Tetrahedron Letters,Vol.23,No.31,pp 3193-3194,1982 0040-4039/82/313193-02$03.00/0
Printed in Great Britain

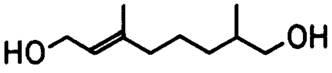
A NOVEL SYNTHESIS OF (E)-3,7-DIMETHYL-2-OCTENE-1,8-DIOL SECRETED BY THE AFRICAN MONARCH USING THE RING-OPENING REACTION OF α-METHYL-β-PROPIOLACTONE

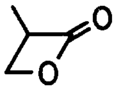
Tamotsu Fujisawa,* Toshio Sato, Tatsuo Kawara, and Atsunari Noda
Chemistry Department of Resources, Mie University, Tsu, Mie 514, Japan

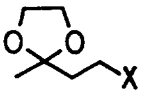
Summary: *The regioselective ring-opening reaction of α-methyl-β-propiolactone with 3,3-ethylenedioxybutylmagnesium bromide in the presence of copper(I) catalyst afforded 2-methyl-6-oxoheptanoic acid, which was easily converted into (E)-3,7-dimethyl-2-octene-1,8-diol in good yield.*

Although (E)-3,7-dimethyl-2-octene-1,8-diol (1) has been characterized as one of the major components of the hairpencil of the *Danaus chrysippus* (African Monarch butterfly),[1] a few reports have been published on the synthesis of 1.[1,2] We now wish to describe a novel method for the synthesis of the monoterpenediol 1, utilizing the regioselective ring-opening reaction of α-methyl-β-propiolactone (2) with Grignard reagent in the presence of a copper(I) catalyst.[3] The lactone 2 provides a useful C_4 building block for terpene synthesis, that is, the key reaction of the lactone 2 with 3,3-ethylenedioxybutylmagnesium bromide (4) furnishes the C_8 skeleton from C_3 to C_8 of the terpenediol 1 with proper functional groups.

One of the starting materials, α-methyl-β-propiolactone (2) is easily available by the cyclization of 3-bromo-2-methylpropionic acid.[4] Another starting material, 3,3-methylenedioxybutyl bromide was easily obtained in 79% yield from 3-buten-2-one, ethylene glycol and hydrogen bromide.[5] The reaction of the lactone 2 with the Grignard reagent 4, prepared in 65% yield from the bromide 3 in THF at room temperature, was performed in THF-Me_2S (30:1) in the presence of copper(I) iodide (2 mol%) at -10 °C for 1.5 h. After treatment of the reaction mixture with 3N HCl aq solution, 2-methyl-6-oxoheptanoic acid (5) was obtained in a yield of 87%; bp 130 °C/1 mmHg (lit.[6] 155 ∿ 156 °C/7 mmHg); NMR (CCl_4) δ 1.12

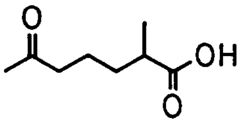

1


2

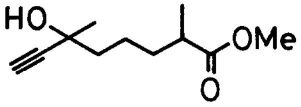

3 X = Br 4 X = MgBr

(3H, d, J = 6 Hz), 1.55 (4H, m), 2.06 (3H, s), 2.30 (3H, m), 9.15 (1H, s); IR 3500 $\sim$ 3000 (broad, OH) and 1710 cm^{-1} (C=O).

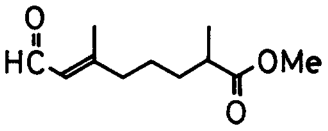
According to the procedure of Erman,[7] introduction of a prenyl alcohol moiety of 1 by two-carbon homologation was achieved by the rearrangement of tertiary propargyl alcohol to α,β-unsaturated aldehyde. Thus, esterification of 5 with diazomethane and addition of lithium acetylide[8] in THF at -78 °C for 2 h gave methyl 2,6-dimethyl-6-hydroxy-7-octynoate (6) in a yield of 97%; bp 160 °C/ 1.5 mmHg; NMR (CCl_4) δ 1.10 (3H, d, J = 7 Hz), 1.38 (3H, s), 1.51 (6H, m), 2.30 (1H, m), 2.35 (1H, s), 3.0 (1H, broad S), 3.60 (3H, s); IR 3450 (OH), 3270 ($\equiv$CH) and 1720 cm^{-1} (C=O). Treatment of the propargyl alcohol 6 with polymeric diphenylsilyl vanadate in xylene under reflux for 2 h gave methyl 2,6-dimethyl-8-oxo-6-octenoate (7) in 82% yield (E:Z = 3:1). The (E)-isomer was easily isolated by VPC (SE 30, 3m, 150 °C); NMR (CCl_4) δ 1.15 (3H, d, J = 7 Hz), 1.55 (4H, m), 1.9 $\sim$ 2.8 (3H, m), 2.17 (3H, s), 3.60 (3H, s), 5.70 (1H, d, J = 8 Hz), 9.75 (1H, d, J = 8 Hz); IR 1720 (ester carbonyl) and 1660 cm^{-1} (aldehyde carbonyl). Reduction of 7 with aluminum hydride in THF at -15 °C for 3 h gave (E)-3,7-dimethyl-2-octene-1,8-diol (1) in 89% yield; NMR (CCl_4) δ 0.85 (3H, d, J = 7 Hz), 1.30 (5H, m), 1.65 (s, 3H), 2.00 (2H, m), 3.00 (2H, broad S), 3.35 (2H, d, J = 6 Hz), 4.05 (2H, d, J = 7 Hz), 5.35 (1H, t, J = 7 Hz); IR 3350 (OH) and 910 cm^{-1} (C=C). Thus, the desired terpenediol 1 was obtained in an overall yield of 46% in five steps starting from the lactone 2.



5



6



7

As mentioned above, the regioselective ring-opening reaction of α-methyl-β-propiolactone as well as β-methyl-β-propiolactone,[9] should provide a promising method for the synthesis of terpenes by a combination with various organometallic reagents, and by further transformation of the carboxylic group to other functional groups.

References

1. J. Meinwald, W. R. Thompson, and T. Eisner, *Tetrahedron Lett.*, 1971, 3485.
2. G. Bidan, J. Kossanyi, V. Meyer, and J. P. Morizur, *Tetrahedron*, 33, 2193 (1977).
3. T. Sato, T. Kawara, M. Kawashima, and T. Fujisawa, *Chem. Lett.*, 1980, 571.
4. H. Johansson, *Chem. Zentralbl.*, 1916, II, 557 [C. A., 11, 2576 (1917)].
5. T. Sato, T. Kawara, K. Sakata, and T. Fujisawa, *Bull. Chem. Soc. Jpn.*, 54, 505 (1981).
6. L. Blaha, J. Weichet, and B. Kakac, *Collect. Czech. Chem. Commun.*, 30, 1214 (1965).
7. M. B. Erman, I. S. Aul'chenko, L. A. Kheifits, V. G. Dulova, J. N. Novikov, and M. E. Vol'pin, *Tetrahedron Lett.*, 1976, 2981.
8. M. M. Midland, *J. Org. Chem.*, 40, 2250 (1975).
9. T. Fujisawa, T. Sato, T. Kawara, A. Noda, and T. Obinata, *Tetrahedron Lett.*, 21, 2533 (1980); T. Sato, T. Kawara, A. Nishizawa, and T. Fujisawa, *ibid.*, 21, 3377 (1980); T. Fujisawa, T. Sato, T. Kawara, and K. Ohashi, *ibid.*, 22, 4823 (1981).

(Received in Japan 30 April 1982)