

A Tandem Cyclization and Hydrogenation of (±)-Citronellal to Menthol over Mixed ZnBr₂/γ-Al₂O₃ and Ni/γ-Al₂O₃ Catalysts

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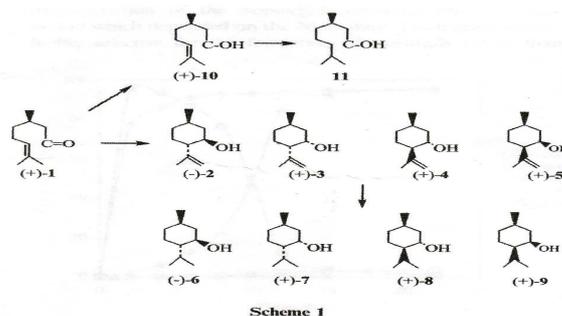
ABSTRACT

A mixture of ZnBr₂/γ-Al₂O₃ and Ni/γ-Al₂O₃ gave a useful dual catalysts system that combines high rate of cyclization of (+) citronellal to isopulegols over zinc dibromide as an acid sites and subsequent hydrogenation of isopulegols to menthols over nickel as a metal sites. The selectivity towards isopulegols and menthols remained high with ZnBr₂ and nickel loading up to 15wt%. A loading of 15 wt% is optimal; lower loadings led to a low rate of hydrogenation, whereas a higher nickel loading appears to block the zinc dibromide Lewis acid sites essential for the cyclization of citronellal. The yield of (±)-menthol over the dual-catalyst system gave good yield (74.82%) and good stereoselectivity towards (-) menthol isomer (68.90%).

KEY WORDS: dual catalysts, cyclization, hydrogenation, (+) citronellal, isopulegols, (-)-menthol.

INTRODUCTION

In the fragrance industry, (-)-Menthol is an important material due to its characteristic peppermint odor [1,2]. It is widely used in pharmaceuticals, cosmetics, toothpastes, chewing gum, cigarettes, and other products. (-)-Menthol is isolated from natural sources, such as the oil of *Mentha arvensis* or *Mentha piperita*. (-)-Menthol can also be synthesized from other terpenoids such as (+)-citronellal, citral, (+)-pulegone, (+)-limonene, (+)-β-pinene, and (+)-δ-2-carene. The cyclization of (±)-citronellal **1** gives four stereoisomers of isopulegol, each of which occurs as a pair of enantiomers : (±)-isopulegol **2**, (±)-neo-isopulegol **3**, (±)-iso-isopulegol **4**, and (±)-neoiso-isopulegol **5** (Scheme 1). Hydrogenation of these isopulegols lead to four pairs of enantiomers : (±)-menthol **6**, (±)-neomenthol **7**, (±)-isomenthol **8**, and (±)-neoisomenthol **9**. Of these (-)-menthol **6** has the most perceptible cooling effect, and hence its selective synthesis is desired [3-12].

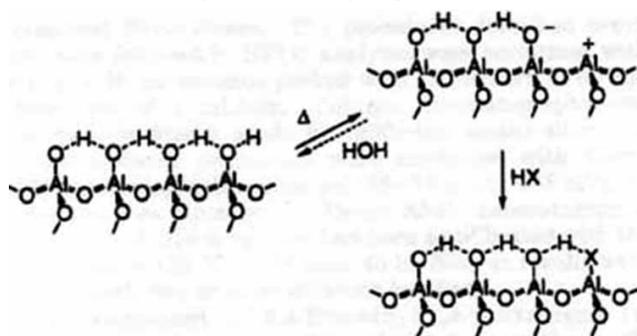


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Several acid catalysts have been investigated in the cyclisation of citronellal, like zeolites [10,11], mesoporous materials [5], zirconia [7]. In the industrial process (–)-isopulegol is crystallized before hydrogenation in order to get a menthol mixture from which (–)-menthol is separated. Racemic menthols can be produced via catalytic hydrogenation of thymol [13] and mixtures of neomenthol, isomenthol and neoisomenthol can be isomerized over heterogeneous catalyst to produce about 65% racemic menthols [13,14].

The combined cyclization to isopulegols and hydrogenation to menthols has been described by Milone *et al.*, [15] for ruthenium on different supports. The silica support had to be acidified to be active for the cyclization of citronellal. At 100% conversion of citronellal, the yield of menthols was 80%, but a rather substantial amount of the fully hydrogenated product, 3,7-dimethyloctanol **11** was formed. Activated carbon was a poor support, even after treatment with HCl. Due to the lack of acid sites, the rate of cyclization was low, and only a 30% combined yield of all menthol isomers was obtained. The addition of ZnBr₂ to Ru/SiO₂ improved the selectivity to (–)-isopulegol **2** reaching 86% selectivity for Zn loading ≥ 4 mmol/g SiO₂ [11]. Ravasio *et al.*, [16], reported that the hydrogenation of (+)-citronellal into menthols over silica-supported copper catalysts required very mild conditions of 0.1 MPa H₂ pressure and 90 °C. A tandem cyclization and hydrogenation of (+)-citronellal **1** to menthol has been described [3] over one-pot dual-catalyst system composed of Zr-beta and Ni/MCM-41. Catalyst system with beta and MCM-41 support gave a diastereoselectivity to (±)-menthol **6**, 93–94%. The nickel loading could be increased up to 15% on MCM-41 but a higher loading of 15 wt% reduced the rate of cyclization but increased the rate of hydrogenation to form more byproducts, citronellol **10** and 3,7-dimethyloctanol **11**.

Cyclisation of citronellal on several solid acid catalysts has been investigated, but few studies deal with the distribution of the stereoisomers formed during the reaction on γ -Al₂O₃ and γ -Al₂O₃ supported catalysts. Unlike silicagel, which is weakly acidic, γ -alumina is basic. In addition to OH groups, the surface of alumina contains oxide ions in the outermost layer and exposed aluminum ions in the next lower layer, which are generated through the loss of chemisorbed water from neighboring OH groups on heating during the manufacturing process (Scheme 2). One manifestation of the resulting basic character is the Cannizzaro oxidation/reduction exhibited by (±)-citronellal **1** and previously observed for a number of other aldehyde. Another is that the first equivalent of an acid is consumed in neutralizing the basic surface [17]. γ -Alumina neutralized with a hydrogen halide exhibits acidic character, apparently due the information of Al-X bonds adjacent to OH groups on the surface (Scheme 2).



Scheme 2

Study that concern on γ -Al₂O₃ as a supported catalysts have investigated [18], during the hydrogenation of very low value mints oils, namely, dementholized oil. Among the different Cu catalysts, they reported that Cu/ γ -Al₂O₃ showed the best activity and selectivity towards a mixture of menthols, while stereoselectivity towards the valuable isomer (–)-menthol **6** can be improved by selectively dehydrogenating the products mixture. In the

hydrogenation of pulegone and *pennyroyal oil*, Cu/ γ -Al₂O₃ catalyst also showed an unprecedented activity allowing complete transformation of the substrate into menthols under very mild experimental conditions (1 atm H₂, 90°C).

In this study, we combined the high diastereoselectivity for the conversion of (+)-citronellal **1** to isopulegols of ZnBr₂/ γ -Al₂O₃ with hydrogenation activity of Ni/ γ -Al₂O₃ to achieve a tandem synthesis of menthols from citronellal. We have reported previously [19] that Ni/ γ -Al₂O₃ show high selectivity for the hydrogenation of (+)-citronellal to menthols, forming (-)-menthol, **6** under very mild experimental conditions (1 atm H₂, 90°C) with yield ~84%. In this paper we present detailed characterization data for ZnBr₂/ γ -Al₂O₃ and Ni/ γ -Al₂O₃ catalysts. The activity and selectivity of dual-catalytic systems of ZnBr₂/ γ -Al₂O₃ and Ni/ γ -Al₂O₃ are optimized and compared. We have also decided to elucidate the influence of the catalysts characteristic in order to get information on the nature of the catalytic active sites.

EXPERIMENTAL

Materials

General remarks: γ -Al₂O₃ (BET=190 m²/g, PV=1.214 cm³/g), ZnBr₂, Ni (NO₃)₂.6H₂O, and methanol, was purchased from MERCK, (*R*)-(+)-Citronellal (>90%) was obtained from fractional distillation under reduced pressure towards Citronella Oil that purchased from Cilacap, Central of Java.

Instrumentation

BET Surface Area Analyzer (Quantachrome NovaWin2), Gas Chromatography (GC-Agilent 7890)

Procedure

Catalyst Preparation and Characterization

ZnBr₂ supported on γ -Al₂O₃ (ZnBr₂/ γ -Al₂O₃) and nickel supported on γ -Al₂O₃ (Ni/ γ -Al₂O₃) were obtained by incipient-wetness impregnation of the support with an aqueous solution of ZnBr₂ and Ni(NO₃)₂ at 30 °C. The ZnBr₂ and nickel loadings on γ -Al₂O₃ were varied from 5 to 15 wt%. After impregnation the samples were dried overnight at 90 °C and calcined in air at 400 °C for 4 h. Before catalytic measurements, the Ni/ γ -Al₂O₃ catalysts were reduced in H₂ (50 ml/min) for 3 h at 500 °C. The surface area and pore volumes were measured by nitrogen adsorption (Quantachrome NovaWin2, Version 2.2).

Catalytic testing

The catalytic tests were performed at 200 °C in a modified reactor glass type using 3 mL of (+)-citronellal (were produced by fractional distilled products from Citronella Oil of *Cimnopogon winterianus*-Java type and were used without further purification), and both of freshly reduced catalyst at a hydrogen pressure of 0.5 g and 0.5 g of ZnBr₂/ γ -Al₂O₃ and Ni/ γ -Al₂O₃ a 1:1 mixture of were tested. Typically, the reaction was conducted in a N₂ atmosphere with stirring for the first hour to allow the cyclization of citronellal to isopulegols. After 1 h, the N₂ atmosphere was replaced with H₂. Samples were removed at regular intervals and analyzed by gas chromatography (HP5 column).

RESULT AND DISCUSSION

Textural properties

The physical properties of the catalysts are summarized in Table 1. The surface area of γ -Al₂O₃ was reduced only slightly (up to 5 m²/g) after impregnation with 5% ZnBr₂. The loss in surface area is due to partial blockage of the micropores. However, the total pore volume, which includes the interparticle pores, remained relatively unchanged. This decrease was more drastic with a loss of more than 140 m²/g for the 15 wt% ZnBr₂

sample. The surface area also decreased after impregnation with nickel. This decrease was more slightly than that for $\text{ZnBr}_2/\gamma\text{-Al}_2\text{O}_3$, with a loss of $15 \text{ m}^2/\text{g}$ for the 15 wt% Ni sample. It can be assumed that nickel clusters in the samples with low metal loading had a narrow size distribution, whereas the cluster size is less uniform in samples with higher loadings.

Table 1. Textural properties of catalyst

	Surface area (m^2g^{-1})	Total pore volume (cc.g^{-1})	Pore diameter (Å)
$\gamma\text{-Al}_2\text{O}_3$	120.50	0.25	29.30
5% $\text{ZnBr}_2/\gamma\text{-Al}_2\text{O}_3^{\text{a}}$	115.37	0.21	24.33
10% $\text{ZnBr}_2/\gamma\text{-Al}_2\text{O}_3^{\text{a}}$	107.10	0.20	28.01
15% $\text{ZnBr}_2/\gamma\text{-Al}_2\text{O}_3^{\text{a}}$	49.80	0.11	24.41
5% $\text{Ni}/\gamma\text{-Al}_2\text{O}_3^{\text{b}}$	118.75	0.23	28.83
10% $\text{Ni}/\gamma\text{-Al}_2\text{O}_3^{\text{b}}$	115.85	0.22	27.95
15% $\text{Ni}/\gamma\text{-Al}_2\text{O}_3^{\text{b}}$	105.05	0.20	27.92

^a = after calcinations

^b = after calcinations and reductions

Catalytic activity of mixture $\text{ZnBr}_2/\gamma\text{-Al}_2\text{O}_3$ and $\text{Ni}/\gamma\text{-Al}_2\text{O}_3$

A dual-catalyst system of $\text{ZnBr}_2/\gamma\text{-Al}_2\text{O}_3$ and $\text{Ni}/\gamma\text{-Al}_2\text{O}_3$ was tested for the one-pot transformation of (+)-citronellal **1** to menthols. The use of $\gamma\text{-Al}_2\text{O}_3$ allows a high metal dispersion on the mesoporous support. A 1:1 ratio of each component was used with a total weight of either 1 g. The ZnBr_2 and nickel loading was 15 wt%. The reaction was carried out under nitrogen for the first hour before hydrogen was introduced. Fig.1 shows typical results of the isomerisation and hydrogenation of (+)citronellal as a function of time. Under the reaction condition used the rate of disappearance of (+)citronellal follows a first-order rate law hence the major products of cyclization formed after 1 h were isopulegols. Beyond this reaction time, the rate of hydrogenation to menthols increased slowly, so that after 6 h, not all of the isopulegols were converted to menthols with (-)menthol **6**, (+)neo-menthol **7**, and (+)iso-menthol **8** in a ratio of 68.9 : 17.85 : 7.86. No (+)neo-isomenthol **9** was detected. Besides the isomeric menthols, other products of citronellal hydrogenation were detected. Citronellol **10** even in first hour were formed, but their concentrations were 0.41%, respectively. The concentration of citronellol **10** reached a maximum at 5 h, and further hydrogenation of the C=C bond no led to 3,7-dimethyloctanol **11** and 3,7-dimethyloctanal **12** was observed, suggesting that over the $\text{Ni}/\gamma\text{-Al}_2\text{O}_3$ catalyst, the carbonyl group in citronellal is preferentially hydrogenated rather than the C=C bond.

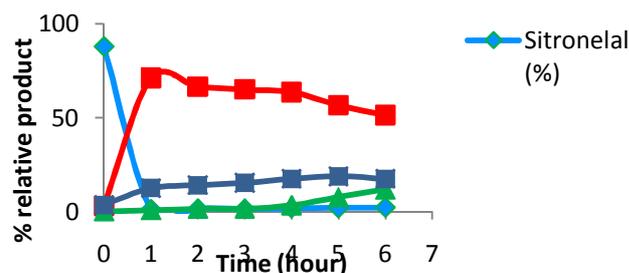


Fig.1 Cyclization and hydrogenation of (+)citronellal over $\text{ZnBr}_2/\gamma\text{-Al}_2\text{O}_3$ and $\text{Ni}/\gamma\text{-Al}_2\text{O}_3$ catalysts with H_2 introduced after 1 hour

CONCLUSION

One-pot dual-catalyst system composed of $\text{ZnBr}_2/\gamma\text{-Al}_2\text{O}_3$ and $\text{Ni}/\gamma\text{-Al}_2\text{O}_3$ gave a slightly higher diastereoselectivity to (-)-menthol **6**, 68.90%. The ZnBr_2 and nickel loading of 15 wt% was effective, but a higher loading of 15 wt% Ni can reduced the rate of cyclization but increased the rate of hydrogenation to form more byproducts, citronellol. Over dual-catalyst system, the rate of cyclization of citronellal to isopulegols was faster than the rate of hydrogenation of citronellal, so that menthols were formed with high yields and only low concentration of by product, citronellol were formed.

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