High-Pressure Acid-Catalyzed Isomerization and Hydration of Fumaric Acid in a Homogeneous Nonisothermal Batch Reactor

Ronald Wbeimar Pacheco Ortiz,[†] Cristina Benincá,[‡] Lúcio Cardozo-Filho,[§,||] and Everton Fernando Zanoelo[*,†]

[†]Department of Chemical Engineering, Federal University of Paraná, Curitiba 81531-970, PR Brazil
[‡]School of Chemistry and Food, Federal University of Rio Grande, Santo Antônio da Patrulha 95500-000, RS Brazil
[§]Department of Chemical Engineering, Universidade Estadual de Maringá, Maringá 87020-900, PR Brazil
[||]Centro Universitário da Fundação de Ensino Octávio Bastos (UNIFEOB), São João da Boa Vista 13874-149, SP Brazil

ABSTRACT: A set of chemical kinetic and phase-transition experiments was performed to investigate the competing conversions of fumaric acid into maleic and malic acids by isomerization and hydration, respectively. The reactions were carried out in sealed stainless steel batch reactors operated up to ~1600 kPa and jacketed with glycerol at 398, 423, 448, and 473 K. The catalyst used was 0.97 M hydrochloric acid. To avoid excessive data near equilibrium, the reaction time was reduced from 720000 to 12600 s as the temperature of the heating fluid was increased. To ensure a homogeneous reaction, the solubility of fumaric acid in water was determined in the temperature range from 293 to 473 K using a high-pressure variable-volume sapphire view cell. The variation in the species concentration with time was determined by HPLC analysis of 12 reaction mixture samples per reaction run conducted twice under identical conditions. The parameters of the Arrhenius equation for the isomerization and hydration reactions were tuned on the kinetic experimental data by applying the Simplex method of optimization ($k_{20} = 1.27 \times 10^{-7}$ s^{-1}, $k_{30} = 1.29 \times 10^{7}$ s^{-1}, $E_{a2}/R = -2815$ K, $E_{a3}/R = 11260$ K).
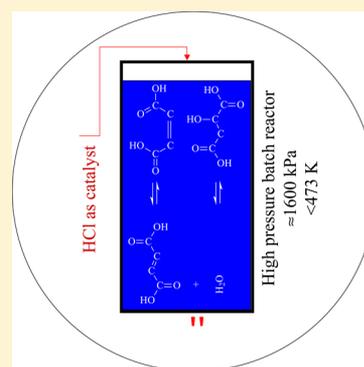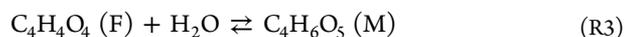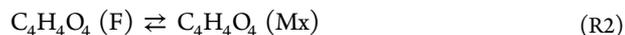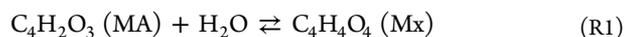
1. INTRODUCTION

Malic acid is the second most important organic acid used as a food additive in the world, behind only citric acid.[1,2] In the past two decades, its overall production and demand have steadily increased at an amazing annual rate of 4−8%, the highest growth rate among all organic acids.[3] The production of approximately 33000 tons in 1992 increased to 55000 tons in 2005, and it is expected to be 88700 tons in 2020.[2,4−7]

Malic acid is manufactured industrially by the bio- and chemical conversions of fumaric acid (F) and maleic anhydride (MA), respectively.[8] However, the enzymatic route is applied to produce L-malic used only for special purposes, and it does not compete with the chemical synthesis of DL- or racemic malic acid (M) widely applied as an acidulant and flavor in the food industry.[3] In fact, only 15% of the malic acid available for market is from biological production.[7]

The three chief reactions for the acid- or base-catalyzed commercial synthesis of DL-malic acid are the hydration reaction of maleic anhydride to form maleic acid (Mx) (reaction R1), the isomerization of maleic acid to fumaric acid (reaction R2) and the conversion of fumaric acid to malic acid by a reaction with H$_2$O (reaction R3).[2,9−11] These reactions are usually carried out at high temperatures (≥423 K) and pressures (1400 kPa) for long reaction times (3−5 h).[2] The reaction product at the exit of the reactor consists of 40−60% malic acid, 40−60% fumaric acid, and residual amounts of maleic acid (2−3%) on a dry basis. Purification is by multiple

stages of precipitation/filtration of fumaric acid at low temperatures (a condition where the solubility of F in water is negligible), followed by crystallization of DL-malic acid that results in a white powder containing less than 1% fumaric acid and 0.05% maleic acid.[2,9,10]

$$C_4H_2O_3 \ (MA) + H_2O \rightleftarrows C_4H_4O_4 \ (Mx) \qquad (R1)$$

$$C_4H_4O_4 \ (F) \rightleftarrows C_4H_4O_4 \ (Mx) \qquad (R2)$$

$$C_4H_4O_4 \ (F) + H_2O \rightleftarrows C_4H_6O_5 \ (M) \qquad (R3)$$

The starting reactant of the chemical mechanism presented above is maleic anhydride, which is an abundantly available petroleum-derived commodity whose toxicity can cause serious health risks to workers who manipulate it in the malic acid industry.[12,13] An interesting substitute for maleic anhydride as a raw material for the chemical production of malic acid is fumaric acid. It is not only a nontoxic compound when ingested,[13] but its use can have important positive impacts on the operating costs that essentially depend on reducing the time of reaction R3. For instance, it is known that the time to reach 99% of the equilibrium conversion of fumaric acid with 0.97 M hydrochloric acid as the catalyst is just approximately 1 h at 473

K and ~1600 kPa.[14] This means a decrease of 2−4 h in the reaction time when compared with that found in typical industrial plants that convert maleic anhydride into malic acid according to reactions R1−R3.

In this framework, the main aim of this study was to investigate the kinetics of reactions R2 and R3 as a chemical mechanism for producing malic acid from fumaric acid using hydrochloric acid (HCl) as the catalyst. It is interesting to highlight that the same suggested mechanism is involved in the production of the same product from maleic acid, but this type of approach to determine the kinetic parameters of reactions R2 and R3 is not currently considered. The kinetics of reaction R3 in the presence of HCl was examined many years ago,[14] but it was based only on experimental data for the conversion of fumaric acid from spectrophotometric analysis and neglected reaction R2. In the current investigation, a more detailed mechanism that involves two simultaneous competing reactions taking place in nonisothermal reactors is considered, as well as the solubility of fumaric acid in water under the same conditions as used for the reaction (to ensure homogeneity of the reaction medium). Moreover, the kinetic parameters were calculated from data on the variations in concentration of three different species with time at four different temperatures emerging from accurate high-performance liquid chromatography (HPLC) analyses.

2. MATERIALS AND METHODS

2.1. Experiments. *2.1.1. Chemicals.* Fumaric, DL-malic, and maleic acids for HPLC analysis were from Sigma-Aldrich (analytical grade, St. Louis, MO). Fumaric and hydrochloric acids used as the starting reactant and catalyst, respectively, in the reaction experiments were purchased from Neon (purity ≥99%, São Paulo, Brazil) and Sigma-Aldrich (37 wt % in H_2O, St. Louis, MO), respectively. Standard and reaction aqueous solutions were prepared with Milli-Q water (Millipore, Bedford, MA). Carbon dioxide necessary to pressurize the apparatus used to determine the solubility of fumaric acid in water above ~373 K was from White Martins (Ponta Grossa, Brazil).

2.1.2. Solubility Experiments. The solubility of fumaric acid in water was measured at temperatures between 293 and 473 K with a phase-equilibrium cell designed to operate at high pressures and temperatures. A CO_2 syringe pump and a high-temperature bath were independently used to reach the desired pressure and temperature, respectively, inside the cell. These variables were also monitored with a pressure transducer and a thermocouple, respectively. A more detailed description of the apparatus is available in the literature.[15]

The applied procedure for the determination of the solubility of F was essentially the same as described in the literature.[16] To summarize, the cell was loaded with a well-known concentration of fumaric acid at ambient temperature, sealed, and kept under agitation with a magnetic stirrer at 500 rpm. The transition from a heterogeneous to a homogeneous phase was visually detected through two sapphire windows as the temperature of the solution was increased. The lowest temperature that allowed for the formation of a transparent aqueous solution was the temperature at which fumaric acid was soluble at the examined concentration. At $T \geq 373$ K, the internal pressure was kept at 2000 kPa by moving a piston that was internally equipped in the view cell. This was done using CO_2 from the syringe pump, which was never in contact with the aqueous solution of fumaric acid.

2.1.3. Reaction Experiments. The reaction experiments were carried out in stainless steel batch reactors that were internally coated with Teflon because of the use of 0.97 M hydrochloric acid as the catalyst. The reaction vessels were vertical cylinders with an internal diameter and height of approximately $(1.6 \pm 0.1) \times 10^{-2}$ and $(6.8 \pm 0.3) \times 10^{-2}$ m, respectively, whose walls thickness was approximately $(1.4 \pm 0.2) \times 10^{-2}$ m. The reactants (H_2O + F) were premixed at ambient temperature, and ~10−14 mL of the prepared solution with an initial concentration of fumaric acid equal to 0.036 ± 0.003 M was charged into each reactor before the reactors were sealed. The reactor contents were not continuously stirred, as a magnetic stirrer could not be used and mechanical agitation cannot be easily applied under high pressure. To have a constant concentration of HCl of 0.97 M, between 0.81 and 1.13 mL of 37% (w/w) HCl was added to the reaction solution. Energy was supplied to the reaction by a nonstirred glycerol bath with proportional−integral−derivative (PID) control of temperature operated at 398, 423, 448, and 473 K (T_∞). The concentrations of F, M, and Mx were determined by collecting aliquots from the reactors at 12 different reaction times for each temperature of the heating fluid presented earlier. The aliquots were immediately refrigerated and stored at 263 K to be examined by high-performance liquid chromatography (HPLC). The reaction experiments were replicated twice.

Because there was heat transfer from glycerol to the liquid reaction mixture, preliminary heating tests were performed under the same conditions as used for the reaction, but with pure water loaded in the reactor kept at atmospheric pressure. The increase of the water temperature was monitored with a calibrated thermocouple (273−623 K, IKA, Cologne, Germany). The purpose of these experiments was to obtain a set of data necessary to determine the overall heat-transfer coefficient that was independent of those used to tune the kinetic parameters of the investigated reactions.

2.1.4. HPLC Analysis. All samples from the reactor, previously filtered through a 33-mm-diameter and 0.22-μm-pore-size high-density polyethylene (HDPE) Durapore membrane, were examined by HPLC in a Shimadzu chromatograph (Prominence LC-20AD, Shimadzu, Kyoto, Japan). It was basically equipped with a degasser (Prominence DGU-20A5), a high-pressure pump that forced the mobile phase (consisting of ultrapure water at pH 2) to flow at 1 mL min^{-1} and 6500 kPa through an adsorption column, an oven to maintain the temperature of the column at 315 ± 0.5 K (Prominence CTO-20A), and a UV detector to monitor the eluted components at wavelengths close to 210 nm (SPD-10AV, Shimadzu, Kyoto, Japan). A 5-μm Allure organic acid packing column (300 × 4.6 mm, Restek, Bellefonte, PA) was used to separate M, F, Mx, and HCl eluted at 3, 6, 12, and 18 min, respectively. These retention times and the concentrations of M, F, and Mx in the reaction mixtures were previously determined by injection of 10 μL of aqueous standard solutions with known concentrations of the species of interest into the column. From these preliminary tests, individual calibration curves for the concentrations of M, F, and Mx as functions of the absorbance of the standard solutions at 210 nm were obtained. The chromatographic conditions were according to the AOAC standard method,[17] as employed in many other investigations reported in the literature to determine organic acids in liquid samples.[18]

2.2. Reaction Kinetic Model. A set of four ordinary differential equations (ODEs) was written from the F, M, and Mx mole balances and from an energy balance on the batch

nonisothermal reactors (eqs 1−4). This system of ODEs was solved numerically with the implicit backward differentiation formula (BDF) method by applying the DASSL routine.[19] Because the kinetic model involves six parameters to be tuned on the experimental results of species concentrations, it was modified to run with the Simplex method of optimization.[20] The objective function to be minimized is given by eq 5.

$$\frac{dC_F}{dt} = -k_2 C_F + \frac{k_2}{K_2} C_{Mx} - k_3 C_F + \frac{k_3}{K_3} C_M \tag{1}$$

$$\frac{dC_{Mx}}{dt} = k_2 C_F + \frac{k_2}{K_2} C_{Mx} \tag{2}$$

$$\frac{dC_M}{dt} = k_3 C_F - \frac{k_3}{K_3} C_M \tag{3}$$

$$\frac{dT}{dt} = U_m(T_\infty - T) \tag{4}$$

$$f = \sum_{i=1}^{n} \left[(C_{F,exp}^i - C_{F,calc}^i)^2 (C_{Mx,exp}^i - C_{Mx,calc}^i)^2 \right] \tag{5}$$

It is worthwhile to remember that water was present in very large excess in the reactors, so the consumption of fumaric acid in reaction R3 is pseudo-first-order (i.e., $k_3 = k_3' C_W$). As a result, the energy balance does not account for the heat added to reaction mixture due to the reactions, but it accounts only for the heat added through the reactor walls.

The forward rate constants k_2 and k_3 in eqs R1−R3 were from the Arrhenius expressions involving the preexponential factors (k_{20} and k_{30}) and the activation energies (E_{a2} and E_{a3}) of the isomerization and hydration reactions (reactions R2 and R3, respectively) as tuned parameters. The dependence of the equilibrium constants (K_j for $j = 2, 3$) on temperature was determined by the van't Hoff equation in its simplified integrated form

$$K_j = K_{j,298} \exp\left[-\frac{\Delta H_{j,298}}{R} \left(\frac{1}{T} - \frac{1}{298} \right) \right] \tag{6}$$

where $K_{2,298}$ and $\Delta H_{2,298}$ were additional model parameters to be tuned on the kinetic experimental results of species concentrations. The same parameters of the van't Hoff equation for reaction R3 were independently tuned on the data for the equilibrium constants for that reaction available in the literature at four different temperatures by the method of Levenberg−Marquardt ($K_{3,298} = 53.8$, $\Delta H_{3,298}/R = -2407$ K).[14,21]

The modified overall heat-transfer coefficient in the conservation energy equation was computed from a large set of data on the temperature of water (74 results) during heating tests performed in the same vessels used as reactors in the reaction experiments. Glycerol at 398, 423, 448, and 473 K was again the heating fluid. The heating of water was described by the algebraic equation that represents the analytical solution of eq 4

$$-\ln\left(\frac{T_\infty - T}{T_\infty - T_{in}} \right) = U_m t \tag{7}$$

where T_∞ is the temperature of the surrounding heating fluid and T_{in} is the initial temperature of water (∼295 K). The method of Levenberg−Marquardt was again used to adjust U_m in the water temperature range from ∼295 K to ∼363 K. This

upper limit of temperature, which is approximately the boiling point of water at atmospheric pressure, was always much lower than the temperatures of the heating fluid because the heating vessel was not sealed.

3. RESULTS AND DISCUSSION

A first notable issue considered in this study was the solubility of fumaric acid in water. The results at temperatures below the boiling point of this solvent at atmospheric pressure when compared to those available in the literature[16,22,23] in the same temperature range promptly validate the experimental procedure currently applied to determine this property (Figure 1). They also confirm that the low solubility of this organic acid
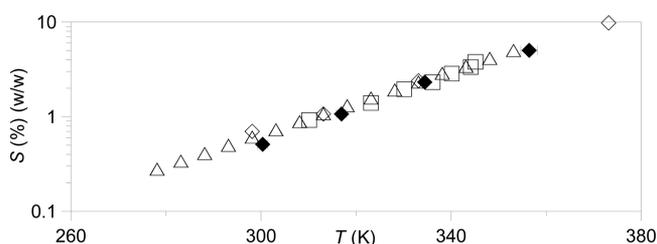
Figure 1. Comparison between the aqueous solubility of fumaric acid determined in this study (solid diamonds) and values reported in the literature below the boiling point of water at atmospheric pressure (open symbols: squares,[16] diamonds,[22] triangles[23]).

in water at ambient temperature is a key limiting factor for its application as an additive in water-based foods, cosmetics, and pharmaceutical products. This is an interesting practical aspect that represents the main reason for converting fumaric acid into malic acid, whose high solubility in water at ∼20 °C (>50% w/w) favors its use as an additive in products that use water as the solvent.[2]

At any rate, for the current purpose, the most relevant data on the solubility of fumaric acid in water are reported in Table 1, which includes the results on solubility from 293 to ∼473 K,

Table 1. Experimental Water Solubility of Fumaric Acid from Ambient Temperature to Approximately the Highest Reaction Temperature Currently Examined (i.e., 473 K)

T (K)	S (%, w/w)	S^a (M)
300	0.5	0.04
317	1.1	0.09
334	2.3	0.19
356	5.0	0.40
376	9.8	0.76
400[b]	20.4	1.47
428	44.6	2.81
462	97.3	4.84

[a]Upper limit of initial concentration of fumaric acid in the reaction mixture was 0.04 M. [b]Approximately equal to the lowest temperature of reaction (398 K).

that is, the temperature range within which the currently examined reactions were performed. Because the solubility of fumaric acid increases almost exponentially with temperature, the solubilities were higher than approximately 20% (mass of FA/mass of H_2O) at the considered reaction temperatures (398−473 K). This means that any aqueous solution of fumaric with a concentration of this reactant lower than approximately

1.45 M is a homogeneous solution. In the current case, the initial concentrations of fumaric acid in the reactors were never higher than 0.04 M, so at least in terms of the solubility of fumaric acid, the examined reaction took place under homogeneous conditions.

To reach the desired reaction temperatures, the reactors were externally heated with glycerol at 398, 423, 448, and 473 K. Because the starting reactant was highly diluted in water, the kinetics of heating was exclusively governed by the rate of heat transfer from glycerol to the bulk reaction mixture. Such a rate of heating is dependent on an overall heat-transfer coefficient that was tuned on an independent set of experimental results for the temperature of water using eq 7. Figure 2 makes clear
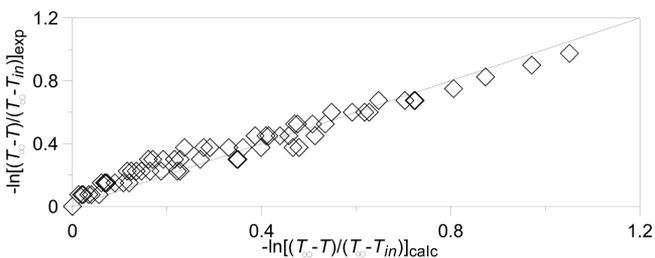

Figure 2. Experimental and calculated (eq 7 based on $U_m = 0.00125$ s^{-1}) temperatures of water in nonisothermal batch reactors heated with glycerol at 398, 423, 448, and 473 K (T_∞) and operated at atmospheric pressure.

that this model (i.e., eq 4 or 7) with a value of $U_m = 0.00125 \pm 0.00006$ s^{-1} is able to describe properly the variation in the reactor temperature with reaction time ($R^2 \approx 0.98$).

The changes in the experimental and calculated concentrations of F, M, and Mx with time from the parallel reactions R2 and R3 are shown in Figures 3−6 at the four different
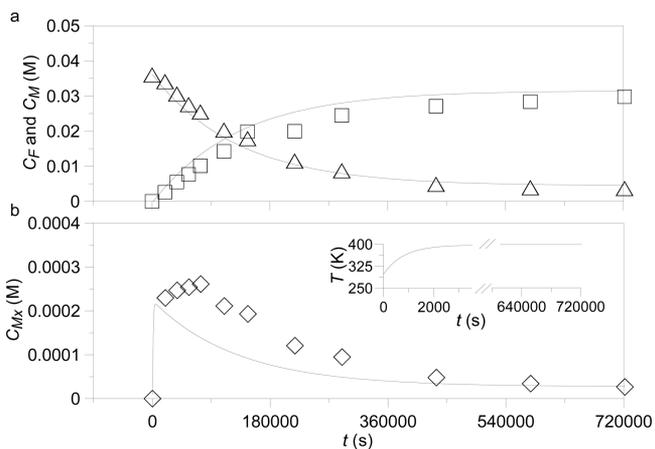

Figure 3. Experimental (symbols) and calculated (solid lines) variations in the concentrations of (a) fumaric acid (triangles) and malic acid (squares) and (b) maleic acid (diamonds) with reaction time in sealed nonisothermal reactors heated from ~298 to 398 K.

investigated temperatures. In a general way, the system of ODEs represented by eqs 1−4 was able to describe the kinetics of consumption of F, as well as the production of M and Mx. The set of tuned model parameters is presented in Table 2. The reliability of k_{30} and E_{a3} was confirmed by a comparison between the forward rate constants for this reaction computed with the Arrhenius expression and those reported in the
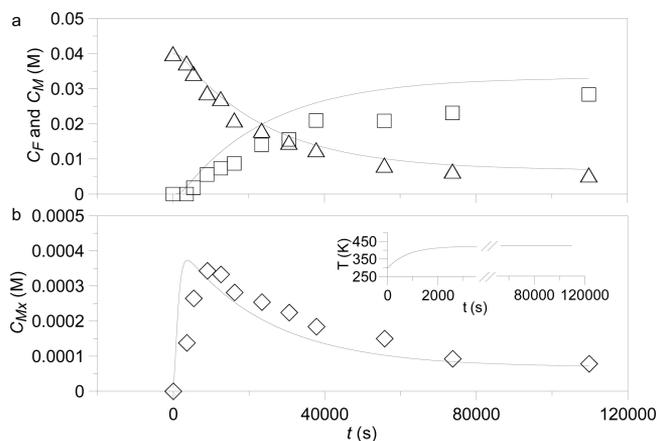

Figure 4. Experimental (symbols) and calculated (solid lines) variations in the concentrations of (a) fumaric acid (triangles) and malic acid (squares) and (b) maleic acid (diamonds) with reaction time in sealed nonisothermal reactors heated from ~298 to 423 K.
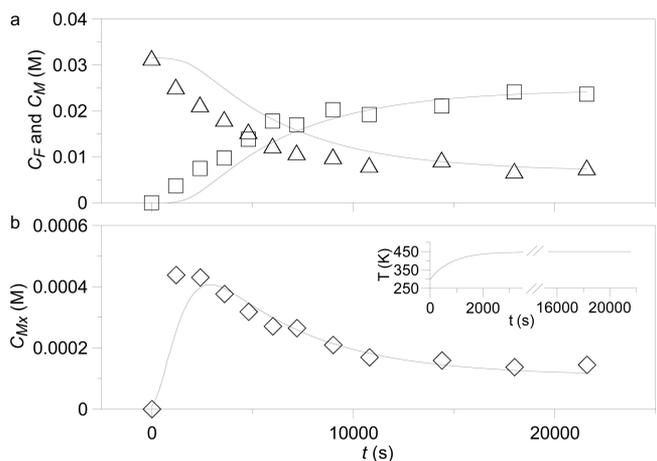

Figure 5. Experimental (symbols) and calculated (solid lines) variations in the concentrations of (a) fumaric acid (triangles) and malic acid (squares) and (b) maleic acid (diamonds) with reaction time in sealed nonisothermal reactors heated from ~298 to 448 K.
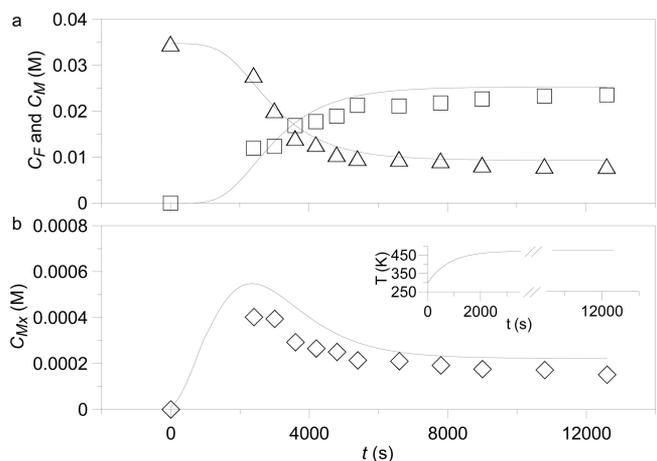

Figure 6. Experimental (symbols) and calculated (solid lines) variations in the concentrations of (a) fumaric acid (triangles) and malic acid (squares) and (b) maleic acid (diamonds) with reaction time in sealed nonisothermal reactors heated from ~298 to 473 K.

Table 2. Tuned Model Parameters

parameter	value
k_{20} (s^{-1})	1.27×10^{-7}
E_{a2}/R (K)	-2815
k_{30} (s^{-1})	1.29×10^{7}
E_{a3}/R (K)	11260
$K_{2,298}$	3.50×10^{-4}
$\Delta H_{2,298}$ (J kmol^{-1})	2.83×10^{7}

literature at the same temperatures and concentration of hydrochloric acid currently considered (see Figure 7a).[14] An
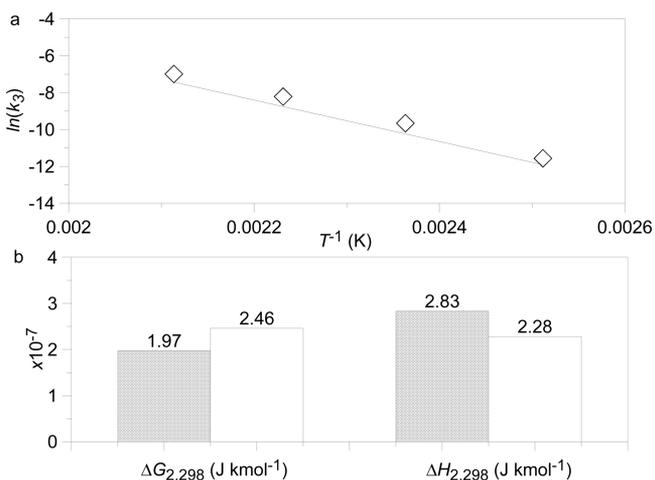
Figure 7. (a) Comparison between the forward rate constants for reaction R3 available in the literature[14] (symbols) and computed with the Arrhenius expression using the tuned values of k_{30} and E_{a3} reported in Table 2 (solid line). (b) Comparison between the primary thermodynamic parameters (Gibbs free energy and enthalpy change at 298 K) for reaction R2 available in the literature[24] (white bars) and those calculated in the current work (dark bars).

analogous analysis was made to validate the tuned value of the heat of reaction R2 ($\Delta H_{2,298}$) and the standard Gibbs free energy change ($\Delta G_{2,298}$) on which $K_{2,298}$ depends (see Figure 7b).[24] In all of these cases, the results from the literature and those currently adjusted from the experimental kinetic data reported in Figures 3−6 are almost the same. However, the tuning procedure was necessary because of the notable sensitivity of species concentrations to uncertainties in these kinetic and thermodynamic parameters.

The residual difference between the calculated conversions of fumaric acid in the current nonisothermal reactors (eqs 1−4 with kinetic parameters from Table 2 at $T_\infty = 398$ K) and those computed with a simplified model (eq 8 with $k_3 = 9.5 \times 10^{-6}$ s^{-1} and $K_3 = 7.31$ from Rozelle and Alberty[14]) that neglects reaction R2 and variations in temperature with time (i.e., $T = 398$ K) further corroborates the reliability of the experimental and numerical procedures involved in the current kinetic investigation (see Figure 8a). Equation 8 is the analytical solution of the separable first-order ODE given by eq 1 with k_2 equal to zero

$$x_F = \frac{K_3}{K_3 + 1}\left\{1 - \exp\left[\frac{-k_3(K_3 + 1)t}{K_3}\right]\right\} \quad (8)$$

In the nonisothermal reactors, T approaches T_∞ as t/t_{max} approaches 0.005 (see the temperature profile in Figure 3b
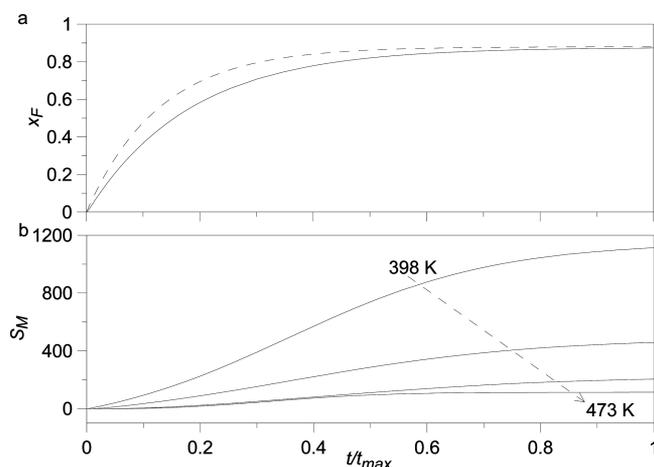
Figure 8. (a) Conversions of fumaric acid calculated with the currently suggested detailed kinetic model (eqs 1−4 with kinetic parameters from Table 2) (solid line) and a simplified kinetic model represented by eq 8 with kinetic parameters from Rozelle and Alberty[14] at $T_\infty = 398$ K (dashed line). (b) Selectivity of malic acid computed as a function of the dimensionless reaction time at the four different investigated T_∞ values ($t_{max} = 720000$ s at $T_\infty = 398$ K, $t_{max} = 109800$ s at $T_\infty = 423$ K, $t_{max} = 21600$ s at $T_\infty = 448$ K, and $t_{max} = 12600$ s at $T_\infty = 473$ K).

when $T_\infty = 398$ K and $t_{max} = 720000$ s), so the nonisothermal behavior plays a minor role in the deviations between the computed conversions obtained by considering the detailed (eqs 1−4) and simplified (eq 8) models. This means that the main reason for the observed deviations is that eq 8 does not account for reaction R2. However, as one can clearly infer from the inverted S curve that represent the decay of C_F with time at $T_\infty = 473$ K (see Figure 6a), the effect of the transient thermal behavior of the examined reactors on the conversion of F is expected to be more prominent at $T_\infty > 398$ K.

For practical purposes, the kinetics of the conversion of fumaric acid and the selectivity of malic acid are the most important responses to be explored. The reason for this is that a rapid conversion of F into products and a high selectivity of M (S_M) can contribute to the reduction of the running costs of the reaction and purification, respectively, of M. In particular, it is interesting to notice that the reaction time to approach equilibrium was sharply reduced from approximately 720000 to 12600 s when the temperature was increased from 293 to 473 K (see Figures 3−6). This suggests that the reactor be operated at high temperatures, but the results for the selectivity of malic acid shown in Figure 8b, obtained by using the equation

$$S_M = \frac{C_M}{C_{Mx}} \quad (9)$$

and in Table 3 at the end of reaction, demonstrate that such a factor (temperature) has an opposite negative effect on S_M.

Table 3. Final Computed Selectivities of Malic Acid As Defined by Eq 9 at Different Reaction Temperatures

T_∞ (K)	t_{max} (s)	S_M
398	720000	1114
423	109800	458
448	21600	205
473	12600	114

In summary, the optimal temperature of reaction depends on a more complex analysis that involves calculating the running costs based on the results of selectivity as well. This is an aspect that depends on the availability of a more detailed kinetic mechanism for the conversion of fumaric acid into products that accounts for the kinetics of reaction R2, a matter that was completely neglected by the only analogous kinetic model available the literature.[14]

4. CONCLUSIONS

The kinetics of the isomerization and hydration of fumaric acid to form maleic and malic acids was experimentally investigated at four different temperatures. The parameters of the Arrhenius expression necessary to calculate the forward rate constants of these different reactions were determined from the experimentally obtained kinetic data ($k_{20} = 1.27 \times 10^{-7}$ s^{-1}, $k_{30} = 1.29 \times 10^{7}$ s^{-1}, $E_{a2}/R = -2815$ K, $E_{a3}/R = 11260$ K). From the same applied procedure of tuning the parameters of the van't Hoff equation, the equilibrium constants of the isomerization reaction were obtained ($K_{2,298} = 3.50 \times 10^{-4}$, $\Delta H_{2,298} = 2.83 \times 10^{7}$ J kmol^{-1}). As far as the authors know, for the reaction that converts fumaric acid into maleic acid, these data are presented in the literature for the first time. For the hydration reaction, the calculated kinetic parameters are important because they confirm the reliability of the only set of forward rate constants for this reaction reported so far.[14]

From a practical point of view, the most useful result is the need to pay attention to the reduction of the selectivity of malic acid when the temperature is increased. This is very important for the purpose of process optimization in terms of running costs, because the same factor has an opposite influence on the reaction time to approach the equilibrium.

A final notable aspect of this study is that it recalls the need for process intensification during the production of malic acid by chemical synthesis. It is motivated by the many reasons that support the commercial importance of this product.

■ AUTHOR INFORMATION

Corresponding Author
*Tel.: + 55 41 33613583. Fax: + 55 41 33613674. E-mail: everton.zanoelo@ufpr.br.

ORCID
Everton Fernando Zanoelo: 0000-0001-9347-4026

Notes
The authors declare no competing financial interest.

■ NOMENCLATURE

C_F = concentration of fumaric acid (mol l^{-1})
C_M = concentration of malic acid (mol l^{-1})
C_{Mx} = concentration of maleic acid (mol l^{-1})
C_W = concentration of water (mol l^{-1})
E_{a2} = tuned activation energy of the isomerization reaction (J kmol^{-1})
E_{a3} = tuned activation energy of the hydration reaction (J kmol^{-1})
i = experimental run i
j = reaction R2, or R3
k_2 = forward rate constant of the isomerization reaction (reaction R2) (s^{-1})
K_2 = equilibrium constant for the isomerization reaction at temperature T

$K_{2,298}$ = equilibrium constant for the isomerization reaction at 298 K
k_{20} = tuned preexponential factor of the isomerization reaction (reaction R2) (s^{-1})
k_3 = forward rate constant of the hydration reaction (reaction R3) (s^{-1})
k_3' = true forward rate constant of the hydration reaction (reaction R3) (l s^{-1} mol^{-1})
K_3 = equilibrium constant for the hydration reaction at temperature T
$K_{3,298}$ = equilibrium constant for the hydration reaction at 298 K
k_{30} = tuned preexponential factor of the hydration reaction (reaction R3) (s^{-1})
P = reaction pressure (kPa)
R = gas constant (J kmol^{-1} K^{-1})
S = solubility of fumaric acid (%, 100 × kg of F/kg of water)
S_M = selectivity of malic acid
t = reaction time (s)
T = reaction temperature (°C)
T_∞ = temperature of the surrounding heating fluid (°C)
U_m = modified overall heat-transfer coefficient (s^{-1})
x_F = conversion of fumaric acid into products
$\Delta G_{2,298}$ = Gibbs free energy change for the isomerization reaction at 298 K (J kmol^{-1})
$\Delta H_{2,298}$ = enthalpy change for the isomerization reaction at 298 K (J kmol^{-1})
$\Delta H_{3,298}$ = enthalpy change for hydration reaction at 298 K (J kmol^{-1})

■ REFERENCES

(1) Francis, F. J. *Wiley Encyclopedia of Food Science and Technology*; Wiley: Hoboken, NJ, 1999.
(2) *Kirk-Othmer Encyclopedia of Chemical Technology*; Wiley: Hoboken, NJ, 2007.
(3) Goldberg, I.; Williams, R. *Biotechnology and Food Ingredients*; Springer: New York, 1991.
(4) Garibay, M. G.; Ramírez, R. Q.; Canales, A. L. M. *Biotecnología Alimentaria*; Limusa: Ciudad de México, 2004.
(5) Huang, J.; Huang, L.; Lin, J.; Xu, Z.; Cen, P. Organic Chemicals from Bioprocesses in China. *Adv. Biochem. Eng./Biotechnol.* **2010**, *122*, 43.
(6) *Malic Acid Market Analysis by Application (Beverages, Confectionary & Food) and Segment Forecast to 2020*; Grand View Research Inc.: San Francisco, 2014.
(7) Lee, B. H. *Fundamentals of Food Biotechnology*; Wiley-Blackwell: New York, 2015.
(8) Zelle, R. M.; de Hulster, E.; van Winden, W. A.; de Waard, P.; Dijkema, C.; Winkler, A. A.; Geertman, J. M. A.; van Dijken, J. P.; Pronk, J. T.; van Maris, A. J. A. Malic acid production by Saccharomyces cerevisiae: Engineering of pyruvate carboxylation, oxaloacetate reduction and malate export. *Appl. Environ. Microb.* **2008**, *74*, 2766.
(9) Cullen, M. A., Jr.; Ingleman, M. (Allied Chemical Corporation). Purification of Malic Acid. U.S. Patent 3,391,187, 1968.
(10) Weinrotter, F.; Schmidt, A.; Gauster, W. (Osterreichische Stickstoffwerke Aktiengesellschaft). Process for the Production of Malic Acid. U.S. Patent 3,875,222, 1975.
(11) Nozaki, K.; Ogg, R., Jr cis-trans Isomerizations. I. The Mechanism of a Catalyzed Isomerization of Maleic Acid to Fumaric Acid. *J. Am. Chem. Soc.* **1941**, *63*, 2583.
(12) Sauer, M.; Porro, D.; Mattanovich, D.; Branduardi, P. Microbial production of organic acids: expanding the markets. *Trends Biotechnol.* **2008**, *26*, 100.
(13) *CAMEO Chemicals*, version 2.7; National Oceanic and Atmospheric Administration (NOAA): Washington, DC, 2016.

(14) Rozelle, L. T.; Alberty, R. A. Kinetics of the acid catalysis of the hydration of fumaric acid to malic acid. *J. Phys. Chem.* **1957**, *61*, 1637.

(15) Pinto, L. F.; Rodriguez-Reartes, S. B.; Corazza, M. L.; Cabral, V. F.; De Araujo, P. H. H.; Madureira, E. H.; Zabaloy, M. S.; Cardozo-Filho, L. Phase behavior of carbon dioxide + medroxyprogesterone acetate system at high pressures. *Fluid Phase Equilib.* **2013**, *349*, 1.

(16) Roa Engel, C. A.; Ter Horst, J. H.; Pieterse, M.; Van Der Wielen, L. A. M.; Straathof, A. J. J. Solubility of Fumaric Acid and Its Monosodium Salt. *Ind. Eng. Chem. Res.* **2013**, *52*, 9454.

(17) Official Method AOAC 986.13: Quinic, Malic, Citric Acid in Cranberry Juice Cocktail and Apple Juice. In *Food Composition, Additives, Natural Contaminants*; AOAC International: Arlington, VA, 1990.

(18) Phillips, M. M.; Case, R. J.; Rimmer, C. A.; Sander, L. C.; Sharpless, K. E.; Wise, S. A.; Yen, J. M. Determination of organic acids in Vaccinium berry standard reference materials. *Anal. Bioanal. Chem.* **2010**, *398*, 425.

(19) Petzold, L. R. A. *Description of DASSL: A Differential/Algebraic System Solver*; Report SAND82-8637; Sandia National Laboratories: Albuquerque, NM, 1982.

(20) Jenson, V. G.; Jeffreys, G. V. *Mathematical Methods in Chemical Engineering*; Academic Press: New York, 1977.

(21) Edgar, T. F.; Himmelblau, D. M. *Optimization of Chemical Processes*; McGraw-Hill: Singapore, 1989.

(22) Weiss, J. M.; Downs, C. R. The physical properties of maleic, fumaric and malic acids. *J. Am. Chem. Soc.* **1923**, *45*, 1003.

(23) Lange, N. A.; Sinks, M. H. The solubility, specific gravity and index of refraction of aqueous solutions of fumaric, maleic and i-malic acids. *J. Am. Chem. Soc.* **1930**, *52*, 2602.

(24) DIPPR *The DIPPR Information And Data Evaluation Manager (DIADEM)*, Version 1.2; AIChE: New York, 2000.