



Solvent-Free Isomerization of 3-carene to 2-carene using Na/o-chlorotoluene Catalyst in Trans-isolimonene Production

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<http://dx.doi.org/10.13005/ojc/330652>

(Received: July 20, 2017; Accepted: August 10, 2017)

ABSTRACT

Trans-isolimonene is one of the important compound in drugs development. This compound can be made by isomerization of inexpensive 3-carene via 2-carene using Na/o-chlorotoluene catalyst in xylene. The existence of xylene as a solvent requires a further separation process that can reduce the efficiency when applied in the bulk industry. The isomerization of 3-carene to 2-carene has been studied in solvent free reaction compared by isomerization without xylene solvent. The result showed that the isomerization can also occur in solvent-free condition. Solvent-free isomerization gave 27.72% of conversion and 83.27% of selectivity while isomerization with solvent gave 23.59% of conversion and 86.87% of selectivity.

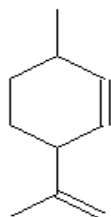
Keywords: 3-carene, 2-carene, Na/o-chlorotoluene, xylene, trans-isolimonene, isomerization.

INTRODUCTION

Trans-isolimonene is one of monoterpenoid compounds that a rare and little-studied substance. It was first synthesized by Tshugaev in 1903¹. Now trans-isolimonene may become a fully accessible monoterpenoid use as one of starting material for some drug compounds development such as in

synthesis of antimalarial drug artemisinin² and synthesis of menthol³. These compounds is rarely found naturally in plants. Several studies have reported that isolimonene found in essential oils of *Citrus medica* and *Citrus reticulata*. The peel oil of *Citrus medica* containi solimonene about 39.37%^{4,5} and 5.87% in *Citrus reticulata* essential oil⁶. The importance of trans-isolimonene compounds in

drugs development not comparable with the availability in nature, therefore sought other methods for producing trans-isolimonene using synthesis way.



trans-isolimonene

Trans-isolimonene can be produced from 2-carene via thermal isomerization, while compound 2-carene was obtained using isomerization of 3-carene. The isomerization of 3-carene to 2-carene is reported to take place in several methods. Over hydrogenation catalysts such as Raney nickel and Pd on carbon, 2-carene was produced in addition to the hydrogenated products under a hydrogen atmosphere but the selectivity of this reactions is low because of hydrogenation to carane⁷. Shimazu, *et al.*,⁸ reported that 3-carene undergoes isomerization to 2-carene over solid bases of MgO and CaO, Ni/SiO₂ catalyst⁹, glaucolite¹⁰, and basic zeolite¹¹. All of these previous methods need high temperature condition and low selectivity of 2-carene.

In this work, we prepared 2-carene from 3-carene using Booth's method¹². The reaction occur at certain temperature with xylene solvent and catalyst Na/*o*-chlorotoluene for 1 night. The existence of xylene solvent requires a separation process using fractional distillation to separate the product from the solvent.

In this study, our objective is to understand the influence of solvent-free isomerization 3-carene to 2-carene on its conversion and selectivity.

MATERIALS AND METHOD

Materials

Sodium metal, 3-carene, and *o*-chlorotoluene were purchased from Merck-Millipore (Germany). Analysis by using Gas Chromatography-Mass Spectrometer (GC-MS) Shimadzu QP2100SP with RTX-5 column.

Isomerisation of 3-carene to 2-carene

With solvent, xylene

A total of 15 mg 3-carene included in the reflux of 500 ml flask along with 15 ml xylene and 0.5 g of sodium metal and 0.5 ml of *o*-chlorotoluene. The mixture refluxed for 12 h, 24 h, and 48 h. respectively. Furthermore, reflux resulting solution is cooled to room temperature. The solution was decanted to separate the catalyst from the solution. Then the solution was analyzed using Gas Chromatography–Mass Spectrometer to determine the equilibrium formation of 3-carene and 2-carene¹².

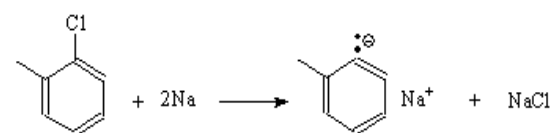
Without solvent, xylene

A total of 30 ml 3-carene included in the reflux of 500 ml flask along with 0.5 g of sodium metal catalyst and 0.5 ml *o*-chlorotoluene. The mixture refluxed for 12, 24, and 48 h. respectively. Furthermore, reflux resulting solution is cooled to room temperature. The solution was decanted to separate the catalyst from the solution. Then the solution was analyzed using Gas Chromatography–Mass Spectrometer to determine the equilibrium formation of 3-carene and 2-carene.

RESULT AND DISCUSSION

Influence of solvent free condition on isomerization 3-carene to 2-carene

The isomerization of 3-carene to 2-carene can be done using alkaline catalyst of sodium/*o*-chlorotoluene. Reaction between sodium metal and *o*-chlorotoluene produces a salt-containing carbanion act as strong base (Scheme 1).



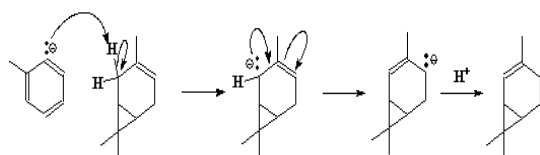
***o*-chlorotoluene**

Scheme. 1

Furthermore, this carbanion take hydrogen atoms on saturated C-C bond of 3-carene causing electron rearrangement to form 2-carene isomer (Scheme 2).

Reaction mechanism that is catalyzed olefin isomerization base is closely related to the chemical nature of the carbanion. Reaction can

occur in a homogeneous solution system and the presence of a strong base catalyst. In the previous study, the solvent xylene used to support the catalyst basicity. The solvent sufficiently suitable to induce the formation of carbanion.



3-carene 2-carene
Scheme. 2

This study has been conducted isomerization of 3-carene to 2-carene without the use of solvent compared to the isomerization with solvent condition. Our objective in this study was to avoid the using solvent in this isomerization reaction. Fig.1. Showed the results of isomerization reaction with solvent xylene and without solvent condition. Both of reactions refluxed for 16 hours.

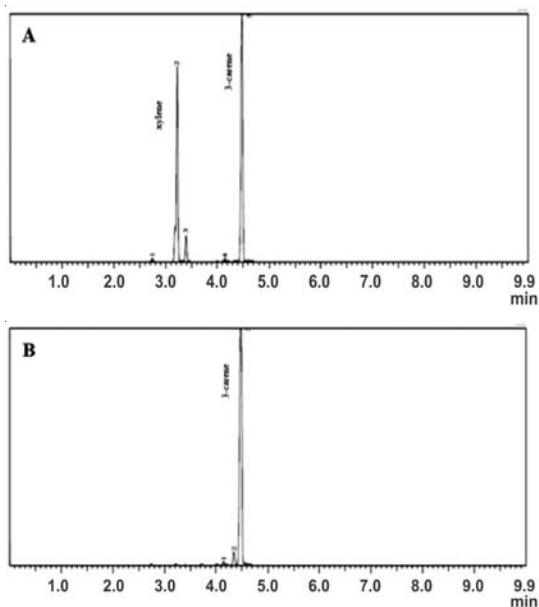


Fig. 1. Chromatograms of isomerization result of 3-carene refluxed for 16 h. (A) with xylene solvent (B) without solvent

Refluxing for 16 h did not give 2-carene product. It need more time to optimize isomerization condition. Addition of reflux time have been observed. Fig.2 demonstrated the result of isomerization for 24 h of refluxing. Solvent-free isomerization also gave product of 2-carene as well as reaction with xylene solvent. At temperature 150-

170°C the thermodynamic equilibrium between 3-carene and 2-carene corresponds to a mixture of 60% of 3-carene and 40% of 2-carene.

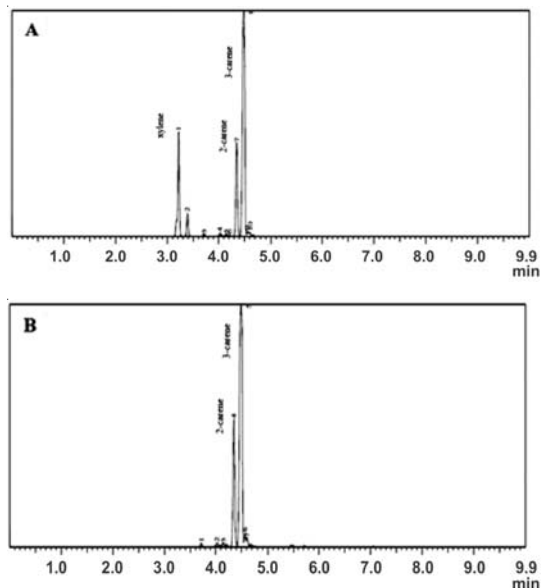


Fig. 2. Chromatograms of isomerization result of 3-carene refluxed for 24 hours (A) with xylene solvent (B) without solvent

Figure.3. showed that more time refluxing for 48 h. also gave 2-carene product but at the same time obtained by-products of *m*-cymene and *p*-cymene.

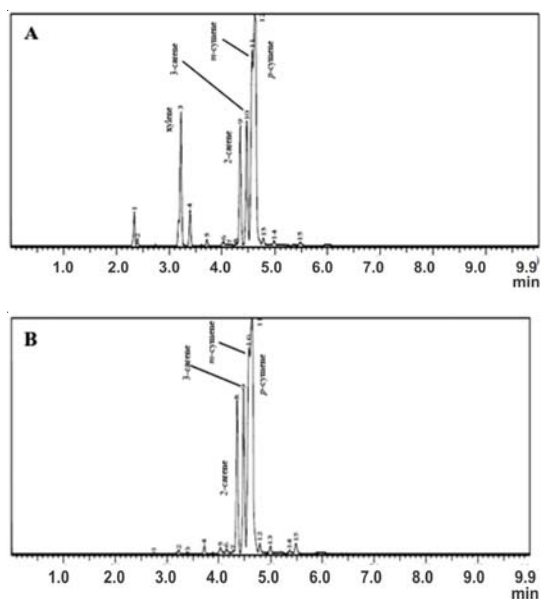
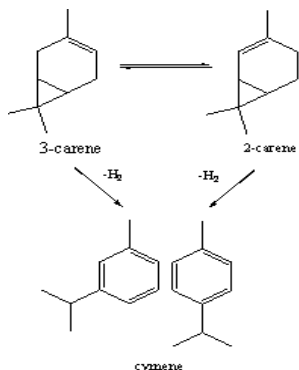


Fig. 3. Chromatograms of isomerization result of 3-carene refluxed for 48 hours (A) with xylene solvent (B) without solvent

According to previous research, cymene can be obtained through dehydrogenation of 3-carene and 2-carene (scheme 3) ⁹.



These results showed that the isomerization also occurs in solvent-free conditions. The optimum result according to this work is the isomerization for 24 h, while the isomerization for 48 h obtained by-products of cymenes.

Conversion and selectivity of isomerization 3-carene to 2-carene

Conversion and selectivity were measured based on the amount of chromatograms area. The conversion of 3-carene (C), selectivity of 2-carene (S) are described by the following equations that $[3c]_0$ represents the initial concentration of 3-carene and $[3c]_t$ and $[2c]_t$ represent the final concentration of 3-carene and 2-carene, respectively.

$$C = ([3c]_0 - [3c]_t) / [3c]_0$$

$$S = [2c]_t / ([3c]_0 - [3c]_t)$$

Conversion of 3-carene in both conditions increased with increasing reaction time (Figure. 4).

The optimum isomerization selectivity of 3-carene to 2-carene was reached when the reaction was conducted in 24 h. refluxing. The selectivity of isomerization with xylene solvent and isomerization without solvent are 86.87% and 83.27%, respectively (Fig.5). There were no significant differences between xylene solvent and without

solvent conditions. It reinforces previous research that isomerization of 3-carene to 2-carene can also be done without using solvent as well as using xylene solvent.

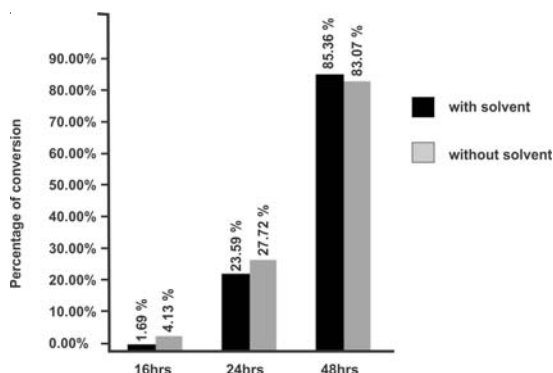


Fig. 4. Conversion of 3-carene to 2-carene

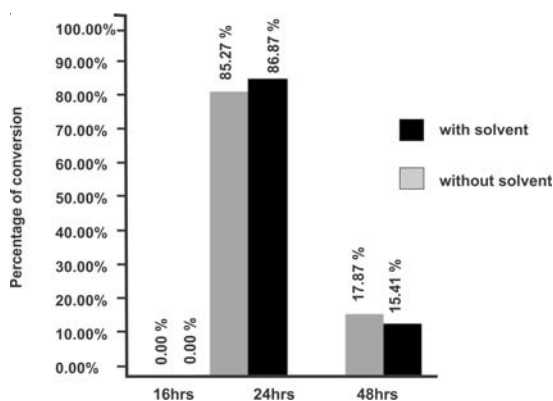


Fig. 5. Selectivity of 3-carene to 2-carene

CONCLUSION

In conclusion, the free solvent isomerization of 3-carene to 2-carene can be done for 24 h. with 27.72% of conversion and 83.27% of selectivity.

ACKNOWLEDGMENTS

This research was financially supported by Scholarship of Indonesian Directorate of Higher Education (DIKTI) and Directorate of Research and Community Service of Islamic University of Indonesia (UII).

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