

## New insight into the kinetics of diisocyanate-alcohol reactions by high-performance liquid chromatography and mass spectrometry

Tibor Nagy,<sup>1</sup> Borbála Antal,<sup>1</sup> Katalin Czifrák,<sup>1</sup> Ildikó Papp,<sup>1</sup> József Karger-Kocsis,<sup>2</sup> Miklós Zsuga,<sup>1</sup> Sándor Kéki<sup>1</sup>

<sup>1</sup>Department of Applied Chemistry, University of Debrecen, H-4032 Debrecen, Hungary

<sup>2</sup>Department of Polymer Engineering, Budapest University of Technology and Economics, H-1111 Budapest, Hungary

Correspondence to: S. Kéki (E-mail: keki.sandor@science.unideb.hu)

**ABSTRACT:** The uncatalyzed reactions of 2,4-TDI (2,4-toluenediisocyanate) and MDI (4,4'-diphenylmethane-diisocyanate) with alcohols including butan-1-ol, butan-2-ol, diethylene glycol monomethylether (DEGME) were studied by high-performance liquid chromatography (HPLC) and electrospray ionization mass spectrometry (ESI-MS). The reactions were carried out at different temperatures from 22°C to 75°C using high molar ratios of alcohols to diisocyanates. It was found that the first isocyanate group of the MDI reacts about 1.5 times faster with the alcohols than the second one. The relative reactivities of the isocyanate groups (para and ortho) of 2,4-TDI as a function of the temperature was also deduced. From the temperature dependence of the rate constants the apparent activation energies were determined. Furthermore, the dependence of the apparent rate constant on the concentration of alcohols was also investigated and a mechanism was proposed for the reaction of diisocyanates with alcohols. © 2015 Wiley Periodicals, Inc. *J. Appl. Polym. Sci.* **2015**, *132*, 42127.

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### INTRODUCTION

The reaction of diisocyanates with alcohols including polyether and polyester polyols is the key process for making polyurethanes with various chemical and mechanical properties.<sup>1</sup> Polyurethanes with broad range of composition and properties can be produced by selecting different isocyanates and polyols thereby varying the reaction conditions. Thus the urethane forming isocyanate-alcohol reaction is invaluable process for the polyurethane industry.<sup>2</sup> Nowadays polyurethanes are used in many areas spanning from foams of various types and coatings<sup>3</sup> to biomedical materials.<sup>4</sup> Recently, polyurethanes have also received considerable interest as shape-memory polymers<sup>5–8</sup> and constituents of self-healing polymers with semi-interpenetrating polymer networks.<sup>9</sup>

The isocyanate-alcohol reactions have been extensively studied from many points of view. The early investigation on this seemingly simple addition reaction was motivated by obtaining information on the reaction order for both the isocyanate and alcohol components. The works showed that the reaction is second order with first-order dependence with the concentration of both the isocyanate and alcohol species.<sup>10</sup> However, at certain

experimental conditions, deviation from the first-order dependence on alcohol concentration was observed. This effect was attributed to the autocatalysis by the reacting alcohol.<sup>11–14</sup> From practical point of view, it is not surprising, however, that many kinetic studies have focused on the reactions taking place between industrially important diisocyanates such as 4,4'-diphenylmethane-diisocyanate (MDI)<sup>15–23</sup> and toluene-diisocyanate (TDI)<sup>24–30</sup> and various alcohols. Moreover, these reactions were studied under very different experimental conditions including e.g. reaction temperature, solvent, reactant concentrations, molar ratios, in the absence or presence of a catalyst, etc. Thus, to compare the reactivities of different diisocyanates toward alcohols is a difficult task because of the lack of finding the same experimental conditions for the diisocyanates to be compared. Furthermore, various experimental tools ranging from dilatometry and titration of the free isocyanate groups<sup>11,22,24</sup> to instrumental methods including liquid chromatography,<sup>16</sup> UV-Vis and fluorescence spectroscopy<sup>17,19</sup> as well as FT-IR spectroscopy<sup>30</sup> are being used for monitoring the isocyanate-alcohol reactions.

In this report, the kinetics of the reactions of diisocyanates (MDI and 2,4-TDI) with alcohols such as butan-1-ol, butan-2-

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ol and diethylene glycol monomethylether (DEGME) performed at different temperatures were studied. These alcohols were applied in high molar ratio to the diisocyanates to provide pseudo-first order kinetics for diisocyanates. The experimental setup allowed the direct comparisons of the reactivities of MDI and 2,4-TDI toward alcohols. The selected alcohols were foreseen to mimic the chain-ends of polymers used in polyurethane chemistry and in the synthesis of polyurethane-based shape memory materials. Butan-1-ol closely resembles the chain-end of poly( $\epsilon$ -caprolactone)-diol, DEGME can mimic the reacting chain end of polyethylene glycol. Butan-2-ol is an appropriate model compound to compare the reactivity of the secondary OH group to that of the primary one on one hand, and to closely model the secondary OH group in glycerol used in making cross-linked polyurethane networks, on the other hand.

## EXPERIMENTAL

### Chemicals

4,4'-Diphenylmethane-diisocyanate (MDI), 2,4-toluenediisocyanate (2,4-TDI), butan-2-ol, diethylene glycol monomethylether (DEGME), acetonitrile (HPLC grade), and toluene were received from Sigma-Aldrich (Taufkirchen, Germany). Toluene was purified and dried according to the well-know procedure.<sup>31</sup> Butan-1-ol and methanol were purchased from Merck (Darmstadt, Germany) and WWR International (Leuven, Belgium), respectively and were used without further purification. Water was purified by a Direct-Q water system (Millipore, Molsheim, France).

### General Procedure for Performing the Reactions of Diisocyanates with Alcohols

Into a flask of 10 mL, dry toluene (5 mL) and calculated amount of diisocyanate (MDI or 2,4-TDI) were introduced under nitrogen atmosphere. The flask was thermostated at a predetermined temperature. After addition of the calculated amount of the corresponding alcohol (butan-1-ol, butan-2-ol, DEGME) the reaction mixture was further diluted with dry toluene to obtain a reaction volume of 10 mL. The initial concentrations of the diisocyanates and the alcohols were 0.01M and 0.65M, respectively. In the experiment aiming the investigation of the dependence of the reaction rate on the initial alcohol concentrations, the alcohol concentrations were varied in the range of 0.3 to 1.6M. For liquid chromatographic and mass spectrometric investigation, after predetermined time intervals, samples of 10  $\mu$ L were taken out from the reaction mixture and added to methanol to quench the unreacted isocyanate groups.

### High-Performance Liquid Chromatography (HPLC)

10  $\mu$ L sample from the solution made by diluting 10  $\mu$ L reaction mixture with methanol to 1000  $\mu$ L (HPLC sample) was injected into the chromatograph system consisting of a Waters 2695 Separations Module equipped with a thermostable autosampler (5°C) and a column module (40°C), a Waters 2996 Photodiode-array detector with a Agilent Zorbax SB-C18 column (4.6 75 mm, 3.5  $\mu$ m) (Agilent technologies, Palo Alto, CA). For the analysis of the products obtained in the reaction of MDI and 2,4-TDI with butan-1-ol and butan-2-ol the isocratic method with an eluent composition of acetonitrile/water (55/45 V/V) at a flow rate of 1.0 mL/min was applied. For the analysis of the reaction products obtained in the reaction of MDI and 2,4-TDI with DEGME iso-

cratic method with an eluent composition of acetonitrile/water (35/65 V/V and 30/70 V/V, respectively) at a flow rate of 1.0 mL/min were used. The separation of the 2,4-TDI isomers from the reaction mixture of 2,4-TDI and DEGME, obtained after quenching, was achieved using an isocratic eluent composition of acetonitrile/water (15/85 V/V) at a flow rate of 1.5 mL/min. The analytes were detected at 245 nm.

### Electrospray Quadrupole Time-of-Flight Mass Spectrometry (ESI-QTOF MS)

The MS measurements were performed with a MicroTOF-Q type Qq-TOF MS instrument (Bruker Daltonik, Bremen, Germany) using an ESI source with positive ion mode. The sample solutions were introduced directly into the ESI source with a syringe pump (Cole-Parmer Ins. Co., Vernon Hills, IL) at a flow rate of 3  $\mu$ L/min. The spray voltage was set to 4 kV. The temperature of the drying gas (N<sub>2</sub>) was kept at 180°C. The MS spectra were accumulated and recorded by means of a digitizer at a sampling rate of 2 GHz. The mass spectra were calibrated externally using the exact masses of the clusters generated from the electrosprayed solution of sodium trifluoroacetate (NaTFA). The recorded mass spectra were evaluated with the DataAnalysis 3.4 software from Bruker.

Samples for the ESI-QTOF MS measurement were prepared as follows: to a 5  $\mu$ L of HPLC sample (10  $\mu$ L reaction mixture diluted with methanol to 1000  $\mu$ L) 10  $\mu$ L sodium chloride solution (20 mM) was added to facilitate the formation of sodiated molecules under electrospray conditions and the mixture was further diluted with methanol to 1000  $\mu$ L.

### Evaluation of the Kinetic Measurements

The reaction steps of MDI with alcohols together with the products obtained after quenching of the reaction mixture with methanol are outlined in Scheme 1.

The corresponding ESI-MS intensities or the peak area obtained from LC-UV measurements were used to calculate the relative concentrations. Thus, the molar fractions of compounds A, B, and C [Scheme 1(b), Figure 1] that can be given by eqs. (1–3).

$$X_A = \frac{I_A}{I_A + I_B + I_C} \quad (1)$$

$$X_B = \frac{I_B}{I_A + I_B + I_C} \quad (2)$$

$$X_C = 1 - X_A - X_B \quad (3)$$

where  $I_A$ ,  $I_B$ , and  $I_C$  are the peak area or the ESI-MS intensity of A, B, and C determined by LC-UV or ESI-MS, respectively.

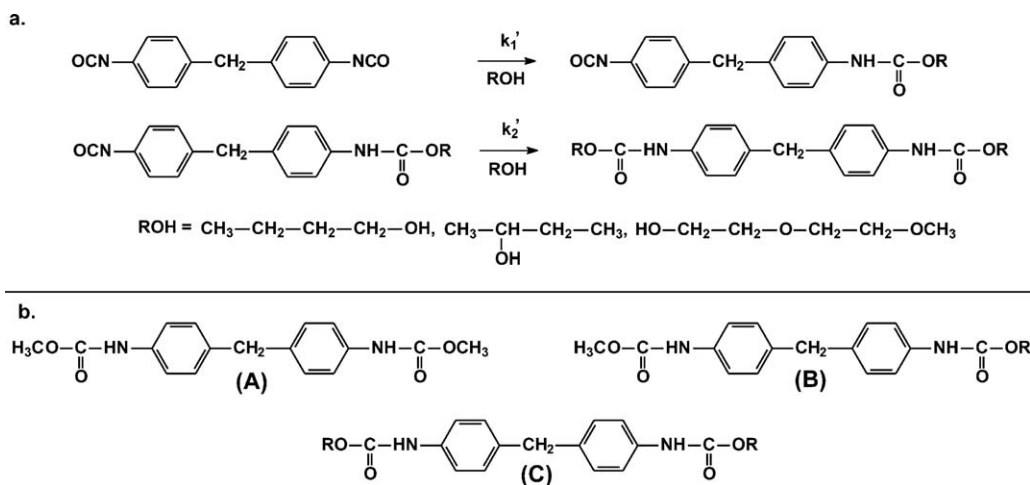
The dependence of the corresponding molar fractions on the reaction time can be expressed by eqs. (4–6), where  $k_1'$  and  $k_2'$  represent the pseudo first-order reaction rate constants.

$$X_A(t) = e^{-2k_1't} \quad (4)$$

$$X_B(t) = \frac{2k_1'}{k_2' - 2k_1'} (e^{-2k_1't} - e^{-k_2't}) \quad (5)$$

$$X_C(t) = 1 - X_A(t) - X_B(t) \quad (6)$$

The reaction path for the reaction of 2,4-TDI with alcohols together with products obtained after quenching are shown in Scheme 2.



**Scheme 1.** The reactions of MDI with alcohols (ROH) (a) and the products obtained after quenching the reaction mixture with methanol (b).

Similarly to the treatment of the MDI-alcohol systems, the corresponding ESI-MS intensities or the peak area obtained from LC-UV measurements were used to calculate, the molar fractions of compounds A, B, C, and D, indicated in Scheme 2(b) [eqs. (7–10)].

$$X_A = \frac{I_A}{I_A + I_B + I_C + I_D} \quad (7)$$

$$X_B = \frac{I_B}{I_A + I_B + I_C + I_D} \quad (8)$$

$$X_C = \frac{I_C}{I_A + I_B + I_C + I_D} \quad (9)$$

$$X_D = 1 - X_A - X_B - X_C \quad (10)$$

where  $I_A$ ,  $I_B$ ,  $I_C$ , and  $I_D$  are the peak area or the ESI-MS intensity of A, B, C, and D determined by LC-UV or ESI-MS, respectively.

Using the reaction scheme presented in Scheme 2, the dependence of the corresponding molar fractions, i.e., product distribution on the reaction time can be given by eqs. (11) to (14), where  $k_1'$ ,  $k_2'$ ,  $k_3'$ , and  $k_4'$  represent the pseudo first-order reaction rate constants.

$$X_A(t) = e^{-(k_1' + k_2')t} \quad (11)$$

$$X_B(t) = \frac{k_1'}{k_3' - k_1' - k_2'} \left[ e^{-(k_1' + k_2')t} - e^{-k_3't} \right] \quad (12)$$

$$X_C(t) = \frac{k_2'}{k_4' - k_1' - k_2'} \left[ e^{-(k_1' + k_2')t} - e^{-k_4't} \right] \quad (13)$$

$$X_D(t) = 1 - X_A(t) - X_B(t) - X_C(t) \quad (14)$$

For the fitting of the parameters of eqs. (4) to (6) and eqs. (11) to (14) to the experimental data a home-made parameter estimation software utilizing the Gauss–Newton–Marquardt procedure was used.<sup>32</sup> [The derivation of eqs. (7) to (14) can be found in the Supporting Information.]

## RESULTS AND DISCUSSION

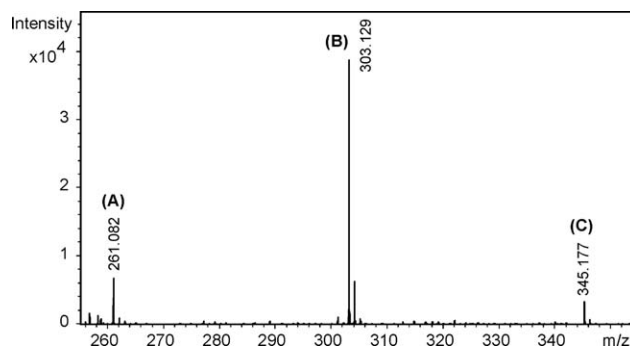
### Reactions of MDI with Alcohols

The ESI-MS spectrum of the quenched reaction mixture obtained from the MDI-butan-1-ol reaction at 55°C and after 12 min reaction time is presented in Figure 1.

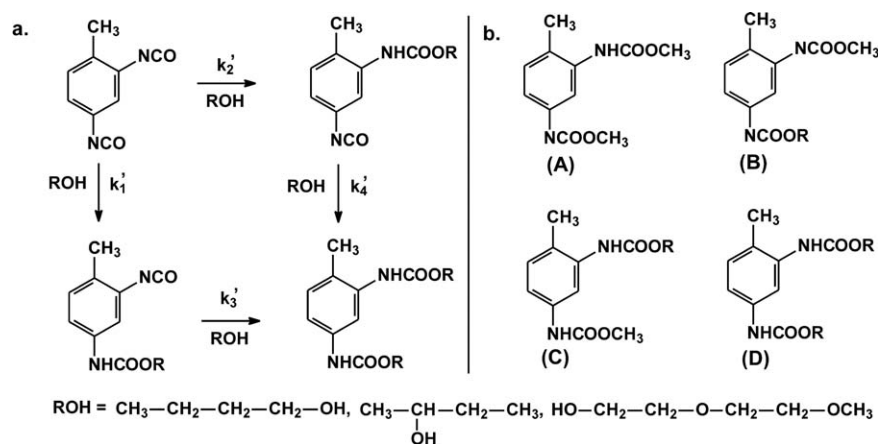
Owing to the mass differences between the methanol and butan-1-ol, the products of the reaction mixture obtained after quenching by methanol can clearly be distinguished (see Figure 1).

In eqs. (1) to (3) it is assumed that all of the three compounds have very similar molar absorption coefficients ( $\epsilon$ ), i.e.,  $\epsilon_A \approx \epsilon_B \approx \epsilon_C$  and possess identical ionization efficiencies in ESI-MS. This is a reasonable assumption considering the very similar structures of A, B, and C (all of the three contain urethane bonds). Indeed, when the sum of peak areas for A, B, and C is plotted as a function of the reaction time no significant change in the sum of peak areas was observed. Hence, this finding indicates very similar molar absorption coefficients for A, B, and C, otherwise changes in the sum of peak areas should have occurred. Furthermore, the molar fractions calculated based on the corresponding ESI-MS intensities and peak areas by LC-UV are in very good agreement as it can be seen in Figure 2.

The observation that the molar fractions obtained from the LC-UV data are very similar to those calculated by using the ESI-MS intensities is valid for all of the three MDI-alcohol systems investigated. To describe the variations of the molar fractions of compounds A, B and as a function of time a consecutive kinetic scheme presented in Scheme 1(a) was applied.



**Figure 1.** ESI-MS spectrum of the reaction mixture obtained from the reaction of MDI with butan-1-ol after reaction time of 12 min. Experimental conditions:  $[\text{MDI}]_0 = 0.01\text{M}$  and  $[\text{butan-1-ol}]_0 = 0.65\text{M}$  and  $T = 55^\circ\text{C}$ .

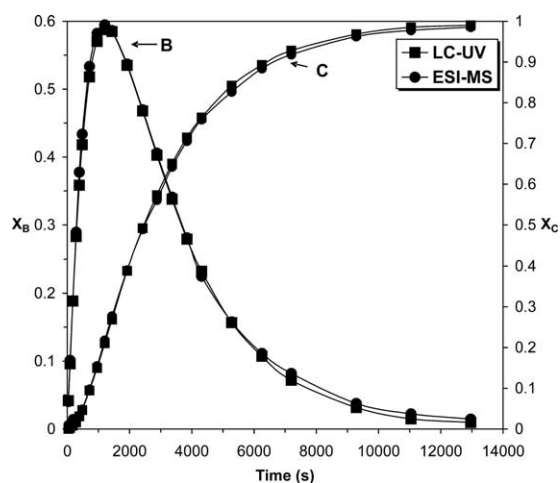


**Scheme 2.** The reactions of 2,4-TDI with alcohols (ROH) (a) and the products obtained after quenching the reaction mixture with methanol (b).

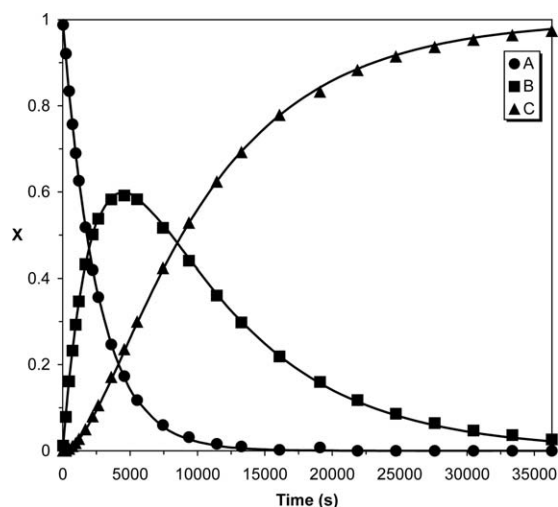
To test the validity of the consecutive kinetic scheme presented in Scheme 1(b) and to determine the values of  $k_1'$  and  $k_2'$ , eqs. (4) to (6) were fitted to the experimental molar fraction versus reaction time data. As an example, Figure 3 shows the result of such a fit.

As seen in Figure 3, the experimental molar fraction versus time curves can be well described using eqs. (4) to (6). It is important to note that all kinetic curves for the MDI-alcohol reactions obey eqs. (4) to (6) and the values of  $k_1'$  and  $k_2'$  determined by LC-UV are very close to those obtained from ESI-MS measurements. However, the values of  $k_2'$  are lower than those of  $k_1'$  by a factor of approximately 1.5. This finding is valid for all the MDI-alcohol reactions investigated. For example, the values of  $k_1'/k_2'$  for the reactions of MDI with butan-1-ol, butan-2-ol, and DEGME at 55°C were determined to be 1.53, 1.69, and 1.58, respectively. The fact that the value of  $k_2'$  is lower than that of  $k_1'$  suggest that the reaction of the second isocyanate group with alcohols proceeds slower after the first isocyanate group has been reacted. Theoretically, it can be

expected that the reactivity of the first isocyanate group, and the isocyanate group remained after the first isocyanate group has been reacted, are equal since no transmission of electronic effect of the formed urethane group toward the remaining isocyanate group may be possible due to the isolated electronic system by the methylene group. However, previous experimental works, published on MDI-alcohol reactions, delivered contradictory results with respect of the values of  $k_1'$  to  $k_2'$ . Huang *et al.*<sup>17</sup> and Sun and Sung<sup>19</sup> found that  $k_1'/k_2' \approx 1$ , which is in good agreement with the theoretical expectation. Other authors<sup>16,23</sup> reported a value of approximately 1.5 for  $k_1'/k_2'$  which is in accordance with our present results. It may be argued that the higher values of the  $k_1'/k_2'$  ratio in our case are due to the assumption made for the molar absorption and ionization efficiencies. However, the validity of this assumption has been checked experimentally as outlined before. Another possible explanation for this discrepancy would be the presence of side



**Figure 2.** Comparison of the ESI-MS and LC-UV results for the product distributions versus reaction time obtained in the MDI-1-butanol reaction at 45°C. Initial concentrations:  $[MDI]_0 = 0.01M$  and  $[butan-1-ol]_0 = 0.65M$ .



**Figure 3.** Variation of the product distributions with the reaction time in the MDI-butan-2-ol reaction at 45°C determined by LC-UV measurements. The solid lines represent the fitted curves using eqs. (4) to (6). Initial concentrations:  $[MDI]_0 = 0.01M$  and  $[butan-2-ol]_0 = 0.65M$ . The fitted parameters are  $k_1' = 1.9 \times 10^{-4} s^{-1}$  and  $k_2' = 1.2 \times 10^{-4} s^{-1}$ .



**Table I.** Apparent Activation Energies for the MDI-Alcohol Reactions Determined by LC-UV and ESI-MS

Alcohol	LC-UV		ESI-MS	
	$E_{a,1}$	$E_{a,2}$	$E_{a,1}$	$E_{a,2}$
Butan-1-ol	$20.5 \pm 2.8$	$23.3 \pm 1.7$	$20.7 \pm 3.0$	$23.5 \pm 0.82$
Butan-2-ol	$25.4 \pm 1.0$	$26.0 \pm 0.1$	$23.5 \pm 3.5$	$23.6 \pm 1.4$
DMGE	$33.1 \pm 0.8$	$36.5 \pm 1.9$	$34.2 \pm 2.3$	$35.2 \pm 1.5$

Activation energies are given in kJ/mol units.

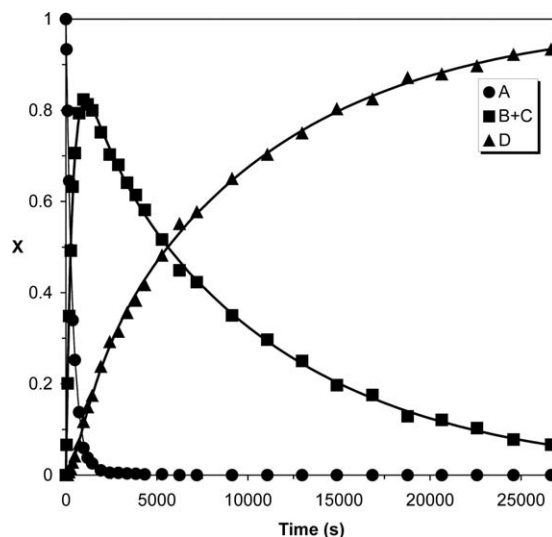
reaction(s) in the MDI-alcohol systems.<sup>1</sup> However, based on the LC-UV and ESI-MS investigation of the reaction products we could not find any experimental proof for the side reactions occurring at significant level under our experimental conditions. Based on our kinetic investigations it can be established that MDI reacts with butan-2-ol approximately three times, while with DEGME 13 times slower than with butan-1-ol. The fact that the MDI-butanol reaction proceeds three times faster than the MDI-butanol-2 reaction is in line with the observations published earlier.<sup>18</sup> From the temperature dependence of  $k_1'$  and  $k_2'$  the apparent activation energies were also determined. The values of the apparent activation energies determined from LC-UV and ESI-MS measurement are compiled in Table I.

As it turns out from the data of Table I, the apparent activation energies calculated from LC-UV data are very similar to those determined by ESI-MS which is not surprising in light of the fact that molar fraction curves by LC-UV and ESI-MS practically match each other (cf. Figure 2). On the other hand, slightly higher apparent activation energies were obtained for the reaction of the second isocyanate group, and the apparent activation energy for the MDI-alcohol reaction increase in the order of butan-1-ol < butan-2-ol < DEGME. The apparent activation energy obtained for the MDI-butanol reaction is about 20 kJ/mol. This value is close to those obtained by Huang *et al.* (17 kJ/mol)<sup>17</sup> and Sun and Sung (13 kJ/mol).<sup>19</sup> (The pseudo first-order rate constant values for the MDI-alcohol reactions can be found in the Supporting Information.)

## REACTIONS OF 2,4-TDI WITH ALCOHOLS

The reactions of 2,4-TDI with alcohols were performed using the same initial reactant concentrations as for the MDI-alcohol systems. This allows us a direct comparison of diisocyanate reactivities toward alcohols. It is noteworthy that the 2,4-TDI-alcohol reaction represents a more complicated kinetic situation compared with the MDI-alcohol since, unlike MDI, the reactivity of the two isocyanate groups in 2,4-TDI is different. To simplify the kinetic scheme the reactivities of the two isocyanate groups in 2,4-TDI have been regarded identical in some reports. It is now widely accepted, however, that the two isocyanate groups should be considered with different reactivities.<sup>1,2</sup>

It is also assumed in eqs. (7) to (10), similarly to those presented for the MDI-alcohol systems, that all of the four compounds have very similar molar absorption coefficients ( $\epsilon$ ), i.e.,  $\epsilon_A \approx \epsilon_B \approx \epsilon_C \approx \epsilon_D$  and possess identical ionization efficiencies



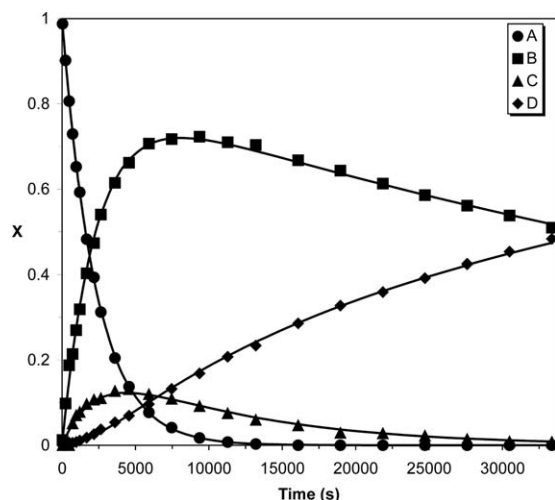
**Figure 4.** Product distributions versus reaction time in the 2,4-TDI-butanol-1-ol reaction at 55°C determined by ESI-MS measurements. The solid lines represent the fitted curves using eqs. (11) to (14). Initial concentrations:  $[2,4\text{-TDI}]_0 = 0.01\text{M}$  and  $[\text{butan-1-ol}]_0 = 0.65\text{M}$ . The fitted parameters are  $k_1' = 2.2 \times 10^{-3} \text{ s}^{-1}$ ,  $k_2' = 4.9 \times 10^{-4} \text{ s}^{-1}$ ,  $k_3' = 9.6 \times 10^{-5} \text{ s}^{-1}$  and  $k_4' = 7.2 \times 10^{-4} \text{ s}^{-1}$ .

in ESI-MS. On the other hand, this is proved indirectly through the comparison of LC-UV and ESI-MS results (see later). As an example, the product distributions for the 2,4-TDI reaction-butanol-1-ol reaction at 55°C as determined by ESI-MS together with the fitted curves to the experimental data using eqs. (7) to (14) are depicted in Figure 4.

It should be noted, however, that in the case of compound B and C only the sum of the molar fractions of B and C can be determined by mass spectrometry since B and C have the same mass, thus these two compounds are indistinguishable from each other by their masses. Because our effort to separate B and C by LC has failed, thus the compounds B and C formed in the 2,4-TDI-butanol-1-ol and 2,4-TDI-butanol-2-ol reactions were co-eluted under HPLC conditions. However, we succeeded to separate B and C obtained from the 2,4-TDI-DEGME reaction. The product distributions for the 2,4-TDI-DEGME reaction at 75°C, as determined by LC-UV, together with the fitted curves of the molar fractions of A, B, C, and D to the experimental values using eqs. (7) to (14) are depicted in Figure 5.

As seen in Figures 4 and 5, eqs. (7) to (14) adequately describes the kinetics of 2,4-TDI-alcohol reactions. Furthermore, in the cases where B and C are not resolved or separated the corresponding rate constants can still be determined. From the dependence of the rate constants  $k_1'$ ,  $k_2'$ ,  $k_3'$ , and  $k_4'$  on the temperature using the Arrhenius plots, i.e., the  $\ln k$  versus  $1/T$  plots, the corresponding apparent activation energies were determined. The Arrhenius plots for the 2,4-TDI-DEGME reaction are shown in Figure 6. The apparent activation energies for the reactions of 2,4-TDI with butan-1-ol, butan-2-ol and DEGME determined by ESI-MS and LC-UV are summarized in Table II.

According to the data of Table II, the apparent activation energies determined by LC-UV are very similar to those obtained by



**Figure 5.** Product distributions versus reaction time in the 2,4-TDI-DMGE reaction at 75°C determined by LC-UV measurements. The solid lines represent the fitted curves using eqs. (11) to (14). Initial concentrations:  $[2,4\text{-TDI}]_0 = 0.01M$  and  $[\text{DMGE}]_0 = 0.65M$ . The fitted parameters are  $k_1' = 3.5 \times 10^{-4} \text{ s}^{-1}$ ,  $k_2' = 8.3 \times 10^{-5} \text{ s}^{-1}$ ,  $k_3' = 1.4 \times 10^{-5} \text{ s}^{-1}$ , and  $k_4' = 1.0 \times 10^{-5} \text{ s}^{-1}$ .

ESI-MS. Furthermore, the reaction of the *para*-isocyanate group requires the lowest activation energy, while that of *ortho*-isocyanate group proceeds via a higher activation energy path for all of the alcohols investigated. These findings are in line with the observations that in the beginning of the reaction a relative fast decrease in the concentration or in the molar fraction of 2,4-TDI can be observed. Further reactions can take place with lower reaction rates resulting in the initial accumulation of the *para*-carbamate derivative (denoted by B after quenching with methanol, see Scheme 2). From the rate constants  $k_1'$ ,  $k_2'$ ,  $k_3'$ , and  $k_4'$  and their temperature dependences, the relative reactivities of the isocyanate groups in different positions as a function of the temperature can also be deduced. The ratio of  $k_1'/k_2'$  gives the relative reactivity of the *para*-isocyanate to the *ortho*-isocyanate group, the ratio of  $k_2'/k_3'$  indicates the relative reactivity of the *ortho*-isocyanate groups when the *para*-isocyanate group is unreacted to the case when it has been reacted (i.e., after carbamate formation), the ratio  $k_1'/k_4'$  informs us on the relative reactivity of *para*-isocyanate groups similarly to the latter case. The ratios of  $k_1'/k_2'$ ,  $k_2'/k_3'$ , and  $k_1'/k_4'$  for the corresponding 2,4-TDI-alcohol reaction as a function of the temperature are plotted in Figure 7.

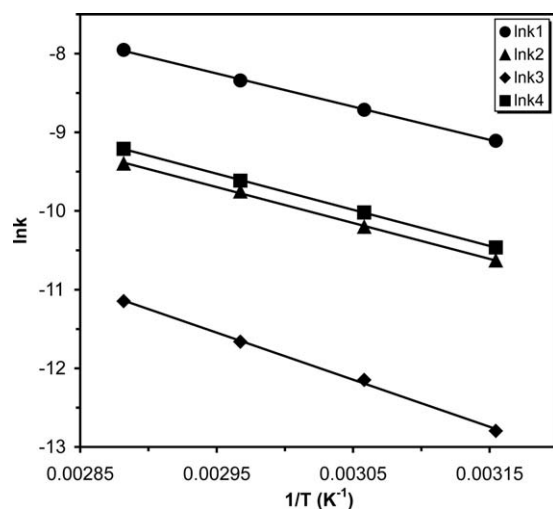
Figure 7(a) reveals that for the 2,4-TDI-DEGME reaction the *para*-isocyanate group is approximately four times more reactive than the *ortho*-isocyanate group and the reactivity ratio is closely independent of the temperature. Moreover, in the case of 2,4-TDI-butan-1-ol and 2,4-TDI-butan-2-ol reactions the reactivity ratios show slight temperature dependences and the reactivity ratios vary approximately between 6 and 3 in the temperature range of 22 to 75°C. Furthermore, according to Figure 7(b), the reactivity of the *ortho*-isocyanate group decreases considerable after the *para*-isocyanate group has been reacted. The ratios  $k_2'/k_3'$  for the 2,4-TDI-butan-1-ol reaction were found to

be about 4 independently of the reaction temperature, while these values show moderate temperature dependence with values of  $k_2'/k_3'$  in the range of 5 to 9 and 9 to 6 for the 2,4-TDI-butan-2-ol and 2,4-TDI-DEGME reactions, respectively. The reactivity of the *para*-isocyanate group decreases also after the *ortho*-isocyanate group has been reacted [Figure 7(c)] similarly to the previous case, however, the decrease in the reactivity after carbamate formation is lower compared with the case when carbamate formation takes place in the *ortho*-position. The values of  $k_1'/k_4'$  show no significant temperature dependence for all the 2,4-TDI-alcohol reactions and the related values are between 3 and 4 [Figure 7(c)]. The facts that the *para*-isocyanate group is more reactive than the *ortho* one, and after carbamate formation the reactivity of the second isocyanate group decreases, are in concert with findings of previous investigations.<sup>24,26,27</sup> These observations can be rationalized as follows: the methyl group, due to its electronic and steric effect, deactivates the isocyanate group in the *ortho*-position more effectively than the one in the *para*-position. On the other hand, a replacement of an isocyanate group by a carbamate one decreases the reactivity of the other isocyanate group since the carbamate group less is electron-pulling substituent than the isocyanate group. This makes the isocyanate group less susceptible for nucleophilic additions with alcohols. (The pseudo first-order rate constant values for the 2,4-TDI-alcohol reactions can be found in the Supporting Information.)

#### Comparison of the Reactivities of Diisocyanates Toward Alcohols

According to our kinetic investigations carried out under identical experimental conditions the following issues can be established for the reactions of diisocyanates toward alcohols. (i) The first isocyanate group (in the *para*-position) of the 2,4-TDI, depending on the reaction temperature and the reacting alcohol, reacts 2.5-3.3 times faster than that of the MDI as shown in Figure 8.

This finding is most probably due to the manifestation of the electron-pulling effect of the *ortho*-isocyanate group making the



**Figure 6.** The  $\ln k$  versus  $1/T$  plots for the 2,4-TDI-DMGE reaction (determined by LC-UV measurements).

**Table II.** Apparent Activation Energies for the 2,4-TDI-Alcohol Reactions Determined by LC-UV and ESI-MS

Alcohol	LC-UV				ESI-MS			
	$E_{a,1}$	$E_{a,2}$	$E_{a,3}$	$E_{a,4}$	$E_{a,1}$	$E_{a,2}$	$E_{a,3}$	$E_{a,4}$
Butan-1-ol	16.8 ± 1.1	25.0 ± 2.3	28.1 ± 0.9	15.4 ± 2.1	17.7 ± 1.3	28.4 ± 1.3	29.4 ± 1.2	14.5 ± 5.3
Butan-2-ol	23.6 ± 2.0	43.5 ± 1.5	24.2 ± 2.2	18.5 ± 3.2	28.0 ± 3.5	34.5 ± 3.8	26.3 ± 3.1	19.1 ± 8.3
DMGE	35.2 ± 0.6	38.2 ± 0.8	49.6 ± 2.1	38.6 ± 0.5	30.6 ± 3.7	46.9 ± 3.9	44.6 ± 7.5	<sup>a</sup>

Activation energies are given in kJ/mol units.

<sup>a</sup>Due to the long reaction time and the relative large scattering in the values of  $k_4'$ ,  $E_{a,4}$  could not be accurately determined by ESI-MS.

*para*-isocyanate group in 2,4-TDI more electrophilic toward alcohols with respect to MDI. For the latter the isocyanate group has less influence on the other isocyanate due to the well-separated electronic structure within the MDI. The reaction of the second isocyanate group, after the first one has been reacted, proceeds slowly with respect to that of the first one, bringing about 20 to 30 times decrease in the effective reactivities, i.e., in the values of  $k_1'/k_3'$ . (ii) The reactivities of both the 2,4-TDI and MDI toward alcohols decrease in the order of butan-1-ol > butan-2-ol > DEGME. This reactivity order can be rationalized by considering that the secondary alcohol is less nucleophilic compared with the primary one, and the ether groups in DEGME add an additional electron-pulling effect on the reactive OH group decreasing its nucleophilicity.

#### Dependence of the Apparent Rate Constant on the Concentration of the Alcohol

We were also interested to determine the dependence of the apparent rate constant on the alcohol concentration. For this reason, the concentrations of the alcohols were varied in a way (i) to maintain high stoichiometric molar ratios of alcohols to diisocyanates and to avoid high alcohol concentration to suppress significant changes in the dielectric constant of the alcohol-toluene mixtures. Note that the latter may affect the rate of the reaction via the well-known Kirkwood relationship.<sup>33</sup> Therefore, the set alcohol concentration range spanned from 0.3M to 1.3M. To simplify the kinetic investigations our attention was focused especially on the consumption of the diisocyanates. Therefore, the effect of the alcohol concentration on the

values of  $k_1'$  and  $k_1' + k_2'$  was thoroughly studied for MDI and 2,4-TDI, respectively. Figure 9 shows the dependence of the apparent rate constant ( $k_{app}$ ) on the alcohol concentration in the MDI versus butan-1-ol, butan-2-ol and DEGME reactions at 45°C.

Fitting power functions to the data of Figure 9(a) the powers for the alcohol concentrations were calculated to be 1.61, 1.72, and 1.86 for the butan-1-ol, butan-2-ol, and DEGME, respectively. These observations suggest that reaction orders for the alcohols are between the first and the second one. Hence, these findings indicate complex dependences of  $k_{app}$  on the alcohol concentration such as the one presented by eq. (15).

$$k_{app} = \frac{a[\text{ROH}]_o^2}{b + [\text{ROH}]_o} \quad (15)$$

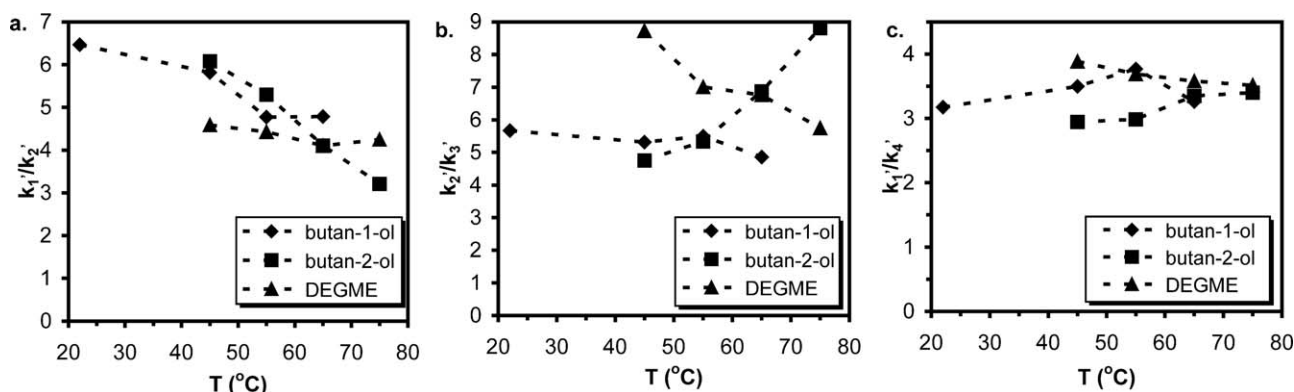
After rearrangement of eq. (15), eq. (16) turns to be:

$$\frac{k_{app}}{[\text{ROH}]_o} = \frac{b}{a} \frac{1}{[\text{ROH}]_o} + \frac{1}{a} \quad (16)$$

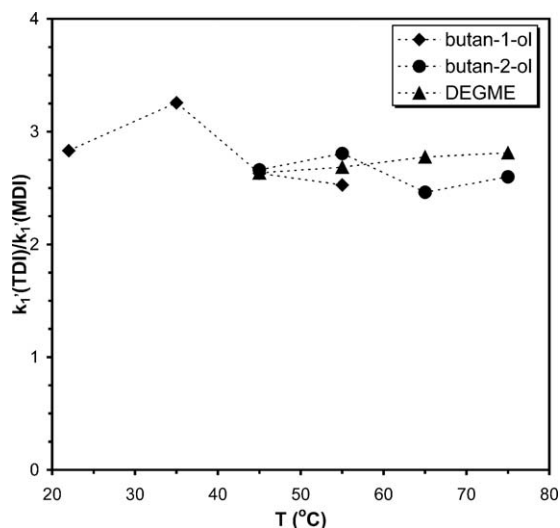
In fact, by plotting  $k_{app}/[\text{ROH}]_o$  as a function of  $[\text{ROH}]_o^{-1}$ , linear relationships were obtained as displayed in Figure 9(b).

The dependence of  $k_{app}$  on the  $[\text{ROH}]_o$  is consistent with the mechanism proposed by Baker and Gaun,<sup>11</sup> and it is presented in Scheme 3. Next we attempt to extend this mechanism to include the uncatalyzed reaction, too.

Assuming steady-states for  $[(^2)\text{OCNR}_1\text{NCO-ROH}]$  and  $[(^1)\text{OCNR}_1\text{NCO-ROH}]$  eq. (17) can be obtained:



**Figure 7.** Variations of the values of  $k_1'/k_2'$  (a),  $k_2'/k_3'$  (b) and  $k_1'/k_4'$  (c) in the 2,4-TDI-alcohol reactions as a function of the temperature.

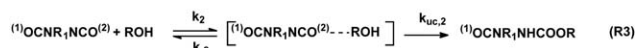
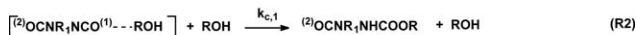
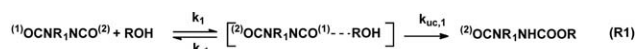


**Figure 8.** Dependence of the values of the ratio  $k_1'(2,4\text{-TDI})/k_1'(\text{MDI})$  on the reaction temperature and the alcohol used, where  $k_1'(2,4\text{-TDI})$  and  $k_1'(\text{MDI})$  stand for the pseudo first-order rate constant for the reaction of alcohols with the first isocyanate group of 2,4-TDI and with that of the MDI, respectively.

$$k_{\text{app}} = \frac{k_1 k_{\text{uc},1} [\text{ROH}]_0}{k_{\text{uc},1} + k_{-1} + k_{\text{c},1} [\text{ROH}]_0} + \frac{k_2 k_{\text{uc},2} [\text{ROH}]_0}{k_{\text{uc},2} + k_{-2} + k_{\text{c},2} [\text{ROH}]_0} + \frac{k_1 k_{\text{c},1} [\text{ROH}]_0^2}{k_{\text{uc},1} + k_{-1} + k_{\text{c},1} [\text{ROH}]_0} + \frac{k_2 k_{\text{c},2} [\text{ROH}]_0^2}{k_{\text{uc},2} + k_{-2} + k_{\text{c},2} [\text{ROH}]_0} \quad (17)$$

where  $k_{\text{uc},1}$  and  $k_{\text{c},1}$  are the rate constant for the uncatalyzed and catalyzed reactions for the first (more reactive) isocyanate group, respectively, while  $k_{\text{uc},2}$  and  $k_{\text{c},2}$  are the rate constant for the uncatalyzed and catalyzed reactions for the second (less reactive) isocyanate group, respectively.

In the case of MDI, the two isocyanate groups have equal reactivity, hence  $k_1 = k_2$ ,  $k_{-1} = k_{-2}$ ,  $k_{\text{uc},1} = k_{\text{uc},2}$  and  $k_{\text{c},1} = k_{\text{c},2}$ . Furthermore, if  $k_{\text{uc},1} \ll k_{\text{c},1} [\text{ROH}]_0$  and  $k_{\text{uc},1} \ll k_{-1}$  are valid in the applied alcohol concentration range, then eq. (17) reduces to eq. (18).



**Scheme 3.** Proposed reaction paths for the reaction of diisocyanates with alcohols.

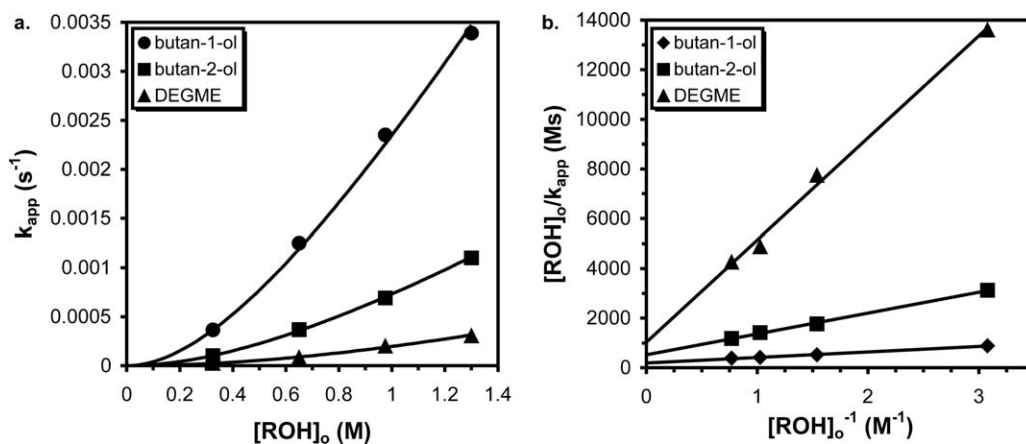
$$k_{\text{app}} \approx \frac{2k_1 k_{\text{c},1} [\text{ROH}]_0^2}{k_{-1} + k_{\text{c},1} [\text{ROH}]_0} \quad (18)$$

Comparing eq. (18) with eq. (17) note that  $a = 2k_1$  and  $b = k_{-1}/k_{\text{c},1}$ . It was found that eq. (18) [and eq. (17)] are capable of describing the dependence of  $k_{\text{obs}}$  on the  $[\text{ROH}]_0$  and that  $k_1$  decreases, while  $k_{-1}/k_{\text{c},1}$  increases in the order of butan-1-ol, butan-2-ol, DEGME. For example,  $2k_1$  values determined for the MDI-alcohol reactions are  $4.9 \times 10^{-3}$ ,  $1.9 \times 10^{-3}$ , and  $1.0 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$ , while values of  $k_{-1}/k_{\text{c},1}$  are 1.1, 1.6, and  $4.2M$  for the butan-1-ol, butan-2-ol, and DEGME, respectively. Similar dependences and tendencies were observed for the 2,4-TDI-alcohol reactions. However, in the case of 2,4-TDI the reactivities of the two isocyanate groups are not equal, the isocyanate group in the *para*-position reacts four to five times faster than the one in the *ortho*-position as we have shown earlier. Assuming similar conditions for the rate constant of 2,4-TDI-alcohol reaction as for those of the MDI-alcohol we get eq. (19).

$$k_{\text{app}} = \frac{k_1 k_{\text{c},1} [\text{ROH}]_0^2}{k_{\text{uc},1} + k_{-1} + k_{\text{c},1} [\text{ROH}]_0} + \frac{k_2 k_{\text{c},2} [\text{ROH}]_0^2}{k_{\text{uc},2} + k_{-2} + k_{\text{c},2} [\text{ROH}]_0} \quad (19)$$

Due to the significant differences in the reactivities of the isocyanate groups in the *para*- and in the *ortho*-positions eq. (19) can be further simplified to obtain eq. (20), which render the observed dependences of the apparent rate constants on the initial alcohol concentration.

$$k_{\text{app}} \approx \frac{k_1 k_{\text{c},1} [\text{ROH}]_0^2}{k_{-1} + k_{\text{c},1} [\text{ROH}]_0} \quad (20)$$



**Figure 9.** Variation of the apparent rate constant ( $k_{\text{app}}$ ) with initial alcohol concentration ( $[\text{ROH}]_0$ ) (a) and the dependence of the values of  $[\text{ROH}]_0/k_{\text{app}}$  with the  $[\text{ROH}]_0^{-1}$  (b) in the MDI-alcohol (butan-1-ol, butan-2-ol, and DEGME) reaction at  $45^\circ\text{C}$  and  $[\text{MDI}]_0 = 0.01M$ .



[The pseudo first-order rate constant values for the diisocyanate-alcohol reactions at different alcohol concentrations and the derivatization of eq. (17) can be found in the Supporting Information.]

## CONCLUSIONS

The progress of the reaction of the MDI and 2,4-TDI with alcohols including butan-1-ol, butan-2-ol, and DEGME at different temperatures were monitored by HPLC coupled with UV detection and off-line electrospray ionization mass spectrometry. ESI-MS proved to be a fast and efficient method to evaluate the reaction products' distribution using the ESI-MS peak intensities. To the best of our knowledge this is the first study applying ESI-MS technique for monitoring the reaction products of diisocyanate-alcohol reactions. According to both HPLC-UV and ESI-MS measurements, the first isocyanate group of the MDI reacts about 1.5 times faster with the alcohols than the second one. The reaction of 2,4-TDI with alcohols showed a more complicated kinetic situation, however, a relatively simple reaction scheme proposed proved to be capable of describing the experimentally observed reaction product distributions. It was further shown the *para*-isocyanate group in the 2,4-TDI reacts faster with alcohols investigated than the first isocyanate group of MDI and that the reactivity of both the 2,4-TDI and MDI toward the alcohols follow the trend: butan-1-ol > butan-2-ol > DEGME. From the temperature dependence of the corresponding rate constants the apparent activation energies were determined. The dependence of the reaction rate on alcohol concentration was also studied and a mechanism similar to that given by Baker and Gaun was proposed.

## ACKNOWLEDGMENTS

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