b. The soil had been composted for 10 years; pH 6.8; temp., 27°C; humidity, 80%. 6a, 6b; 7a, 7b.

50°C, although they are much more reluctantly hydrolyzed at 27°C. Most of these polyesters are degraded by the treatment in activated sludge and by the prolonged soil burial at 27°C. Further work on the biodegradability of these polyesters is currently in progress, and the results will be published elsewhere.

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REFERENCES AND NOTES


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