

Liquid–liquid synthesis of oximes from carbonyl compounds: formation under neutral conditions and degradation at acidic hydrometallurgical process conditions

Kabugo James, Virolainen Sami, Paatero Erkki, Sainio Tuomo

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Complete List of Authors:	Kabugo, James; Outotec (Finland) Oy, Pori Research Center Virolainen, Sami; Lappeenranta University of Technology, Chemical technology Paatero, Erkki; Lappeenranta University of Technology, School of Engineering Science Sainio, Tuomo; Lappeenranta University of Technology, Chemical Technology
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17 6 **Liquid-liquid synthesis of oximes from carbonyl compounds: Formation at**
18 **neutral conditions and degradation at acidic hydrometallurgical process**
19 7
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25 10 James Kabugo^{a, b}, Sami Virolainen^{a*}, Erkki Paatero^a and Tuomo Sainio^a
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29 12

30 13 ^a Lappeenranta University of Technology, Skinnarilankatu 34, FI 53850 Lappeenranta, Finland
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32 14 ^b Outotec (Finland) Oy, Kuparitie 10, 28330 Pori
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55 24 *) Corresponding author, e-mail: Sami.Virolainen@lut.fi . Tel.: +358407093444
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1 ABSTRACT

2 BACKGROUND

3 In order to elucidate kinetics in the synthesis of oxime liquid-liquid extraction reagents, used as
4 ligands in hydrometallurgical copper production, the oximation reactions of salicylaldehyde and
5 2'-hydroxyacetophenone with hydroxylamine were studied in two phase system. Two
6 experimental methods were applied: CSTR reactor under vigorous mixing and batch reactor
7 under normal agitation. The reverse reaction in acidic conditions was also examined, because it
8 results hydroxyoxime reagent losses in copper liquid-liquid extraction process.

9 RESULTS

10 The overall oximation reaction was observed to be of a second order, first order with respect to
11 each reactant. The estimated activation energy for oximation of salicylaldehyde was 34.2 kJ/mol,
12 and interfacial reaction rate constant at 40 °C $4.81 \cdot 10^{-3}$ L/mol/s. Used model, including
13 empirical description for interfacial reactant concentrations, described the salicylaldehyde
14 oximation reaction well in the wide concentration range. In the batch reactor over 0.99
15 conversion for salicylaldehyde was achieved in 15 min at 50 °C, but for 2'-hydroxyacetophenone
16 maximum reaction conversion of only 0.17 was achieved at 70 °C in 60 min. Both, aldoxime and
17 ketoxime, were hydrolyzed into their corresponding carbonyl compounds in presence of 180 g/L
18 sulfuric acid. The ketoxime was completely converted into a ketone, but with the aldoxime
19 equilibrium was observed at 80% reagent degradation.

20 CONCLUSION

21 Liquid-liquid system in neutral conditions is applicable for oximation of especially aldehydes
22 generated by degradation of hydroxyoxime solvent extraction reagents. For ketones the reaction

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3 1 is much slower. The degradation reaction was shown to be significant in conditions similar to
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6 2 copper liquid-liquid extraction stripping stage.
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9 3 Keywords: Hydroxyoximes, aldehyde, ketone, hydroxylamine, hydrolytic degradation
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1 INTRODUCTION

2 Hydroxyoxime ligands, both aldoximes and ketoximes, are extensively used as extractants in
3 hydrometallurgy, for example in the recovery and purification of copper from aqueous pregnant
4 leach solutions [1]. They are also applied as mineral collectors in minerals processing [2].
5 Hydroxyoxime copper reagents are selective, and also otherwise technically very functional to
6 the separation task, but generally regarded expensive due to certain challenges in their
7 manufacturing process.

8 Synthesis of hydroxyoxime ligands from their carbonyl compounds, aldehyde or ketone, is
9 usually done with the use of hydroxylamine or its acid salts [3]. The rates of oximation reactions
10 are notably slow, and may require several hours especially under ambient conditions. This is
11 particularly true for carbonyl compounds with very low solubility in aqueous solutions, like the
12 hydroxyoximes for the copper hydrometallurgy. Several synthesis methods to increase oximation
13 rates have been proposed in literature. These include application of micellar [3-4] and phase-
14 transfer catalysis [5] in liquid-liquid systems, solid-organic systems [6] and single organic phase
15 systems [7-9].

16 The kinetics of the oximation reaction has been studied in the past for various aldehydes and
17 ketones [3, 10]. The reaction rate tends to vary widely among different carbonyl reagents
18 because steric hindrance and electronic effects play an important role in the reactivity of
19 carbonyl compounds [10-13]. Another important factor is the reaction medium, as was observed
20 while developing analytical methods for quantification of aldehydes and ketones in 1960's [14].

21 The reverse reaction to oximation usually occurs via acid catalyzed hydrolysis. This unwanted
22 phenomenon leads to degradation of alkyl hydroxyoximes when they are employed for liquid-
23 liquid extraction of metals in the hydrometallurgical industry [15-18]. In copper liquid-liquid

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3 1 extraction plants, for example, sulfuric acid concentration of 180 g/L is typical in the stripping
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5 2 stage, which favors the hydrolytic degradation [18]. It is known that ketoximes are normally
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7 3 more stable against the hydrolysis than the aldoximes, which is one of the reasons why
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9 4 commercial extractants are often mixtures of aldoximes and ketoximes, although aldoximes are
10
11 5 known to be stronger copper complexants.
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15 6 In this work, the oximation behavior of two selected carbonyl compounds in a liquid-liquid
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17 7 reaction medium are studied. The main objective is to gain fundamental knowledge on the
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19 8 oximation kinetics of salicylaldehyde and 2'-hydroxyacetophenone in a liquid-liquid reaction
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21 9 system. The possibility to intensify the oximation reaction process by employing a flow reactor
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23 10 with short contact time, but efficient mixing, was investigated. The selection of the above
24
25 11 carbonyl reagents was based on their similarity to the precursors of modern, industrially used,
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27 12 hydroxyoxime liquid-liquid extractions reagents, such as 5-nonylsalicylaldoxime and 2-hydroxy-
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29 13 5-nonylacetophenone oxime [1]. Degradation of hydroxyoximes under typical copper stripping
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31 14 conditions was also briefly studied for both salicylaldoxime and 2'-hydroxyacetophenone oxime
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33 15 to demonstrate the reversibility of the studied reaction. The findings from this study support the
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35 16 development of on-site regeneration processes for the degraded hydroxyoxime organic ligands.
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42 **EXPERIMENTAL**

43 **Reagents**

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45 19 The carbonyl reagents, salicylaldehyde and 2'-hydroxyacetophenone, were purchased from
46
47 20 Sigma-Aldrich as analytical grade chemicals. Toluene (technical grade) was used as an organic
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49 21 phase solvent. Hydroxylamine sulfate $(\text{NH}_3\text{OH})_2\text{SO}_4$ and Na_2CO_3 were also of analytical grade
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51 22 (Sigma-Aldrich). Water purified with Centra 60/120 equipment was used in preparation of
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53 23 aqueous solutions.
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1 Analytical method

2 The organic phases were analyzed by gas chromatography (GC) using a non-derivatized method
3 for determination of the carbonyl and oxime mole fractions. A gas chromatograph, Agilent
4 6890N, with 25 m column, flame ionization detection (FID) and helium as a carrier gas was used
5 in the analysis. In the optimized method, the injector and detector temperatures were maintained
6 at 260 °C and 320 °C respectively. The temperature of the column was adjusted according to the
7 following program: temperature was increased from 50 °C to 90 °C at 10 °C/min rate and after
8 that held constant for 2 min. Thereafter it was ramped to 320 °C at 10 °C/min rate, and held
9 constant for 2 min to give a total analysis time of 31 min. Identification of components was done
10 with the help of external standard samples.

11 Experiments in a continuous flow reactor

12 Solutions of approximately 0.8 M salicylaldehyde in toluene and 0.7 M 2'-hydroxyacetophenone
13 (accurate concentration measured by GC) in toluene were prepared and used as stock solutions
14 for the organic phases. The aqueous phase stock solution was 1.7 M (NH₃OH)₂SO₄, which
15 corresponds to 3.4 M hydroxylamine. The pH of the aqueous solution was adjusted to 6.8 with
16 Na₂CO₃. The experiments were done in a 2.5 mL continuous stirred tank-reactor (CSTR)
17 immersed in a water bath and equilibrated to desired temperatures (20-50 °C). Feed solutions
18 were warmed to the corresponding temperatures and pumped through the reactor by use of a
19 peristaltic pump (Ismatec JPN-12 or IPC). Mass flow rates of feed solutions were monitored with
20 the help of balances. Vigorous mixing in the reactor was achieved by using T8 Ultra Turrax high
21 shear mixer (by IKA) at 15000 rpm.

22 During the runs, the aqueous and organic streams were combined in a T-connector just before the
23 reactor. The exact O/A volume ratio was calculated from mass flow data with measured densities

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3 1 of the aqueous and organic phases. The space time in the reactor, and the reaction temperature,
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5 2 were varied. The total volumetric flow rate through the reactor was in the range of 1.6-10
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7 3 mL/min. Under steady state conditions, the extent of the oximation reaction was determined
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9 4 offline through sampling of the dispersion from the reactor outlet. The phases in the samples
10
11 5 were immediately separated with a centrifuge (CINC V-2).
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16 **Experiments in a batch reactor**

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19 7 In batch experiments, the organic phase comprised of 0.84 M of the aldehyde or 0.73 M of the
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21 8 ketone in toluene, and the aqueous phase was 1.7 M $(\text{NH}_3\text{OH})_2\text{SO}_4$ at pH 6.8. For each
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23 9 experiment, 350 mL of aqueous phase was charged into a one-liter reactor and the temperature
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25 10 was adjusted to the desired value. An equivalent volume of the organic phase was added to
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27 11 obtain a phase ratio $O/A = 1$. The content of the reactor was then stirred at 500-900 rpm for an
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29 12 hour at a constant temperature. Samples of the dispersion were collected periodically, and the
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31 13 phases in each sample were separated immediately by using a centrifuge to stop the reaction, and
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33 14 to recover the oximated organic solution. The organic phase was analyzed for oxime and
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35 15 carbonyl groups with the GC method described above.
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41 **Hydrolytic degradation experiments**

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44 17 Oximated organic solutions obtained after batch oximation of salicylaldehyde and
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46 18 2'-hydroxyacetophenone were used as the organic phase for the degradation experiments. Two
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48 19 copper electrolyte solutions, with 30 g/L of Cu and either 180 g/L or 350 g/L of H_2SO_4 , were
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50 20 used. The total volume of the organic phase in each experiment was 400 mL with phase volume
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52 21 ratio $O/A = 1$. The experiments were conducted in 500 mL glass bottles at 40 °C in an orbital
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54 22 shaker for one week. Samples were taken periodically and the recovered organic phases were
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56 23 analyzed for the carbonyl and the oxime functional groups with GC as described above.
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1 THEORY AND MATHEMATICAL MODELLING

2 Oximation takes place in two steps, formation of a carbinolamine intermediate followed by its
3 dehydration, as illustrated in reaction Scheme I. The reaction mechanism for the carbinolamine
4 intermediate formation involves either acid catalyzed amine addition to carbonyl group or a non-
5 catalyzed formation of a zwitterion intermediate, which is converted to a neutral carbinolamine
6 complex after a proton switch either by water or acid catalyzed route [19-21]. Carbinolamine
7 formation rate is known to be influenced by pH and the structural reactivity of the carbonyl and
8 the amine compounds [11-12, 20, 22]. The decomposition of the intermediate into the oxime
9 occurs via acid [11] or base catalyzed dehydration [22-25].

10 The dehydration of carbinolamine proceeds rapidly both at low pH (≤ 2.5) and at high pH (≥ 10)
11 [25] but is slow under neutral and mildly alkaline conditions [12, 20]. For example, the
12 formation of carbinolamine intermediate was reportedly observed in a homogeneous system
13 during oximation of acetone at pH 8.5 but not at pH 2.5 or at pH 10 [25]. Dehydration of the
14 carbinolamine intermediate is considered the rate-determining step under neutral and mildly
15 basic reaction conditions [19]. In a more acidic or alkaline environment, uncatalyzed addition of
16 free base hydroxylamine to the carbonyl group is reported to be the rate-determining step [19-21].
17 It is also important to note that at low pH conditions, hydroxylamine exists mainly in protonated
18 form, which is more stable and less reactive to carbonyl compounds. In neutral and alkaline
19 conditions, most of the hydroxylamine is present in a more reactive free base form, which is
20 susceptible to decomposition even at ambient conditions [26].

21 According to Janakiraman and Sharma, and Fitzpatrick and Gettler [4, 10] the overall oximation
22 reaction is a second order reaction, being first order with respect to both the carbonyl group and
23 hydroxylamine. Shenk [14] suggests a third order or a pseudo-second order reaction including

1 the role of the proton (pH) in the oximation reaction mechanism. Fitzpatrick and Gettler [10] also
 2 concluded, based on their oximation experiments with 11 carbonyl compounds, that the reaction
 3 is irreversible under neutral pH conditions. However, as discussed already in the introduction, it
 4 is known that the hydroxyoxime reagents used in the hydrometallurgical copper processes
 5 undergo hydrolytic degradation under very acidic conditions. The mechanism for this reaction
 6 has been proposed by Hurtado-Guzmán and Menacho [16] and presented in Scheme II.

7 *CSTR model*

8 The continuous reactor was modeled as an ideal CSTR at steady state with two immiscible liquid
 9 phases as the feed. This is well justified based on the analysis of residence time distribution data
 10 reported earlier [27] from the same high-shear mixer reactor. As will be explained below, only
 11 the aldehyde oximation was studied in the CSTR. The mass balances of the reactants A
 12 (salicylaldehyde) and HA (hydroxylamine) over the reactor are

$$13 \quad \dot{V}^{\text{aq}} (c_{\text{HA}}^{\text{aq,feed}} - c_{\text{HA}}^{\text{aq}}) + r_{\text{HA}} a_{\text{int}} V_{\text{R}} = 0 \quad (1)$$

$$14 \quad \dot{V}^{\text{org}} (c_{\text{A}}^{\text{org,feed}} - c_{\text{A}}^{\text{org}}) + r_{\text{A}} a_{\text{int}} V_{\text{R}} = 0 \quad (2)$$

15
 16 In Eqs. (1) and (2), c^{aq} and c^{org} are volumetric concentrations (mol/L) in the bulk of the two
 17 phases, V_{R} is the volume (L) of the dispersion in the reactor and a_{int} is the specific interfacial
 18 area (m^2/L). The volumetric flow rates of the aqueous and organic streams, \dot{V} (L/s), give space
 19 time $\tau = V_{\text{R}} (\dot{V}_{\text{aq}} + \dot{V}_{\text{org}})^{-1}$. Due to vigorous mixing in the high shear mixer, the space time is equal
 20 for the two phases and the organic-to-aqueous phase ratio is $\phi = \dot{V}_{\text{org}} / \dot{V}_{\text{aq}}$.

1 The interfacial area is not known and depends in practice on the droplet size distribution and the
2 phase ratio. Considering that the mixing rate was held constant in the CSTR experiments, and
3 that the phase ratio varied over a narrow range only ($\phi = 0.92 \dots 1.08$), the droplet size
4 distribution is assumed to be independent of phase ratio. The interfacial area is thus related to the
5 phase ratio as

$$a = \delta \frac{\phi}{1 + \phi} \quad (3)$$

7 where δ is an unknown constant characterizing the droplet size distribution. This constant also
8 scales the unit of a from $1/m$ to m^2/L .

10 The rates of formation of A and HA, denoted by r ($\text{mol}/m^2/L$) in the mass balances, are
11 calculated by assuming that the net reaction at the interface is of first order with respect to both
12 reactants [4, 10]

$$r_A = r_{HA} = -k_1(T) q_A q_{HA} \quad (4)$$

14 where k_1 is a reaction rate constant ($m^2/mol/s$) and q denotes the interfacial concentrations
15 (mol/m^2) of the reactants.

17 Considering the high concentration of reactants in most of the experiments, hydroxylamine in
18 particular, the distribution of the reactants between the interface and the bulk phases can be non-
19 linear. In order to account for this phenomenon, the concentrations q in Eq. (4) are calculated
20 with a simple model

$$q_j = \frac{q_{\max,j} b_j c_j^k}{1 + b_A c_A^{\text{org}} + b_{\text{HA}} c_{\text{HA}}^{\text{aq}}} \quad (5)$$

where b and q_{\max} are constants and superscript k refers to the aqueous phase for $j = \text{HA}$ and to the organic phase for $j = \text{A}$. Note that Eq. (5) is used here as an empirical model and not as a thermodynamically consistent interfacial adsorption model. The presence of water and toluene at the interface are not considered and the parameters b and q_{\max} are regarded independent of temperature for simplicity.

In order to reduce the number of parameters, we define the interfacial rate of formation per volume of the dispersion, r'_j (mol/L/s), as

$$r'_j = r_j a_{\text{int}} = -k_1(T) q_{\max,\text{A}} q_{\max,\text{HA}} \delta \frac{b_A b_{\text{HA}} c_A^{\text{org}} c_{\text{HA}}^{\text{aq}}}{1 + b_A c_A^{\text{org}} + b_{\text{HA}} c_{\text{HA}}^{\text{aq}}} \frac{\phi}{1 + \phi} \quad (6)$$

which simplifies to

$$r'_j = -k'_1(T) \frac{c_A^{\text{org}} c_{\text{HA}}^{\text{aq}}}{1 + b_A c_A^{\text{org}} + b_{\text{HA}} c_{\text{HA}}^{\text{aq}}} \frac{\phi}{1 + \phi} \quad (7)$$

where k'_1 is a constant that depends only on temperature according to an Arrhenius type expression

$$k'_1(T) = k_{\text{ref}} \exp\left(\frac{E_a}{R} \left(\frac{1}{T_{\text{ref}}} - \frac{1}{T}\right)\right) \quad (8)$$

where E_a is an apparent activation energy and k_{ref} is the value of k'_1 at an arbitrary reference temperature T_{ref} .

The mass balances were rewritten as in Eqs. (9) and (10) and the concentrations of A and HA in their respective phases at the reactor outlet were solved numerically by using Eqs. (7) and (8) to calculate the rates of formation.

$$c_{\text{HA}}^{\text{aq,feed}} - c_{\text{HA}}^{\text{aq}} + r'_{\text{HA}} \tau (1 + 1/\phi) = 0 \quad (9)$$

$$c_{\text{A}}^{\text{org,feed}} - c_{\text{A}}^{\text{org}} + r'_{\text{A}} \tau (1 + \phi) = 0 \quad (10)$$

Batch reactor model

The concentrations of the reactants in their respective phases in the batch reactor were calculated from the mass balances

$$\frac{dc_{\text{HA}}^{\text{aq}}}{dt} = r'_{\text{HA}} (1 + \phi) \quad (11)$$

$$\frac{dc_{\text{A}}^{\text{org}}}{dt} = r'_{\text{A}} (1 + 1/\phi) \quad (12)$$

where the phase ratio is $\phi = V_{\text{org}}/V_{\text{aq}}$. The interfacial reaction rates were evaluated by using Eqs. (7) and (8).

Parameter estimation

The four parameters of the kinetic model (k_{ref} , E_a , b_A , b_{HA}) were fitted against $N = 120$ CSTR runs at three temperatures and five aldehyde to hydroxylamine concentration ratios by minimizing the sum of weighted squared residuals shown in Eq. (13)

$$RSS = \sum_{k=1}^N \omega_k \left(c_{A,\text{exp},k}^{\text{org}} - c_{A,\text{calc},k}^{\text{org}} \right)^2 \quad (13)$$

Owing to the wide range of concentrations (one decade in both hydroxylamine and salicylaldehyde concentrations) the responses at low concentration were given a higher weight in the parameter estimation by setting $\omega_k = 1/c_{A,\text{exp},k}^{\text{org}}$.

The oximation reaction rate constant in the batch reactor was estimated from data obtained with 500 rpm and 900 rpm stirring rates separately. Although the batch reactor runs were carried out at 323 K only, the value of $k_{\text{ref}}(T=313 \text{ K})$ was estimated instead of the value of $k_1'(T = 323 \text{ K})$ in order to allow more direct comparison of the rate constants obtained in the two kinds of reactors. Due to the limited amount of data, the values estimated from the CSTR experiments were used for E_a , b_A and b_{HA} .

RESULTS AND DISCUSSION

Batch reactor experiments: conversion and reversibility of the oximation reaction

The rates of the forward and reverse reactions of the oximation reaction (see Scheme I and II) depend strongly on pH. In order to justify the assumption of irreversible oximation reaction at the reaction conditions employed here (pH = 6.8), batch reactor experiments were carried out with carbonyl:hydroxylamine molar ratio of ca. 1:4. As observed in Fig. 1, the conversion of salicylaldehyde to salicylaldoxime is practically complete at 20 min. As the excess of hydroxylamine was not very large, this result confirms the assumption in Scheme I that liquid-liquid oximation of salicylaldehyde in toluene/water system can be treated as an irreversible

1 reaction at neutral pH range of the aqueous phase. Considering the low amount of protons
2 present at this pH means that the reaction proceeds with the non-catalytic route.

3 The reverse reaction occurs in concentrated sulfuric acid, as is observed in Fig. 1B. The organic
4 phase was the toluene solution obtained in the oximation reaction experiments and the aqueous
5 phase corresponded to a typical stripping stage of hydrometallurgical copper processing, bearing
6 30 g/L of copper as a sulfate and 180 g/L of sulfuric acid. Hydrolytic degradation of
7 salicylaldoxime was not complete but reached equilibrium within a few hours (the first data point
8 is at 8 h). The equilibrium conversion of the aldehyde degradation was 0.81 and did not change
9 when sulphuric acid concentration was increased to 300 g/L. Under these conditions, the
10 oximation reaction proceeds with the acid-catalyzed pathways in Scheme I.

11 The liquid-liquid reaction of 2'-hydroxyacetophenone with hydroxylamine was found to be very
12 slow at 323 K and also at 343 K. This could stem from lower reactivity of the ketone group
13 compared to the aldehyde group or from its lower affinity to the liquid-liquid interface.
14 According to [28], the octanol-water partition coefficients of 4-hydroxybenzaldehyde and 4'-
15 hydroxyacetophenone, which are structurally very close to the compounds used here, are equal
16 ($\log P_{O/W} = 1.35$). Therefore, it is most likely that the lower reactivity of the ketone is related to
17 steric factors and the electron-withdrawing property of the methyl substituent group.

18 Also the degradation of the ketoxime in concentrated acid is slower than that of the aldoxime
19 (Figs. 1B and C). However, the ketoxime is completely hydrolyzed after approximately 50 h in
20 the batch experiments. It is thus probable that in commercial metals extraction reagents, that are
21 often mixtures of aldoximes and ketoximes, the ketoxime is more stable but, when degraded, it is
22 more difficult to regenerate by carrying out the reoximation reaction. It is important to note that

1 degradation of commercial hydroxyoxime reagents takes place slower than these model
2 compounds due to the long alkyl substitute groups that make them more hydrophobic [18].
3

4 **Kinetics of aldehyde oximation in a CSTR**

5 The reaction kinetics in liquid-liquid oximation of salicylaldehyde with hydroxylamine were
6 investigated in more detail using a CSTR with vigorous high-shear mixing. The experimental
7 results are displayed in Figs. 2 and 3. The feed concentrations of both reactants in their
8 respective phases were varied over a large concentration range. As observed in the experimental
9 data, the reaction is fast at 323 K, yielding approximately 50% conversion with 100 s space time.
10 In the batch reactor, equal conversion required approximately 180 s with the higher stirring rate
11 (900 rpm). It is thus expected that the mass transfer resistances are practically eliminated in the
12 high-shear mixer operating at 15 000 rpm, and the kinetic parameters correspond to the kinetics
13 of the interfacial reaction only.
14 Owing to the high mixing power in the CSTR, the temperature at reactor outlet was typically 1%
15 – 2% higher than the set point. This was attributed to mixing rather than reaction heat because
16 conversion is rather small and a similar temperature effect is observed with this setup also for
17 non-reactive systems. The space time was within $\pm 5\%$ and the phase ratio within $\pm 8\%$ of the set
18 points in the experiments. Accurate values were recorded for each experiment and used in the
19 parameter estimation. Therefore, Figs. 2 and 3 display the experimental data with filled circles
20 and calculated results in parameter estimation with open circles for each CSTR experiment. The
21 solid lines are simulation results showing the dependence of aldehyde concentration at reactor
22 outlet on space time for a fixed set of parameters (T , ϕ , c_A and c_{HA}) that correspond to average of
23 the experimental conditions in each set of experiments.

1 The parameters of the kinetics model in Eqs. (3) to (5) were estimated from the CSTR data as
2 described above and are given in Table 1 together with their 95% confidence intervals. The
3 residuals are shown in Fig. 4. Overall, the fit is good although the data at lowest aldehyde
4 concentration in the feed shows some bias in the relative residuals. This corroborates the
5 assumption in Eq. (3) that the reaction can be regarded irreversible at pH 6.8 in the liquid-liquid
6 system and the kinetics modelled using interfacial concentrations.

7 The activation energy was found to be relatively low, 34.2 kJ/mol, but not in the range of mass
8 transfer limited system. The reaction rate constant from the CSTR data has a relatively large
9 confidence interval. This is due to scatter in the data at high space time values and the fact that
10 the experimental concentration range is quite large. The β parameters describe the distribution of
11 the aldehyde and the amine between bulk phases and the phase boundary where the reaction
12 occurs. The values should be interpreted such that the interphase has a higher A:HA mole ratio
13 than the overall mixture. The fact that the parameters did not tend towards zero during fitting
14 justifies the use of a simple correlation that cannot predict higher concentrations at the interface
15 than in the bulk phases. Excluding the distribution of reactants between the phases (*i.e.*, using Eq.
16 (4) with $q_A = c_A^{\text{org}}$; $q_{HA} = c_{HA}^{\text{aq}}$) lead to doubling of the norm of residuals from 0.115 to 0.218. At
17 the same time, k_{ref} decreased by a factor of 12. E_a increased by only 9% indicating that the
18 distribution of solutes between the bulk and interface is not strongly dependent on temperature.

19 Reaction rate constants were estimated from the batch reactor data as well (Table 1) by using b_A ,
20 b_{HA} , and E_a obtained from the CSTR data. The kinetics appears to be slower in the batch reactor.
21 This is as expected, since the mixing power with the high-shear mixer in the CSTR is
22 significantly higher than with a conventional turbine mixer used in the batch experiments. It is

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3 1 thus concluded that the value of k_{ref} from CSTR data is close to the intrinsic reaction kinetics and
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5 2 is not significantly affected by mass transfer resistance.
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4 **CONCLUSIONS**

5 The results of this work show that oximation of salicylaldehyde with hydroxylamine in a
6
7 toluene-water liquid-liquid system follows an overall second order reaction kinetics at near
8
9 neutral pH. It was shown that in the case of vigorous high-shear mixing in a CSTR, the reaction
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11 kinetics is best modelled by correlating the distribution of the reactants between the bulk phases
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13 and the phase boundary with a simple one-parameter (per reactant) model.
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27 10 The kinetics of salicylaldehyde oximation was found to be much faster than that of 2'-
28
29 hydroxyacetophenone. Moreover, the degradation of the aldehyde, the backwards reaction, was
30
31 not complete in concentrated sulfuric acid / copper sulfate medium, typical for
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33 hydrometallurgical processes, whereas the ketoxime was completely degraded in approximately
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35 50 h. The liquid-liquid system employed here seems suitable for use in industrial production of
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37 aldoxime chemical reagents such as hydroxyaldoxime ligands applied in copper liquid-liquid
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39 extraction.
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For Peer Review

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8 3 **List of figure captions**
9

10
11 4 Figure 1.

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13
14 5 Oximation of 2'-hydroxyacetophenone (squares) and salicylaldehyde (circles) with
15
16 6 hydroxylamine in a batch reactor at pH 6.8 (A). Reaction temperature: 323 K (red, yellow) or
17
18 7 343 K (blue). Stirring rate: 500 rpm (green) or 900 rpm (red, blue). Solid lines: calculated with
19
20
21 8 the batch reactor model. Initial concentrations: 0.73 M for the ketone, 0.84 M for the aldehyde
22
23 9 and 3.4 M for hydroxylamine. Phase ratio = 1.0. Hydrolysis of the corresponding aldoxime (B)
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25
26 10 and ketoxime (C) in 30 g/L CuSO₄ solutions with 180 g/L (red circles) or 300 g/L (crosses)
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28 11 H₂SO₄ at 313 K. Phase ratio = 1.0.
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34 13 Figure 2.

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37 14 Liquid-liquid oximation of salicylaldehyde (in toluene) and hydroxylamine (in water, $c_{\text{HA}}^{\text{feed}} = 3.4$
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39 15 M, pH 6.8) in CSTR. Filled yellow circles: experimental data. Open circles: calculated with
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42 16 exact values of operating conditions (T , τ , ϕ , c_j) in each data point. Lines: calculated using
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45 17 average values of operating conditions.
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51 19 Figure 3.

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54 20 Liquid-liquid oximation of salicylaldehyde (in toluene) and hydroxylamine (water, pH 6.8) in a
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56 21 CSTR. Filled circles: experimental data; magenta: $c_{\text{HA}}^{\text{feed}} = 0.34$ M, green: $c_{\text{HA}}^{\text{feed}} = 1.7$ mol/L, red:
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1 $c_{\text{HA}}^{\text{feed}} = 3.4 \text{ M}$. Open circles: calculated with exact values of operating conditions (T, τ, ϕ, c_j) in
2 each data point. Lines: calculated using average values of operating conditions.

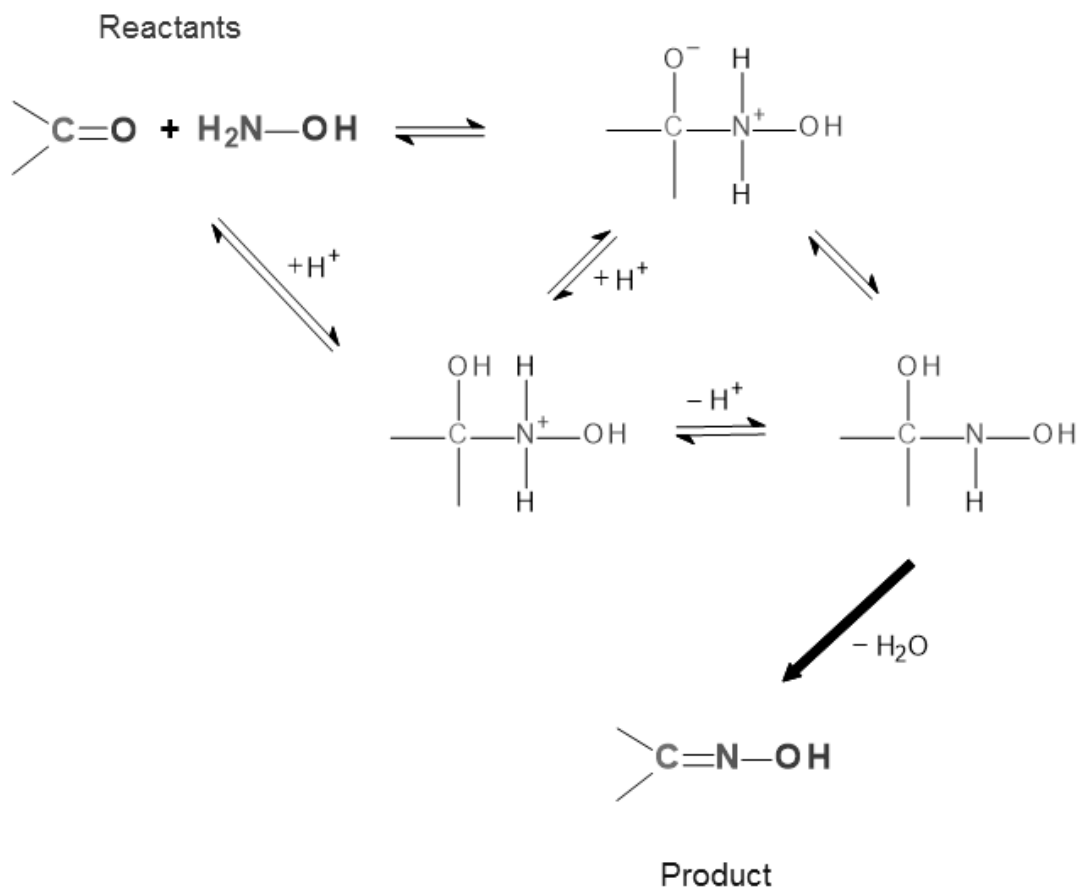
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12 Figure 4

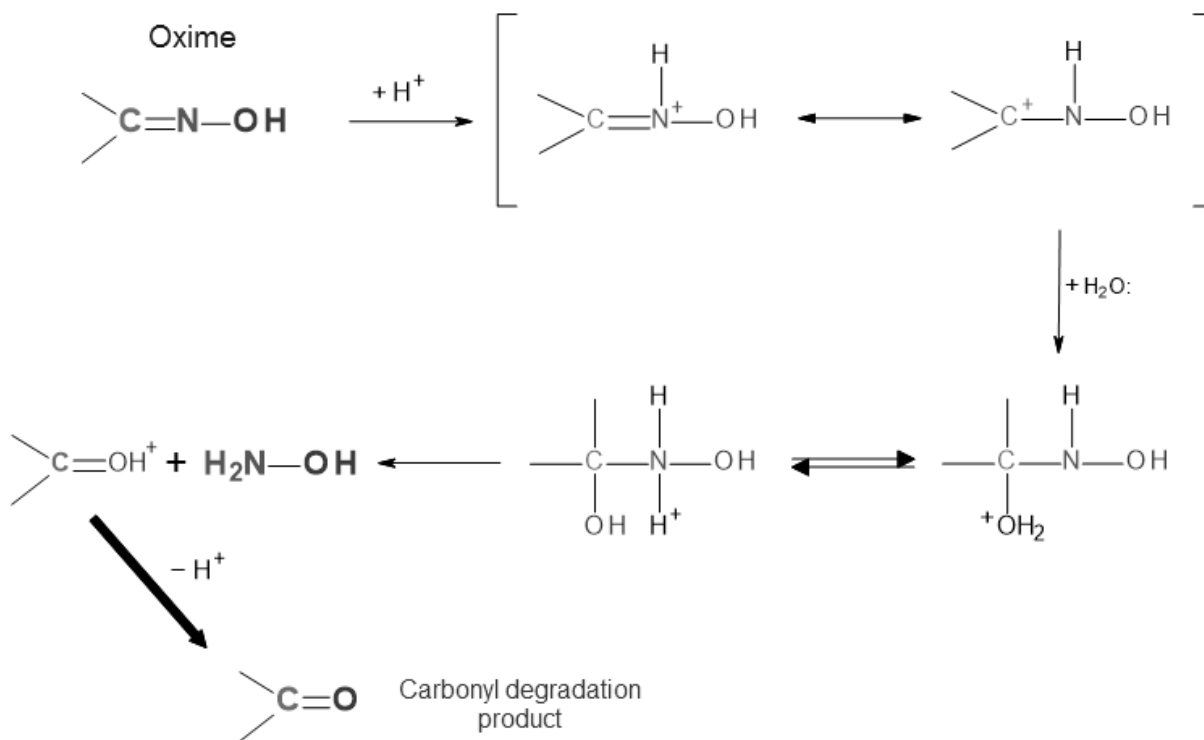
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15 Goodness of fit and residuals in estimation of kinetic parameters for two-phase oximation of
16 salicylaldehyde with hydroxylamine in a CSTR equipped with a high shear mixer. Reaction
17 temperatures: triangle = 293 K, square = 313 K, circle = 323 K. Colors indicate the feed
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8 concentration of hydroxylamine in the aqueous phase: green = 0.34 M, blue = 1.7 M, red = 3.4 M.

Table 1. Parameters of the kinetic model in Eqs. (7) and (8) for oximation of salicylaldehyde (in toluene) with hydroxylamine (in water, pH 6.8) and their 95% confidence intervals. $T_{\text{ref}} = 313$ K.

Parameter	CSTR	Batch (500 rpm)	Batch (900 rpm)
$k_{\text{ref}}(T_{\text{ref}})$, L/mol/s	$(10.55 \pm 4.8) \cdot 10^{-3}$	$(5.82 \pm 0.4) \cdot 10^{-3}$	$(6.58 \pm 0.6) \cdot 10^{-3}$
E_a , kJ/mol	34.7 ± 2.6	–	–
b_A	0.907 ± 0.37	–	–
b_{HA}	0.389 ± 0.14	–	–

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Scheme I

Scheme II

Review

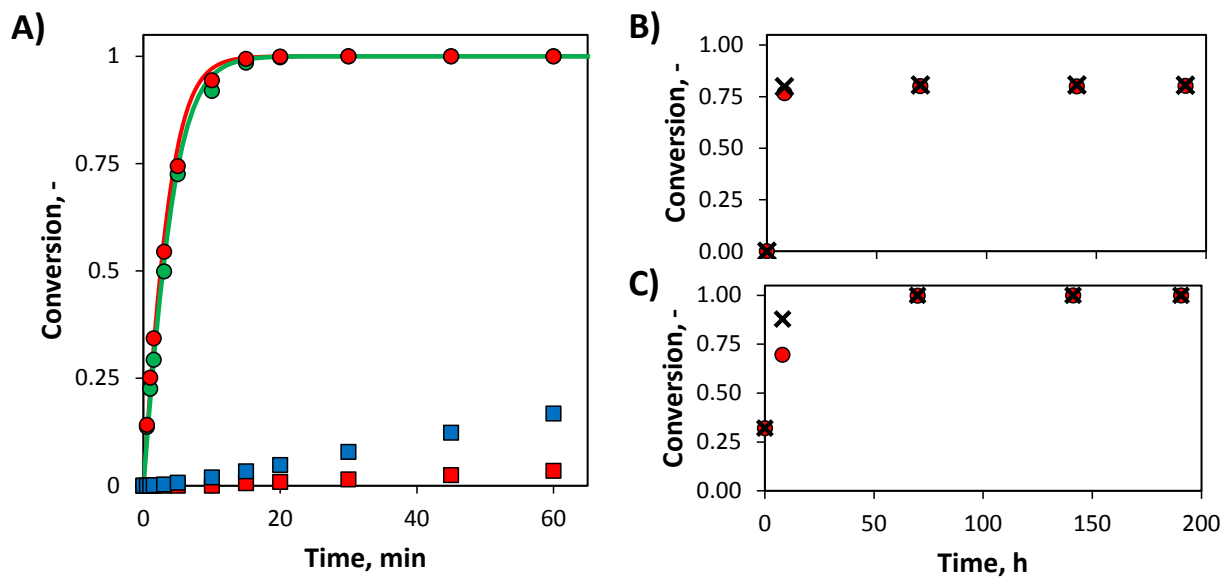


Figure 1.

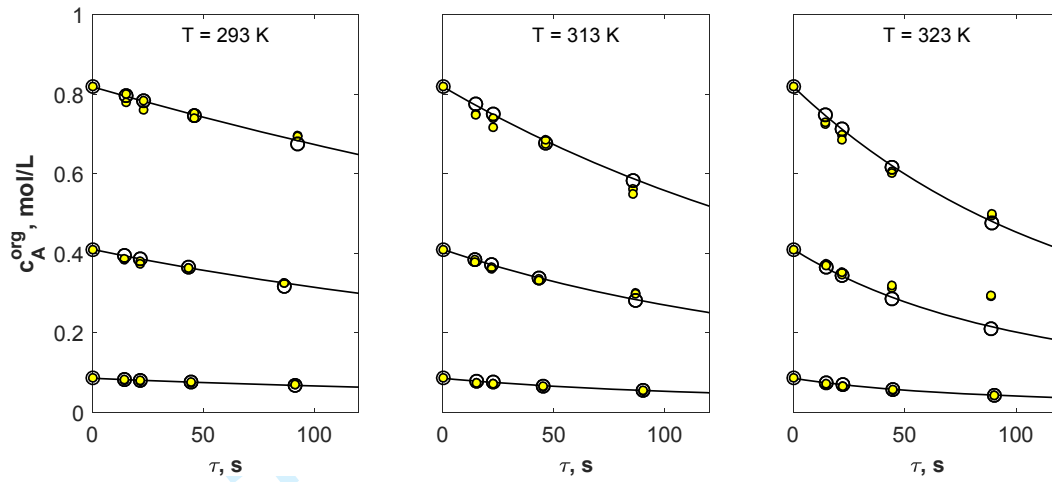


Figure 2.

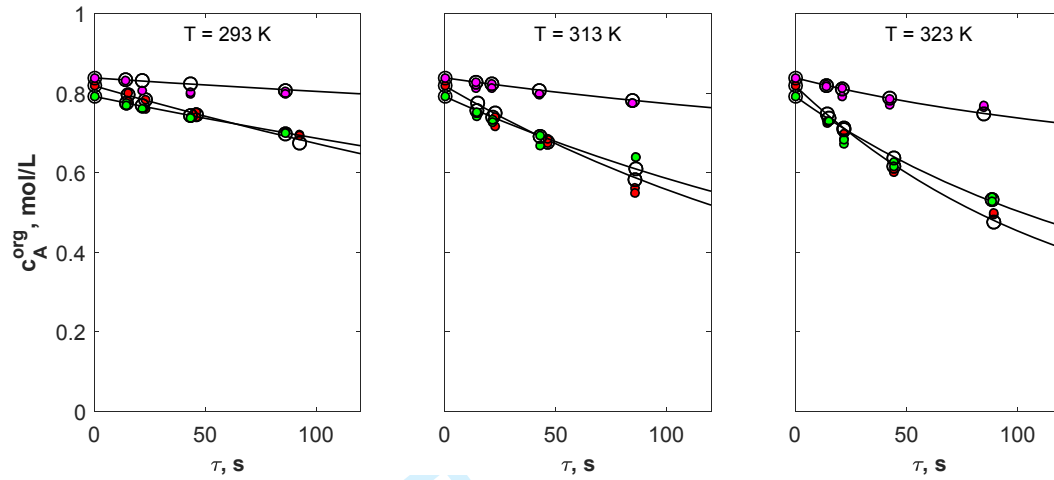


Figure 3.

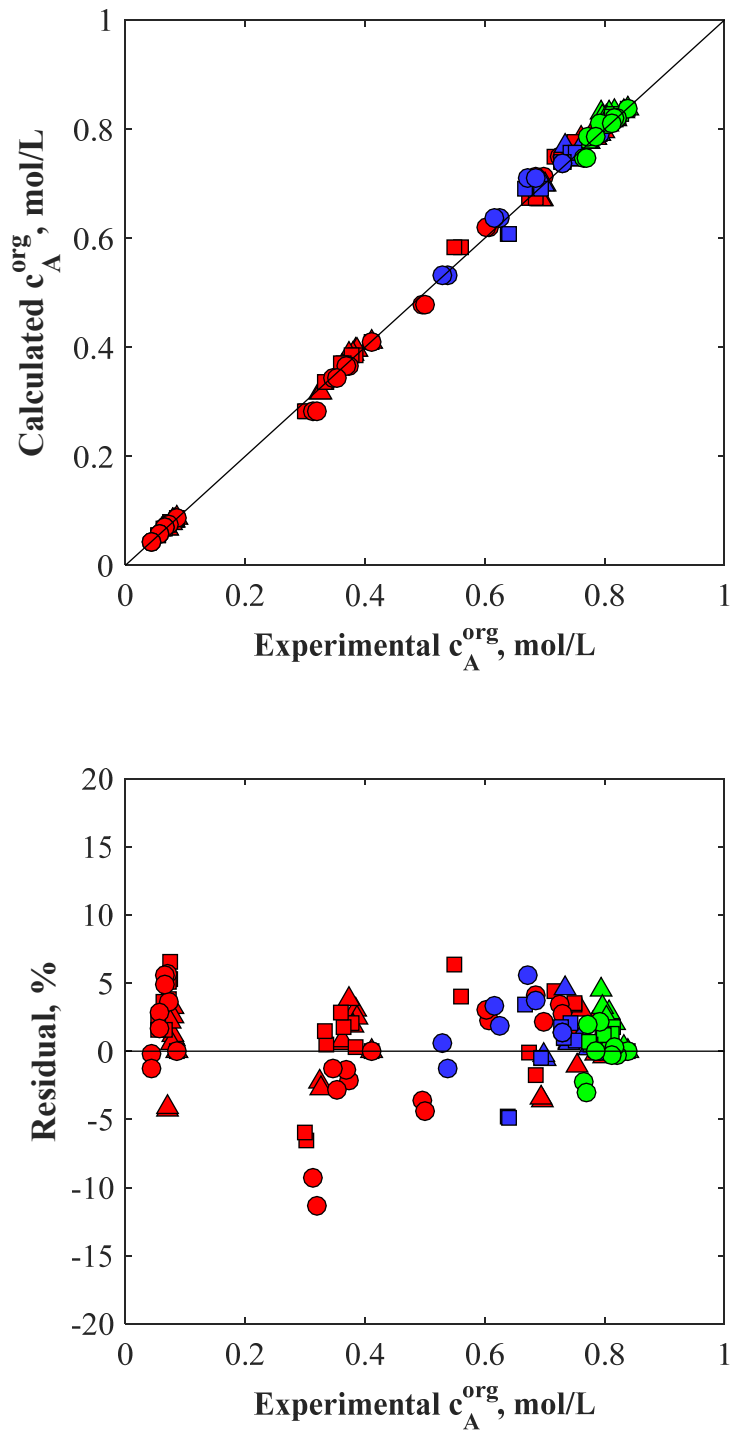


Figure 4.