

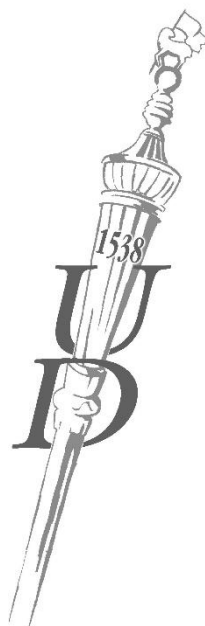
Thesis of doctoral (Ph.D) dissertation

COLLISION INDUCED DISSOCIATION STUDY OF POLYETHERS

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I. INTRODUCTION AND OBJECTIVES

Mass Spectrometry (MS) is a sensitive and selective method which can determine the mass of a molecule by measurement of mass-to-charge ratios of the ions formed when a sample is ionized. The ions are separated, may be fragmented, and detected so that information on the molecular mass and molecule structure can be obtained. Application of mass spectrometry is not limited to chemistry and physics. It has powerful application in medicine and biology as well.

Large molecules like synthetic polymers and biomacromolecules can be analyzed with no or minimal fragmentations using soft ionization technique such as electrospray ionization (ESI). Mass spectrometry can measure molecular weight and molecular formula (high resolution MS). In addition, the structural information of analyte can also be obtained by using tandem mass spectrometry (MS/MS).

There is no doubt about the importance of the polyethers: polyethylene glycol (PEG), polypropylene glycol (PPG), polytetrahydrofuran (PTHF), and propoxylated diethylenetriamine (DETA) polymers are applied in many different areas ranging from industrial to medicinal applications. Thus, studying the structure and properties of these important polyethers by mass spectrometry is interesting from both practical and scientific point of view.

Accordingly, the aims of my PhD studies were the followings: (1) To study the formation and dissociation of polyethers cationized by Na^+ , K^+ and Cs^+ ions, by means of energy-dependent collision-induced dissociation tandem mass spectrometry and to establish the relative gas-phase dissociation energies for binding the alkali ions to polyethers. (2) To develop a simple collision model by implementation of the Rice–Ramsperger–Kassel–Marcus (RRKM) and Rice–Ramsperger–Kassel (RRK) algorithm capable of estimation of the activation energies for the cationized polyethers. (3) To determine the arm-length distribution in the five-arm star

propoxylated diethylenetriamine polyol using tandem mass spectrometry and to get deeper insight into the formation of these polyols.

II. EXPERIMENTAL METHODS

The MS and MS/MS measurements were performed with a MicroTOF-Q type Qq-TOF MS instrument equipped with an ESI source. The sample solutions were introduced directly into the ESI source with a syringe pump at a flow rate of 3 $\mu\text{L}/\text{min}$. The temperature of the drying gas (N_2) was kept at 180°C. The needle voltage was 4 kV. For MS/MS experiments nitrogen gas was used as the collision gas. The pressure in the collision cell was determined to be 8×10^{-3} mbar. The precursor ions for MS/MS were selected with an isolation width of m/z 5. The MS/MS spectra were accumulated and recorded by a digitizer at a sampling rate of 2 GHz. The mass spectra were evaluated with the Data Analysis 3.4 software from Bruker.

For MS^3 experiments, in-source collision-induced dissociation (ISCID) was applied. The mass spectra were calibrated externally using the exact masses of clusters $[(\text{NaTFA})_n + \text{Na}]^+$ generated from the electrosprayed solution of sodium trifluoroacetate (NaTFA).

Source conditions for the TQ (triple quadrupole) measurements were similar to those of Q-TOF and the measurements were performed with a Finnigan TSQ Quantum triple quadrupole mass spectrometer. For the MS/MS experiments argon collision gas was used. The mass spectra were evaluated with the Xcalibur 2.07 software from Thermo Finnigan.

III. NEW SCIENTIFIC RESULTS

1. A simple method was proposed to estimate the relative stabilities of polyethers cationized by alkali metal ions (Na^+ , K^+ and Cs^+)

1.1. It was found that the dominant, and almost unique, process in the MS/MS of the doubly cationized polyethers (PEG, PPG, and PTHF) was the simple loss of a cation from the doubly charged precursor to yield the singly charged product ion.

1.2. It was observed that the collision voltage necessary to obtain 50% fragmentation (CV_{50}) determined for the doubly cationized polyethers increases linearly with the size or degrees of freedom (DOF) for each polyether studied (see Fig. 1).

1.3. The slopes of the CV_{50} versus DOF curves were correlated with the relative gas-phase dissociation energies for binding of alkali ions to polyethers. The relative dissociation energies determined from the corresponding slopes were found to decrease in the order $\text{Na}^+ > \text{K}^+ > \text{Cs}^+$ for each polyether studied, and an order $\text{PPG} \approx \text{PEG} > \text{PTHF}$ can be established for each alkali metal ion (see Fig. 1).

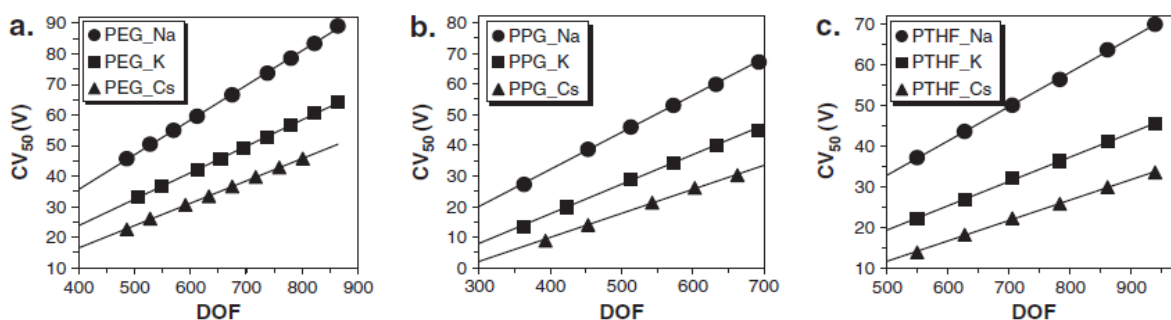


Fig. 1. CV_{50} versus DOF plots for the doubly charged PEG (a), PPG (b) and PTHF (c) cationized with Na^+ , K^+ and Cs^+ ions.

2. A simple collision model for the estimation of activation energy from the survival yields was developed and applied for the fragmentations of polyethers.

2.1. A simple collision model for treating the multiple collisions taking place in quadrupole (Q) type mass spectrometers has been developed. This model is capable of calculating the internal energy increment, the transit time and the exit energy of the ions in Q-type mass spectrometers. The calculations showed that there were good agreements between the results obtained by our model and the SIMION simulation. Implementation of the collision model and Rice–Ramsperger–Kassel–Marcus (RRKM) or Rice–Ramsperger–Kassel (RRK) algorithm into a spreadsheet software allowed a good fitting of the calculated data to the experimental survival yield (SY) *versus* collision energy curve (see Fig. 2). SY is a plot of relative ion intensity ratios of the precursor ion to those of all product ions in which the precursor ion is a function of the collision energy.

2.2. The collision model with the RRKM formalism was used to estimate the efficiencies of the kinetic to internal energy conversion for leucine enkephalin in quadrupole-time-of-flight and triple quadrupole instruments. It was found that reducing the total degree of freedom (DOF) to about one fifth in RRK formalism, the RRK can give comparable results with those of the more complicated RRKM model.

2.3. The critical energy (E_0) of lithiated polyethers including PEG, PPG and PTHF with degrees of freedom similar to that of leucine enkephalin was calculated by this collision model with the RRK formalism. Thus, the RRK model could predict the corresponding rate constant with a reasonable accuracy.

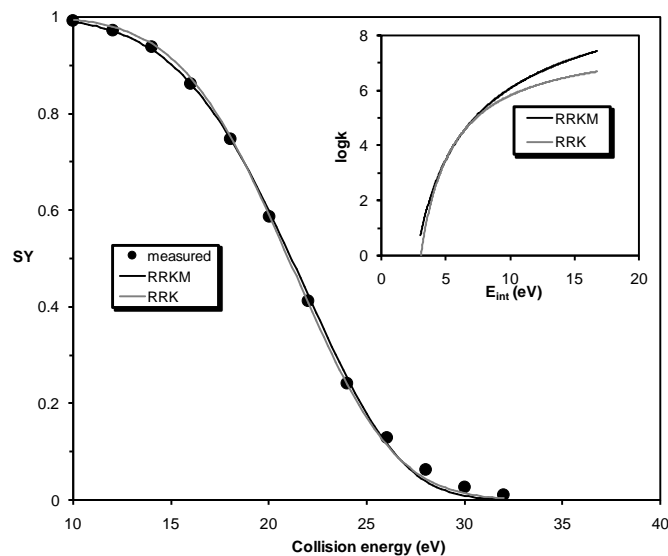
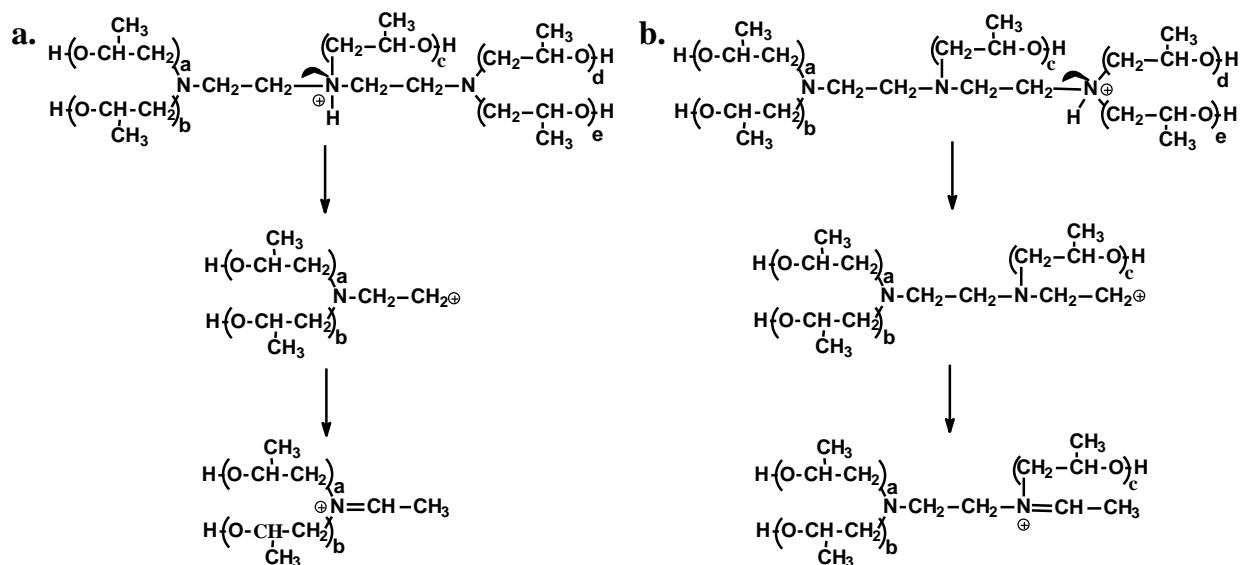


Fig. 2. The SY values for leucine enkephalin as a function of the collision energy.

3. The collision-induced dissociation tandem mass spectrometry of the protonated five-arm star propoxylated diethylenetriamine polyols was investigated under electrospray conditions.

3.1. It was shown that the cleavage of the C-N bonds in the initiator moiety results two product ion series (see Scheme.1). No backbone fragmentation of the polyether chains was observed.



Scheme. 1. Proposed mechanism for fragmentation for the protonated propoxylated diethylenetriamine.

3.2. Binomial distribution was proposed for the description of arm-length distribution. The initiation and propagation process of the oligomers was explored. It was concluded: (1) the repeat units attach to the five arms with approximately the same probability, and (2) the reaction rate of the initiation is greater than that of the chain propagation.

3.3. It was found that there is a linear relationship between the collision energy necessary to obtain 50% fragmentation (CE_{50}) and the number of propylene oxide repeat units.

IV. POSSIBLE APPLICATIONS OF THE RESULTS

Tandem mass spectrometry can be used in quantitative and qualitative analysis of different analytes. Its high sensitivity and selectivity has made it one of the powerful analytical methods. Studying the fragmentation pathways can help to elucidate the fragmentation of similar unknown compounds. The developed simple collision model allows to estimate the transit time and the energetics of fragmentations in collision induced dissociation. Exploring the fragmentation process and determining its basic parameters are important for the development of new mass spectrometric methods. On the other hand, the cationization mechanism which is established in the case of polyethers, let us to use the result in case of other similar types of polymers where the charge is located at initiation moiety. In addition, knowing the affinity of ions to polyethers can also help predicting the fragmentation pathway. We have found the linear relationship between the mass and the fragmentation energy that gave us the practical consequent. As knowing this relationship one can simply adjust the needed collision energy in order to obtain the structurally important fragmentations.

PUBLICATIONS

Publications related to the dissertation:

Ghazaleh Shemirani, Ákos Kuki, Lajos Nagy, Tibor Nagy, Miklós Zsuga, Sándor Kéki. Electrospray ionization tandem mass spectrometry of the star-shape propoxylated diethylenetriamine polyols. *Journal of mass spectrometry*. 50 (2015) 914-917.

IF: 2.379

Ákos Kuki, **Ghazaleh Shemirani**, Lajos Nagy, Miklós Zsuga, Sándor Kéki. Estimation of activation energies from the survival yield curves: a case study for the fragmentation of leucine enkephalin and polyethers by tandem mass spectrometry. *Journal of the american society for mass spectrometry*. 24 (2013) 1064-1071.

IF: 3.193

Ákos Kuki, Lajos Nagy, **Ghazaleh Shemirani**, Antony Memboeuf, László Drahos, Károly Vékey, Miklós Zsuga, Sándor Kéki. A simple method to estimate relative stabilities of polyethers cationized by alkali metal ions. *Rapid communication in mass spectrometry*. 26 (2012) 304-308.

IF: 2.509

Other publication:

Ákos Kuki, Izabella Irsai, Lajos Nagy, **Ghazaleh Shemirani**, Cornelia Majdik, Miklós Zsuga, Sándor Kéki. In-source collision induced dissociation study of polyethers cationized by alkali metal ions. *International journal of mass spectrometry*. 334 (2012) 38-42.

IF: 2.227



Registry number: DEENK/233/2015.PL
Subject: Ph.D. List of Publications

Candidate: Ghazaleh Shemirani
Neptun ID: HOSDWW
Doctoral School: Doctoral School of Chemistry

List of publications related to the dissertation

Foreign language scientific article(s) in international journal(s) (3)

1. **Shemirani, G.**, Kuki, Á., Nagy, L., Nagy, T., Zsuga, M., Kéki, S.: Electrospray ionization tandem mass spectrometry of the star-shaped propoxylated diethylenetriamine polyols.
J. Mass Spectrom. 50 (7), 914-917, 2015. ISSN: 1076-5174.
DOI: <http://dx.doi.org/10.1002/jms.3601>
IF:2.379 (2014)
2. Kuki, Á., **Shemirani, G.**, Nagy, L., Antal, B., Zsuga, M., Kéki, S.: Estimation of Activation Energy from the Survival Yields: Fragmentation Study of Leucine Enkephalin and Polyethers by Tandem Mass Spectrometry.
J. Am. Soc. Mass Spectrom. 24 (7), 1064-1071, 2013. ISSN: 1044-0305.
DOI: <http://dx.doi.org/10.1007/s13361-013-0635-8>
IF:3.193
3. Kuki, Á., Nagy, L., **Shemirani, G.**, Memboeuf, A., Drahos, L., Vékey, K., Zsuga, M., Kéki, S.: A simple method to estimate relative stabilities of polyethers cationized by alkali metal ions.
Rapid Commun. Mass Spectrom. 26 (3), 304-308, 2012. ISSN: 0951-4198.
DOI: <http://dx.doi.org/10.1002/rcm.5307>
IF:2.509





List of other publications

Foreign language scientific article(s) in international journal(s) (1)

4. Kuki, Á., Irsai, I., Nagy, L., **Shemirani, G.**, Majdik, C., Zsuga, M., Kéki, S.: In-source collision induced dissociation study of polyethers cationized by alkali metal ions.
Int. J. Mass Spectrom. 334, 38-42, 2013. ISSN: 1387-3806.
DOI: <http://dx.doi.org/10.1016/j.ijms.2012.10.004>
IF:2.227

Total IF of journals (all publications): 10,308

Total IF of journals (publications related to the dissertation): 8,081

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on the basis of Web of Science, Scopus and Journal Citation Report (Impact Factor) databases.

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