

A NEW METHOD FOR AN EPOXIDATION OF OLEFINS AND ITS APPLICATION
TO A BIOMIMETIC TYPE SYNTHESIS OF MONOTERPENES, LINALYLOXIDES

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Geraniol (1) was transformed into monoterpenes, linalyloxides (4 and 5) along the biogenetic sequence by the oxidation via geranyl o-nitrophenyl selenide (2). This paper also describes a new method for an epoxidation of olefins.

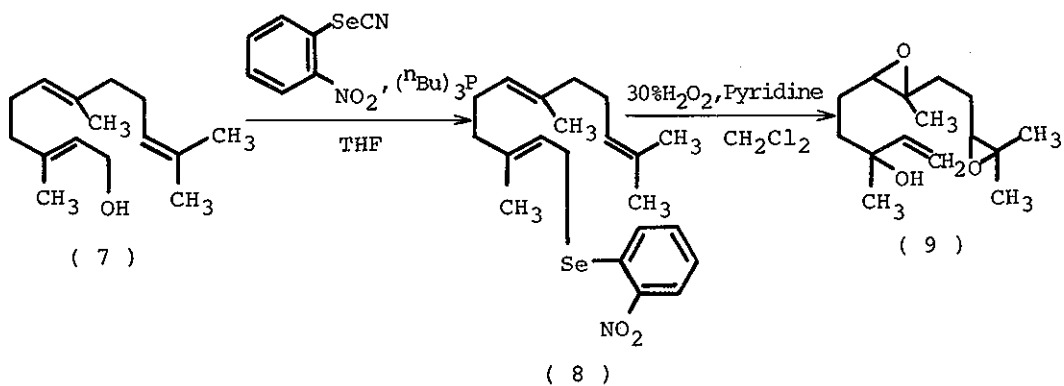
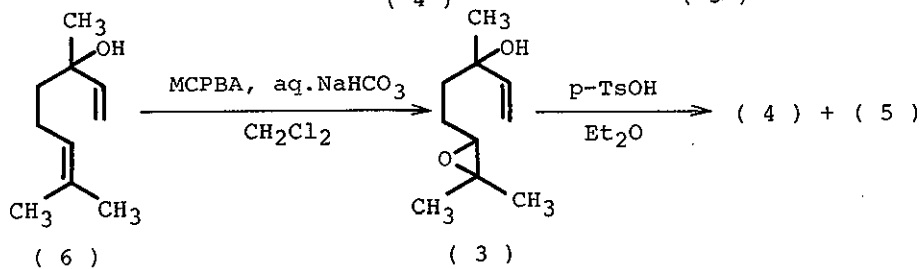
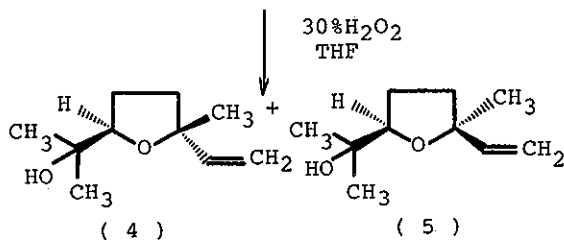
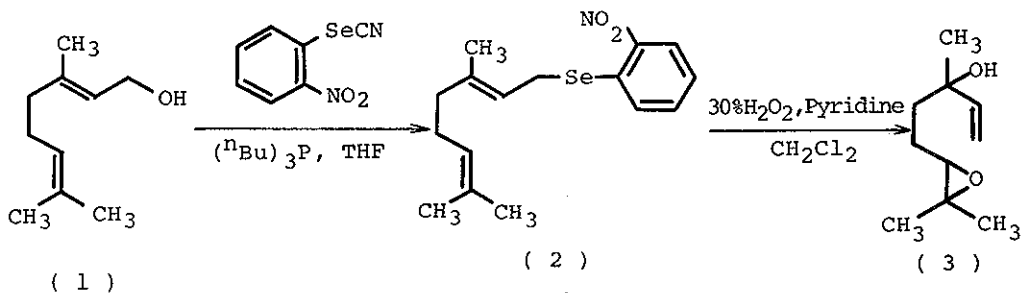
trans- and cis-Linalyloxides, isolated from Lilium makinoi¹ and Humulus lupulus², have been assigned the structure 4 and 5, respectively, by Kotake.¹ The synthesis of these monoterpenes has been achieved by the oxidation of linalool (6), followed by the acidic treatment of the resulting epoxide (3), but a ring opening of 3 has been encountered as an undesired side reaction during the oxidation.^{1,3,4} We have been investigating a biogenetic type synthesis of natural products by using the oxidation as a key reaction^{5,6}, and here we wish to report a total synthesis of trans- (4) and cis-linalyloxides (5) from geraniol (1) along a biomimetic line.

Treatment of geraniol (1) with tri-n-butylphosphine and o-

nitrophenyl selenocyanide in dry tetrahydrofuran gave in a high yield the key intermediate (λ) [m/e 337 and 339 (M^+), (CCl_4) 3.50 (2H, d, J 8 Hz, $-CH_2-SeAr$], which was oxidized in order to get linalool (δ) by a [2.3]sigmatropic rearrangement of the selenoxide derived from the selenide (λ) using the two-phase pyridine buffered 30 % hydrogen peroxide-dichloromethane procedure.^{8,9} Oxidation of λ with an excess of hydrogen peroxide in the procedure mentioned above afforded quantitatively the epoxide (β) [$\delta(CCl_4)$ 1.65 (9H, s, 3 x CH_3), 2.6 (1H, t, J 6 Hz, $\begin{array}{c} H \\ \diagdown \\ C \\ \diagup \\ CH_3 \end{array}$) and 4.8 - 6.1 (3H, m, $-CH=CH_2$)] instead of the expected linalool (δ). Since it has been reported that benzeneselenic acid generated by the elimination of selenoxide group is further oxidized to benzeneseleninic acid with hydrogen peroxide,¹⁰ it might be considered that *o*-nitrobenzeneseleninic acid which was produced during the [2.3]sigmatropic rearrangement of the selenoxide catalyzed the epoxidation of an olefin system. Although the [2.3]sigmatropic rearrangement of selenoxide^{11,12} and the olefin synthesis by the eliminations of phenylselenoxide^{10,13} by using an excess amount of hydrogen peroxide have been reported, no epoxide formation has been described.¹⁴ The structure of this epoxide β was determined by a direct comparison with the authentic sample prepared as follows. Thus oxidation of linalool (δ) with *m*-chloroperbenzoic acid in dichloromethane in the presence of sodium hydrogen carbonate aqueous solution¹⁶ to yield quantitatively the epoxide β which was identical with the sample obtained by the first method in spectral comparisons. Thus, we could demonstrate the new epoxidation reaction.¹⁵

On the other hand, a reaction of the selenide ζ with 30 % hydrogen peroxide in tetrahydrofuran with no buffer gave directly trans- (\mathcal{A}) and cis-linalyloxides (\mathcal{B}) in 40 % and 38 % yield, respectively, via the oxidation of selenide, followed by [2.3]-sigmatropic rearrangement, epoxidation and then ring closure. The spectroscopic data of our products \mathcal{A} and \mathcal{B} were found to be identical with those of the authentic specimens described in the literature.³ Epoxide (\mathcal{C}) was also treated with p-toluenesulphonic acid in ether to give \mathcal{A} and \mathcal{B} in almost identical yields with those of described above.

Analogously, farnesol (η) was transformed to the selenide θ [m/e 405 and 407 (M^+), δ (CCl_4) 3.5 (2H, d, J 8 Hz, $-CH_2-SeAr$), which was subjected to oxidation and rearrangement reaction by using the two-phase pyridine buffered 30 % hydrogen peroxide-dichloromethane procedure to afford the diepoxide [δ (CCl_4) 1.23 (12H, s, 4 x CH_3) and 4.8 - 6.1 (3H, m, $-CH=CH_2$). Thus o-nitrophenylseleninic acid might represent a new catalyst for the epoxidation of substituted olefins by hydrogen peroxide and we could demonstrate the simple synthesis of trans- (\mathcal{A}) and cis-linalyloxides (\mathcal{B}). The scope and limitation of this new catalyst for the epoxidation are under investigation.



References and notes

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