Synthesis and Characterization of Bis(2-hydroxypropyl)amide-Based Hyperbranched Polyesteramides

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ABSTRACT: Polycondensation of 1,2-cyclohexane dicarboxylic anhydride with a calculated molar excess of di-2-propanolamine led to bis(2-hydroxyalkyl)amide based hydroxy-functional hyperbranched polyesteramides in a straightforward manner. Modification reactions of these polymers with lauric esters was conducted in different synthetic approaches. The obtained polymers were characterized by mass spectrometry, using electrospray ionization (ESI) and matrix assisted laser desorption ionization/time-of-flight (MALDI−TOF) techniques, and by size exclusion chromatography in combination with on-line viscosimetry detection (SEC−DV). Comparison of the experimental results with theoretical calculations showed a satisfactory match on molecular weights and polydispersities with fully modified polyesteramides. These values were found to deviate with unmodified and, to a smaller extent, with partially modified polyesteramides. This phenomenon could be attributed to side reactions of the 2-hydroxypropylamide end groups. The lauric ester modified polyesteramides obtained from either consecutive or simultaneous polycondensation and lauric acid esterification were found to be quite similar in structure and molecular weight distribution. This observation underlined the influence of transesterification reactions under the applied conditions.

Introduction

Hyperbranched polymers have been generally recognized as the economically more feasible counterparts of the monodisperse dendrimers.[1,2] Dendrimer molecules are necessarily constructed in a multistep synthesis,[3,4] while hyperbranched molecules can be manufactured in a one-step polymerization procedure.[5,6] The principal concepts of the synthesis of hyperbranched polycondensates were first described by Flory,[7] including the A_2/B_3 and AB_2 reactive systems, in which A and B stand for independent functional groups which are preconditionally only reactive with one another and not among themselves.

Most of the hyperbranched polymers reported are synthesized from AB_2 monomers.[8,9] Polycondensation of n molecules of this monomer type will lead to highly branched treelike structures with one A group and $(n + 1)$ B groups in each molecule. If a particular A group is accidentally reacting with a B group within the same growing chain, a cyclic structure is formed with only B end groups. Reaction of A groups among each other would give rise to formation of very low molecular weight structures instead of polymers; reaction of B groups among each other, on the other hand, will cause gel (i.e., network) formation.

As a consequence of the stochastic nature of this polycondensation, a complex mixture of polymer molecules is obtained. Apart from molecular weight distribution, also an architectural distribution can be envisioned including molecules according to any conceivable branching structure and ranging from linear to strictly dendrimer macromolecules.

To obtain finite molecular weights, use has been made of starter molecules without A groups and more than two B groups.[10,11] Depending on the method of dosing these to the polycondensation reaction, they can also be regarded as chain stoppers.

Our synthetic approach[12,13] as depicted in Scheme 1 bears a strong resemblance with the classic A_2/B_3 approach[7,14] which is unsuitable for higher molecular weights. In our approach, however, one A group denoted "a" of the A_2 compound and one B group denoted "b" of the B_3 component, which is present in molar excess, are preferentially reactive toward each other. In this way, in the prereaction A−a−b−B_2 units (i.e., functional AB_2-type units) are formed while the molar excess of B_3 units is retained in the system. This excess limits molecular weight buildup and eliminates the risk of gel formation at higher molecular weights, contrary to the classical A_2/B_3 approach. Thus, the eventual hyperbranched polymer is composed of n "Aa" units and $(n + 1)$ "B_2b" units and bears $(n + 3)$ B end groups.

The exothermal reaction of 1,2-cyclohexanedicarboxylic acid anhydride and di-2-propanolamine normally leads to a molecule with one carboxylic acid group and two (2-hydroxypropyl)amide groups. This molecule exemplifies the A−a−b−B_2 unit of Scheme 1, in which a−b designates the amide group, and is depicted in Figure 1. A typical molecular structure of a polyesteramide comprising 10 1,2-cyclohexanedicarboxylic anhydride units and 11 di-2-propanolamine units with a more or less stochastic degree of branching $(2D/(2D + L) = 0.45$, according to Frey's definition[15] in which D denotes the number of dendritic units and L denotes linear units), is shown in Figure 2.

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Scheme 1. Polycondensation of Aa and BBb Monomers to a Finite Hyperbranched Structure

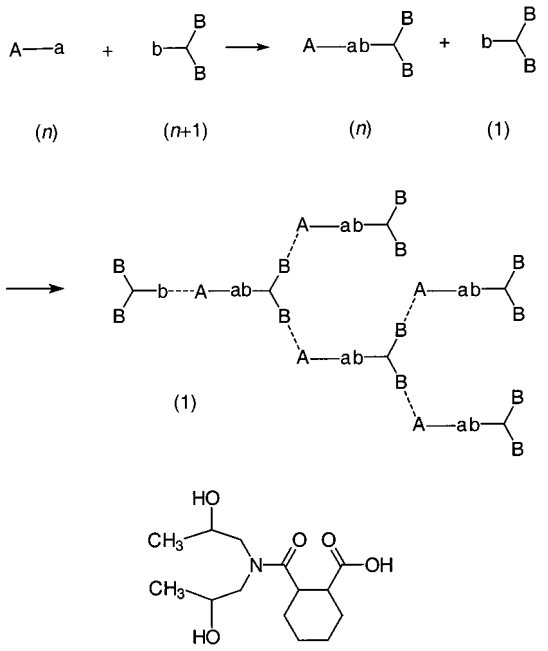


Figure 1. Reaction product from 1,2-cyclohexanedicarboxylic anhydride and di-2-propanolamine.

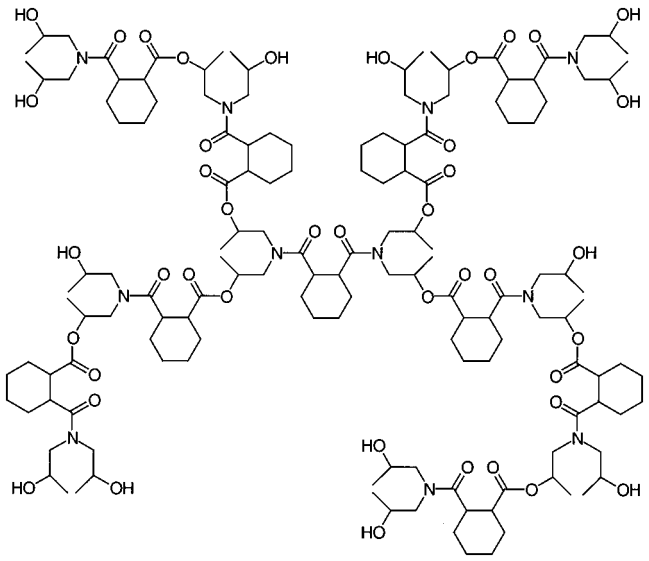
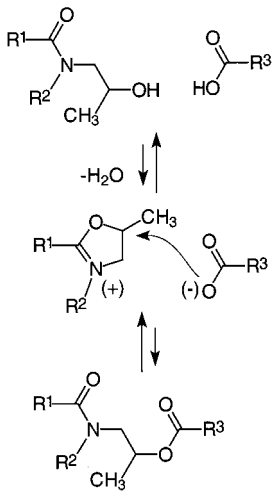


Figure 2. Representation of one possible molecular structure of a polyesteramide comprising 10 anhydride units (**C**) and 11 di-2-propanolamine units (**D**), corresponding to a molecular weight of 4818.

The esterification reaction between a (2-hydroxyalkyl)amide group and a carboxylic acid is known to proceed much faster compared to conventional aliphatic primary or secondary alcohols.[16,17] Instead of an addition−elimination reaction mechanism, the formation of an intermediate oxazolinium−carboxylate ion pair is thought to prevail,[18] which strongly facilitates the esterification reaction (see Scheme 2). Typically, this reaction can take place at temperatures from about 140 °C without a catalyst.

Thus, the formed 2-hydroxyalkyl groups can react readily with the carboxylic acid groups that are formed simultaneously in the anhydride ring-opening reaction. It it also possible to introduce a monocarboxylic acid (A_1)

Scheme 2. Mechanism for the Esterification of (2-Hydroxypropyl)amides via Oxazolinium Carboxylate Ion Pair Formation and Nucleophilic Ring Opening



as a third component in the reaction mixture. In that case, the oxazolinium-carboxylate ion pair formation facilitates both the polycondensation of the A−a−b−B_2 units to a hyperbranched polyesteramide and the esterification of the hydroxyalkyl amide end groups of this polyesteramide with the monocarboxylic acid. These two esterification reactions can take place consecutively in separate reaction steps but also concomitantly. If the composition of the final product distribution is mainly governed by thermodynamic effects, e.g., as a result of the reversibility of the esterification reactions (i.e., hydrolysis, transesterification), it will hardly be influenced by the order of esterification reactions. Consequently, the third component A_1 can in principle be added to the system at any stage of the polycondensation reaction in a single-step procedure without changing the final product mixture.

Depending on the molar ratio of A_1 to the other two components in the system, the monocarboxylic acid can be used merely as end group modifier or as chain stopper. When the amount of monocarboxylic acid m is chosen equal to $(n + 3)$, a polyesteramide is obtained in which all projected B end groups have been modified into esters of A_1. When m is smaller than $(n + 3)$, a partially modified structure is obtained with both esterified and unreacted B end groups. The carboxylic acid A_1 acts as chain stopper when m is chosen in excess of $(n + 3)$.

Results

Computational Methods. The experiments presented in this paper are supported by a theoretical approach. The objective of this approach is to obtain synthetic recipes for a well-defined series of hyperbranched polyesteramides, i.e., a series with a well-defined range of theoretical M_n values and a well-defined degree of substitution of the hydroxyl end groups. After synthesis and characterization, the theoretical M_n and M_w values are compared to the experimental results from SEC (see later, Table 2).

Table 1. Description of the Three Series of Target Molecules

	resin nos.	**D**/**C**	lauric ester modification (DS)
series **I**	**1**−**5**	1.5−1.14	
series **II**	**6**−**11**	1.14 or 1.20	partially (0.20−0.80)
series **III**	**12**−**16**	1.55−1.05	fully

Table 2. Collected Data of Hyperbranched Polyesteramide Resins

					calculated		found (SEC−DV)	
no.	DS	**D**/**C**	target M_n[a]	p_A	M_n[a]	M_w[a]	M_n[a]	M_w[a]
1	0	1.47	0.7	98.8	0.68	1.6	1.5	3.6
2	0	1.35	0.9	98.8	0.87	2.1	1.8	5.9
3	0	1.26	1.2	98.8	1.10	2.9	2.4	11
4	0	1.20	1.5	98.4	1.36	3.9	2.4	59
5	0	1.14	2.0	98.9	1.85	6.1	2.8	250
6	0.2	1.14	2.4	98.6	2.13	6.7	2.8	54
7	0.4	1.14	2.8	97.1	2.11	6.7	2.1	19
8	0.6	1.14	3.1	94.9	1.88	6.0	2.1	12
9	0.6	1.20[b]	2.5	99.1	2.19	5.6	3.0	31
10	0.6	1.20	2.5	99.0	2.17	5.6	2.9	16
11	0.8	1.14	3.4	94.4	1.88	6.1	1.8	8.5
12	1.0	1.55	1.5	91.1	0.95	2.0	1.1	2.5
13	1.0	1.25	2.5	91.5	1.29	3.3	1.4	3.4
14	1.0	1.20	3.0	96.7	2.07	5.6	2.1	6.8
15	1.0	1.13	4.0	89.5	1.41	4.9	1.4	4.9
16	1.0	1.08	6.0	91.1	1.85	8.7	1.6	5.4

[a] 10^3 g/mol. [b] Resin **4** was used as the starting material.

In the past a number of methods for the calculation of the average molecular weights in step polymerizations has been published. The main developments since Flory and Stockmayer have come from Gordon[19] and Dusek[20,21] and from Miller and Macosko.[22] Gordon and Dusek used the stochastic theory of branching processes (cascade theory) and the application hereof to our hyperbranched polyesteramides has been described previously.[23] In this paper, the results derived by Durand and Bruneau[24] are applied. Thereto, the following basic model description was considered.

According to Scheme 1, A, a, B, and b are the functional groups of the monomers Aa (cyclic anhydride) and B_2b (di-2-propanolamine). The reaction between the functional groups a and b is considered to occur instantaneously, while the B_2b component is in excess. This implies that all functional groups a have disappeared before esterification starts. The remaining A groups can react with both functional groups b and B with assumed equal reactivity, reducing the model to a system of AB_2 and B_3 units. Intramolecular reactions leading to cycles are expected to occur; for a calculative approach, however, they have been excluded in our model according to Flory.[7]

The average molecular weights M_n and M_w, as well as the average functionalities f_{nA}, f_{nB}, f_{wA}, and f_{wB} can directly be taken from Durand and Bruneau,[24] who derived general expressions for these moments in such a system. Their expressions take into account the loss of mass due to condensation reactions, assuming that the condensation products are infinitely volatile and directly disappear from the system.

All averages are calculated as a function of conversion p_A (number fraction of reacted A groups). In practice, the conversion of carboxylic acid groups can readily be determined by titration at any stage of the reaction.

The equations are also directly applicable for the single-step polycondensation reaction in which a monofunctional carboxylic acid is added as a third component. Assuming equal reactivities of the respective carboxylic acid groups, the system can simply be considered to consist of monomers AB_2, B_3 and A_1. The system is characterized by the following vectors,[25] in which the monomers AB_2, B_3, and A_1 are denoted *1*, *2*, and *3*, respectively:

$$\text{mole fraction vector: } \boldsymbol{\nu} = [\nu_1, \nu_2, \nu_3];\ \nu_1 + \nu_2 + \nu_3 = 1$$

$$\text{A-functionality vector: } f_A = [f_{A1}, f_{A2}, f_{A3}] = [1, 0, 1]$$

$$\text{B-functionality vector: } f_B = [f_{B1}, f_{B2}, f_{B3}] = [2, 3, 0]$$

$$\text{molecular weight vector: } \mathbf{M} = [M_1, M_2, M_3] = [287, 133, 200]$$

$$\text{A-site fraction vector: } \boldsymbol{\rho}_A = [\rho_{A1}, \rho_{A2}, \rho_{A3}];\ \rho_{A1} + \rho_{A2} + \rho_{A3} = 1$$

$$\rho_{Ai} = \nu_i f_{Ai} / (\Sigma_i\, \nu_i f_{Ai})$$

$$\text{B-site fraction vector: } \boldsymbol{\rho}_B = [\rho_{B1}, \rho_{B2}, \rho_{B3}];\ \rho_{B1} + \rho_{B2} + \rho_{B3} = 1$$

$$\rho_{Bi} = \nu_i f_{Bi} / (\Sigma_i\, \nu_i f_{Bi})$$

$$\text{weight fraction vector: } \mathbf{w} = [w_1, w_2, w_3];\ w_1 + w_2 + w_3 = 1$$

$$w_i = \nu_i M_i / (\Sigma_i \nu_i M_i)$$

The initial average functionalities are defined by the following inner products:

$$f_{nA0} = \boldsymbol{\nu}\cdot\boldsymbol{f}_A \quad f_{nB0} = \boldsymbol{\nu}\cdot\boldsymbol{f}_B$$

$$f_{wA0} = \boldsymbol{\rho}_A\cdot\boldsymbol{f}_A \quad f_{wB0} = \boldsymbol{\rho}_B\cdot\boldsymbol{f}_B$$

$$\zeta_{wA0} = \boldsymbol{\rho}_B\cdot\boldsymbol{f}_A \quad \zeta_{wB0} = \boldsymbol{\rho}_A\cdot\boldsymbol{f}_B$$

The initial average molecular weights are defined by

$$M_{n0} = \nu\mathbf{M} \quad M_{w0} = \mathbf{w}\mathbf{M}$$

$$M_{sA0} = \rho_A\mathbf{M} \quad M_{sB0} = \rho_B\mathbf{M}$$

The conversion p_A (number fraction of reacted A groups) defines the extent of reaction. The stoichiometric ratio r_0 is the number of initially present A groups to the number of B groups.

$$r_0 = (\boldsymbol{\nu}\cdot\boldsymbol{f}_A)/(\boldsymbol{\nu}\cdot\boldsymbol{f}_B) \quad (p_B = r_0 p_A)$$

Finally, M_e is defined as the molecular weight of the byproduct of the forming of a bond between A and B groups, and is 18 (H_2O) in our case.

The number-average molecular weight at conversion p_A is then given by eq 1. The expression for the weight-average molecular weight at conversion p_A needs two more variables (ξ and η[24,25]), as defined in eqs 2 and 3, respectively, and is given in eq 4.

$$M_n = \frac{M_{n0} - p_A f_{nA0} M_e}{1 - p_A f_{nA0}} = \frac{M_{n0} - p_B f_{nB0} M_e}{1 - p_B f_{nB0}} \quad (1)$$

$$\xi = p_A \zeta_{wA0} + \frac{r_0 p_A{}^2 (f_{wA0} - 1)(f_{wB0} - 1)}{1 - p_A \zeta_{wA0}} \quad (2)$$

$$\eta = 1/1(1 - \xi) \quad (3)$$

$$M_w = \frac{M_{n0} M_{w0} - p_A f_{nA0} M_e{}^2}{M_{n0} - p_A f_{nA0} M_e} + \frac{p_A f_{nA0} \eta}{M_{n0} - p_A f_{nA0} M_e} \times \left\{ 2(M_{sA0} - M_e)(M_{sB0} - M_e) + \frac{p_A}{1 - p_A \zeta_{wA0}} (r_0 (f_{wB0} - 1) (M_{sA0} - M_e)^2 + (f_{wA0} - 1)(M_{sB0} - M_e)^2) \right\} \quad (4)$$

The theoretical values of M_n and M_w can directly be compared to the experimental results from SEC. However, for comparison with the results from mass spectrometry, the calculation of the discrete molecular weight distribution would be desired. By using a kinetic method, Yan and Zhou[26] have derived expressions for such a discrete distribution of molecular species as a function of conversion, for a system consisting of AB_2 monomers and a multifunctional core B_f. In our present model $f = 3$ would directly apply. Although Yan and Zhou have also calculated the moments of the distribution, their method was not used for comparison with experimental results in this study because it does not count the core B_f in their degree of polymerization, thereby causing a discrepancy with the results derived by Durand and Bruneau.

Synthesis. Three series (**I**, **II**, **III**) of hyperbranched polyesteramides were synthesized, as listed in Table 1. Series **I** comprises unmodified resins with different 1,2-di-2-propanolamine (**D**)/cyclohexanedicarboxylic anhydride (**C**) ratios, leading to theoretical M_n values at full conversion ranging from 700 for resin **1** to 2000 for resin **5**. Series **II** comprises resins in which the hydroxyl end groups are partially converted to esters of lauric (*n*-dodecanoic) acid. The degree of substitution (DS) is given as the molar fraction of the end groups that have been modified by esterification and is aimed to take values of 0.2, 0.4, 0.6, and 0.8, respectively. Variation in the **D**/**C** ratio is restricted to either 1.14 or 1.20. In series **III**, finally, all resins are fully lauric acid modified (DS = 1) and the **D**/**C** ratios are varied, leading to theoretical M_n values at full conversion ranging from 1500 for resin **12** to 6000 for resin **16**.

For the resins of series **I**, it has been observed that after the solventless and strongly exothermic reaction of the two starting materials, the subsequent polycondensation reaction at 180 °C could be carried through to about 99% chemical conversion at best. Since carboxylic acid groups are theoretically completely consumed in the polycondensation reaction, the residual amount of carboxylic acid as determined by potentiometric titration was taken as a relative quantitative measure of the total chemical conversion p_A. On the basis of the experimental values of p_A, the theoretical M_n and M_w were recalculated in each entry with the help of eqs 1−4.

The second series **II** consists of partially lauroyl-modified polyesteramides.[27] Partial modification of macromolecules introduces two types of heterogeneity in the polymer distributions.[28] For the current modification we assume a purely statistical compositional heterogeneity, in analogy to the stearoyl-modified poly(propyleneimine) dendrimers.[29] The spatial heterogeneity is not considered in the present study.

Again the titrated residual amount of total carboxylic acid was taken as a measure of the chemical conversion, assuming that the differences in reactivity between the carboxylic groups (cyclic anhydride and monocarboxylic acid) are small. They were all prepared in a one-pot, single-step polycondensation at 180 °C in which the polycondensation mixture consisted of the calculated amounts of 1,2-cyclohexanedicarboxylic anhydride, di-2-propanolamine, and lauric acid.

With increasing substitution grades, it became increasingly difficult to reach full chemical conversion within a reasonable amount of time. Because a prolonged reaction time could lead to an increase in side reactions, we chose to prepare the polyesteramides resins **7**, **8**, and **11** (see Table 2) in comparable reaction times, typically about 6 h. As a consequence, progressively decreasing chemical conversions (97%, 95%, and 94%, respectively) were reached and their recalculated (i.e., based on the experimental conversion p_A) number-average molecular weights showed a slightly decreasing tendency in contrast to the originally implied increasing tendency.

To review the effects of possible transesterification reactions on the final molecular weight distribution, the order of esterification reactions was varied in the synthesis of two resins (**9**, **10**) with the same ultimate monomer compositions (**D**/**C** = 1.20, DS = 0.60). Resin **9** was prepared using unmodified polyesteramide **4** as a starting material using lauric acid in a consecutive esterification reaction under identical conditions as applied in the polycondensation of **4**. For a proper comparison with **4** itself, this polyesteramide had to be prepared with a high degree of conversion (99%). This two-step procedure therefore involved a much longer total reaction time (14 h) than in the usual procedure. Polyesteramide **10** was prepared in the usual single-step procedure, in which polycondensation and the lauric acid esterification occur simultaneously, but also with somewhat prolonged polycondensation time (8 h) for comparable chemical conversion.

The third series **III** comprises fully lauroyl-modified polyesteramides with different **D**/**C** ratios. With the exception of **14** (Table 2), a polycondensation time similar to those of the second series was applied in each case, which resulted in overall chemical conversions of about 91%. This reflects the trend as observed in series **II** with increasing substitution grades. Consequently, the recalculated number-average molecular weights differ even more from the originally intended ones than in series **II**. In comparison, polyesteramide **14** was synthesized under prolonged polycondensation conditions (9 h) and was obtained with a much higher chemical conversion of about 97%.

Size Exclusion Chromatography. For comparing molecular weight data of computational methods with experimentally measured ones, a method to establish the absolute molecular weights is required. Conventional SEC was not deemed useful, due to the lack of appropriate (branched) standards for calibration. Therefore, absolute molecular weights were determined on the basis of universal calibration[30] with an on-line differential viscosimetry detection (SEC−DV). The validity of the universal calibration principle for these polymers has been confirmed by determining molecular weights

Table 3. Partial MALDI−MS Spectra of Polyesteramides 6, 7, 8, 11 and 15

m/z	ion	**6**	**7**	**8**	**11**	**15**
	$D - H_2O$					
298	$DL - H_2O + H$	73	87	71	46	46
480	$DL_2 - H_2O + H$	27	13	29	54	54
	$CD - H_2O$					
270	$CD - H_2O + H$	82	77	67	30	21
452	$CDL - H_2O + H$	18	23	33	55	65
634	$CDL_2 - H_2O + H$				15	14
	$CD_2L - H_2O$					
385	$CD_2 - H_2O + H$	58	60	57	6	14
567	$CD_2L - H_2O + H$	36	36	36	30	36
749	$CD_2L_2 - H_2O + H$	6	4	6	40	29
931	$CD_2L_3 - H_2O + H$			1	24	21
	$C_2D_2L - H_2O$					
539	$C_2D_2 - H_2O + H$	80	75	75	13	13
721	$C_2D_2L - H_2O + H$	20	25	25	40	50
903	$C_2D_2L_2 - H_2O + H$				40	37
1085	$C_2D_2L_3 - H_2O + H$				7	
	$C_2D_3L - H_2O$					
654	$C_2D_3 - H_2O + H$	65	75	60		
836	$C_2D_3L - H_2O + H$	28	25	30	8	20
1018	$C_2D_3L_2 - H_2O + H$	7		10	28	30
1200	$C_2D_3L_3 - H_2O + H$				36	30
1382	$C_2D_3L_4 - H_2O + H$				28	20

[a] The figures represent relative intensities normalized to 100% for a chemical composition $C_nD_{n+i}L_m$ with a varying degree *m* of lauroyl (L) substitution.

of collected SEC fractions by mass spectrometry.[31]

For avoiding adsorption and repulsion effects, various solvents have been tested. Reproducible results, listed in Table 2, were finally obtained with dichloromethane as solvent and eluent.

Mass Spectrometry. The strength of MALDI−TOF−MS (matrix-assisted laser desorption ionization time-of-flight mass spectrometry) analysis of synthetic polymers[32] is the capability of oligomer-resolved analysis of molecular weight distributions. Combined with time-lag focusing,[33] this technique allows the qualitative determination of chemical composition including end group identity and functionality type distribution and the extent of cyclization at each degree of polymerization.

A detailed MALDI−TOF−MS study of the unfunctionalized resins of series **I** has been published elsewhere.[34] MALDI is a soft ionization technique and upon ionization generally produces protonated or metal-cationized oligomers. Upon MALD ionization of hyperbranched polyesteramides, however, substantial metastable decay (in-source decay, ISD) of the protonated molecules has been observed in the ion-source of the MS prior to ion extraction.[34,35] The lower mass ends of the MALDI−TOF−MS spectra of unmodified resins mainly contained peaks originating from $[C_nD_{n+1} - H_2O]^+$ and $[C_nD_n - H_2O]^+$ ISD reaction product ions, where C_n denotes the number of 1,2-cyclohexane dicarboxylic acid anhydride moieties and D_n denotes the number of di-2-propanolamine moieties. Pseudomolecular ion peaks of the C_nD_{n+1} and C_nD_{n+1} oligomers were not observed at the high mass end of the MALDI mass spectrum. It is well recognized in the literature[36] that MALDI−MS analysis of polydisperse distributions with PDI > 1.2 leads to severe underestimation of the number-average of the molecular weight distribution.

Partial MALDI−MS spectra of the functionalized resins are compiled in Table 3. They were composed of two series of oligomeric ISD fragment ions with varying

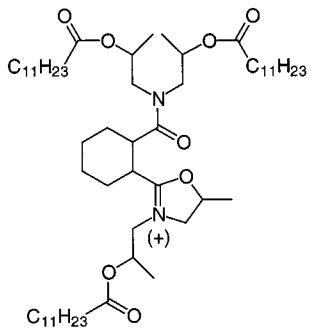


Figure 3. Structure of ISD fragment ion *m/z* 931, $[CD_2L_3 - H_2O + H]^+$.

degree of lauroyl functionalization, i.e., C_nD_n- and C_nD_{n+1}-based ions. Because the concentration of free acid groups is very low, the former are assumed to be cyclic rather than linear structures. The fragment ions generated were found to be lauric acid ester substituted analogues of the ISD fragment ions of the unfunctionalized resins.[34] Peaks originating from protonated intact oligomers, i.e., $[C_nD_{n+1}L_m + H]^+$ and $[C_nD_nL_m + H]^+$ where L_m is the number of lauroyl substituents, were absent. Therefore, functionality distribution information could not be derived. However, the ISD fragment ions did yield pieces of information on the overall structure of the modified resins.

As a typical example, the *m/z* 931 $[CD_2L_3 - H_2O + H]^+$ (Figure 3) is an oxazolinium cation generated by loss of a distal moiety of a lauroyl substituted hyperbranched polyesteramide according to a fragmentation mechanism[34] that resembles the reversal of the esterification mechanism in Scheme 2. The relative intensities of *m/z* 385, 567, 749, and 931 give information on the degree of lauroyl substitution. M/z 385 $[CD_2 - H_2O + H]^+$ is the base peak of the $[CD_2L_m - H_2O + H]^+$ cluster in the MALDI spectrum of compound **6** and carries 58% of the ion current of the CD_2L_m distribution, whereas *m/z* 385 comprises 14% of the CD_2L_m lauroyl distribution of compound **15**. The envelope of the distribution is shifted toward the maximum number of lauroyl substituents for the $[CD_2L_m - H_2O + H]^+$ ISD fragment ion in the series **6**, **7**, **8 11**, and **15**. Similar results are obtained for the DL, CDL, C_2D_2L and C_2D_3L fragment ions, in agreement with the designed increase in degree of substitution (DS = 0.2, 0.4, 0.6, 0.8, and 1.0, respectively).

Because MALDI failed to give information on less abundant oligomer fragments, such as aberrant structures arising from side reactions, polyesteramides **1**, **2**, **6**, **8**, and **15** (DS = 0, 0, 0.2, 0.6, and 1.0, respectively) were analyzed with electrospray ionization (ESI) mass spectrometry as well. In contrast to our previous study in which we used water/methanol as the eluent, the current samples were electrosprayed with THF as eluent, because the lauric acid ester modified polyesteramides were insoluble in water/methanol. Under these conditions ESI led to the formation of sodium cationized $[M + Na]^+$ polyesteramide oligomers. As reported for MALDI, ESI of broad molecular weight distributions also discriminates the high mass tail of the molecular weight distribution. Three series of peaks were observed in the ESI−MS spectrum of unmodified resin **1**. Sodium cationization during ESI produced peaks at *m/z* 425 $[CD_2 + Na]^+$, *m/z* 694 $[C_2D_3 + Na]^+$, *m/z* 963 $[C_3D_4 + Na]^+$, *m/z* 1232 $[C_4D_5 + Na]^+$, *m/z* 1501 $[C_5D_6 + Na]^+$ and *m/z* 1770 $[C_6D_7 + Na]^+$. The cyclic

Table 4. Partial ESI−MS Spectra of Polyesteramides 1, 2, 6, 8 and 15[a]

m/z	ion	**1**	**2**	**6**	**8**	**15**
425	$CD_2 + Na$	85	89	43	12	
540	$CD_3 + Na$	15	11	2		
607	$CD_2L + Na$			39	26	1
722	$CD_3L + Na$			2	2	<0.5
789	$CD_2L_2 + Na$			13	38	31
904	$CD_3L_2 + Na$					
971	$CD_2L_3 + Na$			1	18	45
1086	$CD_3L_3 + Na$					
1153	$CD_2L_4 + Na$				4	23
1268	$CD_3L_4 + Na$					

[a] The figures represent relative intensities are normalized to 100% for the chemical compositions CD_2L_m and CD_3L_m with a varying degree *m* of lauroyl (L) substitution.

C_nD_n-H_2O oligomers give signals at *m/z* 561, 830, 1099, 1368, and 1367. A third series of peaks arises from sodium cationization of C_nD_{n+2} oligomers. The reaction yield of these products as a function of degree of lauric acid ester substitution is examined by comparison of the ESI spectra. The relative intensities of the CD_2L_m and CD_3L_m oligomers are compiled in Table 4. It was found that the formation of the undesired $C_nD_{n+2}L_m$ oligomers decreased as the degree of substitution increased.

Discussion

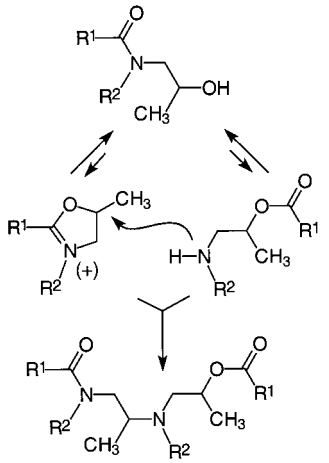
When the experimental SEC−DV results were compared to the calculated molecular mass moments, a close match was observed with the resins of series **III** and some of the resins of series **II** (**8** and **11**, see Table 2). Apparently, a high degree of lauric ester substitution (DS = 0.60 or higher) prevents the occurrence of side reactions that influence the molecular weight distribution. Even in the case of resin **14**, where a prolonged reaction time was applied, no significant deviations from the calculated values were found.

When reviewing the results of series **II**, a distinctively decreasing match of values was noted with decreasing degree of substitution. In the order of resins **15**, **11**, **8**, **7**, **6**, **5** (DS = 1.0, 0.8, 0.6, 0.4, 0.2, and 0.0, respectively), a strong gradual increase in M_w was observed from 5×10^3 to 250×10^3, whereas the calculated values were all in the range $(5-7) \times 10^3$. With respect to M_n, the decrease of degree of substitution only led to significant deviations from the calculated values in resin **6** and unmodified resin **5**.

In series **I**, the M_n and especially the M_w values found with SEC−DV were substantially larger than the a priori calculated values in all cases. The combined observations of the results of series **I** and **II** can be explained by the occurrence of some side reactions between (2-hydroxypropyl)amide end groups leading to chain extension. A proposed mechanism for this side reaction involves nucleophilic ring opening of the oxazolinium ion intermediate by a secondary amine, as depicted in Scheme 3, instead of the associated carboxylate ion (Scheme 2). Secondary amines are present in the polycondensation mixture, either as unreacted di-2-propanolamine or as a result of an acyl shift[37,38] from the hydroxyalkyl amides themselves.

As a consequence of this chain extension aberrant polyesteramides comprising *n* anhydride units and (*n* + 2) di-2-propanolamine units are formed. This is confirmed independently by the ESI mass spectrometry of the resins **1** and **2**, in which substantial amounts of the aberrant structures with (*n* + 2) di-2-propanolamine units have been identified, see Table 4. Furthermore, the presence of tertiary amine groups, directly resulting from this side reaction, in an amount of 0.14 mequiv/g in polyesteramide **4** (next to 0.30 mequiv/g of secondary amine) was established by titration with methylsulfonic acid in the presence of acetic anhydride.[39]

Scheme 3. Proposed Mechanism for the Undesired Reaction of 2-(Hydroxypropyl)amides among Themselves via an Acyl Shift Followed by Ring Opening of the Oxazolinium Ion by the Secondary Amine



This mechanism has been reported earlier[40] to cause multiple chain extension and eventually gelation in attempted syntheses of polyesteramides from cyclic carboxylic anhydrides and diethanolamine instead of di-2-propanolamine. Apparently, the presence of the extra methyl group in the (2-hydroxypropyl)amide moieties (compared to (2-hydroxyethyl)amides) substantially reduces this side reaction but does not eliminate it entirely.

An increase in degree of lauric ester substitution can reduce the amount of chain extension side reactions in two ways. On one hand, the higher concentration of carboxylic acid groups with respect to the amine groups in the system disfavors nucleophilic attack by the amine groups through protonation. On the other hand, the concentration of unreacted (2-hydroxypropyl)amide in the polycondensation mixture decreases faster with progressing chemical conversion.

It was confirmed by the ESI−MS data (Table 4) that the polyesteramides of series **II** contain smaller amounts of aberrant structures with increasing degree of lauric ester substitution.

When the SEC−DV chromatograms of the resins **9** and **10** were compared, a clear similarity was evident (see Figure 4), with respect to the lower molecular weight fractions (<10 103/mol). With both, a M_n of about 3×10^3 was found whereas the calculated values amounted to 2.5×10^3/mol. However, resin **10** that was prepared by consecutive polycondensation and esterification had a higher M_w than **9**. This could be explained by the longer total reaction time, giving rise to a higher extent of chain extension side reactions, as is evident in Figure 4 with respect to the higher molecular weight fractions.

Interestingly, both polyesteramides had a significantly lower M_w than unmodified polyesteramide **4**, which was used as the starting material for **9**. This observation, combined with the similarity of the molecular weight distributions of **9** and **10**, reflects the

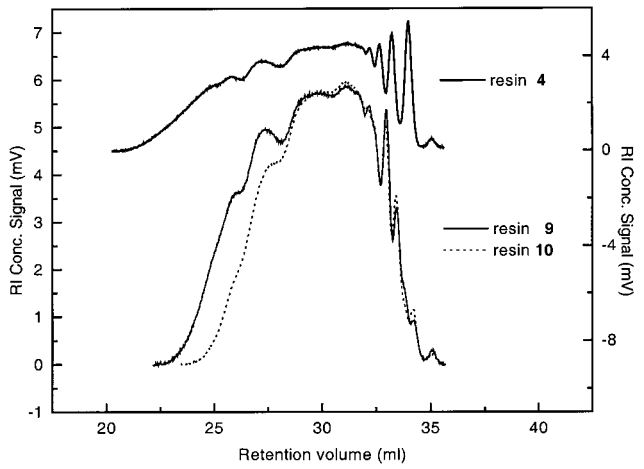


Figure 4. SEC−DV overlay of polyesteramides **4** (right *y* axis), **9** and **10** (left *y* axis).

dominance of transesterification reactions under the applied conditions. The reversibility of the esterification reactions via the oxazolinium−carboxylate ion pair (Scheme 2) offers a very likely basis for ready acid-induced transesterification processes.

Mass spectrometry proved to be a valuable tool for obtaining more detailed information on the molecular structures of the hyperbranched polyesteramides. Although MALDI−TOF−MS failed to monitor pseudo molecular ions, due to in-source decay, the observed fragments were in agreement with the expected structures. Both MALDI−TOF and ESI−MS confirmed the increase of lauroyl substitution of oligomers and fragments as a function of the designed degree of substitution. However, next to the aberrant structures in some samples, both MS techniques revealed the abundance of cyclic structures in all the samples investigated. Although cyclization reactions were expected to occur,[41] even when transesterifications play an important role, they could not be taken into account in our calculative approach. In AB_2-type polycondensations, cyclization effectively lowers the attainable molecular weights.[42] Therefore, the calculated molecular mass moments in this study must be considered as too high. Further studies are underway to take cyclization into account as well.[43]

In this study, no attention was paid to determination of the degree of branching and consequently, the three-dimensional structure of the polyesteramides described. The validity of the universal calibration principle on which the SEC−DV technique is founded, as well as the solute behavior of the polyesteramides as hyperbranched polymeric coils, is described in a parallel study.[31]

Conclusion

Fully lauric acid ester functionalized bis(2-hydroxypropyl)amide-based hyperbranched polyesteramides have been synthesized in a straightforward polycondensation reaction from calculated amounts of 1,2-cyclohexanedicarboxylic acid anhydride, di-2-propanolamine, and lauric acid. Their molecular weight distribution, as determined by SEC−DV, was in accordance with the predicted values obtained by a theoretical approach. Mass spectrometry (MALDI−TOF and ESI) confirmed the expected molecular structures, but also indicated the formation of cyclic structures that were excluded in the calculations.

Table 5. Monomer Compositions of Synthesized Polyesteramides

no.	D^a	C^a	L^a
1	295	232	0
2	285	244	0
3	276	253	0
4	270	260	0
5	267	264	0
6	223	226	85
7	194	197	145
8	215	218	241
9	300[b]		194
10	240	232	289
11	191	193	292
12	175	131	450
13	134	124	282
14	207	200	414
15	139	142	259
16	142	153	245

[a] (grams), **D** = di-2-propanolamine, **C** = 1,2-cyclohexanedicarboxylic anhydride, **L** = lauric acid. [b] Resin **4** (grams).

Polycondensation of 1,2-cyclohexanedicarboxylic acid anhydride and di-2-propanolamine lead to hydroxy functional hyperbranched polyesteramides. Because of side reactions some chain extension occurred during the synthesis, causing deviations from the predicted molecular mass moments. The aberrant structures which result from the side reaction have been identified by mass spectrometry. Partial lauric acid ester functionalized polyesteramides have been synthesized in a similar way. With a high degree of substitution (DS > 0.60) a satisfactory match with the calculated moments was found, while with lower degrees of substitution more deviations were observed. In general, longer reaction times and higher concentrations of 2-hydroxypropylamide end groups in the reaction mixture appeared to enhance the chain extension side reactions.

The partially substituted polyesteramides synthesized by either consecutive or simultaneous polycondensation and lauric acid esterification were found to have similar molecular weight distributions, indicating that transesterification reactions play an important role under the conditions of their preparation.

Experimental Section

A. Synthesis. General Procedure. In a 1 L glass reactor, the calculated amount of di-2-propanolamine (bis(2-hydroxypropyl)amine, Fluka Chemika, 98+%) was introduced under a nitrogen atmosphere. The calculated amount of 1,2-cyclohexanedicarboxylic acid anhydride (hexahydrophthalic anhydride, Acros Organics, 99+%) was then added. As a result of the immediate exothermic reaction, the temperature of the mixture raised to ca. 120 °C. 1-Dodecanoic acid (lauric acid, Acros Organics, 99.5+%) was optionally introduced as well (resins **6**−**8** and **10**−**16** in Table 2), with the total of the calculated amounts of raw materials amounting to about 600 g as tabulated in Table 5. The reaction mixture was then heated to 180 °C. With vigorous stirring, the evolving reaction water was distilled off in 6 h, ultimately under reduced pressure (5 mbar). Aliquots of the resin were taken from the reactor, and their acid concentration was determined (dissolved in THF, titrant = 0.1 N KOH in MeOH, Aldrich). At the desired acid concentration (target: less than 0.04 mmol of carboxylic acid per gram), the hot resin was poured out and cooled to room temperature.

In the synthesis of resin **9**, resin **4** (300 g) was molten in the reactor and heated to 140 °C, after which the lauric acid (194 g) was added and the mixture was polycondensed at 180 °C for 3 h under normal pressure and 4 h under reduced pressure.

Resins **1**−**7** were obtained as slightly yellow glassy masses, the other resins were obtained as yellowish highly viscous liquids.

B. Characterization. The SEC measurements were performed on a Hewlett-Packard chromatograph (HP 1090) equipped with a differential refractometer (RI) and a differential viscosimeter (DV) placed in parallel (Viscotek200).

The polyesteramides were dissolved in dichloromethane (p.a., Merck) at room temperature in a nitrogen atmosphere for at least 4 h; the injection volume was 200 μL. All polymer solutions were filtered using Millex filters (pore size 0.5 μm). Four Polymer Laboratories (PL) mixed C columns were used. The eluent was treated in a degasser (PL-DG 802) prior to use. The measurements were done at room temperature with a flow rate of 1 mL/min.

Molecular weights were determined on the basis of polystyrene standards of PL having known molecular weights in the range (0.58−2880) × 10^3/mol. The intrinsic viscosities of these samples were determined with the DV detector. All data were processed using Trisec 2.70 software (Viscotek). From both the concentration and viscosity chromatograms of the polyesteramide samples, the intrinsic viscosity (η) as a function of elution volume was determined. From these data the average molecular weights (M_n, M_w, and M_z) were calculated using universal calibration.[30]

MALDI−TOF mass spectrometry was carried out using a Perkin-Elmer/Perseptive Biosystems Voyager-DE-RP MALDI−TOF mass spectrometer (PerSeptive Biosytems) equipped with delayed extraction. A 337 nm UV nitrogen laser producing 3 ns pulses was used, and the mass spectra were obtained in the linear and reflectron mode. Samples were prepared by mixing 10 μL of tetrahydrofuran (THF) solution of the polyesteramide sample with 30 μL of a solution of 3 mg/L 2,5-dihydroxybenzoic (DHAB) acid in THF. One microliter of that solution was loaded on the gold−sample plate. The solvent was removed in warm air.

Positive ion electrospray (ESI) mass spectra of the polyesteramides were recorded using a PE Sciex API 150 single quadrupole mass spectrometer (Perkin-Elmer Sciex). The samples were introduced through the electrospray interface by infusion of a THF solution containing 20 μM sodium iodide at 5 μL min^{-1} with a syringe pump (Harvard Apparatus). Nitrogen was used as a nebulizing and curtain gas. The capillary tip was maintained at 3 kV, while the orifice was set at 30 V. Mass spectra were collected in full scan mode, scanning from *m*/*z* 100 to 2000 Da in 30 s. The mass spectral data were processed with the MultiView 1.4 software (PE Sciex).

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