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Molecular rearrangements in longipinane derivatives

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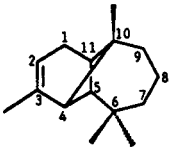
Abstract. Suitable oxygen substituted 2,6,6,9-tetramethyltricyclo[5.4.0.$0^{2,8}$]undec-9-ene (longipinene) derivatives or their saturated analogues, which are both isolated as esters from nature, can be transformed to several new ring-system containing molecules, which include 4,8,8-trimethyl-9-methyleneperhydro-1,5-methanonaphthalene, 4,8,8-trimethyl-9-methylene-1,2,4a,5,6,7,8,8a-octahydro-1,5-methanonaphthalene, 8,8,9-trimethyl-4-methyleneperhydro-1,3,5--methanonaphthalene, 2,6,6,11-tetramethyltricyclo[5.4.0.$0^{4,8}$]undecane, 2,6,6,9-tetramethyltricyclo[5.4.0.$0^{4,8}$]undecane and 4,4,8,9-tetramethylperhydro-1,7-methanonaphthalene derivatives.

INTRODUCTION

Longipinenes deserve their name from the parent hydrocarbon, α-longipinene (1), described as a constituent of *Pinus sylvestris* (1). Compounds with this sesquiterpene skeleton and with different degrees of oxydation (2-3) have been found in *Stevia* (2-6), *Critonia* (3), *Polypteris* (7) and *Artemisia* (8). During the last decade, we established the stereochemistry (5), absolute configuration (6) and conformation (6) of these structurally complex sesquiterpenes and described a full characterization of many of these molecules.



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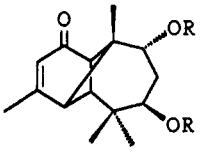

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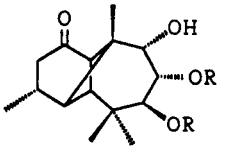

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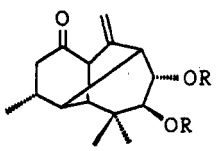
Since these tricyclic strained longipinane and longipinene derivatives offer the possibility to generate new ring systems, because bond migration can be promoted to release the four-membered ring strain, we describe at present the transformation of compounds of types 2-3 into several new ring-system containing molecules.

4,8,8-TRIMETHYL-9-METHYLENEPERHYDRO-1,5-METHANONAPHTHALENE AND 4,8,8--TRIMETHYL-9-METHYLENE-1,2,4a,5,6,7,8,8a-OCTAHYDRO-1,5-METHANONAPHTHALENE DERIVATIVES.

Treatment of **3** (R is angelate) with TsOH affords **4** (R is tiglate) in 93% yield (9). Similarly **3** (R is acetate) was converted to **4** (R is acetate) in 89% yield by means of $BF_3.Et_2O$. However, when the α,β-unsaturated carbonyl analogue of **3** (R is acetate) was treated under the latter reaction conditions, it afforded **5** in only 21% yield, while the conversion of the analogue of **3** (R is acetate) having the secondary methyl group with the β configuration afforded **6** in 64% yield.



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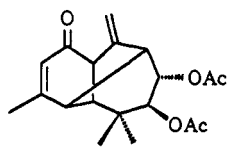

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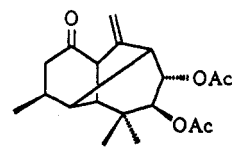

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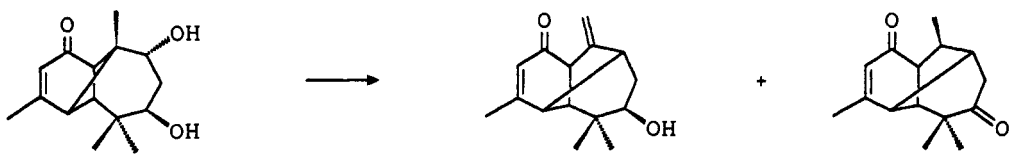
When diol **7** was subjected to the molecular rearrangement with TsOH it afforded **8** in 36% yield and **9** in 54% yield.

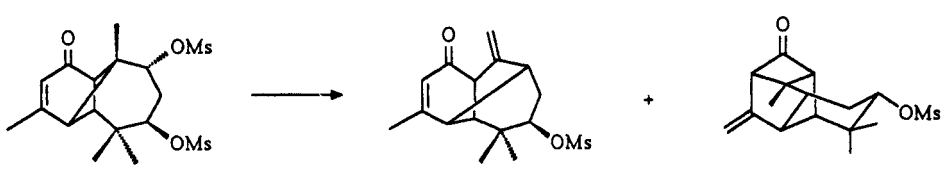


7 8 9

The mechanism for the transformation of **7** to **8** and **9** involves the protonation of the C-9 hydroxyl group to provide the intermediate that meets the requirements for the antiperiplanar C-4/C-10 bond migration. The tertiary carbonium ion at C-10 can eliminate a proton from the methyl group to yield **8**, or it can undergo an intramolecular transannular hydride migration assisted by the C-7 hydroxyl group to provide **9**. This hydride migration was demonstrated by deuterium labeling.

8,8,9-TRIMETHYL-4-METHYLENEPERHYDRO-1,3,5-METHANONAPHTHALENE DERIVATIVE.

Suitable substituted longipinene derivatives can also be rearranged under basic reaction conditions.

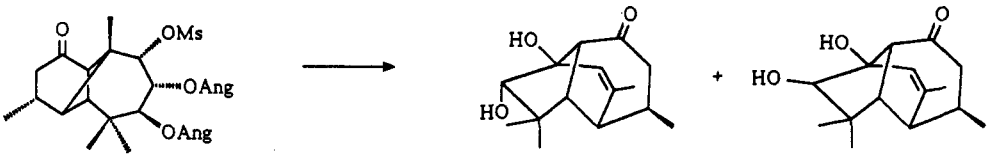


10 11 12

Treatment of dimesylate **10** with KOH afforded the Wagner-Meerwein rearrangement product **11** in 26% yield, together with the further rearranged product **12** in 54% yield. The structure of **11** was tested by correlation with **8**, while that of **12** was verified by X-ray studies.

2,6,6,11-TETRAMETHYLTRICYCLO[5.4.0.$0^{4,8}$]UNDECANE DERIVATIVES.

Treatment of **13** with KOH provided the stereoisomers **14** and **15** in 58% and 21% yield, respectively. The structure and stereochemistry of both reaction products were determined by X-ray studies.

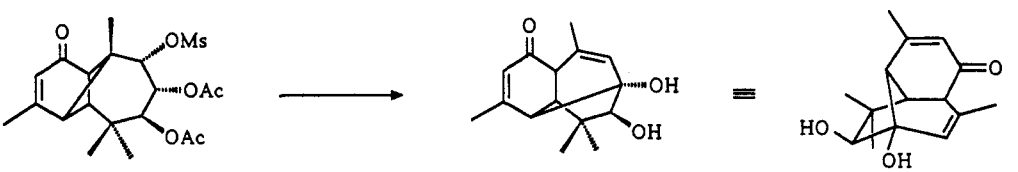


13 14 15

A plausible reaction mechanism assumes the hydrolysis of the angelate groups followed by the subtraction of the proton from the 8-hydroxyl group. An oxygen assisted 1,2-hydride shift from C-8 to C-9 eliminates the mesylate group, to provide a 7-hydroxy-8-ketolongipinane. The 7--hydroxyl group epimerizes to a mixture of two compounds. Each of them can then loose a proton from C-9 and the C-9 carbanion can form a C-9/C-10 double bond with the simultaneous C-10/C-11 bond migration to C-11/C-8.

2,6,6,9-TETRAMETHYLTRICYCLO[5.4.0.$0^{4,8}$]UNDECANE DERIVATIVE.

The double bond on the six-membered ring has a marked influence on the reaction outcome, as is evident when the unsaturated molecule **16** is treated under the basic reaction conditions.

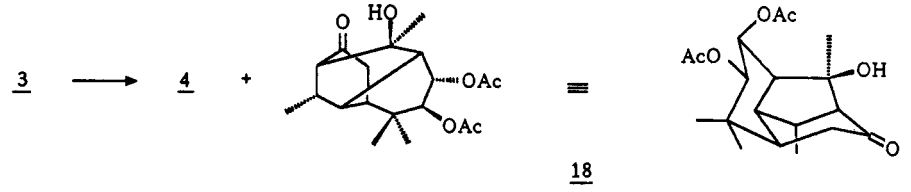


16 17

In this case, **16** provides the single rearrangement product **17** in 67% yield. Here the C-4/C-10 bond migrates to C-4/C-8, instead of the C-10/C-11 bond that migrates when a saturated six-membered ring is present. The structure and stereochemistry of the rearrangement product **17** was again verified by X-ray analysis.

4,4,8,9-TETRAMETHYLPERHYDRO-1,7-METHANONAPHTHALENE DERIVATIVE.

The last molecular rearrangement we describe herein is again performed under acid conditions. Treatment of 3 (R is acetate) with TsOH affords 4 (R is acetate) in 42% yield and the new skeleton containing compound 18 in 33% yield. Its structure and stereochemistry were established by X-ray studies.



18

The reaction mechanism for the transformation assumes the protonation of the 9-hydroxyl group followed by the antiperiplanar bond migration The derived C-10 carbonium ion can trap a molecule of water to provide the tertiary alcohol and the C-10/C-11 bond can migrate to C-2/C-10, which is also *alpha* to the carbonyl group.

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