Thermal Behavior of Head-to-head Coumarin Dimers and Their Lactone-opened Derivatives

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The thermal behavior of head-to-head coumarin dimers and twelve lactone-opened derivatives was investigated. Though the lactone rings in coumarin dimers are very susceptible to nucleophilic ring-opening, heating these derivatives reformed six-membered lactone rings except for certain imide and diamide derivatives. The large neiboring group effect allowed the relactonization by the attack of hydroxyphenyl group to carbonyl carbon in preference to the scission of cyclobutane ring.

Our recent studies on coumarin dimers revealed that the lactone-openig reaction of coumarin dimers[1] and the photoreaction of their lactone-opened derivatives[2,3] are as attractive as their photochemical formation which have been extensively investigated.[4–16] The large strain of the six-four-six fused ring system in coumarin dimers markedly facilitates their lactone-opening reactions by nucleophiles, permitting the smooth reaction with diamines to give high-molecular-weight polyamides. The resulting polyamides show a characteristic photochemical behavior of the transformation of the main chain *via* the asymmetric scission of the cyclobutane rings.[17–19] On the other hand, the thermal degradation of these polyamides was proposed to proceed in quite a different manner to form five-membered imide ring or six-membered lactone ring by the scission of the main chain.[19]

In the previous communication,[20] we briefly reported the thermal behavior of some lactone-opened derivatives of *syn* head-to-head coumarin dimer. In this paper, we wish to present the anomalous thermal reaction of the lactone-opened derivatives of *syn* and *anti* head-to-head coumarin dimers in detail and to discuss these reaction behaviors mainly from the point of neighboring group effect.

Experimental

Materials. *Syn* and *anti* head-to-head coumarin dimers (*syn* dimer (**1**) and *anti* dimer (**2**)) were prepared by the methods of Krauch *et al.*[9] The lactone-opened derivatives were synthesized according to the methods described in the previous paper:[1] *N,N'*-Dibutyl-*c*-3,*c*-4-bis(2-hydroxyphenyl)-*r*-1,*c*-2-cyclobutanedicarboxamide (*syn* dibutyldiamide (**3**)), *N*-butyl-*c*-3,*c*-4-bis(2-hydroxyphenyl)-*r*-1,*c*-2-cyclobutanedicarboximide (*syn* butylimide (**4**)), *N*-phenyl-*c*-3,*c*-4-bis(2-hydroxyphenyl)-*r*-1,*c*-2-cyclobutanedicarboximide (*syn* phenylimide (**5**)), and *N,N,N',N'*-tetrabutyl-*c*-3,*c*-4-bis(2-hydroxyphenyl)-*r*-1,*c*-2-cyclobutanedicarboxamide (*neo* tetrabutyldiamide (**6**)) were prepared from *syn* dimer (**1**). *Anti* dimer (**2**) was converted to 2-ethoxycarbonyl-1-(2-hydroxyphenyl)-1α,2α,2aβ,8bβ-tetrahydro-3*H*-cyclobuta[*c*]chromen-3-one (*anti* monoethyl ester (**7**)), 1-(2-hydroxyphenyl)-2-phenylcarbamoyl-1α,2α,2aβ,8bβ-tetrahydro-3*H*-cyclobuta[*c*]chromen-3-one (*anti* monoanilide (**8**)), 2-butylcarbamoyl-1-(2-hydroxyphenyl)-1α,2α,2aβ,8bβ-tetrahydro-3*H*-cyclobuta[*c*]chromen-3-one (*anti* monobutylamide (**9**)), *t*-3,*c*-4-bis(2-hydroxyphenyl)-*r*-1,*t*-2-cyclobutanedicarboxylic acid (*anti* dicarboxylic acid (**10**)), diethyl *t*-3,*c*-4-bis(2-hydroxyphenyl)-*r*-1,*t*-2-cyclobutanedicarboxylate (*anti* diethyl ester (**11**)), *t*-3,*c*-4-bis(2-hydroxyphenyl)-*r*-1,*t*-2-cyclobutanedianilide (*anti* dianilide (**12**)), *N,N,N',N'*-tetrabutyl-*t*-3,*c*-4-bis(2-hydroxyphenyl)-*r*-1,*t*-2-cyclobutanedicarboxamide (*anti* tetrabutyldiamide (**13**)), and *N,N'*-dibutyl-*t*-3,*c*-4-bis(2-hydroxyphenyl)-*r*-1,*t*-2-cyclobutanedicarboxamide (*anti* dibutyldiamide (**14**)). 2,2'-Dihydroxystilbene was synthesized by the method reported in the literature.[3]

Measurements. TG-DSC curves were recorded on a Rigaku Denki THERMOFLEX TG-DSC with the heating rate of 5 °C/min in a nitrogen stream. IR spectra were recorded on a JASCO IRA-1 spectrophotometer. ^{1}H-NMR spectra were recorded on a HITACHI R-40 spectrophotometer. High performance liquid chromatography (HPLC) was carried out by detecting UV absorbance (at 280 nm) using a Merck LiChrosorb SI60 column (4φ×250 mm) with benzene-ethyl acetate (50:50 or 80:20 v/v%) as an eluent. Thin layer chromatography (TLC) was performed on Merck TLC plates Silica gel 60 F_{254} using the same eluents with HPLC.

Pyrolysis. *A) Pyrolysis in a TG-DSC Pan.* Sample (5—9 mg) was placed in an aluminium pan and heated in the furnace of the TG-DSC instrument under a nitrogen atmosphere. The pyrolyzed products were analyzed by ^{1}H-NMR and IR spectroscopy without purification.

B) Pyrolysis in a Sealed Tube. Sample (*ca.* 10 mg) was placed in a sealed tube under an argon atmosphere and heated in a salt bath. The pyrolyzed product was analyzed by HPLC.

C) Pyrolysis in a Sublimation Tube. Sample (*ca.* 0.2 g) was placed in a sublimation tube and heated in an oil bath under reduced pressure (0.5—1.0 Torr, 1 Torr=133.322 Pa). The product was analyzed by HPLC and IR spectroscopy without purification.

The identification of the pyrolyzed products were accomplished by the comparison of their spectroscopic and HPLC data with those of authentic samples.

Results and Discussion

Thermal Reaction of syn *Head-to-head Coumarin Dimer Derivatives.* The thermal reaction of *syn* dimer (**1**) and its derivatives was investigated on the

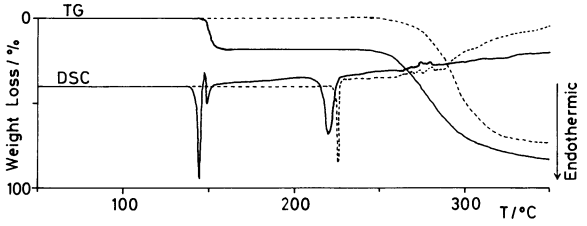


Fig. 1. TG-DSC curves of *syn* dibutyldiamide (**3**) [——] and *syn* butylimide (**4**) [----].

basis of their TG-DSC curves and the data of ^{1}H-NMR, IR, and HPLC analyses of the pyrolyzed products. Figure. 1 shows the TG-DSC curves of *syn* dibutyldiamide (**3**) and *syn* butylimide (**4**). In the TG-DSC curves of *syn* dibutyldiamide (**3**) there were sharp endo- and exothermic peaks at 144 and 147 °C, accompanying with the 16.4% weight loss. These two peaks and weight loss were attributed to melting and decomposition of *syn* dibutyldiamide (**3**) and crystallization of *syn* butylimide (**4**), formed from *syn* dibutyldiamide (**3**) with the elimination of one mole of butylamine (the calculated weight loss is 16.7%). The almost quantitative imide formation was confirmed by comparison of ^{1}H-NMR and IR spectra of the product, obtained by heating *syn* dibutyldiamide (**3**) at 200 °C in a TG-DSC pan, with those of *syn* butylimide (**4**). The thermal reaction in a solution was also carried out and monitored by ^{1}H-NMR spectroscopy. In a DMSO-d_6 solution, *syn* dibutyldiamide (**3**) remained unchanged on standing at 80 °C for 1 h. But the peaks of the cyclobutane ring protons changed completely into those of *syn* butylimide (**4**) on heating at 100 °C for 6.5 h. Moreover, HPLC analysis showed that heating *syn* butylimide (**4**) at 188 to 220 °C under reduced pressure resulted in the complete sublimation of *syn* butylimide (**4**) accompanying with the formation of a small amount of 2,2′-dihydroxystilbene. But, in the products obtained by heating at 270 °C for 3 min in a sealed tube, small amounts of coumarin and *syn* dimer (**1**) were detected along with 2,2′-dihydroxystilbene by HPLC analysis. These results indicate that under rather drastic conditions the symmetric cleavage of the cyclobutane ring *via* an anomalous relactonization occurred certainly in competition with the asymmetric scission of the cyclobutane ring, which would be the single pathway for the degradation at 220 °C.

On the other hand, a complete thermal conversion of *syn* phenylimide (**5**) into *syn* dimer (**1**) was achieved. In the TG-DSC curves of *syn* phenylimide (**5**), a broad endothermic peak in the temperature range of 181—223 °C with the weight loss of 21.4% and a sharp exothermic peak at 190 °C were observed, which correspond to the decomposition of *syn* phenylimide (**5**) with the vaporization of aniline eliminated (the calculated weight loss of aniline is 24.2%) and the crystallization of *syn* dimer (**1**)(Fig.2). Furtheremore, the decomposition mode of *syn* phenylimide (**5**) above 223 °C in TG-DSC curves was essentially the same as that of *syn* dimer (**1**). The product obtained by heating *syn* phenylimide (**5**) at 240 °C in a TG-DSC pan was identified as *syn* dimer (**1**) by ^{1}H-NMR and IR spectroscopy. This relactonization was also observed when a DMSO-d_6 solution of *syn* phenylimide (**4**) was heated at 185 °C for 1 h, giving a mixture of *syn* phenylimide (**4**) and *syn* dimer (**1**) (41:59, based on the peak areas of the cyclobutane ring protons in ^{1}H-NMR spectrum), and the finally decomposed product of *syn* dimer (**1**) was ascertained as coumarin on the basis of spectroscopic data. These thermal behaviors of the lactone-opened derivatives of *syn* dimer (**1**) are summarized in Scheme 1.

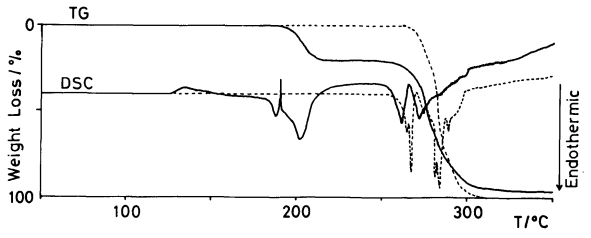


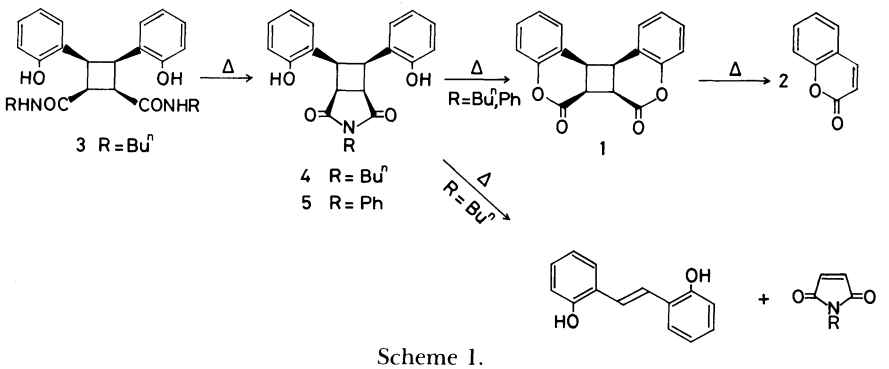
Fig. 2. TG-DSC curves of *syn* dimer (**1**) [----] and *syn* phenylimide (**5**) [——].

The difference in the thermal behaviors of *syn* butylimide (**4**) and *syn* phenylimide (**5**) is interpreted in terms of the electronic nature of their imide linkage. The less electron-donating character of the phenyl group than butyl group lowers the electron density of the imide carbonyl effectively enough to facilitate the nucleophilic attack of 2-hydroxyphenyl group in *syn* phenylimide (**5**).

In spite of the high reactivity of the lactone rings in *syn* dimer (**1**) to nucleophiles, the lactone of a phenolic acid reformed through the elimination of anilino group by the attack of *cis*-positioned 2-hydroxyphenyl group to regenerate *syn* dimer (**1**). It means that anomalously large neighboring group effect plays an important role in these thermal reactions, although phenoxyl group is a very effective leaving group in the lactone-opening reaction of *syn* dimer (**1**) as well as in general substitution reactions.

Thermal Reaction of anti *Head-to-head Coumarin Dimer Derivatives.* The thermal reaction of *anti* dimer (**2**) and its lactone-opened derivatives was investigated by analogous methods.

The thermal reaction of monolactone derivatives of *anti* dimer (**2**) such as *anti* monoethyl ester (**7**), *anti* monoanilide (**8**), and *anti* monobutylamide (**9**) was not clearly distinguished from the TG-DSC curves (Figs. 3—5), but the product sublimed on heating at 300 °C was



Scheme 1.

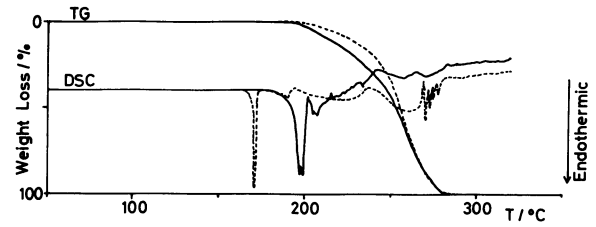


Fig. 3. TG-DSC curves of *anti* monoetyl ester (**7**) [----] and *anti* dietyl diester (**11**) [——].

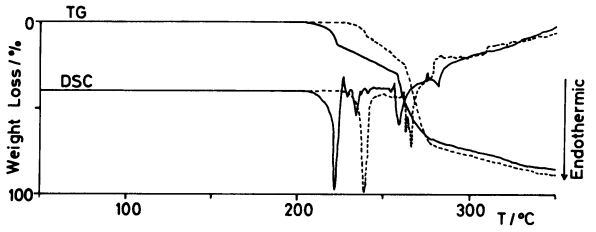


Fig. 4. TG-DSC curves of *anti* monoanilide (**8**) [----] and *anti* dianilide (**12**) [——].

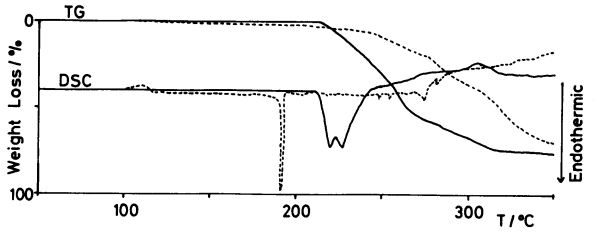


Fig. 5. TG-DSC curves of *anti* monobutylamide (**9**) [----] and *anti* dibutyldimide (**14**) [——].

solely coumarin. To clarify the reaction pathway from monolactone derivatives **7**, **8**, and **9** to coumarin, the heating in a TG-DSC pan was stopped when the weight loss corresponded to the release of one mole of alcohol or amine. The product was proved to be a mixture of the starting material and *anti* dimer (**2**) on the basis of IR and ^{1}H-NMR spectrometric data, indicating that coumarin was produced *via* anomalously relactonized *anti* dimer (**2**). The smooth relactonization was also supported by the following observation: In a DMSO-d_6 solution, *anti* monobutylamide (**9**) turned to a mixture of the starting compound **9**, *anti* dibutyldiamide (**14**), and *anti* dimer (**2**) (70:15:15, based on the peak areas of the cyclobutane ring protons in ^{1}H-NMR spectrum) on heating at 185 °C for 1 h, meaning that *anti* monobutylamide (**9**) slowly decomposed to *anti* dimer (**2**) with the elimination of butylamine, which attacked the residual lactone ring of *anti* monobutylamide (**9**) to give *anti* dibutyldiamide (**14**) (Scheme 2).

In the next stage, the thermal reactions of both lactone-opened derivatives of *anti* dimer (**2**) such as *anti* dicarboxylic acid (**10**), *anti* diethyl diester (**11**), *anti*

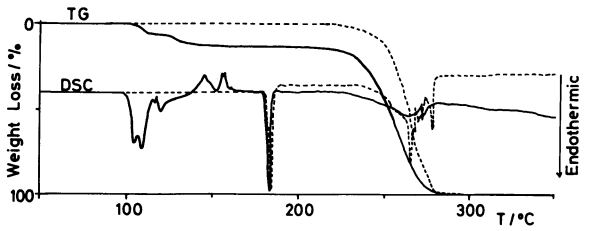


Fig. 6. TG-DSC curves of *anti* dimer (**2**) [----] and *anti* dicarboxylic acid (**10**) [——].

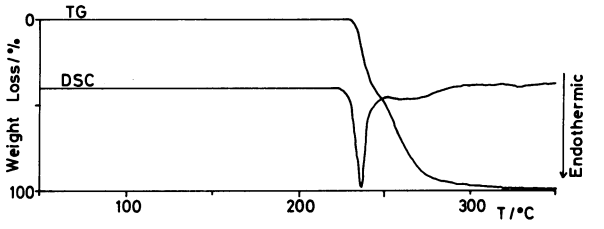
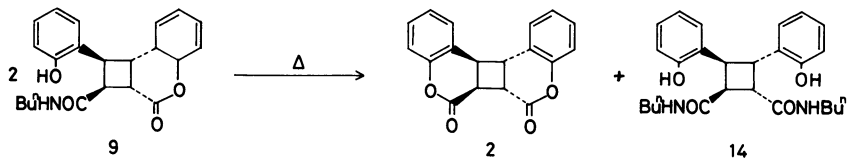


Fig. 7. TG-DSC curves of *anti* tetrabutyldiamide (**13**).

dianilide (**12**), *anti* tetrabutyldiamide (**13**), and *anti* dibutyldiamide (**14**) were carried out. The reactions except for *anti* dibutyldiamide (**14**) were made clear by comparison of their TG-DSC curves with those of the corresponding monolactone compounds **7**—**9** and *anti* dimer (**2**), suggesting that the reaction proceed *via* the monolactone compounds (Figs. 3, 4, 6, and 7). The product, obtained by heating in a TG-DSC pan up to the temperature at which the weight loss corresponded to the release of one mole of water, ethanol, aniline, or dibutylamine, was proved to be a mixture of starting material, the corresponding monolactone derivative, and *anti* dimer (**2**), and further heating was ascertained to give coumarin by TLC analysis and IR and ^{1}H-NMR spectroscopy. But, when *anti* dibutyldiamide (**14**) was heated at 216—217 °C for 30 min (corresponding to the weight loss of one mole of butylamine), the product showed IR absorptions at 1765, 1690, and 1650 cm^{-1} indicating the formation of five-membered imide. However, the thermal reaction of *anti* dibutyldiamide (**14**) in a sublimation tube *in vacuo* at 224—230 °C was found to give only *anti* monobutylamide (**9**) with starting compound **14** by TLC analysis. It is concluded that the both lactone-opened derivative of *anti* dimer (**2**) degradates successively into the corresponding monolactone derivative, *anti* dimer (**2**), and coumarin.

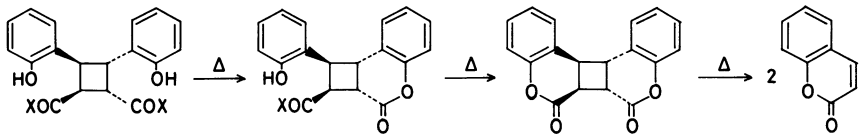
The thermal reactions of *anti* dimer derivatives are summarized in Scheme 3.

Thermal Reaction of neo *Tetrabutyldiamide.* The TG-DSC curves of *neo* tetrabutyldiamide (**6**) in Fig. 8 show gradual weight loss (20.3%) at 170 to 220 °C with an endothermic peak at 170 °C, which corresponds to the loss of one mole of dibutylamine (the calculated weight loss is 23.5%). Then, weight loss restarted at 239 °C and complete weight loss was achieved till



9 2 14

Scheme 2.

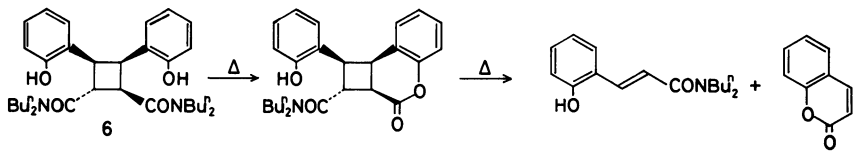


10 X = OH
11 X = OEt
12 X = NHPh
13 X = NBu^n_2
14 X = $NHBu^n$

7 X = OEt
8 X = NHPh
9 X = $NHBu^n$

2

Scheme 3.



Scheme 4.

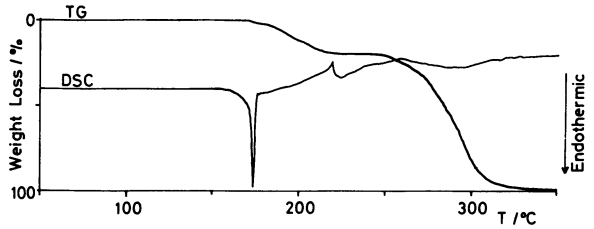


Fig. 8. TG-DSC curves of *neo* tetrabutyldiamide (**6**).

350 °C. At the first stage of this reaction, *cis*-positioned carbonyl and 2-hydroxyphenyl groups were presumed to form six-membered lactone ring with the elimination of one mole of dibutylamine. But further heating did not cause the lactone formation between the *trans*-positioned residual carbonyl and 2-hydroxyphenyl groups but resulted in the scission of the cyclobutane ring (Scheme 4).

In conclusion, the imide formation is prior to other reactions when two carbonyl groups are situated in *cis* position. But, in the case of the imide formation being impossible, the relactonization between the *cis*-positioned 2-hydroxyphenyl and carbonyl groups occurs smoothly, and when both the reactions are impossible, the thermal treatment results in the scission of the cyclobutane ring.

In spite of being effective leaving groups in the nucleophilic lactone-opening reactions, 2-hydroxyphenyl groups attack carbonyl carbons of carboxyl, ester, and even amide to reproduce six-membered lactone rings as a common thermal reaction of these derivatives. This anomalous behavior clearly manifested the contribution of the large neighboring group effect in these reactions. In this point of view, the thermal behavior of coumarin dimer derivaitves is substantially influenced by the configuration of substituents on the cyclobutane ring in the similar manner with the observation in their photocleavage reaction.[3)]

References

1) N. Yonezawa and M. Hasegawa, *Bull. Chem. Soc. Jpn.*, **56**, 367 (1983).
2) M. Hasegawa, Y. Suzuki, and N. Kita, *Chem. Lett.*, **1972**, 317.
3) N. Yonezawa, T. Yoshida, and M. Hasegawa, *J. Chem. Soc., Perkin Trans. 1*, **1983**, 1083.
4) G. Ciamician and P. Silber, *Ber.*, **35**, 4128 (1902).
5) G. Ciamician and P. Silber, *Ber.*, **47**, 640 (1914).
6) R. Anet, *Can. J. Chem.*, **40**, 1249 (1962).
7) K. T. Ström, *Ber.*, **37**, 1383 (1904).
8) G. O. Schenck, I. von Wilucki, and C. H. Krauch, *Chem. Ber.*, **95**, 1409 (1962).
9) C. H. Krauch, S. Farid, and G. O. Schenck, *Chem. Ber.*, **99**, 625 (1966).
10) G. S. Hammond, C. A. Stout, and A. A. Lamola, *J. Am. Chem. Soc.*, **86**, 3103 (1964).
11) H. Morrison, H. Curtis, and T. McDowell, *J. Am. Chem. Soc.*,**88**, 5415 (1966).
12) R. Hoffman, P. Wells, and H. Morrison, *J. Org. Chem.*, **36**, 102 (1971).
13) K. Muthuramu and V. Ramamurthy, *J. Org.Chem.*, **47**, 3976 (1982).
14) J. Bregman, K. Osaki, G. M. Schmidt, and F. I. Sonntag, *J. Chem. Soc.*, **1964**, 2021.
15) N. Ramasubbu, T. N. Guru Row, K. Venkatesan, V. Ramamurthy, and C. N. Ramachandra Rao, *J. Chem. Soc., Chem. Commun.*, **1982**, 178.
16) F. D. Lewis, D. K. Howard, and J. D. Oxman *J. Am. Chem. Soc.*, **105**, 3344 (1983).
17) Y. Suzuki, M. Hasegawa, and N. Nishikawa, *J. Polym. Sci.,Polym. Lett. Ed.*, **11**, 173 (1973).
18) M. Hasegawa, N. Yonezawa, T. Kanoe, and Y. Ikebe, *J. Polym. Sci., Polym. Lett. Ed.*, **20**, 309 (1982).
19) M. Hasegawa, K. Saigo, H. Katsuki, N. Yonezawa, and T. Kanoe, *J. Polym. Sci., Polym. Chem. Ed.*, **21**, 2345 (1983).
20) M. Hasegawa, H. Katsuki, N. Yonezawa, T. Yoshida, and Y. Ikebe, *Chem. Lett.*, **1982**, 1325.