CHEMISTRY LETTERS, pp. 1829-1832, 1986.

Selective Synthesis of 1,3-Dienic Terpenes in a β-Form through Regioselective 1,4-Elimination of Allylic Ethers

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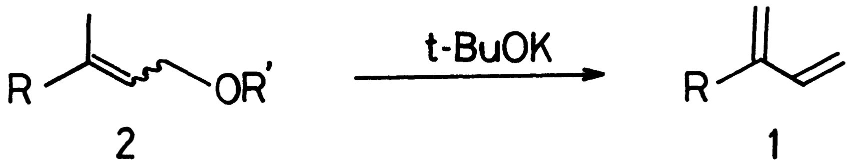
γ-Methyl-substituted allylic ethers proved to be converted into β-substituted dienes exclusively on treatment with t-BuOK in refluxing THF or cyclohexane.

Terpenoids with a β-substituted dienic moiety **1** constitute an important class of compounds in perfumery essential oils. These compounds can be most conveniently synthesized from readily accessible terpene alcohols such as geraniol and farnesol if an appropriate dehydration method or its equivalent process is available. Tanaka and Hata disclosed a base-catalyzed elimination of geranyl- and neryldialkylamines, which, however, suffered from contaminations of various isomers.1) Tsuji and his coworkers2) reported a palladium-catalyzed elimination of geranyl, neryl, and linalyl acetates which also failed to afford the single isomer.3) More recently, the selectivity of the palladium-catalyzed elimination has been improved to a considerable extent by employing allylic amines.4) On the contrary, Negishi et al. found that geranyl and neryl acetates were specifically converted to ocimene and myrcene, respectively, on treatment with propargylzinc bromide in the presence of a palladium catalyst.5) These papers prompted us to describe here our new route for β-substituted dienes.6)

As depicted below (Eq. 1), exposure of γ-methyl-substituted allylic ethers **2** to an excess of t-BuOK in refluxing THF or cyclohexane affords dienes **1** in a β-form exclusively irrespective of the stereochemical purity of starting materials. No other isomers are detectable. When the reaction proceeds rather



(1)

slowly, addition of 18-crown-6 accelerates the rate effectively. The results are summarized in Table 1.

Schlosser and his coworkers reported that disubstituted allylic ethers underwent no elimination but metallation on treatment with their "LICKOR super base".[7,8] Apparently, the present results are ascribable to the presence of the γ-methyl group. t-BuOK attacks the methyl hydrogen preferentially rather than the methylene hydrogen. This explains why the β-isomers are formed exclusively both from trans and cis allylic ethers. It is seen from Fig. 1 as well as Table 1 that the trans isomers are more susceptible to the elimination than the cis counterparts.

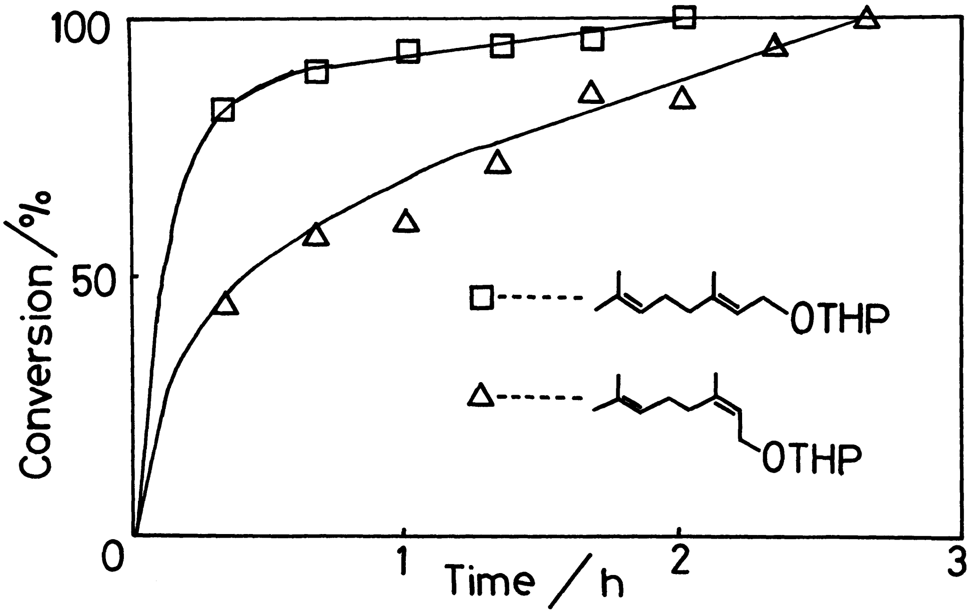
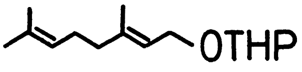
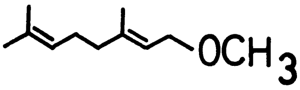
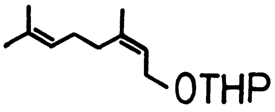
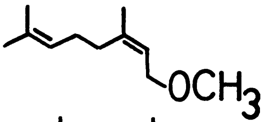
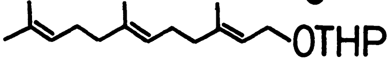
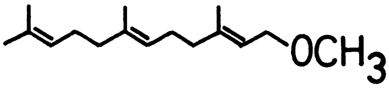
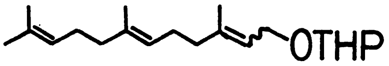
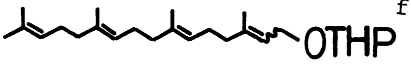
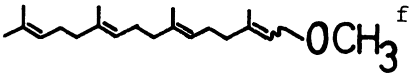


Fig. 1. Time-conversion curves for the reaction of an equimolar mixture of geranyl and neryl ethers with t-BuOK in the presence of 18-crown-6 in THF.

Another notable feature is that tetrahydropyranyl ethers undergo more facile elimination than the corresponding methyl ethers. Apparently, additional coordination of the tetrahydropyranyl oxygen toward potassium facilitates elimination.

Table 1. Conversion of allylic ethers **2** into dienes **1**

2	Solvent	18-Crown-6a)	Reaction time/h	Yield of **1**/%
	THF	A	6	89b)
	CHc)	B	2	73b)
	THF	A	18	41b)
	THF	B	2	76b)
	THF	A	18	83b)
	CHc)	B	4	64b)
	THF	B	7	35b)
	THF	B	2	84d)
	THF	B	7	82d)
 e)	THF	B	7	85d)
 f)	THF	B	7	89d)
 f)	THF	B	8	74d)

a) A: No 18-crown-6 was added; B: two equiv of 18-crown-6 was added.

b) Determined by means of GLC. c) CH: cyclohexane.

d) Isolated yields after column chromatography or distillation.

e) E/Z = 70:30. f) E/Z = 92:8.

Typical procedure is as follows. A THF solution (10 ml) containing farnesyl tetrahydropyranyl ether (306 mg, 1 mmol), t-BuOK (1.25 g, 10 mmol), and 18-crown-6 (532 mg, 2 mmol) was heated at reflux for 2 h. The reaction mixture was extracted with benzene-water. The organic layer was washed with water, dried ($MgSO_4$), and evaporated. Distillation of the residual oil delivered β-farnesene (171 mg, 84%, bp 125 °C/1333 Pa, Kugelrohr bath temperature) which was confirmed by comparison with an authentic sample.

Thanks are due to Prof. M. Schlosser of Universitē de Lausanne for informing us of his results prior to publication.

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(Received June 16, 1986)