

QSPR STUDY OF PHOSPHORIC POLYESTER GLASS TRANSITION TEMPERATURE BY PLS

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Abstract. This paper presents a structure-property study for a series of polyphosphates and polyphosphonates. Structural parameters were derived from the structures of minimum energy obtained by molecular mechanics and the semiempirical molecular orbital PM6 calculations. The influence of monomer structural descriptors of polyphosphates and polyphosphonates on the glass transition temperature was accomplished by Partial Least Squares (PLS). Good correlations of the glass transition temperature with different structural parameters were obtained. Thus, increased number of sulfur atoms present in the molecule, the number of phosphite groups, the polymer polarity and aromaticity are favorable for the glass transition temperature. Increased polymer size, higher polymer flexibility and hydrophobicity decrease the glass transition temperature, in opposition to the hydrophilicity influence.

INTRODUCTION

Studies made on phosphorus containing polymers are steadily developed having in view the polymer range diversification and characterization and their use in varied domains. Phosphoric polyesters, respectively polyphosphonates and polyphosphates are of interest because they confer low flammability on polymers [1].

Much attention has been drawn in recent years towards a new class of biodegradable polymers belonging to polyphosphates and polyphosphonates, which have been investigated as biomaterials in drug delivery, gene delivery, tissue engineering and agricultural [2, 3].

Structure-property study of polyester flexibility, of their capacity of order and also their glass transition temperature was studied by molecular modeling [4]. The semi-rigid

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character of polyesters has been studied by evaluating the rotational barriers measured along the internal bonds of bisphenols which compose the studied polymers.

Glass-transition temperatures of a series of polyphosphonates and polyphosphates containing bisphenol A have been determined experimentally [5, 6, 7, 8].

Principal Component Analysis (PCA) was applied to study the influence of the structural monomer parameters on the glass transition temperature for a series of polyphosphates and polyphosphonates [9].

Quantitative Structure-Property Relationships (QSPR) have been applied to study the glass transition temperatures of low and medium molecular weight homo and copolymers [10]. By multiple linear regression analysis glass transition temperatures for new polymer structures have been proposed.

Resins, plastics and adhesives are usually polymers with high glass transition temperatures. For elastomers and polymers in liquid form a low glass transition temperature is expected.

This paper presents the influence of structural descriptors calculated for monomers of polyphosphates and polyphosphonates (Table 1) on the polymer glass transition temperatures by PLS (Partial Least Squares) [11].

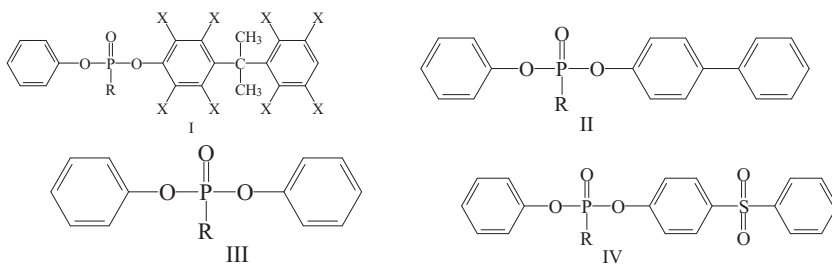
METHODS

Definition of target property and molecular structures

The phosphoric polyesters I (Table 1) were modeled by their monomers obtained from previous studies [12] by molecular modeling calculations. The molecular structure of these polyesters was built by the Chem3D Ultra package [13] and energetically optimized using the MM2 force field. Semiempirical molecular orbital calculations, enabled by MOPAC 2007 program [14], were applied to the lowest energy conformations obtained by molecular mechanics calculations. Thus, the resulted minimized structures were optimized by the semiempirical PM6 Hamiltonian. For each compound the conformation of lowest energy which allowed the construction of polymer structure was considered for further calculations.

The experimental glass transition temperature (T_g) [5, 6, 15] was used as dependent variable for a series of 23 polyphosphates and polyphosphonates (Table 1).

Table 1. Glass transition temperature (T_g) and structural descriptors of polyphosphonates and polyphosphates (I-IV)*



No.	R	X	Hy*	PSA*	nS*	nPO ₃ *	MAXMIN**	μ^{**} (Debye)	ClogP***	T_g (°C)
<i>0</i>	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>	<i>5</i>	<i>6</i>	<i>7</i>	<i>8</i>	<i>9</i>	<i>10</i>
I.1	CH ₃	H	-0.84	45.34	0	1	3.65	1.94	5.95	88 [15]
I.2	OCH ₃	H	-0.81	54.57	0	0	3.68	3.77	5.95	78 [15]
I.3	O(CH ₂) ₃ CH ₃	H	-0.83	54.57	0	0	3.82	2.63	7.54	90 [15]
I.4	(CH ₂) ₃ CH ₃	H	-0.85	45.34	0	1	3.82	2.18	7.54	80 [15]
I.5	C ₆ H ₁₁	H	-0.86	45.34	0	1	3.89	1.99	7.98	93 [6]
I.6	C ₆ H ₅	H	-0.86	45.34	0	1	3.68	2.60	7.38	99 [5]
I.7	OC ₆ H ₁₁	H	-0.84	54.57	0	0	3.66	3.99	7.98	86 [5]
I.8	OC ₆ H ₅	H	-0.84	54.57	0	0	3.89	3.16	7.38	82 [5]
I.9	C ₆ H ₅	Cl	-0.69	45.34	0	1	3.67	2.04	12.61	85 [5]
I.10	OC ₆ H ₅	Cl	-0.67	54.57	0	0	3.79	3.32	12.61	60 [5]
II.11	CH ₃	H	-0.82	45.34	0	1	3.83	4.16	4.97	130[15]
II.12	C ₆ H ₁₁	H	-0.85	45.34	0	1	3.89	2.31	7.00	127 [5]
II.13	C ₆ H ₅	H	-0.85	45.34	0	1	3.68	2.68	6.41	120 [5]
II.14	OC ₆ H ₁₁	H	-0.82	54.57	0	0	3.68	3.70	7.00	116 [5]
II.15	OC ₆ H ₅	H	-0.82	54.57	0	0	3.82	0.25	6.41	112 [5]
III.16	C ₆ H ₁₁	H	-0.81	45.34	0	1	3.89	1.54	5.12	125 [5]
III.17	C ₆ H ₅	H	-0.81	45.34	0	1	3.68	2.70	4.52	112 [5]
III.18	OC ₆ H ₁₁	H	-0.77	54.57	0	0	3.68	1.56	5.12	108 [5]
III.19	OC ₆ H ₅	H	-0.77	54.57	0	0	3.98	0.29	4.52	97 [5]
IV.20	C ₆ H ₁₁	H	-0.77	87.86	1	1	3.89	7.58	5.40	132 [5]
IV.21	C ₆ H ₅	H	-0.77	87.86	1	1	3.96	6.72	4.81	135 [5]

0	1	2	3	4	5	6	7	8	9	10
IV.22	OC ₆ H ₁₁	H	-0.74	97.09	1	0	3.95	6.79	5.40	120 [5]
IV.23	OC ₆ H ₅	H	-0.74	97.09	1	0	3.65	6.96	4.81	130 [5]

* Dragon descriptors: Hy-hydrophilicity, PSA - fragment-based polar surface area, nS-number of sulfur atoms, nPO₃-number of phosphites, ** Descriptors obtained by semiempirical quantum-chemical calculations: MAXMIN-difference between the maximum and minimum atom charge; μ -dipole moment,*** ClogP-octanol-water partition coefficient calculated by the Chem3D Ultra software

Molecular descriptors derived from molecular monomer structures, like: the maximum (QMAX) and minimum (QMIN) atom charge in the monomer molecules, the HOMO and LUMO molecular orbital energies were calculated by the semiempirical PM6 method [14].

The difference between the maximum and minimum atomic charge in a molecule (MAXMIN) was used as a submolecular polarity parameter. From the same quantum-mechanical calculations, dipole moments (μ) were also considered, in order to express possible dipole effects.

Several steric, thermodynamic and hydrophobic descriptors were calculated by the Chem3D Ultra package [13]. Among the steric parameters the Connolly Solvent Accessible Surface Area (SAS), Connolly Molecular Surface Area (MS) and Connolly Solvent-Excluded Volume (SEV) [16] were employed. The hydrophobic (ClogP) parameter and thermodynamic descriptors (like the stretch-bend energy) were also used. The molecular weight (MW) and molar refraction (MR) calculated for the monomers were used as a measure of the bulkiness of the polyesters.

Constitutional, functional groups, empirical and aromaticity descriptors were calculated by the Dragon software [17]. Among them, S_v represents the sum of atomic van der Waals volumes (scaled on Carbon atom), S_p - the sum of atomic polarizabilities (scaled on Carbon atom), nSK - number of non-H atoms, nDB – the number of double bonds, nC-the number of carbon atoms, Mp (mean atomic polarizability), RBN-number of rotatable bonds and RBF- rotatable bond fraction (as constitutional descriptors), HOMA-Harmonic Oscillator Model of Aromaticity index (as aromaticity index), Hy-the hydrophilic factor, Ui-unsaturation index (as empirical descriptors), PSA (fragment-based polar surface area).

The Partial Least Squares (PLS) method

Projections to Latent Structures (PLS) represent a regression technique for modeling the relationship between projections of dependent factors and independent responses. PLS (Partial Least Squares) Regression is a statistical modeling technique with data analysis features linking a block of response variables to a block of explanatory variables [11]. The PLS approach leads to stable, correct and highly predictive models even for correlated descriptors [18].

The PLS method describes the matrix X , of chemical descriptors of the training set by using of principal components-like (PC) models:

$$x_{ik} = \bar{x}_k + \sum_{f=1}^F p_{fk} \cdot t_{if} + e_{ik} \quad (1)$$

where $\bar{x}_k$ denotes the mean of variable k , p_{fk} the loading of variable k in dimension (factor) f , t_{if} the latent variable of compound I and e_{ik} the residuals [19]. The relation between the chemical descriptors and the biological test data is described as a linear model in the latent variables:

$$y_i = \bar{y} + \sum_{f=1}^F b_f \cdot t_{if} + e_i \quad (2)$$

where $\bar{y}$ represents the average of the y -variable and b_f the coefficient in the inner PLS relation between y and the latent variable t_f . PLS calculations were performed by the SIMCA package [20].

RESULTS AND DISCUSSION

The PLS procedure was applied to 54 descriptors derived from the Dragon, Chem3D Ultra and MOPAC softwares to model the glass transition temperatures. Molecular structures were converted into mathematical descriptors which encode the molecular key properties.

Polyester glass transition temperatures were correlated by PLS regression to constitutional, functional, empiric and aromaticity parameters of the studied compounds, which contained relevant information and which had significant contribution to the model. The PLS model was improved based on the DMOX and DMODY distances [21] by omitting 6 compounds (I.9, I.10, III.16-19) from the initial set of compounds, considered to be outliers. For the final PLS model the regression coefficients were transformed as functions of the original variables. The importance of descriptors was evaluated by the VIP (Variable

Influence on Projection) values [22], which summarize the importance of the x variables in the model. VIP values higher than 1.0 were considered (Table 2). The product between the regression coefficient and the corresponding descriptor value defined the descriptor contribution (if positive it increased the glass transition temperatures, if negative it decreased the glass transition temperatures).

Table 2. VIP (Variable Influence on Projection) values and regression coefficients of the final PLS model (in squared parantheses the number of principal components is given)

Descriptor	VIP[2]	Coeff [2]	Descriptor	VIP [2]	Coeff [2]
nCq*	1.76	-0.064	nSO ₂ *	1.28	0.036
nCp*	1.68	-0.070	Me*	1.23	0.016
AMW*	1.54	-0.060	MAXMIN**	1.13	0.027
RBF*	1.53	-0.063	Hy*	1.11	0.022
RBN*	1.53	-0.058	PSA*	1.07	0.023
HOMA*	1.49	0.048	M**	1.05	0.027
Mp*	1.48	0.042	nPO ₃ *	1.04	0.048
MLOGP*	1.47	-0.053	nPO ₄ *	1.04	-0.048
LUMO**	1.47	-0.039	Esb***	1.03	0.045
Mv*	1.47	0.042	nAT*	1.01	-0.030
CLOGP***	1.43	-0.038	Ui*	1.00	0.015
nH*	1.32	-0.034	nBm*	1.00	0.015
Ms*	1.31	0.027	nS*	1.28	0.036
nDB*	1.28	0.036			

* Dragon descriptors; ** quantum-chemical descriptors; *** Chem 3D Ultra descriptors

A final presumed QSPR model containing 17 compounds was obtained with following results: 2 principal components, $R^2X(\text{CUM})=0.511$; $R^2Y(\text{CUM})=0.819$, $Q^2(\text{CUM})=0.725$, where $R^2X(\text{CUM})$ is the fraction of the variation of the X variables explained by the selected component, $R^2Y(\text{CUM})$ is the cumulative sum of squares of the entire Y's explained by all extracted principal components and $Q^2(\text{CUM})$ is the fraction of the total variation of the Y's that can be predicted for all the extracted principal components. The final PLS model

indicated a satisfactory correlation of the glass transition temperatures with the polyester structural descriptors.

From the VIP values of most significant descriptors calculated for the final the PLS model, several structural features important for the polymer glass transition temperatures were obtained. Thus, higher polymer hydrophilicity (Hy) increases the T_g values. An increased number of sulfur atoms (nS) present in the molecule is beneficial for the polymer glass transition temperatures. Same information was found from other descriptors, like: the number of phosphite groups (nPO₃). Polymer polarity, expressed by dipole moment (μ), local polarizability (expressed by MAXMIN), Mp (mean atomic polarizability), PSA (fragment-based polar surface area) was favorable for T_g .

The polymer hydrophobicity (expressed by the ClogP and MlogP descriptors) decreases the glass transition temperature, in opposition to the hydrophilicity influence.

Polymer aromaticity (described by: HOMA, Ui) increases the T_g values. Higher polymer flexibility (expressed by RBN-number of rotatable bonds and RBF- rotatable bond fraction) and increased polymer dimension (expressed by the average molecular weight) is not favorable for the polymer glass transition temperatures.

CONCLUSIONS

This paper presents a structure-property study for a series of polyphosphates and polyphosphonates. They were modeled by their monomers obtained from previous studies by molecular modeling calculations. Structural parameters were derived from the structures of minimum energy. The influence of monomer structural descriptors of polyphosphates and polyphosphonates on their glass transition temperature was accomplished by Partial Least Squares (PLS). Good correlations between the glass transition temperature and different structural parameters were obtained. Thus, higher polymer hydrophilicity increases the T_g values. An increased number of sulfur atoms present in the molecule is beneficial for the polymer glass transition temperatures. Same information was obtained from other descriptors, like: the number of phosphite groups. Polymer polarity was favorable for T_g . The polymer hydrophobicity decreases the glass transition temperature, in opposition to the hydrophilicity influence. Polymer aromaticity increases the T_g values. Higher polymer flexibility and increased polymer dimension is not favorable for the polymer glass transition temperatures.

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