Cyclodextrins in Polymer Synthesis: Influence of Acrylate Side Groups on the Initial Rate of Radical Polymerization of Various Acrylate/Methylated β-cyclodextrin Complexes in Water

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ABSTRACT: Methylated β-cyclodextrin was used to complex the hydrophobic monomers *n*-propyl acrylate (**1**), *n*-butyl acrylate (**2**), *n*-pentyl acrylate (**3**), *n*-hexyl acrylate (**4**), and cyclohexyl acrylate (**5**) respectively yielding the corresponding water-soluble host/guest-complexes **1a**−**5a**. The complexes were polymerized in water by free radical mechanism and the initial polymerization rates (v_0) determined. We found that v_0 increases as follows: **1a** (12.5), **2a** (27.5), **3a** (44.2), **5a** (49.4), **4a** (75.8×10^{-6} mol·L^{-1}·s^{-1}). To investigate the influence of the hydrophobic character of the guest monomers on the reaction rate, the water solubilities of the uncomplexed monomers **1**−**5** were determined by HPLC measurements. It was generally shown that with increase of water solubility of the free monomers the initial reaction rate (v_0) decreases significantly.

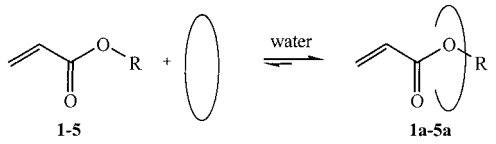
Introduction

We have recently established some potential applications and the broad variability of free radical polymerization of equimolar cyclodextrin complexed monomers in aqueous phase. In this connection we have shown that host/guest-complexes consisting of methylated β-cyclodextrin (Me-β-CD), and e.g., styrene or (meth)-acrylates are generally soluble in water and can be polymerized yielding water insoluble polymers in high yields.[1−9] Besides, some papers and patents appeared describing the use of CDs preferably in catalytic amounts in order to improve, e.g., emulsion polymerizations.[10−13] We generally found that, during the free-radical polymerization of the complexed hydrophobic monomers, the CD ring slips off from the monomer during chain propagation and the polymer precipitates. The CD remains finally in the aqueous phase due to its high water solubility.[1−9] We have also found that the polymerization of water-soluble monomers like *N*-isopropylacrylamide and hydrophobic CD-complexed monomers e.g., styrene can be carried out in water successfully.[3] We also described that the reactivity ratios of the copolymerization of isobornyl acrylate/CD and butyl acrylate/CD complexes ($r_1 = 0.3 \pm 0.1$; $r_2 = 1.7 \pm 0.1$) differ significantly from the *r* values of the uncomplexed monomers in a mixture of DMF/H_2O ($r_1 = 1.3 \pm 0.1$; $r_2 = 1.0 \pm 0.1$).[5] Further more we observed that the overall polymerization rate is approximately proportional to the square root of the initiator concentration.[4] Finally, the molecular weights of polymers obtained from complexes can be controlled very effectively by the use of chain transfer agents.[8,9] Up to now, the influence of the hydrophobic character of acrylate side groups on the initial polymerization rate has not been investigated systematically. Thus, in the present paper we wish to report our new investigation on the kinetics of the free radical polymerization of various hydrophobic acrylates/Me-β-CD complexes in aqueous medium.

Results and Discussion

Methylated β-cylodextrin (Me-β-CD) and the hydrophobic monomers *n*-propyl acrylate (**1**), *n*-butyl acrylate (**2**), *n*-pentyl acrylate (**3**), *n*-hexyl acrylate (**4**), and cyclohexyl acrylate (**5**) respectively were dispersed in water yielding the corresponding equimolar water-soluble host/guest-complexes *n*-propyl acrylate/Me-β-CD (**1a**), *n*-butyl acrylate/Me-β-CD (**2a**), *n*-pentyl acrylate/Me-β-CD (**3a**), *n*-hexyl acrylate/Me-β-CD (**4a**), and cyclohexyl acrylate/Me-β-CD (**5a**) after sonication for some minutes (Scheme 1).

Scheme 1. Complexation of the Acrylates 1−5 with Me-β-CD in Aqueous Medium



No.	R
1/1a	n-propyl
2/2a	n-butyl
3/3a	n-pentyl
4/4a	n-hexyl
5/5a	cyclohexyl

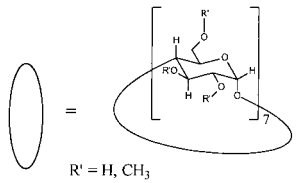


Table 1. R_f Values of Me-β-CD, Free Monomers 1−5 and Complexed Monomers 1a−5a Measured in Methanol/Dichloromethane (9:1 v/v)

Me-β-CD	**1**	**1a**	**2**	**2a**	**3**	**3a**	**4**	**4a**	**5**	**5a**
0.66	0.78	0.54	0.90	0.45	0.88	0.55	0.85	0.77	0.87	0.53

The characterization of the complexes **1a** and **3a**−**5a** was performed using thin-layer-chromatography (TLC) and ^{1}H NMR spectroscopy; the characterization of **2a** is described elsewhere.[5] The R_f values of the complexes **1a** and **3a**−**5a** are significantly lower compared to those of the uncomplexed monomers (Table 1). The spots of the complexed monomers show similar UV activity as the unmodified monomers and in addition they interact

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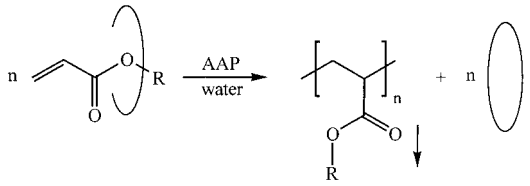
Table 2. Typical ^{1}H NMR Shifts [ppm] of the Terminal Methyl Group of Free Monomers 1−5 and Complexed Monomers 1a−5a (400 MHz, D_2O)

monomer	1	1a	2	2a	3	3a	4	4a
δ [ppm]	0.92	0.99	0.89	1.08	0.86	0.97	0.80	0.92

Scheme 2. Homopolymerization of the Me-β-CD Complexed Monomers 1A−5A



1a-5a **1b-5b**

R = n-propyl, n-butyl, n-pentyl, n-hexyl, cyclohexyl

with iodine like Me-β-CD. This strongly indicates the existence of stable inclusion complexes even under the conditions of chromatographic flow.

We have shown, that the influence of the Me-β-CD cavity on guest monomers can be verified by ^{1}H NMR spectroscopy.[5] For comparison the ^{1}H NMR spectra of all free and complexed monomers were measured in D_2O. For example, the protons of the terminal methyl groups show characteristic differences of chemical shifts to lower field up to 0.19 ppm due to the complexation (Table 2).

For kinetic studies the cyclodextrin complexed monomers **1a**−**5a** were homopolymerized in water by free-radical mechanism using the initiator 2,2′-azobis(2-amidinopropane) dihydrochloride (**AAP**) (Scheme 2).

The concentration−time curves were determined by measuring the concentration of non reacted monomer in the reaction mixture using UV-spectroscopy or high performance liquid chromatography (HPLC). For determination of the initial reaction rate v_0 the concentration−time curves were differentiated. During the first 15 min after initiation $-$d[M]/dt was calculated and plotted vs the reaction time. The extrapolation of $-$d[M]/dt to $t = 0$ leads to the initial reaction rate v_0 [mol·L^{-1}·s^{-1}]. According to this, the initial reaction rates of the homopolymerization of the complexed monomers **1a**−**5a** are summarized in Table 3. It is interesting to note that the initial reaction rate increases from **1a** (12.5 ± 1.18) via **2a** (27.5 ± 0.83) to **3a** (44.2 ± 3.54) to **5a** (49.4 ± 1.18) up to **4a** ((75.8 ± 2.55) × 10^{-6} mol·L^{-1}·s^{-1}). This means that complexes of more hydrophobic monomers react faster than those complexed monomers with a lower hydrophobic character.

To evaluate the influence of the hydrophobic character of the monomers on the initial reaction rates, the water solubilities of the pure monomers **1**−**5** were determined by HPLC (Figure 1). As partially expected, the water solubility increases in the order *n*-hexyl acrylate (**4**), *n*-pentyl acrylate (**3**), cyclohexyl acrylate (**5**), *n*-butyl acrylate (**2**) up to *n*-propyl acrylate (**1**) as summarized in Table 3.

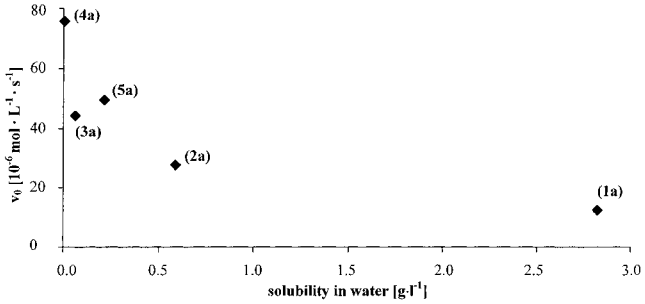


Figure 1. Initial reaction rate v_0 [10^{-6} mol·L^{-1}·s^{-1}] of the Me-β-CD complexed monomers **1a**−**5a** vs the water solubility of the uncomplexed monomers **1**−**5**.

The effect of the reduced water solubility of the monomer is caused by the increasing hydrophobic character of the side groups. Cyclohexyl acrylate (**5**) however is an exception in the series, probably due to the cyclic alkoxy group.

Figure 1 clearly illustrates that the lower the water solubility of the pure monomers the higher the initial reaction rates v_0.

In this connection, it has to be considered that the stability of a host/guest complex generally increases with geometrical fit of the guest in the CD cavity.[14] To achieve prolongation of the growing polymer chain, the CD hosts have to slip off from the monomers. Because of this mechanism, the complex stabilities and dynamics, which are influenced by the sterical demands of the monomers, must also have an influence on the overall rate of polymerization. However, the increasing of the initial reaction rate (v_0) with increasing of hydrophobic character of the complexed monomer seems to be the most important factor of the involved monomers **1**−**4** in the present study. This could be explained by surface interactions between the complexed monomers and the phase separated growing polymer chain. It can be postulated that, the more hydrophobic the monomer, the higher the local concentration of monomer close to the active radical chain end of the polymer. This local concentration effect must lead to higher values of v_0. For example, the voluminous cyclohexyl acrylate/Me-β-CD complex (**5a**) has a significantly higher initial polymerization rate (v_0) than the smaller *n*-propyl acrylate of the complex **1a**, which is the most hydrophilic system in the series.

From the results described above it can be concluded that the hydrophobic character of Me-β-CD entrapped monomers has the strongest influence on the initial polymerization rate of the investigated CD-complexed acrylates.

Materials and Methods

The *n*-butyl acrylate (Fluka Chemie AG, Buchs, Switzerland; purity ≥ 99%), *n*-hexyl acrylate (Acros Organics N.V./S.A., Geel, Belgium; purity ≥ 98%), cyclohexyl acrylate, *n*-pentyl acrylate and *n*-propyl acrylate (Lancaster Synthesis GmbH, Mühlheim, Germany; purity ≥ 97%) were distilled under reduced pressure. The β-cyclodextrin (Me-β-CD) was obtained from Wacker-Chemie GmbH, Burghausen, FRG, with

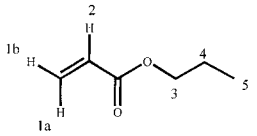
Table 3. Water Solubilities of the Uncomplexed Monomers 1−5 [mol·L^{-1}] and Initial Reaction Rates v_0 of Complexed Monomers 1a−5a [10^{-6} mol·L^{-1}·s^{-1}]

	monomer				
	1/1a	**2/2a**	**3/3a**	**4/4a**	**5/5a**
water solubility of pure monomer [g·L^{-1}]	2.82	5.87·10^{-1}	6.19·10^{-2}	6.44·10^{-3}	2.16·10^{-1}
v_0 of complex [10^6 mol·L^{-1}·s^{-1}]	12.5 ± 1.18	27.5 ± 0.83	44.2 ± 3.54	75.8 ± 2.55	49.4 ± 1.18

an average degree of methylation of about 1.8 per glucose unit. 2,2'-azobis(2-amidinopropane) dihydrochloride was obtained from Wako Chemicals GmbH, Neuss, FRG. Deuterium oxide (99.9 atom-% Deuterium) was purchased from Deutero GmbH, Kastellaun, FRG. Water was demineralized before use. If not mentioned otherwise, all materials were used as received. The supersonic treatment was carried out by use of a Bandelin Sonorex RK 1028 Transistor. The ^{1}H NMR spectra of all monomers were recorded on a Bruker AM 400 (room temperature) in D_2O. The δ scale relative to TMS was calibrated by the deuterium signal of the solvent as internal standard. The TLC analysis was carried out with Merck Silica gel plates 60 F_{254} with methanol/dichloromethane (9:1) as eluent, the spots were visualized by UV fluorescence and by developing with I_2.

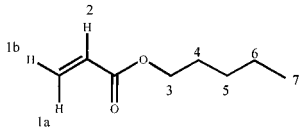
HPLC measurements were performed by the use of a BIOTEC 525 system with a BIOTEC 540 diode array detector at 220 nm and a Knauer RI detector with a ODS-2-Column (5 μm 125 × 4.6 mm) and acetonitrile/water (1:1) as eluent. UV measurements were conducted with an UV 540 system of the company Unicam.

Complexation of Monomers. A 30.2 g (22.7 mmol) sample of Me-β-CD was dissolved in 168 mL of water and 1.48 g of **1** (13.0 mmol) was added. The colorless dispersion was sonicated for 10 min yielding a clear colorless solution of the complexed monomer **1a**. The complexations of **2**−**5** were carried out analogously to **1** using 1.67 g (13.0 mmol) of **2**, 1.84 g (13.0 mmol) of **3**, 2.02 g (13.0 mmol) of **4**, and 2.0 g (13.0 mmol) of **5**. Table 2 shows the R_f values of the complexes compared to uncomplexed monomers. The ^{1}H NMR characterizations of the uncomplexed (**1**, **3**−**6**) and complexed monomers (**1a**, **3a**−**5a**), respectively, are shown in the following tables (400 MHz, D_2O). The ^{1}H NMR characterization of **2a** is described elsewhere.[5]



1, 1a

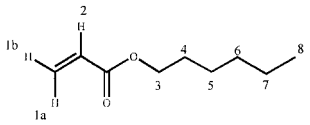
monomer	Peaks of **1**, **1a** [ppm]					
	H-1a	*H-1b*	*H-2*	*H-3*	*H-4*	*H-5*
1	6.40	5.94	6.18	4.13	1.68	0.92
1a	6.39	6.04	6.26	4.17	1.71	0.99



3, 3a

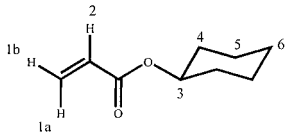
monomer	Peaks of **3**, **3a** [ppm]							
	H-1a	*H-1b*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-7*
3	6.38	5.96	6.19	4.18	1.68	1.33	1.33	0.86
3a	6.37	6.07	6.17	4.20	1.74	1.42	1.42	0.97

Polymerization of the Complexes (1a−5a) in Water. The solution of **1a** described above was heated to 80 °C while being stirred under nitrogen. Then, 194 mg (0.72 mmol) of **AAP** was added. After several minutes an equivalent was taken and poured into 30 mL of cold water. The precipitates were filtered off and the concentration of the nonreacted monomer was measured by UV spectroscopy or HPLC.



4, 4a

monomer	Peaks of **4**, **4a** [ppm]								
	H-1a	*H-1b*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-7*	*H-8*
4	6.23	5.68	6.01	4.02	1.55	1.22	1.22	1.22	0.80
4a	6.37	6.05	6.16	4.17	1.70	1.23	1.25	1.26	0.92



5, 5a

monomer	Peaks of **5**, **5a** [ppm]				
	H-1a	*H-1b*	*H-2*	*H-3*	*H-4 - H6*
5	6.28	5.71	6.05	*	1.75-1.99
5a	6.31	6.05	6.11	4.86	1.80-1.95

* = overlayed by HDO-signal

The polymerizations of **2**−**5** were carried out analogously to **1a**.

Measurement of the Solubility in Water of the Monomers 1−5. An excess of **1** was thoroughly dispersed in water, the phases allowed to separate for 1 day and the monomer concentration in the aqueous phase was determined by HPLC. Measurements of monomers **2**−**5** were carried out analogously to **1**. The solubilities in water are shown in Table 3.

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