

Article

## A Study of the Formation and Stability of N-Alkylbutanimines by <sup>1</sup>H-NMR Spectroscopy

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O estudo da formação de N-alkilbutaniminas obtidas a partir da reação entre aldeídos e aminas primárias foi realizado com o objetivo de determinar as condições experimentais mais apropriadas para a obtenção dessas aldiminas alifáticas. Para isto, foram estudados os efeitos da temperatura da reação, da constante dielétrica dos solventes empregados e do volume dos grupos alquilas substituintes do átomo de nitrogênio no valor da constante de equilíbrio da reação. Os valores das constantes de equilíbrio foram calculados a partir da relação da integração dos sinais de RMN dos hidrogênios dos grupos aldimina e aldeído dos componentes da mistura da reação. O estudo da estabilidade das N-alkilbutaniminas foi realizado considerando a possibilidade de ocorrência de tautomerismo imina-enamina em meio ácido, a presença de hidrogênio alfa ao grupo aldimina e a utilização de solvente de alta constante dielétrica.

The study of the formation of N-alkylbutanimines from the reaction of aldehydes with primary amines was carried out with the objective of determining the most appropriate experimental parameters for their formation. The effects of reaction temperature, dielectric constant of the solvents utilized, and volume of the N-alkyl groups on the equilibrium constant were studied. The equilibrium constants for the formation of N-alkylbutanimines were calculated from the ratio of the integrations of the NMR signals for the hydrogens of the aldimine and aldehyde groups in the reaction mixture. The study of the stability of N-alkylbutanimines was carried out considering the possibility of the occurrence of imine-enamine tautomerism in acidic media, the presence of a hydrogen alpha in the aldimine group, and the utilization of solvents with a high dielectric constant.

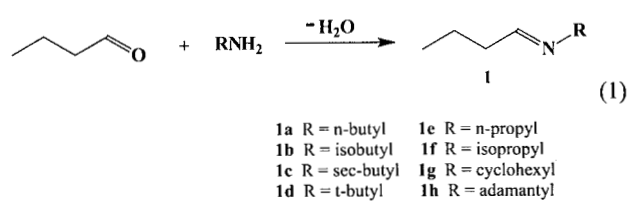
**Keywords:** *aldimines, equilibrium constants, imine-enamine tautomerism, Nuclear Magnetic Resonance*

### Introduction

According to the literature, Schiff bases are aromatic imines whose formation in high yield has been known since the end of the last century<sup>1</sup>. They are stable in the reaction medium in which they are produced, as well as after isolation. These compounds are of great importance as intermediates in the synthesis of biologically active compounds<sup>2</sup>. In addition to their biological importance, Schiff bases have a fundamental role in the synthesis of a series of simple and polymeric substances<sup>3</sup>. On the other

hand, aliphatic imines have been studied very little because of their low stability<sup>4</sup>. The formation of aliphatic aldimines is transitory because, under the conditions described in the literature, they suffer auto-condensation in the reaction medium or after isolation, and are consequently obtained in very low yields<sup>5</sup>.

The present work presents experimental conditions which favor the formation and stability of the N-alkylbutanimines **1a** - **1h**, obtained from butyraldehyde and primary aliphatic amines, as shown in Eq. 1. The effects of temperature, solvent and the structure of the reagents on the



aldimine yield are considered. The formation of N-alkylbutanimines may serve as a model for the preparation of other aliphatic amines.

## Experimental

Thionyl chloride and the solvents pentane, dichloromethane, tetrahydrofuran (THF), diethyl ether, acetonitrile and dimethylsulfoxide (DMSO) were obtained from Merck. Butylamine, isobutylamine, *sec*-butylamine, *t*-butylamine, propylamine, isopropylamine, cyclohexylamine, adamantylamine, butyraldehyde, isobutyraldehyde, aluminum chloride, 2-chloroacetamide, and N-chlorosuccinimide were acquired from Aldrich. Boron trifluoride etherate was obtained from Eastman. Butanoic acid was acquired from Riedel de Haen Ag Seelze. The solvents and reagents were treated as described in the literature<sup>6</sup>. The anhydrous drying agents calcium chloride, magnesium sulfate, potassium carbonate, potassium hydroxide, and sodium sulfate were obtained from Baker, and were utilized with no treatment. The aldehydes were distilled under reduced pressure, washed with aqueous KOH, and distilled at atmospheric pressure. The purified aldehydes were stored at -15 °C under nitrogen and over KOH and distilled twice at atmospheric pressure before use.

The hydrogen NMR spectra were recorded on Varian EM 360-A and Bruker AC 80 spectrometers. The <sup>13</sup>C-NMR spectra were recorded on a Bruker AC 80 instrument operating at 20 MHz. The infrared spectra were recorded on Perkin-Elmer 283B and Mattson Galaxy Series FTIR 3000 spectrophotometers. Refractive indices were obtained on an ABBE Carl Zeiss-Jena refractometer.

The ratio of aldehyde to imine in the reaction mixtures was calculated by the integration of the signals corresponding to the aldehyde hydrogen (near  $\delta$  9.5) and the aldimine hydrogen (near  $\delta$  7.5). An error of 6.5% in the ratio [aldehyde]/[imine] was estimated using standard solutions of chloroform and dichloromethane.

### The effect of drying agent on the reaction yield

Butyraldehyde 0.05 mol was slowly added to a stirred mixture of 0.05 mol of *t*-butylamine, 0.44 mol of pentane and 0.10 mol of anhydrous drying agent in a 3-necked, round-bottomed flask connected to an addition funnel and a reflux condenser with a drying tube. The mixture was stirred for 4 h at room temperature and filtered. The solvent

was distilled at atmospheric pressure, and the aldimine **1d** was distilled under reduced pressure. The drying agents employed were calcium chloride, magnesium sulfate, potassium carbonate, aluminum chloride, boron trifluoride, potassium hydroxide and sodium sulfate.

### The effect of temperature on the reaction equilibrium

Butyraldehyde 0.05 mol was slowly added to a stirred mixture of 0.05 mol of *t*-butylamine, 0.44 mol of pentane and 0.10 mol of anhydrous magnesium sulfate in a 3-necked, round-bottomed flask connected to an addition funnel and a reflux condenser with a drying tube. The mixture was stirred for 150 h at the desired temperature and filtered. Aliquots of the product mixtures were analyzed by <sup>1</sup>H-NMR spectroscopy. The temperatures utilized were 0, 5, 21 and 36 °C.

### The effect of solvent on the reaction equilibrium

Butyraldehyde 0.05 mol was slowly added to a stirred mixture of 0.05 mol of *t*-butylamine, 0.44 mol of solvent and 0.10 mol of anhydrous magnesium sulfate in a 3-necked, round-bottomed flask connected to an addition funnel and a reflux condenser with a drying tube. The mixture was stirred for 140 h at 0 °C and filtered. Aliquots of the product mixtures were analyzed by <sup>1</sup>H-NMR spectroscopy. The solvents utilized were pentane, ether, THF, dichloromethane, acetonitrile, and DMSO (temperature = 21 °C, to avoid freezing). One reaction was carried out without solvent.

### The effect of substituent on the reaction equilibrium

Aldehyde 0.05 mol was slowly added to a stirred mixture of 0.05 mol of *t*-butylamine, 0.44 mol of solvent and 0.10 mol of anhydrous magnesium sulfate in a 3-necked, round-bottomed flask connected to an addition funnel and a reflux condenser with a drying tube. The mixture was stirred for 140 h at 0 °C and filtered. After aliquots for the product mixtures were analyzed by <sup>1</sup>H-NMR spectroscopy (thus affording the  $K_{ap}$  values), the solvent and the aldimines were distilled under reduced pressure. The isolated aldimines remained stable when stored in a desiccator for a 36 month period, as shown by <sup>1</sup>H-NMR analysis. For the reaction with isobutyraldehyde, the amines — butylamine, isobutylamine, *sec*-butylamine, *t*-butylamine, propylamine, isopropylamine, cyclohexylamine and adamantylamine — were used. For the reaction with isobutyraldehyde, only *t*-butylamine was used. The most significant physical data for **1** and **2** are shown below. The procedure described above for the synthesis of the aldimines **1a** to **1h** was also carried out in dichloromethane. The yield presented first in each case is that obtained in pentane, while the yield obtained in dichloromethane is given in parentheses.

*N-Butylbutanimine (1a)*

Yield 94% (92%); bp 44 °C/20 mm;  $n_D^{25}$  1.4016; IR (film)  $\nu$  2950-2850, 1670 (C=N), 1540, 1450, 1375, 1150  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (neat)  $\delta$  0.7-1.1 (m, 6H), 1.2-1.9 (m, 6H), 2.0-2.5 (m, 2H), 3.25 (t,  $J = 6.5$  Hz, 2H), 7.58 (t,  $J = 4.8$  Hz, 1H).

*N-(2-Methylpropyl)butanimine (1b)*

Yield 94% (90%); bp 38 °C/15 mm;  $n_D^{25}$  1.4031; IR (film)  $\nu$  2950-2800, 1670 (C=N), 1460, 1375, 1360, 1120  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (neat)  $\delta$  0.7-1.2 (m, 9H), 1.3-2.0 (m, 3H), 2.0-2.6 (m, 2H), 3.20 (d,  $J = 6.0$  Hz, 2H), 7.60 (t,  $J = 4.2$  Hz, 1H).

*N-(1-Methylpropyl)butanimine (1c)*

Yield 93% (91%); bp 30 °C/15 mm;  $n_D^{25}$  1.4031; IR (film)  $\nu$  2950-2810, 1660 (C=N), 1450, 1375, 1320, 1150  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.8-1.4 (m, 9H), 1.4-2.0 (m, 4H), 2.0-2.6 (m, 2H), 2.7-3.1 (m, 1H), 7.57 (t,  $J = 4.2$  Hz, 1H);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  10.9, 13.7, 19.8, 22.5, 30.7, 37.8, 66.2, 162.2.

*N-(1,1-Dimethylethyl)butanimine (1d)*

Yield 91% (74%); bp 42 °C/23 mm;  $n_D^{25}$  1.4078; IR (film)  $\nu$  3000-2850, 1670 (C=N), 1450, 1360, 1260, 1220, 1090  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.19 (s, 9H), 0.8-1.8 (m, 5H), 2.1-2.4 (m, 2H), 7.59 (t,  $J = 4.7$  Hz, 1H);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  13.8, 19.6, 29.7, 38.3, 56.4, 158.3.

*N-Propylbutanimine (1e)*

Yield 92% (92%); bp 28 °C/26 mm;  $n_D^{25}$  1.4147; IR (film)  $\nu$  2990-2820, 1670 (C=N), 1460, 1370, 1210, 1150, 1100  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.8-1.2 (m, 6H), 1.2-2.0 (m, 4H), 2.0-2.7 (m, 2H), 3.30 (t,  $J = 6.5$  Hz, 2H), 7.60 (t,  $J = 4.6$  Hz, 1H).

*N-(1-Methylethyl)butanimine (1f)*

Yield 94% (89%); bp 25 °C/10 mm;  $n_D^{25}$  1.4045; IR (film)  $\nu$  2950-2850, 1660 (C=N), 1460, 1375, 1270, 1150, 1120  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.8-1.2 (m, 9H), 1.2-1.8 (m, 2H), 2.0-2.5 (m, 2H), 3.26 (m,  $J = 6.4$  Hz, 1H), 7.70 (t,  $J = 5.0$  Hz, 1H).

*N-Cyclohexylbutanimine (1g)*

Yield 94% (86%); bp 52 °C/20 mm;  $n_D^{25}$  1.4160; IR (film)  $\nu$  2950-2800, 1670 (C=N), 1580, 1450, 1370, 1340, 1250, 1210, 1150  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.8-1.2 (m, 3H), 1.2-2.0 (m, 12H), 2.0-2.5 (m, 2H), 2.7-3.2 (m, 1H), 7.63 (t,  $J = 4.7$  Hz, 1H).

*N-Adamantylbutanimine (1h)*

Yield calculated by  $^1\text{H-NMR}$  44% (29%); IR (film)  $\nu$  2980-2800, 1665 (C=N), 1455, 1370, 1200, 1140  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.8-2.5 (m, 20H), 7.74 (t,  $J = 4.5$  Hz, 1H).

*N-(1,1-Dimethylethyl)-2-methylpropanimine (2)*

Yield 56%; bp 34 °C/20 mm;  $n_D^{25}$  1.4075; IR (film)  $\nu$  3000-2850, 1670 (C=N), 1450, 1385, 1365, 1110;  $^1\text{H-NMR}$  (neat)  $\delta$  1.03 (d,  $J = 2.0$  Hz, 6H), 1.13 (s, 9H), 1.8-2.1 (m, 1H), 7.60 (d,  $J = 4$  Hz, 1H).

*The synthesis of N-(1,1-dimethylethyl)-2,2-dichlorobutanimine (3) and N-(1,1-dimethylethyl)-2-chlorobutanimine (4)*

Anhydrous magnesium sulfate 0.20 mol and 0.40 mol of N-chlorosuccinimide were added to a solution of 0.10 mol of **1d** in 100 mL pentane with stirring in an ice bath. The mixture was allowed to warm to room temperature, and was filtered after stirring for 24 h. After distillation of the pentane at atmospheric pressure, the products were distilled under reduced pressure.

*N-(1,1-dimethylethyl)-2,2-dichlorobutanimine (3)*

Yield 46%; bp 75 °C/20 mm (Lit.:<sup>7</sup> bp 45 °C/9 mm); IR (film)  $\nu$  1670 (C=N);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.93 (t,  $J = 6.4$  Hz, 3H), 1.19 (s, 9H), 2.45 (q,  $J = 6.4$  Hz, 2H), 7.64 (s, 1H);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  9.53, 29.1, 36.7, 56.8, 91.1, 154.6.

*N-(1,1-dimethylethyl)-2-chlorobutanimine (4)*

Yield 21%; bp 68 °C/20 mm (Lit.:<sup>7</sup> bp 56-58 °C/12 mm); IR (film)  $\nu$  1665 (C=N);  $^1\text{H-NMR}$  (neat)  $\delta$  1.03 (t,  $J = 7.0$  Hz, 3H), 1.19 (s, 9H), 2.0-2.8 (m, 2H), 3.91 (m, 1H), 7.62 (d,  $J = 5.6$  Hz, 1H).

*The synthesis of 1,2-dichloroethanimine (5)*

Thionyl chloride 1.51 mol was added with stirring at 0 °C to a solution of 0.154 mol of  $\alpha$ -chloroacetamide in 50 mL benzene in a 3-necked, round-bottomed flask connected to an addition funnel and a reflux condenser with a drying tube. After the addition was complete, the mixture was refluxed for 144 h, and the benzene and unreacted thionyl chloride were distilled at atmospheric pressure. Ether 100 mL and 100 mL of 20% HCl were added to the residue. The phases were separated and the aqueous phase was extracted with ether. The organic phases were combined and dried over  $\text{Na}_2\text{SO}_4$ . The solvent was distilled at atmospheric pressure and the product was distilled under reduced pressure.

### 1,2-dichloroethanimine (5)

Yield 27.8%; bp 90 °C/10 mm. IR (film)  $\nu$  3600-2800, 2000, 1720, 1650, 1400  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (neat)  $\delta$  3.35 (s, 1H), 5.10 (s, 2H).

### The determination of the stability of the aldimines

Butanoic acid 0.005 mol was added to a solution of 0.10 mol of aldimine in 0.44 mol of solvent. The mixture was stirred at room temperature and aliquots of the product mixtures were analyzed by  $^1\text{H-NMR}$  spectroscopy. The aldimines utilized were **1a** -**1h**, **3**, **4** and **5**. When the reaction was carried out in DMSO or water, butanoic acid was not added to the mixture and aliquots were analyzed by  $^1\text{H-NMR}$  over a 240 h period.

## Results and Discussion

### The study of the Formation of N-Alkylbutanimines

The effect of the drying agent on the yield was determined using the agents listed in Table 1. As can be seen, acidic drying agents furnished the lowest yields. The highest yield was obtained using magnesium sulfate, and this substance was employed in the subsequent studies.

The N-alkylbutanimines are in dynamic equilibrium with the reactant aldehydes and amines (Eq. 1). In order to determine the experimental conditions which favor the shift of this equilibrium toward the products, the effects of temperature, the dielectric constant of the solvent, and the volume of the N-alkyl group on the apparent equilibrium constant for the reaction were determined. The true equilibrium constant for this reaction was difficult to determine because the product water formed a separate phase. Instead, the apparent equilibrium constant,  $K_{\text{ap}}$ , as defined by Eq. 2, was determined.

$$K_{\text{ap}} = \frac{K}{[\text{H}_2\text{O}]} = \frac{[\text{amine}]}{[\text{aldehyde}]^2} \quad (2)$$

**Table 1.** Yields of N-(1,1-dimethylethyl)butanimine (**1d**) obtained from the reaction of *t*-butylamine with butyraldehyde in pentane in the presence of various anhydrous drying agents.

Drying agent	Yield (%)
CaCl <sub>2</sub>	28
MgSO <sub>4</sub>	91
KOH	85
Na <sub>2</sub> SO <sub>4</sub>	68
K <sub>2</sub> CO <sub>3</sub>	19
AlCl <sub>3</sub>	52
BF <sub>3</sub>	0
---	23 <sup>a</sup>

<sup>a</sup> This yield was obtained in the absence of a drying agent.

Table 2 presents the values of  $K_{\text{ap}}$  calculated for the formation of **1d** from *t*-butylamine and butyraldehyde in pentane in the presence of magnesium sulfate at different temperatures. The results shown in Table 2 indicate that an increase in temperature favors the formation of the imine, in spite of the fact that the literature states that the reaction between aldehydes and primary amines is highly exothermic<sup>8</sup>. However, to facilitate the NMR analysis, the following studies of the effects of the solvent and substituent on  $K_{\text{ap}}$  were carried out at 0 °C.

The effects of the solvent dielectric constants on the values of  $K_{\text{ap}}$  for the formation of **1d** from butyraldehyde and *t*-butylamine at 0 °C in the presence of magnesium sulfate are shown in Table 3. A comparison of the  $K_{\text{ap}}$  values with the dielectric constants of the solvent employed in the reaction showed no correlation.

Finally, the steric effects of the substituents on the amine and aldehyde were studied. The reaction of butyraldehyde with *t*-butylamine in pentane at 0 °C in the presence of magnesium sulfate showed the lowest  $K_{\text{ap}}$  (156.0  $\text{M}^{-1}$ ) when compared to the results of the other amines with the

**Table 2.**  $K_{\text{ap}}$  values calculated at different temperatures for the formation of N-(1,1-dimethylethyl)butanimine (**1d**) obtained from *t*-butylamine and butyraldehyde in pentane in the presence of magnesium sulfate.

Temperature (°C)	[aldehyde]/[imine] ( $\pm$ 6.5%)	$K_{\text{ap}}$ ( $\text{M}^{-1}$ )
0	0.084	156
5	0.053	380
21	0.029	1154
36	0.025	1690

**Table 3.**  $K_{\text{ap}}$  values for the formation of **1d** from butyraldehyde and *t*-butylamine in different solvents at 0 °C in the presence of magnesium sulfate.

Solvent	Dielectric constant	[aldehyde]/[imine] ( $\pm$ 6.5%)	$K_{\text{ap}}$ ( $\text{M}^{-1}$ )
no solvent	---	0.026	1560.0
pentane	2.7	0.084	156.0
ether	4.3	0.121	76.2
THF	7.6	0.099	112.0
CH <sub>2</sub> Cl <sub>2</sub>	9.1	0.173	39.5
CH <sub>3</sub> CN	38.1	0.117	29.1 <sup>a</sup>
DMSO	45.0	0.000	$\infty^b$

<sup>a</sup> The reaction in acetonitrile did not reach equilibrium because of the reaction of the amine with acetonitrile. An increase in the ratio [aldehyde]/[amine] occurred with time. In this case the  $K_{\text{ap}}$  value corresponds to the results obtained one hour after initiating the reaction. <sup>b</sup> The reaction in DMSO at 21 °C was irreversible, with no  $^1\text{H-NMR}$  signal corresponding to the aldehyde hydrogen being detected after 1.5 h.

same aldehyde. This amine has a more voluminous alkyl group bound to the nitrogen than the other amines studied. The  $K_{ap}$  value for the reaction with adamantylamine was  $1008.3 \text{ M}^{-1}$ . The steric effects of the adamantyl group are smaller because of its rigidity. The reactions of butyraldehyde with the remaining amines all had  $K_{ap}$  values equal to or approaching infinity, since these amines are less sterically hindered, and the products show little or no steric interaction. Similarly, the  $K_{ap}$  values for the reactions of butyraldehyde with *t*-butylamine and adamantylamine in dichloromethane under the same conditions were  $39.5 \text{ M}^{-1}$  and  $79.5 \text{ M}^{-1}$ , respectively, whereas the reactions with the remaining amines were irreversible. Thus, the smaller the steric effect of the group bound to the amine nitrogen, the greater was the relative concentration of the product imine (larger  $K_{ap}$ ).

With respect to the effects of branching on the aldehyde, the  $K_{ap}$  value for the reaction of isobutyraldehyde with *t*-butylamine (Eq. 3) in pentane at  $21^\circ \text{C}$  in the presence of magnesium sulfate was  $43.9 \text{ M}^{-1}$  after 90 h, much lower than that for the reaction of butyraldehyde with the same amine ( $1154.0 \text{ M}^{-1}$ ). Hence, the steric effect of a methyl group alpha on the carbonyl of the aldehyde also causes a reduction in the yield of the aldimine.

#### The stability of the N-alkylbutanimines

The aldimines **1a-h** were stable in the reaction medium, as well as after isolation. Since the literature states that the aliphatic aldimines are unstable<sup>9</sup>, a more detailed study of their stability was undertaken. In this study, two considerations which could favor the auto-condensation of these compounds were taken into account: 1) the aldehyde could be contaminated with the corresponding carboxylic acid; 2) the presence of a hydrogen alpha to the carbonyl group would be necessary for the occurrence of imine-enamine tautomerism.

#### The effect of the presence of acid in the medium

Since aldehydes are rather easily oxidized to the corresponding carboxylic acids, it is to be expected that the reaction medium may be contaminated by these acids<sup>10</sup>. Such contamination was verified by gas chromatographic analysis of the aldehydes employed in these studies even after purification by the methods normally described in the literature<sup>6</sup>.

In order to determine the effect of the presence of a carboxylic acid on the stability of the aliphatic aldimines, the reaction of butyraldehyde with primary amines was carried out in the presence of catalytic amounts of butanoic

acid. Fig. 1 shows the  $^1\text{H-NMR}$  spectra of aliquots of the reaction mixture of butyraldehyde with *sec*-butylamine before (Fig. 1A) and after (Fig. 1B) the addition of catalytic quantities of butanoic acid. The triplet at  $\delta 7.57$  is characteristic of the hydrogen of the aldimine group in **1c**. This signal was modified after the addition of butanoic acid (Fig. 1B). The same behavior was observed with the other aldimines studied, the aldimines being transformed into other products in the presence of butanoic acid<sup>11</sup>.

It has been shown that the addition of Lewis acids such as aluminum chloride or boron trifluoride to the reaction mixture caused the condensation of the N-alkylbutanimines, resulting in low yields of aldimines (Table 1). This fact explains observations recorded in the literature where aliphatic aldimines were obtained in lower yields when drying agents or activators of the aldehyde group with electrophilic properties were employed<sup>12</sup>.

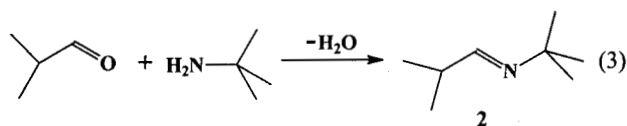
Potassium hydroxide has been cited as the most appropriate drying agent for the removal of water in the formation of aliphatic amines<sup>3c,13</sup>. Undoubtedly, this is because of the fact that it also removes any carboxylic acids which may be present. In the present study, however, the best yields were obtained when magnesium sulfate was used as the drying agent, as long as the medium was acid-free.

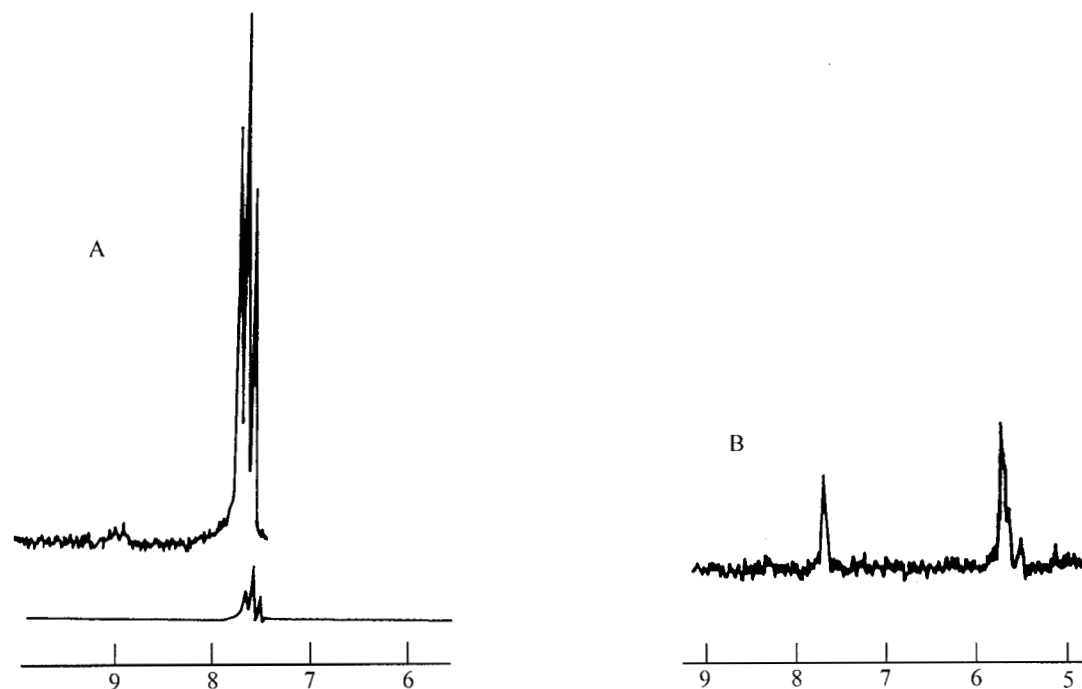
#### The necessity of an alpha hydrogen in the aldimine

If the reaction of the aliphatic aldimines to form secondary products involves a condensation reaction, the presence of a hydrogen alpha in the aldimine group is necessary. This fact was demonstrated by the formation and subsequent treatment of N-(1,1-dimethylethyl)-2,2-dichlorobutanamine (**3**) with butanoic acid. In this case, the aldimine remained stable under the reaction conditions, no alteration being observed in the  $^1\text{H-NMR}$  spectra of **3** after the addition of butanoic acid. The relative stability of the aromatic aldimines would, of course, be due primarily to the absence of alpha hydrogens in these molecules<sup>14</sup>. Similar results have been observed with hexafluoro-2-propylimine<sup>15</sup>. The stability of N-(1,1-dimethylethyl)-2-chlorobutanamine (**4**) and 1,2-dichloroethanimine (**5**) was also verified, these substances bearing an alpha hydrogen. After the addition of butanoic acid to the reaction medium,  $^1\text{H-NMR}$  spectra indicated the formation of additional products which were not identified.

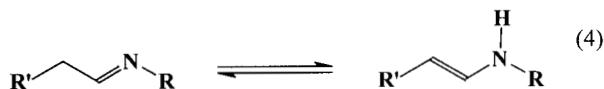
#### The occurrence of imine-enamine tautomerism

The necessity of an alpha hydrogen and the instability of the aliphatic aldimines are related to the possibility of forming an enamine in the reaction medium, as shown in Eq. 4<sup>16</sup>. According to the literature, the position of the imine-enamine equilibrium is strongly shifted in the direction of the imine<sup>17</sup>, and is significantly influenced by the structural characteristics of the imine<sup>18</sup>. Imine-enamine



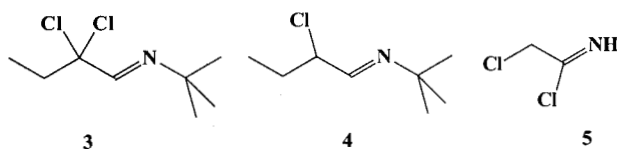


**Figure 1.** Partial  $^1\text{H-NMR}$  spectra of aliquots of the reaction mixture of butyraldehyde with *sec*-butylamine, at  $0\text{ }^\circ\text{C}$  in pentane in the presence of magnesium sulfate: (A) without butanoic acid, and (B) 4 h after the addition of catalytic quantities of butanoic acid.



tautomerism is favored in acidic media<sup>12a-c,19</sup>, in the presence of primary and secondary amines<sup>20</sup>, or in a solvent with high polarizability<sup>21</sup>.

Thus, it would be expected that the aldimine would be less stable in DMSO, a solvent of high polarizability, because of the presence of the enamine form. The  $^1\text{H-NMR}$  spectra of the products obtained from the reaction of butyraldehyde with *t*-butylamine in DMSO after 240 h exhibited no triplet near  $\delta$  7.60 characteristic of the hydrogen of the aldimine group. This fact suggests that the aldimine is unstable under these conditions. On the other hand, no signals between  $\delta$  4.5 and 5.5, characteristic of the enamine form, exist in the spectra, nor were they observed at various intervals during the period from 4 to 240 h. This fact may be due to the low concentration of the enamine in the reaction medium and its rapid conversion to by-products. Even so, it may be that the instability of the aldimine in DMSO is due to the formation and rapid transformation of the enamine form.



The reaction of butyraldehyde with primary amines was carried out in the absence of a solvent and drying agent. Thus, in the presence of water, the aldimines suffered slow transformation. Water, a solvent with a high dielectric constant, favors the imine-enamine tautomerism and, consequently, the transformation of the aldimines into other products.

## Conclusion

The conditions described in the literature for the synthesis of aliphatic aldimines do not eliminate the contamination by the carboxylic acid derivative of the aldehyde. The presence of this acid provokes the reaction of the aldimine. This fact may explain the importance of potassium hydroxide as a drying agent, which would also neutralize any acid present. Once the absence of acid is guaranteed, the presence of a drying agent in the reaction medium is important because it favors the shift of the equilibrium in the direction of the aldimine and also inhibits the reaction of the product to form by-products. The presence of voluminous alkyl groups inhibits the formation of the aldimine.

Based on the study of the stability of the *N*-alkylbutanimines, it may be concluded that aliphatic aldimines are stable under conditions which do not favor imine-enamine tautomerism. Thus, aldimines are stable in the absence of acid and in solvents with a low dielectric constant. These results may serve as a model for other aliphatic aldimines, permitting their synthesis and use as intermediates in the synthesis of other compounds. It is possible to predict

which conditions favor the formation of N-alkylalkanamines in relatively high yields and their use without the formation of by-products.

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