

Production of a low-cost scavenger resin to capture aldehydes and ketones in solutions

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ABSTRACT: Over the past years, polymer-supported reagents have been extensively studied and used in various applications. One class of such reagents is called “scavengers,” which can be used to easily eliminate compounds in a solution. The present work describes the production of a resin that can be used for scavenging ketones and aldehydes using low-cost reagents and simple reaction steps, named here Amb15-Iso. This resin is obtained by reacting a low-cost commercial sulfonyl resin, Amberlyst-15, with isoniazid, a drug used for the treatment of tuberculosis. Acetone and isobutyraldehyde were used as carbonyl compound models. The reactions were monitored in-line by ATR-FTIR and results showed that the polarity of the solvent influences the kinetics of the production of the resin and water proved to be the fastest solvent. For the scavenging of acetone and isobutyraldehyde, two factors showed to have an impact in the amount of compounds captured: the polarity of the solvent and the solubility of water in the solvent. The capacity of scavenging acetone in water varied from 0.11 to 0.28 mmol per gram of resin, depending on the initial acetone concentration. The equilibrium of this reaction was modeled and the equilibrium constant was calculated to be $0.63 \pm 0.07 \text{ L mol}^{-1}$. The resin was also recycled and tested in a second round of scavenging and results showed that there was not much difference between the new resin and the recycled one, proving that the Amberlyst-15 could be reused for a second cycle of scavenging. © 2015 Wiley Periodicals, Inc. *J. Appl. Polym. Sci.* **2015**, *132*, 42291.

KEYWORDS: applications; separation techniques; spectroscopy

Received 5 December 2014; accepted 1 April 2015

DOI: 10.1002/app.42291

INTRODUCTION

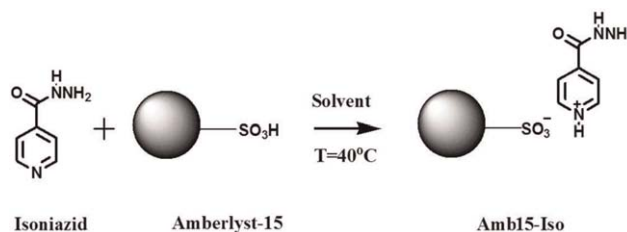
Polymer-supported reagents have been a growing research interest over the past few years because of their easy recovery at the end of a chemical process. Such reagents can be divided into three classes: stoichiometric reagents, catalysts, and scavengers. The stoichiometric reagents and the catalysts participate directly as part of the reaction itself, while the scavenger resins are typically applied after the reaction has occurred.^{1,2} Each of these classes, through the help of combinatorial chemistry, have been used in the synthesis of numerous compounds.^{3–7} Scavenging resins are mainly used for the removal of impurities and/or excess reagent in the reaction medium; this has been demonstrated as one of the major advantages of this technique in that the product of the reaction is not impaired since the residuals can be removed from the aqueous or organic solution.^{8,9} This purification technique consists of the capture of a determined

component (the nonreacted reagent, impurities, or co-products) through reaction with a group that is part of the resin, which can then be removed by filtration.

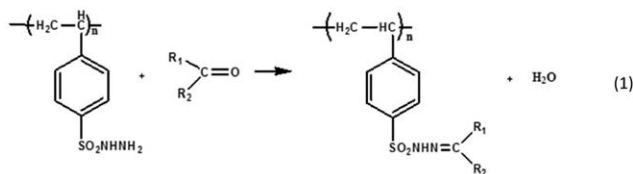
Several polymer-supported scavenging resins are known and can be selectively applied to different types of impurities.^{3,10–13} One such extensively used application is the capture of carbonyl compounds, such as ketones and aldehydes, from a solution; these molecules react with a hydrazine/hydrazide group forming a hydrazone. This reaction has been previously described in the literature.⁷ In 1979, Emerson *et al.* proposed the production of a resin that consisted of a highly reticulated matrix of polystyrene-divinylbenzene with functionalized groups of sulfonyl hydrazine that could be used for scavenging.¹⁴ The reaction of this resin is shown in the following equation, where R_1 and R_2 can be either a hydrogen or an alkyl group.

Additional Supporting Information may be found in the online version of this article

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Scheme 1. Reaction of isoniazid with Amberlyst-15 to produce the new resin Amb15-Iso.



This resin has been commercially produced and can be purchased for the scavenging of aldehydes and ketones. However, because of its high-cost and time-consuming synthesis, large-scale use of this product is too expensive, and the technique is not often employed.^{14,15} The substitution of the resin for a less expensive one could provide a possible solution for extensive scavenging applications.

The present work presents the synthesis of a resin similar to the commercial one mentioned above, with a process involving the use of low-cost reagents and simple reaction steps. This resin is obtained by reacting a low-cost commercial sulfonamide resin, Amberlyst-15, with isoniazid, which is a drug used in the treatment of tuberculosis. The production of the new resin, Amb15-Iso, was performed in three different solvents: water, ethanol, and 1,4-dioxane. Amb15-Iso can be used for capturing carbonyl compounds. For the model presented in this work, acetone and isobutyraldehyde were used to evaluate the performance of Amb15-Iso as a scavenger reagent for ketones and aldehydes. The resin was

also tested for its recyclability in a second round of scavenging. All the reactions were monitored in-line by Attenuated Total Reflectance – Fourier Transform Infrared (ATR-FTIR).^{16,17}

EXPERIMENTAL

Apparatus

A ReactIR 45m (Mettler Toledo) was used to measure and monitor the reactions. It was equipped with a DS Micro Flow Cell and an AgX 9.5mm × 2m Fiber (Silver Halide) with a diamond crystal, and with an MCT Detector using HappGenzel apodization. The samplings were made in the ranges of 4000 to 650 cm^{-1} and 2000 to 650 cm^{-1} with a wavenumber resolution of 8, with 15-second intervals between each spectrum.

All reactions were carried out in a 100 mL reactor controlled by an EasymaxTM Workstation (Mettler Toledo). The temperature of the reaction was kept at a constant 40°C by regulation with a Pt100 temperature sensor and through a Peltier System jacket. The medium was stirred at 150 rpm using a magnetic stirrer. The reaction medium was fed through the ATR-FTIR equipment using a ProMinent® Beta® pump.

Isoniazid and the Amberlyst-15 resin were reacted, and then acetone and isobutyraldehyde were incorporated (as models for the scavenging of carbonyl compounds). Both types of reactions were performed using different solvents.

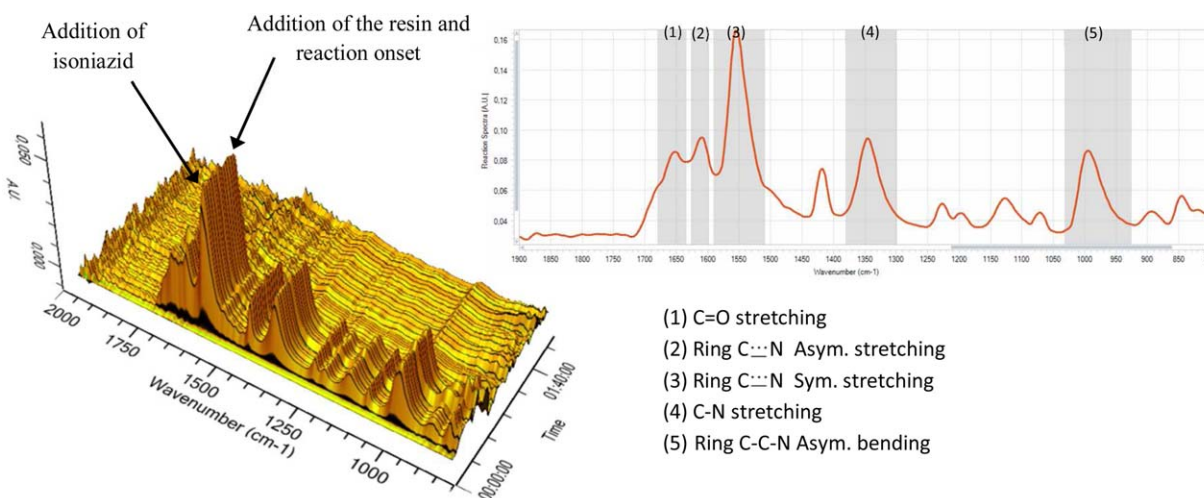


Figure 1. Time-dependent 3D ATR-FTIR graph of the incorporation reaction of isoniazid in water (pure solvent spectrum subtracted) and one selected spectrum of the isoniazid in water with descriptions of its major bands.¹⁸ [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Table I. Capacity of Incorporation of Isoniazid by the Resin in the Different Solvents Tested

Solvent	Total capacity (mmol g ⁻¹)	Standard deviation	t-Value ^a
Water	1.98	0.08	-
Ethanol	2.02	0.06	0.88
1,4-Dioxane	2.07	0.05	2.00

^aA t-test for the independent samples was performed in relation to the water values with $\alpha = 0.05$, where t-critical is 2.77.

Procedure

The resin used for the experiments was pretreated with a 10% solution of sulfuric acid, washed with water until a neutral pH was obtained, and then posteriorly washed with methanol. Subsequently, the resin was left to dry in an oven for 12 hours at 50°C, and then stored in a desiccator.

For the preparation of the incorporated resin (Amb15-Iso), 2 g of isoniazid was added to a reactor containing 40 mL of the solvent (water, ethanol, or 1,4-dioxane). The system was maintained at a constant temperature of 40°C, at a stirring rate of 150 rpm. After the solubilization of isoniazid, 5.0 g of the pretreated Amberlyst-15 resin were added to the medium and the reaction was monitored until the end using ATR-FTIR.

For the scavenging reaction, two models were chosen representing a ketone and an aldehyde. For the ketone reaction, 600 μ L of acetone was added to 40 mL of the solvent (water, ethanol, and 1,4-dioxane). For the aldehyde reaction, 150 μ L of isobutyraldehyde was added to 40 mL of the solvent (ethanol, 1,4-dioxane, dichloromethane and hexane). The system was kept at a temperature of 40°C, at a stirring rate of 150 rpm. Then 5.0 g of the Amb15-Iso resin was added and the reaction was monitored by ATR-FTIR until scavenging equilibrium was achieved.

To calculate the capacity of scavenging, the capture of acetone in water was chosen as the reaction model. To quantify the concentration, an analytical curve was constructed using 10 standard solutions (six training and four test points) and a PLS

regression was used. For the modeling, the infrared region selected was from 1810 to 955 cm⁻¹, using the first derivative, mean centering, scaling and with one latent variable.

For the recovery of the resin, 5.0 g of the Amb15-Iso previously used in the capture of acetone was added to 50 mL of a 25% solution of sulfuric acid and the system was kept at a temperature of 50°C, at a stirring rate of 150 rpm. The release of the hydrazide/hydrazone was monitored by ATR-FTIR until equilibrium was achieved.

In each case, the resin was isolated, washed with water/ethanol, and then left to dry at 50°C for 12 h.

RESULTS AND DISCUSSION

Maximum Incorporation of Isoniazid by the Amberlyst-15 Resin

For the production of the scavenger resin proposed in this work, it was necessary to incorporate the isoniazid molecules into the raw structure of Amberlyst-15. Since isoniazid has a basic nitrogen in the pyridine ring, it reacts with the Amberlyst-15 sulfonic acid group to form a salt, as shown in Scheme 1.

The reactions were monitored in-line using real time ATR-FTIR, which shows the absorption of each molecule in solution. We evaluated the preparation of Amb15-Iso in three different solvents: water, ethanol, and 1,4-dioxane. Figure 1 shows a time-dependent 3D graph of the reaction of isoniazid with Amberlyst-15 in water.

The spectra shown in Figure 1 correspond only to the isoniazid absorption bands, as the solvent peaks were subtracted from the raw spectra. It can be seen that before isoniazid addition, there were no absorptions, and as the Amberlyst-15 was added, the band signals decreased, indicating that isoniazid was being removed from the solution. The ATR-FTIR probe can detect only substrates present in solution; therefore, as the isoniazid is incorporated into the resin, its concentration decreases, and so does its signal.

The reactions of isoniazid with Amberlyst-15 were performed in triplicate for each of the three solvents. A t-test was performed

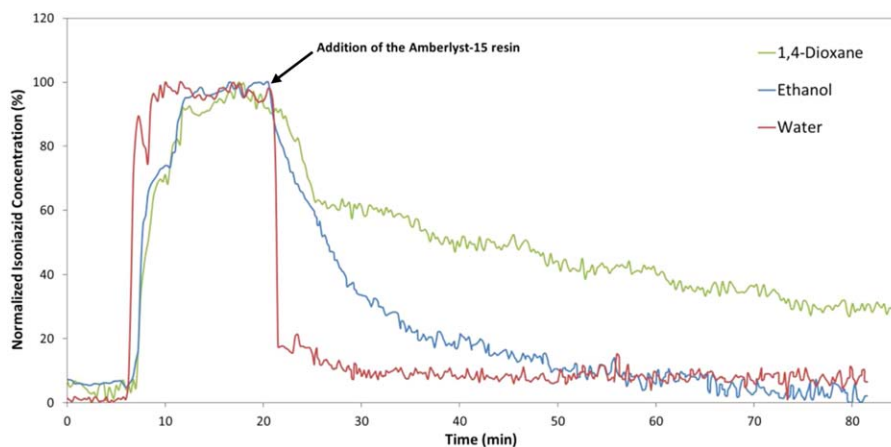
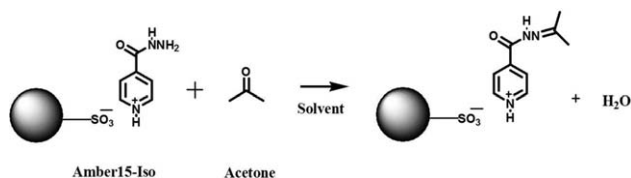


Figure 2. Normalized trends for the incorporation of isoniazid by the Amberlyst-15 resin measured by ATR-FTIR. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



Scheme 2. Reaction of the Amber15-Iso resin with a ketone (acetone) in the scavenging process.

to determine if the mean capacities of incorporation for the three solvents were the same, according to the deviation over the triplicates. The capacity was defined as the number of moles of isoniazid captured, calculated gravimetrically by the difference of weight between the Amberlyst-15 and the Amb15-Iso, per grams of raw resin. The results are shown in Table I.

As shown by the calculated t -values, the incorporation was not greatly affected by the solvent itself. In this statistical test, a hypothesis is created in which two mean values are compared, taking their variances into account. For this hypothesis to be true, the calculated t -value should be smaller than the t -critical tabulated for this degree of freedom; otherwise, the hypothesis is false and the means are different. In this case, the mean capacity of incorporation of the isoniazid in water is statistically the same as the one in ethanol and 1,4-dioxane with a certainty of 95%. This shows that changing the solvent does not influence how much isoniazid can be incorporated into the resin, and hence, how much of the product (Amb15-Iso resin) can be produced. Since water is the most accessible solvent and is much greener than the other two, it appears to be the best option for the solvent in the reaction.

Even though it does not affect the equilibrium itself, changing the solvent greatly affects the kinetics of the incorporation. Figure 2 shows the normalized trends regarding the monitoring of isoniazid in solution.

The results presented in Figure 2 indicate that the polarity of the solvent is crucial in the evaluation of the kinetics, since the reaction depends on the isoniazid molecules being carried into the inside structure of the resin in order to react with the

sulfonic acid group. Since water is the most polar solvent, it interacts better with the isoniazid molecules, having the fastest kinetics and achieving equilibrium in around 5 min, while ethanol takes about 40 min, and dioxane can take more than an hour. Besides being the best solvent for the incorporation and production of the resin, water is a cleaner and cheaper solvent, making it the best candidate for scaling-up this process.

The resin produced showed an average capacity of loading of 2 mmol g^{-1} , while the commercial resin has a capacity of $1.5\text{--}3.0 \text{ mmol g}^{-1}$. This also indicates that the resin proposed here can be considered similar regarding the number of reacting sites when compared to the commercial sulphonyl hydrazine resin.

After production, the resin was washed, dried, and tested in order to determine if the incorporated isoniazid would once again be released into a new batch of solvent. The results showed that the resin remained intact and no isoniazid was released, as presented in the supporting information file. This means that the produced resin is viable for usage, without loss of power, after addition in a new solution.

Capture of Acetone and Isobutyraldehyde by the Amb15-Iso Resin

The produced resin can be used for the scavenging of aldehydes and ketones present in solutions. The isoniazid group reacts with the carbonyl compound, as shown in Scheme 2 for the reaction with acetone.

Figure 3 shows the infrared 3D graph of the acetone capture by the Amb15-Iso in water.

The spectra presented in Figure 3 show that after the addition of acetone, three main absorptions occurred (1710 , 1365 , and 1230 cm^{-1}), referent to the C=O and C-O stretch bands. As soon as the Amb15-Iso resin was added to the solution of acetone in water, a decrease in the acetone absorption intensities indicate the decrease of acetone concentration in solution. Aiming to check if the diminution in the absorption intensities is actually related to the formation of the hydrazone and not to a physical process such as adsorption in the resin, a test was conducted where Amberlyst-15 was added instead of Amb15-Iso. In

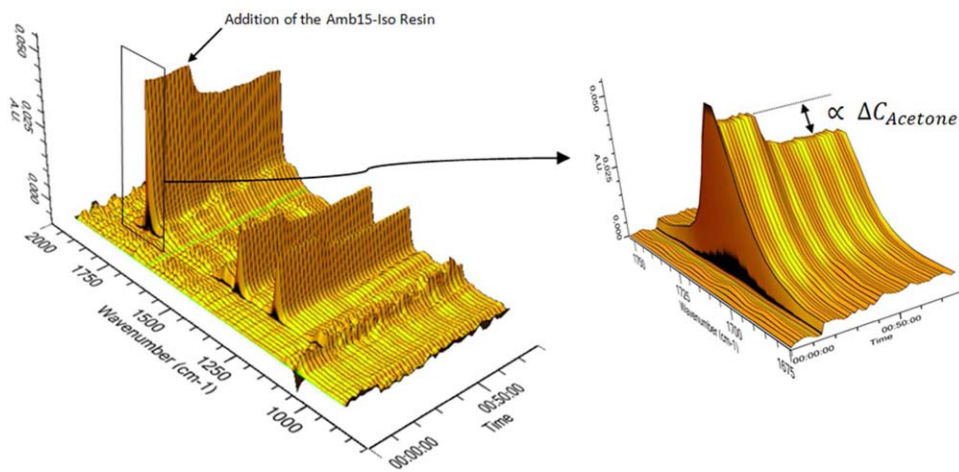


Figure 3. Time-dependent 3D ATR-FTIR graph of the acetone capture by reaction with Amb15-Iso (pure solvent spectrum subtracted) and the decreasing carbonyl band as the reaction occurs. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

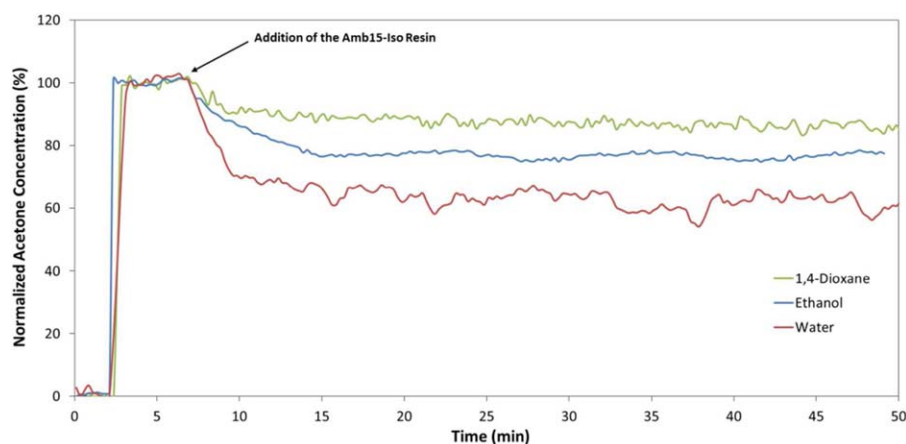


Figure 4. Normalized trends for the capture of acetone by the Amb15-Iso resin measured by ATR-FTIR in the different solvents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

this case, the concentration of acetone remained constant, proving that the absorption decrease genuinely comes from the reaction. This result is presented in the Supporting Information file.

In order to check the effect of the solvent in the kinetics of hydrazone formation, a comparison between the diminution of acetone concentration is presented in Figure 4.

It can be seen that in each case, there was a decrease in the acetone concentration, meaning that the scavenging occurred for all three solvents. However, the amount of acetone removed from solution increased as the polarity of the solvent increased. This shows that the resin can be used to capture ketone molecules in various media and solvents. The acetone in solution was not entirely reacted, and so the concentration did not decrease to zero, but the use can still be made in order to remove smaller quantities of these compounds.

As a model for the scavenging of aldehydes, the reaction of the Amb15-Iso with isobutyraldehyde was chosen, illustrated in Scheme 3.

The reaction was monitored using ATR-FTIR, as with the acetone reaction, to evaluate the trend of the carbonyl band. The reactions were performed in four different solvents, varying their polarity, to check if the resin would be able to scavenge in these different conditions and determine its kinetics. Figure 5 shows the results of the diminution of the isobutyraldehyde concentration in each solvent.

As can be seen in Figure 5, the scavenging was successful and part of the aldehyde present in each solvent was captured. In

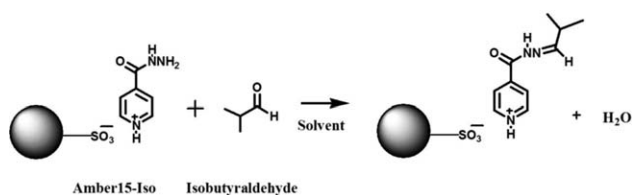
comparison to the scavenging of acetone, the application for this molecule showed to be more efficient, where a maximum decrease of about 80% of the infrared signal in ethanol and hexane was observed, while for the acetone the maximum decrease was about 40% (in water). Isobutyraldehyde was not tested in water because of miscibility problems. Regarding the polarity of the solvents, a trend can be observed if hexane is ignored, where its increase also increased the amount of carbonyl compounds captured from solution. This agrees with what was observed in the scavenging of acetone, where polarity played a major role in this equilibrium. However, hexane (one of the most nonpolar solvents) showed a similar result to that with ethanol. This can be explained by the water solubility in the solvent. For the other three solvents, water is very soluble or has some solubility (as in the case of dichloromethane). For hexane, this solubility is about 9.5 mg L^{-1} at 25°C [19], which means water being produced leave the solvent phase, and hence decrease the water concentration around the sites in the resin. This also acts in the equilibrium, increasing the amount of carbonyl compounds being scavenged.

Finally, for the scavenging of acetone in water, a test was also performed to calculate the capacity of scavenging by the Amb15-Iso. For that, an analytical curve of acetone in water was constructed using the ATR-FTIR equipment and used to quantify the concentration of acetone in four different prepared solutions, with varying initial concentrations. The amount of acetone captured was calculated from the variation in the concentration before and after the addition of the resin, and the capacity was calculated using the below equation:

$$\text{Capacity} = (C_{\text{final}} - C_{\text{initial}}) \times V_{\text{sol}} / m_{\text{res}} \quad (2)$$

In this equation, C_{final} and C_{initial} are the concentration of acetone before and after the addition of the resin, respectively, V_{sol} is the volume of the solution and m_{res} is the mass of the resin used for the scavenging. Figure 6 shows the graph of the calculated capacity for four different initial concentrations of acetone in solution, using the Amb15-Iso in a batch system.

It can be seen in Figure 6 that the capacity of scavenging is dependent on the initial concentration of acetone, which can be



Scheme 3. Reaction of the Amb15-Iso resin with an aldehyde (isobutyraldehyde) in the scavenging process.

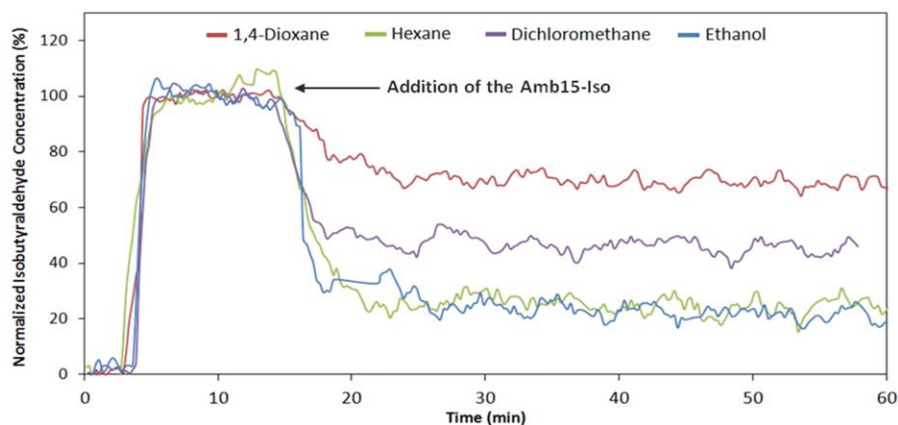


Figure 5. Normalized trends for the capture of isobutyraldehyde by the Amb15-Iso resin measured by ATR-FTIR in the different solvents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

explained by the equilibrium law. The equilibrium equation can be described in a similar way to the one of a normal ionic exchange resin, and the following equation shows the case for the Amb15-Iso applied in the scavenging of acetone.

$$\frac{K}{V_{sol}} = \frac{n_{acet}^{capt}}{(n_{sit} - n_{acet}^{capt})(n_{acet}^o - n_{acet}^{capt})} \quad (3)$$

In the equation, K is the equilibrium constant, V_{sol} is the volume of the solution, n_{acet}^{capt} is the number of moles of acetone captured by the resin, n_{sit} is the number of reaction sites present in the resin (containing the isoniazid molecules), and n_{acet}^o is the initial number of moles of acetone in the solution. From the points in Figure 6, the equilibrium constant was estimated to be $0.63 \pm 0.07 \text{ L mol}^{-1}$ and is valid for the capture of acetone in water. The capacity of the acetone scavenging in water can also be calculated from eqs. (2) and (3), and is also shown in Figure 6.

The capacity of the initial concentration of acetone tested varied from 0.11 to 0.28 mmol of acetone per gram of resin. This value is still lower than the total capacity of approximately 2 mmol per gram of resin, which is the total number of moles of isoniazid in the resin. It should be emphasized that the system described in this work functions as a batch system. The use of the resin in a continuous system could present a higher efficiency of acetone removal; this is not the goal of the present

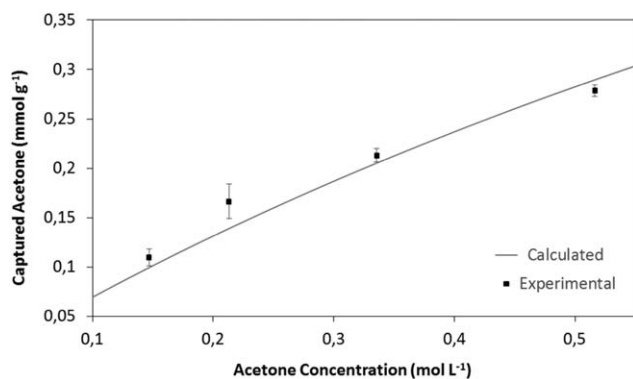


Figure 6. Capacity of the acetone scavenged in water by the Amb15-Iso resin in a batch system.

research, however, and this aspect will be pursued in future work.

Recovery of the Amberlyst-15 Resin

One of the advantages of working with Amberlyst-15 resin is its potential for easy regeneration. In a solution containing an excess of hydronium ions, it starts to compete with the pyridine ring attached to the sulfonic group in the resin, in a way that this molecule is released from its matrix and the original resin is reconverted. Tests were performed in order to obtain maximum recovery, and it was seen that a solution of 25% sulfuric acid is the most efficient way for the regeneration. Higher concentrations lead to easier destruction of the resin's matrix, disabling it for reuse in future scavenging processes.

The recovery process was also monitored using ATR-FTIR in order to observe the release of the hydrazide/hydrazone molecules that were contained in the previously used resins. Figure 7(a) shows the normalized trend of the concentration of the molecules being released from the resin.

This recuperation is very fast, taking only about 10 min until equilibrium is achieved. In order to check if the resin was indeed reverted to the Amberlyst-15 form, the solid phase spectrum of the resin was taken and compared to a never-before-used Amberlyst-15 resin and the Amb15-Iso resin, as shown in Figure 8.

It can be seen that in the spectrum from the recovered resin (I), the major band from the hydrazide/hydrazone, the carbonyl band that appears at around 1700 cm^{-1} in the resin's matrix, disappeared. The spectrum is fairly close to the one from the never-used Amberlyst-15 (III), meaning that the recuperation was successful. However, it could not be guaranteed that all the sites were recovered and some isoniazid molecules might have been retained in the resin. Nevertheless, the objective at this point was to evaluate the reuse of the recovered resin for further cycles of scavenging.

The recovered resin was retreated with isoniazid. Figure 7(b) shows a comparison between the scavenging of acetone by the newly produced Amb15-Iso and the recovered Amberlyst-15. It can be seen that there is little difference between the two, which

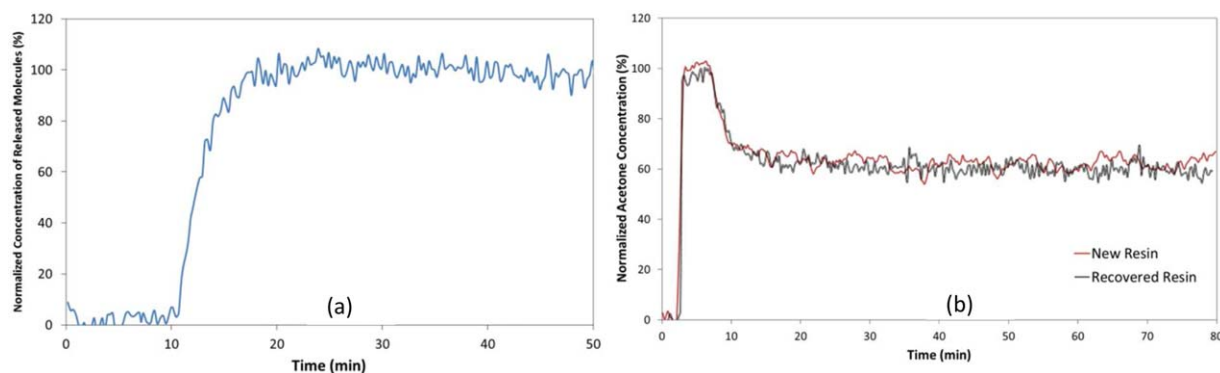


Figure 7. (a) Normalized trend of the concentration of molecules being released from the resin; and (b) Normalized trends for the capture of acetone by the new and recovered Amb15-Iso. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

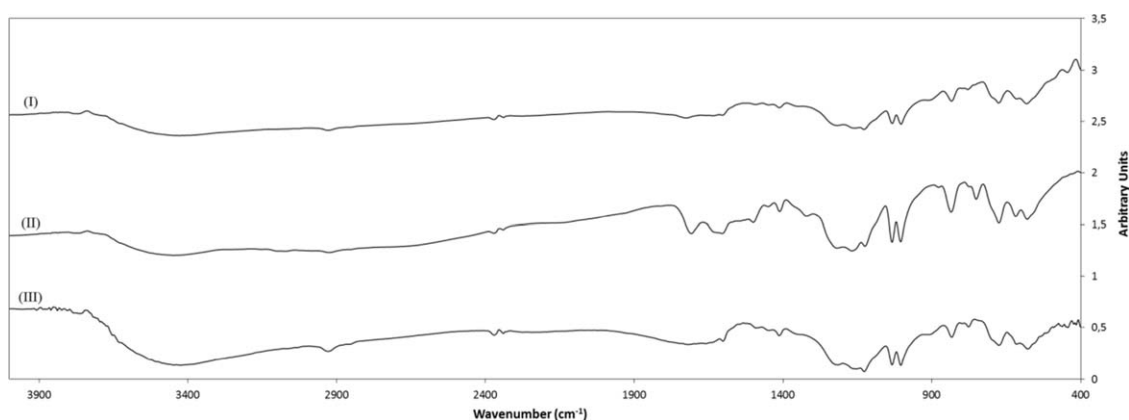


Figure 8. FTIR spectra of the solid phase resins: (I) recovered Amberlyst-15, (II) Amb15-Iso, and (III) new Amberlyst-15.

shows that the resin can be recovered and reused for a new cycle of scavenging. However, further study should be conducted to evaluate how many cycles the resin is able to endure.

CONCLUSION

The production of the Amb15-Iso resin showed that regardless of the type of solvent, the equilibrium does not change and the amount of isoniazid that can be incorporated into the resin remains the same. The kinetics of the reaction, however, increase significantly as the polarity of the solvent increases, since the reaction depends on the isoniazid molecules interacting with the molecules of the solvent and being carried inside the resin in order to react with the sulfonic group. For the scavenging of acetone in all three solvents—water, ethanol, and 1,4-dioxane—as the polarity increased, the amount of acetone captured also increased. As for the scavenging of isobutyraldehyde, another factor showed to be of importance in the equilibrium: the solubility of water in the solvent. For this molecule, polarity defined the equilibrium for ethanol, dichloromethane, and 1,4-dioxane, but for hexane, the water solubility had a great impact, increasing the amount captured.

The capacity of scavenging of acetone in water was tested and the analysis with ATR-FTIR showed that the amount captured

varied with the initial concentration of acetone in water, with values measured experimentally from 0.11 to 0.28 mmol per gram of resin. This value was lower than the total number of moles of isoniazid in the resin, and can be improved if the system is made continuous. The equilibrium was modeled for this reaction and the equilibrium constant was calculated to be $0.63 \pm 0.07 \text{ L mol}^{-1}$.

The resin was also recycled and tested for a second round of scavenging. Results showed that the hydrazide/hydrazone attached to the sulfonic groups in the resin could be released by using a 25% solution of sulfuric acid. This resin could be used for another round of incorporation of isoniazid and scavenging of acetone, and the results showed that there was an insignificant difference between the new resin and the recycled one, which confirms that the resin could be recovered and reused for a new cycle of scavenging.

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