

One-pot menthol synthesis from citronellal on polymer supported catalyst

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Highlights

- Successful synthesis of an active heterogenous catalyst for one-pot isomerization process.
- The mechanical mixture of ZnCl₂@pDVB and palladium on different supports for menthol synthesis was tested to obtain an intensified concept.
- The deactivation of palladium on carbon deactivation studies.

1. Introduction

Palladium nanoparticles are extensively used for the preparation of catalysts for both oxidation and reduction reactions and their oxidation state is often crucial for the activity and selectivity of the process. To limit coalescence, palladium nanoparticles are typically dispersed on several supports, such as activated carbon, silica, titanium oxide, as well as a variety of macro- and mesoporous materials, including polymers [1]. Innovative approaches have been applied on palladium-based catalysis in liquid-phase processes, especially when palladium nanoparticles immersed in ionic liquids inside the pores have been used for catalytic hydrogenation of citral and other polyfunctional molecules. Menthol is indeed an important chemical, widely used in flavoring applications as well as in pharmaceutical and cosmetic products. Although it can be extracted from natural sources such as peppermint, the increasing request prompted the development of synthetic routes. Among those, the Takasago process represents the most applied industrial approach [2]. The process is based on the telomerization of myrcene with diethylamine to N,N-diethylgeranylamine, which is then isomerized to (+)-citronellal enamine, using rhodium BINAP catalyst. Similar synthetic approaches, based on an acid catalyzed isomerization and the subsequent hydrogenation of the obtained intermediates, have been developed to obtain (-)-menthol from citronellal and citral. We are now investigating this synthetic route, exploiting the use of the polymer supported palladium catalyst in this selected organic reaction, where both the acidity and metal functions are needed [3,4,5].

2. Methods

The first task is the synthesis of a suitable acid catalyst for the isomerization of citronellal to isopulegol. To this end, a mesoporous polydivinylbenzene has been used as support for the Lewis acid, ZnCl₂, by deposition on the catalytic support. Several experiments have been carried out to determine the role of the support and the effect of the amount of Lewis acid on the catalyst performance.

The first experiments were performed at a selected interval of initial concentration, temperature and pressure. In a typical experiment, the catalyst was swollen for two hours at 70°C and 10 atm in an autoclave, whereas the citronellal solution was preheated in a separated chamber to be later injected into the reactor vessel. Liquid-phase samples were withdrawn from the autoclave at several reaction times through a dedicated sampling valve, allowing a precise description of the progress of the reaction, analyzed by gas chromatography.

The acid catalyst was functionalized with Pd nanoparticles, to prepare a bifunctional material for the one pot synthesis of (-)-menthol from citronellal, in the presence of molecular hydrogen. Several tests with mechanical mixtures of the acid catalyst and palladium on carbon have been performed. The experimental equipment for catalyst screening and kinetic studies consisted of a pressurized autoclave (Parr), equipped with a heating system, agitator, thermocouple, cooling loop and sampling line. The

equipment included a separate preheating chamber, which allows the injection of the reagent solution after the pretreatment of the catalyst *in situ* in the autoclave.

3. Results and discussion

In the first part of the project, the research was concentrated on the identification of the best catalyst for the acid isomerization: several routes were screened starting from polydivinylbenzene and ZnCl_2 as the Lewis acid. It can be concluded that a minimum amount of 30% of ZnCl_2 is necessary to perform the reaction until its thermodynamic equilibrium with a conversion of 85% and a selectivity towards (-)-isopulegol diastereoisomer of 35%. TEM characterizations were performed to study the morphology of the catalyst, as well as ICP leaching tests to ensure that the catalyst remained in the solid phase.

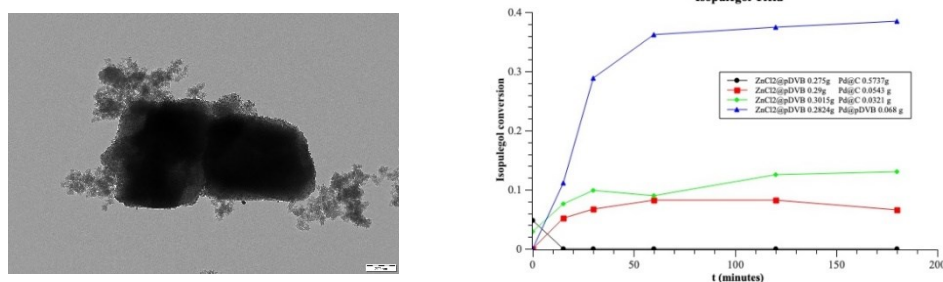


Figure 1. HR-TEM characterization of $\text{ZnCl}_2(30\%)\text{@pDVB}$ and isopulegol yield with $\text{ZnCl}_2(30\%)\text{@pDVB}$ and Pd@C as catalyst.

The reaction was then implemented to cover the hydrogenation reaction of (-)-isopulegol to menthol, performed with a mechanical mixture of palladium on different supports and the acidic catalyst synthesized.

Several experiments confirmed that decreasing the quantity of palladium on carbon as hydrogenating catalyst, the selectivity towards the desired product increased. However, deactivation of the catalyst was observed and studied when in combination with the presence of zinc chloride deposited on the mesoporous resin.

4. Conclusions

We were able to associate the activity of the catalytic material to the presence of large crystals, bearing smaller ZnCl_2 crystallites (ca. 10 nm) on the surface, which are only present in the catalyst synthesized with the combination of THF and water as the swelling solvent. The experiments performed with a mechanical mixture of the catalyst with acid sites and palladium on different supports allowed us to individuate the precise proportion that gives a higher menthol yield. The deactivation of the palladium catalyst has been observed and is now investigated to fully comprehend the mechanism of the process and which species is responsible for the isomerization and, hence, the catalyst deactivation.

References

- [1] Liu, F., Meng, X., Zhang, Y., Ren, L., Nawaz, F., Xiao, F., *Journal of Catalysis*, 2010, 271, 52-58
- [2] Dylong, D., Hausoul, P., Palkovits, R., Eisenacher, M., *Flavour Fragr. J.*, 2022, 37, 195-209
- [3] Milone, C., Gangemi, C., Neri, G., Pistone, A., Galvagno, S., *Appl. Chem. A: General*, 2000, 199, 239-244
- [4] Mäki-Arvela, P., Kumar, N., Nieminen, V., Sjöholm, R., Salmi, T., Murzin, D., *Journal of Catalysis*, 2004, 225, 155-169
- [5] Mäki-Arvela, P., Simakova, I., Vajglová, Z., Murzin, D., *Catalysis surveys*, 2023, 27, 2-19

Keywords

Menthol, polydivinylbenzene, citronellal, batch reactor