

Allylic Oxidation of Myrcene

Ayşe MAKASÇI¹, Hüseyin ANIL²

Abstract: In this study, allylic oxidation reaction of open chain monoterpene, myrcene was studied. Our aim was to obtain pine-bark insect pheromones ipsdienol from myrcene. In the experiments, chromium trioxide (CrO₃), CrO₃-pyridine complex, pyridinium chlorochromate (PCC), tert-butyl hydroperoxide (t-BuOOH) and tert-butyl perbenzoate (TBPB) were chosen as oxidants, benzotrifluoride, dichloromethane, acetonitrile, CCl₄, acetanhydride, benzene, acetic acid, ethylacetate ve glacial acetic acid as solvents, while some salts of Cu(I) and Cu(II) compounds and together with L-prolin, S-prolin, SeO₂ and PdCl₂ were used as catalysts. Reaction products were determined by GC-MS analysis. The conversion of myrcene to ipsdienol was not so successful. Because, myrcene tends to isomerisation to different cyclic and open chain compounds before its allylic oxidation could occur. In the allylic oxidation reaction of particularly, the conversion of myrcene to ipsdienol could have been obtained with BTF only.

Keywords: Allylic oxidation, α -pinene, myrcene, ipsdienol.

Mirsen'in Allilik Oksidasyonu

Özet: Bu çalışmada, açık zincirli monotermen olan mirsenin allilik yükseltgenme reaksiyonları incelenmiştir. Burada amaçlanan, çam kabuk böceği feromonu olan , mirsenin ipsdienole dönüştürülmesidir. Bu çalışmada yükseltgen olarak kromtrioksit (CrO₃), kromtrioksit-piridin kompleksi, piridinyum klorokromat (PCC), tersiyer butil hidroperoksit (t-BuOOH) ve tersiyer butil perbenzoat (TBPB), solvent olarak benzotriflorür (BTF), diklorometan, asetinitril, CCl₄,asetanhidrit, benzen, asetik asit, etil asetat ve glasiyel asetik asit, katalizör olarak ise bazı Cu(I) ve Cu(II) tuzları, bakır tuzları ile birlikte L-prolin, S-prolin kompleksleri, SeO₂ ve PdCl₂ kullanılmıştır. Sözü edilen katalizörler ve yükseltgenler ile farklı yöntemler uygulanmış ve reaksiyon sonucunda oluşan ürünler GC-MS ile belirlenmiştir. Mirsenin ipsdienole dönüştürülmesinde yeterince başarı sağlanamamıştır; çünkü,mirsenin allilik yükseltgenmeye uğramadan önce bazı halkalı ve açık zincirli bileşiklere izomerleştiği gözlenmiştir. Mirsenin allilik yükseltgenmesinde en iyi verimler, yükseltgen olarak piridinyum klorokromatın kullanılmasıyla elde edilmiştir. Ayrıca çözücü olarak benzotriflorür (BTF)'ün kullanılması yükseltgenme ürünleri veriminin daha da artmasını sağlamıştır. Özellikle, mirsenin ipsdienole dönüştürülmesi ancak bu çözücünün kullanılması ile gerçekleştirilebilmiştir.

Anahtar Sözcükler: Allilik yükseltgenme, α -pinen, mirsen , ipsdienol.

¹ Mugla University, Department of Chemistry, 48100 Mugla-TURKEY mayse@mu.edu.tr

² Ege University, Department of Chemistry, 35100 Bornova İzmir-TURKEY

Introduction

In this study, the syntheses of ipsdienol which is important pheromones, from terpenic hydrocarbons such as myrcene was aimed. It is noticed that there is a steep increase in the use of pheromones in order to struggle against pine bark pests which damage pine trees. It is very important to fight against the pests by using pheromones instead of agricultural pesticides for environmental and ecological balance. Synthesis and production of pheromones to struggle against the pine damagers bark pests in pine trees is highly important from both scientific and economic points of view.

Pheromone, is a kind of chemical substance which is secreted by the pest to the outside and creates a specific stimulation to the other individuals of the same species. Male and female pests have to join for breeding (gamogenesis). One way for the encountering of pests is via pheromones secreted. It is thought to war against to pests by utilizing the pheromone secretion of pests and this method is started to be applied now.

During the flying season, adult males of *Ips sexdentatus*, after leaving the pupas and entering the new host tree, produce ipsdienol which is the aggregation pheromone. (s)-cis-Verbenol that is bark-broody substance and increases attractive effect, come into being after contacting with alpha-pinene resin of the host tree. Many researchers have determined ipsdienol, aminitol, ipsenol, cis-verbenol and methylbutenol compounds in the aggregation pheromone produced by *Ips Sexdentatus*.

It is known that pheromones produced by every bark pest species have different compounds and have a proximity with the terpenes of host tree. Besides, it is also known that the reaction of bark pests against to different isomers of the same compounds is different.

Allylic oxidation belongs to an important group of olefin oxidations and remains a reaction of considerable value in organic synthesis. These allylic oxidation reactions have been traditionally performed with chromium reagents, as CrO_3 -pyridine complex, chromium trioxide and 3,5-dimethylpyrazole, pyridinium chlorochromate (PCC), pyridinium dichromate (PDC), sodium chromate and sodium dichromate in acetic acid (Fig. 1).

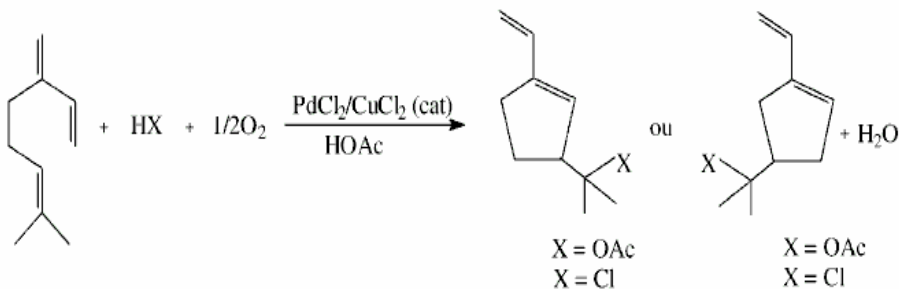


Figure 1 Myrcene undergoes an intramolecular oxidative cyclization combined with nucleophilic addition which leads to products with cyclopentane structure.

Materials and Methods

1. Instrumentation

Gas chromatographic (GC) analyses were performed on an HP 6890 gas chromatograph with a split-splitless injector and HP Agilent 6890 Series autosampler was used. Separation was achieved HP-1 MS capillary column with a 60 m x 0.32 mm I.D., coated with methyl siloxane (0.25 μm film thickness) and helium (45 mL/minute) as carrier gas, and with an HP 5973 MSD Hewlett-Packard mass-selective detector. Mass detector transfer line temperature, 280°C, solvent delay time, 3.5 minute. The oven temperature was set at 70°C, increased at the rate of 6°C/minute to 210°C and then held for 1 minute. The injector temperature was 250°C pressures 17.5 psi. The sample was injected in split mode (50:1 split ratio). The carrier gas flow 2.5 mL/minute. Data

analyses were performed using the Hewlett-Packard Chemstation software and "Wiley 275.L" Library Search.

2. Experimental

Myrcene was used as substrates. Ipsdienol was synthesized.

Method 1.

In a typical procedure, a mixture of myrcene (1 mL), BTF (1 mL), CCl₄ (4 mL) and pyridinium chlorochromate (124.8 mg) was dissolved by stirring and the mixture was kept in the fridge at +4°C for oxidation and waited for 2 days. After waiting, the mixture was washed with water and shaken with CCl₄. The mixture was washed with water and shaken with CCl₄. The mixture was refluxed and boiled for 1 hour, with 1% KOH for alkaline hydrolysis. The mixture was washed with aqueous saturated solution of NaHCO₃ and extracted with CH₂Cl₂, dried over Na₂SO₄. Products were identified by GC-MS.

Method 2.

Into a 25 mL round-bottomed flask containing pyridinium chlorochromate (5.2 mL) and BTF (1 mL) was added commercial aqueous t-BuOOC(O)Ph (0.6 mL). After stirring for 2 minutes, myrcene was added and the flask was closed with a plastic top. The mixture was stirred at room temperature and then filtered through a plug alumina the reaction mixture was diluted with 50 mL of saturated NaHCO₃ aqueous solution extracted with 2x20 mL of ethylacetate. The ethylacetate layer was washed with water and dried over MgSO₄. Products were identified by GC-MS.

Method 3.

Into a 25 mL round-bottomed flask containing CrO₃ (29.5 mg) and BTF (1 mL) was added, commercial aqueous 70% t-BuOOH (0.64 mL). After stirring for 2 minutes, myrcene (1 mL) was added, and the flask was closed with a plastic top. The mixture was stirred at room temperature. Then filtered through a plug alumina. The filtrate was evaporated. The filtrate was washed with Et₂O. The oxidized compounds were identified by GC-MS.

Method 4.

A mixture of Cu₂O (17.4 mg), S-prolin (58.6 mg), myrcene (1 mL) was dissolved by stirring and heating in 5 mL of acetonitrile. Addition of t-BuOOC(O)Ph (0.39 mL) to the resulting colorless solution led immediately to a deep blue coloration. Then the blue color changed to green. The reaction mixture was cooled to room temperature, diluted with 50 mL saturated NaHCO₃ aqueous solution and extracted with 2x10 mL of Et₂O. The ether layer was washed with water and dried over MgSO₄. Products were identified by GC-MS.

Method 5.

A mixture of Cu₂O (14.3 mg), L-prolin (57.7 mg), acetic acid (1 mL) and myrcene (1 mL) was dissolved by stirring and heating in 5 mL acetonitrile. Addition of TBPB (0.39 mL) to the resulting colourless solution led immediately to a deep blue coloration. The resulting mixture was waited for 2 hours. After this time the blue color changed to green. The reaction mixture was cooled to room temperature, diluted with 50 mL of saturated NaHCO₃ aqueous solution and extracted with 2x10 mL of Et₂O. The ether layer was washed with water and dried over MgSO₄. Products were analyzed by GC-MS.

Results

Table 1 Some of the products determined by GC-MS in the allylic oxidation of myrcene according to Method-1

Products	Yield (%)
Ipsdienol	4.90 %
Limonene	1.36 %
p-Cymene	0.89 %
Carveol	0.27 %

Table 2 Some of the products determined by GC-MS in the allylic oxidation of myrcene according to Method-2

Products	Yield (%)
Ipsdienol	3.72 %
Limonene	10.58 %
β -Pinene	5.51 %
Limonene oxide	1.09 %
Camphene	0.99 %
p-Cymene	1.07 %

Table 3 Some of the products determined by GC-MS in the allylic oxidation of myrcene according to Method-3

Products	Yield (%)
Ipsdienol	1.81 %
Limonene	14.71 %
Carvone	1.68 %

Table 4 Some of the products determined by GC-MS in the allylic oxidation of myrcene according to Method-4

Products	Yield (%)
Limonene	4.75 %
Camphene	17.38 %

Table 5 Some of the products determined by GC-MS in the allylic oxidation of myrcene according to Method-5

Products	Yield (%)
Limonene	15.13 %
Camphene	4.58 %

Discussion

In coniferous trees, some compounds which have pheromone activities are being used for the biotechnical fight against bark beetles. It is known that α -pinene which has two different enantiomers is a substance of great importance in the host tree. When bark insects are exposed to the terpenes of the host tree, they excrete some oxygenated monoterpenes with pheromone activity.

In the study, the compounds including oxygene and ketone groups with pheromone activity have been realized deriving from α -pinene and its enantiomers .It is understood that allylic oxidation procedures are suitable to obtain cis- and trans-verbenol, cis-, trans- and rasemic verbenone and ipsdienol, which are found at various pine species and known with pheromone activity. An imported pheromone preparate, which is currently at used for biotechnical fighting

against the insects of *pinus brutia*, includes 75% *cis-verbenol*. It is thought that the excretion of pests can be used against them and has been started too apply.

Many researchers have detected *ipsdienol*, *aminitol*, *ipsenol*, *cis-verbenol* and *methylbutenol* compounds in the aggregation pheromone produced by *Ips sexdentatus*. *Ipsdienol*, *aminitol* or *ipsenol* which have effect on the pests are used in different ways. In addition, pheromones with trade marks *pheroprax* or *iplure*, which are the mixtures of *ipsdienol* (*aminitol* or *ipsenol*) + *cis-verbenol* + *methylbutenol* are widely used to fight against pests.

The conversion of *myrcene* to *ipsdienol* was also studied in different experimental conditions. Noticeable yields of *ipsdienol* were obtained by using PCC as oxidant, BTF and CH_2Cl_2 as solvent. It was also observed that *myrcene*, through fast reactions has converted to cyclic and open chain monoterpenes. The conversion of *myrcene* to *ipsdienol* was not so successful. Because, *myrcene* tends to isomerisation to different cyclic and open chain compounds before its allylic oxidation could occur. In the allylic oxidation reaction of particularly, the conversion of *myrcene* to *ipsdienol* could have been obtained with BTF only.

Acknowledgements

I also express my gratitude to Prof.Dr.İşık TUĞLULAR, Director of Center for drug Research & Pharmacokinetic and Applications (ARGEFAR), Ege University. I express my gratitude to Research Funds of both Muğla University and Ege University for providing financial supports to my study.

References

- [1] Arizona Chemical, **The Flavor And Fragrance High Production Volume Consortia The Terpene Consortium, Test Plan For Bicyclic Terpene Hydrocarbons**. Private Communication To FFHPVC, Arizona Chemical 1-46 (1996).
- [2] Ailton, J., Oliver, G., Howarth, W., Gusevskaya, E.V., **Palladium catalyzed oxidation of monoterpenes: novel oxidation of myrcene with dioxygen**, *Journal of Molecular Catalysis A: Chemical*, 3570: 1-8 (2002).
- [3] Andrus, M. B., and Lashley, J. C., **Copper catalyzed allylic oxidation with peresters**, *Tetrahedron*, 58: 845-866 (2002).
- [4] Andrus, M.B., Chen, X., **Catalytic enantioselective allylic oxidation of olefins with copper (I) catalysts and new perester oxidants**, *Tetrahedron*, 53(48), 16229-16240 (1997).
- [5] Boitsov, S., Riahi, A., Muzart, J., **Chromium (VI) oxide-catalyzed oxidations by t-butyl hydroperoxide using benzotrifluoride as solvent**, *C. R. Acad. Sci. Paris, Serie IIC, Chimie/Chemistry*, 3: 747-750 (2000).
- [6] Bras, J.L., Muzart, J., **Selective copper-catalyzed allylic oxidations using a 1/1 ratio of cycloalkene and tert-butylperbenzoate**, *Journal of Molecular Catalysis A: Chemical*, 3578: 1-5 (2002).
- [7] Brunel, J.M., Legrand, O., Buono, G., **Recent advances in asymmetric copper allylic oxidation of olefins**, *C. R. Acad. Sci. Paris, t:2, Serie IIC*, 19-23 (1999).
- [8] Calogirou, A., Larsen, B.R., Kotzias, D., **Gas-phase terpene oxidation products: a review**, *Atmospheric Environment*, 33: 1423-1439 (1999).
- [9] Dauben, W.G., Lorber, M., Fullerton, D.S., **Allylic oxidation of olefins with chromium trioxide-pyridine complex**, *J. Org. Chem.*, 34(11): 3587-3592 (1969).
- [10] Geron, C., Rasmussen, R., Arnts, R.R., Guenther, A., **A review and synthesis of monoterpene speciation from forest in the United States**, *Atmospheric Environment*, 34: 1761-1781 (2000).

- [11] Gusevskaya, E., Gonsalves, J.A., **Palladium (II) catalyzed oxidation of naturally occurring terpenes with dioxygen**, *Journal of Molecular Catalysis A: Chemical*, 121: 131-137 (1997).
- [12] Lajunen, M.K., **Co(II) catalyzed oxidation of α -pinene by molecular oxygen. Part III**, *Journal of Molecular Catalysis A: Chemical*, 169: 33-40 (2001).
- [13] Lajunen, M.K., Maunula, T., Koskinen, A.M.P., **Co(II) catalyzed oxidation of α -pinene by molecular oxygen. Part II**, *Tetrahedron*, 56: 8167-8171 (2000).
- [14] Levina, A., and Muzart, J., **Enantioselective allylic oxidation in the presence of the Cu(I)/Cu(II)-proline catalytic system**, *Tetrahedron: Asymmetry*, 6(1): 147-156 (1995).
- [15] Locwood, G.B., **Techniques for gas chromatography of volatile terpenoids from a range of matrices**, *Journal of Chromatography A*, 936: 23-31 (2001).
- [16] Murphy, E.F., Mallat, T., Baiker, A., **Allylic oxofunctionalization of cyclic olefins with homogeneous and heterogeneous catalysts**, *Catalysis Today*, 57: 115-126 (2000).
- [17] Muzart, J., **Synthesis of unsaturated carbonyl compounds via a chromium-mediated allylic oxidation by 70% tert.butylhydroperoxide**, *Tetrahedron Letters*, 28(40): 4665-4668 (1987).
- [18] Rothenberg, G., Wiener, H., Sasson, Y., **Pyridines as bifunctional co-catalysts in the CrO₃-catalyzed oxygenation of olefins by t.butyl hydroperoxide**, *Journal of Molecular Catalysis A: Chemical*, 136: 253-262 (1998).
- [19] Silva, A.D., Patitucci, M.L., Bizzo, H.R., Elia, E.D., Antunes, O.A.C., **Wacker PdCl₂-CuCl₂ catalytic oxidation process: oxidation of limonene**, *Catalysis Communication*, 3: 435-440 (2002).
- [20] Silva, M.J., Gusevskaya, E.V., **Palladium-catalyzed oxidation of monoterpenes: novel tandem oxidative coupling-oxidation of camphene by dioxygen**, *Journal of Molecular Catalysis A: Chemical*, 176: 23-27 (2001).
- [21] Yüksel, B., Doğu Ladini (Picea Orientalis (L.) Link.) **Ormanlarında Zarar Yapan Böcek Türleri İle Bunların Yırtıcı Ve Parazitleri**, *Doğu Karadeniz Ormancılık Araştırma Müdürlüğü Dergisi, Teknik Bülten*, No: 4,6, (1998).
- [22] Zondervan, C., Feringa, B.L., **Remarkable reversal of the non-linear effect in the catalytic enantioselective allylic oxidation of cyclohexene using copper proline complexes and t-butyl hydroperoxide**, *Tetrahedron: Asymmetry*, 7(7): 1895-1898 (1996).