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# THE REACTION OF 2-FLUOROPYRIDINIUM SALT WITH NEROL AND GERANIOL. NON-ENZYMIC BIOGENETICLIKE CYCLIZATION TO LIMONENE

Susumu KOBAYASHI, Mikio TSUTSUI, and Teruaki MUKAIYAMA
Department of Chemistry, Faculty of Science,
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

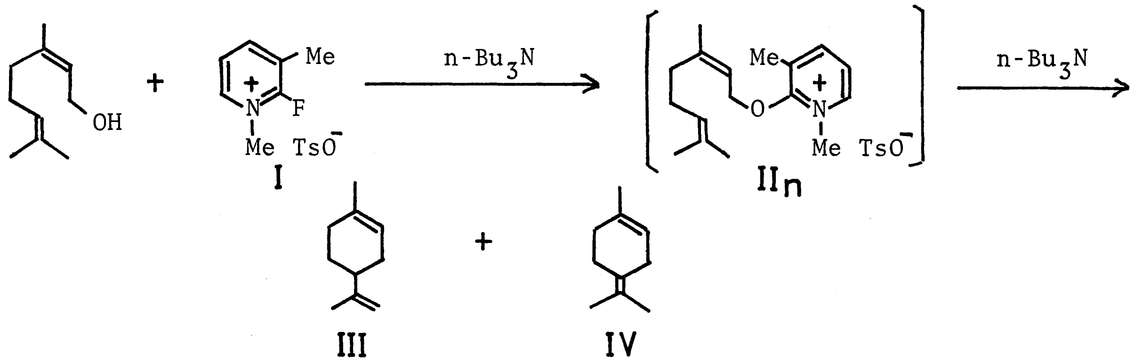
Treatment of nerol with 2-fluoropyridinium salt and tri-n-butylamine at -40°C afforded cyclic monoterpenes, mainly limonene, in high yields. The reaction of geraniol with 2-fluoropyridinium salt is also described.

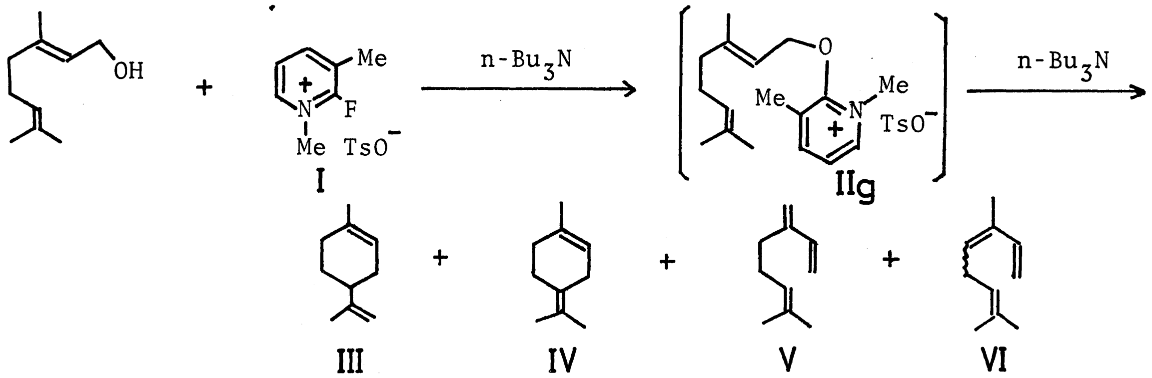
Naturally occurring terpenes are derived directly, or by way of stereospecific cyclizations and rearrangements, from the acyclic precursors such as geraniol, or farnesol.[1] Non-enzymic biogeneticlike conversion of such a precursor to the other terpenes has been of much interest and widely investigated.[2] In this communication we wish to report the dehydrative conversions of nerol and geraniol to the cyclic and acyclic monoterpenes, mainly limonene, under a very mild condition by the use of 2-fluoropyridinium salt and tri-n-butylamine.

Different from the case of primary, secondary or benzylic alcohols,[3] it was found that 2-alkoxypyridinium salt, $II_n$ or $II_g$, prepared from 2-fluoro-1,3-dimethylpyridinium tosylate and nerol or geraniol, was unstable and readily converted to monoterpene hydrocarbons and 1,3-dimethyl-2-pyridone. When nerol was allowed to react with 2-fluoropyridinium salt I and tri-n-butylamine in methylene chloride at -40°C for 7 hr, limonene (III) and terpinolene (IV) were produced in 82% and 15%yield, respectively. The structures were confirmed by the gaschromatographic comparison with the authentic samples, and the yields were determined by glc (PEG 20M) using β-pinene as an internal standard. Varying the reaction conditions, the reactions of nerol or geraniol with 2-fluoropyridinium salt were examined, and the results are summarized in the table.

The cis configuration of 2,3-double bond in the nerol moiety of $II_n$ causes the close proximity with $C_1$ carbon and 6,7-double bond, and this leads to both the high reactivity and the high product selectivity. Thus none of the uncyclized product, myrcene (V) and occimene(VI) were detected when the reaction was carried out at low temperature. However, when the same reaction was carried out at r.t., myrcene and occimene were also formed about total 10∼15% yield along with the cyclized products.

In a typical procedure, a methylene chloride solution (5ml) of nerol (156.1mg, 1.0mmol) and tri-n-butylamine (456.1mg, 2.5mmol) was added to 2-fluoro-1,3-dimethylpyridinium tosylate (I) (350.7mg, 1.2mmol) at -78°C under an argon atmosphere. The reaction mixture was stirred at -40°C for 7 hr. After quenching with water, followed by the addition of hexane (20ml), the organic layer was successively washed with





The Reaction of 2-Fluoropyridinium Salt with Nerol and Geraniol

| alcohol | temp. (°C) | time (hr) | Yield (%)<br>III | <br>IV | <br>V | <br>VI |
|---|---|---|---|---|---|---|
| nerol | -40 | 7 | 82 | 15 | – | – |
| geraniol | -5 | 20 | 41 | 3 | 7 | 7 |
| | r.t. | 3 | 40 | 4 | 17 | 21 |

saturated potassium hydrogensulfate solution, water and saturated sodium chloride solution.

In the case of the reaction of geraniol, the ratio of acyclic monoterpenes to cyclic monoterpenes was increased as was expected.

The noteworthy features of the present method are; 1) limonene and other monoterpenes are obtained directly from nerol or geraniol, 2) reaction condition is very mild, and 3) yields are high.

Application to the other sesquiterpene alcohols is now in progress.

## References

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