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Rearrangement Processes in the Bicyclo[3.2.1]heptane Moiety of 12,17-Bifunctionalized *ent*-Beyer-15-enes

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Abstract: *Several rearrangements of 17-mesyloxy and 12,17-dimesyloxy derivatives of ent-beyer-15-enes were carried out. Rearrangement processes mainly occurred with the participation of the functional group at C-12, although the group at C-17 and the C-15/C-16 double bond aided in an observed 16(13)→12/11(12)→13 double rearrangement. The influence of the groups at C-12 and their stereochemistry, of the mesyloxy groups at C-17 and of the C-15/C-16 double bond is studied and the stereochemistry of the observed rearrangement processes is discussed.*

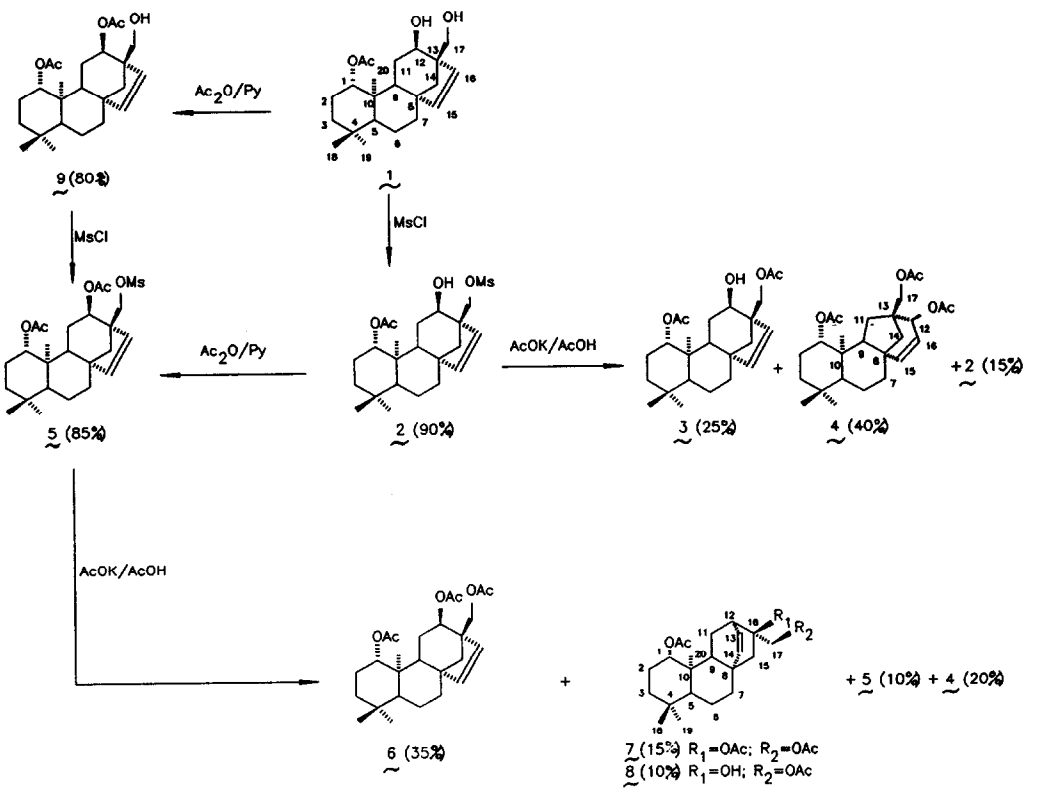
INTRODUCTION

The rearrangement of tetracyclic diterpenoids has been extensively studied in the last two decades. In general, the rearrangements studied in solvolytic reactions[1-5] or from epoxy compounds[6-12] were carried out on starting material with only one functional group present in the moiety of the molecule capable of undergoing rearrangement. On some occasions, the double bond originally present in the natural skeleton was hydrogenated before setting up the rearrangement experiment. However, we think that the presence of other functional groups near the leaving group may have a decisive quali-or/and quantitative influence on the course of the reaction, as reported in the conversion of *ent*-beyer-15-ene to *ent*-atis-13-ene[13,14], in the ruthenium-catalyzed rearrangement of epoxybeyeranes functionalized at C-14[15] or in the acid-catalyzed rearrangement of the *ent*-beyer-15-en-12-one system[16]. In this work we present the results of the rearrangement of *ent*-beyer-15-enes functionalized at C-12 and C-17 to study the influence of the presence/absence of functional groups in these positions, principally of the C-15/C-16 double bound, and to compare the results with those described by McAlees and McCrindle in their general scheme of rearrangement of tetracyclic diterpenoids functionalized at C-12[5].

RESULTS AND DISCUSSION

Treatment of *ent*-1ß-acetoxy-12α,17-dihydroxybeyer-15-ene (1-acetyljativatriol,**1**[17]) with mesyl chloride (MsCl) at room temperature yielded its 17-mesyl derivative (**2**, 90%) which afterward was treated with AcOK/AcOH for 24 hours under reflux (see Experimental part), after which starting material (**2**, 15%), 1,17-diacetyljativatriol[18] (**3**, 25%) and a rearranged product (**4**, 40%) were isolated (Scheme I). This rearranged product (**4**), the main product of this process, was a triacetyl derivative (MS, see Experimental part; ^{1}H NMR, Table I; ^{13}C NMR, Table III), with one acetoxymethylene (situated at a quaternary carbon) and two acetoxymethine groups. One of these can be attributed to the original group at C-1 of the unaltered A ring, but the other one cannot be situated at C-12 of an *ent*-beyer-15-ene system. In the new skeleton, this acetoxymethine group, with a ^{1}H NMR signal at δ 4.98 (1H, d, J=3.9 Hz), was allylic to a double bond, which was proved by double resonance experiments. Moreover, the ^{13}C NMR chemical shift of C-9 was very different (δ 40.50) to that of *ent*-beyer-15-ene products (δ 49.32 for product **2**).

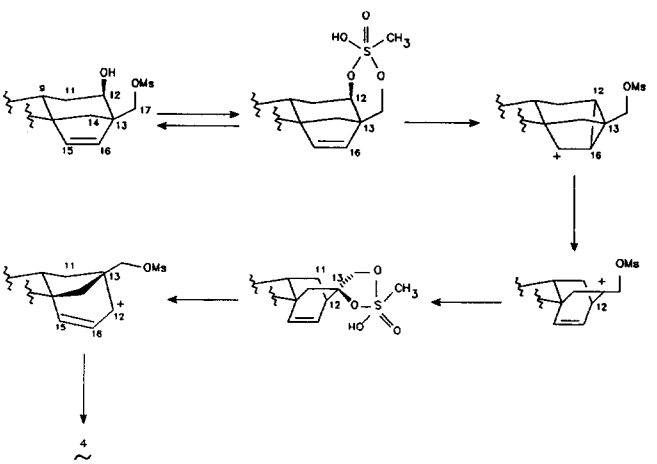
SCHEME I



Solvolysis of *ent*-12α-tosyloxybeyerane, described by Coates & Bertram[3] and McAlees & McCrindle[4], gave *ent*-atisane. *ent*-Atisene compounds were also obtained by rearrangements of 12,17-isopropylidene or 12,17-thiocarbonyl derivatives of 1-acetyljativatriol[14]. However, the skeleton now obtained was not an *ent*-atisene, because four non-oxygenated quaternary carbons and two non-oxygenated methine carbons were present in the ^{13}C NMR spectra of **4**, and irradiation of the proton geminal to the allylic acetoxy group transformed the signal of the olefin H-15 (δ 5.54, dd, J_1=9.5, J_2=3.9Hz) into a doublet (J=9.5 Hz).

The configuration at C-12 can be easely deduced by consideration of the coupling constant of its proton (J=3.9 Hz) and the dihedral angles for the two possible configurations calculated after the observation of Dreiding models (40 and 75° respectively). Taking into account the influence of the electronegativity of the acetoxy group on the coupling constant, its observed value (3.9 Hz) was in accord with an R configuration (near 4 Hz is described[19]), whereas for the S configuration a coupling constant near zero was expected. In addition, C/H correlation experiments were performed to assign the chemical shifts of protons at C-11 and C-15. Subsequent n.O.e difference experiments desmonstrated the spatial proximity between H-12 and *ent*-11ß-H, H-16 and the C-20 methyl group and between *ent*-11α-H and the acetoxymethylene group of C-17. Thus, product **4** must be the result of a 16(13)→12/11(12)→13 double rearrangement process. This structure was proposed as a possibility in the general rearrangement scheme of 12α and 12ß-hydroxybeyeranes by McAlees et all[5], but not isolated. Thus, the hydroxyl group at C-12 is likely to participate in this process, as shown in Chart I.

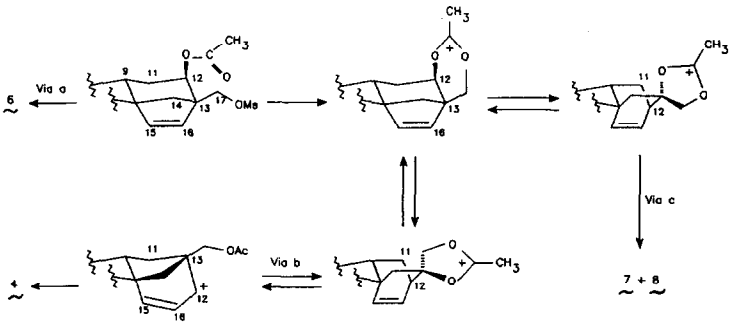
CHART I



To prove the participation of the hydroxyl group at C-12, we acetylated the starting material **2** to obtain the diacetyl derivative **5**, which was treated under the same conditions as **2**. In this case, the rearranged product **4** was also obtained, but the yield was only 20%. The product of acetolysis at C-17 was the main one isolated from this process. Moreover, starting product (**5**, 10%) and the atisene products **7**[13](15%) and **8**[13](10%) were isolated (Scheme I). In this case, solvolysis of the mesyloxy group at C-17 and participation of the acetoxy group at C-12,as indicated in Chart II, seemed reasonable. The main process

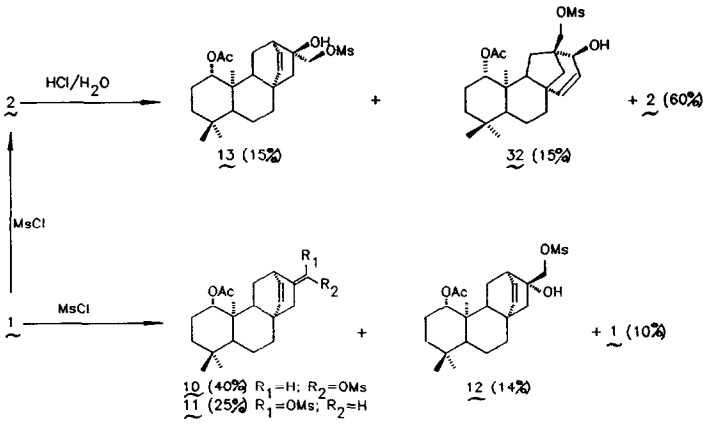
in the reaction was the direct acetolysis at C-17 (*via* a) and the more classical rearrangement toward *ent*-atis-13-ene compounds (*via* c) was more extensive than the double rearrangement (*via* b). It seems clear that the rearrangement of **2** and **5** could occur (except for product **6**), with the participation of both groups at C-12 and C-17.

CHART II



To prove if the process was initiated at C-12, we mesylated product **1** at reflux to obtain a dimesylate, that was not isolated. In this case, the atisene compounds **10**(40%), **11**(25%) and **12**(14%) were isolated (Scheme II). The structures of **10** and **11** can be deduced from comparison with the data of *ent*-atis-13,16-diene compounds previously described[20]. Products **10** and **11** were unstable and evolved to aldehyde compounds.

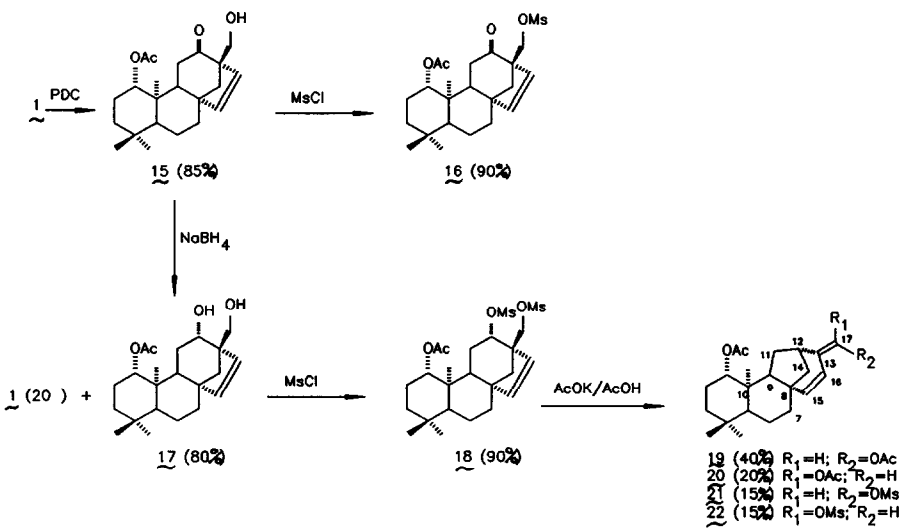
SCHEME II



The structure of product **12** can be deduced from comparison with the data of its 16-epimer compound **13**, obtained by mesylation of the natural product **14** (1-acetylsideritol[13]). The ^{13}C NMR data of both epimer products (**12** and **13**) were, as expected, very similar with the exception of C-13, C-14 and C-15, and especially C-16 and C-17 (see Table II). As can be seen, all the products (**10-12**) isolated in this process had an *ent*-atisene skeleton, and maintained the original mesyloxy group at C-17.

The oxidation of **1** gave ketone **15**[14] (Scheme III), which was mesylated to give **16**.This product, after 35 hours at reflux under conditions of acetolysis, was recovered unaltered. Hence, for this type of process,the participation of a 12-oxy group seems to be necessary.

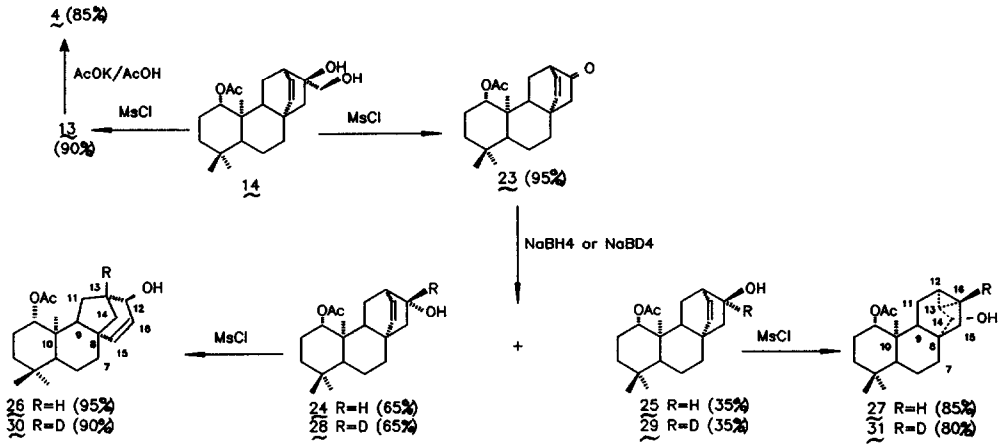
SCHEME III



To study the influence of the stereochemistry of the hydroxyl group at C-12, on the process, ketone **15** was reduced to give *ent*-12ß (**17**, 70%[14]) and *ent*-12α-hydroxyl derivatives (**1**, 30%) (Scheme III). Mesylation of **17** at room temperature produced dimesyl derivative **18**, which was acetolysed under reflux for 24 hours in a form similar to that described for mesylate **2**. In this manner, rearranged products **19** (40%), **20** (20%), **21** (15%) and **22** (15%) were obtained. All these products (**19-22**) showed similar ^1H and ^{13}C NMR spectra (Tables I, III and IV), although with the difference of an acetoxy group (**19** and **20**) or a mesyloxy group (**21** and **22**). The skeleton of all these four products was the result of the expected rearrangement toward *ent*-14(13)→12-beyerene compounds[5], although with a 13(17),15-diene system, previously described[21]. All four of these products maintained one function at C-17: an acetoxy group in the case of **19** and **20** and a mesyloxy group in the case of products **21** and **22**. We carried out a series of n.O.e.-difference experiments on products **19** and **20** to elucidate the configuration at C-13 of the pairs of compounds. Irradiation at H-17 of **19** gave positive n.O.e. with H-12 (δ 2.66, m, $w_{½}$=9 Hz). However, similar irradiation on H-17 of product **20** did not give n.O.e. with H-12, but did give such an effect with H-16 (δ 6.23, d, J=11Hz). Thus, products **19** and **21** are E-isomers of **20** and **21** respectively (Z-isomers).

Evidently, the configuration at C-12 was decisive in the development of the reaction. Thus, the starting material with *ent*-12α functions evolved toward the two-facedly rearranged compounds. On the other hand, the mesylation at reflux of *ent*-12α-hydroxy compound (**1**) yielded *ent*-atis-13,16-diene compounds. As the *ent*-12ß-hydroxybeyerane and *ent*-12ß-hydroxybeyer-15-ene compounds readily evolved toward *ent*-atisane[3] or *ent*-atisene compounds[13,14], the formation of di-*abeo* compounds such as **4** may well have occurred *via* the *ent*-atis-13-ene compound. To prove this hypothesis we performed the acetolysis of 17-mesyl derivative **13** of the *ent*-atis-13-ene natural product **14**[13] (Scheme IV) under the same conditions as described for the acetolysis of **2**.In this way, only product **4** (80%) was isolated. Hence, it seems clear that bicyclo[2.2.2]octane partial structure may have provided the means for the formation of products like **4** from *ent*-beyer-15-ene compounds, but only from starting material without an original leaving group situated at C-12 in *ent*-beyer-15-ene, which principally evolved towards *ent*-atis-13,16-diene compounds.

SCHEME IV



Similar behavior was described for the *ent*-atis-13-ene compound functionalized at C-16 (but not in C-17) which yielded, by treatment with MsCl, *ent*-13,16-diene compounds independent of its configuration at C-16[20]. However, it is reasonable to think that the rearrangement to 11(12)→13-*abeo* compound from *ent*-atis-13-ene compounds may be favored by a 16-*exo* leaving group or by *exo*-assistance at C-16 by the mesyloxy group present at C-17. To test the influence of the configuration of the possible intermediate in this rearrangement at C-16, we oxidized the natural *ent*-atis-13-ene **14** with $NaIO_4$ to give ketone **23**[20] which was then treated with $NaBH_4$ to give *ent*-16R,17-nor-atis-13-ene derivative **24** (65%) and its 16S-epimer **25** (35%) (Scheme IV). The configurations at C-16 of both epimers were determined by the ^{13}C NMR chemical shift of C-11 (δ 26.93 and 22.66 for **24** and **25** respectively, see Table IV) and, after the assignment of the chemical shift to the protons at C-11 (C/H correlation, COSY), by one and two dimensional n.O.e. experiments. Thus, we proved that H-16ß of alcohol **24** was spatially near to H-11ß

(δ 1.38). The H-16 of its epimer compound **25**, was near the latter's H-13 (see Table II). However, the main result of the reduction of ketone **23** was the *exo*-epimer **24**. Mesylation of **24** at room temperature gave, after 24 hours of reaction, products **26** (95%).

The spectroscopic behavior of **26** indicated that this product was a 17-*nor*-derivative of **4**, although without an acetate group at C-12. Several homo-decoupling experiments indicated that the new hydroxyl group at C-12 (δ 3.74) was coupled to H-13 (J=3.3 Hz) and that H-16 was coupled in addition to H-12, with H-15 (J=9.6 Hz) and H-13 (W coupling, J=1.9 Hz). The configuration at C-12 was determined as S on the basis of the value of the H-12/H-13 coupling constant and several n.O.e.-difference experiments which carried out after identification of the chemicals shifts of the protons by C/H correlation. Thus, irradiation at δ 3.74 (H-12) gave positive n.O.e. for H-13, H-16 and *ent*-11ß-H (δ 0.96, 1H, ddd, J_1=14, J_2=9, J_3=2 Hz). On the other hand, irradiation at H-14 gave a clear n.O.e with 3H-20, which confirmed stereochemical characteristics of C and D rings of this molecule. Thus, the rearrangement of 16-*exo* hydroxyl compound **24** gave 11(12)→13-*abeo* compounds. However, the *endo* isomer **25** gave the *ent*-17-*nor*-trachylobane derivative **27** in the same mesylation reaction as described for **24**, although slowly (48 hours) (Scheme IV). The proton geminal to the hydroxyl group at C-14 gave a singlet signal at δ 4.11 (1H, bs). The ^{13}C NMR spectrum of **27** gave three new methine groups at δ 17.23 (two) and 24.85 (one methine group). C/H correlation indicated overlapping of the methine group at δ 17.23, and correlation with protons at δ 0.96, 1.32 and 1.38. The configuration at C-14 was determined by n.O.e-difference experiments, as irradiation at H-14 produced positive n.O.e. with one of the previously described protons (δ 1.38) and an excellent n.O.e with the methyl group of C-20 (and vice versa), which indicated an 14-R configuration in this compound **27**.

To assign the chemical shifts of the cyclopropane moiety and the possible hydride shift in the rearrangements of **24** and **25**, respectively , we reduced ketone **23** with $NaBD_4$ to give the 16-deuterated compounds **28** and **29** (*exo* and *endo* respectively) (Scheme IV). The treatment of **28** with MsCl under the same conditions as described for **24**, gave only one compound **30** (Scheme IV), whose spectroscopic studies confirmed the structure proposed for **26**. The treatment of **29**, as described for **25**, gave only product **31** (Scheme IV), whose ^{13}C NMR spectrum indicated that only the C-16 carbon (δ 17.23) was deuterated. C/H correlation thus allowed us to assign the chemical shift δ 1.32 to H-16, and the n.O.e.-difference experiment described above, indicated a chemical shift δ 1.38 to H-13 (and δ 24.85 to C-13); hence we assigned δ 0.96 and δ 17.23 to H-12 and C-12 respectively.

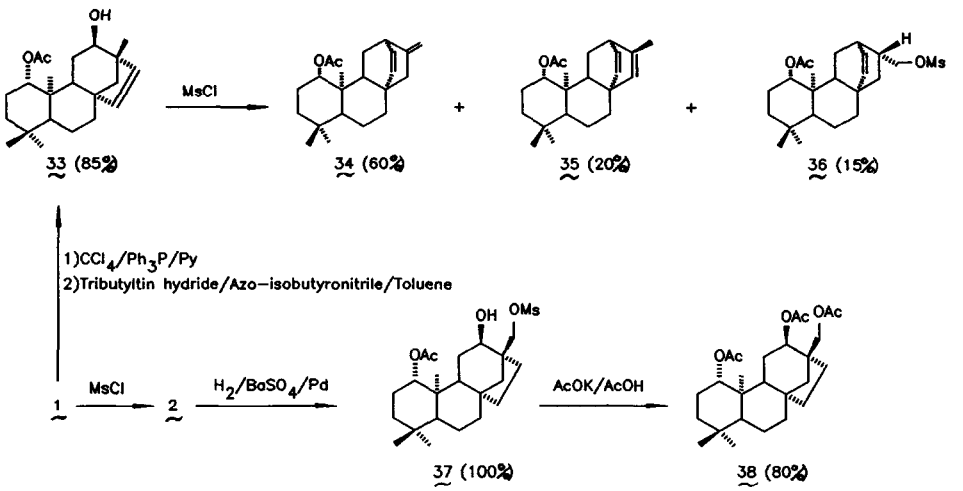
It was therefore evident that the configuration at C-16 and the assistance of the mesyloxy group at C-17 were decisive in determining the skeleton obtained. The 17-mesyloxy group must act with an *exo*-assistance at C-16 of the *ent*-atis-13-ene skeleton in the 11(12)→13-*abeo* rearrangement. However, when the leaving group was a 16-*endo* mesyloxy group, *ent*-atis-13,16-diene (**10, 11**) and *ent*-17-*nor*-trachylobane (product **27**) were obtained.

In addition to obtaining di-*abeo* compounds (like **4**) by acetolysis processes, we found that treatment of starting material **2** with diluted HCl at room temperature during a few minutes produced monorearranged (*ent*-atisene compound **13**, 25%) and two-facedly rearranged product (**32**, 15%) (Scheme II). Treatment under such conditions of *ent*-beyerene (**1**) and *ent*-atisene (**14**) compounds did not produce any transformation.

Product **33** was obtained from compound **1** by chlorination at C-17 with CCl_4/PPh_3 and by treatment of 17-chloro derivative with tri-n-butyltin hydride[23,24] to give the 17-deoxy compound **33** (Scheme V).This product **33**, by treatment with MsCl at room temperature for 24 hours, gave the *ent*-atis-13,16-

diene **34** (main product[20], 60%), the *ent*-atis-13,15-diene (**35**[20], 20%) and the *ent*-1ß-acetoxy-17-mesyloxy-16S-atis-13-ene **36** (15%). The chemical shift of C-9 of product **36** was characteristic of *ent*-atis-13-ene compounds, and the observed deshielding of C-11 indicated that the mesyloxymethylene group at C-16 was *exo* (for both see Table IV). This process was parallel with that described for *ent*-12α-tosyl derivatives[3], with the exception of product **36**, in which a functionalization at the methyl group of C-17 was produced. This possibility was not considered in the case of rearrangement of saturated compounds[3]. Presumably, product **36** could be formed through the diene **34** after protonation of the C-13/C-14 double bond, the formation of trachylobane-like structure, mesylation at C-17 and the formation of *ent*-atis-13-ene compound with the possible assistance of the mesyloxy group at C-17.

SCHEME V



In the light of these findings, the presence of a mesyloxy group (or another one as an acetoxy group, as explained in Chart II) at C-17 was decisive, this group assisting at the *exo*-face at C-16 of the rearranged *ent*-beyer-15-ene or *ent*-atis-13-ene. We think that the *exo*-assistance, or the presence of 16-*exo*-group (as in **24** or **28**), is necessary, although the formation of products like **4** was suggested through 16-*endo* intermediates on occasion of the study of the cleavage of the cyclopropane ring of *ent*-trachylobane compounds with thallic acetate[25]. Moreower, to test the influence of the double bond of the starting *ent*-beyer-15-ene we hydrogenated the starting material (**2**) to give product **37**, which was acetolyzed under the same conditions as **2**. In this form, in addition to starting material **37** (15%), the triacetyl derivative **38** (80%) was isolated (Scheme V).

We therefore think that the presence of double bond was necessary to stabilize the carbocation at C-12 of di-*abeo* compounds like compound **4**, in a parallel form to described in the acid rearrangement of *ent*-12-ketobeyer-15-ene system[16]. The new acetoxy group at C-12 of product **38** indicated that the mesyloxy group at C-17 also takes part in the process, but the impossibility of the above mentioned carbocation forming in detectable amounts ruled out evolution toward di-*abeo* compounds.

The results obtained in this work suggest that the study of rearrangements of unsaturated and/or polyfunctionalized tetracyclic diterpenes would yield further valuable data.

TABLE I

Hydr.	2	4	5	8	10	11	12	13	15	16	18	19	20	21	22
H-1	4.49q J_1=4.9Hz J_2=10.7Hz	4.43q	4.49q	4.56q	4.52q	4.51q	4.55q	4.55q J_1=5.4Hz J_2=10.5Hz	4.46q	4.45q	4.46q J_1=4.8Hz J_2=10.8Hz	4.47q	4.46q	4.47q	4.46q
H-11	---	---	---	---	---	---	---	---	2.58dd J_1=9.6Hz J_2=17.1Hz	2.59dd J_1=9.9Hz J_2=17Hz	---	---	---	---	---
H-11	---	---	---	---	---	---	---	---	2.09dd J_1=7.3Hz J_2=17.1Hz	2.08dd J_1=7.4Hz J_2=17Hz	–	---	---	---	---
H-12	3.87m $W_{1/2}$=4.9Hz	4.98d J=3.9Hz	4.94m $W_{1/2}$=7.5Hz	2.45m $W_{1/2}$=11Hz	2.90m $W_{1/2}$=10.5Hz	2.87m $W_{1/2}$=10.5Hz	3.02m $W_{1/2}$=10Hz	2.53m $W_{1/2}$=12Hz	---	---	4.74dd J_1=6.6Hz J_2=9.1Hz	---	---	---	---
H-13	---	---	---	6.05t J_1=10.5Hz J_2=7.5Hz	6.10t J_1=10Hz J_2=7.5Hz	6.08t J_1=10Hz J_2=7.5Hz	6.10t J_1=7.9Hz J_2=7.4Hz	6.09t J_1=7.8Hz J_2=7.4Hz	---	---	---	2.66m $W_{1/2}$=9Hz	3.28m $W_{1/2}$=9Hz	2.68mm $W_{1/2}$=9.2Hz	3.27m
H-14	---	---	---	5.86d J=10.5Hz	5.85d J=10Hz	5.87d J=10Hz	6.04d J=7.6Hz	5.89d J=7.9Hz	---	---	---	---	---	---	---
H-15	5.76Q_{AB} J=5.8Hz	5.92bd J=9.5Hz	5.77Q_{AB} J=6Hz	---	---	---	---	---	5.83Q_{AB} J=6Hz	5.70Q_{AB} J=5.7Hz	5.51Q_{AB} J=5.8Hz	6.23d J=11Hz	5.86d J=7.5Hz	6.18d J=11Hz	5.87d J=8Hz
H-16	5.83Q_{AB} J=5.8Hz	5.54dd J_1=9.5Hz J_2=3.9Hz	5.91Q_{AB} J=6Hz	---	---	---	---	---	6.13Q_{AB} J=6Hz	6.16Q_{AB} J=5.7Hz	6.01Q_{AB} J=5.8Hz	5.82d J=11Hz	5.73d J=7.5Hz	5.94d J=11Hz	5.75d J=8Hz
H-17	3.89Q_{AB} J=9.7Hz	3.71Q_{AB} J=12Hz	3.86Q_{AB} J=10.5Hz	3.72Q_{AB} J=12Hz	6.35	6.16	4.16Q_{AB} J=11Hz	3.93Q_{AB} J=10Hz	3.69Q_{AB} J=12Hz	4.30Q_{AB} J=10.2Hz	3.99Q_{AB} J=9.6Hz	6.84sa	6.86s	6.25s	6.28s
H-17	4.40Q_{AB} J=9.7Hz	4.25Q_{AB} J=12Hz	4.20Q_{AB} J=10.5Hz	3.82Q_{AB} J=12Hz	---	---	4.48Q_{AB} J=10Hz	3.84Q_{AB} J=10Hz	3.53Q_{AB} J=12Hz	4.24Q_{AB} J=10.2Hz	4.40Q_{AB} J=9.6Hz	---	---	---	---
Me	0.80s	0.78s	0.82s	0.75s	0.75s	0.76s	0.75s	0.75s	0.80s	0.82s	0.81s	0.84s	0.84s	0.81s	0.82s
Me	0.82s	0.82s	0.84s	0.81s	0.80s	0.80s	0.82s	0.82s	0.86s	0.86s	0.85s	0.84s	0.84s	0.84s	0.84s
Me	0.85s	0.87s	0.86s	0.87s	0.86s	0.87s	0.87s	0.88s	0.89s	0.89s	0.90s	0.87s	0.87s	0.87s	0.87s
MeCOO	1.96s	1.96s	1.97s	1.97s	1.95s	1.95s	1.98s	1.98s	1.98s	1.97s	2.00s	1.96s	1.98s	1.98s	1.95s
MeCOO	---	2.01s	2.04s	2.08s	---	---	---	---	---	---	---	2.13s	2.16s	---	---
MeCOO	---	2.01s	---	---	---	---	---	---	---	---	---	---	---	---	---
$MeSO_2$	2.99s	---	2.97s	---	2.96s	2.98s	3.01s	3.03s	---	3.02s	2.99s	---	---	3.01s	3.03s
$MeSO_2$	---	---	---	---	---	---	---	---	---	---	3.02s	---	---	---	---

TABLE II

Hydr.	23	24	25	26	27	28	29	30	31	32	33	34	36	37	38
H-1	4.56q J_1=4.7Hz J_2=10.9Hz	4.51q	4.56q	4.46q J_1=5.4HZ J_2=10.7Hz	4.48q	4.53q	4.56q	4.47q	4.47q	4.48q	4.50q J_1=4.8Hz J_2=10.9Hz	4.54q	4.56q	4.52q	4.52q
H-12	2.99m $W_{1/2}$=12Hz	2.58m $W_{1/2}$=12Hz	2.47m $W_{1/2}$=12Hz	3.74bt J_1=J_2=3.3Hz	0.96	2.61	2.47	3.75	—	3.88d J=3.5Hz	3.58m $W_{1/2}$=5.2Hz	2.89m $W_{1/2}$=6Hz	2.54m	3.75m	4.79m
H-13	6.11m $W_{1/2}$=4Hz	6.05t J_1=5.9Hz J_2=2.0Hz	6.04t J_1=7.5Hz J_2=10Hz	2.29m $W_{1/2}$=12Hz	1.38	6.06	6.05	---	—	5.61dd J_1=9Hz J_2=4.5Hz	---	6.14	6.00t	—	—
H-14	6.09m $W_{1/2}$=4Hz	6.02d J=5.9Hz	5.87d J=10Hz	—	4.11sa	6.03	5.88	---	4.10	5.86d J=9Hz	—	5.90	5.95d	---	---
H-15	---	---	---	5.80d J=9.6Hz	1.30	---	---	5.80	---	---	5.54Q_{AB} J=5.7Hz	1.83	---	---	---
H-16	---	3.87dt	3.71m $W_{1/2}$=13Hz	5.49dq J_1=9.6Hz J_2=3.7Hz J_3=1.9Hz	1.32	---	---	5.49	---	---	5.71Q_{AB} J=5.7Hz	---	---	---	---
H-17	---	---	---	---	---	---	---	---	---	3.99Q_{AB} J=12Hz	1.02s	4.68	3.73m	4.4q J=9.5Hz	4.06q J=10.9Hz
H-17	---	---	---	---	---	---	---	---	---	4.53Q_{AB} J=12Hz	1.02s	4.48	3.73m	3.86q J=9.5Hz	3.71q J=10.9Hz
Me	0.78s	0.71s	0.74s	0.75s	0.80s	0.74s	0.76s	0.76s	0.80s	0.76s	0.81s	0.77s	0.75s	0.80s	0.81s
Me	0.81s	0.79s	0.80s	0.81s	0.83s	0.81s	0.80s	0.83s	0.84s	0.82s	0.83s	0.82s	0.82s	0.84s	0.85s
Me	0.87s	0.84s	0.87s	0.85s	1.06s	0.86s	0.86s	0.86s	1.07s	0.87s	0.84s	0.88s	0.87s	1.05s	1.05s
MeCOO	1.95s	1.96s	1.97s	1.96s	1.98s	1.98s	1.97s	1.97s	1.98s	1.98s	1.96s	1.97s	1.98s	1.99s	1.98s
MeCOO	---	---	---	---	---	---	---	---	---	---	---	---	---	---	1.99s
MeCOO	---	---	---	---	---	---	---	---	---	---	---	---	---	---	2.01s
$MeSO_2$	---	---	---	---	---	---	---	---	---	3.01s	—	---	2.96s	2.98s	---

TABLE III

Carbon	1	2	4	5	6	10	11	12	13	14	15	16	18	19	20
1	82.13	81.98	81.67	81.82	81.88	82.79	82.85	82.76	82.96	83.10	81.56	81.44	81.64	81.69	81.75
2	24.92	24.88	24.19	24.97	24.98	24.79	24.83	24.64	24.71	24.71	24.70	24.67	24.83	24.43	24.45
3	39.21	39.19	39.88	39.31	39.33	39.59	39.51	39.48	39.52	39.49	39.24	39.17	39.17	40.08	40.10
4	32.97	32.95	32.61	33.04	33.04	32.88	32.75	32.93	32.89	32.82	32.93	32.80	33.00	32.73	32.72
5	55.11	55.08	55.25	55.03	55.07	54.58	54.60	54.49	54.56	54.58	54.48	54.37	54.77	55.62	55.69
6	19.96	19.86	18.17	19.78	19.82	18.88	18.87	18.79	18.86	18.86	19.82	19.69	19.64	18.48	18.46
7	36.91	36.64	35.54	36.55	36.70	36.95	37.02	36.36	37.43	37.03	36.38	36.14	35.96	36.16	36.32
8	49.74	49.26	44.62	48.91	48.78	38.87	38.75	38.77	39.03	38.99	49.28	49.48	48.88	45.25	45.02
9	49.31	49.32	60.50	39.31	49.31	52.49	52.28	52.02	52.02	52.22	54.25	54.16	51.64	64.84	64.04
10	41.72	41.70	41.14	41.77	41.77	41.94	41.90	41.86	41.86	41.85	41.79	41.75	41.95	41.35	41.35
11	32.65	32.04	31.89	28.72	28.81	30.68	30.53	23.45	24.11	24.29	39.11	38.64	30.46	32.19	31.37
12	70.31	65.21	73.13	68.65	69.11	37.13	36.68	37.77	38.53	38.33	213.21	207.89	78.89	37.39	33.35
13	53.10	52.31	121.57	50.84	50.61	130.21	129.85	128.65	130.71	131.28	62.54	60.24	51.58	130.80	132.90
14	48.84	47.71	140.39	48.55	48.96	137.39	137.76	138.91	137.20	136.45	52.69	52.12	53.12	45.89	45.02
15	138.36	138.74	41.80	139.89	139.23	41.04	41.00	45.32	48.58	49.24	140.55	141.38	140.28	138.69	139.95
16	132.54	131.82	44.99	130.96	132.07	132.97	133.04	91.42	74.58	76.07	131.95	130.45	127.53	122.15	118.72
17	68.79	72.35	67.83	70.34	65.65	126.28	125.82	68.92	76.05	69.63	64.04	69.05	70.13	126.70	124.64
18	32.97	32.95	33.02	33.07	33.09	33.24	33.20	33.22	33.22	33.18	32.85	32.80	33.02	33.15	33.18
19	21.45	21.42	21.23	21.57	21.59	21.63	21.63	21.78	21.81	21.77	21.31	21.26	21.48	21.30	21.28
20	10.97	10.92	12.17	10.74	10.73	11.58	11.62	11.88	11.72	11.62	11.09	11.08	11.38	12.48	12.41
MeCOO	22.08	22.02	21.71	21.81	21.84	21.68	21.60	21.91	21.92	21.95	21.95	21.91	21.74	21.91	21.99
MeCOO	----	----	20.81	21.42	20.92	----	----	----	----	----	----	----	----	20.84	20.94
MeCOO	----	----	21.23	----	21.47	----	----	----	----	----	----	----	----	----	----
MeCOO	170.96	170.87	171.00	170.85	170.85	170.51	170.51	170.49	170.64	171.04	170.51	170.39	170.84	170.95	170.99
MeCOO	----	----	170.73	170.34	170.95	----	----	----	----	----	----	----	----	168.18	168.25
MeCOO	----	----	170.47	----	171.12	----	----	----	----	----	----	----	----	----	----
$MeSO_2$	----	37.00	----	37.39	----	35.77	35.73	35.72	37.43	----	----	37.11	37.39	----	----
$MeSO_2$	----	----	----	----	----	----	----	----	----	----	----	----	38.44	----	----

TABLE IV

Carbon	21	23	24	25	26	27	28	29	30	31	33	34	36	37	38
1	81.61	82.67	83.01	83.20	81.82	83.43	82.94	83.16	81.84	83.43	82.05	82.99	82.94	83.05	83.11
2	24.41	24.73	24.99	24.83	24.36	25.03	24.93	24.81	24.39	25.03	24.90	24.86	24.93	24.80	25.04
3	40.01	39.46	39.76	39.70	38.87	39.75	39.65	39.64	38.79	39.63	39.25	39.62	39.62	40.74	40.91
4	32.70	32.91	33.00	32.94	32.65	32.91	32.93	32.94	32.68	32.97	32.99	32.93	32.94	32.98	33.09
5	55.55	54.56	54.89	54.77	55.47	54.09	54.78	54.70	55.49	55.09	55.13	54.73	54.71	55.51	55.61
6	18.38	18.40	18.92	18.96	18.22	19.50	18.83	18.94	18.25	19.49	19.93	18.98	18.99	20.02	19.85
7	35.95	35.99	37.47	37.11	35.82	30.95	37.36	37.05	35.84	30.96	37.06	37.19	37.63	39.13	39.40
8	45.38	41.51	38.49	38.42	43.77	45.77	38.41	38.38	43.84	45.78	48.20	39.71	37.34	45.13	45.94
9	64.48	52.39	51.73	53.33	60.79	55.09	51.64	53.30	60.80	54.43	49.16	52.74	52.14	52.00	52.19
10	41.27	42.00	42.09	42.08	41.25	42.38	41.99	42.04	41.27	42.38	41.71	42.00	42.03	42.25	42.24
11	31.80	27.52	26.93	22.66	26.92	20.66	26.79	22.60	26.84	20.65	32.56	31.20	29.99	32.39	27.54
12	37.06	49.49	39.22	38.83	72.63	17.23	39.03	38.70	72.62	17.15	71.10	42.10	32.14	69.58	73.10
13	136.28	127.40	128.62	130.89	39.46	24.85	128.47	130.79	39.75	24.76	50.02	131.29	129.43	47.41	44.71
14	45.80	139.18	138.53	137.69	39.99	71.80	138.61	137.72	40.02	71.85	52.90	134.81	137.85	45.04	46.37
15	142.40	50.00	49.88	47.45	139.43	39.54	49.70	47.34	139.53	39.53	137.40	45.37	40.05	31.63	32.80
16	117.62	213.06	70.57	68.93	124.55	17.23	69.30	69.15	124.54	17.25	136.98	150.33	37.94	30.85	32.06
17	124.24	----	----	----	----	----	----	----	----	----	21.30	103.25	73.33	74.85	67.83
18	33.12	33.25	33.35	33.25	33.11	32.96	33.30	33.27	33.13	32.97	33.00	33.31	33.32	33.08	33.28
19	21.28	21.81	21.95	21.87	21.27	21.95	21.83	21.64	21.29	21.53	21.48	21.90	21.90	21.56	21.78
20	12.47	12.01	11.86	11.95	12.23	12.30	11.84	11.97	12.26	12.32	10.93	11.66	11.66	11.89	11.40
MeCOO	21.91	21.97	21.89	21.87	21.86	21.99	21.99	21.99	21.89	22.00	22.07	21.90	21.91	22.08	20.91
MeCOO	----	----	----	----	----	----	----	----	----	----	----	----	----	----	21.39
MeCOO	----	----	----	----	----	----	----	----	----	----	----	----	----	----	21.70
MeCOO	170.97	170.47	170.71	170.66	170.89	170.70	170.77	170.71	170.92	170.65	170.71	170.84	170.77	170.84	170.87
MeCOO	----	----	----	----	----	----	----	----	----	----	----	----	----	----	170.67
MeCOO	----	----	----	----	----	----	----	----	----	----	----	----	----	----	171.24
$MeSO_2$	37.06	----	----	----	----	----	----	----	----	----	----	----	37.63	36.97	----

EXPERIMENTAL SECTION

Melting points (Kofler apparatus) are uncorrected. The NMR spectra (300 MHz ^1H and 75.47 MHz ^{13}C) were obtained with a Bruker AM--300 spectrometer equipped with a process controller and an array processor. Samples were dissolved in $CDCl_3$. The assignments of ^{13}C chemical shifts were made with the aid of distortionless enhancement by polarization transfer (DEPT) using a flip angle of 135°. Monodimensional n.O.e.-difference experiments were performed by irradiation for 4 s in series of 8 scans with alternate on-resonance and off-resonance. Bruker's programs were used for COSY (45°), NOESY, CONOESY (90°) and C/H correlation. The optical rotations were measured on a Perkin-Elmer 240 polarimeter. IR spectra were recorded in a FT-IR-Nicolet 20 SX spectrometer. Mass spectra were obtained on a Hewlett-Packard 5988-A spectrometer (CI,methane). Silica gel SDS 60 Å CC (40-60 μm) was used for flash chromatography. The colums were pressurized to 0.1 atm with air. CH_2Cl_2 or $CHCl_3$ containing increasing amounts of acetone was used as eluent. Analytical plates (silica gel Merck G) were visuallized by spraying with H_2SO_4-AcOH, followed by heating at 120°C for 5 min.

GENERAL MESYLATION PROCEDURE.-

Product (30 mg) was dissolved in 2 mL of pyridine and treated with MsCl (0.01 mL) at room temperature for 24 h or under reflux for 4 h. After this time, the reaction products were dropped in a solution of 50 mL of $KHSO_4$ (10%), extracted with 50 mL of CH_2Cl_2, dried over anhydrous $NaSO_4$ and the solvent was evaporated at reduced pressure.

GENERAL ACETOLYSIS PROCEDURE.-

Mesylate (50 mg) was dissolved in 2 mL AcOK/AcOH (0.5 N), the mixture refluxed for 24 h and then neutralized with $NaHCO_3$, extracted with CH_2Cl_2, dried over anhidrous Na_2SO_4 and the solvent evaporated.

MESYLATION OF *ent*-1ß-ACETOXY-12α-DIHYDROXYBEYER-15-ENE (**1**).-

Product **1** (200 mg) isolated according to reference 22 treated with MsCl as previously described above, gave, after CC, *ent*-1ß-acetoxy-17mesyloxy-12α-hydroxybeyer-15-ene (**2**) (180 mg, 90%): Colorless gum; $[\alpha]_D$ +18° ($CHCl_3$, c 1); IR μ_{max}($CHCl_3$): 3530, 2945, 1718 and 1174 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 441 ($[M+1]^+$, 2 %), 285 (60), 363 (100). Anal. Calcd for $C_{23}O_6H_{36}S$: C, 62.73; H, 8.18. Found: C, 62.80; H, 8.35.

ACETOLYSIS OF PRODUCT **2**.-

Mesylate **2** (150 mg) was treated with AcOK/AcOH as described above under General Acetolysis Procedure to give, after CC: *ent*-1ß,17-diacetoxy-12α-hydroxybeyer-15-ene (**3**) (37 mg, 25%), *ent*-1ß,12α,17-triacetoxy-16(13)→12,11(12)→13-di*abeo*beyer-15-ene (**4**) (60 mg, 40%) and the starting product (**2**) (23 mg, 15%). Product **3**: known product[18]. Product **4**: mp : 87-89°C; $[\alpha]_D$ -12° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2948, 1737 and 1246 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 447 ($[M+1]^+$, 1%), 387 (100), 327 (20). Anal. Calcd for $C_{26}O_6H_{38}$: C, 69.96; H, 8.52. Found: C, 69.88; H, 8.48.

ACETYLATION OF PRODUCT **2**.-

Acetylation of 300 mg of product **2** with 7 mL Ac_2O and 14 mL pyridine at r.t. for 48 h, gave *ent*-1ß,12α-diacetoxy-17-mesyloxybeyer-15-ene (**5**) (255 mg, 85%) as a colorless gum; $[\alpha]_D$ +43° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2945, 1720 and 1170 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 483 ($[M+1]^+$, 1%), 363 (40), 423 (100). Anal. Calcd for $C_{25}O_7H_{38}S$: C,62.24; H, 7.88. Found: C, 61.87; H, 8.20.

ACETOLYSIS OF PRODUCT 5.-

Treatment of 200 mg of product **5** with AcOK/AcOH in the usual manner gave: (**4**) (40 mg, 20%) and the previously described compounds *ent*-1ß,12α,17-triacetoxybeyer-15-ene[18] (**6**) (70 mg, 35%), *ent*-1ß,16α,17-triacetoxyatis-13-ene[13] (**7**) (30 mg, 15%) and *ent*-1ß,17-diacetoxy-16α-hydroxyatis-13-ene[13] (**8**) (20 mg, 10%) and the starting product (**5**) (20 mg, 10%).

DIMESYLATION AND REARRANGEMENT OF PRODUCT 1.-

Three products were isolated, after CC, when dimesylation of product **1** (150 mg) was attempted with MsCl/pyridine (0.12 mL) under conditions of reflux (24 h): (E)-*ent*-1ß-acetoxy-17-mesyloxyatis-13,16-diene (**10**) (60 mg, 40%), (Z)-*ent*-1ß-acetoxy-17mesyloxyatis-13,16-diene (**11**) (37 mg, 25%) and *ent*-1ß-acetoxy-16ß-hydroxy-17-mesyloxyatis-13-ene (**12**) (20 mg, 14%). Product **10**: mp : 123-25°C; $[\alpha]_D$ -16° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2950, 1720 and 1165 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 423 ($[M+1]^+$, 1%), 269 (48), 365 (100). Anal. Calcd for $C_{23}O_5H_{34}S$: C, 65.40; H, 8.06. Found: C, 65.44; H, 8.12. Product **11**: mp : 127-29°C; $[\alpha]_D$ -8° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2945, 1720 and 1160 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 423 ($[M+1]^+$, 2%), 269 (43), 365 (100). Anal.Calcd for $C_{23}O_5H_{34}S$: C, 65.40; H, 7.58. Found: C, 65.38; H, 8.02. Product **12**: Colorless gum; $[\alpha]_D$ +15° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3520, 2945, 1720 and 1170 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 441 ($[M+1]^+$, 2%), 423 (10), 379 (17), 321 (14), 285 (42), 363 (100).

ACID TREATMENT OF PRODUCT 2.-

Product **2** (150 mg) was dissolved in Cl_2CH_2 (20 mL), washed with a diluted solution of HCl (20 mL, 0,1N) during a few minutes, neutralized with $NaHCO_3$, extracted with CH_2Cl_2, dried over anhidrous $NaSO_4$ and the solvent evaporated. After CC, the following products were isolated: *ent*-1ß-acetoxy-16ß-hydroxy-17-mesyloxyatis-13-ene (**13**) (37 mg, 15%), *ent*-1ß-acetoxy-12α-hydroxy-17-mesyloxy-16(13)→12,11(12)→13-di*abeo*beyer-15-ene (**32**) (22 mg, 15%) and starting product (**2**) (60 mg, 40%). Product **13**: mp : 174-76°C; $[\alpha]_D$ +6.4° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3505, 2944, 1718 and 1174 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 441 ($[M+1]^+$, 1%), 285 (37), 363 (100). Anal. Calcd for $C_{23}O_6H_{36}S$: C,62.73; H, 8.18. Found: C, 62.54; H, 8.14. Product **32**: Colorless gum; $[\alpha]_D$ -14° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3510, 1740 and 1245 cm^{-1}; ^1H NMR: see Table II; MS, m/z (%): 441 ($[M+1]^+$, 1%), 366 (38), 383 (100).

MESYLATION OF *ent*-1ß-ACETOXY-12α,17-DIHYDROXYATIS-13-ENE (**14**).- 100 mg of **14**, isolated as indicated in reference 22, was treated with 0.035 mL of MsCl. Work-up proceeded in the usual form, and after CC, product (**13**) (90 mg, 90%) was obtained.

ACETOLYSIS OF PRODUCT 13.-

Product **13** (80 mg) was dissolved in AcOK/AcOH (3 mL) and stirred under reflux for 24 h. Work-up proceeded in the usual manner, and after CC, product **4** (68 mg, 85%) was isolated.

OXIDATION OF PRODUCT 1.-

100 mg of **1** was oxidized with pyridinium dichromate[22], to give, after CC, *ent*-1ß-acetoxy-17-hydroxy-15-en-12-one (**15**) (85 mg, 85%). mp : 61-63°C; $[\alpha]_D$ -3.63 ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3450, 1750,and 1730 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 361 ($[M+1]^+$, 1%), 241 (89), 229 (93), 301 (100). Anal. Calcd for $C_{22}O_4H_{32}$: C, 73.33; H, 17.78. Found: C, 73.60; H, 8.67.

MESYLATION OF PRODUCT 15.-

90 mg of product **15** was mesylated with MsCl (0.03 mL). The solution was kept at room temperature for 24 h as described above. After CC, *ent*-1ß-acetoxy-17-mesyloxybeyer-15-en-12-one (**16**)

(80 mg, 90%) was isolated. mp : 133-35°C; $[\alpha]_D$ +40° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3075, 1748 and 1732 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 439([M+1]$^+$, 1%), 283 (48), 379 (100). Anal. Calcd for $C_{23}O_6H_{34}S$: C, 63.01; H, 7.76. Found: C, 62.96; H, 7.92.

ACETOLYSIS OF PRODUCT **16**.-

Product **16** (70 mg) was treated with AcOK/AcOH for 24 h under reflux, after which only **16** (66 mg, 95%) was isolated.

REDUCTION OF PRODUCT **15**.-

$NaBH_4$ (900 mg) was added to a stirred solution of product **15** (450 mg) in i-PrOH (25 mL) at room temperature for 30 min. The reaction mixture was acidified with dil. HCl, extracted with CH_2Cl_2, dried with $NaSO_4$ and concentrated in vacuo. Chromatography on a silica gel column yielded *ent*-1ß-acetoxy-12ß,17-dihydroxybeyer-15-ene (**17**) (360 mg,80%) and product **1** (90 mg, 20%). Product **17**: mp : 180°C; $[\alpha]_D$ +68° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3525, 2946, 1720 and 1170 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 363 ([M+1]$^+$, 2%), 285 (55). Anal. Calcd for $C_{22}O_4H_{34}$: C, 72.93; H, 9.39. Found: C, 72.74; H, 9.43.

MESYLATION OF PRODUCT **17**.-

Treatment of **17** (220 mg) with MsCl (0.15 mL) under the same conditions as described above gave *ent*-1ß-acetoxy-12ß,17-dimesyloxybeyer-15-ene (**18**) (198 mg, 90%). mp : 185-87°C; $[\alpha]_D$ +39° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2945, 1720 and 1175 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 519 ([M+1]$^+$, 1%), 459 (26), 362 (40), 284 (60), 79 (100). Anal. Calcd for $C_{24}O_8H_{38}S_2$: C, 55.60; H, 7.34. Found: C, 55.72; H, 7.36.

ACETOLYSIS OF PRODUCT **18**.-

Product **18** (200 mg) was treated with AcOK/AcOH as indicated above, yielding four products after CC: (E)-*ent*-1ß,17-diacetoxy-14(13)→12-*abeo*beyer-13(17),15-diene (**19**) (80 mg, 40%), (Z)-*ent*-1ß,17-diacetoxy-14(13)→12-*abeo*beyer-13(17),15-diene (**20**) (40 mg, 20%), (E)-*ent*-1ß-acetoxy-17-mesyloxy-14(13)→12-*abeo*beyer-13(17),15-diene(**21**) (30 mg, 15%) and (Z)-*ent*-1ß-acetoxy-17-mesyloxy-14(13)→12-*abeo*beyer-13(17),15-diene (**22**) (30 mg, 15%). Product **19**: mp : 141-43°C; $[\alpha]_D$ +32.6° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2945, 1718, 1163 and 1165 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 387 ([M+1]$^+$, 2%), 327 (78), 267 (18), 285 (100). Anal. Calcd for $C_{24}O_4H_{34}$: C, 74.61; H, 8.81. Found: C,74.42; H, 8.97. Product **20**: mp : 137-39°C; $[\alpha]_D$ +7.3° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2947, 170, 1160 and 1163 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table III; MS, m/z (%): 387 ([M+1]$^+$, 2%), 327 (55), 267 (15), 285 (100). Anal. Calcd for $C_{24}O_4H_{34}$: C, 74.61; H, 8.81. Found: C, 74.24; H, 8.78. Product **21**: mp : 128-30°C; $[\alpha]_D$ 42.8° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2945, 1720, 1160 and 1162 cm^{-1}; ^1H NMR: see Table I; ^{13}C NMR: see Table IV; MS, m/z (%): 423 ([M+1]$^+$, 8%), 327 (12), 267 (80), 363 (100). Anal. Calcd for $C_{23}O_5H_{34}S$: C, 65.40; H, 8.06. Found: C, 64.98; H, 8.44. Product **22**: mp : 130-32°C; $[\alpha]_D$ +4.5° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2945, 1719, 1162 and 1165 cm^{-1}; ^1H NMR: see Table I; MS, m/z (%): 423 ([M+1]$^+$, 6%), 327 (8), 267 (82), 363 (100). Anal. Calcd for $C_{23}O_5H_{34}S$: C, 65.40; H, 8.06. Found: C, 65.04; H, 8.40.

OXIDATION OF PRODUCT **14**.-

Product **14** (500 mg), dissolved in $MeOH/H_2O$, was added a flask containing 500 mg $NaIO_4$ dissolved in 3 mL water (in an ice bath with magnetic stirring). Then 200 mg of $NaHCO_3$ was also added. A white precipitate of the nonsoluble product appeared and, after CC, *ent*-1ß-acetoxy-17-*nor*atis-13-en-16-one (**23**) (475 mg, 95%) was obtained. mp : 113-15°C; $[\alpha]_D$ +2° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2947, 2870, 1728 and 1243 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 331 ([M+1]$^+$,

100%), 271 (82), 229 (11), 273 (26). Anal. Calcd for $C_{21}O_3H_{30}$: C, 76.36; H, 9.09. Found: C, 76.15; H, 8.99.

REDUCTION OF PRODUCT **23**.-

Product **23** (200 mg) was dissolved in EtOH (8 mL) and 100 mg $NaBH_4$ was added. The mixture was stirred at room temperature for 2 h. After CC, *ent*-1ß-acetoxy-16ß-hydroxy-17-*nor*atis-13-ene (**24**) (130 mg, 65%) and *ent*-1ß-acetoxy-16α-hydroxy-17-*nor*atis-13-ene (**25**) (70 mg, 35%), were isolated. Product **24**: mp : 135-36°C; $[\alpha]_D$ +2.5° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3343, 2929, 2871, 2850 and 1245 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 333 ([M+1]$^+$, 1%), 273 (59), 256 (16), 228 (20), 78 (33), 255 (100). Anal. Calcd for $C_{21}O_3H_{32}$: C, 75.90; H, 9.64. Found: C, 75.67; H, 9.50. Product **25**: mp : 164-65°C; $[\alpha]_D$ +1.3° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3343, 2940, 2871, 2870, 1728 and 1246 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 333 ([M+1]$^+$, 1%), 273 (50), 256 (20), 228 (22), 78 (35), 255 (100). Anal. Calcd for $C_{21}O_3H_{32}$: C, 75.90; H, 9.64. Found: C, 75.73; H, 9.54.

MESYLATION AND REARRANGEMENT OF PRODUCT **24**.-

Product **24** (100 mg) was treated with MsCl (0.02 mL) at room temperature in the usual manner to give, after CC, *ent*-1ß-acetoxy-12α-hydroxy-16(13)→12,11(12)→13-17-*nor*beyer-15-ene (**26**) (95 mg, 95%). mp : 129-30°C; $[\alpha]_D$ +2° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3323, 2948, 2868, 1736 and 1240 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 333 ([M+1]$^+$, 1%), 273 (34), 257 (41), 217 (36), 107 (86), 91 (100). Anal. Calcd for $C_{21}O_3H_{32}$: C, 75.90; H, 9.64. Found: C, 75.65; H, 9.68.

MESYLATION AND REARRANGEMENT OF PRODUCT **25**.-

Treatment of **25** (100 mg) with MsCl (0.02 mL) under the same conditions as described for product **24**, gave, after CC, *ent*-1ß-acetoxy-14R-hydroxy-17-*nor*trachylobane (**27**) (85 mg, 85%). mp : 162-64°C; $[\alpha]_D$ +1.5° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3484, 2932, 2871, 1717 and 1269 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 333 ([M+1]$^+$, 2%), 273 (71), 256 (21), 228 (24), 255 (100). Anal. Calcd for $C_{21}O_3H_{32}$: C, 75.90; H, 9.64. Found: C, 75.98; H, 9.42.

REDUCTION OF PRODUCT **23** WITH $NaBD_4$.-

Treatment of product **23** (200 mg) with $NaBD_4$ under the same conditions as in treatment with $NaBH_4$ gave, after CC: *ent*-1ß-acetoxy-16ß-hydroxy-16α-deuterio-17-*nor*atis-13-ene (**28**) (130 mg, 65%) and *ent*-1ß-acetoxy-16α-hydroxy-16ß-deuterio-17-*nor*atis-13-ene (**29**) (70 mg, 35%). Product **28**: mp : 144-45°C; $[\alpha]_D$ +2.3° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3328, 2926, 2871, 1728 and 1246 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 334 ([M+1]$^+$, 1%), 316 (12), 274 (70), 257 (20), 256 (100). Product **29**: mp : 171-72°C; $[\alpha]_D$ +1.5° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3484, 2945, 2853, 1718 and 1241 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 334 ([M+1]$^+$, 1%), 316 (11), 275 (18), 257 (20), 256 (100).

MESYLATION AND REARRANGEMENT OF PRODUCT **28**.-

Mesylation of product **28** (100 mg) under the same conditions that described above for product **24** gave, after CC, *ent*-1ß-acetoxy-12α-hydroxy-13-deuterio-16(13)→12,11(12)→13-di*abeo*-17-*nor*beyer-15-ene (**30**) (90 mg, 90%). mp : 145-47°C; $[\alpha]_D$ +2.2° ($CHCl_3$, c 1); IR μ_{max}($CHCl_3$): 3403, 2944, 2870, 1736 and 1245 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 334 ([M+1]$^+$, 1%), 316 (45), 257 (22), 256 (96), 274 (100).

MESYLATION AND REARRANGEMENT OF PRODUCT **29**.-

Treatment of product **29** (100 mg) in the usual manner with MsCl gave, after CC, *ent*-1ß-acetoxy-14R-hydroxy -16-deuterio- 17-*nor*trachylobane (**31**) (80 mg, 80%). mp : 127-29°C; $[\alpha]_D$ +9.8° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3439, 2918, 2853, 1735 and 1236 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 334 ([M+1]$^+$, 4%), 316 (20), 275 (20), 257 (15), 256 (60), 274 (100).

DEHYDROXYLATION OF PRODUCT 1.-

Product **1** (300 mg) was firstly treated with $Py/Cl_4C/Ph_3P$ and afterward with tributyltin hydride/α,α'-azo-isobutyronitrile/toluene as described in references 23 and 24. After CC, *ent*-1ß-acetoxy-12α-hydroxybeyer-15-ene (**33**) (225 mg, 85%), was obtained. mp : 135-37°C; $[\alpha]_D$ +48.5° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3448, 2947, 2868, 1735 and 1245 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 347 ($[M+1]^+$, 2%), 329 (46), 269 (98), 243 (30), 287 (100). Anal. Calcd for $C_{22}O_3H_{34}$: C, 76.30; H, 8.93. Found: C, 76.35; H, 9.89.

MESYLATION OF PRODUCT 33.-

Product **33** (150 mg) was treated with MsCl in the usual manner to give the compounds previously described[20] (**34**) (90 mg, 60%) and (**35**) (30 mg, 20%) and *ent*-1ß-acetoxy-17-mesyloxyatis-13-ene (**36**) (22.5 mg, 15%). Product **36**: Colorless gum; $[\alpha]_D$ +18.6° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2931, 2842, 1732 and 1247 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 425 ($[M+1]^+$, 2%), 366 (23), 329 (22), 270 (21), 269 (97), 365 (100).

HYDROGENATION OF PRODUCT 2.-

Hydrogenation of 120 mg of **2**, dissolved in 10 mL EtOH using $Pd(5\%)/BaSO_4$ as a catalyst, was carried out at room temperature and 5 atm. of H_2 pressure for 2h. After CC, *ent*-1ß-acetoxy-12α-hydroxy-17-mesyloxybeyerane (**37**) (120 mg, 100%), was isolated. Colorless gum; $[\alpha]_D$ +23° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 3528, 2946, 2871, 1731, 1249 and 1174 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 443 ($[M+1]^+$, 4%), 366 (24), 287 (33), 269 (25), 365 (100). Anal. Calcd for $C_{23}O_6H_{38}S$: C, 62.44; H, 8.60. Found: C, 62.08; H, 8.97.

ACETOLYSIS OF PRODUCT 37.-

Product **37** (90 mg) was treated with AcOK/AcOH as described above under General Acetolysis Procedure. After CC, *ent*-1ß,12α,17-triacetoxybeyerane (**38**) (72 mg, 80%). Product **38**: mp : 136-38°C; $[\alpha]_D$ +25.7° ($CHCl_3$, c 1); IR μ_{max} ($CHCl_3$): 2948, 2871, 1735 and 1245 cm^{-1}; ^1H NMR: see Table II; ^{13}C NMR: see Table IV; MS, m/z (%): 447 ($[M+1]^+$, 1%), 389 (88), 330 (23), 328 (15), 269 (40), 329 (100). Anal. Calcd for $C_{26}O_6H_{38}$: C, 69.96; H, 8.52. Found: C, 69.98; H, 8.48.

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