Zárójelentés

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In our research kinetics of aromatic and aliphatic isocyanates in the presence of alcohols and industrially important crosslinking agents was studied. Furthermore, sucrose containing polyurethanes (SPURs) were prepared from polycaprolactone diol and 1,6-hexamethylene diisocyanate and the isocyanate-alcohol “click” reaction was successfully used for molecular information storage.

1st year

In the first year SPURs were synthetized, in the syntheses sucrose was used as crosslinking agent. The designed polyurethanes obtained are potentially suitable for biological, pharmaceutical applications. In order to fulfill these requirements all reactants and solvents were selected according to the proposal of EUR-8 Pharmacopoeia. The first step of the synthesis work was the preparation of the prepolymer from polycaprolactone diol (PCLD) and 1,6-hexamethylene diisocyanate (HDI) in melt. The prepolymers formed in the reactions were characterized by matrix assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). After the characterization sucrose (used as crosslinking agent) was added to the prepolymer. In this reaction the main polymers were obtained from the reaction between the isocyanate group of the prepolymer chains and the 6 and 6’ primary OH groups of sucrose. Then the crosslinking reactions were taken place by the reaction between the excess free isocyanate groups of prepolymer and the residual primary hydroxyl group (in the 1’ position) of sucrose. It was found that the reactivity of the free OH groups of sucrose were different. Moreover, the swelling experiments of the SPUR samples using solvents with different polarities revealed that the highest degree of swelling took place in dimethyl-sulfoxide while in hexane and water the degrees of swelling was low. The crosslink densities calculated from the data of swelling experiments decreased with the increasing sucrose content. The reason of this finding is the different reactivities of OH groups of sucrose. If the prepolymer concentration was significantly higher than that of the sucrose the excess of prepolymer could react with the secondary OH groups of sucrose resulting in increasing crosslink densities. According to the mechanical tests the SPUR samples showed high elongation values, i.e., high flexibilities as it can be seen in Table 1.

Table 1. Uniaxial tensile mechanical properties of SPURs

Sample	Elastic Modulus (MPa)	Ultimate Elongation (%)	Stress at Break (MPa)
SPUR-1	5.0 ± 0.4	810 ± 110	22.6 ± 2.2
SPUR-2	3.3 ± 0.8	800 ± 40	14.8 ± 6.4
SPUR-3	2.1 ± 0.3	940 ± 330	15.8 ± 1.0
SPUR-4	2.8 ± 0.3	945 ± 110	24.3 ± 4.7
SPUR-5	5.3 ± 0.6	1100 ± 80	26.3 ± 1.3

To interpret and approve the decreasing of the crosslink densities with increasing sucrose content kinetic study was performed between the sucrose (S) and phenyl isocyanate (PI) in DMSO solvent. In order to achieve pseudo first-order reaction the sucrose was applied in high molar excess to isocyanate (the molar ratio of S/PI was 16/1). Under these reaction conditions monosubstitued glucose derivatives were formed. The reaction was quenched by methanol and the products formed were separated and detected by HPLC-UV (Fig. 1).

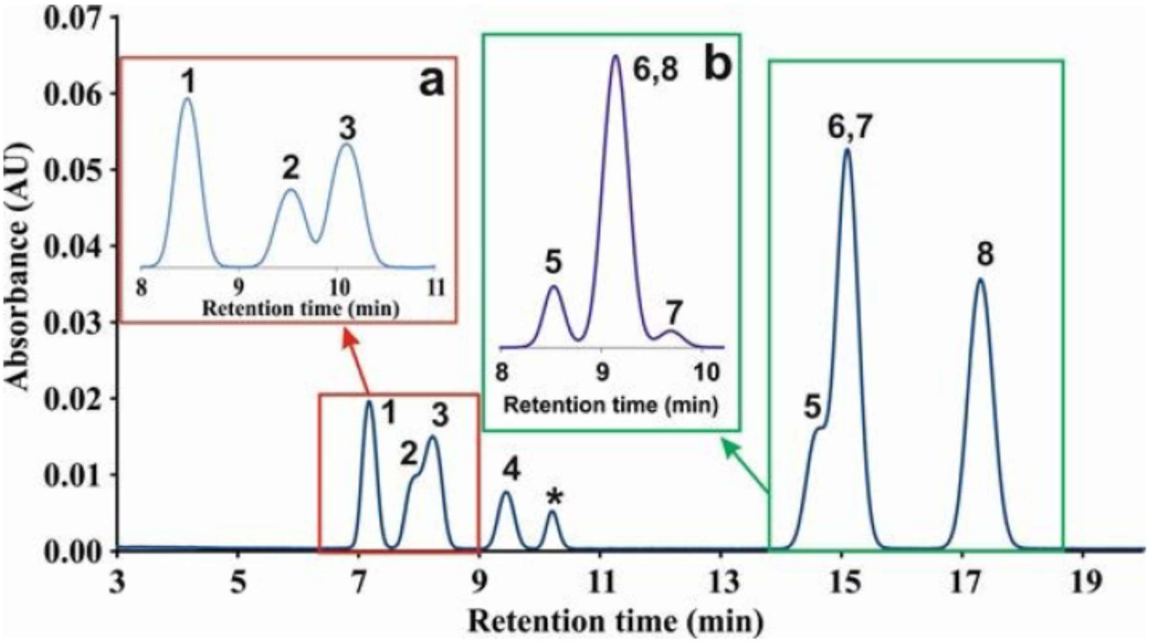

Figure 1. The HPLC-UV chromatogram using a C18 column and recorded at λ = 233 nm for the reaction mixture formed by the reaction of sucrose with phenyl isocyanate. The insets a and b represent the zoomed chromatograms using C18 (at different eluent composition) and phenyl columns, respectively. The peak denoted by asterisk (*) represents the aniline formed from the reaction of PI and moisture contamination.

Based on the UV areas of the peaks appeared in the chromatogram the absolute and relative reactivities were determined. The results However, further measurements were performed to attempt assigning the rate constants to the corresponding sucrose`s OH group. The reaction between the phenyl isocyanate and the sucrose was achieved with labeled sucrose (13C-atom at C-1 position in the glucose moiety). Then the products formed in the reaction was studied by HPLC-MS/MS measurements. Based on the typical fragmentation of the sucrose under ESI-MS/MS conditions the rate constants could be divided into two groups: the one associated with reaction of phenyl isocyanate with the glucose and the other with that of the fructose moiety of sucrose. Furthermore, the 2D-NMR measurements showed that the most reactive moieties were the three primary OH groups of the sucrose. Moreover, the Mulliken charges were calculated for the sucrose since a nucleophylic addition took place between the OH group and the isocyanate therefore, it was believed that the higher was the extent of the negative charge on the OH group and the positive charge on the carbonyl carbon of the isocyanate the higher was the reactivities towards each other. Based on the results the following reactivity order was found (relative reactivities are showed in brackets):

k(OH)6`(1) > k(OH)6(0.84) > k(OH)1`(0.31) > k(OH)3(0.25) > k(OH)4(0.23) > k(OH)2(0.13) > k(OH)4`(0.11) > k(OH)3`(0.09)

2nd year

As a continuation of our research in the isocyanate topic we focused our attention on the reaction of 1,3-xylylene diisocyanate (1,3-XDI) with aliphatic alcohols of different alkyl chain length and polyols. The aromatic isocynates (such as MDI, TDI) are frequently used for the production of polyurethane-based goods. However, the polyurethanes (PU) containing aromatic isocyanates possess poor light stability and show coloration upon aging. In contrast, the aliphatic isocyanates (such as HDI) show good resistance to light furthermore, the PU foams produced are softer than the MDI or TDI based PUs. The favorable properties of the aliphatic and aromatic isocyanates are alloyed in the XDI based PU products so the use of XDI in the PU chemistry becomes more and more significant. Therefore, industrial and scientific point of view the kinetic study of XDI and the knowledge of the mechanism of the reaction taking place between XDI and various alcohols are essential.

The reactions between the 1,3-XDI and alcohols including alcohols with varying alkyl chain lengths and low molecular weight polyols (such as monomethoxylated polyethylene glycol (mPEG) and polytetrahydrofuran (PTHF)) were achieved in dry toluene solvent in the absence of catalyst. The concentrations of the 1,3-XDI and the alcohols or polyol in the reaction mixture were 0.01 and 0.65 M, respectively. At appropriate reaction times sample was taken out the reaction mixture and it was quenched by methanol. The reaction was monitored by high-performance liquid chromatography (HPLC) using PDA detector at 210 nm. As it turns out from the concentrations the alcohol was applied in high molar excess to 1,3-XDI providing pseudo-first-order reaction kinetics. The mole fractions at the individual reaction times were calculated by the peak area fractions obtained from the HPLC chromatograms. It was found that the ratio of the rate constants determined for the two isocyanate groups (k_1 and k_2) was approximately 1. That indicates that there is no significant substitution effect, so the reactivity of the residual isocyanate group does not change after the first one has reacted. Furthermore, it was shown that the reaction rate constants was increased with increasing chain length (k_1 values at 80 oC from 1-propanol to 1-hexanol: 0.0166 min-1; 0.0187 min-1; 0.0219 min-1; 0.0341 min-1). The activation parameters (pre-exponential factor and activation energy) were also determined in the 50-80 ºC temperature range. The activation energies were determined in a range from 25 to 39 kJ/mol for the different alcohols (Table 2).

Table 2 The values of the natural logarithm of the apparent pre-exponential factors ($A_{1,\mathrm{app}}$ and $A_{2,\mathrm{app}}$) and activation energies ($E_{1\mathrm{a,app}}$ and $E_{2\mathrm{a,app}}$)

Apparent activation parameters	Alcohol			
	1-propanol	1-butanol	1-pentanol	1-hexanol
$\ln(A_{1,\mathrm{app}}\ [\mathrm{min}^{-1}])$	5.05±0.76	5.76±0.65	6.33±0.79	9.04±0.33
$E_{1\mathrm{a,app}}$ [kJ/mol]	26.9±2.1	28.7±1.8	29.8±2.1	36.6±0.9
$\ln(A_{2,\mathrm{app}}\ [\mathrm{min}^{-1}])$	4.55±0.68	6.48±0.63	7.53±0.76	9.64±0.57
$E_{2\mathrm{a,app}}$ [kJ/mol]	25.6±1.9	31.0±1.8	33.4±2.1	38.6±1.6

Then the isocyanate alcohol “click” reaction was successfully used for molecular storage of information. Recently, there is an increasing need for alternatives to existing data storage technologies and a very promising alternative way to the current digital storage system is the use of natural and synthetic molecules. The urethane bond formed by the reaction of isocynates and alcohols may be capable for using urethanes as molecular storage systems owing to its high stability at environmental conditions. In this research, the capability of encoding information using a homologous series of monodisperse monomethoxypolyethylene glycols (mPEG), with a number of ethylene oxide units ranging from nEO = 5 to 8, and monodisperse linear aliphatic isocyanates containing a number of CH2 units from 3 to 7, was demonstrated. In the presence of tin(II) 2-ethyl-hexanoate catalyst the mPEG was reacted with aliphatic isocyanate at room temperature. In this “click” reaction 20 different mPEG-OCONHR oligomers were synthetized and then used to encode information in binary sequences using a MALDI sample plate and employing the common dried-droplet sample preparation method capable of encoding 20 bit (2.5 byte). The information stored in the spots on the MALDI sample carrier was read by MALDI-TOF mass spectrometer. Owing to the similarity of the molecules synthetized and their high ionization efficiencies the MALDI-TOF MS signal intensities from each compound was so strong and unambiguous that complete decoding could be performed in each case.

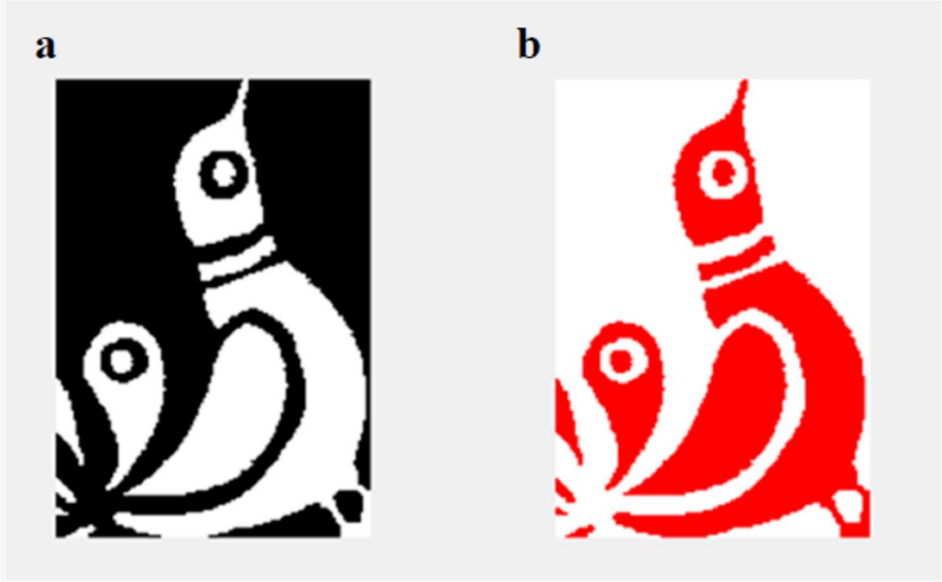

Figure 2. An original picture on a "Matyó" embroidery (bird pattern, 126x184 pixel) used for encoding information (**a**) and its Run Length Encoding (RLE) compressed version as decoded by MALDI-TOF MS (**b**).

The capability of the method to store data was demonstrated by writing and reading a text file, visualizing a picture on a "Matyó" embroidery (Fig. 2) and encoding an audio file containing the tune of an old popular American ballad written in Musical Instrument Digital Interface (MIDI) sequence. The reading of information was achieved with 100% efficiency in all cases.

3rd year

As it turned out our previous results the crosslinking agent had a significant role on the properties of polyurethanes. Thus in our next research the kinetics of some commonly used crosslinking agents (such as glycerol, sucrose, sorbitol) with phenyl isocyanate was studied. The reactions were performed in high molar excess of one of the reactants obtaining pseudo-first-order rate dependencies. The reactions where crosslinking agents were applied in high molar excess to isocyanate was monitored by HPLC-UV measurements. The separation of the reaction products was achieved by C18 HPLC column using UV detection at 233 nm. It was found that the primary hydroxyl groups of glycerol were four times reactive than the secondary one. However, in the case of sorbitol, the two primary OH groups were found to be the most reactive, and the reactivity of hydroxyl groups decreased in the order of kOH(6)(8.43) > kOH(1)(6.91) > kOH(5)(1.19) > kOH(2)(0.98) > kOH(3)(0.93) > kOH(4)(0.64), where the numbers in the subscript and in the brackets denote the position of OH groups and the pseudofirst- order rate constants, respectively. The assignments of the rate constants to the corresponding OH group of sorbitol were performed by density functional theory (DFT) calculations (Atomic Polar Tenzor (APT) charges of OH groups and dipole moments of monosubstituted sorbitol derivatives were calculated).

The reactions were also achieved using the phenyl isocyanate in high molar excess in the reaction mixture. For sucrose (Fig 3) and sorbitol, the reactions were monitored by MALDI-TOF mass spectrometry and the evaluation of the data was performed using a simplified reaction scheme owing to the huge number of derivatives likely formed in these reactions. For elimination of mass discrimination and ionization efficiency differences of the reaction products obtained under MALDI conditions derivatization was applied by p-tolyl isocyanate.

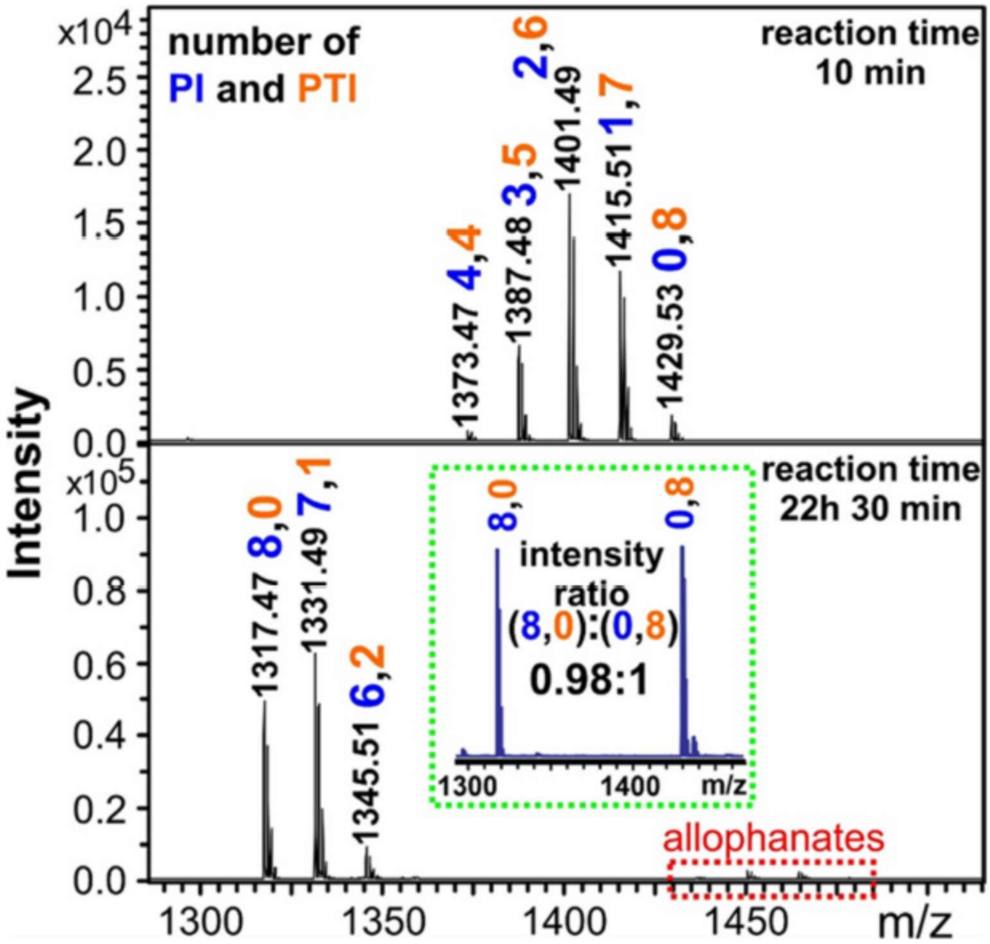

Figure 3. MALDI-TOF MS spectra of the reaction mixture of sucrose and phenyl isocyanate (PI) recorded at 10 min and 1350 min reaction times after derivatization with p-tolyl isocyanate (PTI). The numbers above the mass peaks represent the number of PTI and PI units attached to the sucrose. The inset shows the spectrum of sucrose derivatized completely with PI (8,0) and PTI (0,8) at 1:1 molar ratio.

It was found that the reactivity of the unreacted OH groups significantly decreases by increasing the number of the phenyl isocyanate moieties attached to the crosslinking agent. For instance, the difference between the first and last reaction rate constants of sucrose was determined to be ca. two orders of magnitude. Based on the results, the kinetically equivalent functionality (f_k) of each crosslinking agent was determined and found to be 2.26, 2.26, and 2.96 for glycerol, sorbitol, and sucrose, respectively.

4th year

As a continuation of our previous work various polymer polyol crosslinking agents were studied in the presence of phenyl isocyanate such as Pentaerythritol (PE), Trimethylol propane (TMP), ethoxylated (PEEO) and propoxylated (PEPO) pentaerythritol oligomers as well as Petol PA 500-5D (a propoxylated diethylenetriamine with 5 arms). The polyols were applied in high molare excess to phenyl isocyanate obtaining in this way pseudo first-order rate dependency. The reactions were monitored by HPLC-UV measurements, and C18 recersed phase column was used for the separation of reaction products formed. It was found that trimethylol propane (kTMP = 0.0819 min-1), due to its electron donating group, was slightly more reactive than pentaerythritol (kPE = 0.0700 min-1). Moreover, ethoxylated and propoxylated derivatives were found less reactive than PE, which can be explained by the electron withdrawing property of alkoxy groups. In addition, Petol PA 500-5D was determined to be the most reactive polyol, which is ascribed to the fact that it carries some catalytic properties similarly to other tertiary amine catalysts.

Moreover, the reactions were carried out in the presence of high isocyanate molar excess to polyols studying the influence of the phenyl isocyanate attached to the polyol on the unreacted OH groups. In cases of PE and TMP the reaction products were separated and the reaction was monitored by HPLC-UV measurement, however for the monitoring of the reactions of PEEO, PEPO and Petol PA-500-5D MALDI-TOF MS was applied. The results clearly showed that the reactivity of the unreacted OH groups significantly changed upon reaction in the case of PE and TMP, while for the polymer polyols steric and inductive effects slightly modified the relative reactivities of OH groups in each crosslinking agent (Table 2 shows the results for PEEO and PEPO).

Table 2. The determined pseudo first-order rate coefficients for the reaction of PEEO and PEPO with PI. Reaction conditions: [PEEO]0 = 0.0187 M, [PEPO]0 = 0.0187 M, [PI]0 = 0.45 M, solvent = DMSO, temperature = 30 °C. The numbers in the brackets next to the rate coefficients represent the number or PI units attached to the alcohol.

Rate coefficient	k x 10^2 (min^{-1}) (PEEO)	Rate coefficient	k x 10^2 (min^{-1}) (PEPO)
$k_{PEEO(0)}$	13.71	$k_{PEPO(0)}$	7.62
$k_{PEEO(1)}$	11.27	$k_{PEPO(1)}$	6.67
$k_{PEEO(2)}$	9.95	$k_{PEPO(2)}$	5.92
$k_{PEEO(3)}$	8.81	$k_{PEPO(3)}$	5.25

After the research of polyols and aromatic isocyanates the kinetics of the urethane forming reactions of aliphatic isocyanates such as hexamethylene diisocianate (HDI), 4,4′-dicyclohexyl-methane-diisocyanate) (HMDI) and isophorone diisocyanate (IPDI) with butan-1-ol were systematically studied by electrospray ionization mass spectrometry (ESI-MS). Unlike the aromatic isocyanates the aliphatic ones have no appropriate UV absorption thus in order to eliminate ionization efficiency differences of the reaction products we used perdeuterated butan-1-ol (i.e., d9-butan-1-ol) for quenching the reaction mixture. Providing in this way that the intensity ratios detected under MS conditions correspond to the molar ratios. The corresponding rate coefficients were determined and reactivities of the diisocyanates were found to decrease in the order of the HDI > IPDI > HMDI. The distribution of the reaction products against time and the fitted curves (dashed line) for HMDI are shown in Fig. 4.

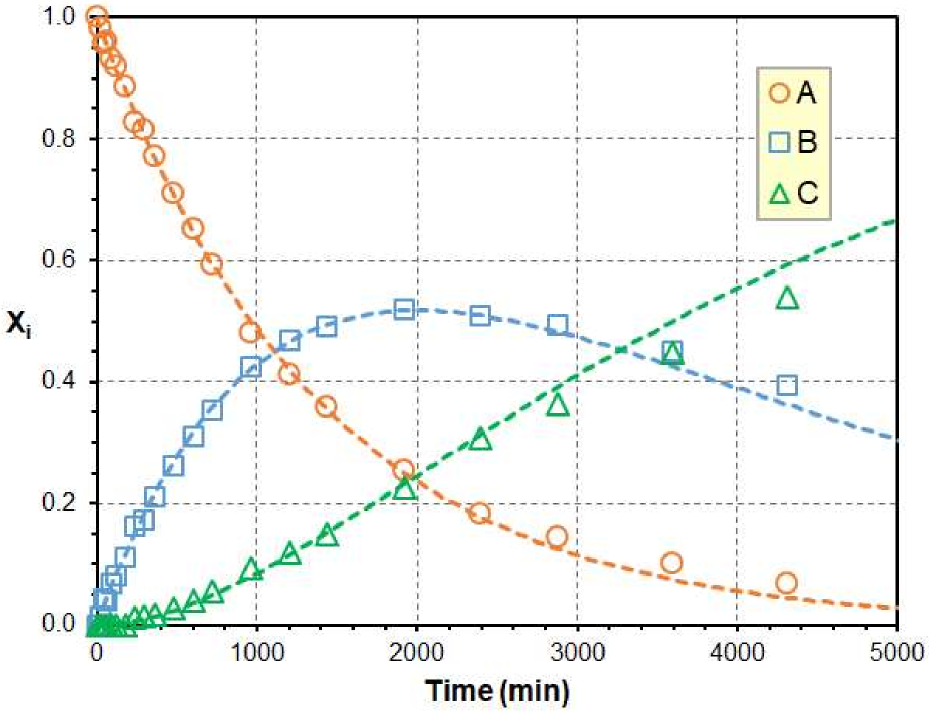

Figure 4. Product distributions versus reaction time in the uncatalyzed HMDI-butan-1-ol reaction at 80 °C recorded by ESI-MS. Initial concentrations of HMDI and butan-1-ol are 0.01 M and 0.64 M, respectively. The symbols: orange (initial isocyanate (X_A)); blue (once-reacted isocyanate (X_B)); green (twice-reacted isocyanate (X_C))

It was found that the second isocyanate group in HDI, due to the ring formation by intramolecular hydrogen bond, reacted faster with butan-1-ol after the first isocyanate moiety had reacted. This phenomenon was interpreted by the formation of hydrogen bonded ring that was confirmed by DFT calculation. Nevertheless, the reactivity of the second isocyanate moiety (after the first one has reacted) did not change significantly in the case of HMDI, only a slight negative substitution effect could be recognized, while for IPDI the trend, must likely due to steric hindrances, decreased considerably.

Published articles

1. Lajos Nagy, Miklós Nagy, Bence Vadkerti, Lajos Daróczi, György Deák, Miklós Zsuga, Sándor Kéki: Designed Polyurethanes for Potential Biomedical and Pharmaceutical Applications: Novel Synthetic Strategy for Preparing Sucrose Containing Biocompatible and Biodegradable Polyurethane Networks, Polymers 2019, 11(5), 825; DOI: 10.3390/polym11050825

2. Lajos Nagy, Bence Vadkerti, Gyula Batta, Péter Pál Fehér, Miklós Zsuga, Sándor Kéki: Eight out of Eight: A Detailed Kinetic Study on the Reactivities of the Eight Hydroxyl groups of Sucrose with Phenyl Isocyanate, New Journal of Chemistry 2019, DOI: 10.1039/C9NJ03569A

3. Lajos Nagy, Anett Juhász, Miklós Zsuga, Sándor Kéki: Uncatalyzed urethane forming reaction of 1,3-xylylene diisocyanate with aliphatic alcohols of varying chain lengths and polyols, eXPRESS Polymer Letters 2020, 14, 336; DOI: 10.3144/expresspolymlett.2020.28

4. Lajos Nagy, Ákos Kuki, Tibor Nagy, Bence Vadkerti, Zoltán Erdélyi, Levente Kárpáti, Miklós Zsuga, Sándor Kéki: Encoding Information into Polyethylene Glycol Using an Alcohol-Isocyanate “Click” Reaction, International Journal of Molecular Sciences 2020, 21, 1318; DOI: 10.3390/ijms21041318

5. Nagy L.; Vadkerti B.; Lakatos C.; Feher P.P.; Zsuga M.; Keki S.: Kinetically equivalent functionality and reactivity of commonly used biocompatible polyurethane crosslinking agents, International Journal of Molecular Sciences, 22(82), Article number 4059 (page: 19) (2021), doi: 10.3390/ijms22084059

6. Vadkerti, B., Juhász, A., Lakatos, C., Zsuga, M., Kéki, S., Nagy, L.: Reactivity of multi-arm polyols towards isocyanates, New Journal of Chemistry, 46(20), 9871-9879 (2022), doi: 10.1039/d2nj01103d

Under submission for publication

Anett Juhász, Uneri Haymana Serra, Csilla Lakatos, Bence Vadkerti, Anita Rágyanszki, Ödön Farkas, Sándor Kéki, Lajos Nagy: The kinetics of uncatalyzed and catalyzed urethane forming reaction of aliphatic diisocyanates with butan-1-ol (2023)

Conference presentation

1. Nagy Lajos, Nagy Tibor, Kuki Ákos, Oláh Réka, Lakatos Csilla, Zsuga Miklós, Kéki Sándor: A 2,6-toluilén-diizocianát alkoholokkal történő reakciójának kinetikai vizsgálata katalizátor nélkül és katalizátor jelenlétében XXIV. Nemzetközi Vegyészkonferencia, 2018. október 24-27.

2. CZIFRÁK Katalin, LAKATOS Csilla, ZSUGA Miklós, KÉKI Sándor: Poliuretán alapú vitrimerek előállítása és vizsgálata, XXV. Nemzetközi Vegyészkonferencia, Kolozsvár, Románia, 2019. Október 24-26.

3. KORDOVÁN Marcell, NAGY Lajos, NAGY Miklós, VADKERTI Bence, DARÓCZI Lajos, DEÁK György, ZSUGA Miklós, KÉKI Sándor: Új típusú poliuretánok előállítása szacharóz, 1,6-hexametilén, diizocianát (HMDI) és ε-kaprolakton felhasználásával, XXV. Nemzetközi Vegyészkonferencia, Kolozsvár, Románia, 2019. Október 24-26.

4. LAKATOS Csilla, CZIFRÁK Katalin, KOVÁCS István Gergő, ZSUGA Miklós, KÉKI Sándor: Poli(ω-pentadekalakton)-t tartalmazó poliuretánok előállítása és vizsgálata, XXV. Nemzetközi Vegyészkonferencia, Kolozsvár, Románia, 2019. Október 24-26.

5. VADKERTI Bence, NAGY Lajos, BATTA Gyula, FEHÉR Péter Pál, ZSUGA Miklós, KÉKI Sándor: A szacharóz reakciója fenil-izocianáttal, XXV. Nemzetközi Vegyészkonferencia, Kolozsvár, Románia, 2019. Október 24-26.

Poster

1. Lajos Nagy, Bence Vadkerti, Gyula Batta, Péter Pál Fehér, Miklós Zsuga, Sándor Kéki: Detailed kinetic study on the reactivities of the eight hydroxyl groups of sucrose in urethane

forming reaction (poszter), International Mass Spectrometry Conference (IMSC) Abstract Book, Maastricht, Hollandia (2022. 08.27.-09.02.)

2. Bence Vadkerti, Lajos Nagy, Ákos Kuki, Tibor Nagy, Zoltán Erdélyi, Levente Kárpáti, Miklós Zsuga, Sándor Kéki: Information coding by peg – aliphatic isocyanate reaction and decoding by MALDI-TOF MS (poszter), International Mass Spectrometry Conference (IMSC) Abstract Book, Maastricht, Hollandia (2022. 08.27.-09.02.)