Synthesis, characterization and molecular dynamics simulation of dendronized poly(3,5-diphthalimido-alkylphenyl methacrylate)s

Nancy Alvarado[1], **Luz Alegría**[2], **Claudia Sandoval**[3], **Ligia Gargallo**[4], **Angel Leiva**[1], **Deodato Radic**[1], [*]

Abstract: Dendronized methacrylates containing 3,5-diphthalimidoalkylphenyl moieties (with ethyl, propyl or butyl spacer groups) were synthesized. These monomers were then polymerized using radical polymerization. Monomers and polymers were characterized using Fourier transform infrared spectroscopy (FT-IR) and nuclear magnetic resonance methods (^{1}H NMR and ^{13}C NMR). Molecular weight was estimated by multi-angle static light scattering (MALS). Molecular dynamics simulation was performed to evaluate the conformational radius of gyration (R_g) and the end-to-end distance (r_{ee}). Different spatial arrangements depending on the length of the spacer group are observed.

Keywords: poly(phtalimidoalkyl methacrylate), dendronized polymers, spacer groups, molecular dynamics simulation, radius of gyration, end-to-end distance.

Synteza, charakterystyka i symulacje metodą dynamiki molekularnej dendry-merycznych poli(metakrylanów 3,5-diftalimidoalkilofenylu)

Streszczenie: Zsyntezowano dendrymeryczne metakrylany zawierające ugrupowania 3,5-diftalimido-alkilofenylowe (z etylowymi, propylowymi lub butylowymi grupami dystansującymi), a następnie monomery te poddano polimeryzacji rodnikowej. Do określenia struktury wyjściowych monomerów oraz otrzymanych polimerów zastosowano spektroskopię w podczerwieni z transformacją Fouriera (FT-IR) i metody magnetycznego rezonansu jądrowego (^{1}H NMR i ^{13}C NMR). Oznaczono również masę cząsteczkową polimerów metodą wielokątowego rozpraszania światła (MALS). Symulacje metodą dynamiki molekularnej pozwoliły na wyznaczenie konformacyjnych promieni bezwładności (R_g), a także odległości między końcami łańcucha (r_{ee}). Zaobserwowano różne układy przestrzenne, których rodzaj zależał od wielkości grupy dystansującej.

Słowa kluczowe: poli(metakrylan ftalimidoalkylu), polimery dendrymeryczne, grupy dystansujące, symulacja metodą dynamiki molekularnej, promień bezwładności, odległość między końcami łańcucha.

Dendronized polymers can be considered as linear macromolecules that bear pendant monodisperse dendrons along the backbone which are recognized as an important alternative structure [1, 2]. These are novel macromolecules whose nanoscale size, rigidity and functionality can be controlled with precision by tuning molecular architecture [2—6]. These dendritic macromolecules are characterized by a central poly-functional core, branching units and end groups. From the core there arise successive layers of monomer units with branching points in each monomer unit. This special spatial arrangement gives rise to a chemical structure that can adopt a cylindrical shape, where the periphery consists of a large number of chain ends. They have a highly functional globular structure that „resembles" proteins [7—9] and there is interest in developing applications in medicine [10—13], surface science [14, 15] and catalysis [16—18].

The aim of the present work was the synthesis, characterization and conformational analysis of dendronized poly(methacrylate)s containing phthalimidoalkyl moieties in the side chain, with different spacer groups. The effect of the side chain structure and the bulkiness and length of the spacer group on the conformational behavior and stiffness of the polymers is also another objective of this work.

[1] Pontificia Universidad Católica de Chile, Depto Química Fisica, Facultad de Química, Casilla 306, Santiago 22, Chile.

[2] Universidad Austral de Chile, Facultad de Ciencias de la Ingeniería, Centro de Docencia de Ciencias Básicas para Ingeniería, Casilla 567, Valdivia, Chile.

[3] Universidad Autónoma de Chile, Edificio Centro de Salud y Deportes, El Llano Suibercaseaux 2801, San Miguel, Santiago, Chile.
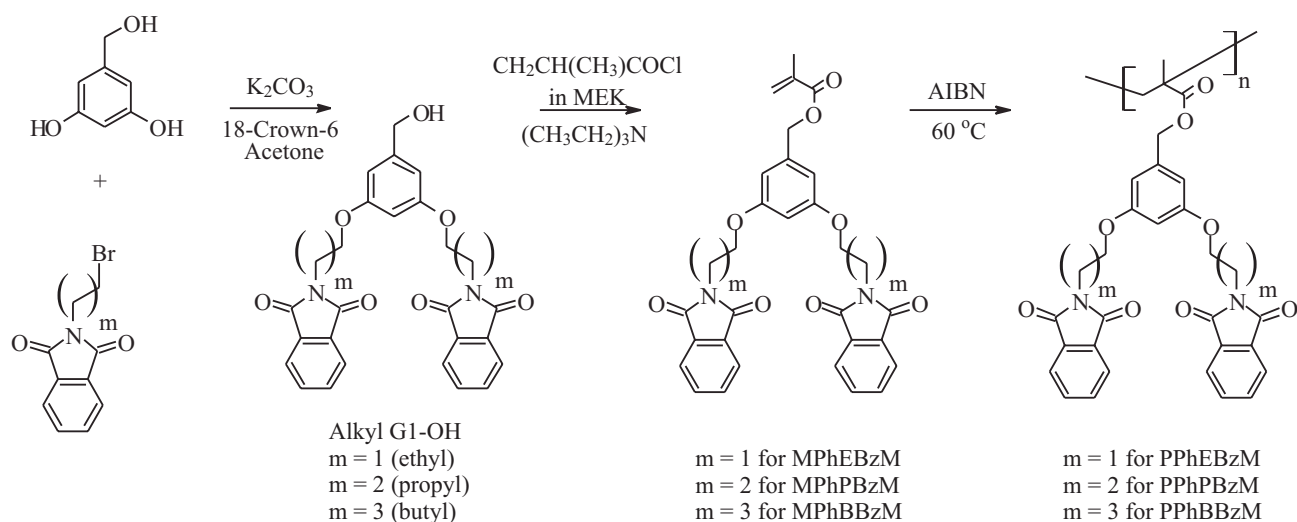
[4] Universidad de Tarapacá, General Velásquez 1775, Arica, Chile.

[*] Author for correspondence; e-mail: dradic@puc.cl

<div style="column-count:2">

EXPERIMENTAL PART

Materials

Dendritic benzyl alcohols, *i.e.* alkylphthalimidoalkylbenzyl alcohols (PhABz-OH), were obtained by mixing the appropriate *N*-allylphthalimide bromide (2.00 equiv., Aldrich, 99 %), 3,5-dihydroxybenzylalcohol (1.00 equiv., Aldrich, 99 %), dried potassium carbonate (2.5 equiv., ISN, 99.8 %) and 18-crown-6 (0.2 equiv., Aldrich, 99 %) in dry acetone, heated at reflux temperature and stirred under inert atmosphere. The crude product was purified using silica gel column chromatography, eluted with CH_2Cl_2/ethyl acetate mixture that gradually increased in the percentage of ethyl acetate.

Bruker Vector 22 spectrophotometer using KBr discs. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker AM-200 and AM-400 spectrometers using tetramethylsilane as internal reference.

The mass-average molecular weights ($\overline{M}_w$) of polymers were determined with multi-angle static light scattering (MALS) method using a DAWN EOS and an Optilab DSP detector from Wyatt technology working online with three PLgel mixed — c Polymer Labs columns.

Thermal properties were determined using differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA). The glass transition, melting and crystallization temperatures (T_g, T_m and T_c, respectively) of the pure and dry polymers were measured with a Mettler 821 calorimetric system and the data were processed using

</div>

Scheme A

<div style="column-count:2">

Monomers, *i.e.* phthalimidoethylbenzyl methacrylate (MPhEBzM), phthalimidopropylbenzyl methacrylate (MPhPBzM) and phthalimidobuthylbenzyl methacrylate (MPhBBzM) were obtained according to Scheme A. The appropriate dendritic benzyl alcohol (1.00 equiv.) were mixed with triethyl amine (1.00 equiv., Sigma-Aldrich, 99 %) and methacryloyl chloride (1.05 equiv., synthesized in our laboratories) in methylethylketone (Sigma-Aldrich, 99 %) and stirred under inert atmosphere. The crude product was purified by flash chromatography eluted with CH_2Cl_2. Monomers were polymerized at 333 K in bulk under N_2 atmosphere in the presence of α,α′-azobisisobutyronitrile (AIBN, 0.025 % in bulk, Fluka, 98 %) as initiator.

Methods of testing

Fourier transform infrared spectroscopy (FT-IR) and nuclear magnetic resonance methods (^{1}H NMR i ^{13}C NMR) were used to determine the structure of monomers and polymers. FT-IR spectra were recorded on a

the STAR^e program. Dry nitrogen was used as purge gas and thermograms were measured in the range of 273 to 473 K at the scan rate of 20 deg/min. Thermal degradation temperatures (*TDT*) were determined using Mettler Toledo TGA/SDTA 851 apparatus. The scans were performed at temperatures ranging between 25 °C and 700 °C at the heating rate of 10 deg/min under nitrogen environment. The amounts of the samples used were 5—10 mg using 40 µl alumina pans. Data were processed using STAR^e software version 8.1 from Mettler-Toledo.

Molecular dynamics simulations

Molecular dynamics (MD) simulations were carried out for three dendronized polymer (DP) systems. Twenty monomeric units for each dendronized polymer (DP) were built to the poly(phthalimidoethyl benzyl methacrylate), poly(phthalimidopropyl benzyl methacrylate) or poly(phthalimidobuthyl benzyl methacrylate) (PPhEBzM, PPhPBzM and PPhBBzM, respectively) to compare the physicochemical properties of the first gene-

</div>

ration dendrimers (G_1-DP). Discover module of the Material Studio program (Accelerys) was used to carry out both minimization and molecular dynamics protocols. Structures were minimized in 5000 iterations. The steepest descent and conjugated gradient methods were used for this purpose. MD simulations were performed in vacuum for each DP and consistent-valence force field (CVFF) [19] was appropriate to obtain the atomic parameters. The canonical NVT ensemble [the ensemble systems all at constant number of particles (N), volume (V) and temperature (T)] were considered to the molecular dynamics for all the systems. The radius of gyration (R_g) and end-to-end distance (r_{ee}) parameters were calculated from MD simulation trajectories. In order to know the DP's conformations a collection of 100 frames for each DP were selected from MD simulation trajectories.

RESULTS AND DISCUSSION

Synthesis and characterization of PhABz-OH, MPhABzM and PPhABzM

PhABz-OHs were synthesized by reaction of the appropriate *N*-alkyl phthalimide bromide with 3,5-dihydroxybenzylalcohol, where alkyl (A) was ethyl (E) or propyl (P) or butyl (B) as described in Scheme A. PhEBzOH, PhPBzOH and PhBBzOH purified products gave a colorless powder with the yield of 30, 32 and 34 %, respectively. The corresponding monomers MPhEBzM, MPhPBzM and MPhBBzM obtained from the PhABzMs and methacryloyl chloride was a yellow powder for MPhEBzM, and colorless powder for the other two monomers an the yield were 25, 30 and 45 %, respectively. Alcohols and monomers were characterized by spectroscopic measurements. The results of FT-IR, ^{1}H NMR and ^{13}C NMR measurements are collected in Table 1. The presented spectroscopic characterization is in agreement with the expected chemical structure.

Monomers were polymerized by radical polymerization and the pure polymers were characterized by ^{1}H NMR and FT-IR measurements. The results are presented in Table 2. The spectroscopic data for the polymers are in agreement with the expected chemical structure.

$\overline{M}_w$ of the polymers determined by multi-angle static light scattering method were 10500, 9800 and 7200 for PPhEBzM, PPhPBzM and PPhBBzM, respectively. The dendronized polymers were characterized also by DSC and TGA. Table 3 compiles the values of thermal properties for the three polymers. In the case of PPhEBzM, the polymer behaves as a semi-crystalline material, with $T_m = 358$ K and $T_c = 335$ K. It is interesting to note that the T_g value of PPhBBzM is lower than that of PPhEBzM, although the molar volume of the side chain is larger but the insertion of a spacer -CH_2- group increases the flexi-

T a b l e 1. The spectroscopic characterization of monomers

Spectroscopic method	Polymer		
	MPhEBzM	MPhPBzM	MPhBBzM
^{1}H NMR (δ in ppm)	1.99 (t, 3H, J=1.0 Hz, CH_3), 3.60 (t, 4H, CH_2-N), 4.10 (t, 4H, CH_2-O-Ar), 5.03 (d, 2H, J=10 Hz, CH_2-Ar), 5.81 (d, 1H, J=1 Hz, CH vinyl), 6.06 (d, 2H, J=16 Hz, H-Ar), 6.22 (d, 1H, J=1 Hz, H vinyl), 6.85(dd, 1H, J=10 y 16 Hz, H-Ar), 7.83 (m, 8H, H-Ar, phthalimide)	1.97 (t, 3H, J=1.0 Hz, CH_3), 2.10 (m, 4H, CH_2-CH_2-CH_2), 3.80 (t, 4H, CH_2-N), 4.00 (t, 4H, CH_2-O-Ar), 5.08 (d, 2H, J=10 Hz, CH_2-Ar), 5.69 (d, 1H, J=1.5 Hz, CH vinyl), 6.27 (d, 1H, J=1.5 Hz, H vinyl), 6.47 (d, 2H, J=15 Hz, H-Ar), 6.65 (dd, 1H, 15 Hz, H-Ar), 7.72 (m, 8H, H Ar, phthalimide)	1.81 (m, 8H, -CH_2-CH_2-), 2.00 (t, 3H, CH_3), 3.71 (t, 4H, CH_2-N), 4.13 (t, 4H, CH_2-O-Ar), 5.08 (t, 2H, CH_2-Ar), 5.55 (d, 1H, CH vinyl), 5.71 (d, 1H, CH vinyl), 6.29 (t, 1H, J= ? Hz, H-Ar), 6.41 (t, 1H, H-Ar), 6.71 (t, 1H, H-Ar), 7.72 (m, 8H, H-Ar phthalimide)
^{13}C NMR	17.94, 28.23, 39.28, 104.44, 123.50, 123.62, 129.05, 131.58, 131.81, 134.23, 134.51, 135.72, 163.06, 166.45, 167.7	18.39, 26.44, 35.42, 65.74, 65.92, 101.66, 107.64, 113.39, 115.74, 123.30, 133.96, 138.33, 141.87, 154.05, 159.88, 168.37, 174.03	18.38, 25.28, 26.50, 37.65, 67.18, 67.39, 101.57, 107.15, 110.35, 123.26, 127.41, 132.03, 133.99, 135.79, 143.53, 159.91, 160.21, 165.88, 166.52
FT-IR (ν in cm⁻¹)	3093 (CH_3), 3046 (CH=CH, Ar), 2914 (CH_2), 1771 (C=O), 1716 (C=O), 1396 (C-N), 1070 (C-O, ester), 1376 (C-N), 1155 (C-O, ester)	2950 (CH_3), 2934 (CH=CH, Ar), 2880 (CH_2), 1764 (C=O), 1705 (C=O)	2943 (CH_3), 3061 (CH=CH, Ar), 2874 (CH_2), 1771 (C=O), 1712 (C=O), 1148 (C-O, ester)

T a b l e 2. The spectroscopic characterization of polymers

Spectroscopic method	Polymer		
	PPhEBzM	PPhPBzM	PPhBBzM
^{1}H NMR	1.92 (m, 3H, CH_3), 2.04 (m, 2H, CH_2), 4.07 (t, 4H, CH_2-N), 4.27 (t, 4H, CH_2-O-Ar), 5.34 (m, 2H, CH_2-Ar), 6.10 (m, 2H, H-Ar), 6.75 (m, 1H, H-Ar), 7.87 (m, 8H, H-Ar, phthalimide)	1.91 (m, 3H, CH_3), 2.04 (m, 2H, CH_2), 2.14 (m, 4H, CH_2-CH_2-CH_2), 3.63 (t, 4H, CH_2-N), 3.94 (t, 4H, CH_2-O-Ar), 5.15 (m, 2H, CH_2-Ar), 6.27 (m, 2H, H-Ar), 6.35 (m, 1H, H-Ar), 7.75 (m, 8H, H-Ar, phthalimide)	1.67 (m, 8H, -CH_2-CH_2-), 1.96 (m, 3H, CH_3), 2.01 (m, 2H, CH_2), 3.57 (t, 4H, CH_2-N), 3.94 (t, 4H, CH_2-O-Ar), 5.34 (m, 2H, CH_2-Ar), 6.25 (m, 2H, H-Ar), 6.38 (m, 1H, H-Ar), 7.85 (m, 8H, H-Ar, phthalimide)
FT-IR (ν in cm⁻¹)	2980 (CH_3), 2880 (CH_2), 1760 (C=O), 1380 (C-N)	2950 (CH_3), 2890 (CH_2), 1740 (C=O), 1360 (C-N)	3050 (CH_3), 2900 (CH_2), 1770 (C=O), 1390 (C-N)

bility, lowering T_g. In the case of PPhBBzM, the T_g value increases due to the increase in the molar volume of the side chain, irrespective of the two -CH$_2$- spacer groups, what indicate that the effect of the volume of the side chain is more important than that of the flexibilization due to the insertion of the aliphatic chains. This is a normal behavior in the sense that flexibility and molar volume of the side chain have contrary effects.

T a b l e 3. Thermal properties of prepared polymers [glass transition temperature (T_g), thermal decomposition temperature (TDT), melting temperature (T_m), and crystallization temperature (T_c)]

Polymer	T_g, K	TDT, K	T_m, K	T_c, K
PPhEBzM	360	588	358	335
PPhPBzM	352	719	—	—
PPhBBzM	365	765	—	—

Molecular dynamics simulations

The radius of gyration (R_g) and end-to-end distance (r_{ee}) parameters were evaluated from MD simulation trajectories and discussed in order to study the variation of the stiffness due to the increase in the number of carbon atoms in the side chain of the dendrons. R_g can be defined as:

$$R_g^2 = \left\langle \frac{1}{N\left(\sum R_i^2\right)} \right\rangle \tag{1}$$

where: R_i — the distance of atom i from the mass center, N — the total number of atoms.

On the other hand, r_{ee} parameter is given by the equation:

$$r_{ee} = \Sigma l_i \tag{2}$$

where: l_i — the vector along the backbone bond i, n — the number of backbone bonds in the molecule.

R_g and r_{ee} were evaluated in the regions where the energies were stable and 100 frames were considered for this purpose.

The variations of R_g with respect to frame number of the MD simulation for obtained polymers are shown in Fig. 1. The values of R_g^2 are 2.46, 2.50 and 2.71 nm^2 for PPhEBzM, PPhPBzM and PPhBBzM, respectively. For PPhEBzM, the variation of R_g is lower than those for PPhPBzM and for PPhBBzM is the largest. For the last one, the behavior can be attributed to the increased flexibility. PPhBBzM has a larger side chain compared with PPhEBzM and PPhPBzM, which may be indicative of increased flexibility. The increase in length of the spacer group also enhances thermal resistance of polymers. This was confirmed by the increasing values of TDT from 588 K for PPhEBzM to 765 K for PPhPBzM.

Indeed these results are in agreement with the results of T_g measurements. T_g decreases as the number of carbon atoms in the side chain increases, nevertheless in the case of the propyl derivative it decreases due to the inser-
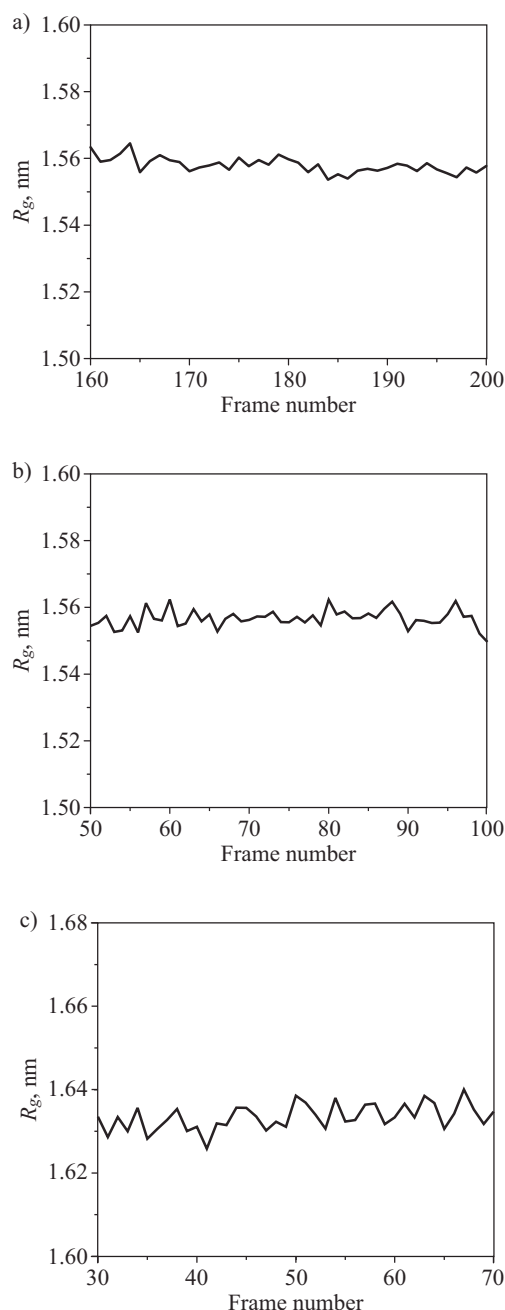
Fig. 1. Variation of gyration radius (R_g) with the frame number for: a) PPhEBzM, b) PPhPBzM, c) PPhBBzM

tion of a flexible -CH$_2$ group. According as the side chain increases the T_g of a polymer decreases because free volume increases (chain have a larger space to move), which implies that it is more flexible. Therefore this directly affects the overall flexibility of the polymer, resulting in a greater movement of the side chain.

The conformations of obtained polymers are shown in Fig. 2. It can be observed that these polymers adopt similar conformations, a helical-like structure, probably due to the similarity of sizes in the side chain of the dendron and also because the fluctuations of R_g are relatively similar. However, PPhEBzM adopts a structure very different to those of the other DPs. This structure was found to be similar to a rod-like polymer. This was confirmed by results of calori-
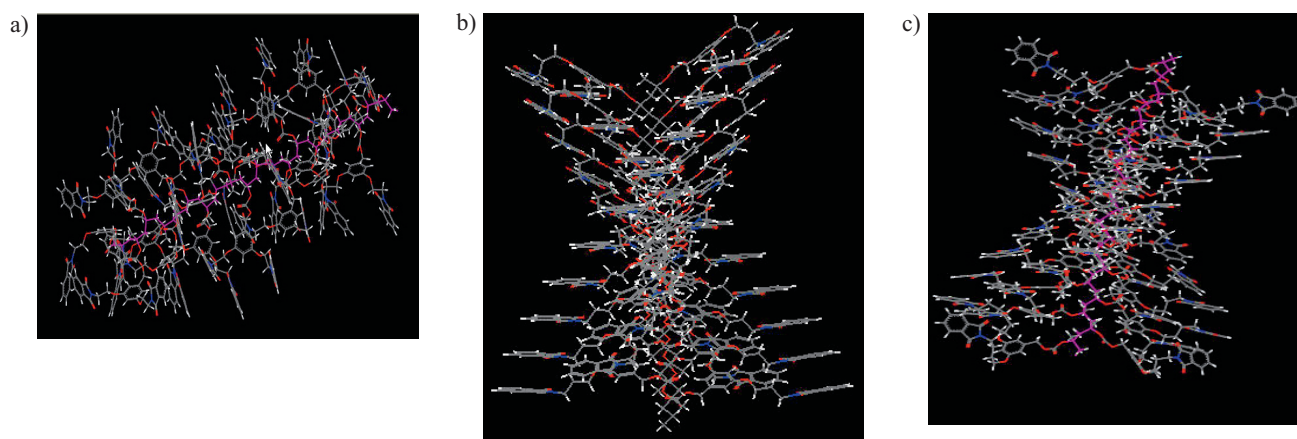
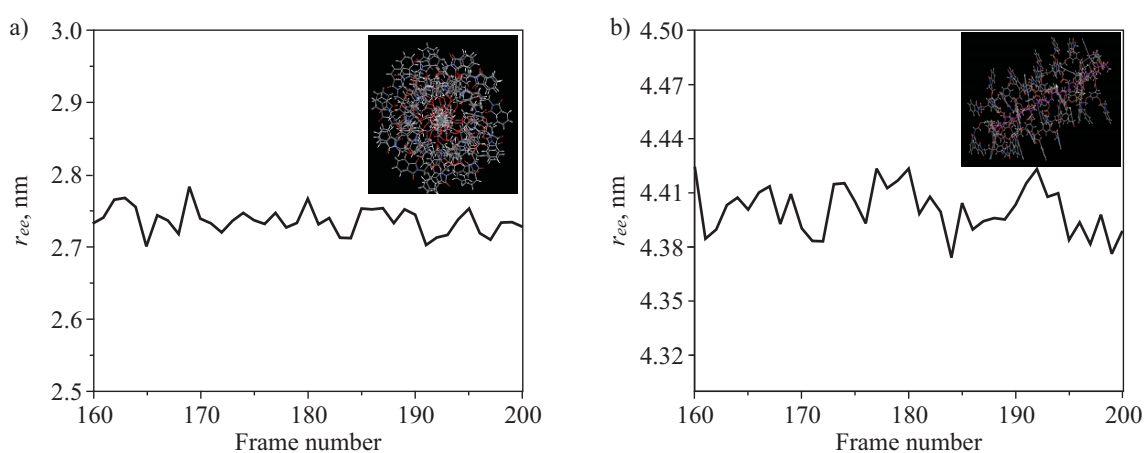**Fig. 2. The conformation of: a) PPhEBzM, b) PPhPBzM, c) PPhBBzM**

Fig. 3. Variation of end-to-end distance (r_{ee}) with the frame number for PPhEBzM: a) crosswise variation, b) longitudinal variation

metric measurements (T_m and T_c). This feature of PPhEBzM gives less flexibility compared to PPhPBzM and PPhBBzM. Because PPhEBzM has a crystalline structure, the r_{ee} value was calculated. The crosswise and longitudinal r_{ee} were calculated in order to study the differences in the flexibility between the backbone and dendrons of PPhEBzM and results are presented in Fig. 3. The crosswise variation of r_{ee} was calculated, taken into account the carbon atoms of the rings and backbone carbon atoms. A slight variation in the curve was observed obtaining an average radius of 2.8 nm to crosswise r_{ee}. In the case of the longitudinal r_{ee} the head and tail carbon atoms of the backbone were included to calculate the property, but higher fluctuations were observed and an average value of 4.3 nm was obtained for the longitudinal r_{ee}. This behavior is attributed to the movement of the backbone compared with the more restricted motions of the dendrons. This means that in the case to PPhEBzM has more degrees of freedom to move along the chain, not being so in the case of the dendrons.

spacer groups adopt semi-helicoidal structures. Experimental and theoretical analyses are in good agreement in these systems. The thermal behavior of the polymers follows a trend which is consistent with their chemical structures and in this family of polymers it could be considered as a good starting point to the synthesis of new dendronized polymers. The conformation obtained for PPhEBzM was different compared with PPhPBzM and PPhBBzM. A rod-like structure to PPhEBzM was obtained. This result was in agreement with the calorimetric results for this semi-crystalline polymer. The stiffness of PPhEBzM was higher compare to PPhPBzM and PPhBBzM.

CONCLUSIONS

The synthesis of dendronized poly(phthalimidoalkyl methacrylate)s shows that polymers with different

REFERENCES

[1] Guo Y.F., van Beek J.D., Zhang B.Z. *et al.*: *Journal of the American Chemical Society* **2009**, *131*, 11 841.
      http://dx.doi.org/10.1021/ja9032132

[2] Schlüter A.D., Rabe J.P.: *Angewandte Chemie International Edition* **2000**, *39*, 864. http://dx.doi.org/10.1002/(SICI)1521- -3773(20000303)39:5<864::AID-ANIE864>3.0.CO;2-E

[3] Percec V., Imam M., Peterca M., Leowanawat P.: *Journal of the American Chemical Society* **2012**, *134*, 4408. http://dx.doi.org/10.1021/ja2118267

[4] Bertran O., Zhang B., Schlüter A.D. *et al.*: *The Journal of Physical Chemistry C* 2015, *119* (7), 3746. http://dx.doi.org/10.1021/jp510586r

[5] Yan X., Jiang B., Cook T. *et al.*: *Journal of the American Chemical Society* **2013**, *135*, 16813. http://dx.doi.org/10.1021/ja4092193

[6] Shu L., Schlüter A.D., Ecker C. *et al.*: *Angewandte Chemie International Edition* **2001**, *40*, 4666. http://dx.doi.org/ 10.1002/1521-3773(20011217)40:24<4666::AID-ANIE4666> 3.0.CO;2-1

[7] Xin J., Chen T., Lin Z. *et al.*: *Chemical Communications* **2014**, *50*, 6491. http://dx.doi.org/10.1039/C4CC00617H

[8] Zeng H., Little C., Tiambeng T. *et al.*: *Journal of the American Chemical Society* **2013**, *135*, 4962. http://dx.doi.org/10.1021/ja400986u

[9] Grotzky A., Altamura E., Adamcik J. *et al.*: *Langmuir* **2013**, *29*, 10831. http://dx.doi.org/10.1021/la401867c

[10] Kumari M., Gupta S., Achazi K. *et al.*: *Macromolecular Rapid Communications* **2015**, *36*, 254. http://dx.doi.org/10.1002/marc.201400467

[11] Nielsen M.M., Dimitrov I., Takamuku S. *et al.*: *Fuel Cells* **2013**, *13*, 342. http://dx.doi.org/10.1002/fuce.201200192

[12] Khandare J., Calderón M., Dagia N., Haag R.: *Chemical Society Reviews* **2012**, *41*, 2824. http://dx.doi.org/10.1039/C1CS15242D

[13] Niea N., Tua Q., Wanga J. *et al.*: *Colloids and Surfaces B: Biointerfaces* **2012**, *97*, 226.

[14] Bini D., Russo L., Battocchio Ch. *et al.*: *Organic Letters* **2014**, *16*, 1298. http://dx.doi.org/10.1021/ol403476z

[15] Iqbal P., Rawson F., Ho W. *et al.*: *ACS Applied Materials & Interfaces* **2014**, *6*, 6264. http://dx.doi.org/10.1021/am501613c

[16] Li N., Zhao P., Igartua M. *et al.*: *Inorganic Chemistry* **2014**, *53*, 11 802. http://dx.doi.org/10.1021/ic5021498

[17] Deraedt C., Pinaud N., Astruc D.: *Journal of the American Chemical Society* **2014**, *136*, 12 092. http://dx.doi.org/10.1021/ja5061388

[18] Li N., Echeverría M., Moya S. *et al.*: *Inorganic Chemistry* **2014**, *53*, 6954. http://dx.doi.org/10.1021/ic500861f

[19] Dauber-Osguthorpe P., Roberts V., Osguthorpe D. *et al.*: *Proteins: Structure, Function, and Bioinformatics* **1988**, *4*, 31. http://dx.doi.org/10.1002/prot.340040106