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HIGHLY STEREOSELECTIVE SYNTHESES OF NEROL AND GERANIOL

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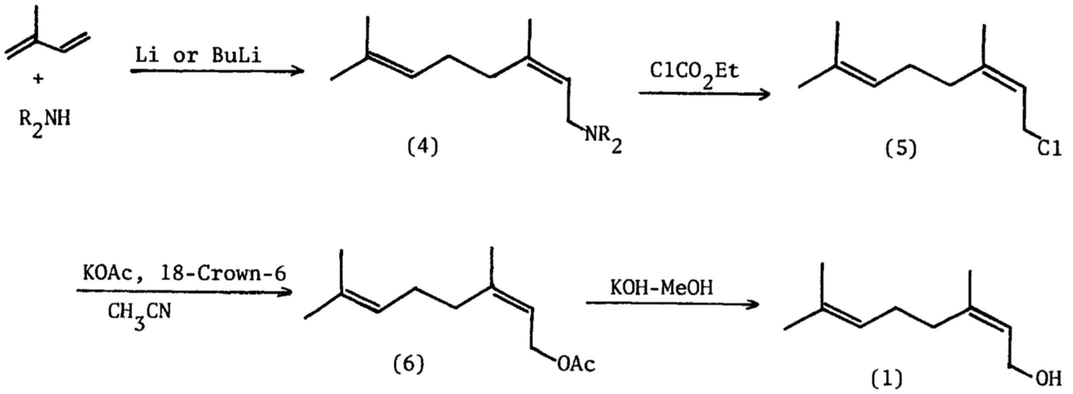
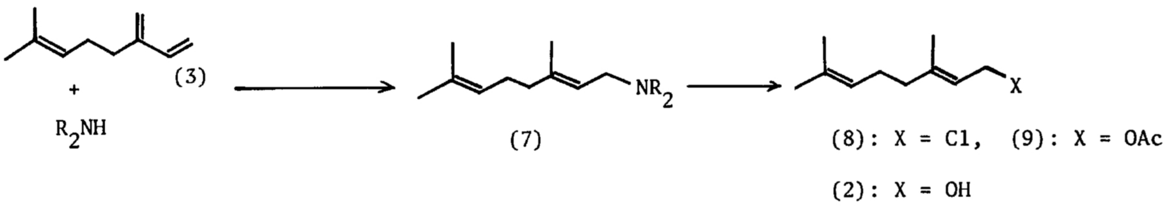
A highly stereoselective synthesis of nerol (1) was accomplished using the telomerization process of isoprene. Geraniol (2) was also synthesized from myrcene (3).

Much attention has been recently paid to the stereospecific syntheses of acyclic terpenoids.$^{1)}$ However, the highly stereoselective syntheses of nerol (1) and geraniol (2) utilizing the telomerization has not been reported. We herein describe a highly stereoselective and simple route to (1) and (2) from isoprene and myrcene (3), respectively.



N,N-Dialkylnerylamine (4), a key intermediate$^{2)}$ for the syntheses of acyclic monoterpenoids, was prepared in ca. 85% yield by the lithium- or butyllithium-catalyzed telomerization$^{3)}$ of isoprene with dialkylamine (R_2NH; R = Me, Et, and n-Pr) in benzene at 65°C. N,N-Dipropylnerylamine (4) was found to be easily transformed into neryl chloride (5)$^{4)}$ on treatment with an excess of ethyl chloroformate at 30°C for 8 h in 84% yield, and (5) was then allowed to react with potassium acetate in dry acetonitrile in the presence of 18-Crown-6$^{5)}$ at 60°C for 4 h to afford neryl acetate (6) in 96% yield. Treatment of (6) with 15% potassium hydroxide-methanol solution at room temperature gave pure nerol (1) (Z : E = 99.5 : 0.5)$^{6)}$ in 94% yield.$^{7)}$

On the other hand, geraniol (2) was synthesized from myrcene (3)$^{8)}$ according to the following scheme.



The stereoselective preparation of N,N-dipropylgeranylamine (7) was carried out in 80% yield using the lithium-catalyzed reaction of (3) with dipropylamine in benzene at 50°C for 20 h. The similar treatment of (7) with ethyl chloroformate gave geranyl chloride (8)$^{9)}$ in 87% yield, which was then converted into geranyl acetate (9) by the reaction with potassium acetate in the presence of 18-Crown-6. Hydrolysis of (9) with potassium hydroxide-methanol solution gave geraniol (2) (E : Z = 98 : 2)$^{6)}$ in 85% yield based on (8).$^{7)}$

REFERENCES AND FOOTNOTES

1) S. Kobayashi and T. Mukaiyama, Chem. Lett., 705 (1974); M. Ohki and K. Mori, Agr. Biol. Chem., 38, 177 (1974); L. J. Altman, L. Ash and S. Marson, Synthesis, 129 (1974); K. Sato, S. Inoue and S. Morii, Chem. Lett., 747 (1975); G. Cahiez, D. Bernard and J. F. Normant, Synthesis, 245 (1976); F. Derguini-Boumechal, R. Lorne and G. Linstrumelle, Tetrahedron Lett., 1181 (1977) and references cited therein.

2) K. Takabe, T. Katagiri and J. Tanaka, Tetrahedron Lett., 3005 (1975); idem., Chem. Lett., 1031 (1975); M. Tanaka and G. Hata., Chem. & Ind., 330 (1976); idem., ibid., 202 (1977).

3) K. Takabe, T. Katagiri and J. Tanaka, Tetrahedron Lett., 4009 (1972).

4) Neryl chloride (5) could be also obtained from N,N-dimethyl- and diethylnerylamine in 73% and 75% yields, respectively.

5) C. L. Liotta, H. P. Harris, M. McDermott, T. Gonzalez and K. Smith., Tetrahedron Lett., 2417 (1974).

6) The ratio was determined by GLC (PEG 6000, 160°C)

7) The structures of the products were verified by compatible spectral data.

8) Recently, we reported that myrcene (3) could be directly prepared from isoprene [K. Takabe, A. Agata, T. Katagiri and J. Tanaka, Synthesis, 306 (1977).]

9) (8) was also prepared from N,N-dimethyl- or diethylgeranylamine obtained by the BuLi-catalyzed reaction of (3) with dimethylamine or diethylamine.

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