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Cyclodextrins in Polymer Synthesis: Free Radical Polymerization of a *N*-Methacryloyl-11-aminoundecanoic Acid/β-Cyclodextrin Pseudorotaxane in an Aqueous Medium

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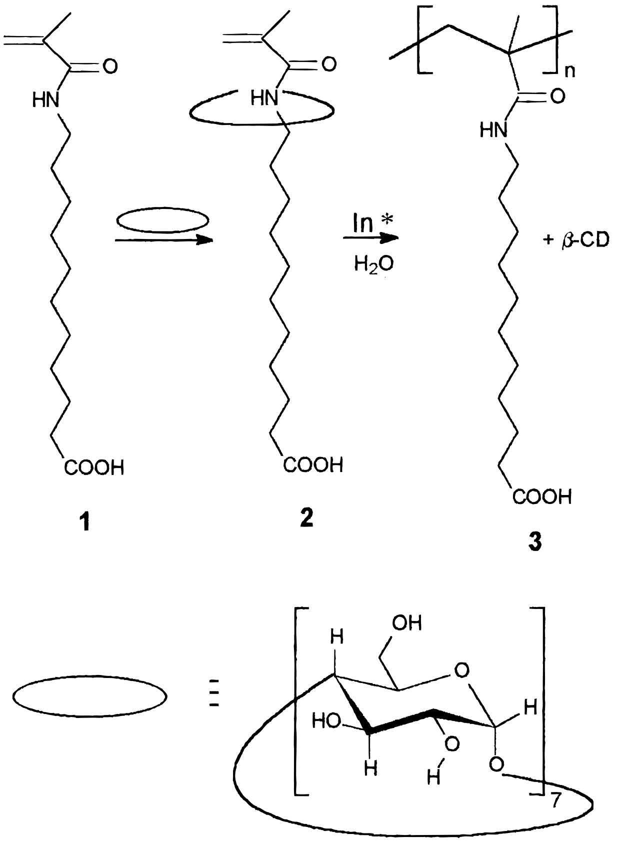
ABSTRACT: The relatively hydrophobic monomer *N*-methacryloyl-11-aminoundecanoic acid (**1**) was incorporated as a guest into the cavity of β-cyclodextrin (β-CD) as a host, yielding the water-soluble monomer *N*-methacryloyl-11-aminoundecanoic acid/β-CD pseudorotaxane (**2**). This pseudorotaxane was polymerized radically in an aqueous medium by use of the water soluble azoinitiator 2,2′-azobis(N,N′-dimethylenisobutyramidine). The obtained poly(*N*-methacryloyl-11-aminoundecanoic acid) (**3**) was insoluble in water because of a nearly quantitative unthreading of the cyclodextrin during the polymerization. It was found that the precipitation polymerization of *N*-methacryloyl-11-aminoundecanoic acid/β-CD pseudorotaxane in water occurred much faster compared to the polymerization of the uncomplexed *N*-methacryloyl-11-aminoundecanoic acid in a homogeneous DMSO/water solution (4/1 v/v) under similar conditions.

Introduction

Cyclodextrins are well-known to form inclusion pseudorotaxanes with suitable organic molecules in a key−lock type geometry.[1] Accordingly, they may be used, for example, as a catalyst in organic syntheses.[2−4] During the last few years, some interest has been focused on threading cyclodextrins onto different kinds of linear polymers to carry out the formation of main chain polyrotaxanes.[5−9] In this connection, we have succeeded in synthesizing a series of new side-chain polyrotaxanes, containing noncovalently anchored cyclodextrins, via polymer analogous condensations of corresponding semirotaxanes onto functionalized comblike polymers.[10−13]

Very recently[14,15] we described the syntheses of 2,6-(di-*O*-methyl)-β-cyclodextrin-complexes from hydrophobic monomers and their polymerization behavior in water.[16−19] Until now, however, only methylated cyclodextrin was used as a host molecule for methacrylic monomers because of its excellent solubility in organic solvents and in water. In this paper we wish to report on the synthesis of a new pseudorotaxane type based on the relatively hydrophobic *N*-methacryloyl-11-aminoundecanoic acid as a guest monomer and unmodified β-cyclodextrin as the host component. The paper also deals with the polymerization behavior of this pseudorotaxane in an aqueous medium.

Scheme 1. Preparation and Polymerization of the Pseudorotaxane 2



In *= 2,2'-azobis(N,N'-dimethyleneisobutyramidine)

Results and Discussion

The water soluble *N*-methacryloyl-11-aminoundecanoic acid/β-CD complex (**2**) was obtained from solution (Scheme 1). β-CD was dissolved in water at 65 °C, and then the crystalline powder of *N*-methacryloyl-11-aminoundecanoic acid (**1**) was added at once. The resultant suspension was stirred until a clear solution was formed, and then the water was evaporated. The structure of this complex was proved by use of standard methods. For example, in thin-layer chromatography the R_f values for the complex **2** (R_f(ethyl acetate) = 0) and the guest **1** (R_f(ethyl acetate) = 0.43) were significantly different. The comparison of the ^{1}H NMR spectra of **1** and **2** showed that some of the signals of the guest in the complex **2** are influenced due to guest−host interactions. Additionally, the FT-IR spectra of the complexed (**2**) and uncomplexed guest molecule (**1**) showed that the carbonyl bands of the complexed monomer are shifted significantly to higher frequencies from 1708 to 1712 cm^{-1} (acid group) and from 1537 to

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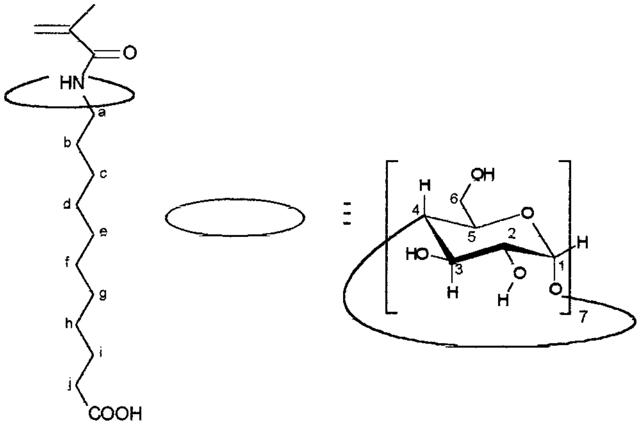

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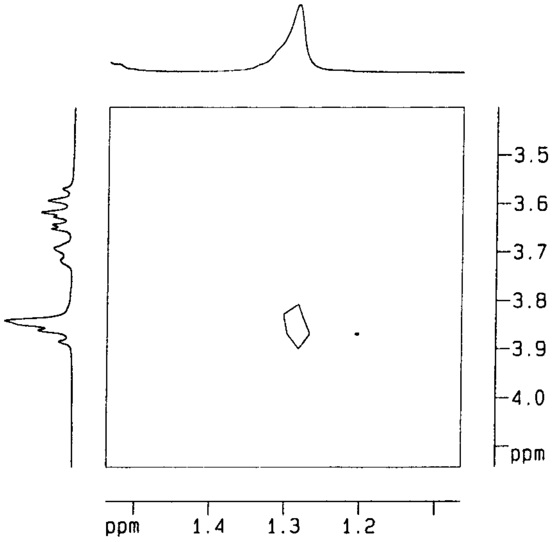

Figure 1. Correlated regions of the 2D NOESY spectrum of pseudorotaxane **2** in D_2O at room temperature.

1541 cm^{-1} (amide group). The bands at 3049 and 1613 cm^{-1}, which are assigned to the vinyl group of the guest, could not be monitored in the spectra of the complex because these signals overlap with the OH signals of the β-cyclodextrin. For the same reason, a reasonable shift of the characteristic absorption of the amide group in the region of 3300−3350 cm^{-1} could not be detected. For the investigation of the pseudorotaxane topology, a 2D NOESY spectrum (Figure 1) of pseudorotaxane **2** was measured in D_2O. The NOESY spectrum showed cross-peaks between the C_3C_5 cyclodextrin protons at 3.83−3.89 ppm and the protons of the methylene chain at 1.28 ppm of the guest. These signals reflect interactions between the intraannular protons of the cyclodextrin (C_3C_5) and the methylene chain of the guest, which only appear if the guest penetrates into the cavity of the cyclodextrin. It is worthwhile to mention that cross-peaks between the C_2C_4 cyclodextrin protons at 3.57−3.71 ppm and the protons of the guest−methylene chain at 1.28 ppm do not exist. This indicates that the observed cross-peaks mentioned above are not the result of interactions between the external C_6 cyclodextrin protons and the guest protons which are located at the outside of the cylcodextrin. This also confirms the formation of an inclusion complex. In addition to the spectroscopic characterization, we have performed thermal measurements by use of differential scanning calorimetry (DSC). Accordingly, the complex **2**, a physical mixture of **1** and β-CD (1/1 mol) and the pure β-CD were investigated. The results of these measurements (all second heating) are illustrated in Figure 2. The physical mixture of **1** and β-CD shows an endothermic melting point transition at 51 °C that can be assigned to the melting of the phase-separated monomer **1**. In contrast to this, both, the pseudorotaxane **2** and the pure β-CD do not show any endothermic transition in this temperature range. This fact can be taken as a further hint[20] for the formation of an inclusion complex.

As an additional characteristic feature, it is interesting to mention that the cyclodextrin component of the pseudorotaxane **2** can be selectively degraded in the presence of amyloglucosidase in aqueous medium yielding the water-insoluble, uncomplexed monomer **1**, which precipitates.

The probability of homopolymerization of the pseudorotaxane may be low due to the bulky cyclodextrin. The external dimensions of the β-CD are 1.53 nm in diameter and 0.78 nm in length.[21] The included guest **1** is a long molecule with a maximum diameter of about 0.45 nm.[22] It was found that despite the relatively huge CD ring, pseudorotaxane **2** could be homopolymerized very easily in water initiated with the water-soluble free radical initiator 2,2′-azobis(*N*,*N*′-dimethyleneisobutyramidine).

It was observed that, immediately after the water solution was heated, precipitation occurred. The precipitated product was determined by ^{1}H NMR spectroscopy to be the homopolymer of **1**, which contained only a trace of cyclodextrin (4.9 mol %). The amount of cyclodextrin in the polymer was determined by ^{1}H NMR spectroscopy. The ratio of the monomer unit in polymer per cyclodextrin was calculated from the methylene protons integral (2.0) at 2.17 ppm and the cyclodextrin integral (1.47) at 3.1−3.7 ppm under consideration of the number of protons which cause the signals. The existence of some β-CD residues can also be determined by elemental analysis.

This means in general that unthreading of the ring component must preferentially occur during the approach of the monomers to the growing radical end groups. The yield of the polymer was around 93% after 24 h at 70 °C. The M_n of **3** was $\geq$ 630 kg/mol. In contrast the polymerization of **1** under nearly the same conditions in homogeneous DMSO/H_2O (4/1 vol.) solution did not run very well. The ^{1}H NMR spectrum of the isolated product showed that only a small conversion to the polymer (33%) was achieved. According to GPC measurements also the molecular weight of the polymer (M_n $\geq$ 200 kg/mol) is much lower compared to the value of polymer obtained from the complex.

Conclusion

It can be concluded that synthesis of the poly(*N*-methacryloyl-11-aminoundecanoic acid) (**3**) can be performed in water as solvent via an unthreading process without using any organic solvent or protective colloids. Only the use of unmodified β-CD as a complexing agent for the monomer **1** is necessary to produce polymer in high yield and relatively high molecular weights.

Experimental Section

Materials and Methods. The synthesis of *N*-methacryloyl-11-aminoundecanoic acid (**1**) is described elsewhere.[23] Amyloglucosidase was obtained from Sigma; 1,4-α-D-glucan-

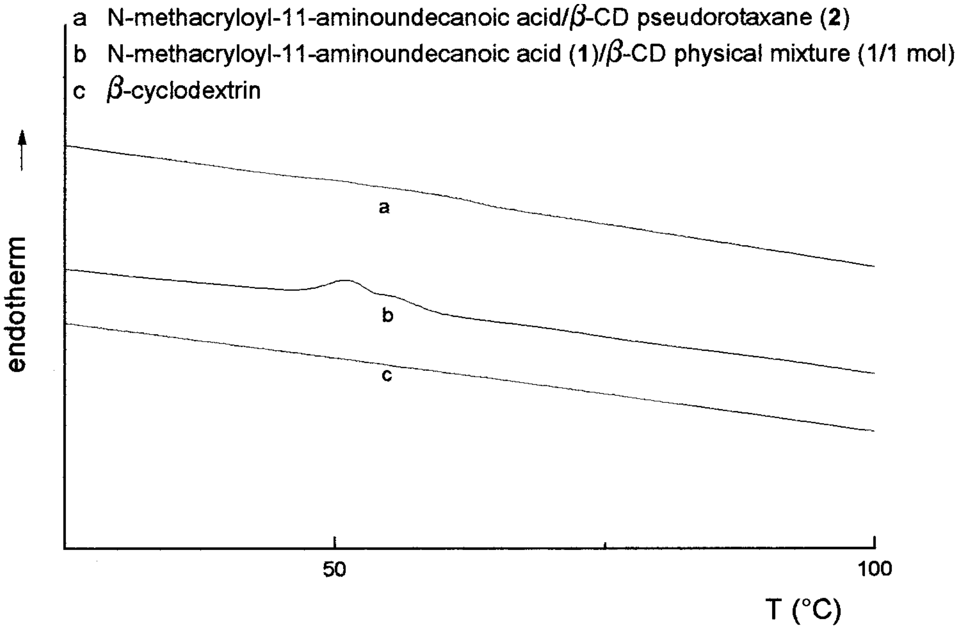

Figure 2. Differential scanning calorimetry of **2** (a), mixture of **1** + β-CD (1/1 mol) (b), and β-CD (c) (second heating for all DSC curves).

glucohydrolases in a mixture of glucose (1 M) in water was used (type "*Aspergillus niger*" (EC 3.2.1.3); 30−60 U/mg). Heptakis(β-cyclodextrin) was obtained from Merck. 2,2′-Azobis(*N*,*N*′-dimethyleneisobutyramidine) was obtained from Wako Chemicals. If not mentioned otherwise, the materials were used as received. Films for thin-layer chromatography (SiO_2 with fluorescence indicator, 254 nm) were obtained from Merck.

Instruments. ^{1}H NMR spectra and the 2D NOESY were obtained at 400.1 MHz on a Bruker ARX 400 spectrometer. FT-IR spectra of KBr pellets were recorded with a Nicolet 5SXB. Differential scanning calorimetry (DSC) (DSC7, Perkin-Elmer) applied heating and cooling rates of 10 °C/min. Molar masses of the polymers were measured by GPC (Waters, UltraStyragel, eluent DMF). The column combination (10^5, 10^4, 10^3, 500, and 100 Å was calibrated with polystyrene standards.

***N*-Methacryloyl-11-aminoundecanoic acid/β-Cyclodextrin Pseudorotaxane (2).** A 1.00 g (0.88 mmol) sample of β-cyclodextrin was dissolved in 20 mL of water at 65 °C. To the clear solution was added 0.237 g (0.88 mmol) of *N*-methacryloyl-11-aminoundecanoic acid (**1**). The suspension was stirred for 24 h at 65 °C. Then an optically clear solution was obtained. The water was removed by evaporation, and the solid product was dried for 24 h at 40 °C in a vacuum. Yield: 1.21 g (98%).

^{1}H NMR (d_6-DMSO): δ [ppm] = 5.60 (s, 1H, $=CH_2$), 5.27 (t, 1H, $=CH_2$, $J = 1.5$ Hz), 3.07 (q, 2H, $-CONHCH_2$, $J = 6.6$ Hz), 2.16 (t, 2H, $HOOCCH_2$, $J = 7.4$ Hz), 1.83 (s, 3H, $-CH_3$), 1.47 (pt, 2H, $HOOCCH_2CH_2$, $J = 7.1$ Hz), 1.41(pt, 2H, $-CONHCH_2CH_2$, $J = 6.8$ Hz), 1.23 (s, 12H, $-CONH(CH_2)_2(CH_2)_6(CH_2)_2$-COOH); cyclodextrin signals δ [ppm] 5.65 (s, 2H, OH, C2′, C3′)δ [ppm] 4.82 (s, 1H, CH, C1′), 4.39 (s, 1H, OH, C6′), 3.69−3.52 (m, 3H, C3′, C5′, C6′), 3.38−3.27 (m, 2H, CH, C2′, C4′).

FT-IR (KBr): $\tilde{\nu}$ [cm^{-1}] = 3435 (ν_{OH}), 2926, 2855 (ν_{CH}), 1712 (ν_{CO}), 1542 (ν_{CO}), 950 (δ_{CH}).

Anal. Calcd for [$C_{57}H_{97}NO_{38}$]: C, 48.75; H, 6.96. Found: C, 48.45; H, 7.12.

Enzymatically Catalyzed Degradation of 2. *N*-Methacryloyl-11-aminoundecanoic acid/β-cyclodextrin pseudorotaxane (**2**), 0.51 g (0.36 mmol), was dissolved in 40 mL of water containing 5 mL of the enzyme solution (Amyloglucosidase from *A. niger*) at pH 5. This solution was stirred for 3 d at 40 °C, whereby the precipitation started after about $^1/_2$ h. After 3 d, cyclodextrin was degraded completely.

TLC: **1**, R_f(ethyl acetate) = 0.43; **2**, R_f(ethyl acetate) = 0.

Poly(*N*-methacryloyl-11-aminoundecanoic acid) (3) from Water. *N*-Methacryloyl-11-aminoundecanoic acid/β-cyclodextrin pseudorotaxane (**2**) 2.81 g (2 mmol) was dissolved in 45 mL of water at 65 °C. The clear solution was flushed with argon for 15 min, then 25 mg (0.1 mmol) 2,2′-azobis(N,N′-dimethyleneisobutyramidine) was added, and the solution was stirred for 24 h at 70 °C. The precipitated polymer was filtered off, washed with water, and dried in a vacuum at 40 °C. Yield: 0.50 g (93%).

^{1}H NMR (d_6-DMSO): δ [ppm] = 2.88 (2H, $-CONHCH_2$), 2.17 (2H, $HOOCCH_2$), 1.48 (2H, $HOOCCH_2CH_2$), 1.36 (2H, $-CONHCH_2CH_2$), 1.24 (12H, $-CONH(CH_2)_2(CH_2)_6(CH_2)_2$-COOH), 0.78 (3H, $-CH_3$); cyclodextrin signals δ [ppm] 3.2−3.7 (greatly widen).

FT-IR (KBr): $\tilde{\nu}$ [cm^{-1}] = 3375 (ν_{OH}), 2955, 2845 (ν_{CH}), 1710 (ν_{CO}), 1620, 1530 (ν_{CO}), 1020.

Anal. Calcd for [$C_{15}H_{27}NO_3$]$_{20.4}$/[$C_{56}H_{98}O_{35}$]: C, 63.69; H, 9.58. Found: C, 63.05; H, 9.68.

SEC (polystyrene-standard, DMF): $\bar{M}_w$ = >950 kg/mol; $\bar{M}_n$ = >630 kg/mol; $\bar{M}_w/\bar{M}_n = 1.5$

Poly(*N*-methacryloyl-11-aminoundecanoic acid) (3a) from Water/DMSO Solution. *N*-Methacryloyl-11-aminoundecanoic acid (**1**) 0.538 g (2 mmol) was dissolved in 19.2 mL of DMSO and 4.8 mL of water. Then, 25 mg (0.1 mmol) of 2,2′-azobis(N,N′-dimethyleneisobutyramidine) was added to the solution, and after the solution was flushed with argon, it was stirred for 24 h at 70 °C. The product was isolated by pouring the solution into 400 mL of water. The precipitated product was filtered off and dried at 40 °C in a vacuum. Yield: 0.48 g (89%, contains unpolymerized monomer).

^{1}H NMR (d_6-DMSO): δ [ppm] = 5.61 (s, 1H, $=CH_2$, monomer), 5.27 (t, 1H, $=CH_2$, $J = 1.4$ Hz, monomer), 3.08 (q, 2H, $-CONHCH_2$, monomer), 2.90 (2H, $-CONHCH_2$, polymer), 2.17 (2H, $HOOCCH_2$, monomer + polymer), 1.84 (s, 3H, $-CH_3$, monomer), 1.50−1,36 (4H, $HOOCCH_2CH_2$, $-CONHCH_2CH_2$, monomer + polymer), 1.24 (12H, $-CONH(CH_2)_2(CH_2)_6(CH_2)_2$-COOH, monomer + polymer), 0.78 (3H, $-CH_3$, polymer).

FT-IR (KBr): $\tilde{\nu}$ [cm^{-1}] = 3300 (ν_{NH}), 2900, 2835 (ν_{CH}), 1694 (ν_{CO}), 1640, 1603, 1520 (ν_{CO}), 1208, 1180, 910.

Anal. Calcd for [$C_{15}H_{27}NO_3$]$_n$: C, 66.88; H, 10.10. Found: C, 66.24; H, 9.50.

SEC (polystyrene standard, DMF): $\bar{M}_w$ = >650 kg/mol; $\bar{M}_n$ = >200 kg/mol; $\bar{M}_w/\bar{M}_n = 3.3$.

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References and Notes

(1) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springer: Berlin, 1978.

(2) Griffiths, D. W.; Bender, M. L. *J. Am. Chem. Soc.* **1973**, *95*, 1679−1680.

(3) Monflier, E.; Fremy, G.; Castanet, Y.; Mortreux, A. *Angew. Chem.* **1995**, *107*, 2450−2452.

(4) Rezac, M.; Breslow, R. *Tetrahedron Lett.* **1997**, *38*, 5763−5766.

(5) Harada, A. *Acta Polym.* **1998**, *49*, 3−17.

(6) (a) Bheda, M. C.; Engen, P. T.; Gibson, H. W. *Prog. Polym. Sci.* **1994**, *19*, 843−945. (b) Gong, C.; Glass, T. E.; Gibson, H. W. *Macromolecules* **1998**, *31*, 308−313. (c) Gong, C.; Gibson, H. W. *Angew. Chem.* **1998**, *110*, 323−327.

(7) (a) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725−2828. (b) Philp, D. Stoddart, J. F. *Angew. Chem.* **1996**, *108*, 1242−1286,

(8) Weickenmeier, M.; Wenz, G. *Macromol. Rapid Commun.* **1997**, *18*, 117−1123.

(9) Herrmann, W.; Keller, B.; Wenz, G. *Macromolecules* **1997**, *30*, 4966−4972.

(10) Born, M.; Ritter, H. *Angew. Chem.* **1995**, *107*, 342−344.

(11) Born, M.; Koch, T.; Ritter, H. *Acta Polym.* **1994**, *45*, 68−72.

(12) Born, M.; Ritter, H. *Macromol. Rapid Commun.* **1991**, *12*, 471−476.

(13) Noll, O.; Ritter, H. *Macromol. Rapid Commun.* **1997**, *18*, 53−58.

(14) Jeromin, J.; Ritter, H. *Macromol. Rapid Commun.* **1998**, *19*, 377−379.

(15) Jeromin, J.; Noll, O.; Ritter, H. *Macromol. Chem. Phys.* **1998**, *199*, 2641−2645.

(16) Lau, W., Rohm and Haas Company: Eur. Pat. Appl., 1996; Vol. 125, 59402 CA.

(17) Leyrer, R. J.; Wildburg, G.; Haunschild, A., BASF A.-G., Ludwigshafen, Germany, Ger. Offen., 1996; Vol. 129, 68159 CA.

(18) Leyrer, R.; Mathauer, K.; Roser, J.; Wildburg, G., BASF A.-G., Ludwigshafen, Germany, Eur. Pat. Appl., 1997; Vol. 127: 109383 CA.

(19) Schornick, G.; Kistenmacher, A.; Ritter, H.; Jeromin, J.; Noll, O.; Born, M., BASF A.-G., Ludwigshafen, Germany, Ger. Offen., 1997; Vol. 126: 277902 CA.

(20) Szente, L., *Comprehensive Supramolecular Chemistry*, Pergamon: Oxford, England, 1996; Volume 3, p 268.

(21) Szejtli, J. *Kontakte (Darmstadt)* **1988**, 1, 31−36.

(22) MM+ calculation by Hyper Chem Release 4, HyperCube Inc. 1994.

(23) Rehse, H.; Ritter, H. *Macromol. Chem.* **1988**, 189, 529−539.

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