heterocyclic carbenes [4].
Many procedures have been developed to generate a broad range of differently substituted imidazoles [5]. Although there is a wide variety of synthetic routes towards imidazoles, only a few studies exist for the synthesis of 1,2,4,5-tetrasubstituted imidazoles which are mostly performed via multistep routes or via a trisubstituted 1H-imidazole in which the nitrogen is substituted in the final step.

Using the modified Radziszewski reaction [6] (Figure 1), a procedure has been optimized for the generation of tri- and tetrasubstituted imidazoles via micoreactor technology. Optimization included the search for a suitable solvent mixture, temperature and reaction time. Finally, the generality of the optimized reaction was tested using different starting materials.

It was possible to create a variety of tri- and tetrasubstituted imidazoles in moderate to good yields (up to 1.6 g/h) via a continuous procedure [7].

\[
\begin{align*}
\text{R}_1 & \xrightarrow{\text{H}_{\text{N}}^{\text{O}} - \text{O}} \text{R}_2 + \text{R}_3 + \text{H}_{\text{N}}^{\text{O}} \\
\text{R}_1 & \xrightarrow{\text{H}_{\text{N}}^{\text{O}} - \text{O}} \text{R}_2 + \text{R}_3 + \text{H}_{\text{N}}^{\text{O}} \\
\text{R}_1 & \xrightarrow{\text{H}_{\text{N}}^{\text{O}} - \text{O}} \text{R}_2 + \text{R}_3 + \text{H}_{\text{N}}^{\text{O}} \\
\text{R}_1 & \xrightarrow{\text{H}_{\text{N}}^{\text{O}} - \text{O}} \text{R}_2 + \text{R}_3 + \text{H}_{\text{N}}^{\text{O}} \\
\end{align*}
\]

*Figure 1: Imidazole formation through a 4-CR*

References:

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**Sono-enzymatic coloration of wool**

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Laccase from *Trametes villosa* was tested in combination with ultrasound to improve coloration of wool by "in situ" radical polymerization of catechol. Catechol and catechol/laccase solutions, in presence of wool, were treated at 30 and 50 °C without and with ultrasound at 20 kHz at different power intensities (3, 10, 20, 35 and 42 W). The results were analyzed by spectrophotometric and HPLC analyses. No coloration was observed in the sonicated catechol system due to the formation of hydroxyl radicals that attack the phenol molecules in solution or in the collapsed cavitation bubbles interface.

Catechol in this condition does not polymerize and degrades in biodegradable and colorless products such as carboxylic acids. However, in the sonicated laccase/catechol system a large polymerization was observed even more than the laccase/catechol stirring system. The degree of enzymatic coloration of wool fabrics, measured by spectrophotometric analysis, has showed a linear correlation at 50 °C between the absorbance and the ultrasound power intensity in a direct correlation. The HPLC (High Performance Liquid Chromatographie) analyses of the sonicated system have confirmed the formation of a larger quantity of polymer in respect to the stirred system as well as the production of polymers with higher molecular weight. In presence of laccase, the direct ultrasound catechol degradation showed lower kinetic than the ultrasonic enhanced catechol polymerization due to the indirect physical and chemical ultrasound effects on the enzyme.

This study have demonstrated that the ultrasound waves improve the diffusion processes and may also have positive effect on the laccase active center structure. Moreover the hydroxyl radicals produced by ultrasound can react with the intermediate molecules produced by the enzyme, enhancing the enzymatic catechol polymerization.