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(S)-(+)-Dihydromyrcene in the Directed Synthesis of Insect Pheromones

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Abstract

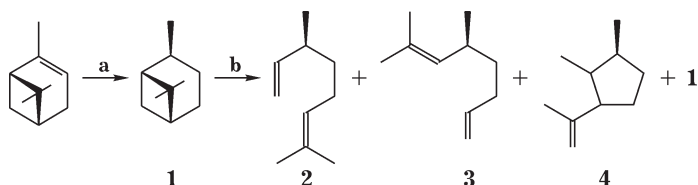
Via the selective oxidative transformations of double bonds in (+)-(3*S*)-3,7-dimethylocta-1,6-diene (dihydromyrcene), the main thermolysis product of (+)-*cis*-pinane, efficient schemes are developed for the synthesis of a number of optically active insect pheromones.

Key words: (S)-(+)-dihydromyrcene, pheromones, oxidation, ozonolysis

The thermolysis product of (+)-*cis*-pinane **1** contains a mixture of isomeric hydrocarbons **2** : **3** : **4** : **1** at an approximatratio 55 : 7 : 10 : 28 (Scheme 1), among those the most important isomer is presented by (+)-(3*S*)-3,7-dimethylocta-1,6-diene (dihydromyrcene) **2** used in the synthesis of *exo* and *endo* insect hormones [1].

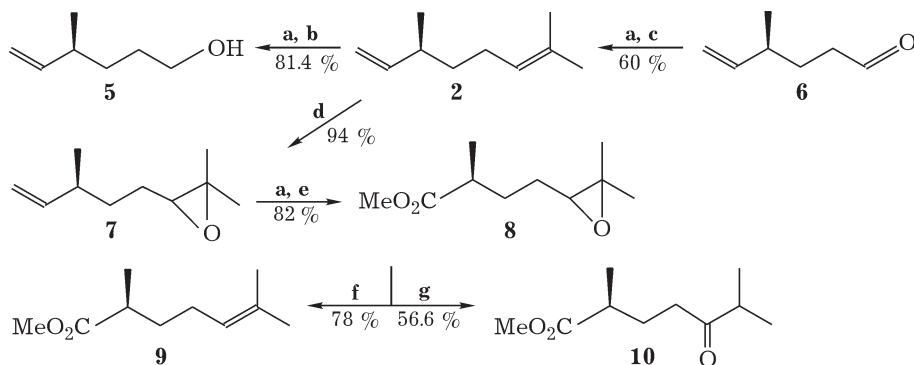
The extraction of pure diene **2** from the mixture of isomers by means of distillation is

a laborious procedure. We proposed an alternative pathway based on the selective oxidative transformations of double bonds. It was established that dihydromyrcene **2** could be subjected to the selective transformation in a mixture of compounds **1–4** by means of partial ozonolysis of a thermolytic product of (+)-*cis*-pinane **1**, which leads to the cleavage of a trisubstituted double bond in diene (Scheme 2). The further reduction of the peroxide prod-



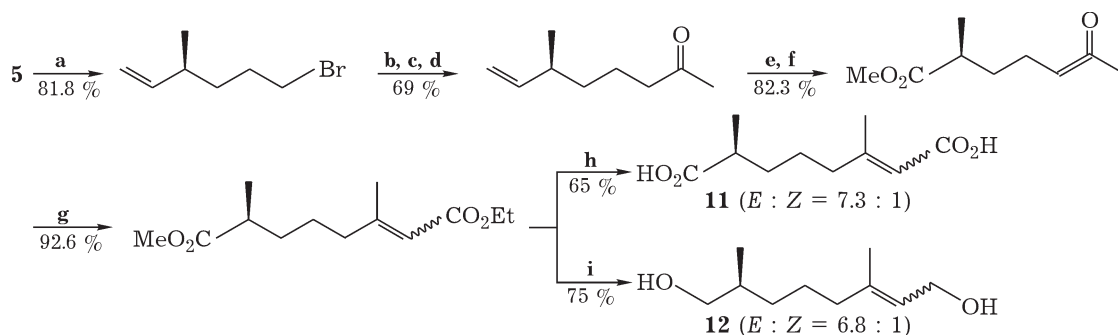
Reagents and conditions: a. H₂/Ni. b. 510–550 °C.

Scheme 1.



Conditions: **a.** O_3 , CH_2Cl_2 -MeOH, -70°C ; **b.** NaBH_4 ; **c.** Me_2S ; **d.** $t\text{-BuOOH}$, $\text{Mo}(\text{CO})_6$; **e.** Et_3N , Ac_2O ; **f.** AlI_3 , PhH ; **g.** MgI_2 , CH_3CN .

Scheme 2.



Conditions: **a.** PBr_3 , Py ; **b.** Mg , THF ; **c.** CH_3CHO ; **d.** PCC ; **e.** O_3 , CH_2Cl_2 -MeOH; **f.** Et_3N , Ac_2O ; **g.** $(\text{MeO})_2\text{P}(\text{O})\text{CH}_2\text{CO}_2\text{Et}$, EtONa , THF ; **h.** NaOH , H_2O ; **i.** DIBALH .

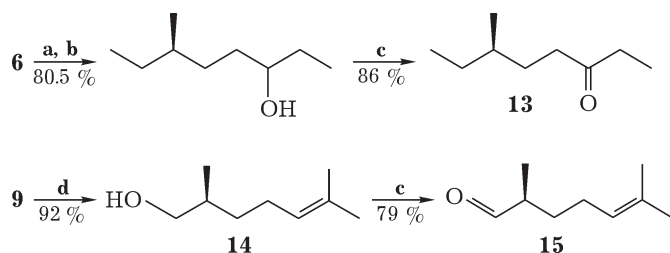
Scheme 3.

ucts of ozonolysis using NaBH_4 results in the formation of alcohol **5**, whereas the use of Me_2S as a reducer leads to the formation of aldehyde **6**. In some cases, in order to obtain target chiral block-synthons from diene **2** one needs to perform the terminal double bond cleavage with conserving the isopropenyl fragment. The selective protection of the trisubstituted double bond in this fragment can be provided owing to the oxidation thereof into epoxide **7**. Compounds **5-7** can be readily isolated

with the purity level of 94–97% from the isomeric mixture of hydrocarbons by means of fractional distillation under reduced pressure.

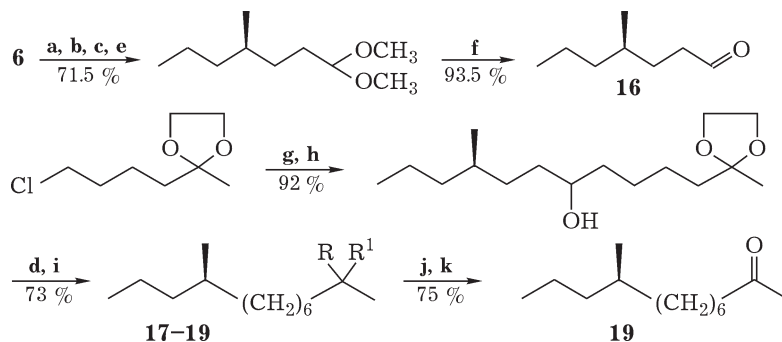
The further ozonolytic cleavage of the terminal double bond in compound **7** and the removal of epoxy protection in the resulting ester **8** via the action of AlI_3 leads to the formation of ester **9**. Replacing the AlI_3 by MgI_2 results in the formation of ketoester **10**.

Alcohol **5** served a synthon in the synthesis of the pheromones of Chinese bean weevil



Conditions: **a.** EtMgBr , Et_2O ; **b.** H_2 , Pd-C ; **c.** PCC ; **d.** DIBALH .

Scheme 4.



$\text{R} + \text{R}^1 = \text{OCH}_2\text{CH}_2\text{O}$ (**17**); $\text{R} = \text{H}$, $\text{R}^1 = \text{OH}$ (**18**); $\text{R} + \text{R}^1 = \text{O}$ (**19**). **17** : **18** : **19** = 1 : 2 : 1.

Conditions: **a**. TsOH, MeOH; **b**. $\text{BF}_3 \cdot \text{Et}_2\text{O}$, NaBH_4 ; **c**. H_2O_2 -NaOH; **d**. TsCl, Py; **e**. MeMgI, Li_2CuCl_4 , Et_2O -THF; **f**. HCl, MeOH- H_2O ; **g**. Mg; **h**. **16**; **i**. LiAlH_4 ; **j**. HCl, Me_2CO ; **k**. PCC.

Scheme 5.

(2*E*,7*S*)-3,7-dimethylocta-2-endioic acid **11** and African monarch butterfly (2*E*,7*S*)-3,7-dimethylocta-2-ene-1, 8-diol **12** (Scheme 3) [2].

Basing on compounds **6** and **9** we have developed synthetic schemes for the pheromones of ants belonging to genera *Crematogaster* *Myrmica* (6*R*)-6-methyloctane-3-one **13** (2*S*)-2,6-dimethylheptyl-5-ene-1-ol **14** and corresponding aldehyde **15** (Scheme 4) [3].

Aldehyde **6** was also used in the synthesis of (*R*)-(-)-methyltridecane-2-one **19** (Scheme 5), that represents a sex pheromone of a saw-worm such as aspen leaf beetle [4].

CONCLUSION

Thus, basing on the products of selective oxidative transformations of (*S*)-(+)-dihy-

dromyrcene we have developed efficient pathways for the synthesis of a number of optically active insect pheromones.

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