

Short thesis for the degree of doctor of philosophy (PhD)

**Investigation of the Reactions of Polyols and Diisocyanates Using
Liquid Chromatography and Mass Spectrometry**

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Introduction and objectives

The use of plastics is extremely diverse, present in almost every area of our lives: in households, electronics, vehicles, healthcare, as well as in space exploration. Polyurethane (PU) plastics are among the most successful and versatile products on the global market. Their production occurs through the polyaddition reaction of polyisocyanates and polyols. Aliphatic and cycloaliphatic diisocyanates are isocyanates where the isocyanate functional group is attached to an aliphatic or cycloaliphatic carbon chain. Their main representatives include hexamethylene diisocyanate (HDI), isophorone diisocyanate (IPDI), and 4,4-dicyclohexylmethane diisocyanate (HMDI). Xylene diisocyanate (XDI) is positioned between aliphatic and aromatic diisocyanates in terms of its properties. The reactivity of aliphatic isocyanates is much lower than that of aromatic isocyanates. The polyurethanes made from them are characterized by excellent weather resistance, light stability, high temperature resistance, and a low yellow index. The utilization of these properties finds application in industries such as aviation, aerospace, solar energy, and other high-end manufacturing of railway and automotive equipment with such specific requirements.

Our goal was to study the reactions between HDI, IPDI, HMDI, XDI, alcohols, and polyols. Among the alcohols, we used low molecular weight alcohols (propanol, butanol, pentanol and hexanol), diethylene glycol monomethyl ether (DEGME), and methoxylated polyethylene glycol (mPEG) for the experiments. The reactions were carried out at different temperatures, and the activation energies were calculated from the obtained results. To monitor the reactions, mass spectrometry and liquid chromatography were used, providing qualitative and quantitative information about the product distribution. To support our experimental results and gain a deeper understanding of the reaction mechanisms, we performed theoretical (quantum chemical) calculations as well.

Applied methods and equipment

In my work, we investigated the kinetics of XDI reactions with alcohols of various alkyl chain lengths, mPEG, and PTHF. The temperature dependence of the reaction with aliphatic alcohols was studied in the range of 50-80 °C. We conducted the reactions of aliphatic diisocyanates (HDI, HMDI, IPDI) with butanol at different temperatures (50-80°C), both with and without catalysis, and with the use of tin(II) (2-ethylhexanoate) catalyst. The effect of catalyst concentration on the reaction was studied in the range of 0.001-0.005 M. To achieve pseudo-first-order kinetics, we used a large molar excess of alcohol compared to diisocyanates. Dried toluene was employed as the solvent and the reactions were carried out under a nitrogen atmosphere. The reaction was stopped at appropriate intervals by adding methanol to the reaction and samples were taken from the reaction mixture. Since aliphatic diisocyanates have no chromophore group suitable for UV absorption, thus, we used MS detection, instead. For quenching and monitoring the reactions by MS, we applied d₉-butyl alcohol. The reactions were followed using HPLC with a diode array detector (PDA) for XDI, and the samples were detected at $\lambda = 210$ nm. ESI-MS mass spectra for the reactions of HDI, HMDI, and IPDI were recorded using a MicrOTOF-Q QqTOF-MS system, and the data evaluation was performed using the DataAnalysis 3.4 software by Bruker. Our experimental results were also supported by quantum chemical calculations. Gaussian16 software was used for the calculations. Geometrical optimization was performed using the B3LYP method with the 6-31+G(d) basis set. Frequencies were calculated on the optimized structures to determine the thermodynamic properties of the reaction mechanism. To confirm the reaction energy profile, intrinsic reaction coordinate (IRC) calculations were applied to the transition state structures. All calculations were performed at 298.15 K, 1 atm pressure, and in toluene using the Polarizable Continuum Model (PCM) solvent model.

New scientific results

1. We determined the apparent (pseudo-first-order) rate constants and activation parameters for the reactions of 1,3-xylene diisocyanate with alcohols of different chain lengths. We found that the apparent rate constants ($k_{1,app}$ and $k_{2,app}$) for both isocyanate groups increased with the increasing number of carbon atoms in the alcohols.

We demonstrated that for alcohols from 1-propanol to 1-hexanol, both $k_{1,app}$ and $k_{2,app}$ values increased with the increasing number of carbon atoms. The ratio of $k_{1,app} / k_{2,app}$ remained close to 1, indicating that the completion of the first reaction did not affect the reactivity of the second isocyanate group.

By examining the temperature dependence of the reaction (Figure 1), we showed that the $k_{1,app}$ values increased approximately two to four times (and this was also true for $k_{2,app}$ values), which indicates relatively low activation energies for these urethane-forming reactions.

We concluded that the increase in k_{app} values with chain length can be explained by the fact that in a non-polar medium, such as toluene, the alcoholic OH-group is more accessible to the reacting isocyanate group because longer alkyl chains are more effectively solvated by the surrounding non-polar solvent molecules.

Table 1. Apparent (pseudo-first-order) rate coefficients for the reaction of 1,3-XDI with various alcohols

Apparent rate coefficients	Alcohol			
	1-propanol	1-butanol	1-pentanol	1-hexanol
$k_{1, app} \cdot 10^2 [\text{min}^{-1}]$	$1,66 \pm 0,02$	$1,87 \pm 0,02$	$2,19 \pm 0,03$	$3,41 \pm 0,05$
$k_{2, app} \cdot 10^2 [\text{min}^{-1}]$	$1,57 \pm 0,02$	$1,74 \pm 0,02$	$2,18 \pm 0,03$	$3,18 \pm 0,05$

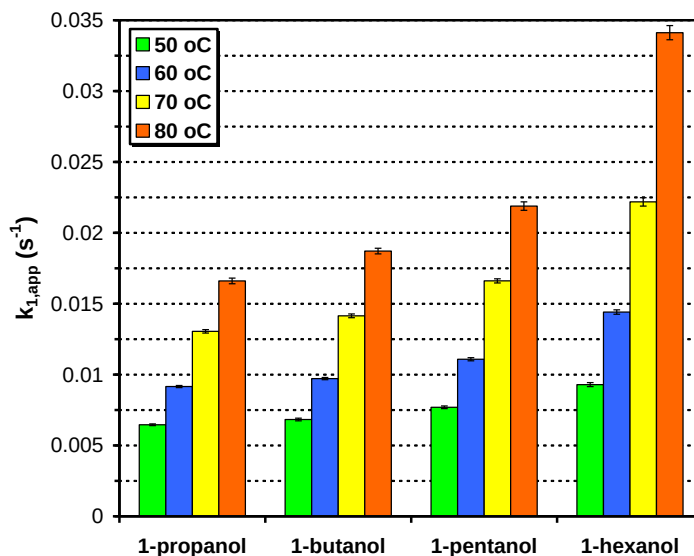


Figure 1. The change of the value of $k_{1,app}$ with the length of the alkyl chain and the temperature.

Experimental conditions: $[1,3\text{-XDI}]_0 = 0.01\text{ M}$, $[\text{Alcohol}]_0 = 0.65\text{ M}$

The kinetic data were evaluated using the logarithmic form of the Arrhenius equation, from which the apparent activation energies ($E_{a,app}$) and pre-exponential factors (A_{app}) were determined.

2. We established that the product distribution of the polymer-polyol-isocyanate reaction can be predicted using rate constants obtained from a much simpler system that mimics the corresponding polymer-polyol isocyanate reaction.

For modeling the reactions of 1,3-XDI and mPEG, we used DEGME to mimic the polymer polyol chain ends. By using the apparent rate constants obtained from the 1,3-XDI-DEGME reaction kinetics. We also demonstrated that the product distribution curves calculated with these apparent rate constants fit well with the experimental curves for the 1,3-XDI-mPEG reaction.

We determined the apparent rate constants, which are significantly smaller compared to those for alkyl chain alcohols. The lower reactivity of DEGME towards isocyanates is due to the inductive effect of the ether oxygen atom, which reduces the partial negative charge on the oxygen atom of the reacting OH group of DEGME.

We validated that the product distributions calculated from the kinetic data derived from DEGME matched well with the experimental results for the 1,3-XDI and mPEG reaction, confirming that the product distribution of a polymer-polyol system reaction can be predicted using the kinetic data of a simpler model compound.

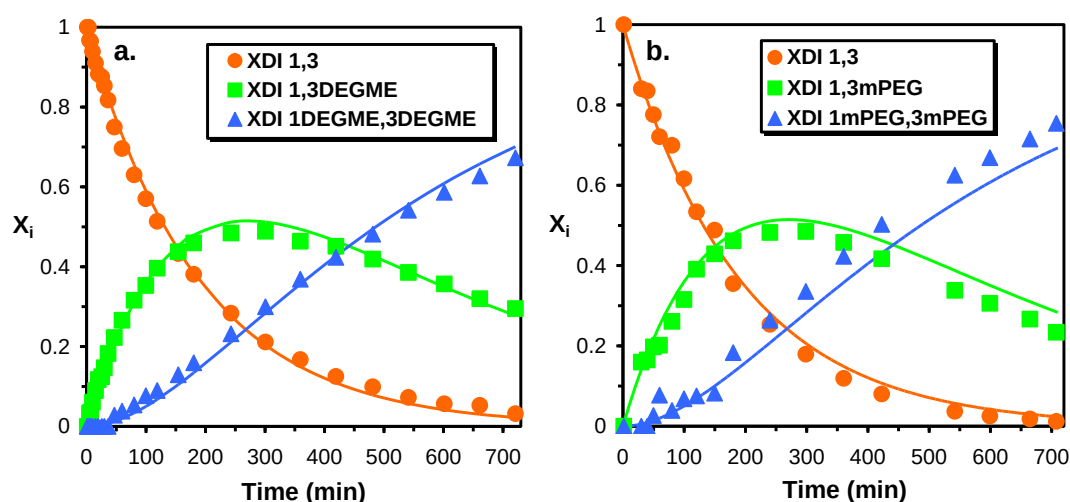


Figure 2. Product distributions as a function of reaction time for the reaction of 1,3-XDI with (a) DEGME and (b) mPEG (kinetic parameters used in the calculation were derived from the 1,3-XDI–DEGME reaction).

Experimental conditions: $[1,3\text{-XDI}]_0 = 0.01 \text{ M}$, $[\text{DEGME}]_0 = 0.65 \text{ M}$, $[\text{mPEG}]_0 = 0.65 \text{ M}$, $T = 80 \text{ }^\circ\text{C}$

3. We demonstrated that the products formed in the reaction of low molecular weight PTHF with 1,3-XDI can be separated by HPLC based on the number of repeating units of PTHF, and we confirmed that the apparent rate constants depend on the chain length.

The reaction of 1,3-XDI with PTHF resulted in products that were separated by HPLC according to the total number of repeating units in PTHF. First, the separated peaks were correspondingly summed to get molar fractions of non-reacted, mono-reacted, and di-reacted isocyanates. In the next step, we determined the distribution of all individual oligomer products based on UV absorption, using phenyl-isocyanate as the chromophore. Based on this, we concluded that in the case of mono-reacted diisocyanate products, the PTHF oligomers contained 2, 3, 4, and 5 repeating units, while in di-reacted diisocyanates, the reacted PTHF had 4, 5, 6, 7, 8, and 9 repeating units. We found that the obtained k_{app} values were smaller than those for alkyl chain alcohols, supporting further the fact that the presence of an oxygen atom reduces the reactivity of the reacting OH group.

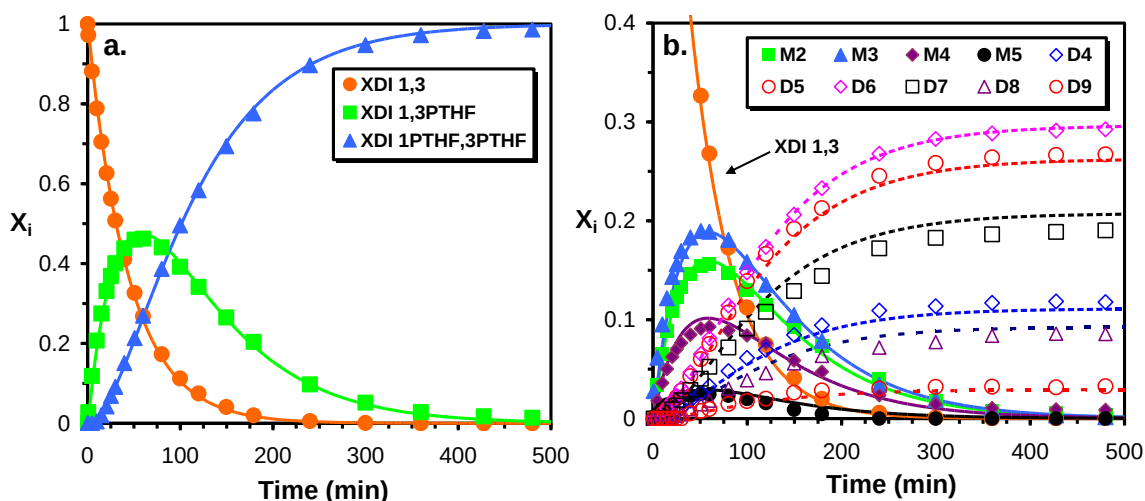


Figure 3. (a) Plots of the product distributions against time for the reaction between 1,3-XDI and PTHF using the sum of the oligomer HPLC peak area and (b) using the individual oligomer HPLC peak area.

Experimental conditions: $[1,3\text{-XDI}]_0 = 0.01 \text{ M}$, $[\text{PTHF}]_0 = 0.32 \text{ M}$, $T = 80 \text{ }^\circ\text{C}$

4. We determined the apparent rate constants and activation parameters of the uncatalyzed reactions of HDI, HMDI, and IPDI with butan-1-ol. Quantum chemical calculations confirmed that in the case of HDI, the higher reactivity of the isocyanate group can be attributed to the formation of ring structures involving N-H-N and N-H-O hydrogen bonds. We demonstrated that a linear correlation exists between the apparent rate constant and the concentration of the tin(II)-2-ethylhexanoate catalyst.

We proved that the ESI-MS intensity ratio of the mono- and di-reacted urethanes formed in reactions with d₉-butan-1-ol reflects the corresponding concentration ratios, making the method suitable for monitoring these reactions.

We confirmed that, based on the apparent rate constants ($k_{i,app}$), the reactivity order of the aliphatic diisocyanates is as follows: HMDI < IPDI < HDI < 1,3-XDI. In the case of IPDI, it was observed that following the reaction of the first isocyanate group, the reactivity of the second isocyanate group decreases, meaning that k_1 is greater than k_2 . In contrast, the opposite trend was observed for HDI: after the first reaction, the second isocyanate group becomes more reactive, i.e., k_1 is smaller than k_2 .

We revealed that for HDI, the increased reactivity of the second isocyanate group may be caused by the formation of ring structures stabilized by N-H-N and N-H-O hydrogen bonds and this effect was also confirmed by DFT calculations.

We established that the same trend (HMDI < IPDI < HDI) is valid in the presence of tin(II)-2-ethylhexanoate catalyst as in the uncatalyzed reactions. We investigated the effect of catalyst concentration on the reaction in the range of 0.001–0.005 M and demonstrated that a linear relationship exists between the apparent rate constant and the concentration of the tin(II)-2-ethylhexanoate catalyst.

Table 2. The pseudo first-order rate coefficients for the uncatalyzed reactions of HDI, HMDI and IPDI with butan-1-ol at different temperatures

Rate coefficient ($\text{M}^{-1}\text{min}^{-1}$) $\times 10^4$	HDI	HMDI	IPDI
50 °C			
k_1	$5,02 \pm 0,08$	$0,99 \pm 0,02$	$3,72 \pm 0,08$
k_2	$6,72 \pm 0,14$	$0,92 \pm 0,08$	$1,70 \pm 0,04$
60 °C			
k_1	$7,21 \pm 0,06$	$1,05 \pm 0,01$	$4,37 \pm 0,09$
k_2	$10,64 \pm 0,13$	$1,01 \pm 0,03$	$1,89 \pm 0,11$
70 °C			
k_1	$10,20 \pm 0,35$	$2,54 \pm 0,05$	$10,53 \pm 0,19$
k_2	$16,61 \pm 1,10$	$2,27 \pm 0,04$	$5,45 \pm 0,11$
80 °C			
k_1	$13,11 \pm 0,10$	$3,61 \pm 0,02$	$12,33 \pm 0,23$
k_2	$25,62 \pm 0,26$	$3,29 \pm 0,04$	$6,42 \pm 0,35$

5. Our experimental results were supported by quantum chemical calculations for the reactions of XDI, HDI, HMDI, and IPDI with butanol. We showed that among the concentric monobutanol, di-, and tributanol mechanisms, the experimentally determined activation energies are consistent with the results of the tributanol mechanism. We demonstrated that in the case of HDI, among the N–H–N and N–H–O bonds, the formation of N–H–N bond is energetically more favorable.

We established that in the case of XDI, HDI, HMDI, and IPDI, the energy barrier is too high for the concentric monobutanol mechanism.

We confirmed that the activation energies obtained for the di- and tributanol mechanisms are consistent with the experimentally determined values.

In the case of N–H–N and N–H–O cyclic transition states, we found that only with HDI do we approach the experimentally obtained values, and between the two mechanisms, the N–H–N pathway is energetically more favorable.

For IPDI, in agreement with our experimental observations, we demonstrated that the reactivity of the second isocyanate group is reduced compared to the first isocyanate group.

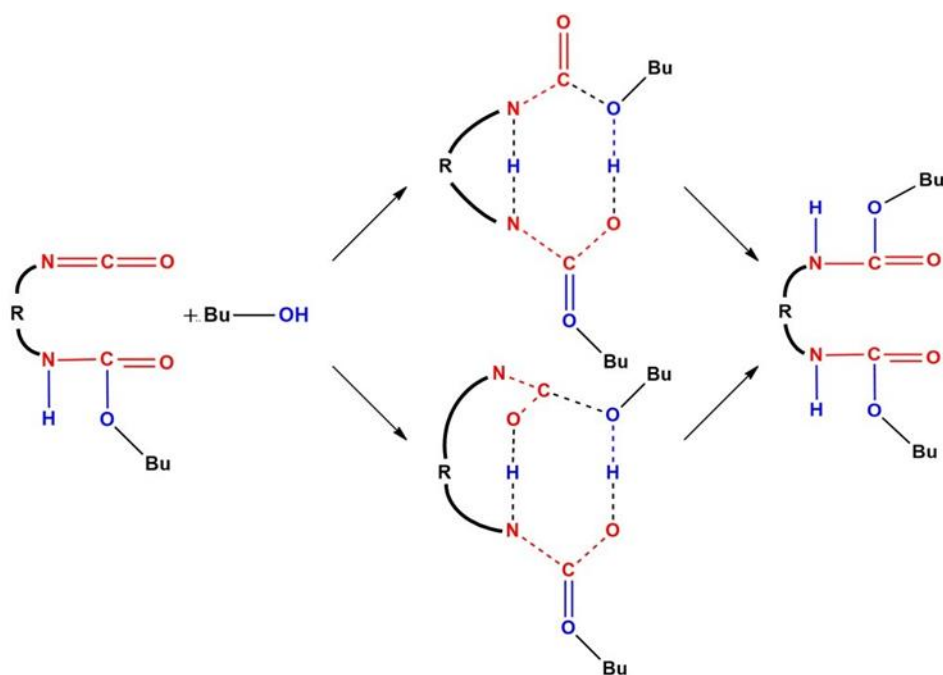


Figure 4. Structure of the intramolecular rings formed in the transition state during the reaction of the second isocyanate group (N–H–N ring, N–H–O ring)

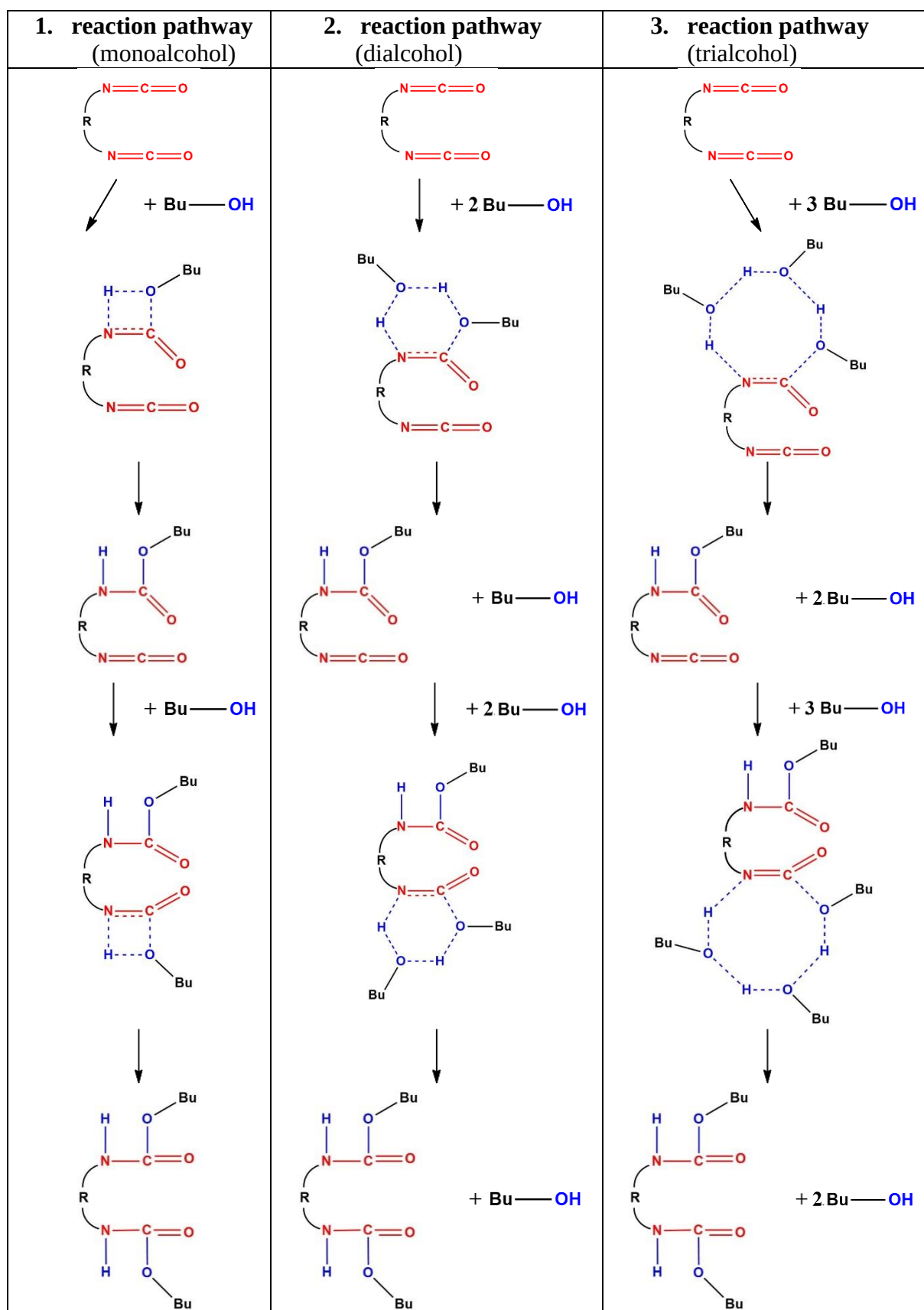


Figure 5. Urethane formation mechanisms investigated in our calculations

Possible application of the results

In polyurethane production, a deeper understanding of the reaction mechanisms and reactivity differences between various aliphatic and cycloaliphatic diisocyanates provides an opportunity to target the properties of the products more precisely. As a result, prepolymers with desired reactivity profiles can be produced, optimized for different processing conditions (e.g., temperature, time, viscosity). By considering the reactivity order, more selective reactions can be carried out, such as the synthesis of block copolymers or specific structures of crosslinked materials. The design of reactions with bio-based polyols also becomes predictable.

Moreover, this opens up possibilities for developing new, specialized application areas where precise reaction control is crucial. The emergence of aliphatic diisocyanates in biomedical materials is due to numerous advantages they offer, which aromatic diisocyanates cannot provide. They are characterized by lower toxic and allergenic effects, making them safer for medical applications. They are more flexible, more stable, and provide a more environmentally friendly alternative from a sustainability perspective.

Aliphatic diisocyanates also offer promising applications in the aerospace industry due to their many advantages in extreme environments. They are primarily useful in the production of polyurethane-based materials, composites, and coatings that require specific mechanical, thermal, and chemical resistance. They can be used for the insulation of spacecraft, lightweight and strong structural components for space probes and satellites, astronaut suits, and composites and coatings that can withstand the extreme conditions of outer space.

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List of publications related to the dissertation

Foreign language scientific articles in Hungarian journals (1)

1. Nagy, L., **Juhász, A.**, Zsuga, M., Kéki, S.: Uncatalyzed urethane forming reaction of 1,3-xylylene diisocyanate with aliphatic alcohols of varying chain lengths and polyols.
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Foreign language scientific articles in international journals (1)

2. **Juhász, A.**, Üneri, H. S., Lakatos, C., Vadkerti, B., Rágyanszki, A., Farkas, Ö., Kéki, S., Nagy, L.:
The kinetics of uncatalyzed and catalyzed urethane forming reactions of aliphatic diisocyanates with butan-1-ol.
New J. Chem. 47 (34), 16096-16107, 2023. ISSN: 1144-0546.
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List of other publications

Foreign language scientific articles in international journals (1)

3. Vadkerti, B., **Juhász, A.**, Lakatos, C., Zsuga, M., Kéki, S., Nagy, L.: Reactivity of multi-arm polyols towards isocyanates.
New J. Chem. 46, 9871-9879, 2022. ISSN: 1144-0546.
DOI: <https://doi.org/10.1039/D2NJ01103D>
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Hungarian abstracts (3)

4. Vadkerti, B., Lakatos, C., Üneri, H. S., Rágyanszki, A., Farkas, Ö., **Juhász, A.**, Zsuga, M., Kéki, S., Nagy, L.: Alifás diizocianátok és butan-1-ol reakcióinak kinetikai vizsgálata = Kinetic study of the reactions between aliphatic diisocyanates and butan-1-ol.
In: XXIX. Nemzetközi Vegyészkonferencia = 29th International Conference on Chemistry.
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5. Vadkerti, B., **Juhász, A.**, Lakatos, C., Zsuga, M., Kéki, S., Nagy, L.: Polimer poliolkok és fenil-izocianát reakcióinak kinetikai vizsgálata = Kinetic study of reactions of polymer polyols and phenyl-isocyanate.
In: XXVIII. Nemzetközi Vegyészkonferencia = 28th International Conference on Chemistry.
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6. Nagy, L., Vadkerti, B., **Juhász, A.**, Lakatos, C., Zsuga, M., Kéki, S.: Négy- és ötkarú polimer poliolkok reaktivitásának vizsgálata fenil-izocianát jelenlétében = Reactivity of four- and five-arm industrially important polymerpolyols in the presence of phenyl isocyanate.
In: XXVII. Nemzetközi Vegyészkonferencia = 27th International Conference on Chemistry.
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