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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.

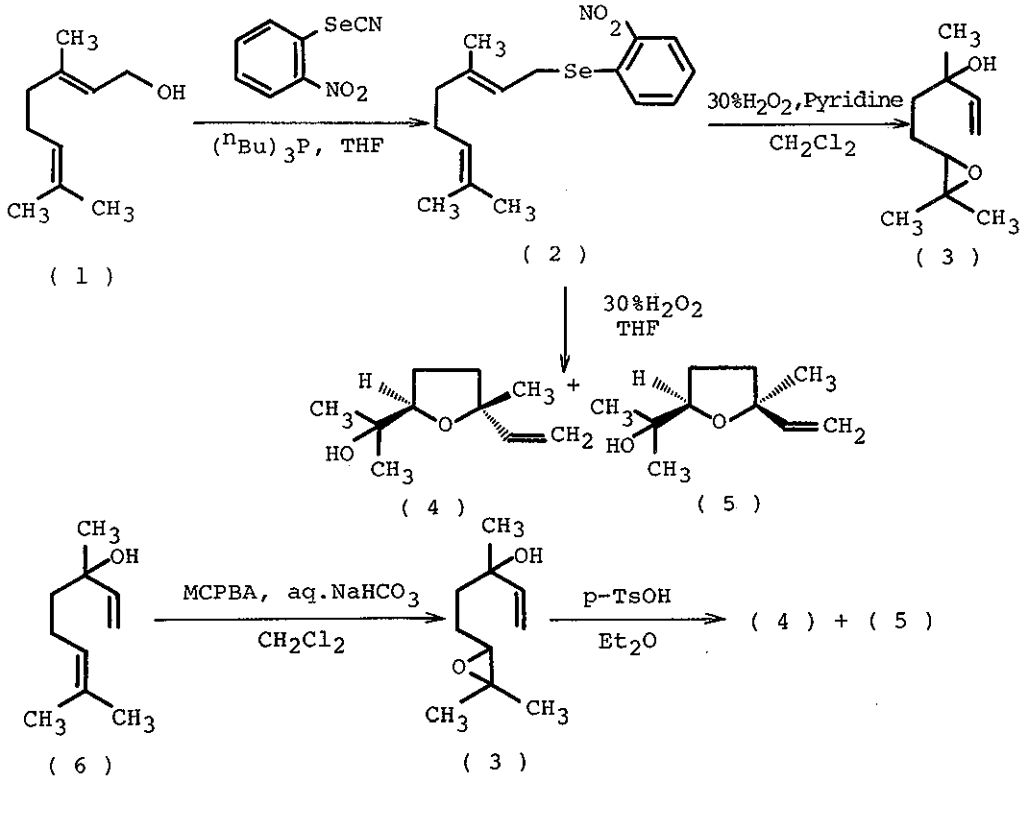
trans- and cis-Linalyloxides, isolated from Lilium makinoi[1] and Humulus lupulus[2], have been assigned the structure 4 and 5, respectively, by Kotake.[1] The synthesis of these monoterpenes has been achieved by the oxidation of linalool (6), followed by the acidic treatment of the resulting epoxide (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.

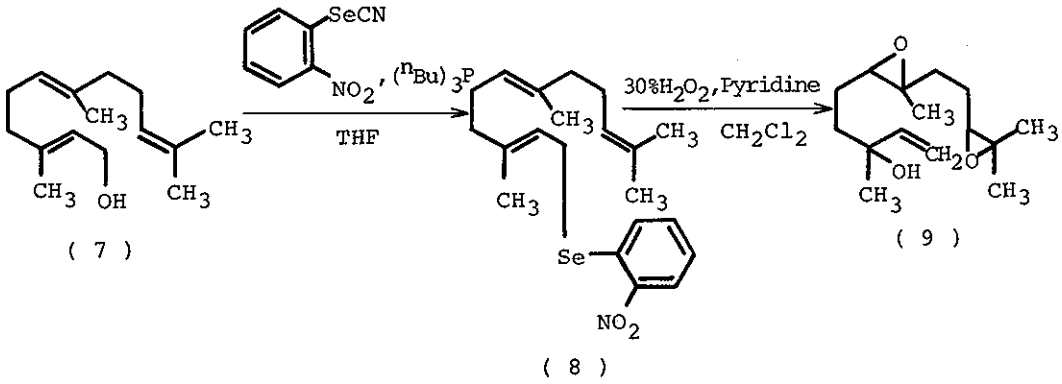
Treatment of geraniol (1) with tri-n-butylphosphine and o-

nitrophenyl selenocyanide in dry tetrahydrofuran gave in a high yield the key intermediate (2) [m/e 337 and 339 (M^+), (CCl_4) 3.50 (2H, d, J 8 Hz, -C<u>H</u>$_2$-SeAr], which was oxidized in order to get linalool (6) by a [2.3]sigmatropic rearrangement of the selenoxide derived from the selenide (2) using the two-phase pyridine buffered 30 % hydrogen peroxide-dichloromethane procedure.[8,9] Oxidation of 2 with an excess of hydrogen peroxide in the procedure mentioned above afforded quantitatively the epoxide (3) [$\delta(CCl_4)$ 1.65 (9H, s, 3 x CH_3), 2.6 (1H, t, J 6 Hz,  and 4.8 - 6.1 (3H, m, -C<u>H</u>=C<u>H</u>$_2$)] instead of the expected linalool (6). Since it has been reported that benzeneselenic acid generated by the elimination of selenoxide group is furhter 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 3 was determined by a direct comparison with the authentic sample prepared as follows. Thus oxidation of linalool (6) with m-chloroperbenzoic acid in dichloromethane in the presence of sodium hydrogen carbonate aqueous solution[16] to yield quantitatively the epoxide 3 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 2 with 30 % hydrogen peroxide in tetrahydrofuran with no buffer gave directly trans- (4) and cis-linalyloxides (5) 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 4 and 5 were found to be identical with those of the authentic specimens described in the literature.[3] Epoxide (3) was also treated with p-toluenesulphonic acid in ether to give 4 and 5 in almost identical yields with those of described above.

Analogously, farnesol (7) was transformed to the selenide 8 [m/e 405 and 407 (M^+), δ (CCl_4) 3.5 (2H, d, J 8 Hz, $-C\underline{H}_2$-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, $-C\underline{H}=C\underline{H}_2$). 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- (4) and cis-linalyloxides (5). The scope and limitation of this new catalyst for the epoxidation are under investigation.


SeCN
NO2
(nBu)3P, THF
NO2
Se
30%H2O2,Pyridine
CH2Cl2
OH
(1)
(2)
(3)
30%H2O2
THF
(4)
(5)
MCPBA, aq.NaHCO3
CH2Cl2
p-TsOH
Et2O
(4) + (5)
(6)
(3)


SeCN
NO2, (nBu)3P
THF
30%H2O2,Pyridine
CH2Cl2
OH
Se
NO2
(7)
(8)
(9)

References and notes

1 T. Okazaki, A. Ohsuka, and M. Kotake, J. Chem. Soc. Japan, 1973, 359.

2 Y. Naya and M. Kotake, J. Chem. Soc. Japan, 1968, 89, 113.

3 D. Felix, A. Melera, J. Seibl, and E. sz. Kovats, Helv. Chim. Acta, 1963, 46, 1513.

4 E. Klein, H. Farnow, and W. Rojahn, Annalen, 1964, 675, 73.

5 T. Kametani, M. Takemura, M. Ihara, K. Fukumoto, and K. Takahashi, Heterocycles, 1977, 6, 99.

6 T. Kametani and K. Fukumoto, Synthesis, 1972, 657; T. Kametani, K. Fukumoto, and F. Satoh, Bioorg. Chem., 1974, 3, 430.

7 P. A. Grieco, S. Gilman, and M. Nishizawa, J. Org. Chem., 1976, 41, 1485.

8 H. J. Reich, J. M. Renga, and I. L. Reich, J. Org. Chem., 1974, 39, 2133.

9 H. J. Reich, J. Org. Chem., 1975, 40, 2570.

10 K. B. Sharpless and R. F. Laner, J. Amer. Chem. Soc., 1973, 95, 2697.

11 K. B. Sharpless and R. F. Laner, J. Amer. Chem. Soc., 1972, 94, 7154.

12 H. J. Reich, J. Org. Chem., 1975, 40, 2570.

13 K. B. Sharpless and R. F. Laner, J. Org. Chem., 1974, 39, 429.

14 Hydrogen peroxide in the presence of Selenium dioxide has been reported to hydroxylate[14a], acetoxylate[14b], and epoxidize[14c] the olefins.

a) N. Sonoda and S. Tsutsumi, Bull. Chem. Soc. Japan 1965, 38, 958.

b) K. A. Javaid, N. Sonoda, and S. Tsutsumi, Tetrahedron Letters, 1969, 4439.

c) M. Sumimoto, T. Suzuki, and T. Kondo, Agric. and Biol. Chem. (Japan), 1974, 38, 1061.

15 In contrast to the epoxidation of olefinic alcohol by tert-butylhydroperoxide catalyzed by transition metal[15a,b], the olefins removed from the hydroxyl group were epoxidized.

a) K. B. Sharpless and R. C. Michaelson, J. Amer. Chem. Soc., 1973, 95, 6136.

b) S. Tanaka, H. Yamamoto, H. Nozaki, K. B. Sharpless, R. C. Michaelson, and J. D. Cutting, J. Amer. Chem. Soc., 1974, 96, 5254.

16 W. K. Anderson and T. Veysoglu, J. Org. Chem., 1973, 38, 2267.

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