Chinese Chemical Letters Vol. 13, No. 6, pp 495 – 496, 2002
http://www.imm.ac.cn/journal/ccl/html

Ferric Chloride Catalyzed Isomerization and Cyclization of Geraniol, Linalool and Nerol

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Abstract: Ferric chloride catalyzes the isomerization and cyclization of geraniol, linalool and nerol in acetonitrile giving α-terpineol in good to high yields.

Keywords: $FeCl_3$, catalysis, cyclization, geraniol, linalool, nerol, α-terpineol.

Geranyl pyrophosphate, linalyl pyrophosphate and neryl pyrophosphate are known to be important precursors for biosynthesis of cyclic terpenoids, and a variety of cationic intermediates have been suggested to be involved in their skeletal rearrangements[1]. Ferric chloride has recently been used as a Lewis acid to catalyze Friedel-Crafts reactions[2], synthesis of esters and acetals[3], α-glycosidation of peracetylated sugars[4] and cyclization of 2-(trimethylsilylmethyl) pentadienal[5]. Therefore, it is of interest to see if ferric chloride could also catalyze the isomerization and cyclization of acyclic terpenols. We wish to report herein a preliminary result on isomerization and cyclization of geraniol, linalool and nerol by the action of ferric chloride in acetonitrile.

The terpenol (3 mmol) and ferric chloride were dissolved in 50 mL of acetonitrile and stirred at room temperature for 4 h, then the products were analyzed by TLC and GC. α-Terpineol was separated chromatographically on a silica gel column and identified by ^1H and ^{13}C NMR and MS spectroscopy. Geraniol produced linalool and/or α-terpineol, while linalool produced geraniol and α-terpineol. Nerol gave geraniol, linalool and α-terpineol. It was found that the product distribution and the yield depended significantly on the amount of ferric chloride and the content of water in the solvent. When anhydrous ferric chloride was used in anhydrous acetonitrile the yields of the products are very low. However, ferric chloride hexahydrate ($FeCl_3 \cdot 6\ H_2O$) could efficiently catalyze the reactions giving high yield of the cyclization product. But addition of small amount of water would retard the reaction. The optimum mole ratio of $FeCl_3 \cdot 6\ H_2O$ for this reaction was found to be two equivalents in anhydrous acetonitrile, one equivalent is not enough. Under this condition α-terpineol was the predominant product from all of the three terpenols. Representative results are listed in **Table 1**.

It is seen from **Table 1** that geraniol and nerol could isomerize to linalool in appreciable amount, while both geraniol and linalool could not transfer to nerol. In addition, in dry acetonitrile all of the three terpenols gave the cyclized α-terpineol as the predominant product. Therefore, it is reasonable to assume that α-terpineol could

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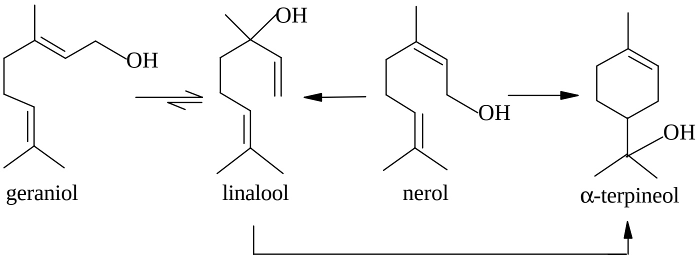
Table 1 Isomerization of terpenols catalyzed by 2 equivalents of $FeCl_3 \cdot 6H_2O$

Substrate	Products and yield (%)			
	geraniol	linalool	nerol	α-terpineol
geraniol	74a trace^b	26^a 4^b		none^a 53^b $<10^c$
linalool	4^a trace^b	90^a 5^b		6^a 65^b $20\text{-}30^c$
nerol	4^a	23^a trace^b	56^a trace^b	17^a 94^b $65\text{-}80^c$

a. In CH_3CN containing 5% of water (v/v); b. In anhydrous CH_3CN; c. Yield from mineral acid catalyzed reactions (see ref. 6).

be directly formed from linalool and nerol, and the latter could also isomerize to linalool. In addition, an equilibrium existed between geraniol and linalool which is favorable to the latter as depicted in **Scheme 1**. Similar equilibrium and isomerization have been observed in the mineral acid catalyzed isomerization of these terpenols[6], but the yields of the cylization product are much lower as listed in **Table 1**.

Scheme 1



In conclusion, this work demonstrates that ferric chloride hexahydrate in acetonitrile can efficiently catalyze the cyclization of geraniol, linalool and nerol giving high yield of α-terpineol.

Acknowledgment

The authors thank the National Natural Science Foundation of China (Grant No. 29972018) for financial support.

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Received 28 Septembber, 2001