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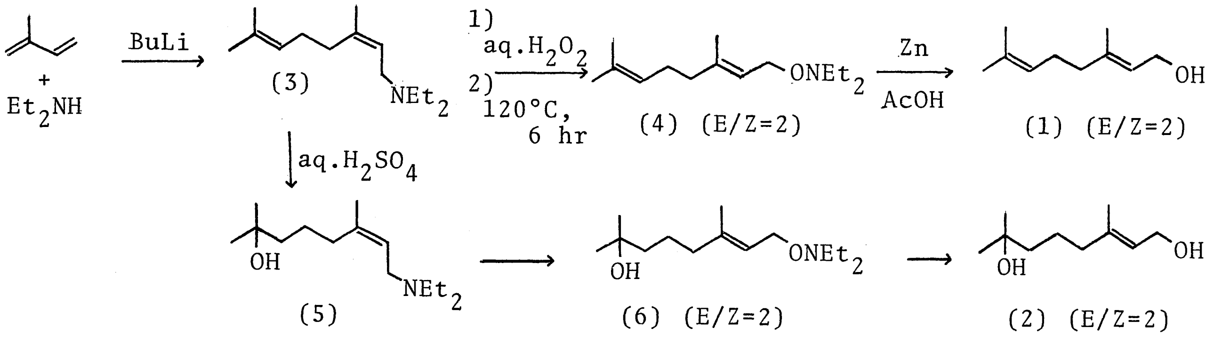
A NEW ROUTE TO 3,7-DIMETHYL-2,6-OCTADIEN-1-OL AND 3,7-DIMETHYL-2-OCTENE-1,7-DIOL FROM ISOPRENE

Kunihiko TAKABE, Takao KATAGIRI, and Juntaro TANAKA
Department of Synthetic Chemistry, Faculty of Engineering,
Shizuoka University, Hamamatsu 432

A convenient synthetic method for 3,7-dimethyl-2,6-octadien-1-ol (1) (geraniol and nerol) and 3,7-dimethyl-2-octene-1,7-diol (2), involving the anionic telomerization of isoprene and the rearrangement of amine oxide was established. The overall yields of (1) and (2) (E/Z ratio=2) from isoprene were 61 and 44%, respectively.

The step-wise synthesis of polyisoprenoid alcohols has been well established$^{1)}$, but new preparations are still being described$^{2)}$. To our knowledge, however, the selective synthesis of 3,7-dimethyl-2,6-octadien-1-ol (geraniol and nerol) (1) and 3,7-dimethyl-2-octene-1,7-diol (hydroxygeraniol and hydroxynerol) (2) by the telomerization or the oligomerization of isoprene has not been reported$^{3)}$. We herein describe a new route to (1) and (2) from isoprene.



N,N-Diethylnerylamine (3)$^{4)}$ was prepared by the butyllithium-initiated telomerization of isoprene with diethylamine (5 : 1) in a benzene-ether solution at 55°C for 30 hr in an 80% yield. To a methanol solution of (3) was added dropwise aqueous hydrogen peroxide (30%) under ice-cooling. The mixture was allowed to warm to room temperature and then left for 15 hr. The excess hydrogen peroxide was destroyed by the addition of a small amount of platinum oxide$^{5)}$. After removal of the solvents under reduced pressure, the crude amine oxide was obtained quantitatively. A benzene solution of this amine oxide was heated at 115-125°C for 6 hr in a sealed tube and then the distillation of the products gave O-(3,7-dimethyl-2,6-octadienyl)-N,N-diethylhydroxylamine (4) in an 81% yield.

[(4); bp 95-97°C/2.0mmHg, ir(neat, cm^{-1}): 1660, 1015 and 823, nmr(CCl_4,δ): 1.07(6H,t,J=7.0Hz), 1.50-1.76(9H,m), 2.61(4H,q,J=7.0Hz), 4.08(2H,bd,J=7.0Hz), 4.82-5.42(2H,m), 1.90-2.16(4H,m).].

Reductive N-O bond fission[6] of (4) with zinc dust in acetic acid at 27°C for 15 hr gave (1) (a ca. 2 : 1 mixture of geraniol and nerol)[7] in a 94% yield.

3,7-Dimethyl-2-octene-1,7-diol (2) was synthesized as follows; N,N-Diethylnerylamine (3) was hydrated by aqueous sulfuric acid at 45°C for 5 hr to give N,N-diethyl(6,7-dihydro-7-hydroxyneryl)amine (5) in a 93% yield.

[(5); bp 115-117°C/3.0mmHg, ir(neat, cm^{-1}): 3380, 1660, 1190, 1155 and 830, nmr(CCl_4,δ): 0.91(6H,t,J=7.0Hz), 1.07(6H,s), 1.23-1.47(4H,m), 1.64(3H,bs), 1.72-2.12(2H,m), 2.46(4H,q,J=7.0Hz), 2.24(1H,bs), 2.86(2H,d,J=7.0Hz), 5.13(1H,t,J=7.0Hz)].

The subsequent treatment of (5) as mentioned above afforded a ca. 2 : 1 mixture of hydroxygeraniol and hydroxynerol (2) in a combined yield of 59% from (5) through the hydroxylamine (6).

[(6); bp 120-125°C/1.5mmHg, ir(neat, cm^{-1}): 3390, 1660, 1145, 1015 and 825, nmr(CCl_4,δ): 1.08(6H,t,J=7.0Hz), 1.12(6H,s), 1.28-1.55(4H,m), 1.55-1.77(3H,m), 1.80-2.20(2H,m), 2.63(4H,q,J=7.0Hz), 4.09(2H,bd,J=7.0Hz), 5.00-5.42(1H,m)].

[(2); bp 105-109°C/0.45mmHg, ir(neat, cm^{-1}): 3350, 1660, 1145, 1000 and 830, nmr(CCl_4,δ): 1.13(6H,s), 1.27-1.52(4H,m), 1.62 and 1.69(3H,s), 1.80-2.20(2H,m), 3.29(2H,s), 4.00(2H,bd,J=7.0Hz), 5.02-5.52(1H,m)].

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References and Notes

1) P. de Mayo "The Chemistry of Natural Products" ed. by K. W. Bentley, Vol. 2, Interscience Publ., New York, (1959).
2) For recent examples of the synthesis of acyclic terpenes see: S. Kobayashi and T. Mukaiyama, Chem. Lett., 705 (1974). M. Ohki and K. Mori, Agr. Biol. Chem., 38, 177 (1974). G. Cardillo, M. Content and S. Sandri, Tetrahedron Lett., 2215 (1974). L. J. Altman, L. Ash and B. Marson, Synthesis, 129 (1974). B. S. Pitzele, J. S. Baran and D. H. Steinman, J. Org. Chem., 40, 269 (1975). M. Hidai, M. Ishiwatari, H. Yagi, E. Tanaka, K. Onozawa and Y. Uchida, Chem. Commun., 170 (1975).
3) It is well-known that the cationic telomerization of isoprene with carboxylic acid or prenyl chloride affords a mixture of geranyl, neryl, linalyl, lavandulyl and -terpinyl derivatives. [J. Tanaka, T. Katagiri and T. Takeshita, Nippon Kagaku Zasshi, 89, 65 (1968). K. V. Leets, Zh. Obshch. Khim., 28, 3096 (1958).].
4) K. Takabe, T. Katagiri and J. Tanaka, Tetrahedron Lett., 4009 (1972).
5) The platinum oxide was recovered by filtration.
6) V. Rautenstrauch, Helv. Chim. Acta, 56, 2492 (1973).
7) The structures of the products were verified by compatible spectral data (ir, nmr and mass spectra).

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