ISSN 0023-1584, Kinetics and Catalysis, 2012, Vol. 53, No. 1, pp. 25–35. © Pleiades Publishing, Ltd., 2012.

# Kinetic Modelling of Synthesis of N-Aminopiperidine from Hydroxylamine-O-Sulfonique Acid and Piperidine[1]

**E. Labarthe, A.-J. Bougrine, V. Pasquet, and H. Delalu**

*Laboratoire Hydrazines et Composés Energétiques Polyazotés, Université Claude Bernard Lyon 1, France*

*e-mail: veronique.pasquet@univ-lyon1.fr*

Received March 15, 2011

**Abstract**—A new route to synthesize N-aminopiperidine (NAPP) from hydroxylamine-O-sulfonique acid (HOSA) and piperidine was described. Kinetics of the reaction was investigated to optimize the conditions of the synthesis. Since the reaction is fast, this study was carried out in a diluted medium ($10^{-3}$ to $10^{-2}$ mol/l). To determine the concentration of the reaction product, NAPP was allowed to react with formaldehyde and the product was analysed by UV and HPLC techniques. The formation of NAPP is consistent with the first-order reaction to two reagents, governed by the nucleophilic substitution via SN2 mechanism. Oxidation of NAPP by HOSA was identified as the main secondary reaction which consistently reduced the yield of NAPP. A number of differential equations were elaborated and solution of these equations serves to predict the behavior of the system as a function of the reagent concentrations, pH and temperature. From the corresponding mathematical treatment a unique implicit expression was derived that characterizes the reaction medium. It was found that the $[PP]_0/[HOSA]_0$ molar ratio ($p$), the initial concentrations of $[PP]_0$ and $[HOSA]_0$, the ratio of rate constants $k_2/k_1$ and temperature are the only parameters that affect the yield of NAPP from HOSA. The results calculated from this model are in good agreement with the experimental data and they can be used to determine the optimal conditions of the reaction.

**DOI:** 10.1134/S0023158412010041

N-aminopiperidine (**NAPP**) is a precursor for the pharmaceutical industry; it is used for plant protection, in cosmetology and photographic chemistry. NAPP is used to prepare derivatives from tetrazolinone in manufacturing weed killers. Other applications are the fabrication of paper and transparent recording films, the formulation of inhibitors and substances resistant to amine based solvents.

NAPP synthesis by the Raschig process has already been optimized in our laboratory [1, 2]. It involves the selective synthesis based on monochloramine that can be conducted with any organic solvent at low cost and without polluting reagents. However, monochloramine is unstable and must be used immediately.

Accordingly, a new synthesis route was introduced with hydroxylamine-O-sulfonique acid (**HOSA**). This synthesis process has many advantages: it is as clean as the Raschig process (water chemistry and no pollutant reagents), HOSA is more stable than monochloramine, it is easier to store, it can be processed in more concentrated solutions and finely, the synthesis can be operated batchwise or continuously.

Due to its flexibility to fluctuations in the international market, a commercialization of the process can be expected. The commercial route to hydrazines can be upscaled for industrial production.

Here we disclose the information on kinetic parameters of the reaction HOSA with piperidine that is important to optimize this process.

## EXPERIMENTAL PART

### *Reagents*

Water was passed through an ion-exchange resin. All the salts used (NaOH, $Na_2SO_4$, $Na_2SO_4 \cdot 10H_2O$, $BaCl_2$, $Na_2HPO_4$ and $KH_2PO_4$) were products of reagent grade (99%) purity (Chimie-plus, Merck and Acros).

Samples of Hydroxylamine-O-Sulfonique Acid (**HOSA**) were of reagent (97%) grade purity supplied by ISOCHEM and Aldrich. Piperidine (**PP**) and N-aminopiperidine (**NAPP**) were supplied by Aldrich, with reagent grade purities of 99 and 97% respectively.

Azopiperidine (TTZ) was produced by oxidation of NAPP by HOSA. It was prepared at 20°C with a pH 13.7 ([NaOH] = 0.5 mol/l) by mixing two 100 mL aqueous solutions of HOSA and NAPP. A white product precipitated, which was filtered, washed with cold water (5°C), and then dried under low pressure.

### *Analyses*

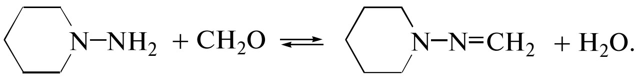
NaOH and piperidine concentrations were determined, by using an automatic titration apparatus, Metrohm Titrino 702 SM, with a glass electrode (reference: calomel electrode, KCl saturated solution).

---

[1] The article is published in the original.

The concentration of $SO_4^{2-}$ ion was determined by conductometric titration using freshly prepared solutions of barium chloride.

NAPP concentration was determined using the UV spectrometric method developed in our laboratory [3]. The method is based on the reaction of NAPP with formaldehyde to give hydrazone chromophore (methylene-piperidin-1-yl-amine: **FNAPP**) according to the following scheme:



FNAPP

The spectrometer used was a VARIAN CARY 100 Scan apparatus with double beam equipped with a data acquisition system.

Gaz chromatography (**GC**) was used to monitor concentrations of PP and NAPP in the course of the synthesis in concentrated medium. The samples were diluted in methanol before injection into the chromatograph (injected amount: 1 μl). Triglyme was used as the internal standard. The apparatus was a Hewlett Packard 6890A equipped with EPC modules (Electronic Pneumatic Control) to control and measure all flow rates and gas pressures in different compartments of the chromatograph. System data acquisition was managed by Chemstation HP 3365 software. The column used was a 30 m long HP-Innowax capillary with an internal diameter of 250 μm and a film thickness of 1 μm packed with polyethylene glycol.

High performance liquid chromatography (**HPLC**) analyses were performed to determine NAPP concentration during degradation kinetics. The apparatus was a Hewlett Packard 1100 chromatograph combined with a UV detector. The system data acquisition was managed by the same software (Chemstation HP 3365). The column was an Eclipse ODS XDB-C8 column (length = 150 mm, diameter 3 mm), equipped by a pre-column for the basic injections. The mobile phase was a mixture of $H_2O/CH_3CN$ and the loop injection volume was 20 μl, with the flow, composition and wavelength depending on the constituents to be analysed. A standard curve was constructed using a series of mixtures with concentrations close to those expected.

Gas chromatography coupled with mass spectrometry (**GCMS**) was used to quantify and characterize molecules such as PP, NAPP or Tetrazene. The spectrometer was a 5970 Agilent Technology spectrometer equipped with a quadripolar analyser. Chemstation software was used.

## RESULTS AND DISCUSSION

### *HOSA Stability in Basic Medium*

To study kinetics of the reaction between HOSA and piperidine, the stability of HOSA must be determined as a function of time. Several works have been carried out in basic medium: Steinmetz, Robinson and Ackermann [4] studied the kinetics of HOSA alkaline hydrolysis at 26.6°C, the concentration of NaOH between 0.1 and 1.5 mol/l and constant ionic strength ([NaCl] = 1.5 mol/l).

The first stage is a limiting step, corresponding to the formation of hydroxylamine that reacts with HOSA ($NH_2OSO_3H$) *via* the following fast consecutive parallel reactions:

$$NH_2OSO_3^- + OH^- \xrightarrow{k_a} NH_2OH + SO_4^{2-},$$

$$2NH_2OSO_3^- + 2NH_2OH + 2OH^- \xrightarrow{k_b} N_2 + N_2H_4 + 2SO_4^{2-} + 4H_2O,$$

$$2NH_2OSO_3^- + N_2H_4 + 2OH^- \xrightarrow{k_c} N_2 + 2NH_3 + 2SO_4^{2-} + 2H_2O,$$

with the rate $v = k[NH_2OSO_3^-][M]$ where at $M = OH^-$ $k_a = 0.11 \times 10^{-2}$ l $mol^{-1}$, $min^{-1}$, at $M = NH_2OH$ $k_b = 9.6$ l $mol^{-1}$ $min^{-1}$ and at $M = N_2H_4$ $k_c = 6.0$ l $mol^{-1}$ $min^{-1}$.

Global stoichiometry and the reaction rate can then be deduced ($k_b > k_c \gg k_a$):

$$3NH_2OSO_3^- + 3OH^- \rightarrow N_2 + NH_3 + 3SO_4^{2-} + 3H_2O,$$

$$-\frac{d[NH_2OSO_3^-]}{dt} = k_a[NH_2OSO_3^-][OH^-].$$

Another work, carried out by Matsuguma and Audrieth [5] the stability of NaOH (0.12 mol/l) and HOSA (0.1 mol/l) mixtures at temperatures of 6 and 23°C as a function of time was reported. The curves describing the results led to a rate constant of the same order ($k_a \approx 0.14 \times 10^{-2}$ l $mol^{-1}$ $min^{-1}$). These results were confirmed by a test carried out in our laboratory (iodometric titration).

Under these conditions and in the presence of piperidine, the rate of disappearance of HOSA includes 2 terms, one being related to its hydrolysis:

$$-\frac{d[HOSA]}{dt} = k_1[HOSA][PP] + k_a[HOSA][OH^-]$$

$$\text{at } t = 0.$$

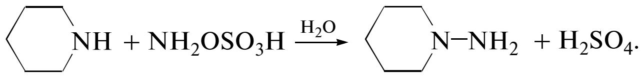
During the first moments of the reaction, the preceding reaction can be written as:

$$-\left(\frac{d[HOSA]}{dt}\right)_0 = \left(\frac{d[NAPP]}{dt}\right)_0 + k_a[HOSA]_0[OH^-]_0.$$

Measurement of slopes at the outset for the [NAPP] = *f*(*t*) curves shows that the second term is negligible (0.3%) under the experimental conditions studied.

### *Kinetic Study of HOSA—Piperidine Reaction in Basic Medium*

This reaction requires an SN2 type nucleophilic substitution mechanism.



NAPP formation kinetics was first studied at $T$ = 20°C. As the reaction rate is high, the tests were carried out in diluted medium with reagent concentrations varying from $10^{-3}$ to $10^{-2}$ mol/l. The formation rate of NAPP is expressed by the relation:

$$v_1 = \frac{d[NAPP]}{dt} = k_1[HOSA]^{\alpha}[PP]^{\beta}, \qquad (1)$$

where $k_1$, $\alpha$ and $\beta$ are the rate constant of the reaction versus NAPP and the partial orders versus the reagents HOSA and piperidine, respectively.

The reaction of HOSA on piperidine leads to the formation of 2 protons that are immediately neutralized by NaOH ($pK_{\alpha}(PP)$ = 11.123 [6]). Under these conditions, pH remains constant with a value determined by NaOH concentration. This gives the following theoretical stoichiometric relations:

$$-\frac{d[HOSA]}{dt} = -\frac{d[PP]}{dt} = \frac{d[NAPP]}{dt}.$$

The kinetics of this reaction was studied with excess piperidine to limit NAPP oxidation by HOSA. Since HOSA proportioning is not easily and instantaneously accessible, the rate laws were established by measuring the time dependence of the NAPP concentration under optimal reaction rate conditions. The kinetic parameters were determined by integration, considering $\alpha = \beta = 1$.

NAPP concentration was determined by UV analysis: after sampling, the reaction was immediately terminated by quantitatively transforming NAPP into hydrazone followed by dilution of the product was in a buffer solution with pH 6.88. The concentration of NAPP was determined from the optical density ($A$) obtained at wave lengths $\lambda_1$ = 208 and $\lambda_2$ = 236 nm:

$$\begin{aligned} Abs^{\lambda_1} &= \varepsilon^{\lambda_1}_{CH_2O}\, l[CH_2O] + \varepsilon^{\lambda_1}_{FNAPP}\, l[FNAPP], \\ Abs^{\lambda_2} &= \varepsilon^{\lambda_2}_{CH_2O}\, l[CH_2O] + \varepsilon^{\lambda_2}_{FNAPP}\, l[FNAPP], \end{aligned} \qquad (2)$$

where $l$ is: length of optical thickness (1 cm), $\varepsilon$—coefficients of molar extinction of $CH_2O$ and FNAPP at $\lambda_1$ and $\lambda_2$.

The instantaneous concentrations of piperidine and HOSA were determined experimentally from the NAPP concentration by using the following equation: $[PP]_t = [PP]_0 - [NAPP]_t$ that is to say $a = a_0 - u$, and $[HOSA]_t = [HOSA]_0 - [NAPP]_t$ that is to say $x = x_0 - u$.

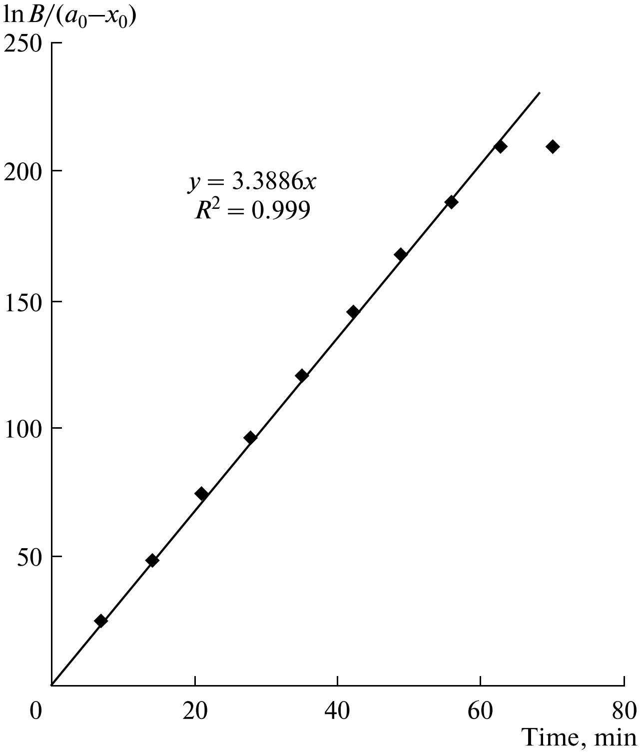


**Fig. 1.** Kinetics of NAPP formation. Determination of $k_1$. $B = \frac{x_0(a_0-u)}{a_0(x_0-u)}$.

The reaction scheme can then be written as:

$$NH_2OSO_3H + C_5H_{10}NH \xrightarrow{k_1} C_5H_{10}NNH_2 + H_2SO_4,$$

$$2NaOH + H_2SO_4 \rightarrow Na_2SO_4 + 2H_2O,$$

$$\Rightarrow NH_2OSO_3H + C_5H_{10}NH + 2NaOH \rightarrow C_5H_{10}NNH_2 + Na_2SO_4 + 2H_2O.$$

Denoting the concentrations of NAPP, HOSA and piperidine by $u$, $x_0$ and $a_0$ respectively, the evolution of the system is expressed by relation (4) that is given by integrating differential Eq. (3):

$$\int_0^u \frac{du}{(x_0 - u)(a_0 - u)} = \int_0^t k_1 dt, \qquad (3)$$

$$\frac{1}{a_0 - x_0} \ln\left(\frac{x_0(a_0 - u)}{a_0(x_0 - u)}\right) = k_1 t. \qquad (4)$$

The experimental results are collected in Table 1. As an example, Fig. 1 shows the first term of Eq. (4) plotted as a function of time for a reaction mixture of mole ratio $p = [C_5H_{10}NH]_0/[NH_2OSO_3H]_0 = 10$ ($[NH_2OSO_3H]_0 = x_0 = 1.23 \times 10^{-3}$ mol/l, $[C_5H_{10}NH]_0 = a_0 = 1.23 \times 10^{-2}$ mol/l, $[NaOH]_0 = 5.33 \times 10^{-2}$ mol/l).

Linearity of the plot indicates that the first-order kinetics in two reagents. A linear section of the plot

**Table 1.** Experimental data of NAPP formation kinetics in basic medium

| Time, min | *Abs* | | [NAPP] × $10^3$, mol/l | $\ln Abs/(a_0 - x_0)$ | $k_1$, l $mol^{-1}$ $min^{-1}$ |
|---|---|---|---|---|---|
| | 208 nm | 236 nm | | | |
| 7 | 0.585 | 0.468 | 0.32 | 24.525 | 3.50 |
| 14 | 0.703 | 0.641 | 0.55 | 48.646 | 3.48 |
| 21 | 0.801 | 0.779 | 0.72 | 74.165 | 3.53 |
| 28 | 0.872 | 0.872 | 0.84 | 96.094 | 3.43 |
| 35 | 0.909 | 0.938 | 0.93 | 120.36 | 3.44 |
| 42 | 0.956 | 0.999 | 1.01 | 145.29 | 3.46 |
| 49 | 0.977 | 1.034 | 1.06 | 167.14 | 3.41 |
| 56 | 0.988 | 1.058 | 1.09 | 188.30 | 3.36 |
| 63 | 1.001 | 1.079 | 1.12 | 209.07 | 3.32 |
| 70 | 1.023 | 1.091 | 1.12 | 209.47 | 2.99 |

$[NH_2OSO_3H]_0 = x_0 = 1.23 \times 10^{-3}$ mol/l, $[C_5H_{10}NH]_0 = a_0 = 1.23 \times 10^{-2}$ mol/l, $[NaOH]_0 = 5.33 \times 10^{-2}$ mol/l, $T = 20°C$.

extends to $t \le 60$ min, the point where a degree of conversion $\varepsilon = (x_0 - x)/x_0$ is equal to 0.9. The deviation observed beyond a value of 60 min is related to the profile of the curve [NAPP] = *f*(*t*) directly calculated from the relation (2) (Fig. 2). A straight line obtained during the first 60 min of reaction passes close to the origin with slope of 3.39 l $mol^{-1}$ $min^{-1}$ and a correlation coefficient $R^2 = 0.999$. The reaction rate established in relation to HOSA ($\varphi = [NAPP]_\infty/[HOSA]_0$) is close to 91%.

To verify the rate law at 20°C, a similar treatment was carried out for reagent mixtures with different compositions. The results are given in Table 2: the values of $k_1$ are quite constant. This gives $k_1 = \dfrac{d[NAPP]/dt}{[HOSA][PP]} = 3.39 \pm 0.10\,l\,mol^{-1}\,min^{-1}$ at 20°C.

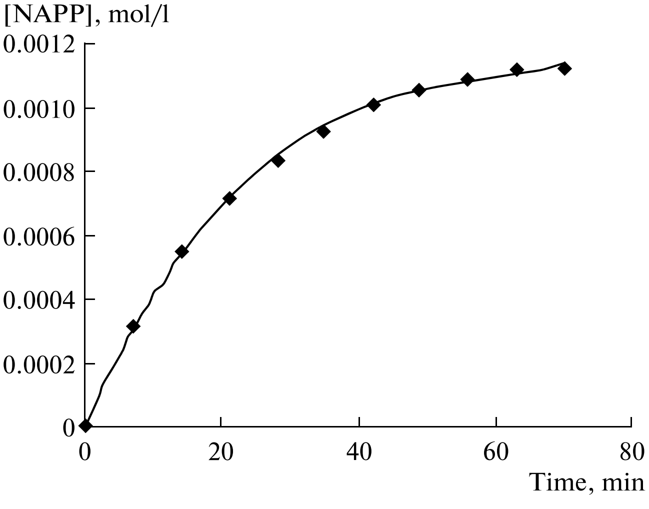


**Fig. 2.** Kinetics of NAPP formation in basic medium. Evolution of NAPP concentration through time, calculated from equation (2).

**Effect of temperature.** The influence of temperature was studied between 10 and 25°C for constant concentrations of HOSA and piperidine, equal to $1.25 \times 10^{-3}$ and $1 \times 10^{-2}$ mol/l respectively. The variation of $k_1$ with temperature obeys Arrhenius equation:

$$k = A\exp(-E/RT),$$

where $A$ is the Arrhenius pre-exponential factor (l $mol^{-1}$ $min^{-1}$), $E$—activation energy (J/mol), $R$—perfect gas constant (8.314472 J $K^{-1}$ $mol^{-1}$), $T$—temperature (K).

Curve $\ln(k_1) = f(1/T)$ is described by a straight line with slope $-E_1/R$ and intercept point $\ln A_1$. It serves to determine the activation energy $E_1$ and the factor $A_1$. This gives $k_1 = 1.5 \times 10^{10} \exp(-54.1/RT)$.

The activation enthalpy and entropy are determined from the relations:

$$\Delta H_1^{0\#} = E_1 - RT, \quad \Delta S_1^{0\#} = R\ln(A_1 h/ek_BT), \qquad (5)$$

$k_B$ and $h$, representing the Boltzmann constant and the Planck constant respectively ($k_B = 1.380 \times 10^{-23}$ J/K, $h = 6.623 \times 10^{-34}$ Js). At $T = 25°C$, $\Delta H_1^{0\#} = 51.6$ kJ/mol, $\Delta S_1^{0\#} = -58.6$ J $K^{-1}$ $mol^{-1}$, $\Delta G_1^{0\#} = 69.0$ kJ/mol.

### *Kinetics of NAPP Degradation in Basic Medium*

The deviation observed at the end of the reaction is due to a partial oxidation of hydrazine by HOSA. To quantify this phenomenon, a kinetic and mechanistic study was carried out under the same conditions as described above.

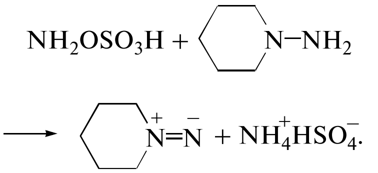
The GC–MS analysis of the reaction medium showed that degradation essentially leads to a linear tetrazene [7] or azopiperidine which was identified and characterized. Tests were performed in basic medium for concentrations of NAPP and HOSA between $2.5 \times 10^{-3}$ and $1.5 \times 10^{-2}$ mol/l. Tests per-

**Table 2.** Determination of the rate constant of the reaction between HOSA and PP ($k_1$) in basic medium. Influence of the initial reagent concentrations

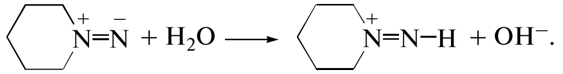
| $[HOSA]_0 \times 10^3$, mol/l | $[PP]_0 \times 10^2$, mol/l | $[NaOH]_0 \times 10^2$, mol/l | $p$ | $k_1$, l mol$^{-1}$ min$^{-1}$ | $R^2$ |
|---|---|---|---|---|---|
| 1.24 | 0.15 | 5.45 | 1.19 | 3.26 | 0.992 |
| 1.24 | 0.37 | 5.52 | 3 | 3.39 | 0.997 |
| 1.30 | 0.78 | 5.57 | 6 | 3.42 | 0.995 |
| 1.20 | 0.96 | 5.55 | 8 | 3.32 | 0.996 |
| 1.23 | 1.23 | 5.33 | 10 | 3.39 | 0.999 |
| 1.22 | 1.46 | 5.55 | 12 | 3.57 | 0.999 |
| 1.29 | 1.02 | 3.16 | 8 | 3.27 | 0.996 |
| 1.25 | 1.00 | 7.04 | 8 | 3.50 | 0.996 |

formed in more concentrated medium led to the precipitation of azopiperidine.

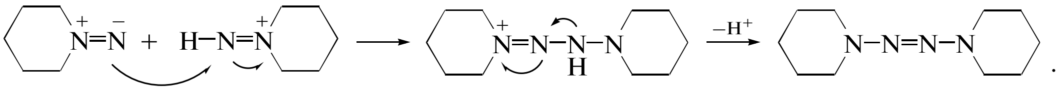
The first step corresponds to the formation of a diazene:



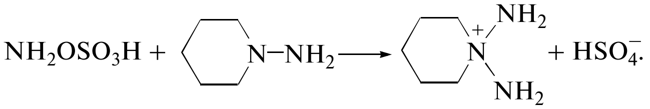
In aqueous medium, diazene can be considered as a base, able to capture a proton according to the following acid-base equation:



Diazene can be in its conjugate form in a weakly basic medium. In this case, azopiperidine is obtained by rapid dimerization between the molecular form and the protonated form of cycloamonitrene:



In this reaction, the yield of tetrazene per NAPP consumed was between 74 and 80%, providing evidence of a competing reaction. The literature indicates the existence of a triazium salt [8–10] whose reaction mechanism corresponds to an $S_N2$ amino reaction.



Since this reaction is secondary, the reaction used for modelling is that which leads to the formation of diazene.

**Kinetic aspect.** As the formation of diazene is stoichiometric (unity), the NAPP degradation rate is expressed by the relation:

$$v = -\frac{d[NAPP]}{dt} = k_2[HOSA]^{\alpha}[NAPP]^{\beta}, \qquad (6)$$

where $k_2$, $\alpha$ and $\beta$ are the degradation rate constant of NAPP and the partial orders to the reagents, HOSA and NAPP respectively.

The kinetics was followed in oxidative and basic medium, i.e. in the presence of HOSA taken in 5 and 8 fold excess. The data were monitored as the NAPP concentration plotted as a function of time.

After sampling, the reaction was immediately terminated by quantitatively transforming NAPP into hydrazone followed by dilution of the product was in a buffer solution with pH 6.88. Then, the concentration in the sample was determined by HPLC at wavelength $\lambda = 236$ nm. Following this, the HOSA concentration could be evaluated for each moment of the reaction. Defining the amount of reacted NAPP as $\delta$, the HOSA concentration can be calculated from the following relation:

$$[HOSA]_t = [HOSA]_0 - ([NAPP]_0 - [NAPP]_t) = [HOSA]_0 - \delta,$$

that is to say $x = x_0 - (u_0 - u) = x_0 - \delta$.

Figure 3 gives the concentration of NAPP as a function of time for a mixture with following initial concentrations:

$$[NH_2OSO_3H]_0 = 1.25 \times 10^{-2}\ \text{mol/l},\ [C_5H_{10}NNH_2]_0 = 2.50 \times 10^{-3}\ \text{mol/l},\ [NaOH]_0 = 5.5 \times 10^{-2}\ \text{mol/l}.$$

As the evolution of the degradation products is independent of the reagents, the yield depends only on the first reaction step. The kinetic parameters were determined by using an integration procedure similar to that described above and assuming a partial order of 1 for each of the reagents.

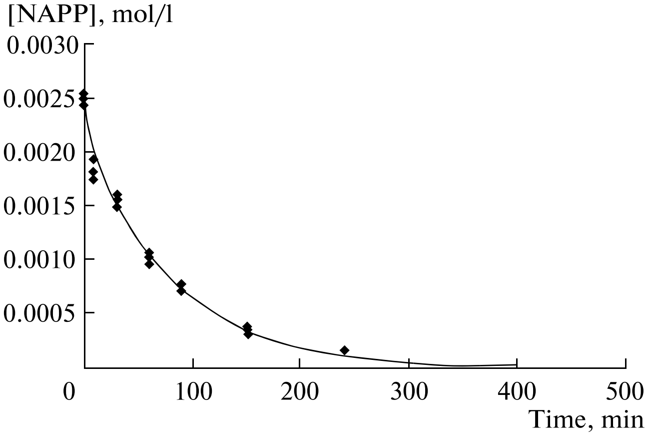


**Fig. 3.** Kinetics of NAPP oxidation by HOSA. Evolution of NAPP concentration through time.

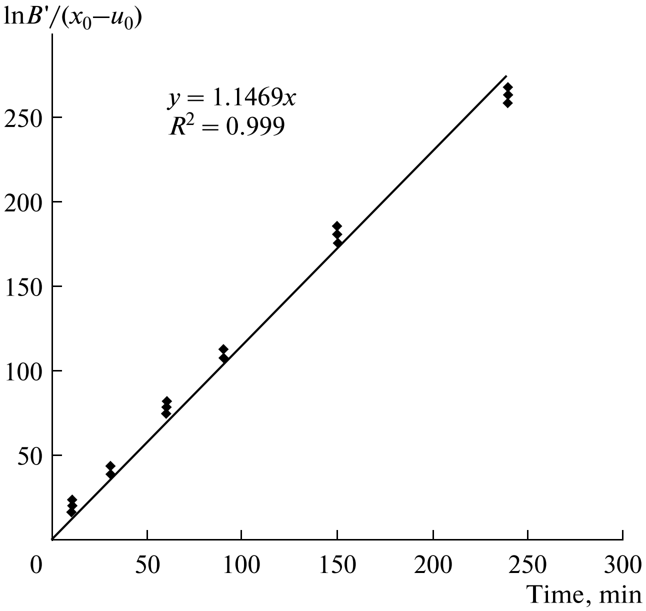


**Fig. 4.** Kinetics of NAPP degradation. Determination of $k_2$. $B' = xu_0/x_0u$

Concentrations of NAPP at the initial time and at $t$, are defined as $u_0$ and $u$, respectively, likewise for HOSA they are $x_0$ and $x$. Thus, by writing $a_0 = u_0 - x_0$, and observing that $x = u - u_0 + x_0 = u - a_0$, the integration of Eq. (6) gives the following expressions:

$$\int_0^u -\frac{du}{u(a_0+u)} = \int_0^t k_2 dt, \tag{7}$$

$$\frac{1}{x_0-u_0}\ln\left(\frac{u_0x}{x_0u}\right) = k_2t. \tag{8}$$

To illustrate the use of this expression, Fig. 4 shows the first term of the Eq. (8) plotted as a function of time for a reaction mixture at 20°C and a mole ratio $p = 5$ ($[NH_2OSO_3H]_0 = x_0 = 1.25 \times 10^{-2}$ mol/l, $[C_5H_{10}NNH_2]_0 = u_0 = 2.50 \times 10^{-3}$ mol/l, $[NaOH]_0 = 5.5 \times 10^{-2}$ mol/l). We observe that the first- rate law is obeyed without deviation up to the completion of the reaction (250 to 300 min). Thus, the reagents are not involved in a secondary reaction process. A similar treatment was carried out for a series of mixtures with different reagent concentrations. The results are given in Table 3. The values obtained are fairly constant. At $T = 20°C$ we obtain:

$$k_2 = -\frac{d[NAPP]/dt}{[HOSA][NAPP]} = 1.17 \pm 0.04\ \mathrm{l\ mol^{-1}\ min^{-1}}.$$

**Influence of temperature.** The effect of temperature was studied between 20 and 35°C for HOSA and NAPP at constant concentrations of $1.28 \times 10^{-2}$ and $2.50 \times 10^{-3}$ mol/l respectively. The variation of $k_2$ with temperature obeys Arrhenius law. This gives $k_2 = 1.83 \times 10^{11}\exp(-62.8/RT)$. The thermodynamic activation values at $T = 25°C$ are as follow:

$$\Delta H_2^{0\#} = 60.4\ \mathrm{kJ/mol}, \quad \Delta S_2^{0\#} = -38\ \mathrm{J\ K^{-1}\ mol^{-1}}, \quad \Delta G_2^{0\#} = 71.6\ \mathrm{kJ/mol}.$$

### *Formulation of a Kinetic Model in Basic Medium*

Consistent with the foregoing dada, we can suggest a plausible sequence of reactions for the synthesis NAPP with HOSA:

$$NH_2OSO_3H + OH^- \rightarrow NH_2OSO_3^- + H_2O, \tag{I}$$

$$NH_2OSO_3^- + C_5H_{10}NH \xrightarrow{k_1} C_5H_{10}NNH_2 + HSO_4^-, \tag{II}$$

$$OH^- + HSO_4^- \rightarrow SO_4^{2-} + H_2O, \tag{III}$$

$$C_5H_{10}NNH_2 + NH_2OSO_3^- \xrightarrow{k_2} C_5H_{10}N^+{=}N^- + NH_4^+ + SO_4^{2-}, \tag{IV}$$

$$OH^- + NH_4^+ \xrightarrow{k_2'} NH_3 + H_2O, \tag{V}$$

$$2C_5H_{10}N^+{=}N^- \rightarrow C_5H_{10}NN{=}NNC_5H_{10}. \tag{VI}$$

The excess NaOH ensures a stoichiometry of unity versus the reagents, since neutralisation reactions (III) and (V) are instantaneous. The useful step of the synthesis is reaction (II). This reaction is bimolecular and first order in the reagents. Reaction (IV) is consecutive-parallel. Indeed, as NAPP is formed, it is partially oxidised by $NH_2OSO_3^-$ to give an intermediate compound, diazene (IV), which then dimerizes to form azopiperidine (VI).

**Table 3.** Determination of the rate constant of the oxidation of NAPP by HOSA ($k_2$) at 20°C

| $[NH_2OSO_3H]_0 \times 10^2$, mol/l | $[C_5H_{10}NNH_2]_0 \times 10^3$, mol/l | $[NaOH]_0 \times 10^2$, mol/l | $p$ | $k_2$, l mol$^{-1}$ min$^{-1}$ | $R^2$ |
|---|---|---|---|---|---|
| 1.25 | 2.50 | 7.50 | 5.1 | 1.13 | 0.989 |
| 1.50 | 2.50 | 7.50 | 6 | 1.20 | 0.991 |
| 1.74 | 2.50 | 7.50 | 7 | 1.18 | 0.996 |
| 1.25 | 2.50 | 5.50 | 5 | 1.14 | 0.986 |
| 1.28 | 2.50 | 9.50 | 5.1 | 1.18 | 0.989 |

It is now possible to evaluate the instantaneous concentrations of the main products and the predictive calculation of the yield versus the reagent concentrations, pH and temperature. To approach calculations, the system of differential equations defined by the rate laws of the previous reactions needs to be solved. By designating the concentrations of HOSA, piperidine, NAPP, NaOH and diazene, at instant $t$, by $x$, $a$, $u$, $b$ and $f$ respectively, the synthesis is described by the following system of differential equations:

$$\frac{dx}{dt} = -k_1xa - k_2xu, \tag{9}$$

$$\frac{da}{dt} = -k_1xa, \tag{10}$$

$$\frac{du}{dt} = k_1xa - k_2xu, \tag{11}$$

$$\frac{db}{dt} = -2(k_1xa + k_2xu), \tag{12}$$

$$\frac{df}{dt} = k_2xu, \tag{13}$$

with the initial conditions $x = x_0$, $a = a_0$, $b = b_0$ and $u = f = 0$.

In particular, we note

$$\frac{db}{dt} = 2\frac{dx}{dt}.$$

This system of equations can be solved numerically by the Runge–Kutta method. However, a semi-algebraic resolution was sought that permits evaluation of the behaviour of the system in time by using a single implicit equation and analytical relations. It also allows a direct access to the final yields on the basis of reagent concentration ratios and temperature ignoring the time factor. To achieve this, $t$ is eliminated between Eqs. (9) and (10):

$$\frac{dx}{da} = 1 + \frac{k_2}{k_1}\frac{u}{a}. \tag{14}$$

Ratio $k_2/k_1$ depends only on ionic strength and temperature. Equation (14) is integrable, expressing $u = f(a)$.

Accordingly, we can modify Eqs. (11) and (10) dividing limb by limb:

$$\frac{du}{da} = -1 + r\frac{u}{a} \quad \text{with} \quad r = \frac{k_2}{k_1}.$$

The integration of this equation leads to:

$$u = \frac{1}{r-1}a\left[1 - \left(\frac{a}{a_0}\right)^{r-1}\right]. \tag{15}$$

Equation (15) permits verifying that $u = 0$ when $a = a_0$.

Substitution of Eq. (15) in Eq. (14) yields a differential equation whose resolution leads to the following implicit equation:

$$(x_0 - x) - (a_0 - a)\frac{2r-1}{r-1} + \frac{a_0}{r-1}\left[1 - \left(\frac{a}{a_0}\right)^{r}\right] = 0. \tag{16}$$

Therefore the final NAPP concentration ($u_\infty$) can be deduced from Eq. (15):

$$u_\infty = \frac{1}{r-1}a_\infty\left[1 - \left(\frac{a_\infty}{a_0}\right)^{r-1}\right]. \tag{17}$$

The instantaneous diazene concentration is obtained from the material balance related to NAPP, combining Eqs. (10), (11) and (13). That gives at $t = \infty$:

$$f_\infty = \sum_{\mathrm{i}} p_i = (a_0 - a_\infty) - \frac{a_\infty}{r-1}\left[1 - \left(\frac{a_\infty}{a_0}\right)^{r-1}\right]. \tag{18}$$

The intermediate concentrations of piperidine ($a$), HOSA ($x$) and NAPP ($u$) can be related to time by resolving the integral obtained from Eqs. (10) and (16):

$$t = \frac{1}{k_1}\int_{\mathrm{a}_0}^{\mathrm{a}_t} -\frac{da}{a[x_0 - g(a, a_0, r)]}$$

with $g(a, a_0, r) = (a_0 - a)\frac{2r-1}{r-1} + \frac{a_0}{r-1}\left[1 - \left(\frac{a}{a_0}\right)^{r}\right]$.

### *Determination of the Parameters Controlling the Synthesis*

The previous equations may be applied to predict the evolution of the system under specific experimen-

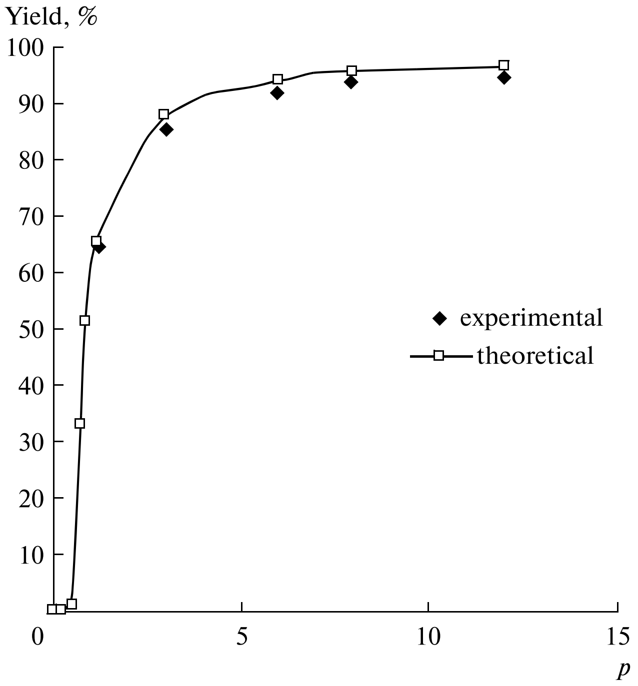


**Fig. 5.** Evolution of NAPP yield with reagents ratio $p$ in concentrated medium at $[\mathrm{NaOH}]_\infty = 0.05$ mol/l, $T = 20°\mathrm{C}$, $k_{1\mathrm{exp}} = 3.39\ \mathrm{l\ mol^{-1}\ min^{-1}}$ and $k_{2\mathrm{exp}} = 1.17\ \mathrm{l\ mol^{-1}\ min^{-1}}$.

tal conditions, but they do not refer to the parameters that affect the yield, especially the initial concentration ratios defined by the relation:

$$p = \frac{[\mathrm{C_5H_{10}NH}]_0}{[\mathrm{NH_2OSO_3H}]_0}.$$

**Table 4.** Influence of the reagents ratio ($p$) on NAPP yield in concentrated medium at $[\mathrm{NaOH}]_\infty = 0.1$ mol/l and $T = 20°\mathrm{C}$

| $p = a_0/x_0$ | Initial reagents concentrations, mol/l | | |
|---|---|---|---|
| | $[\mathrm{C_5H_{10}NH}]_0$ | $[\mathrm{NaOH}]_0$ | $[\mathrm{HOSA}]_0$ |
| 1.2 | 0.10 | 0.21 | 0.08 |
| 1.2 | 0.30 | 0.55 | 0.25 |
| 1.2 | 0.50 | 0.89 | 0.42 |
| 3 | 0.50 | 0.37 | 0.16 |
| 6 | 0.50 | 0.21 | 0.08 |
| 8 | 0.50 | 0.17 | 0.06 |
| 12 | 0.50 | 0.13 | 0.04 |

Introducing this parameter into the Eq. (16) we have:

$$1 - p\left(1 - \frac{a_\infty}{a_0}\right)\frac{2r-1}{r-1} + \frac{p}{r-1}\left[1 - \left(\frac{a_\infty}{a_0}\right)^r\right] = 0. \qquad (19)$$

Taking into account the reagent material balances at $t_\infty$:

$$x_0 = u_\infty + 2f_\infty,$$

$$a_0 - a_\infty = u_\infty + f_\infty.$$

Then, by eliminating the term related to NAPP oxidation between the two previous equations and by noting $\varphi_\mathrm{u} = u_\infty/x_0$, one obtains

$$\frac{a_\infty}{a_0} = 1 - \frac{\varphi_u + 1}{2p}.$$

The substitution of this expression in Eq. (19) leads to the following implicit general equation:

$$1 - (\varphi_u + 1)\frac{2r-1}{2(r-1)} + \frac{p}{r-1}\left[1 - \left(1 - \frac{\varphi_u + 1}{2p}\right)^r\right] = 0.$$

This equation clearly shows that NAPP yield ($\varphi_u$) depends only on $p = a_0/x_0$ and on $r = k_2/k_1$, $r$ being only a function of pH and temperature. We can verify that when $r \to 0$ ($k_2 = 0$), yield $\varphi_u \to 1$. The yields related to amine and diazene are deduced directly:

$$\varphi_a = \frac{u_\infty}{a_0 - a_\infty} = \frac{2\varphi_u}{\varphi_u + 1} \quad \text{and} \quad \varphi_f = \frac{1 - \varphi_u}{2}.$$

### *Validation of the Model and Determination of Optimal Conditions*

The results obtained by the theoretical study were verified by experiments conducted in a concentrated medium at a temperature of 20°C for different ratios $p$ (1 to 12) and for increasing reagent concentrations. The amount of sodium hydroxide needed to neutralise all the $\mathrm{H^+}$ ions involved in NAPP formation and maintain a final sodium hydroxide concentration equal to 0.05 mol/l was calculated.

**Influence of the *p* ratio.** The experiments were carried out at 20°C, by varying the concentration of HOSA, while maintaining constant temperature and final NaOH concentration. Piperidine and HOSA volumes were equal to 100 ml. Table 4 gives the initial reagent concentrations and Table 5 gives the molar composition at $t = 0$ and $t = \infty$, and the NAPP yield $\varphi_u$. Figure 5 shows that the yield increases by 30% when $p$ increases from 1.2 to 12. The theoretical curve agrees with the experimental points.

NAPP yield increases with ratio $p = [\mathrm{PP}]_0/[\mathrm{HOSA}]_0$. For $p = 6$, the yield reaches 90%. Beyond this value, doubling the ratio leads only to a negligible increase in the yield ($\varphi = 94.1\%$ for $p = 6$, $\varphi = 96.5\%$ for $p = 12$). Thus ratio $p = 8$ was used for synthesis under optimal conditions.

**Effect of temperature.** The influence of temperature was studied between 10 and 80°C for a final concentration of NaOH equal to 0.05 mol/l and for a ratio

**Table 5.** Formation of NAPP. Experimental results

| $p = a_0/x_0$ | Real concentration in the reaction medium, mol/l | | | | Yield $\varphi_u = u_\infty/x_0$, % | |
|---|---|---|---|---|---|---|
| | $t = 0$ | | $t = \infty$ | | | |
| | $[NaOH]_0$ | $[HOSA]_0$ | $[NaOH]_\infty$ | $[NAPP]_\infty$ | exp. | theor. |
| 1.2 | 0.11 | 0.04 | 0.05 | 0.03 | 65.9 | 65.6 |
| 1.2 | 0.28 | 0.13 | 0.05 | 0.09 | 66.0 | 65.6 |
| 1.2 | 0.45 | 0.21 | 0.05 | 0.13 | 64.5 | 65.6 |
| 3 | 0.19 | 0.08 | 0.05 | 0.07 | 85.9 | 87.7 |
| 6 | 0.11 | 0.04 | 0.05 | 0.04 | 91.8 | 94.1 |
| 8 | 0.09 | 0.03 | 0.05 | 0.03 | 93.9 | 95.6 |
| 12 | 0.07 | 0.02 | 0.05 | 0.02 | 94.6 | 96.5 |

$p = 1.2$. The initial reagent concentrations were as follows: $[C_5H_{10}NH]_0 = 0.50$ mol/l; $[NaOH]_0 = 0.89$ mol/l; $[NH_2OSO_3H]_0 = 0.42$ mol/l. For this experiment, 100 ml of aqueous HOSA solution was introduced into 100 ml of a mixture of piperidine and NaOH. Table 6 gives the corresponding yields.

The higher the temperature the lower the yield. Thus NAPP must be synthesized at a low temperature, i.e. 20°C.

**The evolution of NAPP at industrial concentration.** Figure 6 presents the kinetic curves obtained by modelling the behaviour of the system under conditions which include reagent concentrations approaching those used in industry, i.e. the addition of an aqueous HOSA solution of 32% w/w to a mixture of NaOH and piperidine at 20°C. The initial concentrations of the reaction mixture are as follows: $[HOSA]_0 = 0.69$ mol/l, $[PP]_0 = 5.55$ mol/l, $[NaOH]_0 = 1.39$ mol/l, $p = 8$.

The reaction is almost terminated at $t = 0.35$ min, corresponding to a NAPP yield close to 96%.

### *Kinetics of NAPP Formation in Buffer Medium*

A kinetic study of NAPP formation was carried out to verify that the results obtained in basic medium can be used in buffer medium (pH 11–12). The methodology is similar to that applied to the data for basic medium. The reaction scheme is as follows:

$$NH_2OSO_3H + C_5H_{10}NH \xrightarrow{k_3} C_5H_{10}NNH_2 + H_2SO_4,$$

$$2C_5H_{10}NH + H_2SO_4 \rightarrow (C_5H_{10}NH_2)_2^+SO_4^{2-},$$

$$\Rightarrow NH_2OSO_3 + 3C_5H_{10}NH \rightarrow C_5H_{10}NHH_2 + (C_5H_{10}NH_2^+)_2SO_4^{2-}.$$

Under these conditions, pH is controlled through time by the buffer mixture PP—$(PPH^+)_2SO_4^{2-}$. Therefore PP is consumed by both reaction with HOSA and by protonation. The latter reaction contributes to a slowdown in the rate of NAPP formation. The following theoretical stoichiometric relations can be written:

$$-\frac{d[HOSA]}{dt} = -\frac{1}{3}\frac{d[PP]}{dt} = \frac{d[NAPP]}{dt}.$$

By designating the concentrations of NAPP, HOSA and piperidine at the initial time by $u$, $x_0$ and $a_0$ respectively, the integration of the previous relations gives:

$$\int_0^u \frac{du}{(x_0 - u)(a_0 - 3u)} = \int_0^t k_3 dt,$$

$$\frac{1}{a_0 - 3x_0}\ln\left(\frac{x_0(a_0 - 3u)}{a_0(x_0 - u)}\right) = k_3 t.$$

**Table 6.** Influence of temperature on the NAPP yield in concentrated medium at $p = 1.2$ and real concentration $[NaOH]_\infty = 0.05$ mol/l

| $T$, °C | $\varphi_u$, % | |
|---|---|---|
| | exp. | theor. |
| 20 | 64.5 | 65.6 |
| 50 | 58.9 | 59.2 |
| 80 | 53.2 | 53.6 |

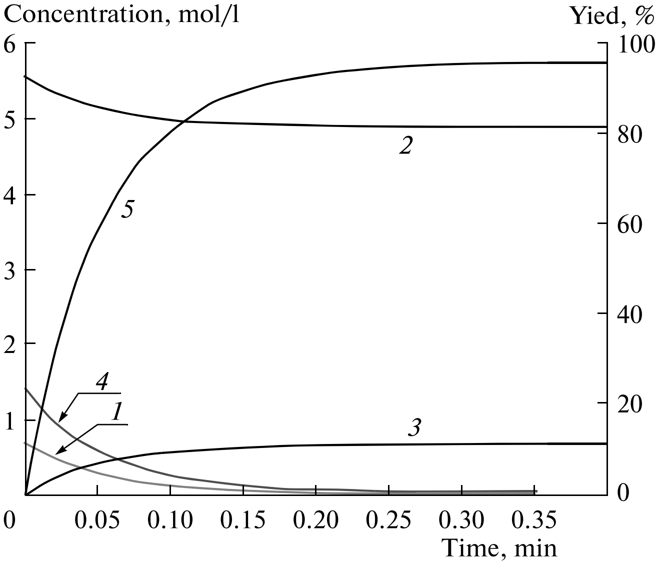


**Fig. 6.** Evolution of HOSA (*1*), PP (*2*), NAPP (*3*) and NaOH (*4*) and yield (*5*) during the reactions in basic medium and under industrial conditions.

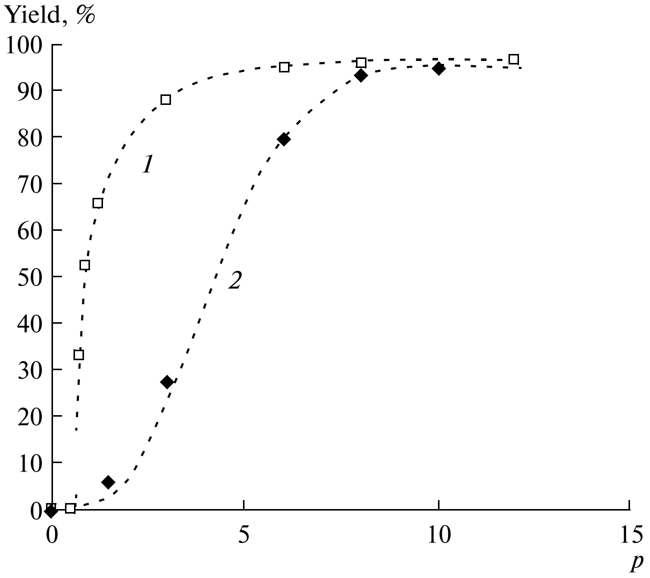


**Fig. 7.** Evolution of NAPP yield in basic (*1*) and in buffer (*2*) mediums.

The results are presented in Table 7. The values obtained are fairly constant. The following expression can be deduced at $T = 20°C$:

$$k_3 = \frac{d[NAPP]/dt}{[HOSA][PP]} = 2.56 \pm 0.08 \, l \, mol^{-1} \, min^{-1}.$$

The influence of temperature was studied at temperatures between 5 and 25°C for constant concentrations of HOSA and piperidine equal to $1.25 \times 10^{-3}$ and $1.5 \times 10^{-2}$ mol/l respectively. The variation of $k_3$ with temperature obeys Arrhenius law. Thus we can write:

$$k_3 = 5.99 \times 10^{10} \exp\left(-\frac{58.2}{RT}\right).$$

The activation parameters at 25°C can be deduced:

$$\Delta H_3^{0\#} = 55.7 \text{ kJ/mol}, \quad \Delta S_3^{0\#} = -47 \text{ J K}^{-1}\text{mol}^{-1}.$$
$$\Delta G_3^{0\#} = 69.7 \text{ kJ/mol}.$$

Figure 7 shows the evolution of NAPP yield in basic medium and in buffer medium. The curves have the same shape but in buffer medium, the inflexion point appears later. This is due to partial protonation of the amine by the $H^+$ ions stemming from the formation of NAPP in buffer medium.

For $p = 8$, the yields are very similar to those obtained in basic medium. Under these conditions, it is possible to synthesize NAPP in buffer medium, with the optimal parameters being established in basic medium.

## CONCLUSION

NAPP synthesis using hydroxylamine-O-sulfonic acid (HOSA) is a new and promising process. It was therefore desirable to study reaction mechanisms. The results indicate that the formation of NAPP is the first- order reaction to two reagents, piperidine and HOSA described by a nucleophilic substitution mech-

**Table 7.** Determination of rate constant of reaction between HOSA and PP ($k_3$) at 20°C in buffer medium

| $[NH_2OSO_3H]_0 \times 10^3$, mol/l | $[C_5H_{10}NH]_0 \times 10^3$, mol/l | $p$ | $k_3$, l mol$^{-1}$ min$^{-1}$ | $R^2$ |
|---|---|---|---|---|
| 1.25 | 10.7 | 8.6 | 2.41 | 0.9992 |
| 1.25 | 12.5 | 10.0 | 2.54 | 0.9998 |
| 1.26 | 14.7 | 11.6 | 2.50 | 0.999 |
| 1.25 | 17.7 | 14.2 | 2.76 | 0.9994 |

anism of $S_N2$ type. The main secondary reaction identified was NAPP oxidation by HOSA which consistently decreased NAPP yield. This reaction occurred in 2 consecutive steps: the formation of a diazene followed by dimerization to tetrazene.

The study of the different parallel reactions resulted in a system of differential equations. By solving these equations it was possible to find expressions that predict the evolution of the system as a function of the reagent concentrations, pH and temperature. A mathematical treatment was used to characterize the reaction medium from a unique implicit equation. The equation clearly shows that the $p$ molar ratio, the initial concentrations $[PP]_0/[HOSA]_0$, the rate constant ratio $k_2/k_1$ and temperature are the only parameters that affect the yield of NAPP from converted [HOSA]. The curves obtained according to the model agree well with the experimental curves. This provides evidence of the validity of the model that makes it possible to determine optimal conditions for the reaction:

$$[HOSA]_0 = 0.69\ \text{mol/l},\quad [PP]_0 = 5.55\ \text{mol/l},\quad p = 8,$$
$$\text{pH } 11\text{–}12,\ T = 20°\text{C}.$$

Thus NAPP was synthesised by fast and selective reaction with a yield around 96%. This study was first carried out in basic medium and then in buffer medium with fairly similar results.

## REFERENCES

1. Jain, S.R. and Chellappa, D., *Proc. Indian Acad. Sci. Chem. Sci.*, 1985, vol. 95, no. 4, p. 381.
2. Darwich, C., *French Thesis Univ. Claude Bernard Lyon 1*, 2005, vol. 29, p. 2005.
3. Delalu, H. and Marchand, A., *Anal. Chim. Acta,* 1992, vol. 266, p. 39.
4. Steinmetz, W.E., Robinson, D.H., and Ackermann, M.N., *Inorg. Chem.*, 1975, vol. 14, p. 421.
5. Matsuguma, H.J. and Audrieth, L.F., *J. Inorg. Nucl. Chem.*, 1959, vol. 12, p. 186.
6. *CRC Handbook of Chemistry and Physics*, Lide, D.R., Ed., Boca Raton, Fla.: CRC, 2003–2004, 84th ed., p. 8.
7. Stradi, R., *Atti Accad. Naz. Lincei Cl. Sci. Fis. Mat. Nat. Rend.*, 1947, vol. 43, p. 350.
8. Linke, K.H. and Turley, R., *Z. Naturforsch., A: Phys. Sci.*, 1973, vol. 28b, p. 781.
9. Sommer, F., Schluz, O.F., and Nassau, M., *Z. Anorg. Allg. Chem.*, 1925, vol. 147, p. 142.
10. Freyer, D., Voigt, W., and Kohnke, K., *Eur. J. Solid State Inorg. Chem.,* 1998, vol. 35, p. 595.