Transformations of Monoterpene Epoxides in Supercritical Fluids

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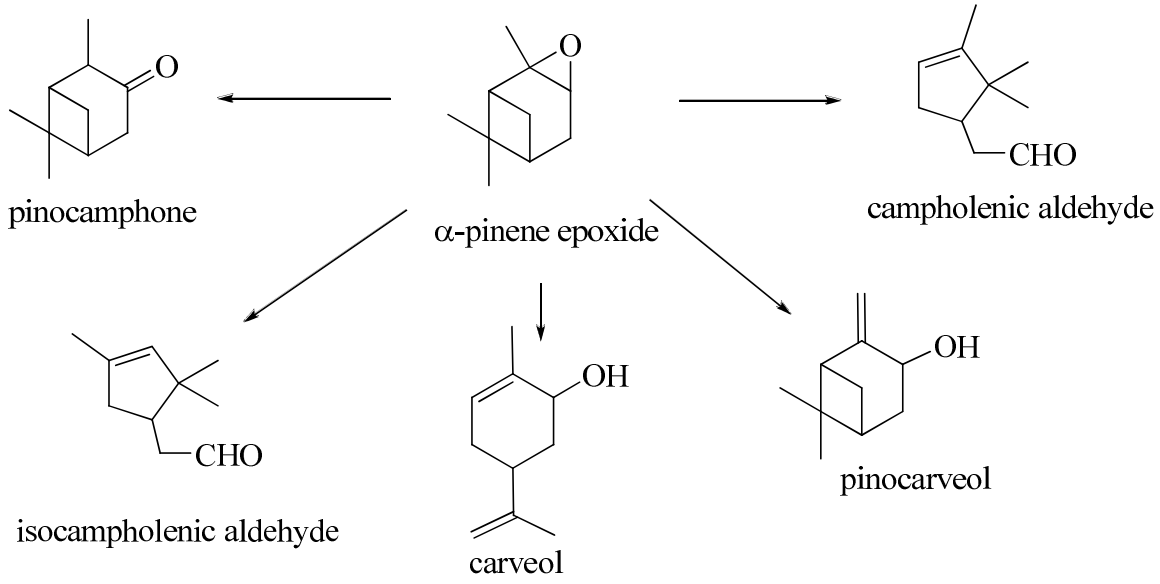
Monoterpenes and they epoxides are a valuable renewable starting material for pharmaceutical and cosmetic industries, in the production of flavorings, pesticides, etc. However, the transformations of these compounds, especially epoxides, in acid media due to isomerization and polymerization reactions may give not only the target products, but also a number of different compounds. Moreover serious environmental problems caused by large amount of toxic acid-containing waste. Reactions based on the transformations of monoterpene epoxides in supercritical solvents can be considered as an alternative to conventional methods.

The present work is the first study of α- and β-pinene epoxides and verbenol epoxide transformations in supercritical two-component fluid containing CO_2 and isopropyl alcohol. The use of supercritical CO_2 allowed us to decrease the critical temperature of solvent in comparison with that of pure alcohol, and thus to perform the reaction in supercritical region at a lower temperature. The reaction were conducted in a flow-type reactor with residence time up to 4 min.

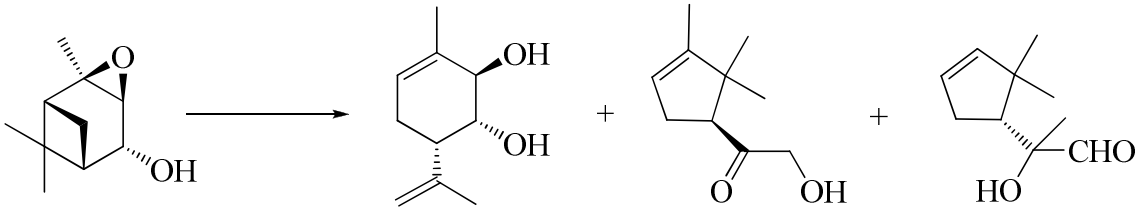
Campholenic aldehyde, the key compound for synthesis of some sandalwood scented substances [1], and carveol were shown to be the main products of α-pinene epoxide reactions in supercritical solvents containing water [2]. In the absence of water, isomerization of α-pinene epoxide in supercritical solvent yields campholenic aldehyde and pinocamphone, with their total amount in the reaction mixture attaining 80% [2]. In this case, judging from the composition of products being formed, the occurrence of two parallel processes can be assumed: thermal isomerization of α-pinene epoxide and its acid-catalyzed isomerization.



One of the main identified products of verbenol epoxide transformations in supercritical fluid containing CO_2 and isopropyl alcohol was para-menthadiol **1** with high anti-

parkinsonian activity [3]. Preparative isolation of compound **1** followed by analysis by chiral GC-MS proved that the isomerization of verbenol epoxide to **1** proceeded stereospecifically [4].

In contrast to α-pinene epoxide transformations, the presence of water caused no essential changes in product distribution. The presence of triethylamine suppressed the rearrangements; obviously the reaction has cationic character.



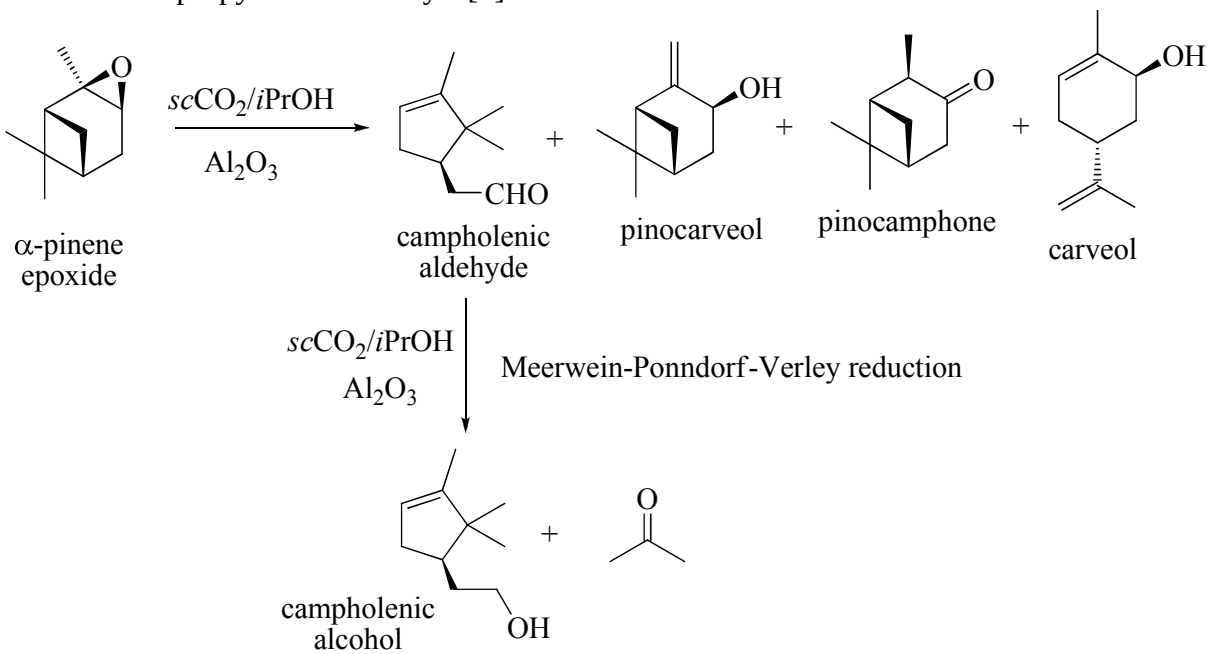
verbenol epoxide
ee 72%

1
ee 72%

α-Campholenic alcohol and its derivatives exhibit valuable organoleptic properties [5]. The well-established scheme of the compound synthesis includes the acid-catalyzed isomerization of α-pinene epoxide that causes the formation of campholenic aldehyde followed by its isolation [6]; in the second stage, aldehyde is reduced to α-campholenic alcohol by using $LiAlH_4$ [7].

We have found that the use of a system consisting of flow-type reactor, supercritical fluid containing isopropanol/CO_2 and alumina as a catalyst allows the one-pot isomerization of α-pinene epoxide into campholenic aldehyde and Meerwein-Ponndorf-Verley (MPV) reduction of the aldehyde to the α-campholenic alcohol [8].

The MPV reaction is one of efficient and highly selective methods for the reduction of carbonyl compounds into substituted alcohols bearing a large variety of functional groups. The classical MPV reaction uses reducing agent isopropanol, which converts to acetone, and aluminum isopropylate as a catalyst [9].



α-pinene epoxide

campholenic aldehyde

pinocarveol

pinocamphone

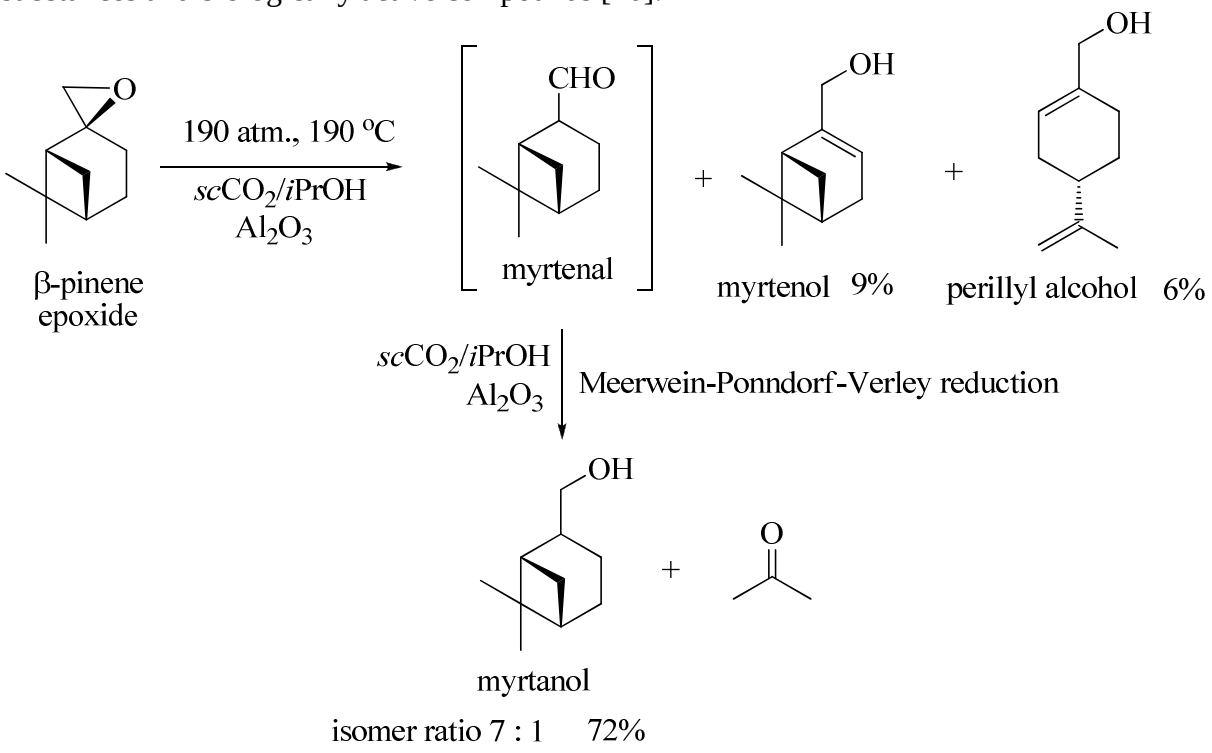
carveol

campholenic alcohol

It is noticeable that despite the formation of two carbonyl compounds in the reaction, i.e. campholenic aldehyde and pinocamphone, only aldehyde is reduced to alcohol, while ketone remains unchanged.

The reaction mixture was prepared at 200 °C and separated by column chromatography on SiO_2. α-Campholenic alcohol and pinocamphone were obtained as the main products; their yields were 40% and 31%, respectively. In addition, pinocarveol was found with a yield of 4%.

Obtaining *trans*-myrtanol from β-pinene through the formation of intermediate β-pinene epoxide and myrtenal is another interesting process; it is based on the opening of the epoxide ring followed by the reduction process. Myrtanol is used in the syntheses of metal-organic substances and biologically active compounds [10].



Transformations of β-pinene epoxide occurring under supercritical solvent conditions in the presence of Al_2O_3 at 190 °C led to the formation of *trans*- and *cis*-myrtanol (their total content was 72%, the ratio of the isomers was 7 : 1, according to the GC-MS data), which were most likely the products of MPV reduction of the intermediate compounds, *trans*- and *cis*-myrtanals [8]. In addition, myrtenol and perillyl alcohol, minor products of epoxide isomerization, were found in the reaction mixture.

Thus the transformations of epoxides in supercritical solvents of different compositions can be considered as new methods of obtaining the target isomerization products at short residence time in a continuous mode.

Acknowledgements

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