# Salicylic Acid Nitration by Means of Nitric Acid/Acetic Acid System: Chemical and Kinetic Characterization

Roberto Andreozzi,<sup>†</sup> Marisa Canterino,<sup>†</sup> Vincenzo Caprio,<sup>†</sup> Ilaria Di Somma,<sup>\*,†</sup> and Roberto Sanchirico<sup>‡</sup> Università di Napoli "Federico II", p.le V. Tecchio, 80-80125 Naples, Italy, and Istituto di Ricerche sulla Combustione (CNR), p.le V. Tecchio, 80-80125 Naples, Italy

#### Abstract:

The nitration of salicylic acid by means of HNO<sub>3</sub>/AcOH is investigated, and the results are compared with those obtained using different nitrating systems: HNO<sub>3</sub>/H<sub>2</sub>SO<sub>4</sub>/H<sub>2</sub>O (mixed acid), HNO<sub>3</sub>/Ac<sub>2</sub>O/AcOH, aqueous HNO<sub>3</sub> (70% by weight) at 343 K. Little differences are found in terms of yield of the desired product (5-nitrosalicylic acid) among HNO<sub>3</sub>/AcOH mixture, mixed acid, and HNO<sub>3</sub>/Ac<sub>2</sub>O/AcOH systems, aqueous HNO<sub>3</sub> giving the poorest results. However according to the data collected during the present investigation the use of the system HNO<sub>3</sub>/AcOH presents some advantages with respect to the others for the separation and purity of desired product, waste minimization, and safety improvements. The reaction kinetics for the nitration of salicylic acid with this system is also investigated. A global second-order kinetic law (one for the substrate, one for nitric acid) is used in the analysis of the data collected for the formation of the two mononitroderivatives (3nitro- and 5-nitrosalicylic acids) and of the side product 2-nitrophenol.

### 1. Introduction

Nitrations are among the most common reactions carried out at industrial scale. Nitrated products are used directly or as intermediates in dyes, explosives, pesticides, and the pharmaceutical industry.<sup>1,2</sup> Although these reactions have been widely studied in the past,<sup>3,4</sup> the interest is still alive from theoretical and practical points of view. The most common nitrating system currently adopted at the industrial scale is represented by the classic mixed acid (HNO<sub>3</sub>/H<sub>2</sub>-SO<sub>4</sub>/H<sub>2</sub>O). Among the drawbacks associated to its use, poor selectivity, waste disposal, and process safety are often reported. With respect to the last aspect, it is useful to remember that, due to its exothermic behaviour and to the inherent thermal instability of the products, nitrations are along with polymerizations among the most dangerous reactions due to the thermal runaway phenomena at industrial levels. It is evident that, in view of an industrial process

 Olah, G. A.; Malhotra, R.; Narang, S. C. Organic Nitro Chemistry Series-Nitration Methods and Mechanisms; VCH: New York, 1989. implementation, this factor should be considered extensively from the early stages of the process development.

The present work aims at studying the nitration of salicylic acid (AS) for the production of 5-nitrosalicyclic acid by comparing the effectiveness of different nitrating systems. This compound is an important intermediate for chemical and pharmaceutical industries. The derivative amine (mesalazine) is currently used as active species for the treatment of various pathologies such as ulcerative colitis and Crohn's disease.<sup>5,6</sup> From a literature survey it is highlighted that there are two nitrating systems that have been normally adopted for the production of the target compound: HNO<sub>3</sub>/H<sub>2</sub>SO<sub>4</sub>/  $H_2O$  (mixed acid)<sup>7,8</sup> and HNO<sub>3</sub> (70% by weight) at 343 K.<sup>8-10</sup> A further system that, from literature indications, could be used in this process is the mixture HNO<sub>3</sub>/Ac<sub>2</sub>O/AcOH. In fact this system has been found to give good results in the nitration of deactivated substrate.<sup>11</sup> Unfortunately the HNO<sub>3</sub>/ Ac<sub>2</sub>O/AcOH system evolves through the formation of acetylnitrate, an unstable intermediate, thus resulting in a less safe process.<sup>12–14</sup> On the basis of these considerations a further system that could be proposed for the production of 5-nitrosalicylic acid is the mixture HNO<sub>3</sub>/AcOH. The elimination of acetic anhydride could result into a reduction in the formation of the acetylnitrate. This last system shows some additional useful advantages in a possible industrial application with respect to the use of HNO<sub>3</sub> at 70% by weight. In fact the reactivity of the system HNO<sub>3</sub>/AcOH allows working at a temperature lower than that used with the sole HNO<sub>3</sub> thus resulting in a more inherently safe process. Moreover, it is possible to separate the desired product at high purity by filtration. Simple considerations may not allow us to establish what is the safest nitrating system between mixed acid and HNO<sub>3</sub>/AcOH mixture. From a general point of view it can be put forward that both of them may originate runaway phenomena as a result of a loss

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<sup>\*</sup> Corresponding author. Telephone: +39 081 7682225. Fax: +39 081 5936936. E-mail: idisomma@unina.it.

<sup>&</sup>lt;sup>†</sup> Università di Napoli "Federico II".

<sup>&</sup>lt;sup>‡</sup> Istituto di Ricerche sulla Combustione (CNR).

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Table 1. Experimental conditions adopted in preliminary runs

no.	system	<i>T</i> [K]	$[\text{mol} \times 10^{-2}]$	$n_{\mathrm{HNO}_3}$ [mol × 10 <sup>-</sup> 2]	$n_{\rm AcOH}$ [mol × 10 <sup>-</sup> 2]	$n_{\mathrm{H}_2}\mathrm{SO}_4$ [mol × 10 <sup>-</sup> 2]	$n_{Ac_2}O$ [mol × 10 <sup>-</sup> 2]	$n_{\rm AS}/n_{\rm HNO_3}$
1 2 3 4	mixed acid HNO <sub>3</sub> /Ac <sub>2</sub> O/AcOH HNO <sub>3</sub> /AcOH HNO <sub>3</sub> (w/w 70%)	288 288 288 343	0.60 0.60 0.60 0.43	3.0 3.0 3.0 1.3	1.46 1.46	6.1	0.60	1/5 1/5 1/5 1/3

of the thermal control with a possible accidental triggering of the decomposition of the intermediate and product nitroderivatives. Safety investigations on these aspects for the system HNO<sub>3</sub>/AcOH are reported by the authors elsewhere.<sup>12</sup> Moreover, at least in principle, the possibility cannot be ruled out of detonation of the mixture HNO<sub>3</sub>/AcOH if properly initiated and confined. However no data are available in the literature for a HNO<sub>3</sub>/AcOH mixture as diluted as those used in the present investigations.<sup>15</sup>

In the present work the nitration by HNO<sub>3</sub>/AcOH is studied from chemical and kinetic points of view. A comparison of the yields of 5-nitrosalicylic acid obtained with this system with those found in the nitration of salicylic acid by means of the other three systems is also performed.

#### 2. Experimental Section

**2.1. Materials and Methods.** For all isothermal experiments a jacketed glass magnetically stirred (volume:  $2.0 \times 10^{-2}$  L) reactor has been used. The temperature has been kept at a desired value by using (cooling fluid: water) a Julabo F32 refrigerated/heating circulator. With the main system (HNO<sub>3</sub>/AcOH) all runs have been carried out by charging the solution of acetic acid and substrate in the reactor and then adding nitric acid in batch mode.

The concentration of the involved species as a function of reaction time has been recorded by submitting chemically quenched samples (with the addition of a solution of urea and methanol) collected during the experiments to HPLC analysis using a Hewlett-Packard model 1100 II, equipped with a UV—vis detector and a Phenomenex Synergi 4  $\mu$  polar RP/80A column. The following operating conditions have been adopted: the mobile phase has been formed by 80% of a buffer solution (vol %: CH<sub>3</sub>OH 5%, H<sub>3</sub>PO<sub>4</sub> 0.4%, H<sub>2</sub>O 94.6%) and 20% of acetonitrile; the signals have been acquired at 240, 280, 350 nm; the column temperature has been kept at 298 K; and the flow rate was set at 1 × 10<sup>-3</sup> L·min<sup>-1</sup>.

For all the experiments analytical grade reagents have been used ( $H_2SO_4$  98% by Fluka and the others by Sigma Aldrich).

Due to the lower solubility of mononitroderivative acids with respect to salicylic acid, in some runs a heterogeneous final mixture has been obtained. In this case both to confirm the information concerning the global yields and to characterize the solid, the runs have been performed twice, once separating the solid from the liquid phase and once recovering the whole reactor content.

In the first case, the final mixture has been filtered, and the solid recovered has been washed with cold water, dried, and weighed. In the second case, the whole reactor content has been quenched with urea, and the resulting samples dissolved in methanol. The collected solutions have been then submitted to HPLC analysis.

#### **3. Results and Discussions**

**3.1. Preliminary Experiments.** Aiming both to verify the data reported in the literature<sup>7–11</sup> and to highlight the differences among the systems investigated in the present work, a series of preliminary nitrations of the substrate has been performed. The nitration of salicylic acid has been thus studied by using  $HNO_3/H_2SO_4/H_2O$  (the mixed acid), aqueous  $HNO_3$  (70% by weight),  $HNO_3/Ac_2O/AcOH$ , and  $HNO_3/AcOH$  systems. Their main characteristics and the adopted operating conditions are reported in Table 1.

For system no. 1 of Table 1 (mixed acid) the ratio  $n_{\rm HNO3}/n_{\rm H_2SO_4} = 1/2$  has been used in all the runs which have been carried out. The nitrating system has been prepared directly in the reactor, and salicylic acid added after the reaction temperature has been stabilized. The gathered data indicate a total yield of 50.4% mol/mol and a purity of the separated 5-nitrosalicylic acid of 68% w/w, with 32% of 3-nitrosalicylic acid, after a reaction time of 135 min.

For system no. 2 of Table 1, the runs have been carried out charging the reactor with the solution of acetic acid/ acetic anhydride/substrate; once the reaction temperature has been stabilized 1.89 g of concentrated nitric acid have been added in batch mode to the mixture. The chemical analysis allowed deriving a total yield in 5NS of 50.3% and a purity of the solid of 75%.

For system no. 4 salicylic acid has been added to 1.176 g of the aqueous solution of nitric acid previously charged in the reactor. During this phase the evolution of red fumes has been observed. The system has been kept under isothermal conditions for 60 min and then cooled at 298 K. A homogeneous system has been collected at the end of the run, directly diluted in methanol, and submitted to HLPC analysis. A total yield in the desired product of 40.9% has been recorded.

Also in the case of the alternative system of nitration here proposed, HNO<sub>3</sub>/AcOH mixtures (no. 3), in all the adopted experimental conditions the formation of a solid has been verified.

To assess the influence of the feed ratio, salicylic acid/ nitric acid, on yields and purity of the precipitated solid, a series of runs ( $n_{AS}/n_{AcOH} = 0.4$  in all cases) has been carried out with an  $n_{AS}/n_{HNO_3}$  ratio equal to  $^{1}/_{5}$ ,  $^{1}/_{7}$ , and  $^{1}/_{10}$ . The mean values obtained for the total yields, the purity of the recovered solid, defined as the weight percentage of 5-nitrosalicylic acid, and the molar percentage of formed 5-nitrosalicylic acid which precipitates are shown in Figure 1.

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*Figure 1.* Total yields, purity, and precipitated amount of 5-nitrosalicylic acid against the molar ratio  $n_{AS}/n_{HNO_3}$  obtained at 288 K for the system AS/HNO<sub>3</sub>/AcOH.



*Figure 2.* Best results for the total yield and purity obtained using the various nitrating systems.

The results in this figure point out that, as the molar ratio  $n_{\rm AS}/n_{\rm HNO_3}$  decreases, the percentage of formed 5-nitrosalicylic acid present as precipitated solid with respect to the total amount formed slightly decreases, whereas the solid purity increases, the yield for this product remaining practically constant. It is noteworthy to observe that for a ratio  $n_{\rm As}/n_{\rm HNO_3} = 1/10$  more than 92% of 5-nitrosalicylic acid which formed during the reaction separates from the solution and that 96% by weight of the recovered solid is represented by this isomer.

In Figure 2 the results obtained in the nitration of salicylic acid with all the systems adopted in the present study are compared. For the system HNO<sub>3</sub>/AcOH the data collected in the runs with a  $n_{\rm AS}/n_{\rm HNO_3}$  ratio equal to  $1/_5$  have been inserted in this figure to make the comparison easier.

The data shown in the figure indicate that the system  $HNO_3/AcOH$  is the most interesting among those tested in the present work. In fact, although for three of them (nos. 1, 2, and 3, Table 1), both comparable yield and selectivity are obtained, the adoption of the  $HNO_3/AcOH$  system makes it possible to eliminate the use of sulfuric acid (with respect to mixed acid) with reduced problems of waste disposal and that of acetic anhydride (with respect to the system 2), leading to a more inherently safe nitrating system. The proposed system presents some advantages also with respect to the use of aqueous  $HNO_3$  solutions being capable of the latter, ensuring only a lower yield for 5-nitrosalicyclic acid (Figure 2) at a significantly higher working temperature.

**3.2. Kinetic Assessment.** On the basis of the abovereported considerations it is evident the importance of achieving a kinetic characterization of the nitration process of salicylic acid by means of the mixture HNO<sub>3</sub>/AcOH. To this aim a series of isothermal experiments (T = 285, 288,293, and 298 K) with the following initial concentrations,



*Figure 3.* Concentration profiles in the nitration of salicylic acid with the system HNO<sub>3</sub>/AcOH (T = 298 K): AS, salicylic acid; 5NS, 5-nitrosalicylic acid; 3NS, 3-nitrosalicylic acid; 2NP, 2-nitrophenol.

Scheme 1. AS, salicylic acid; 5-NS, 5-nitrosalicylic acid; 2-NP, 2-nitrophenol; 3-NS, 3-nitrosalicylic acid



 $C_{\text{SA}}(0) = 0.053 \text{ mol } \text{L}^{-1}, C_{\text{HNO}_3}(0) = 0.265 \text{ mol } \text{L}^{-1}, \text{ and} C_{\text{AcOH}}(0) = 17.5 \text{ mol } \text{L}^{-1} (n_{\text{AS}}/n_{\text{HNO}_3} = \frac{1}{5})$  has been performed.

The reaction development has been monitored submitting to HPLC analysis the samples withdrawn from the reactor at fixed intervals of time and quenched with urea.

In Figure 3 the data collected during a run performed at 298 K are shown. The profiles in Figure 3 indicate that the main products of reaction are 5-nitrosalicylic (5-NS) and 3-nitrosalicylic acid (3-NS) with a minor occurrence of 2-nitrophenol (2-NP), whose presence could be ascribed to an ipsonitration process involving the substrate.<sup>1</sup> Trace concentrations of 3,5-dinitrosalicylic acid (3,5-DNS), 2,4-dinitrophenol (2,4-DNP), and 2,6-dinitrophenol (2,6-DNP) have been also recorded in all the runs. All the results gathered during this set of experiments are summarized in the reactions in Schemes 1 and 2.

Only scant indications<sup>2</sup> have been found in the literature on the reaction kinetics for the adopted nitrating system. In particular, it has been reported that, depending on the nature of the substrate, its initial concentration and that of nitric acid and water, its reaction order may be zero or  $1,^2$  although no clear indications on how to determine the correct value have been given. After a preliminary analysis of the results collected during the present investigation, which easily allowed ruling out zero-order kinetics with respect to the substrate, a possible scheme for the nitration of salicylic acid has been proposed (Scheme 3).

It has been reported<sup>2</sup> that nitric acid exists almost completely not dissociated in a solvent like acetic acid, and therefore, if it is assumed that the rate of the step (c) is fast *Scheme 2.* 5NS, 5-nitrosalicylic acid; 2NP, 2-nitrophenol; 3NS, 3-nitrosalicylic acid; 3,5DNS, 3,5-dinitrosalicylic acid; 2,4DNP, 2,4-dinitrophenol; 2,6DNP, 2,6-dinitrophenol



#### Scheme 3. ArH: aromatic compound

$$2 \text{ HNO}_{3} \xrightarrow{K_{A}} \text{ NO}_{2}^{+} + \text{ NO}_{3}^{-} + \text{ H}_{2}\text{O} \quad (a)$$

$$ArH + \text{ NO}_{2}^{+} \xrightarrow{k} \text{ ArNO}_{2} + \text{ H}^{+} \quad (b)$$

$$H^{+} + \text{ NO}_{3}^{-} \xrightarrow{Fast} \text{ HNO}_{3} \quad (c)$$

with respect to that of (b), the following condition  $C_{\text{NO}_2^+} \cong C_{\text{NO}_3^-}$  holds. In light of this assumption the equilibrium constant  $K_A$  [step (a)] can be written as

$$K_{\rm A} = \frac{C_{\rm NO_2^+}^2 C_{\rm H_2O}}{C_{\rm HNO_3}^2} f$$

in which f takes into account the activity coefficients of the species in the equilibrium (a).

The nitronium ion concentration can be thus calculated as

$$C_{\text{NO}_{2}^{+}} = \sqrt{\frac{K_{\text{A}}}{C_{\text{H}_{2}\text{O}}}} C_{\text{HNO}_{3}} \frac{1}{\sqrt{f}}$$

and the following relationship is derived for the reaction rate

$$-\frac{\mathrm{d}C_{\mathrm{ArH}}}{\mathrm{d}t} = kC_{\mathrm{NO}_{2}^{+}}C_{\mathrm{ArH}} = k\sqrt{\frac{K_{\mathrm{A}}}{C_{\mathrm{H}_{2}\mathrm{O}}f}}C_{\mathrm{HNO}_{3}}C_{\mathrm{ArH}} \cong k'C_{\mathrm{HNO}_{3}}C_{\mathrm{ArH}} (\mathrm{d})$$

Equation (d) indicates that according to the proposed reaction scheme (Scheme 3) the nitration of an aromatic species with theHNO<sub>3</sub>/AcOH mixture proceeds in agreement with a second-order kinetic law, the kinetic constant being dependent upon the reciprocal of the root square of the water concentration.

If it is possible to neglect in eq (d) the contribution of the water formed during the nitration process and the changes of f, the ratio under the square root keeps constant. A set of runs at different initial water concentrations has been performed to confirm the dependence found in relationship (d). In each run the concentration decay of salicylic acid has



# **Figure 4.** $1/k_{\rm S}^2$ against the multiplier g for the runs performed at different initial water content.

been recorded, and an experimental kinetic constant  $(k_S)$  for the nitration has been derived modeling collected data by means of a simple second-order rate law.

On the basis of relationship (d) in which

$$k' = k \sqrt{\frac{K_{\rm A}}{C_{\rm H_2O}f}} = k'' \frac{1}{\sqrt{C_{\rm H_2O}}} = k_{\rm S}$$
 (e)

squaring and taking the reciprocal of (e) it is possible to obtain the following relationship:

$$\frac{1}{k_{\rm S}^2} = \frac{C_{\rm H_2O}}{k''^2}$$
(f)

A linear relationship could be thus expected by plotting  $1/k_{\rm S}^2$  against  $C_{\rm H_2O}$ .

In Figure 4 the plot obtained by using the data collected during the experiments at varying initial water contents is shown. The diagram of the figure confirms the rate dependence upon water concentration found in relationship (f).

The overall second-order kinetic equation (d) has been considered also for the ipsonitration process (reaction 3 of Scheme 1)<sup>16</sup> leading to the following mass-balance equations according to Schemes 1 and 2 (for each reaction the kinetic constant is given by  $k_i = k_{i0} \exp(-E_i/RT)$ ):

$$\frac{dC_{5NS}}{dt} = k_1 C_{AS} C_{HNO_3} - k_4 C_{5NS} C_{HNO_3} - k_5 C_{5NS} C_{HNO_3}$$
(1)

$$\frac{dC_{3NS}}{dt} = k_2 C_{AS} C_{HNO_3} - k_8 C_{3NS} C_{HNO_3} - k_9 C_{3NS} C_{HNO_3}$$
(2)

$$\frac{dC_{2NP}}{dt} = k_3 C_{AS} C_{HNO_3} - k_6 C_{2NP} C_{HNO_3} - k_7 C_{2NP} C_{HNO_3}$$
(3)

$$\frac{dC_{AS}}{dt} = -k_1 C_{AS} C_{HNO_3} - k_2 C_{AS} C_{HNO_3} - k_3 C_{AS} C_{HNO_3}$$
(4)

$$\frac{\mathrm{d}C_{\mathrm{HNO}_3}}{\mathrm{d}t} = 2\,\frac{\mathrm{d}C_{\mathrm{AS}}}{\mathrm{d}t} + \frac{\mathrm{d}C_{\mathrm{5NS}}}{\mathrm{d}t} + \frac{\mathrm{d}C_{\mathrm{3NS}}}{\mathrm{d}t} + \frac{\mathrm{d}C_{\mathrm{2NP}}}{\mathrm{d}t} \tag{5}$$

The values for the kinetic parameters of the reaction 4-9 have been taken from the results of a recent investigation of the authors<sup>17</sup> (see Table 2).

The system of eqs 1-5 has been solved in an optimization procedure in which the concentration profiles, calculated at

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<sup>(17)</sup> Andreozzi, R.; Caprio, V.; Di Somma, I.; Sanchirico, R. J. Hazard. Mater. 2006, 134, 1–7.

Table 2. Kinetic constants of reactions 4-9 (L mol<sup>-1</sup> s<sup>-1</sup>)

				· · · · · ·
	285 K	288 K	293 K	298 K
$egin{array}{c} k_4 \ k_5 \ k_6 \ k_7 \ k_8 \ k_9 \end{array}$	$\begin{array}{c} 5.16 \times 10^{-9} \\ 1.86 \times 10^{-9} \\ 9.38 \times 10^{-6} \\ 6.20 \times 10^{-6} \\ 6.01 \times 10^{-8} \\ 1.10 \times 10^{-7} \end{array}$	$\begin{array}{c} 9.76 \times 10^{-9} \\ 3.39 \times 10^{-9} \\ 1.64 \times 10^{-5} \\ 1.11 \times 10^{-5} \\ 1.15 \times 10^{-7} \\ 2.17 \times 10^{-7} \end{array}$	$\begin{array}{c} 2.75 \times 10^{-8} \\ 8.93 \times 10^{-9} \\ 4.06 \times 10^{-5} \\ 2.83 \times 10^{-5} \\ 3.29 \times 10^{-7} \\ 6.56 \times 10^{-7} \end{array}$	$\begin{array}{c} 7.47 \times 10^{-8} \\ 2.78 \times 10^{-8} \\ 9.74 \times 10^{-5} \\ 7.03 \times 10^{-5} \\ 9.07 \times 10^{-7} \\ 1.91 \times 10^{-6} \end{array}$



*Figure 5.* Calculated (continuous line) and experimental data (symbols) for the run performed at 298 K: AS, salicylic acid; 5NS, 5-nitrosalicylic acid; 3NS, 3-nitrosalicylic acid; 2NP, 2-nitrophenol.



*Figure 6.* Calculated (continuous line) and experimental data (symbols) for the run performed at 285 K: AS, salicylic acid; 5NS, 5-nitrosalicylic acid; 3NS, 3-nitrosalicylic acid; 2NP, 2-nitrophenol.



*Figure 7.* Calculated (continuous line) and experimental data (symbols) for the run performed at 288 K: AS, salicylic acid; 5NS, 5-nitrosalicylic acid; 3NS, 3-nitrosalicylic acid; 2NP, 2-nitrophenol.



*Figure 8.* Calculated (continuous line) and experimental data (symbols) for the run performed at 293 K: AS, salicylic acid; 5NS, 5-nitrosalicylic acid; 3NS, 3-nitrosalicylic acid; 2NP, 2-nitrophenol.



*Figure 9.* Predicted (continuous line) and experimental data (symbols) for the run performed at 293 K with a starting substrate concentration equal to 0.084 mol/L: AS, salicylic acid; 5NS, 5-nitrosalicylic acid; 3NS, 3-nitrosalicylic acid; 2NP, 2-nitrophenol.

different temperatures, have been compared with the experimental data. Some examples of comparison between calculated (continuous line) and experimental data (symbols) are shown in Figure 5-8.

As a result of this optimization procedure, the kinetic parameters for reactions 1, 2, and 3 (Scheme 1) have been evaluated (Table 3).

The model so obtained has been validated by means of data recorded during a set of runs performed at starting conditions different from those adopted during the parameter estimation. In Figure 9 an example is shown of a comparison among the concentrations predicted by the model, using the kinetic values reported in Tables 2 and 3 and those experimentally recorded in a run with an initial substrate concentration two times higher than those previously used.

These results indicate that the proposed model well predicts the behaviour of the studied system at varying experimental conditions.

Table 3. Kinetic parameters assessed for the reaction reported in Scheme 1

$k_{10} [\mathrm{L} \mathrm{mol}^{-1} \mathrm{s}^{-1}]$	$E_1$ [kJ mol <sup>-1</sup> ]	$k_{20}$ [L mol <sup>-1</sup> s <sup>-1</sup> ]	$E_2$ [kJ mol <sup>-1</sup> ]	$k_{30}$ [L mol <sup>-1</sup> s <sup>-1</sup> ]	$E_3$ [kJ mol <sup>-1</sup> ]
$(2.53\pm0.15)\times10^{+19}$	$124.37\pm0.17$	$(1.38 \pm 0.11) \times 10^{+19}$	$123.90\pm0.17$	$(5.37 \pm 1.2) \times 10^{+18}$	$124.66\pm0.42$

# 4. Conclusion

The nitration of salicylic acid has been studied using different systems: mixed acid, mixture HNO<sub>3</sub>/Ac<sub>2</sub>O/AcOH, mixture HNO<sub>3</sub>/AcOH, and aqueous HNO<sub>3</sub> (70% by weight) at 343 K. The results collected during the present investigation indicate that with all the adopted systems the main reaction products are 3-nitro- and 5-nitrosalicylic acid with a minor occurrence of 2-nitrophenol which forms through an ipsonitration mechanism. Small differences have been observed among the first three systems in terms of the overall yield for 5-nitrosalicylic acid, aqueous nitric acid solutions giving the poorest results. However the system HNO<sub>3</sub>/AcOH demonstrated some advantages with respect to the others for the separation and purity of desired product, waste minimization, and safety improvements. Kinetic investigations performed on salicylic acid nitration with this system allowed assessing that the nitration and ipsonitration are both regulated by a second-order kinetic law. The use of this

kinetic law for the analysis of the data collected during the nitration experiments made it possible to identify kinetic parameters for the formation of the two mononitroderivatives and 2-nitrophenol.

## SYMBOL LIST

k	Pre-exponential factor of <i>i</i> th reaction (rate law d	lepending)
E	Activation energy of <i>i</i> th reaction (kJ mol <sup><math>-1</math></sup> )	
k	Kinetic constant of <i>i</i> th reaction (rate law dependence)	nding)
ŀ	Universal constant of gas (J mol <sup>-1</sup> K <sup>-1</sup> )	
t	Time (s)	
0	Concentration of <i>j</i> th species (mol $L^{-1}$ )	
K	Equilibrium constant (mol L <sup>-1</sup> )	

Received for review July 24, 2006.

OP060148O