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Kinetics of a Diels−Alder Reaction of Maleic Anhydride and Isoprene in Supercritical CO_2

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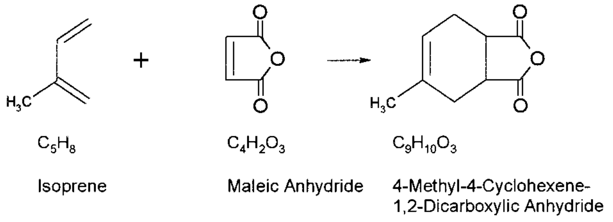
The kinetics of the reaction of maleic anhydride and isoprene in supercritical carbon dioxide was studied over an extended concentration range, from 5×10^{-5} to 1.3×10^{-2} mole fractions of both maleic anhydride and isoprene at 60 °C and pressure 100 atm. The apparent rate constant of the reaction was found to be concentration dependent, in contradiction with the literature data. The results are interpreted in terms of limited solubility of maleic anhydride in supercritical CO_2. The solubility of maleic anhydride in supercritical carbon dioxide was directly measured by sampling and analyzing the supercritical phase. The observed sharp increase in the apparent rate constant of the reaction between maleic anhydride and isoprene correlates with the solubility of maleic anhydride in supercritical carbon dioxide. The interpretation was confirmed using visual observations of the phase behavior. The rate constant of the reaction measured under the true supercritical, single phase, conditions is $k_x = (17.0 \pm 1.3)$ hr^{-1} (mole fraction units, 60 °C, pressure 100 atm).

Introduction

During the past decade, supercritical fluids (SCF) received significant attention as prospective solvents for organic synthetic reactions.[1−29] Supercritical carbon dioxide is considered to be a prospective environmentally friendly replacement of organic solvents.[2,25] From the engineering point of view, supercritical fluids as reaction media can be advantageous due to the increase of the number of the process parameters—both temperature and pressure can be used to control chemical reactions.[2,6,9,10,14,15,20,21,24−28] From the fundamental point of view, supercritical fluids represent new class of solvents with some properties intermediate between the gas and the liquid phases and with other properties that are found neither in the gas nor in the liquid phases. Because of the high isothermal compressibility in the vicinity of the critical point, some reactions exhibit very large activation volumes and, hence, strong pressure dependencies. Examination of the pressure effects allows better understanding of the solvent effect on the reaction rates.[16−24,28]

Supercritical carbon dioxide is one of the most studied supercritical fluids. Carbon dioxide has low critical temperature ($T_c = 304.2$ K) and a moderate critical pressure ($p_c = 73.8$ atm) and represents a prospective medium for reactions involving nonpolar or slightly polar reactants and transition states.[2] Diels−Alder cycloaddition is one of the classes of organic synthetic reactions intensively studied in supercritical carbon dioxide.[6−12,14,15,26−29] One of the model cycloaddition reactions, reaction of maleic anhydride with isoprene (reaction 1), was one of the first reactions studied in supercritical CO_2.



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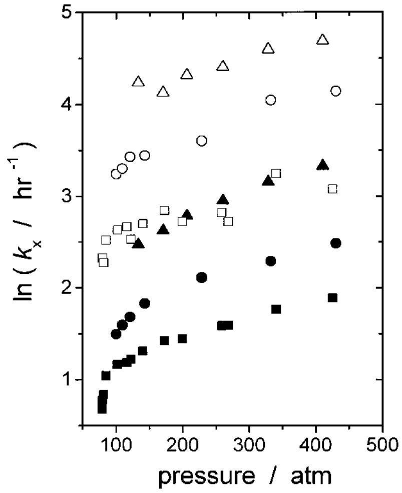

Figure 1. Rate constants of reaction 1 measured by Paulaitis and Alexander.[6,7] Filled symbols, rate constants reported in 6, 7, open symbols are the rate constants recalculated in this work based on the raw data and the formulas taken from 7 (see Appendix). The reactor temperature was 35 °C (squares), 45 °C (circles), and 60 °C (triangles). The mole fractions of maleic anhydride were $(3.4-5.2) \times 10^{-3}$ at 35 °C, $(3.3-3.6) \times 10^{-3}$ at 45 °C, and 2.5×10^{-3} at 60 °C. Isoprene was in excess from 1.5 to 3 times.

Paulaitis and Alexander performed extensive investigation of the kinetics of reaction 1 in supercritical carbon dioxide.[6,7] Effects of both temperature and pressure on the rate constant were investigated. Strong dependence of the rate constant on pressure at 35 °C (near the critical temperature of CO_2, $T_c =$ 31 °C) was observed (Figure 1, filled symbols) as expected based on the solvatochromic shift measurements.[18,19]

Currently, reaction 1 is considered to be a classical example of a Diels−Alder reaction in supercritical carbon dioxide and is widely cited in the literature on the reactions in supercritical media.[2,13,24]

In the course of our experiments, we used reaction of maleic anhydride with isoprene (reaction 1) as a model reaction with the main purpose to validate the experimental approach and the procedures. In our measurements of the rate constant of reaction

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1, the results of the original works of Paulaitis and Alexander[6,7] were not reproduced. Because of the model nature of reaction 1 to the field, an extensive study on the kinetics of this reaction was undertaken. In contrast to the works of Paulaitis and Alexander,[6,7] we found the apparent rate constant of reaction 1 to be concentration dependent over the range of the mole fractions studied, $5 \times 10^{-5} - 1.3 \times 10^{-2}$.

Recently, Renslo et al.[14] and Lin and Akkerman[26] have reexamined the earlier results of Ikushima et al.[9,10] on the regioselectivity of another Diels–Alder reaction in supercritical carbon dioxide. They concluded that the results of Ikushima et al.[9,10] on the reaction between isoprene and methyl acrylate in carbon dioxide were obtained in a two-phase system, rather than in the true single supercritical phase. Lin and Akkerman[26] also measured the apparent rate constant of this reaction at a single temperature and pressure while varying the compositions of the reaction mixture. Variation of the composition of the reaction mixture leads to the change of the nature and the number of phases. The apparent rate constants measured in the single supercritical phase and in the two-phase (gas–liquid) system differ significantly.[26] This recent research showed the importance of understanding the phase behavior for kinetic studies in supercritical fluids.

The presence of a second (liquid) phase could affect the reaction rate in several ways. Both acceleration and deceleration of the overall reaction are possible, depending on both the reaction rate constants in the two phases and their composition. If the liquid phase is enriched by both reactants, then the acceleration of the overall reaction is anticipated even for equal intrinsic reaction rate constants in both phases. If the reactants are partitioned between the two phases then the deceleration of the overall reaction could be expected. And, finally, the rate constants in the supercritical and the liquid phases could differ due to the solvent effects.

The concentration dependence of the apparent rate constant for reaction 1 observed in the current work was considered as an indication of the complications caused by the phase behavior of the reactive system. Two reasons for the phase nature change or the multiple phase formation were indicated in the literature: the limited solubility of the reactants and the shift of the phase boundaries and the critical point in the presence of the reactants. Generally, visual phase observation is used to verify the presence (or absence) of another phase.[14,26,28] However, this approach does not guarantee a single-phase environment, or even correct phase identification, since the visual observation of a small amount of liquid phase is difficult.[26]

The effects of the reagents on the phase behavior (such as the limited solubilities, phase boundaries and the critical point shift) are expected to vanish at very low concentrations of the reactants. Therefore, a different approach was chosen in this work. The approach consists of measuring the apparent rate constant down to very low reactant concentrations. The observation of the independence of the apparent rate constant of the reactant concentration at low concentrations serves as the criterion of a true single-phase system. When possible, the presence of several phases derived based on the presumed interference with the kinetic measurements are verified by the visual liquid phase observations using a view cell.

Experimental Section

Reagents. Maleic anhydride (Aldrich, mp 54–56 °C, bp 200 °C) was purified by vacuum sublimation. Maleic acid was the only impurity detected in maleic anhydride. The content of maleic acid in the commercial reagent was about 3 wt %. After the sublimation, the content of maleic acid was less than 0.4 wt %. Several experiments were performed using nonpurified maleic anhydride to establish the effect of maleic acid.

Maleic acid (Aldrich, mp 140–142 °C, 99%) was used without further purification.

Analysis of maleic anhydride on the content of maleic acid was based on the large difference in the solubilities of these substances in benzene (0.024 wt %[30] and 5.5 wt % (this work) at 25 °C for maleic acid and maleic anhydride, respectively). Weighed samples of maleic anhydride were dissolved in measured volumes of benzene. Dissolution of samples of the original (nonpurified) maleic anhydride resulted in white suspensions, whereas dissolution of samples of purified maleic anhydride lead to clear transparent solutions. The solid particles were separated by filtration, the precipitate was dried and weighed. The precipitate was analyzed by HPLC using an ion exclusion column (Waters IC–Pak Ion-Exclusion, 7.8 × 300 mm with Waters 484 Tunable Absorption detector). The content of maleic acid in the precipitate was determined to be 100%. The lower limit of the maleic acid content in maleic anhydride detectable by this analytical procedure (limited by the solubility of maleic acid in benzene) is about 0.4 wt %.

Isoprene (Aldrich Chem. Co., bp 34 °C, mp −146 °C, 99%) was used either without additional purification or after vacuum distillation. No effect of the distillation of isoprene on the measured rate of reaction 1 was observed.

Supercritical grade carbon dioxide (Liquid Carbonic Co. or Matheson Co.) was purchased in cylinders pressurized by helium to about 110 atm. The content of helium in CO_2 withdrawn from the cylinders was analyzed using mass-spectrometer and was about 2.5 vol %. The amount of carbon dioxide in the reactor was calculated from the reactor volume, temperature and pressure using eq 2:

$$n = \frac{pV}{ZRT} \tag{2}$$

The compression factors of carbon dioxide were taken from literature.[31] For reference, the compression factor at 60 °C and 100 atm is 0.548.

Kinetic Measurements. The experimental setup is shown in Figure 2. Reaction of maleic anhydride with isoprene was studied in a batch stirred high-pressure temperature controlled reactor (Autoclave Engineering, 300 cm^3 volume). In the experiments, weighed samples of maleic anhydride were loaded into the reactor. Then the reactor was sealed and flushed with carbon dioxide to remove air. After flushing the reactor was filled to a 98% fraction of the target CO_2 pressure (100 atm in the majority of the experiments). The second (liquid) reactant (isoprene) was initially loaded into a small auxiliary cylinder (10 cm^3). After the partial loading of the reactor with CO_2, isoprene was flushed into the reactor with an additional amount of carbon dioxide. Carbon dioxide was added until the desired pressure is reached. The reaction mixture was stirred using ordinary Teflon coated magnetic bar through the nonmagnetic stainless steel bottom wall of the reactor. The majority of the experiments were performed with the stoichiometric mixtures of the reactants. Additional series of experiments were performed with varying the amount of isoprene while keeping the amount of maleic anhydride constant to verify the effect of isoprene on the apparent rate constant of the reaction.

In the course of reaction, small portions (ca. 1 cm^3) of the reaction mixture were sampled and expanded through a $^1/_8$ in.

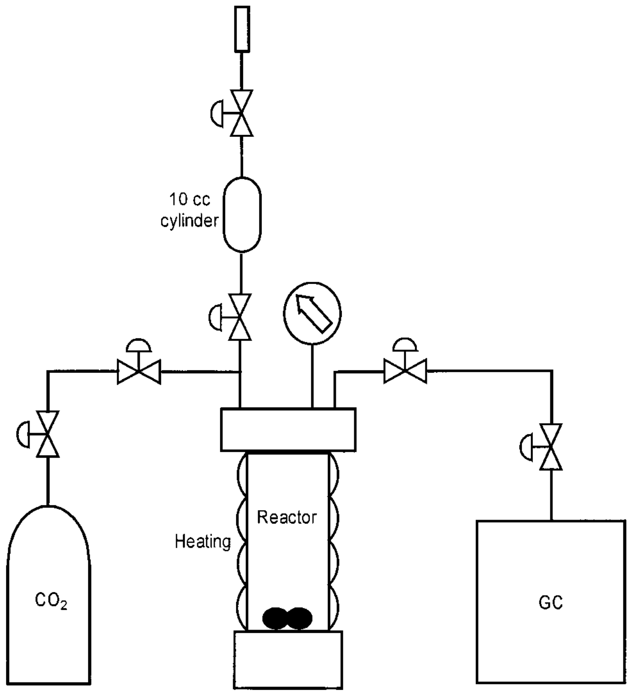

Figure 2. Experimental setup. High-pressure temperature controlled stirred batch reactor coupled to a GC.

stainless steel tube connected to a 1 cm^3 sampling loop of a GC (HP-5790A). The sampling volume was kept at temperature of 60 °C.

The gas-phase samples were analyzed on-line using gas chromatography to measure the concentration of isoprene. An 8 ft × $^1/_8$ in. SS 1% Alltech AT-1000 on 60/80 Graphpack-GB column and FID were used for the GC analyses. The column and the detector temperatures were 210 °C and 260 °C, respectively. The GC was calibrated using liquid isoprene/hexane mixtures. Isoprene peak area has been found to vary linearly with the isoprene concentration.

Solubility Measurements. The measurements of the solubility of maleic anhydride in SC CO_2 were performed using HPLC analysis of the samples withdrawn from the reactor. Weighed samples of maleic anhydride were loaded in the reactor. The reactor was filled with CO_2. After heating to a supercritical temperature, a fraction of the mixture was withdrawn from the top of the reactor to a 10 cm^3 cylinder, which was then slowly discharged. The precipitated maleic anhydride was washed from the sampling volume with acetonitrile, the resulting solutions were analyzed using HPLC (Alltech Adsorbosphere column, packing, C18; particle size, 5 μm; length × ID, 250 × 4.6 mm; and Waters 484 Tunable Absorbance UV detector). In additional experiments, the UV absorption of maleic anhydride in acetonitrile was characterized. Maleic anhydride dissolved in acetonitrile exhibits the validity of Beer's law over a wide concentration range (0.05−1000 ppm), the maximum molar absorption coefficient is $\epsilon_{10} = 1.3 \times 10^4$ liter mol^{-1}cm^{-1} at $\lambda = 207$ nm.

Visual Observation of the Phase Behavior in SC CO_2. A view cell similar to that described in ref 32 was used for the visual observations of the phase behavior of mixtures of maleic anhydride, isoprene and carbon dioxide. The cell (aperture ca. 1 cm, internal length 0.7 cm, volume 1.1 cm^3) was equipped with two $^1/_4$ in. thick fused silica windows. The cell was immersed into a heated stirred temperature controlled water bath. A magnetic bar was used to provide mixing of the content of the cell through the bottoms of the cell and the bath. Additional magnetic bars provided stirring of water in the bath.

Phase behavior was observed in the binary (CO_2−maleic anhydride) and the ternary (CO_2−maleic anhydride−isoprene) systems. In the experiments with the binary system, weighed samples of maleic anhydride (0.8−3.2 mg) were loaded into the cell immersed into the water bath at 43 °C. The cell was filled with a precalculated amount of carbon dioxide. During the loading of carbon dioxide, maleic anhydride melted due to the melting point depression by a SCF,[6] forming liquid droplets. After achieving the required pressure and temperature, the observation was continued for a period of 2 h. This time is longer than the estimated mixing time even if it was controlled exclusively by diffusion (40 min) and guaranties mixing of the components by diffusion alone (the estimate is based on the diffusion coefficient of ca. 10^{-4} cm^2/s, as for naphthalene in SC CO_2 at 60 °C and 100 atm[33,34]). The actual mixing time was much shorter due to the efficient forced mixing provided by a rotating magnetic bar inside the cell.

In the experiments with the ternary system (CO_2−maleic anhydride−isoprene), loading of the components was performed in two steps (similar to the procedure used in the kinetic measurements). First, maleic anhydride was loaded and the cell together with an auxiliary heated volume was filled with a predetermined required amount of carbon dioxide. After injection of the second reactant, the cell was immersed into the preheated water bath. The desired pressure was achieved in ca. 1−2 min. The presence (or absence) of a liquid phase was observed through the cell window.

Results and Discussion

Kinetics of Reaction 1 in Nitrobenzene and SC CO_2. According to the literature data, reaction of maleic anhydride with isoprene both in liquid solutions[35,36] and in SCF[6,7] solutions is a simple bimolecular reaction. First, we measured the rate constant of the liquid-phase reaction in nitrobenzene. For reference, measured in this work rate constant at 28 °C in nitrobenzene is 1.98 ± 0.33 L/mol hour. This is in agreement with the results of Snycker and Eckert,[36] $k = 2.73 \pm 0.08$ L/mol hrs at 35 °C and 1.11 ± 0.07 L/mol hour at 21 °C. The apparent activation energy for this reaction in nitrobenzene is 12.6 kcal/mol.[36]

In supercritical fluids, second order rate constants are usually reported in the mole fraction units, k_x.[2] The rate constant in terms of mole fractions is defined by eq 3

$$\frac{\mathrm{d}x_A}{\mathrm{d}t} = -k_x x_A x_B \tag{3}$$

The rate constant in terms of mole fractions, k_x, is related to the common, concentration based bimolecular rate constant

$$k_x = k[S] \tag{4}$$

where $[S] = n_{\text{solvent}}/V$ is the molar concentration of the solvent, n_{solvent} is the amount of the solvent in the reactor (number of moles) and V is the reactor volume.

The experimental kinetic curves were fitted by eq 5, which is the result of integration of eq 3 with a proper initial conditions, using k_x' as a fitting parameter

$$I_{IP} = I_{IP}^{0} \frac{(\eta_0 - 1)\exp\left(-k_x'\left(1 - \frac{1}{\eta_0}\right)t\right)}{\eta_0 - \exp\left(-k_x'\left(1 - \frac{1}{\eta_0}\right)t\right)} \tag{5}$$

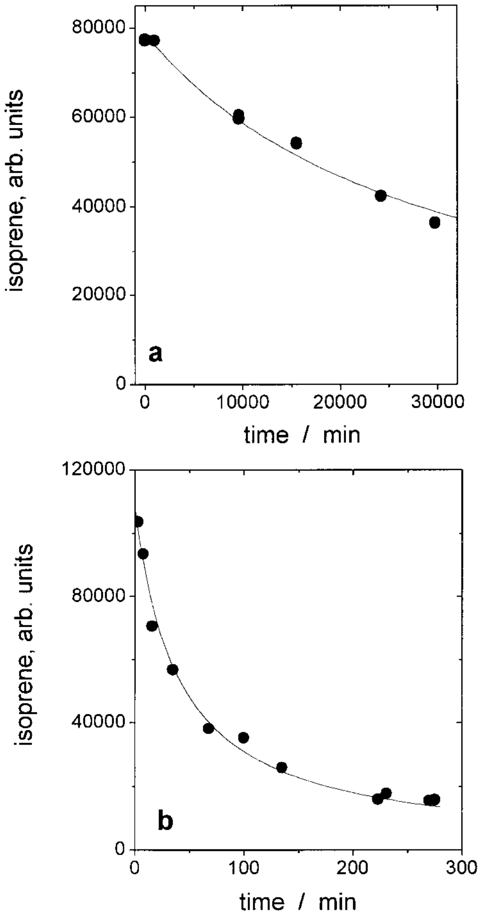

Figure 3. Sample isoprene concentration temporal profiles in reaction with maleic anhydride in supercritical carbon dioxide. Circles, experimental points; solid lines, fits using eq 5. Experimental conditions: temperature 60 °C, pressure 100 atm, stoichiometric mixtures. The ratios of the loaded amounts (numbers of moles) of maleic anhydride to the number of moles of CO_2 were 9.25×10^{-5} (**a**) and 9.25×10^{-3} (**b**).

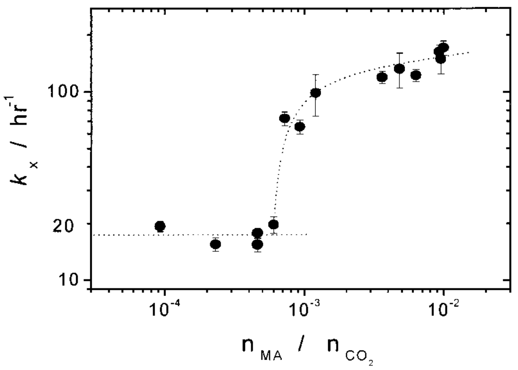

Figure 4. Dependence of the apparent rate constant of reaction 1 on the loaded mole fraction of maleic anhydride (stoichiometric conditions). Temperature 60 °C, pressure 100 atm. Horizontal dotted line, the rate constant of reaction 1 measured in this work. Curved dotted line, a spline line through the experimental points.

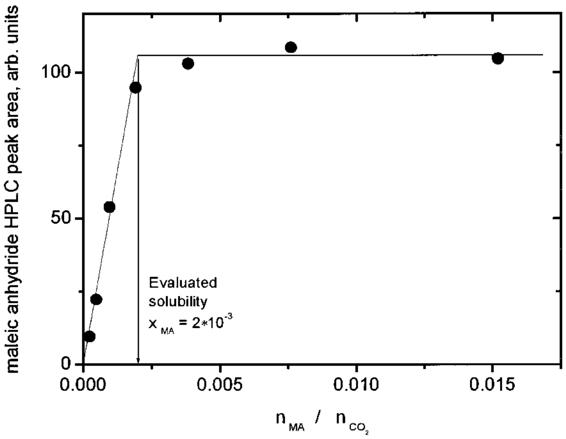

Figure 5. Determination of the solubility of maleic anhydride in SC CO_2 at 60 °C and 100 atm. The HPLC peak area of maleic anhydride from the samples obtained by washing the sampling volume with acetonitrile is plotted vs the ratio of the loaded number of moles of maleic anhydride to the number of moles of CO_2 (see text).

where $k_x' = k_x x_{MA}^0$, $\eta_0 = x_{MA}^0/x_{IP}^0 = n_{MA}^0/n_{IP}^0$, I_{IP} is the peak area of isoprene GC peak at time t, I_{IP}^0 is the initial peak area of isoprene, x_{IP}^0 and x_{MA}^0 are the initial mole fractions of isoprene and maleic anhydride, respectively. Typical examples of kinetic curves and fits by eq 5 are shown in Figure 3.

Dependence of the Apparent Rate Constant on the Concentration of Maleic Anhydride and the Correlation with the Solubility of Maleic Anhydride in SC CO_2. The experiments described in this section were performed at temperature 60 °C and pressure 100 atm. Reaction 1 was studied over a wide range of the reactant concentrations. Typical kinetic curves are shown in Figure 3. The apparent second-order rate constant of reaction 1 measured in this work exhibit dependence on the concentration of maleic anhydride. For example, for the kinetic curve **a** in Figure 3, which corresponds to a low (about 10^{-4}) mole fraction of maleic anhydride, the apparent rate constant, $k_x^{app} = 18.5 \pm 1.2$ h^{-1}. For the kinetic curve **b**, which corresponds to a much higher (about 10^{-2}) mole fraction of maleic anhydride, $k_x^{app} = 156 \pm 15$ h^{-1}.

The dependence of the apparent rate constant on the loaded amount of maleic anhydride is shown in Figure 4. The main feature of this dependence is a sharp rise in the apparent rate constant at the mole fraction of maleic anhydride of ca. 7×10^{-4}. At low concentrations of maleic anhydride ($x_{MA} < 0.0007$), the apparent rate constant is independent of the maleic anhydride mole fraction. At the mole fraction of 7×10^{-4}, the apparent rate constant sharply increases reaching values factor of 5 to 10 higher than that measured at low concentrations.

The sharp, "threshold-type" concentration dependence of the apparent rate constant indicates a possibility of a phase transition. To verify this hypothesis, additional experiments aimed at the determination of the solubility of maleic anhydride in SC CO_2 were performed. In these experiments, the content of maleic anhydride in the supercritical phase was measured as a function of the amount of maleic anhydride loaded in the reactor. The results are shown in Figure 5. At low concentrations, the content of maleic anhydride in the supercritical phase linearly increases with the total (loaded) amount. When the solubility is reached no further increase of the amount of maleic anhydride in the supercritical phase is observed. For the specific conditions shown in Figure 5, the sharp break in the dependence is observed at $x_{MA} \approx 2 \times 10^{-3}$, which gives the solubility of maleic anhydride in SC carbon dioxide at these conditions. This result correlates with the observed concentration dependence of the apparent reaction rate constant shown in Figure 4. At low concentrations, the reaction occurs in the only existing supercritical phase. At $x_{MA} > 2 \times 10^{-3}$, the reaction occurs presumably mainly in the liquid phase presumably enriched with the reactants, which leads to a larger apparent rate compared to the true, single supercritical phase, rate constant of the reaction.

As it was mentioned in the Introduction, the increase of the reaction rate in a two-phase system is possible, even if the rate

TABLE 1: Results of the Visual Observation of the Phase Behavior in the Binary (maleic anhydride/carbon dioxide) and Ternary (maleic anhydride/isoprene/carbon dioxide) Systems using a View Cell (aperture diameter ca. 1 cm, internal length 0.7 cm, and volume 1.1 cm^3)[a]

experiment no.	solutes	solute mole fraction (by load)[b]	T, °C	pressure, atm	observed no. of phases
1	maleic anhydride	1.1×10^{-3}	60	100	one
2	maleic anhydride	2.2×10^{-3}	60	100	uncertain (one or two)
3	maleic anhydride	4.4×10^{-3}	60	100	two
4	maleic anhydride	2.5×10^{-3}	60	133	two
5	maleic anhydride isoprene	2.5×10^{-3} 3.7×10^{-3}	60	133	two

[a] Stirring with a magnetic bar, observation time 2 h. Each observation was repeated two times. [b] The ratio of the loaded amount (numbers of moles) of the solute and the amount of carbon dioxide.

constants in the both phases are equal. Possible effect of the liquid phase on the apparent rate constant was estimated as follows. It is assumed that the kinetics of reaction 1 is monitored via the concentration of isoprene. In a single-phase system the initial reaction rate is

$$W_{01} = -\mathrm{d}[\mathrm{IP}]/\mathrm{d}t = k[\mathrm{IP}][\mathrm{MA}] = k\mathrm{n}_{\mathrm{IP}}\mathrm{n}_{\mathrm{MA}}/V^2 \qquad (6)$$

where [IP], [MA], n_{IP} and n_{MA} are the molar concentrations and the numbers of moles of isoprene and maleic anhydride, V is the volume of the reactor. In a two-phase system, the overall reaction rate is

$$W_{02} = -\mathrm{d}(n_{\mathrm{IP}}/V)/\mathrm{d}t = -\mathrm{d}((n_{\mathrm{IP},1}+n_{\mathrm{IP},2})/V)/\mathrm{d}t = -\mathrm{d}(([\mathrm{IP}]_1V_1 + [\mathrm{IP}]_2V_2)/V)/\mathrm{d}t \qquad (7)$$

where $n_{\mathrm{IP},1}$, $n_{\mathrm{IP},2}$, $[\mathrm{IP}]_1$, and $[\mathrm{IP}]_2$ are the numbers of moles and the molar concentrations of isoprene in supercritical and liquid phase, respectively. V_1 and V_2 are the volumes of the supercritical and the liquid phases. The reaction rates in the supercritical and the liquid phases are

$$-\mathrm{d}[\mathrm{IP}]_1/\mathrm{d}t = k[\mathrm{IP}]_1[\mathrm{MA}]_1 \qquad (8)$$

$$-\mathrm{d}\ [\mathrm{IP}]_2/\mathrm{d}t = k_2[\mathrm{IP}]_2[\mathrm{MA}]_2 \qquad (9)$$

where $[\mathrm{MA}]_1 = n_{\mathrm{MA},1}/V_1$, $[\mathrm{MA}]_2 = n_{\mathrm{MA},2}/V_2$, $n_{\mathrm{MA},1}$ and $n_{\mathrm{MA},2}$ are the molar concentrations and numbers of moles of maleic anhydride in the supercritical and liquid phase, k and k_2 are the (concentration based) reaction rate constants in the gaseous and liquid phases. Assuming constant volume of the liquid phase (V_2 = const), eqs 7−9 could be rearranged

$$W_1 = k\mathrm{n}_{\mathrm{IP},1}\mathrm{n}_{\mathrm{MA},1}/(VV_1) + k_2n_{\mathrm{IP},2}n_{\mathrm{MA},2}/(VV_2) \qquad (10)$$

Finally, assuming equal rate constants in both phases ($k_2 = k$), and the volume of the liquid-phase much smaller than the volume of the reactor ($V_2 \ll V_1 \approx V$), eqs 6 and 10 lead to

$$W_{01}/W_{02} = n_{\mathrm{IP},1}n_{\mathrm{MA},1}/(n_{\mathrm{IP}}\ n_{\mathrm{MA}}) + Vn_{\mathrm{IP},2}n_{\mathrm{MA},2}/(V_2n_{\mathrm{IP}}n_{\mathrm{MA}}) \qquad (11)$$

For the overall mole fractions of maleic anhydride and isoprene in the reactor (at 60 °C, 100 atm) of ca. 0.004 (two times higher than the solubility of maleic anhydride at these conditions), the measured reaction rate is ca. 10 times larger than that expected in the single-phase system. Estimating the volume of the liquid phase (which contains a half of the total amount of maleic anhydride) as $V_2 \approx 0.4$ cm^3, the experimentally observed 10-fold increase in the reaction rate could be explained if the liquid phase contains only ca. 2.5% (ca. 0.02 cm^3 of liquid at room temperature) of the total amount of isoprene. The estimate above supports a possible drastic effect of the presence of a small amount of liquid phase on the apparent rate constant due to the solely concentration effects. The relative contributions of the effect of the reactants concentration and the possible solvent effects to the apparent reaction rate in the two-phase region could not be separated based on the available experimental data.

It should be noted that there is no exact correspondence of the concentration dependence of the apparent rate constant and the measured solubility of maleic anhydride. There exists a transition region (in the vicinity of $x_{\mathrm{MA}} \approx 0.001$), in which maleic anhydride in the binary system maleic anhydride−carbon dioxide is completely dissolved but the apparent rate constant is already ca. 7 times higher than that measured at lower concentrations. This observation suggests that there is an influence of another component of the reaction mixture (isoprene) on the phase coexistence boundaries.

The reaction product, MCDA, is also expected to have low solubility in supercritical carbon dioxide. Precipitation of MCDA in the course of the reaction cannot be ruled out. However, there were no indications that possibly precipitating MCDA affects the reaction rate. No deviations from the second-order kinetic law, which could be attributed to the product formation, were observed.

Visual Verification of the Phase Behavior in the Binary (CO_2−Maleic Anhydride) and the Ternary (CO_2 − Maleic Anhydride − Isoprene) Systems. The results of the solubility measurements of maleic anhydride in supercritical carbon dioxide and the interpretation of the observed dependence of the apparent rate constant on the amount of the reactants were verified by the visual observation of the phase behavior. The results of these observations are summarized in Table 1.

Experiments 1−3 in Table 1 describe the behavior of maleic anhydride in SC CO_2 at the conditions of the current work (60 °C, 100 atm). In the experiment #1, the loaded mole fraction of maleic anhydride, 1.1×10^{-3}, was considerably smaller than the measured solubility of maleic anhydride in supercritical carbon dioxide (2×10^{-3}). In these experiments, droplets of a liquid phase on the cell windows visible in the beginning of the experiments disappeared in 2 min. The solution was transparent and has appearance similar to that of pure carbon dioxide. When the loaded mole fraction of maleic anhydride was considerably higher than the solubility (4.4×10^{-3}, experiment #3), droplets of a liquid phase on the cell windows were unambiguously observed for the whole duration of the experiment (ca. 2 h). In the experiment #2 with the loaded mole fraction of 2.2×10^{-3} (which is ca. 10% higher than the measured solubility of maleic anhydride), no certain conclusions on the presence of the liquid phase were derived. Although there were tentative indications on the presence of the liquid phase in this case, the amount was too small to make a definite conclusion. The results of the experiments #1−#3 (Table 1) are in agreement with the measured solubility of maleic anhydride in supercritical carbon dioxide (Figure 5).

Additional experiments (experiments #4 and #5 in Table 1) were designed to verify whether a single phase or two phases are present under the experimental conditions of the work of Paulaitis and Alexander.[6,7] The experiments were performed at 60 °C, 133 atm, and the loaded mole fraction of maleic anhydride 2.5×10^{-3} (the set of the experimental conditions of work[7] closest to the experimental conditions of the current work). In the binary system, maleic anhydride/carbon dioxide (experiment #4) two phases (gaslike and liquid) were unambiguously observed during the whole observation time (2 h). This infers that the solubility of maleic anhydride in supercritical carbon dioxide at 60 °C and 133 atm is lower than the mole fraction of maleic anhydride used in the experiments of Paulaitis and Alexander (2.5×10^{-3},[7]). However, this observation is not sufficient to unambiguously prove that the experiments in refs 6,7 were performed in a two-phase system because the second reactant (isoprene) might serve as a cosolvent. To check this possibility, experiment 5 (Table 1) was performed in the ternary (maleic anhydride/isoprene/carbon dioxide) system. The experimental conditions were the same as the experimental conditions of one of the experimental points measured at 60 °C and 133 atm of Paulaitis and Alexander.[7] Droplets of a liquid phase were observed during 2 h of the observation period (in the experiments of Paulaitis and Alexander the first sample was withdrawn 1 h after the loading of isoprene[7]). In conclusion, the current experiments with the view tube unambiguously demonstrate that at least at some experimental conditions used in the previous works[6,7] both the binary (maleic anhydride/carbon dioxide) and ternary (maleic anhydride/isoprene/carbon dioxide) mixtures are in the two-phase region.

Another important issue is whether the homogeneous phase, which fills the whole reactor is a true supercritical or a liquid phase. Recently, Lin and Akkerman[26] estimated the critical conditions of reactive mixtures used in several earlier studies of Diels−Alder reactions in supercritical carbon dioxide using the group contribution method.[37] According to their estimates, under the conditions used in these previous studies[9,10,14,19,29] the shift of the critical point due to the presence of the reactants could be large (e.g., 60 degrees Celsius[9,10]). On the basis of the estimates performed Lin and Akkerman[26] concluded that a number of earlier studies were presumably performed either in a two-phase region[9,10] (which was confirmed by the visual observation of the second phase in refs 14,26) or in a single liquid-phase region, but not in the supercritical fluid.[14,19,29]

We used the recommendations of Reid et al.[38] to evaluate the critical parameters of both the binary and the ternary systems formed by carbon dioxide, maleic anhydride, and isoprene. When the mole fractions of the solutes are smaller than 0.0007 (the concentration range in which the measured apparent rate constant of reaction 1 is independent of the concentration of the reactants), the estimated differences between the critical parameters (T_c, p_c) of the mixtures and of pure CO_2 are less than 4 °C and 1 atm, respectively. Therefore, the single phase observed in our experiments at 60 °C and 100 atm over this concentration range is the supercritical phase.

The current kinetic measurements are consistent with both the solubility measurements and the visual observations of the phase behavior in this work. The disagreement with the previous studies[6,7] is apparent and significant. Beyond the explanation given above, a number of hypothetical sources of errors were initially investigated in an attempt to find another explanation for this discrepancy. These experiments are described in the next section.

Analysis of Possible Sources of Errors. The following possible sources of experimental errors were identified and assessed:

1. *Carbon Dioxide Composition in the Reactor*. Supercritical carbon dioxide obtained from the cylinders pressurized with helium contains small amount of helium, which is dissolved in the liquid carbon dioxide in the cylinders. Carbon dioxide withdrawn from the cylinders was analyzed using mass-spectrometry. The mole fraction of helium was determined to be 2.5%. This small helium impurity is expected to have only minor effects both on the media properties and the rates of chemical reactions.

2. *Impurities in Isoprene*. No impurities in isoprene were found by the GC analysis. Vacuum distillation of isoprene has no effect on the reaction rate. No dependence of the apparent rate constant on the concentration of isoprene was found within the experimental accuracy (10%).

3. *Influence of Water*. It could be speculated that traces of water (if exist) in the reaction mixture might have an effect on the reaction rate via the mechanism of acid catalysis. Addition of 0.01 mole fraction of water to the reaction mixture did not affect the reaction rate within the experimental accuracy 10%.

4. *Effect of Maleic Acid or other Impurities in Maleic Anhydride*. Maleic acid was the only impurity found in maleic anhydride. The content of maleic acid in the commercial reagent was about 3%. It was purified to better than 0.4% using the procedure described earlier.

Maleic acid might affect the measured rate of reaction 1 in two ways. First, it could affect the phase coexistence boundary. Second, it could have a catalytic effect on reaction 1. Catalysis of Diels−Alder reactions by Lewis acids was observed in the liquid phase[39] as well as in supercritical carbon dioxide.[8,10]

No effect of the addition of maleic acid (up to 3 wt %) on the solubility of maleic anhydride in supercritical carbon dioxide was observed in the current work. Purification of the commercial reagent (3 wt % maleic acid) to less than 0.4 wt % had no effect on the measured solubility of maleic anhydride in supercritical carbon dioxide.

No effect of either maleic anhydride purification (from 3 wt % to < 0.4 wt %) or maleic acid addition (to 10 wt %) on the apparent rate constant of reaction 1 was observed at “high” concentrations ($x_{MA} \approx 0.01$), where the apparent rate constant has maximum. At low concentrations ($x_{MA} < 0.001$), purification of maleic anhydride also has no effect on the reaction rate. However, at low concentrations ($x_{MA} < 0.001$) addition of large amounts of maleic acid (up to $x_{acid} \approx 0.1\ x_{MA}$) lead to the acceleration of the reaction by a factor of 2. This allows to estimate an upper limit on the possible effect of maleic acid on the reaction rate in the current experiments as < 4%.

Comparison of the Current and Previous[6,7] Works. On the basis of the discussion above the following conclusions were derived. Only the experiments that were performed at sufficiently low concentrations of maleic anhydride (<0.0007) reflect the true supercritical phase reaction rate constant. Averaging the rate constants values obtained at low mole fractions of maleic anhydride ($x_{MA} < 0.0007$, the five low concentration points in Figure 4) yielded $k_x = (17.0 \pm 1.3)\ \text{hr}^{-1}$. This is the value for the rate constant of reaction between isoprene and maleic anhydride in SCF CO_2 at 60 °C and 100 atm measured in the current work.

The earlier experiments[6,7] have been performed in a two-phase system. The initial concentrations of maleic anhydride in these experiments were too high, and the reaction presumably occurred in a liquid-phase enriched with the reactants.

A problem was encountered when we attempted to reanalyze the raw data from the original works of Paulaitis and Alexander.[6,7] We failed to obtain the rate constants reported in refs 6 and 7 from the raw data published in ref 7 (see Appendix).

The processing of the original raw data from[7] using the procedure described in refs 6,7 (Figure 1, open triangles) resulted in the rate constant $k_x \approx 50$ h^{-1} at 60 °C, 100 atm and the mole fraction of maleic anhydride of 0.0025 (presumably in the two-phase region). This rate constant is ca. 3 times larger than the rate constant measured in this work under the true single-phase supercritical conditions at the same temperature and pressure. Our measurements at a larger mole fraction of maleic anhydride (0.0025, which presumably corresponds to a two-phase region) resulted in k_x of ca. 100 h^{-1} (Figure 4). This is ca. factor of 2 larger than the value obtained from the original experimental results of.[6,7] It should be noted, however, that the mole fraction of isoprene used in refs 6, 7 was ca. 1.5 times larger than in our measurements. This could lead to different relative amounts of the liquid and supercritical phases in these two measurements.

An additional reason for the difference in the apparent rate constants measured in two-phase systems could be in the difference in the experimental procedures used. In the current work, the mole fractions of isoprene in the samples obtained from the gas phase were measured (Figure 3b). In refs 6, 7, both maleic anhydride (MA) and MCDA were sampled from the gas phase, but only the ratios of the mole fractions of MA and MCDA in the samples are available.[7] In a two-phase system, the ratio of the mole fractions of two components in the gas phase is not necessarily equal to the ratio of their mole fractions in the overall system.

In addition, in two-phase systems the sampling procedure used in both earlier[6,7] and this work is not well-defined. Stirring the reaction mixture could (and, presumably, does) lead to the formation of small aerosol-like particles of the liquid phase with a long sedimentation time. For example, estimated sedimentation time for micron-sized particles is ca. 2 h. After stirring is stopped, these aerosol-like particles are still sampled together with the gas phase. The samples obtained in this way might reflect the composition intermediate of these of the supercritical and the liquid phases.

The main purpose of this work was to reveal and to avoid multiphase problems with the purpose of measuring the rate constant under true, single-phase, supercritical conditions.

Conclusions

Kinetics of reaction of isoprene and maleic anhydride in supercritical carbon dioxide was investigated at 60 °C and 100 atm over an extended range of the reactant concentrations. The measured rate constant in the mole fraction units, $k_x = (17.0 \pm 1.3)$ hr^{-1}, is in discrepancy with the literature data.[6,7] The observed disagreement is explained based on the low solubility of maleic anhydride in supercritical CO_2. The interpretation was confirmed by the visual observation of another (liquid) phase under the experimental conditions of the earlier works.[6,7] Presumably, the results of the earlier studies[6,7] reflect the reaction kinetics in the liquid phase. Both the original rate constants of reaction 1 reported in ref 7 and the rate constant recalculated in the current work from the original data exhibit *positive* pressure dependencies (Figure 1). Positive pressure dependencies infer negative apparent volume of activation. Our preliminary results obtained in the true one-phase supercritical conditions indicate strong *negative* pressure dependencies of the rate constant of reaction 1. Detailed investigation of the pressure dependence of the rate constant of reaction 1 is in progress.

Appendix

Recalculation of the Rate Constants of Reaction 1 Using Both the Raw Kinetic Data and the Procedure from 7. In the original work,[7] reaction between isoprene and maleic anhydride (further − IP and MA, respectively) in SCF CO_2 was studied by monitoring both MA and the reaction product, 4-methyl-4-cyclohexene-1,2-dicarboxylic anhydride (further, MCDA). Small portions of the reaction mixture were withdrawn using an auxiliary volume. The volume was discharged and washed with dichloromethane. The resulting solutions of MA and MCDA in dichloromethane were analyzed using gas chromatography.

The raw kinetic data are reported in ref 7, Appendix C. The tables contain parameter S as a function of time. The parameter S is defined as the ratio of the adduct GC peak area and the total MA + MCDA GC peak areas

$$S \equiv \frac{MCDA_{\mathrm{PeakArea}}}{MCDA_{\mathrm{PeakArea}} + MA_{\mathrm{PeakArea}}} \tag{A1}$$

The experimental conditions, the amounts of MA and IP loaded into the reactor, and other pertinent parameters for each kinetic run are also available. This allows recalculation of the rate constants using the same procedure as used in ref 7. The procedure consists of the following steps:

1. Parameter S (the GC peak area fraction of MCDA) is converted to parameter W (the weight fraction of MCDA in the mixture of MA and MCDA):

$$W \equiv \frac{m_{\mathrm{MCDA}}}{m_{\mathrm{MA}} + m_{\mathrm{MCDA}}} = S + (S - S_2)(C_1 + C_2(2S - 1) + C_3(2S - 1)^2) \tag{A2}$$

where m_{MA} and m_{MCDA} are the masses of MA and MCDA, respectively; C_i's are the coefficients obtained from the calibration procedure (ref 7 Appendix B): $C_1 = 0.9596$; $C_2 = -0.5804$; $C_3 = 0.3273$.

2. The mole fraction of MCDA, α, is calculated based on the weight fraction, W:

$$\alpha \equiv \frac{n_{\mathrm{MCDA}}}{n_{\mathrm{MA}} + n_{\mathrm{MCDA}}} = \frac{1}{1 + \frac{M_{\mathrm{MCDA}}}{M_{\mathrm{MA}}}\left(\frac{1}{W} - 1\right)} \tag{A3}$$

where n_{MA}, n_{MCDA}, M_{MA}, M_{MCDA} are the amounts (numbers of moles) of MA and MCDA and the molar masses of MA and MCDA, respectively.

3. The initial moler fractions of MA and IP in the reaction mixture, $x_{\mathrm{MA}}{}^0$ and $x_{\mathrm{IP}}{}^0$, are calculated.

4. The mole fraction of the reaction product, x_{MCDA}, is calculated based on the values of α and $x_{\mathrm{MA}}{}^0$:

$$x_{\mathrm{MCDA}} = \alpha x_{\mathrm{MA}}{}^0 \tag{A4}$$

This mole fraction is calculated for different reaction times.

TABLE 2: Raw Kinetic Data and Other Pertinent Information for Calculation of the Rate Constants Taken from 7[a]

MA, 10^{-3} mol	IP, 10^{-3} mol	T, °C	pressure, atm	CO_2 molar vol, cm^3/mol	time, hr	parameter S	$F(t)$, (ref 7)	$F(t)$, recalculated using eqs A1−A5	k_x from[7]	k_x recalculated using eqs (A1−A5)
3.997	9.547	35	199	50.83	2.0	0.3558	9.37	61.01	4.1	15.2
					4.0	0.5117	16.60	96.47		
					6.0	0.637	25.96	133.89		
					8.5	0.7232	36.68	169.64		
					11	0.7719	45.48	196.34		
1.175	1.841	60	133	82.66	1	0.1768	11.63	90.25	11.5	69.2
					2	0.3126	24.89	178.87		
					3	0.4027	36.01	247.53		
					4	0.4799	47.79	314.92		
					5	0.5332	57.76	368.14		

[a] Reactor volume 38.3 cm^3. Parameter S is defined by eq A1. Parameter $F(t)$ is defined by eq A5.

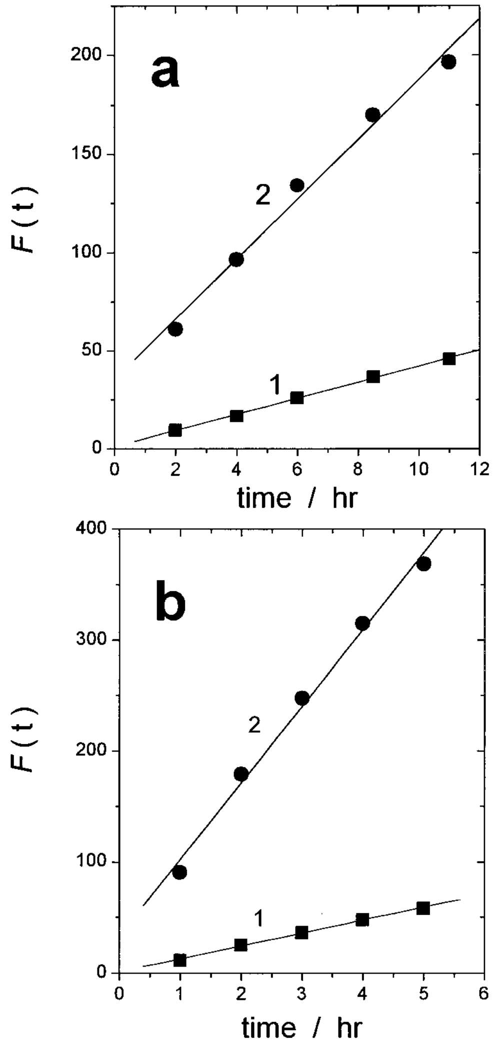

Figure 6. Examples of the recalculation of the rate constants of reaction 1 from the original raw data of ref 7. **a:** 35 °C, 199 atm; **b:** 60 °C and 133 atm. The slopes of the solid straight lines (obtained by linear regression) yield the rate constants of the reaction ($F(t) = 1/x_{MA}^{0} - x_{IP}^{0}) \ln(x_{IP}^{0}(x_{MA}^{0} - x_{MCDA})/x_{MA}^{0}(x_{IP}^{0} - x_{MCDA}) = k_x t$). The values of $F(t)$ for curves 1 are taken from 7. The values of $F(t)$ for curves 2 are recalculated from the raw kinetic data taken from 7 using eqs A1−A5. The rate constants, $k_x = 4.1$ and $15.2\ h^{-1}$ (**a**) and $k_x = 11.5$ and $69.2\ h^{-1}$ (**b**) for curves 1 and 2, respectively.

5. Finally, the reaction rate constant in the mole fraction units, k_x, is calculated using equation A5:

$$k_x t = F(t) \equiv \frac{1}{x_{MA}^{0} - x_{IP}^{0}} \ln\left(\frac{x_{IP}^{0}(x_{MA}^{0} - x_{MCDA})}{x_{MA}^{0}(x_{IP}^{0} - x_{MCDA})}\right) \quad (A5)$$

Two detailed examples of the rate constant recalculation are given in Table 2 and shown in Figure 6. The absolute values of the recalculated rate constants deviate significantly (by a factor of 5) from those originally reported in ref 7. The reason for this difference is not resolved. Both the originally reported constants and the recalculated rate constants at 60 °C and 100 atm are in disagreement with the results of the current work. The pressure dependencies of both the originally reported and the recalculated rate constants based on the raw data from[7] are shown in Figure 1.

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