Univ. Sci. 25 (3): 385-407, 2020.
doi: 10.11144/Javeriana.SC25-3.sozp

ORIGINAL ARTICLE

# Synthesis of zeolites P and evaluation of their activity as new and reusable heterogeneous catalysts in a three-component ABB' Povarov model reaction

**Jefersson A. López[1], Robert A. Toro[1], Arnold R. Romero Bohórquez[2], Jose H. Quintana[3] & José A. Henao[1,*]**

**Edited by**
Juan Carlos Salcedo-Reyes
(salcedo.juan@javeriana.edu.co)

1. Grupo de Investigación en Química Estructural (GIQUE), Escuela de Química, Facultad de Ciencias, Universidad Industrial de Santander, Ciudadela Universitaria, A-A. 678, Bucaramanga, Santander, Colombia.

2. Grupo de Investigación en Compuestos Orgánicos de Interés Medicinal (CODEIM), Parque Tecnológico Guatiguará, Universidad Industrial de Santander, A.A. 678, Piedecuesta, Colombia.

3. Grupo de Investigación en Biocalorimetría, Departamento de Química, Universidad de Pamplona, Km 1 vía Bucaramanga, Pamplona, Colombia.

* jahenao@gmail.com

**Received:** 31-07-2019
**Accepted:** 23-07-2020
**Published on line:** 30-12-2020

**Citation:** López JA, Toro RA, Romero Bohórquez AR, Quintana JH, Henao JA. Synthesis of zeolites P and evaluation of their activity as new and reusable heterogeneous catalysts in a three-component ABB' Povarov model reaction, *Universitas Scientiarum,* 25 (3): 385-407, 2020. doi: 10.11144/Javeriana.SC25-3.sozp

**Funding:**
Vicerrectoría de Investigación y Extensión and Laboratorio de Difracción de Rayos-X, Universidad Industrial de Santander.

**Electronic supplementary material:**
N.A.

## Abstract

A Na-P zeolite was synthesized and subjected to ion exchange with $Ca^{2+}$, $Cu^{2+}$, $Al^{3+}$, and $In^{3+}$, and supported with $H^{+}/NH_4Cl$ ($NH_4$-P) by *in situ* reaction of EtOH and $NH_4Cl$. All the exchanged zeolites showed catalytic activity in the ABB' Povarov reaction. However, zeolite $NH_4$-P promoted a better yield. In all reactions two products were obtained, 2,6-dimethyl-4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinoline and 1-(1-(4-methylphenylamino)ethyl)pyrrolidin-2-one. Synthesis using zeolite P as catalyst proves to be a simple method with high yields, short reaction times and easy preparation. The catalyst can be recovered by filtration and reused up to three times in good yields.

**Keywords:** Tetrahydroquinolines; Povarov reaction; zeolite P; powder diffraction.

## Introduction

In organic synthesis, the use of solid acid catalysts such as clays and zeolites has attracted attention in recent years due to its environmental compatibility, possible reuse, high selectivity, non-corrosiveness, low cost, and simplicity of operation [1]. Reactions catalyzed with clays and zeolites are more economical and benign to the environment. Such compounds, both in their natural form and after ion exchange, act as Brönsted and Lewis acids. This allows them to function as efficient catalysts for various organic reactions. Recently, several immobilization methods have been developed in organic synthesis with the main objective of creating cleaner and cheaper processes than traditional ones [2]. The importance of catalysis in green chemistry, as a route to develop low-cost synthetic methodologies, has generated attention due to the potential for obtaining and isolating products in a short time and the possibility of reusing the catalyst.

Zeolites act as microporous and mesoporous molecular sieves due to their many empty spaces in their three-dimensional structure. This can greatly improve reaction rates by combining the spatial confinement of the reagents that decrease the reaction frequency factor and by providing catalytic active sites which decrease the activation energy [3, 4]. In addition to being able to influence the selectivity of the reaction. For example, Gomez *et al.* [5] have used different microporous and mesoporous materials as catalysts in the Diels-Alder and retro-Diels-Alder reaction between cyclopentadiene and *p*-benzoquinone. Olmos and colleagues carried out a catalytic study with faujasite-type zeolites and metal-exchanged USY in Aza-Diels-Alder reactions [6]. This work confirmed that before, during, and after the reaction, the zeolite undergoes changes in its structure, showing good performance and efficiency as a free and reusable heterogeneous catalyst for the synthesis of tetrahydroquinolines.

Zeolites have become materials of great interest due to their use as catalysts in different applications. Zeolites are commonly used is in the oil refinement industry [7], employed to filter linear molecules. Due to the particular characteristics of zeolites, they are currently being used as catalysts in the production of many chemical products.

The use of zeolites as catalysts in organic synthesis constitutes an emerging field, there is however literature covering the synthesis of some N-heterocycles on acid zeolites [8], zeolite-promoted synthesis of non-fused heterocycles [2], and the use of copper zeolites for the synthesis of heterocycles [8-10] among others. Several reports have been published that emphasize the many aspects of the synthesis of heterocycles on solid supports; Candeias and Afonso [2] underlined the importance of zeolites as heterogeneous catalysts in the synthesis of heterocyclic compounds. Zeolites are efficient catalysts in the synthesis of arylaminotetrazoles [11] and triazoles [12], and their catalytic activity has been demonstrated in the Michael addition, condensation, and esterification reactions [13, 14]. However, to the best of our knowledge, Zeolites have not been employed in ABB' Povarov reactions.

The Povarov reaction describes a domino Mannich/Friedel-Crafts reaction between an aromatic imine and an alkene that produces a tetrahydroquinoline. The quinolones and tetrahydroquinolines are structural fragments of importance in the area of natural bioactive products. The Povarov reaction between an aniline-derivative, an imine, and an electron-rich alkene is one of the most useful methods for the synthesis of tetrahydroquinoline derivatives. Povarov reactions are classified in different categories, including the one-pot ABC reaction, that uses aniline, aldehydes, and activated alkenes; and the ABB’ reaction, which uses anilines and two equivalents of a dienophile. Although this reaction was first described by Povarov in the 1960s, it remained relatively dormant until the discovery of its efficient catalysis by Lewis acids [15]. After this development, many groups have used the Povarov reaction as a more efficient method for the synthesis of tetrahydroquinoline derivatives.

The study and optimization of synthetic routes for tetrahydroquinolines has generated the need to increase the efficiency of these reactions. Numerous Lewis and Brönsted acid catalysts have been used. In general, $InCl_3$ gives better reaction yields [16]. However, this compound is a homogeneous catalyst that cannot be recovered, it is expensive, and is a contaminating reagent. For this reason, a great variety of agents have been studied to replace $InCl_3$ as a catalyst of this reaction.

In this work, we studied the synthesis of zeolites M-P (M = Na, In, Al, Ca, and Cu), supported with $H^+/NH_4Cl$ ($NH_4$-P), and their respective catalytic activity in a model ABB’ Povarov reaction. Their application in the Povarov reaction is only a modest contribution to demonstrate their catalytic behavior. The zeolites and the reaction’s adducts were characterized by IR spectroscopy, X-ray fluorescence and X-ray diffraction techniques.

## Material and Methods

### Measurements

The atomic absorption spectrophotometry (AA) analysis of the sodium aluminate used was carried out on a Perkin Elmer 372 spectrophotometer using an aluminum lamp. Quantification was performed with a calibration curve with a range of aluminum solutions: 6 mg/L 12 mg/L, 18 mg/L, 24 mg/L, and 30 mg/L. The determination of silicon was carried out on a Thermo Electron S Series spectrophotometer. A calibration curve was obtained with Si solutions with concentrations of 30 mg/L, 60 mg/L, 90 mg/L, 120 mg/L, and 150 mg/L. X-ray fluorescence (XRF) analyses were performed using a Bruker Model S8-TIGER 4kW wavelength dispersive X-ray fluorescence spectrometer.

The data were recorded using a Rhodium (Rh) tube and a scintillation detector (heavy elements) coupled to a flow detector (light elements). The data were analyzed using the Quant-Express method (Fundamental Parameters). Powder diffraction patterns were recorded on a Bruker D8-ADVANCE diffractometer operating at 40 kV and 40 mA, with a Bragg-Brentano geometry using CuK$\alpha$ radiation ($\lambda = 1.5406$ ). The graphical representation of the patterns corresponds to the values of intensities (y axis) as a function of the Bragg angle ($2\theta$) (x axis). The patterns were analyzed with DIFFRAC.EVA for the identification of crystalline phases using the Powder Diffraction File PDF-2 [17].

### Synthesis of zeolite Na-P

A total of 0.05 g of NaF (1.2 mmol) were mixed with 0.1 g (0.3 mmol) of ethylenediaminetetraacetic acid (EDTA). Sodium aluminate and sodium silicate were added dropwise with stirring at room temperature. The mixture was refluxed at 180 °C for 6 hours, allowed to cool, filtered, and dried at 90 °C. Four trials were performed with the following Si/Al ratios, 2.4; 2.8; 3.2, and 3.6. To study the importance of EDTA in the synthesis, the same procedure was carried out without adding EDTA. The solids obtained from the syntheses were characterized by X-ray fluorescence and X-ray diffraction.

### Ionic exchange and support with $H^+/NH_4Cl$

Solutions of $CuCl_2$, $CaCl_2$, $InCl_3$, and $AlCl_3$ (all four at 0.01 M) were prepared. The zeolites were activated by heating at 300 °C for three hours, were subjected to water extraction with a vacuum pump and allowed to cool to room temperature. A total of 10 mL of the metal solution (M-chloride, M= Cu, Ca, In, and Al) were added with constant stirring at 50 °C for 2 hours. The obtained solids were filtered, washed, and dried at 90 °C. The zeolites supported with $HCl/NH_4Cl$ ($NH_4$-P) were prepared in a beaker with 0.3 g of zeolite, 0.1 g (1.9 mmol) $NH_4Cl$, and 15 mL of ethanol. The mixture was heated at 50 °C to dryness.

### Catalytic activity over the ABB' Povarov reaction

A total of 0.3 g (2.8 mmol) of 4-methylaniline (1), dissolved in acetonitrile and 0.8 g (7.2 mmol) of N-vinyl-2-pyrrolidone (2), were mixed for 10 minutes. Then, 0.3 g of the zeolite M-P were added under constant stirring for 30 minutes and then under reflux at 60 °C for 6 hours. **Fig. 1** shows the reaction model and the products obtained in the synthesis: 2,6-dimethyl-4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinoline (3) and 1-(1-(4-methylphenylamino)ethyl)pyrrolidin-2-one (4). The reaction was

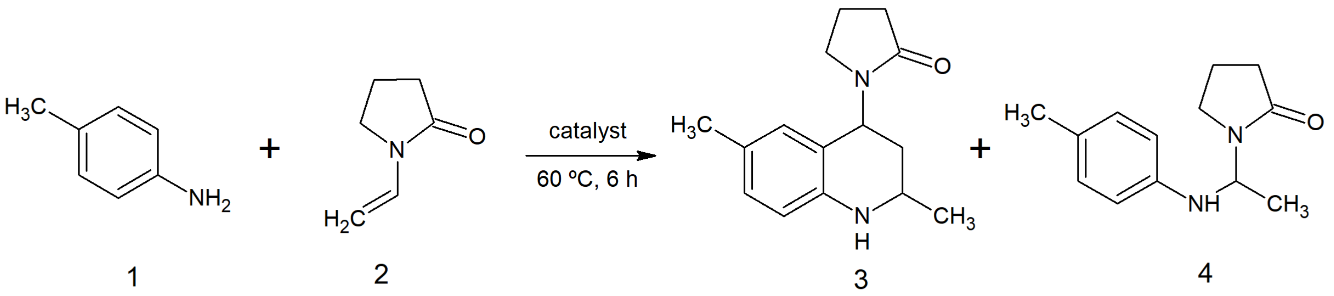

**Figure 1.** Scheme of the ABB' Povarov reaction.

monitored by thin layer chromatography on Silufol $UV_{254}$® plates, developed in a light chamber at 254 nm or iodine until completion of the reaction time. Adducts were extracted with ethyl acetate by collecting the organic phase over anhydrous $Na_2SO_4$, followed by column chromatography using silica as the stationary phase and a petroleum ether/ethyl acetate mixture as the mobile phase.

## Catalytic activity study

A series of experiments were conducted to study the variables influencing the catalysis of the ABB' Povarov reaction using the synthesized zeolites P. The solids exchanged and the zeolites used as support were arranged to verify their action as catalysts:

- (i) Test of $NH_4$-P catalytic activity with different alcohols: Tests were carried out using methanol, ethanol, and isopropanol on the supported zeolites.
- (ii) Reaction temperature test: The reaction was studied at different temperatures: 25 °C, 40 °C, 50 °C, and 60 °C.
- (iii) Stirring test: The reactions were compared under stirring at 300 rpm and without stirring.
- (iv) Catalyst equivalent test: The minimum amount of zeolite needed to obtain high reaction yields was studied.
- (v) Catalytic test in different solvents: The versatility of the catalyst in different solvents was studied in $H_2O$, MeCN, dioxane, MeOH, and EtOH.

### Reusing zeolite $NH_4$-P as a catalyst

The capacity of the solid to be reused was evaluated in 3 reaction cycles. Each cycle was repeated with three different zeolite treatments: (1) zeolite recovered by washing with ethyl acetate; (2) zeolite washed with ethyl acetate, 15 mL of ethanol, and heating to dryness; and (3) washing with ethyl acetate, 15 mL of ethanol and 0.1 g (1.9 mmol) of $NH_4Cl$, and heating to dryness. The different washes were performed to establish the treatment necessary for the solid to maintain its catalytic activity after being used in the reaction.

## Results and Discussion

### Synthesis of Zeolite Na-P

The synthesis of zeolite Na-P was carried out under reflux at 180 °C for 6 hours, with varying concentrations of the precursors in Si/Al ratios: 2.4, 2.8, 3.2 and 3.6. **Fig. 2** shows the powder diffraction patterns of the materials obtained from each process. The powder patterns of the synthesis products

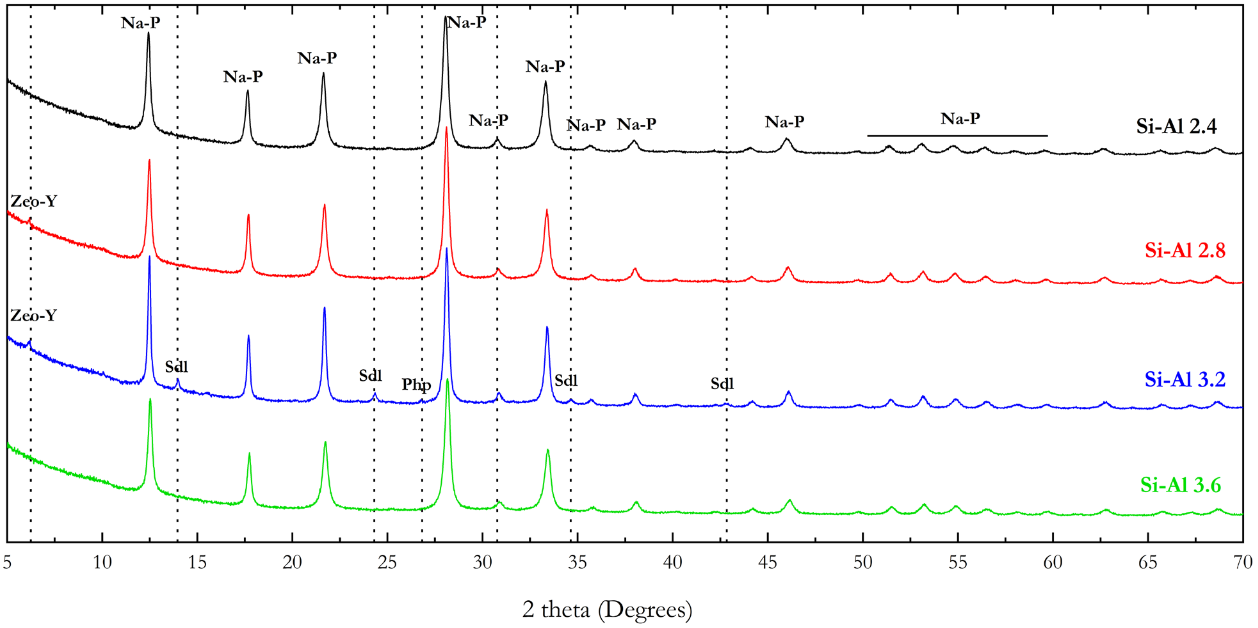

**Figure 2.** Powder diffraction patterns of zeolites Na-P synthesized with different Si/Al ratios: Si/Al = 2.4 (black), Si/Al = 2.8 (red), Si/Al = 3.2 (blue), and Si/Al = 3.6 (green). The powder patterns of the products of the synthesis with Si/Al = 2.4 and 3.6, match the Na-P zeolite phase. In the others patterns the crystalline phases Na-P zeolite, *sodalite* (Sdl), *phillipsite* (Php), and zeolite Y (Zeo-Y) were identified.

with Si/Al = 2.4 and 3.6 (Si-Al 2,4 and Si-Al 3,6 in Fig. 2) match the crystalline phase of zeolite Na-P (PDF-2: 00-039-0219). On the other hand, in the powder patterns of the products with Si/Al of 2.8 and 3.2 (Si-Al 2,8 and Al-Si 3,4 in Fig. 2), the crystalline phase zeolite Na-P, *sodalite* (Sdl, PDF-2: 01-071-5356), *phillipsite* (Php, PDF-2: 04-011-2575) and zeolite Y (Zeo-Y, PDF-2: 01-073-4042) were identified. The peak positions ($2\theta$) and the values of relative intensity (I/Io) of each phase identified in the diffraction patterns of all the M-P zeolites presented in this work are shown in the supplementary material.

To assess the influence of EDTA as a template, the reaction was carried out under the same conditions without EDTA. Under these conditions a pattern composed by several crystalline phases was obtained (**Fig. 3**): Na-P (PDF-2: 00-039-0219, 01-071-0962), *sodalite* (Sdl, PDF-2: 01-071-5356 and 00-037-0476), zeolite X (Zeo-X, PDF-2: 00-038-0237), zeolite A (Zeo-A, PDF-2: 01-071-0370), *garronite* (Grn, PDF-2: 04-011-7946), and *phillipsite* (Php, PDF-2: 04-011-2575). This result highlights the key role of EDTA as the main phase for obtaining zeolite Na-P.

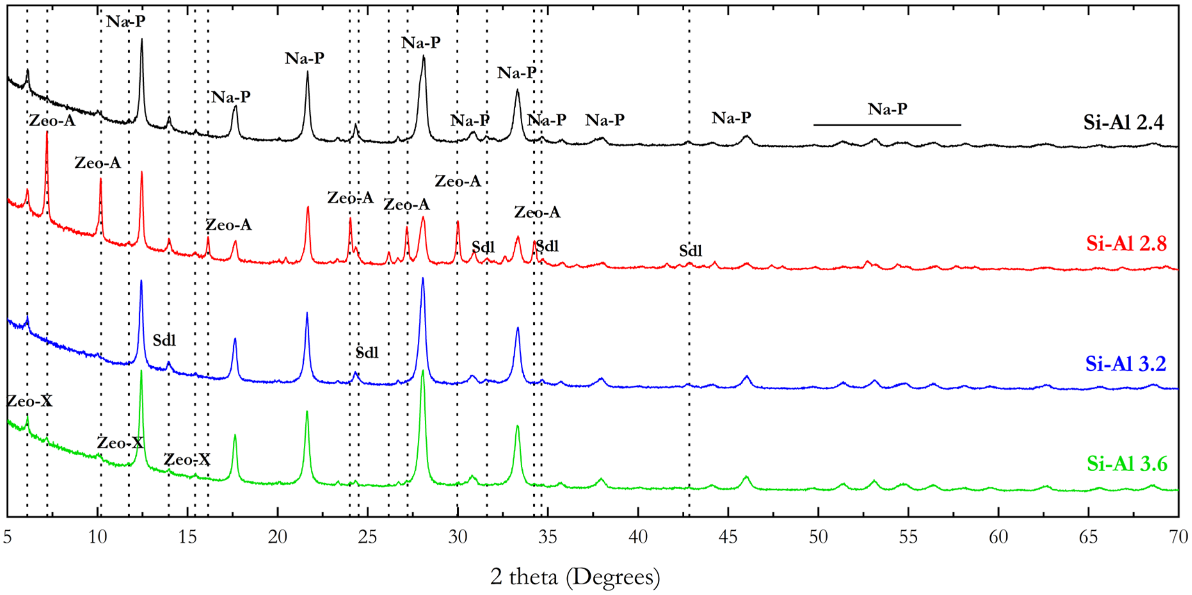

**Figure 3.** Powder diffraction patterns of zeolite Na-P synthesized without EDTA: Si/Al = 2.4 (black), Si/Al = 2.8 (red), Si/Al = 3.2 (blue), and Si/Al = 3.6 (green). The powder patterns show several crystalline phases: Na-P zeolite, *sodalite* (Sdl), zeolite X (Zeo-X), zeolite A (Zeo-A), *garronite* (Grn), and *phillipsite* (Php). These results indicate that EDTA is important for obtaining zeolite Na-P as the main phase.

## Ionic exchange

The zeolites subjected to ion exchange were analyzed by XRF to determine the percentage of metals exchanged in each solid. Analyses were performed using the Quant-Express method (Fundamental Parameters). The results of the elemental analyses are presented in the **Table 1**. It is worth mentioning that the percentage exchanged in the Al-P material was not determined because some of the aluminum may not be exchanged.

The diffraction patterns for each of the solids obtained from the exchange processes are shown in **Fig. 4**. The powder pattern of the material obtained by calcium exchange (CaP in Fig. 4) revealed the presence of Ca-P zeolite (PDF-2: 00-039-1374) and of *sodalite* (Sdl, PDF-2: 00-037-0476). The pattern of the solid obtained from the copper exchanged (Fig. 4) crystallized with the structure of the zeolite type Mg-*gismondine* (PDF-2: 00-044-0052). Three peaks of lower intensity at 14.024°, 24.401°, and 35.628° ($2\theta$) corresponded to a *sodalite* phase (Sdl, PDF-2: 01-074-3649).

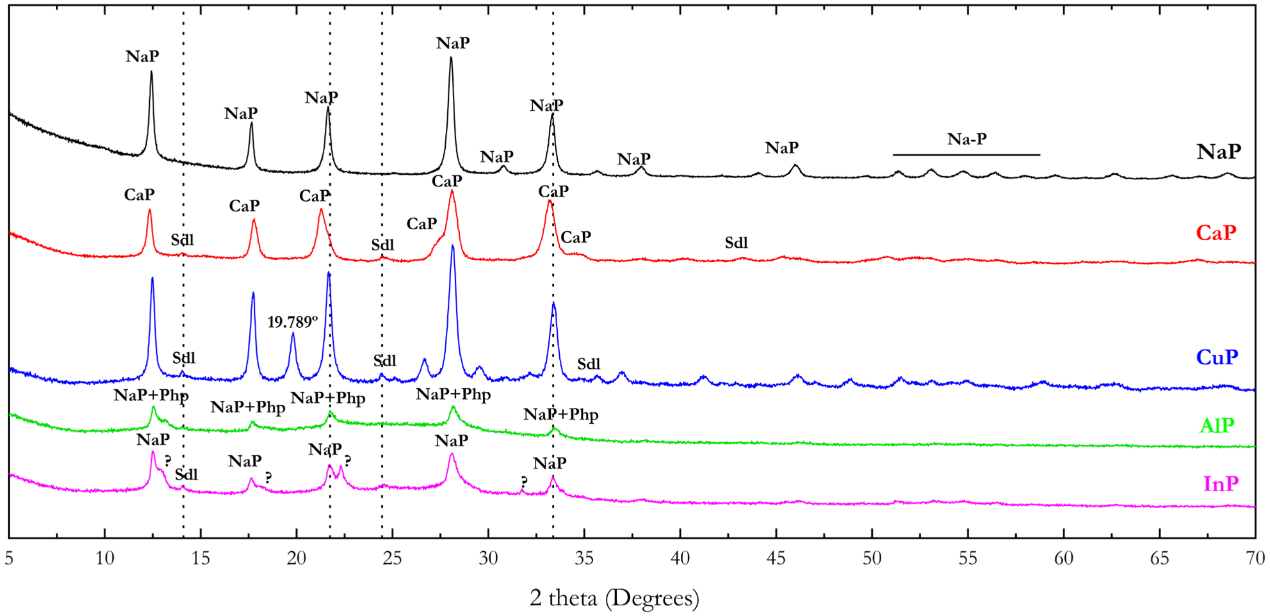

**Figure 4.** Powder diffraction patterns for the zeolites M-P obtained from the exchange processes: zeolite Na-P (black), zeolite Ca-P (red), zeolite Cu-P (blue), zeolite Al-P (green), and zeolite In-P (pink). The powder pattern of the material obtained by calcium exchange coincides with a Ca-P and *sodalite* (Sdl); the solid obtained from the Cu exchanged shows an unidentified phase and *sodalite*; the zeolite exchanged with Al and In match Na-P. In the XRD pattern of Al-P the *phillipsite* (Php) phase was identified.

**Table 1.** Elemental analysis of exchanged zeolites M-P (M= Na, Ca, Cu, Al, and In). The percentage ratio was determined by X-ray fluorescence analysis.

| | Na-P | Ca-P | Cu-P | Al-P | In-P |
|---|---|---|---|---|---|
| **Element** | **Proportion** | | | | |
| Si | 22.42 % | 22.86 % | 22.80 % | 27.16 % | 26.75 % |
| Al | 16.61 % | 16.69 % | 17.02 % | 20.06 % | 19.15 % |
| In | --- | --- | --- | --- | 0.27 % |
| Cu | --- | --- | 8.09 % | --- | --- |
| Ca | --- | 11.99 % | 0.09 % | 0.05 % | 0.07 % |
| Na | 14.95 % | 1.61 % | 6.31 % | 2.75 % | 4.42 % |

For the zeolites exchanged with Al and In (AlP and InP in Fig. 4), no matches were found in the database. The powder patterns showed a decrease in crystallinity and revealed the presence of several crystalline phases, Furthermore, some unidentified peaks were likely to correspond to the exchanged zeolite. The powder pattern of Al-P showed peaks of zeolite Na-P (PDF-2: 01-071-0962), *phillipsite* (Php, PDF-2: 01-072-4634), and sodium aluminum silicate hydrate (*, PDF-2: 00-039-0217). On the other hand, Na-P (PDF-2: 01-071-0962) and *sodalite* (Sdl, PDF-2: 00-037-0476) phases were identified in the In-P pattern.

## Zeolites supported with $H^{+}/NH_4Cl$, $NH_4$-P

The incorporation of $H^{+}$ on the surface of the zeolite was carried out in situ as described by Lyi [18]. The reaction occurred between $NH_4Cl$ and ethanol according to the chemical reaction shown in **Eq. 1** Since the reaction takes place upon heating without alcohol boiling, $H^{+}$, NaCl, and $NH_4Cl$ are supported on the surface of the zeolite.

$$Na^{+}+NH_4Cl+CH_3CH_2OH\rightarrow CaCl+H^{+}+CH_3CH_2O^{-}NH_4^{+} \tag{1}$$

Different processes occur on the surface of the zeolite. First, $H^+$ ions and $NH_4Cl$ are supported on the surface. Then, exchange of ammonia by sodium of the zeolite occurs promoting the formation of NaCl. Third, there is absorption of $NH_4Cl$ in the pores of the zeolite as well as other processes as described by Lyi in his study. The powder pattern of the supported $NH_4$-P zeolite (**Fig. 5**) shows the presence of Halite (Hl, PDF-2: 00-070-2509) and $NH_4Cl$ (PDF-2: 00-001-0674). The presence of these salts reflects the reaction between the residual $Cl^-$ and $Na^+$ of the zeolite. For sodium to react with the remaining chlorine, it must be removed from the structure through exchange with ammonia. The peaks in the powder pattern showed a shift to higher values of $2\theta$ and a variation in the intensities, indicating modification of the structure.

Removal by washing of the ammonium salt supported on the surface of the solid was not performed since it is an agent involved in the catalysis of the organic reaction. This mutual involvement is described by Brosius, who used ammonium salts supported on zeolites as catalysts in the synthesis of tetrahydroquinolines [19].

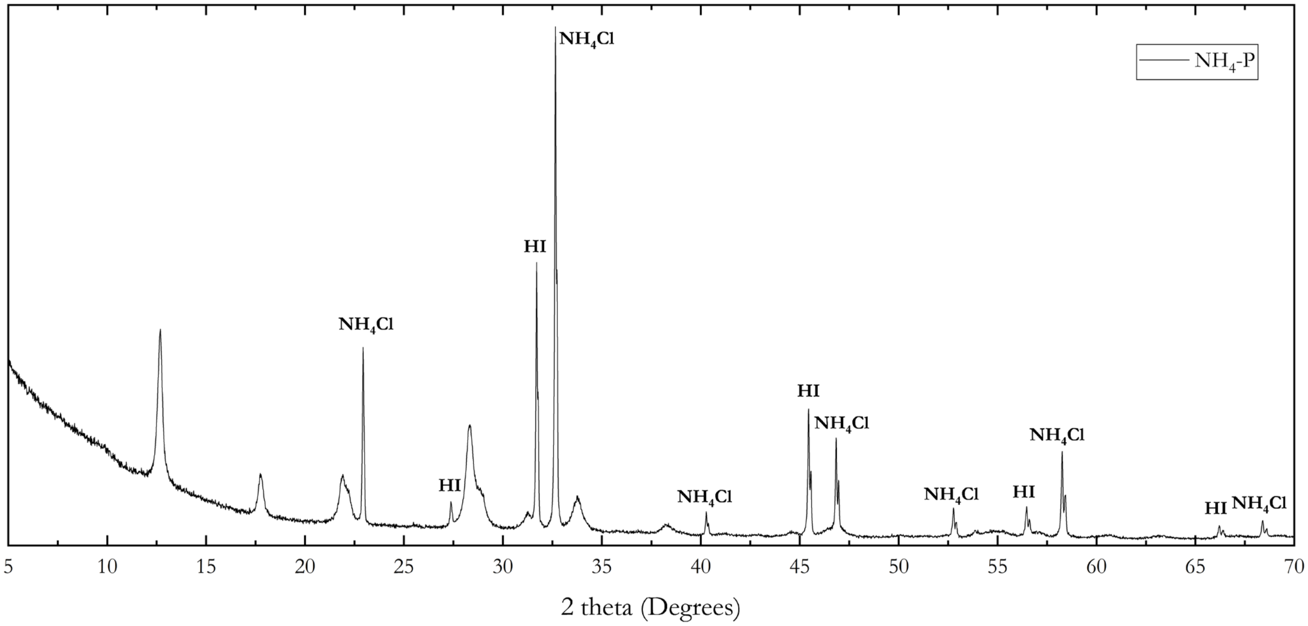

**Figure 5**. Powder diffraction patterns of $NH_4$-P zeolite. The powder pattern of $NH_4$-P shows the presence of *halite* (Hl, NaCl) and $NH_4Cl$, indicating the reaction between residual $Cl^-$ and $Na^+$ from the zeolite.

## Catalysis of the ABB' Povarov reaction by zeolite P

Zeolite catalytic activity has been directly associated with reaction yield. For this reason, different reactions with $InCl_3$ as a catalyst were conducted the results are summarized in **Table 2**. According to the literature, when $InCl_3$ is employed as a catalyst of the ABB' Povarov reaction, the adduct 3 is reported as the only product of the reaction [17, 20]. In our experiment, reactions took place at room temperature and the products 3 and 4 were obtained in a 1:2 ratio. These results (products 3 and 4 obtained) have not been previously reported in the literature for these reaction conditions.

Zeolites Na-P and Ca-P did not promote the ABB' Povarov reaction (**Table 3**), which is an expected fact since these metals do not generate acidic sites in the zeolite structure. The other M-P zeolites (M = In, Al, and Cu), promoted the synthesis of products with yields lower than those obtained with $InCl_3$. However, they promoted the formation of the two products, showing that these solids are not selective in the promotion of a single product. The zeolite supported with $H^+/NH_4Cl$ ($NH_4$-P) showed higher yield values compared to the exchanged zeolites M-P under the same reaction conditions. These were selected for the study of the catalytic activity in the ABB' Povarov reaction. Zeolites M-P and $NH_4$-P (supported, $NH_4$-P) had the ability to promote the synthesis of products 3 and 4, simultaneously (Table 3). In all the reactions carried out to study the catalytic activity of zeolite $NH_4$-P, product 4 was obtained in higher yield compared to product 3. Only product 4 obtained through the Povarov reaction is reported in the literature and this result is explained by the inductive effects of catalysts [20], which can be the same as zeolitic catalysts, given the electrostatic interactions in its surface.

## Spectroscopic Characterization of the adducts of the ABB' Povarov reaction

ABB' Povarov reaction products were characterized using FT-IR and NMR spectroscopy. In all cases, product 3 was an amber oily liquid. Inspection of the FT-IR spectrum signals revealed a simple band at 3 392 $cm^{-1}$ in the absorption region of the secondary amines corresponding to N-H bond stretching. A strong and intense band at 1 635 $cm^{-1}$ was observed; it marked the carbonyl of the pyrrolidinyl ring due to the strain vibration of this group. The signals between 2 900 and 2 950 $cm^{-1}$ were caused by vibrations of the C-H, $-CH_2$, and $-CH_3$ groups of the aromatic ring. Finally, the band at 1 506 $cm^{-1}$ corresponded to the bending vibration of the N-H bond. Product 4 was obtained as a brown-white solid. The FT-IR of this compound showed the N-H stretch bands at 3 331 $cm^{-1}$ and the carbonyl of the pyrrolidinyl

**Table 2.** Reaction yields using InCl3 as catalyst in the ABB' Povarov reaction. Note that product 4 is always obtained in greater proportion.

| Catalyst | Time | Temperature | Product 3 | Product 4 |
|---|---|---|---|---|
| ---- | 12 h | 50 °C | --- | --- |
| $InCl_3$ | 3 h | Room temperature | 29.2 % | 62.0 % |
| $InCl_3$ | 6 h | 50 °C | 4.4 % | 92.9 % |

ring at 1 661 $cm^{-1}$. The bands of aromatic C-H and $-CH_2$ and $-CH_3$ groups appeared between 2 850-2 970 $cm^{-1}$ and the bending of the N-H bond at 1 529 $cm^{-1}$.

$^1$H-NMR and $^{13}$C-NMR spectra of product 3 confirms the structure of the compound: $^1$H-NMR (400 MHz, $CDCl_3$) $\delta$ (ppm): 6.70 (1H, d, J = 7.5 Hz), 6.52 (1H, d, J = 7.5 Hz), 6.37 (1H, t, J = 7.5 Hz), 5.31 (1H, dd, J = 12.0, 6.0 Hz), 4.13 (1H, br s), 3.50-3.40 (1H, m), 3.15-3.00 (1H, m), 2.95-2.85 (1H, m), 2.30-2.20 (2H, m), 1.94 (3H, s), 1.90-1.80 (2H, m), 1.75-1.66 (1H, m), 1.65-1.50 (1H, m), and 1.13 (3H, d, J = 6.3 Hz). $^{13}$C-NMR (100 MHz, $CDCl_3$) $\delta$ (ppm): 176.3, 146.4, 130.4, 125.2, 123.3, 119.9, 117.8, 49.7, 48.6, 43.8, 35.8, 32.5, 23.4, 19.8, and 18.5. The spectra of product 4 are similar to those reported by Jiang [20], showing the chemical nature of the compound. $^1$H-NMR (100 MHz, $CDCl_3$) $\delta$ (ppm): 1.45 (d, J = 6.5 Hz, 3H), 1.86-1.98 (m, 2H), 2.10 (s, 3H) , 2.42 (t, J = 7.4 Hz, 2H), 3.16-3.22 (m, 1H), 3.32-3.45 (m, 1H), 3.65 (br s, 1H), 5.70 (q, J = 6.5 Hz, 1H), 6.42 (d, J = 7.8 Hz, 2H), 7.12 (d, J = 7.8 Hz, 2H) . $^{13}$C-NMR (100 MHz, DMSO-d6) $\delta$ (ppm): 175.1, 142.5, 130.4, 126.9, 113.1, 57.3, 40.7, 31.9, 21.1, 19.8, and 18.2.

## Catalytic activity study of $NH_4$-P zeolites

Once the catalytic solid was chosen, tests were performed to verify the conditions that regulate the supported zeolite as a catalyst. These tests were not done to optimize the reaction but were carried out to study the variables that condition the catalytic activity of the zeolite.

**Table 3**. Yields using exchanged and supported zeolites as catalysts in the ABB' Povarov reaction. The M-P zeolites (M = In, Al, and Cu) promote the synthesis of the two products in the reaction with yields lower than those obtained with $InCl_3$. On the other hand, the zeolite supported with $H^+/NH_4Cl$ ($NH_4$-P) showed higher yield values under the same reaction conditions.

| Zeolite | Product 3 | Product 4 |
|---|---|---|
| Na-P | --- | --- |
| Ca-P | --- | --- |
| Al-P | 15.7 % | 28.9 % |
| In-P | 21.3 % | 30.2 % |
| Cu-P | 10.1 % | 26.7 % |
| $NH_4$-P Cycle 1 | 34.3 % | 48.4 % |
| $NH_4$-P Cycle 2 | 24.6 % | 37.5 % |

Test of $NH_4$-P catalytic activity with different alcohols: The solvent is of importance in the supported zeolite due to its role in the production of $H^+$. The size of the alcohol can promote changes in the catalytic activity of the solid, increasing the yields of the reaction [19]; these differences are listed in **Table 4**. The use of ethanol instead of methanol led to an increase in the yields of both products, with a tendency to favor the formation of product 3. In the other catalytic activity tests, ethanol was selected as the precursor of $H^+$ *in situ* in the zeolite due to its lower cost and shorter time of reaction and of heating.

Stirring test: Stirring is an important factor within the kinetics of the reaction. Without stirring, no product was obtained after six hours of reaction, however after 98 hours product 4 was formed. The reaction occurred via heterogeneous catalysis and the stirring allowed a greater interaction between the surface of the solid and the precursors. The reactions were carried out under constant stirring at 300 rpm.

**Table 4**. Catalytic activity with different alcohols for the *in situ* reaction of $H^+$ on zeolite Na-P. Ethanol as a reaction medium increases the yield of the reaction favoring the formation of product 3.

| Zeolite | Product 3 | Product 3 |
|---|---|---|
| $NH_4$-P (MeOH) | 9.5 % | 39.7 % |
| $NH_4$-P (EtOH) | 31.6 % | 58.6 % |
| $NH_4$-P (Isopropanol) | 31.6 % | 60.7 % |

Reaction temperature test: The catalytic activity of the solid improved as temperature increased (**Table 5**). At 60 °C and 70 °C (and above) the reaction yields were similar. This behavior indicates that at higher temperatures the catalytic activity will not increase significantly, possibly because the catalyst has achieved the maximum combined yield of 96 % for both products.

Catalyst equivalent test: The catalytic activity was directly proportional to the amount of zeolite used in the reaction. As shown in **Table 6**, the minimum amount required for maximum yield was 0.3 g of zeolite. The yield of the reaction decreased with smaller amounts of the zeolite, while at higher yields the reaction rate was similar.

Catalytic test in different solvents: The influence of the nature of the solvent on the model reaction promoted by the zeolite was studied. The best reaction yield was obtained with acetonitrile as the solvent (product 3: 34.9 % and product 4: 61.4 %). However, good reaction yields were also observed with the use of water (product 3: 19.4 % and product 4: 51.2 %), methanol (product 3: 23.8 % and product 4: 56.3 %), and ethanol (product 3: 22.6 % and product 4: 55.3 %). Although the use of water as the reaction medium has been reported, we observed that the reaction can also be carried out in methanol and ethanol, which are environmentally benign solvents.

**Table 5**. Reaction temperature test using $NH_4$-P (EtOH) as catalyst. A rise in temperature increases the yield of the reaction, therefore improving the catalytic activity of zeolite $NH_4$-P.

| Zeolite | Temperature | Product 3 | Product 4 |
|---|---|---|---|
| $NH_4$-P (EtOH) | Room temp. | --- | --- |
| $NH_4$-P (EtOH) | 40°C | 8.4 % | 23.6 % |
| $NH_4$-P (EtOH) | 50°C | 31.6 % | 55.6 % |
| $NH_4$-P (EtOH) | 60°C | 34.9 % | 61.4 % |
| $NH_4$-P (EtOH) | 70°C | 35.4 % | 61.1 % |

## Reusing zeolite $NH_4$-P as a catalyst

Zeolite $NH_4$-P was recovered from the reaction medium by simple filtration and treated with different washing cycles, as described in experimental section 2.6. We observed that once the zeolite dries, it can be reused in two more cycles of the same reaction for 6 hours at 60 °C. The solid washed with ethyl acetate (treatment 1, cycle 2) showed low reaction yields, about half of that obtained in cycle 1, and continued to decrease until the third cycle (**Table 7**). This behavior indicates that this method is inefficient for the solid to maintain its catalytic property. The second treatment showed good results, with yields similar to the initial ones for cycle 2 and with good yields for cycle 3. These results may be attributed to the presence of adsorbed $NH_4Cl$ on the surface of the solid that can react with the ethanol added generating more protons, therefore promoting a good catalytic activity when the catalyst is reused. The best results were obtained for treatment 3. Treatment 2 and treatment 3 regenerated the catalytic property of the solid, demonstrating that the supported zeolite P is an efficient and reusable catalyst for the synthesis.

In the reaction, the zeolite lost, on average, 30 % of its mass. Despite this loss, the catalyst/precursor ratio was maintained by performing the following reaction cycles. The zeolite lost crystallinity due to the acid reactions that are generated on the surface of the solid during its catalytic participation

**Table 6**. Catalyst equivalent test using $NH_4$-P (EtOH) as catalyst. The minimum amount required for maximum yield is 0.3 g and the yield of the reaction decreases with smaller amounts of the zeolite.

| $NH_4$-P | Product 3 | Product 4 |
|---|---|---|
| 0.10 g | 7.4 | 38.2 % |
| 0.15 g | 16.3 % | 43.7 % |
| 0.30 g | 34.9 % | 61.4 % |
| 0.60 g | 31.8 % | 62.1 % |

in the synthesis. However, the material maintained its catalytic activity after amorphization. This result is relevant since it is possible to synthesize amorphous solids of lower costs which

**Table 7**. Zeolite $NH_4$-P with different treatments and its reuse in several reaction cycles. Treatment 1: solid washed with ethyl acetate. Treatment 2: zeolite washed with ethyl acetate, ethanol, and heat to dryness. Treatment 3: washing with ethyl acetate, ethanol and $NH_4Cl$ solution, and heat to dryness. The solid with treatment 1 shows low reaction yields and continues to decrease until the third cycle. The second treatment shows good results, and treatment 3 shows the best results.

| $NH_4$-P | $NH_4$-P | Product 3 | Product 4 |
|---|---|---|---|
| Treatment (1) Cycle2 | 0.22 g | 24.6 % | 37.5 % |
| Treatment (1) Cycle3 | 0.14 g | 17.2 % | 24.4 % |
| Treatment (2) Cycle2 | 0.20 g | 31.4 % | 55.26 % |
| Treatment (1) Cycle3 | 0.15 g | 26.7 % | 43.6 % |
| Treatment (3) Cycle2 | 0.21 g | 32.5 % | 58.3 % |
| Treatment (3) Cycle3 | 0.14 g | 33.1 % | 56.2 % |

can be used as catalysts. Thus, zeolite P functionalized as catalytic support can improve the yield of products via ABB' Povarov reaction and maintain its catalytic activity for at least three cycles of reaction regardless of the loss of crystallinity during the reactions.

## Conclusion

The zeolites P prepared were shown to be effective catalysts for the synthesis by a model ABB' Povarov reaction, promoting the formation of two products that have been previously obtained separately, depending on the reaction conditions. Of the zeolites synthesized, those supported with $H^+/NH_4Cl$ led to the higher yields and can be reused for up to three reaction cycles. Although the $NH_4Cl$-P zeolite exhibited amorphization and mass loss during its application as a catalyst, it maintained its catalytic activity when treated with EtOH or EtOH/$NH_4Cl$. This method proves to be simple and efficient, with short reaction times and high yields. The $NH_4$-P zeolite catalyst can be recovered by conventional filtration and reused up to three times. Currently, more experiments are underway with the goal to explain the reactivity and selectivity of this zeolite as a catalyst.

## Acknowledgements

The authors acknowledge the support of Vicerrectoría de Investigación y Extensión and Laboratorio de Difracción de Rayos-X, Universidad Industrial de Santander, Bucaramanga, Colombia for recording X-ray fluorescence and X-ray diffraction data.

## Conflict of interests

The authors declare having no conflict of interests.

## References

[1] Krishna VV, Narender N. Synthesis of N-heterocyclic compounds over zeolite molecular sieve catalysts: an approach towards green chemistry, *Catalysis Science and Technology*, 2: 471-487, 2012.

doi: 10.1039/c2cy00162d

[2] Candeias NR, Afonso CAM. Preparation of non-fused heterocycles in zeolites and mesoporous materials, *Journal of Molecular Catalysis A: Chemical*, 242(1): 195-217, 2005.

doi: 10.1016/j.molcata.2005.07.042

[3] Corma A. State of the Art and Future Challenges of Zeolites as Catalysts, *Journal of Catalysis*, 216: 298-312, 2003.

doi: 10.1016/S0021-9517(02)00132-X

[4] Corma A, Garcia H. Lewis acids: from conventional homogeneous to green homogeneous and heterogeneous catalysis, *Chemical Review*, 103(11): 4307-4365, 2003.

doi: 10.1021/cr030680z

[5] Gomez MV, Cantin A, Corma A, de la Hoz A. Use of different microporous and mesoporous materials as catalyst in the Diels-Alder and retro-Diels-Alder reaction between cyclopentadiene and p-benzoquinone, *Journal of Molecular Catalysis A: Chemical*, 240(1): 16-21, 2005.

doi: 10.1016/j.molcata.2005.06.030

[6] Olmos A, Rigolet S, Louis B, Pale P. Design of Scandium-Doped USY Zeolite: An Efficient and Green Catalyst for Aza-Diels-Alder Reaction, *The Journal of Physical Chemistry C*, 116:13661-13670, 2012.

doi: 10.1021/jp303169h

[7] Joshi SS, A. Bhatnagar, V.V. Ranade. Industrial Catalytic Processes for Fine and Specialty Chemicals. Chapter 8: Catalysis for Fine and Specialty Chemicals. 2016 Elsevier Inc. 317-392.

[8] Chassaing S, Bénéteau V, Pale P. Green catalysts based on zeolites for heterocycle synthesis, *Current Opinion in Green and Sustainable Chemistry*, 10: 35-39, 2018.

doi: 10.1016/j.cogsc.2018.02.007

[9] Chassaing S, Bénéteau V, Louis B, Pale P. Zeolites as Green Catalysts for Organic Synthesis: the Cases of H-, Cu- & Sc-Zeolites, *Current Opinion in Green and Sustainable Chemistry*, 21: 779-793, 2017.

doi: 10.2174/1385272820666160525130204

[10] Keller M, Sido A, Pale P, Sommer J. Copper(I) Zeolites as Heterogeneous and Ligand-Free Catalysts: [3+2] Cycloaddition of Azomethine Imines, *Chemistry a European Journal*, 15: 2810-2817, 2009.

doi: 10.1002/chem.200802191

[11] Nasrollahzadeh M, Habibi D, Shahkarami Z, Bayat Y. A general synthetic method for the formation of arylaminotetrazoles using natural natrolite zeolite as a new and reusable heterogeneous catalyst, *Tetrahedron*, 65: 10715-10719, 2009.

doi: 10.1016/j.tet.2009.10.029

[12] Bénéteau V, Olmos A, Boningari T, Sommer J, Pale P. Zeo-click synthesis: CuI-zeolite-catalyzed one-pot two-step synthesis of triazoles from halides and related compounds, *Tetrahedron Letters*, 51: 3673-3677, 2010.

doi: 10.1016/j.tetlet.2010.05.036

[13] Bakavoli M, Sabzevari O, Rahimizadeh M. H-Y-zeolites induced heterocyclization: Highly efficient synthesis of substituted-quinazolin-4(3H)ones under microwave irradiation, *Chinese Chemical Letters*, 18: 533-535, 2007.

doi: 10.1016/j.cclet.2007.03.029

[14] Nagendrappa G. Organic synthesis using clay and clay-supported catalysts, *Applied Clay Science*, 53: 106-138, 2011.

doi: 10.1016/j.clay.2010.09.016

[15] Forero JSB, Junior JJ, da Silva FM. The Povarov Reaction as a Versatile Strategy for the Preparation of 1,2,3,4-Tetrahydroquinoline Derivatives: An Overview, *Current Organic Synthesis*, 13: 157-175, 2016.

doi: 10.2174/1570179412666150706183906

[16] Varma PP, Srinivasa A, Mahadevan KM. Efficient $InCl_3$/ $H_2O$-catalyzed one-pot stereoselective synthesis of cis-2-methyl4-amido-1,2,3,4-tetrahydroquinoline derivatives, *Synthetic Communications*, 41: 2186-2194, 2011.

doi: 10.1080/00397911003650453

[17] Gates-Rector S, Blanton T. The Powder Diffraction File: a quality materials characterization database, *Powder Diffraction*, 34(4):352-360, 2020.

doi: 10.1017/S0885715619000812

[18] Lyi N, Yamada H. Efficient decarbonation of carbonate-type layered double hydroxide (CO32−LDH) by ammonium salts in alcohol medium, *Applied Clay Science*, 65-66: 121-127, 2012.

doi: 10.1016/j.clay.2012.05.001

[19] Brosius RG. Vapour-phase synthesis of 2-methyl- and 4-methylquinoline over BEA zeolite, *Journal of Catalysis*, 239(2):362-368, 2006.

doi: 10.1016/j.jcat.2006.02.015

[20] Jiang R, Xu HY, Xu XP, Chu XQ, Ji SJ. Direct alkylation of indoles and amines by tert-enamides: facile access to pharmaceutically active 2-oxo-1-pyrrolidine analogues, Organic and Biomolecular Chemistry, 9:5659-5669, 2011.

doi: 10.1039/c1ob05546a

## Síntesis de zeolitas P y evaluación de su actividad como catalizadores heterogéneos nuevos y reutilizables en una reacción modelo de Povarov de tres componentes ABB'

**Resumen:** Se sintetizó una zeolita Na-P y se sometió a intercambio iónico con $Ca^{2+}$, $Cu^{2+}$, $Al^{3+}$ y $In^{3+}$ y soportada con $H^{+}/NH_4Cl$ ($NH_4$-P) por reacción *in situ* de EtOH y $NH_4Cl$. Todas las zeolitas intercambiadas mostraron actividad catalítica en la reacción de Povarov ABB'. Sin embargo, la zeolita $NH_4$-P promovió un mejor rendimiento. En todas las reacciones se obtuvieron dos productos: 2,6-dimetil-4-(2-oxopirrolidina-1-yl)-1,2,3,4-tetrahidroquinolina y 1-(1-(4-metilfenilamino)etil)pirrolidina-2-uno. La síntesis usando zeolita P como catalizador prueba ser un método simple con altos rendimientos, tiempos de reacción cortos y fácil preparación. El catalizador se puede recuperar por filtración y reutilizar tres veces con buenos rendimientos.

**Palabras clave:** Tetrahidroquinolinas; reacción de Povarov; zeolita P; difracción en polvo.

# Síntese de zeólitos P e avaliação de sua atividade como catalizadores heterogêneos novos e reutilizáveis em uma reação modelo de Povarov de três componentes ABB'

**Resumo:** Sintetizou-se um zeólito Na-P e se submeteu a intercambio iônico com $Ca^{2+}$, $Cu^{2+}$, $Al^{3+}$ e $In^{3+}$ e suportada com $H^{+}/NH_4Cl$ ($NH_4$-P) por reação *in situ* de EtOH e $NH_4Cl$. Todas os zólitos trocados mostraram atividade catalítica na reação de Povarov ABB'. Entretanto, o zeólito $NH_4$-P promoveu um melhor rendimento. Em todas as reações se obtiveram dois produtos: 2,6-dimetil-4-(2-oxopirrolidina-1-il)-1,2,3,4-tetrahidroquinolina e 1-(1-(4-metilfenilamina)etil)pirrolidin-2-ona. A síntese usando zeólito P como catalizador provou ser um método simples com altos rendimentos, tempos de reação curtos e fácil preparação. O catalizador pode ser recuperado por filtração e reutilizado três vezes com bons rendimentos.

**Palavras-chave:** Tetrahidroquinolinas; reação de Povarov; zeólito P; difração em pó.

**Jeferson Andres López Jaimes**

Chemist and PhD. Student in materials engineering at the Universidad Industrial de Santander (UIS), Colombia, with experience in the characterization of crystalline materials by X-ray diffraction techniques, spectroscopic and thermal methods, chromatographic analysis and materials science with mention in biomaterials.

ORCID: 0000-0002-7482-3961

**Robert Antonio Toro Hernández**

Chemist and PhD. in Applied Chemistry in the mention of Materials Studies graduated from the Universidad de Los Andes in Mérida, Venezuela, and Post-doctorate at the Grupo de Investigación en Química Estructural (GIQUE) from the Universidad Industrial de Santander (UIS), with experience in the characterization of crystalline materials by X-ray diffraction techniques, spectroscopic and thermal methods. Currently, I provide my services in the Laboratorio de Rayos X of the UIS-PTG for the characterization of polymorphs of active pharmaceutical ingredients.

ORCID: 0000-0003-4198-0028

**Arnold R. Romero Bohórquez**

Received her B.S. degree, with Cum Laude mention, and Doctor Degree with honors in Chemistry from the Universidad Industrial de Santander (UIS) in Bucaramanga, Colombia. Her skills including the synthesis of heterocyclic compounds with potential biological activity. Currently, he works as an Associate Professor of the Department of Chemistry at UIS, and also he is the director of the research group CODEIM, where he leads the design & synthesis laboratory.

ORCID: 0000-0003-3479-3865

## Jose Hernando Quintana Mendoza

Chemist graduated from the Universidad de Pamplona, with experience in the synthesis and characterization of zeolites, I have worked as a University Chemistry teacher for five years and carried out research and development of materials. I have a certificate as an implementer and auditor in environmental management systems (ISO 14001), quality management (ISO 9001: 2015) and, occupational health and safety management (Decree 1072: 2015).

ORCID: 0000-0002-7107-5830

## José Antonio Henao Martínez

Chemist and MSc from the Universidad Industrial de Santander and PhD. in Applied Chemistry in the mention of Materials Studies graduated from the Universidad de Los Andes in Mérida, Venezuela, and Post-Doctorate at the Instituto Zuliano de Investigaciones Tecnológicas (INZIT)", Maracaibo, Venezuela, with experience in the characterization of organic and inorganic crystalline and vitreous materials by X-ray techniques, actually director of the Laboratorio de Rayos X of the UIS-PTG.

ORCID: 0000-0002-2887-1532