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Oxidative Transformations of the Side-chains in the (12*E*)- and (12*Z*)-Abienols

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The reaction of (12*E*)-abienol (*3*) with *m*-chloroperbenzoic acid in chloroform yields, in addition to compounds *4*–*7*, two unexpected products which have now been formulated as the (12*R*,13*R*,14*R*)- and (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanols (*1*, *2*) on the basis of chemical results and X-ray analysis.

A probable route to *1* and *2* involves attack of the peracid on the 14,15-double bond in *3* and rearrangement to the (12*R*,13*E*)- and (12*S*,13*E*)-8,12-epoxy-13-labden-15-ols (*18*, *19*), which are then epoxidized. Its existence is borne out by the fact that *18* and *19* can be trapped from an epoxidation reaction carried out in a two-phase buffered system, and by the observation that both *18* and *19* undergo rapid and stereoselective epoxidations. Such a reaction sequence is of less importance for (12*Z*)-abienol (*22*), which furnishes compounds *29*–*32* by preferential attack of the peracid on the 12,13-double bond.

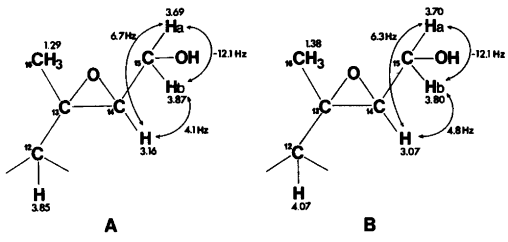
Alcohols *18* and *19* have been synthesized from (12*Z*)-abienol (*22*) *via* a stereospecific lead tetraacetate oxidation, which affords as the major products the (12*R*,13*S*)- and (12*S*,13*R*)-8,12-epoxy-14-labden-13-oyl acetates (*23*,*24*). The latter compounds were subjected to palladium(II)-catalyzed allylic rearrangements giving *25* and *26*, respectively, which were hydrolyzed.

A comparison of spectral data indicates that carterochaetol, previously formulated as (12*R*,13*Z*)-8,12-epoxy-13-labden-15-ol (*33*), is identical with (12*S*,13*E*)-8,12-epoxy-13-labden-15-ol (*19*). A revision of the stereochemistry at C-12 is also suggested for 16-hydroxycarterochaetol (*35*).

In a previous communication [1] we described the preparation of four tobacco diterpenoids:[2–4] The (12*R*,13*S*)- and (12*S*,13*R*)-8,12-epoxy-14-labden-13-ols (*4*, *5*) and the (12*R*,13*S*)- and (12*S*,13*R*)-8,13-epoxy-14-labden-12-ols (*6*, *7*) by treatment of (12*E*)-abienol (*3*) with *m*-chloroperbenzoic acid in chloroform. Two products of higher polarity, constituting some 20 % of the reaction mixture, were also obtained. We now report the stereostructures of these and discuss the mechanism of their formation in the light of results obtained by chemical transformations.

RESULTS

The two polar oxidation products (*1*, *2*) were identified as isomers of 8,12-13,14-diepoxy-15-labdanol on the basis of the following evidence. Both compounds (*1*, *2*) had the composition $C_{20}H_{34}O_3$ and gave rise to monoacetates (*8*, *9*) on acetylation. The allocation of the hydroxyl group in *1* and *2* to partial structures A and B, respectively, was determined by proton spin decoupling and spin simulation experiments. Additional support for these assignments was provided by the ^{13}C NMR spectra, which, besides



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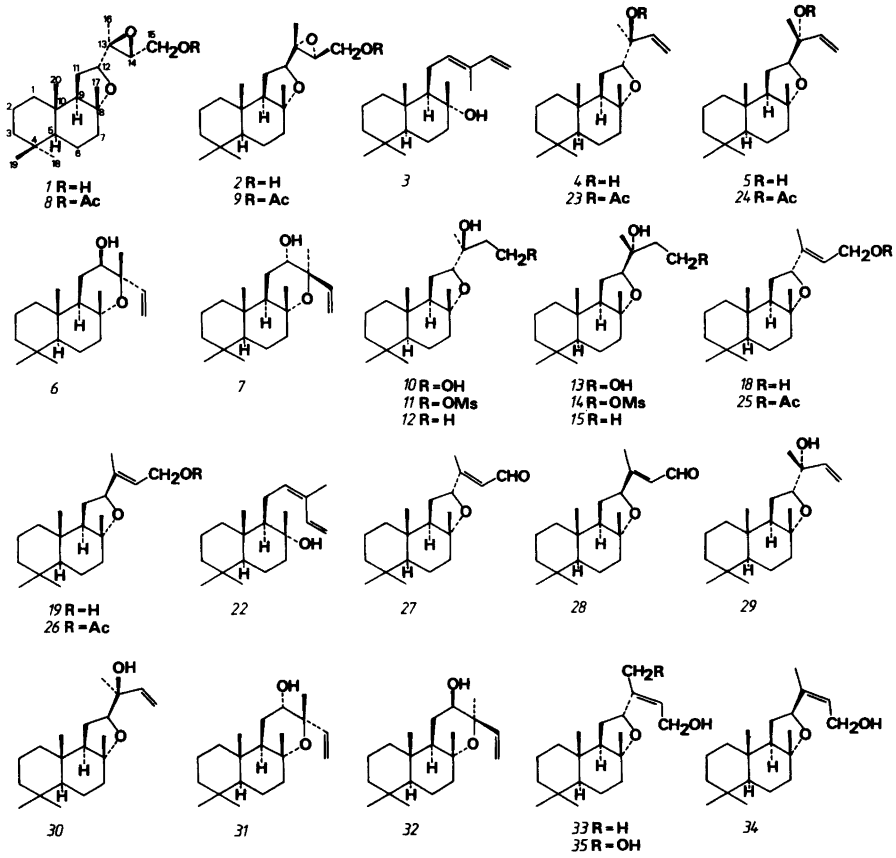


the C–15 resonance, present at δ 61.0 for *1* and at δ 60.9 for *2*, contained signals attributed to C-13 and C-14 at δ 61.6 (s) and 62.1 (d) for *1* and at δ 61.8 (s) and 60.1 (d) for *2* (*cf.* Table 1).

The presence of the 8,12-epoxy group followed from the chemical shift values of the signals due to the remaining oxygen-carrying carbon atoms, δ 81.8 (s) and 79.2 (d) for *1* and δ 81.1 (s) and 80.4 (d) for *2*.

The stereochemistry at C-12 and C-13 in alcohol *1* was deduced to be *R,R* by chemical correlation. Reduction using LAH converted alcohol *1* to a diol (*10*), which was reacted with methanesulfonyl chloride in pyridine. The monomesylate formed (*11*) was reduced using LAH to give a product, which was identical to (12*R*,13*S*)-8,12-epoxy-13-labdanol (*12*).

In a similar manner, alcohol *2* was converted *via* diol *13* and monomesylate *14* to (12*S*,13*R*)-8,12-epoxy-13-labdanol (*15*), hence demonstrating that its stereochemistry at C-12 and C-13 is *S,S*. While the assignment of an *R*-chirality to C-14 in alcohol *1* rests on chemical correlations detailed below, X-ray analysis was used to complete the determination of the stereochemistry of alcohol *2*.

Alcohol *2* formed needle-shaped crystals of space group $P2_1$. The crystal data, obtained on a Philips PW 1100 diffractometer, are: a=12.693, b=7.376 and c=11.116 Å, β=112.02°, Z=2. The present *R*-value including anisotropic thermal parameters for all non-hydrogen atoms is 0.098; location of the hydrogen atoms and further refinement being under way.[5] A stereoscopic view, which summarizes the X-ray results and demonstrates that alcohol *2* is (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanol, is shown in Fig. 1.

Three routes, A, B and C in Scheme 1, may be invoked to account for the generation of alcohols *1* and *2*. In route A, (12*E*)-abienol (*3*) is converted *via* the intermediacy of epoxides *16*

Table 1. Carbon-13 chemical shifts and assignments for compounds *1, 2, 8–10, 12, 13, 15, 18, 19* and *23–26.*[a].

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	C-16	C-17	C-18	C-19	C-20
1	40.0	18.4	42.4	33.1	57.4	20.6	39.7	81.8	59.9	36.4	25.3	79.2	61.6	62.1	61.0	12.9	21.4	33.5	21.1	14.8
2	40.0	18.4	42.4	33.1	57.0	21.0	40.3	81.1	60.6	36.3	23.7	80.4	61.8	60.1	60.9	14.7	24.1	33.5	21.0	15.6
8 [b]	40.0	18.4	42.5	33.1	57.4	20.6	39.7	81.7	59.9	36.4	25.4	78.5	61.4	58.6	63.2	13.4	21.4	33.6	21.1	14.8
9 [c]	40.1	18.5	42.5	33.1	57.1	21.0	40.4	81.0	60.7	36.4	23.7	80.0	61.4	56.8	63.1	15.0	24.0	33.5	21.0	15.6
10	39.8	18.3	42.4	33.0	57.3	20.5	39.6	81.2	60.0	36.3	23.9	81.6	74.5	38.9	58.9	22.4	21.3	33.5	21.1	14.7
12	39.9	18.4	42.5	33.1	57.4	20.6	39.8	80.9	60.4	36.4	23.8	81.9	73.9	29.9	7.7	22.9	21.3	33.6	21.1	14.8
13	40.2	18.5	42.5	33.1	57.1	21.4	40.9	81.1	60.9	36.4	23.8	85.8	73.6	38.8	58.9	23.9	25.4	33.5	21.0	16.0
15	40.3	18.5	42.6	33.2	57.2	21.5	41.0	80.8	61.1	36.5	24.3	85.8	72.5	30.1	7.9	23.7	25.4	33.6	21.0	16.0
18	39.7	18.4	42.5	33.1	57.3	20.6	39.9	81.3	59.2	36.3	28.2	79.6	140.0	123.7	59.2	12.9	21.6	33.5	21.1	15.0
19	40.1	18.4	42.5	33.1	57.2	21.0	40.6	81.3	61.0	36.4	28.8	81.9	140.2	122.0	59.1	13.4	24.8	33.5	21.0	15.8
23 [d]	40.0	18.3	42.4	33.0	57.4	20.5	39.6	81.2	59.5	36.2	24.4	80.3	84.0	139.4	114.9	18.9	21.3	33.5	21.1	14.8
24 [e]	40.2	18.5	42.5	33.1	57.2	21.3	40.9	81.5	60.6	36.4	24.1	85.3	83.4	139.6	114.6	20.0	25.1	33.5	21.0	15.9
25 [f]	39.9	18.4	42.5	33.1	57.3	20.6	39.7	81.2	59.1	36.2	28.2	79.3	142.3	118.4	61.0	13.1	21.5	33.5	21.1	15.0
26 [g]	40.6	18.4	42.5	33.1	57.1	21.0	40.1	81.2	61.0	36.3	28.8	81.6	142.7	116.6	61.0	13.6	24.6	33.5	21.0	15.8

[a] δ-Values in $CDCl_3$ relative to TMS. [b] $OCOCH_3$ 20.8. [c] $OCOCH_3$ 170.8; $OCOCH_3$ 20.8. [d] $OCOCH_3$ 169.7; $OCOCH_3$ 22.3. [e] $OCOCH_3$ 169.9; $OCOCH_3$ 22.1. [f] $OCOCH_3$ 170.9; $OCOCH_3$ 21.0. [g] $OCOCH_3$ 170.9; $OCOCH_3$ 21.0.

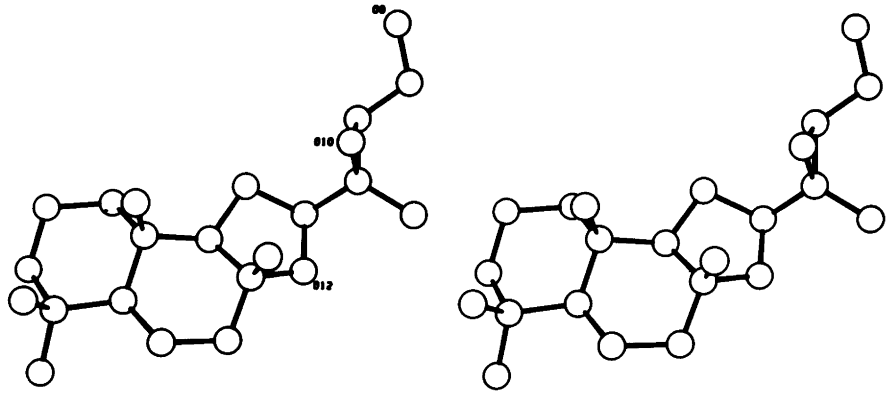


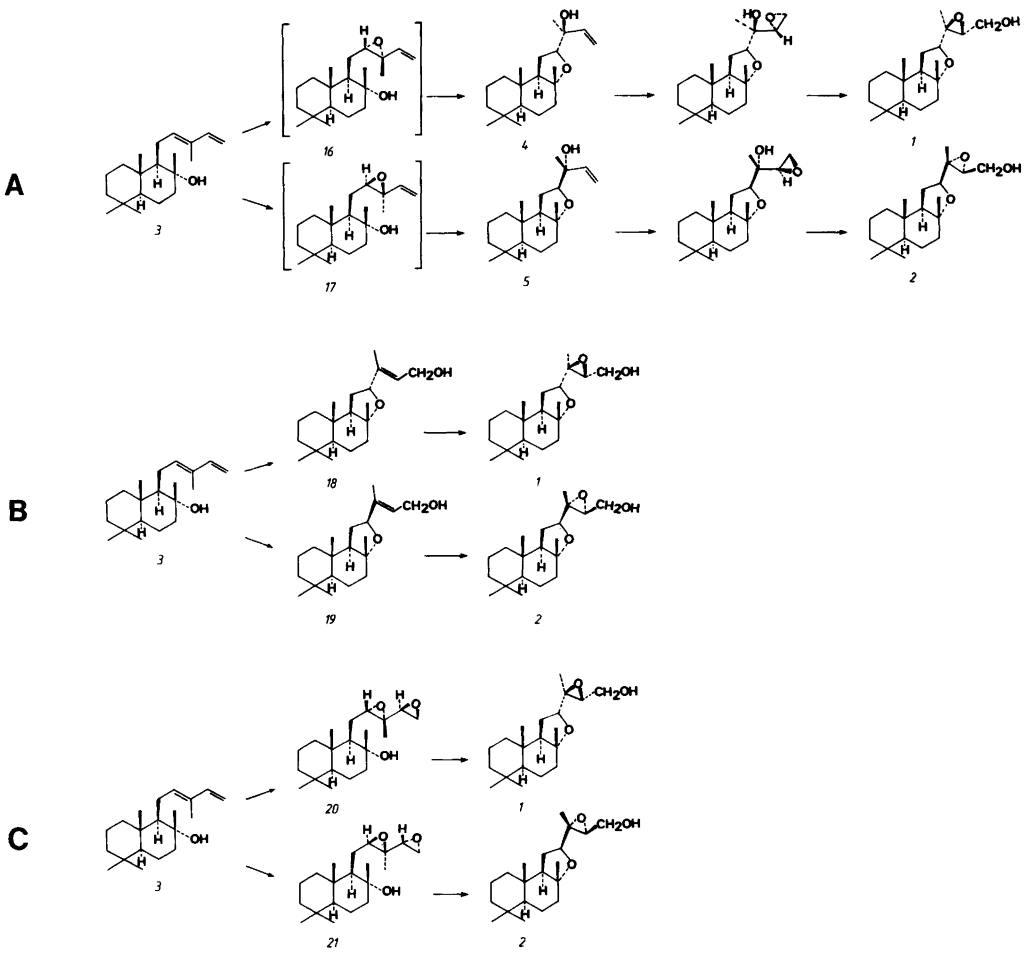
Fig. 1. A stereoscopic view of (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanol (*2*).

and *17*, or equivalent peracid complexes, to the 8,12-epoxides *4* and *5*, which undergo epoxidation of the 14,15-double bond and subsequent rearrangement. This possibility was ruled out, however, since *4* was recovered unchanged after treatment with *m*-chloroperbenzoic acid in chloroform for 2 h, *i.e.* the reaction time normally needed to convert (12*E*)-abienol (*3*) to alcohols *1* and *2*. Route B would involve an initial attack of peracid on the 14,15-double bond in (12*E*)-abienol (*3*), accompanied by acid-induced rearrangements to give alcohols *18* and *19*, which are rapidly and stereospecifically epoxidized. The formation of alcohols *1* and *2* *via* route C would require the intermediate 12,13-14,15-diepoxides *20* and *21* to have (12*S*,13*R*,14*S*)- and (12*R*,13*S*,14*R*)-stereochemistry, respectively. These two diastereoisomers are actually those expected to arise from (12*E*)-abienol (*3*), since the initially generated monoepoxides would exist mainly in s-*trans* conformations and attack of the peracid would occur *anti* to the epoxide oxygen.[6]

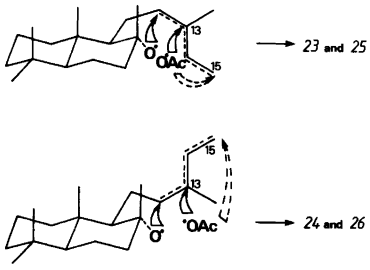
In order to evaluate the importance of routes B and C we decided to prepare the (12*R*,13*E*)- and (12*S*,13*E*)-8,12-epoxy-13-labden-15-ols (*18*, *19*) and to study the products of their epoxidation reactions. To this end (12*Z*)-abienol (*22*) was initially treated with lead tetraacetate (LTA) in benzene. Four products were obtained. The major two, which gave rise to alcohols *4* and *5* on alkaline hydrolysis, were identified as the (12*R*,13*S*)- and (12*S*,13*R*)-8,12-epoxy-14-labden-13-oyl acetates *23* and *24*, respectively. The minor two products (*25*, *26*) proved to be identical to the rearrangement products obtained by reacting acetates *23* and *24* with bis(acetonitrile)palladium(II) chloride in tetrahydrofuran. Their ^{1}H NMR spectra included signals due to a vinylic methyl group, a CH_2–OAc group and an olefinic proton. They were hence formulated as the (12*R*,13*E*)- and (12*S*,13*E*)-8,12-epoxy-13-labden-15-oyl acetates (*25*, *26*), the *E*-geometries assigned to their 13,14-double bonds being consistent with the proposed mechanism of the allylic rearrangement reaction [7] (for conclusive evidence, see below).

The LTA reaction deserves additional comments. Firstly, it follows that (12*Z*)-abienol (*22*) on LTA treatment in pure benzene gives rise to 8,12-epoxides (*23*–*26*) only. Addition of pyridine does not affect the outcome of this reaction. These results contrast with findings for other γ,δ-unsaturated alcohols, *e.g.* 4-penten-1-ol [8] and β-ionol,[9] which yield mixtures of tetrahydrofurans and tetrahydropyrans when the reaction is carried out in benzene, while tetrahydrofurans are the predominant products (98 %) from 4-penten-1-ol, when pyridine is present.[9] This sensitivity to experimental conditions has been associated with the reaction mechanisms involved; *i.e.* the reaction is likely to proceed by an ionic or concerted mechanism in benzene, while in the presence of pyridine a radical mechanism has been found to be operative.[9] Whether this implies that the diene (12*Z*)-abienol (*22*) reacts by a radical mechanism under both reaction conditions is presently unclear.

Secondly, the reaction of (12*Z*)-abienol (*22*)



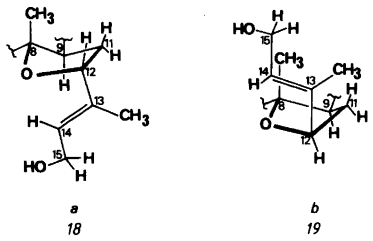
Scheme 1. Proposed routes for the formation of *1* and *2* from (12*E*)-abienol (*3*).



Scheme 2. Formation, assuming a radical mechanism, of *23–26* by LTA oxidation of (12*Z*)-abienol (*22*).

with LTA is stereoselective. The generation of the major acetates *23* and *24* is explained by attachment of the acetoxy radical (or ion) to C–13 from the side shown in Scheme 2, while attack on C–15 would yield the minor acetates *25* and *26*.

Alkaline hydrolysis of acetates *25* and *26* furnished the target alcohols *18* and *19*, respectively. In order to confirm the geometries assigned to the 13,14-double bond in these four compounds (*18, 19, 25, 26*), alcohols *18* and *19* were oxidized using manganese dioxide to the corresponding aldehydes *27* and *28*. Their ^{1}H



a *b*
18 *19*

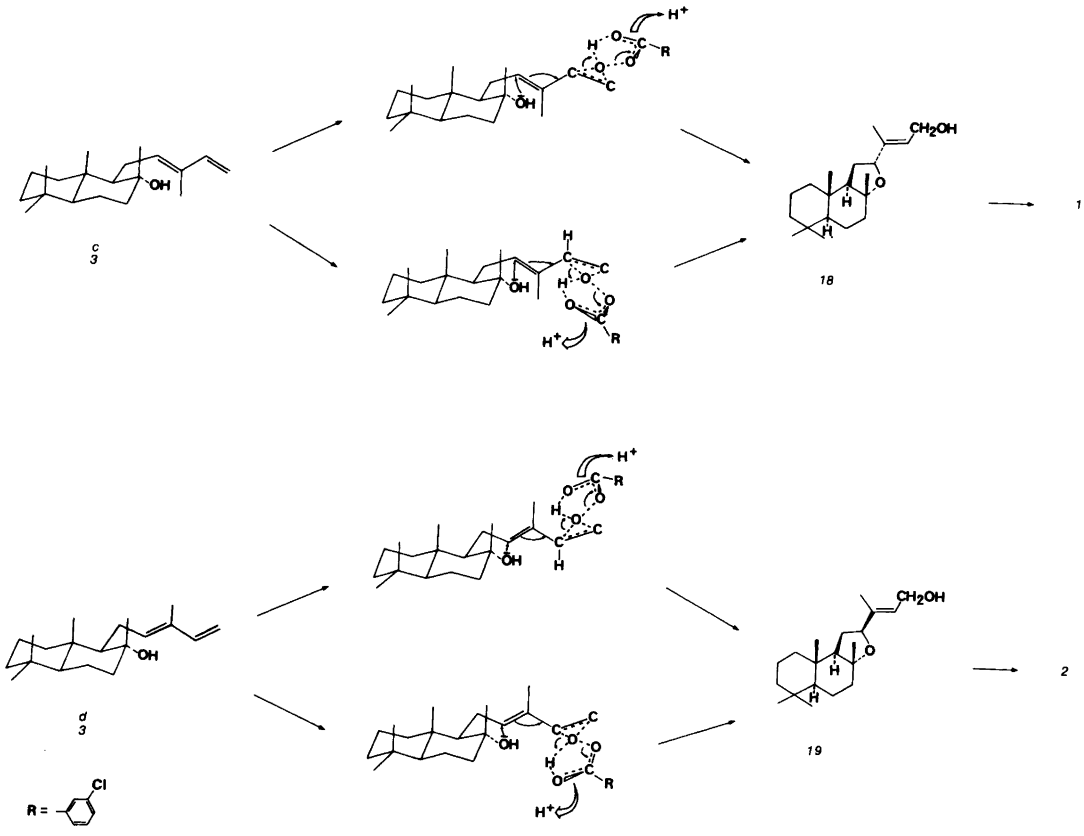
Scheme 3. Reacting conformers in the epoxidation of *18* and *19*.

NMR spectra displayed signals due to H–16 at δ 2.13 and at δ 2.12, respectively, shieldings which are only consistent with *E*-geometries.[10]

The reaction of alcohol *19* with *m*-chloroperbenzoic acid in chloroform proceeded rapidly and virtually stereospecifically with formation of an epoxide, which was identical with (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanol (*2*). Epoxidation of alcohol *18* occurred in a similar manner yielding an epoxide indistinguishable from epoxide *1*. The latter is consequently fully characterized as (12*R*,13*R*,14*R*)-8,12-13,14-diepoxy-15-labdanol.

The outcome of these reactions is explained if conformer *a* of alcohol *18* and *b* of alcohol *19* (Scheme 3), which appear to be energetically favoured, are the reacting species. Their geometries also allow the possibility of anchimeric assistance from the 8,12-ether oxygen and the hydroxyl group at C-15. Such cooperative effects have previously been found to lead to high stereospecificity in the epoxidation of allylic alcohols with peracids.[11]

The experimental results obtained are hence consistent with the formation of alcohols *1* and *2* *via* route B but do not exclude the existence of route C. Further insight into the reaction details



Scheme 4. Mechanisms for the formation of *18* and *19* from (12*E*)-abienol (*3*).

was next sought by treatment of (12*E*)-abienol (*3*) with *m*-chloroperbenzoic acid in a biphasic solvent system consisting of diethyl ether and aqueous sodium bicarbonate.[12,13] No acid-sensitive 1,2-epoxides, *i.e. 16, 17* or *20, 21,* were detected. However, the lower reaction efficiency under these conditions permitted the trapping of alcohols *18* and *19*.

Thus, one route to alcohols *1* and *2* is evidently initiated by attack of peracid on the terminal 14,15-double bond in (12*E*)-abienol (*3*). It is reasonable to assume that the overall process to alcohols *18* and *19* is concerted and since *trans*-products are formed exclusively, the rearrangements are likely to take place in all-*trans* conformers such as *c* and *d* of (12*E*)-abienol (*3*). While the peracid attack has been envisaged in Scheme 4 to occur on both sides of the 14,15-double bond, the steric requirements for the process are evidently very strict in other respects. This follows from the observation that a corresponding process, which would compete with the preferential formation of compounds *29–32 via* epoxidation of the 12,13-double bond, is of little importance in (12*Z*)-abienol (*22*).

In conclusion we wish to comment upon the structural assignments of a few naturally occurring 8,12-epoxy bridged labdanoids. Carterochaetol, a compound isolated from *Carteothamnus anomalochaeta,*[15] has been formulated as (12*R*,13*Z*)-8,12-epoxy-13-labden-15-ol (*33*) mainly on the basis of spectral evidence. A comparison of the published spectral data with those of alcohols *18* and *19* suggests, however, that carterochaetol is identical with the latter, *i.e.* its structure is (12*S*,13*E*)-8,12-epoxy-13-labden-15-ol (*19*). Support for this view is also provided by the spectral congruity of carterochaetol acetate and acetate *26* and by the fact that the ^{1}H NMR data previously reported for the two synthetic C–12 epimers of 8,12-epoxy-13*Z*-labden-15-ol (*33, 34*) [16] are different from our data for alcohol *19*.

16-Hydroxycarterochaetol (*35*), another naturally occurring 8,12-epoxylabdanoid, which has been isolated from a few *Silphium* species,[17] has previously been assigned a 12*R*-stereochemistry. However, its ^{13}C NMR spectrum displays the C-17 signal at δ 24.5, a chemical shift value only consistent with a 12*S*-stereochemistry (*cf.* Table 1 and Ref. 14). As a consequence, the configuration at C-12 may also have to be revised in compounds which have been chemically correlated with 16-hydroxycarterochaetol.

EXPERIMENTAL

With the exception of accurate mass measurements, which were carried out on a Kratos MS 50 Stereo DS 55 SM/DS 55 S mass spectrometer-computer system and some of the ^{1}H NMR spectra, which were recorded on a Varian XL-200 spectrometer, the instruments specified in Ref. 18 were used.

Experimental details for the preparation and isolation of the (12*R*,13*R*,14*R*)- and (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanols (*1, 2*) have been given previously.[1]

(12*R*,13*R*,14*R*)-8,12-13,14-Diepoxy-15-labdanol (*1*) had m.p. 126–127 °C; $[\alpha]_D$ –3.7° (*c* 0.30, $CHCl_3$) (Found: $M^{\cdot+}$ 322.2511. Calc. for $C_{20}H_{34}O_3$: 322.2508); IR (CCl_4) bands at 3610 and 3430 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.83 (s)/0.83 (s)/0.88 (s) (H-18/H-19/H-20) and 1.13 (s, H-17) (for other ^{1}H NMR data see partial structure A); MS [*m/z* (%, composition)]: 322 (M, 1), 307 (17), 291 (7, $C_{19}H_{31}O_2$), 277 (1), 262 (8, $C_{18}H_{30}O$), 247 (2, $C_{17}H_{27}O$), 235 (20, $C_{16}H_{27}O$ and $C_{15}H_{23}O_2$), 217 (11, $C_{16}H_{25}$ and $C_{15}H_{21}O$), 206 (5), 191 (100), 175 (5), 163 (3), 149 (6), 137 (38), 123 (22), 109 (28), 95 (30), 81 (24), 69 (37), 55 (22) and 43 (39).

(12*S*,13*S*,14*S*)-8,12-13,14-Diepoxy-15-labdanol (*2*) had m.p. 176–178 °C; $[\alpha]_D$ –15.3° (*c* 0.40, $CHCl_3$) (Found: $M^{\cdot+}$ 322.2512. Calc. for $C_{20}H_{34}O_3$: 322.2508); IR (CCl_4) bands at 3610 and 3440 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.82 (s)/0.84 (s)/0.89 (s) (H-18/H-19/H-20) and 1.15 (s, H-17) (for other ^{1}H NMR data see partial structure B); MS [*m/z* (%)]: 322 (M, 1), 307 (28), 291 (4), 277 (3), 262 (11), 247 (5), 235 (10), 217 (7), 191 (100), 177 (13), 163 (5), 149 (9), 137 (38), 123 (26), 109 (31), 95 (33), 81 (29), 69 (36), 55 (23) and 43 (33).

*Preparation of the (12*R*,13*R*,14*R*)- and (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanoyl acetates* 8 *and* 9. Acetylation using acetic anhydride in pyridine converted *1* and *2* into the (12*R*,13*R*,14*R*)- and (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanoyl acetates *8* and *9*, respectively.

(12*R*,13*R*,14*R*)-8,12-13,14-Diepoxy-15-labdanoyl acetate (*8*) had IR (CCl_4) bands at 1745 and 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.83 (s)/0.83 (s)/0.88 (s) (H-18/H-19/H-20), 1.13 (s, H-17), 1.31 (s, H-16), 2.10 (s, OCOC*H*$_3$), 3.18 (dd, *J*=4 and 7 Hz, H-14), 3.85 (m, H-12), 4.06 (dd, *J*=7 and –12 Hz, H-15a) and 4.37 (dd, *J*=4 and –12 Hz); MS [*m/z* (%)]: 364 (M, 2), 349 (14), 304 (3), 289 (3), 262 (5), 235 (17), 217 (15), 191 (100), 177

(18), 163 (8), 149 (14), 137 (46), 123 (32), 109 (43), 95 (48), 81 (42), 69 (57), 55 (35) and 43 (89).

(12*S*,13*S*,14*S*)-8,12-13,14-Diepoxy-15-labdanoyl acetate (*9*) had IR (CCl_4) bands at 1745 and 1230 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.82 (s)/0.84 (s)/0.87 (s) (H-18/H-19/H-20), 1.14 (s, H-17), 1.39 (s, H-16), 2.10 (s, $OCOCH_3$), 3.11 (dd, J=4 and 7 Hz, H-14), 4.07 (dd, J=7 and –12 Hz, H-15a), 4.10 (m, H-12) and 4.38 (dd, J=4 and –12 Hz, H-15b); MS [*m/z* (%)]: 364 (M, 2), 349 (32), 304 (3), 289 (3), 262 (16), 247 (8), 235 (7), 217 (6), 191 (100), 175 (20), 163 (7), 149 (15), 137 (39), 123 (32), 109 (36), 95 (43), 81 (36), 69 (38), 55 (31) and 43 (83).

*Conversion of (12*R*,13*R*,14*R*)-8,12-13,14-diepoxy-15-labdanol (1) to (12*R*,13*S*)-8,12-epoxy-13-labdanol (12).* An ethereal solution of 35 mg of *1* was refluxed with excess LAH for 1 h. Work-up and chromatography over silica gel afforded 30 mg of (12*R*,13*S*)-8,12-epoxy-13,15-labdanediol (*10*), which had ^1H NMR ($CDCl_3$): δ 0.83 (s)/0.83 (s)/0.87 (s) (H-18/H-19/H-20), 1.15 (s)/1.22 (s) (H-16/H-17) and 3.9 (overlapping signals, H-12, H-15a and H-15b).

A solution of 25 mg of *10* in 5 ml of pyridine was left with 20 µl of methanesulfonyl chloride at room temperature for 2 h. The reaction mixture was diluted with water and extracted with ether. The ether extract was washed with aqueous H_2SO_4 (10 %), sodium bicarbonate and water. Removal of solvent gave 12 mg of (12*R*,13*S*)-8,12-epoxy-13-hydroxy-15-labdanoyl methanesulfonate (*11*), which had ^1H NMR ($CDCl_3$): δ 0.83 (s)/0.83 (s)/0.88 (s) (H-18/H-19/H-20), 1.15 (s)/1.19 (s) (H-16/H-17), 3.02 (s, OSO_2CH_3), 3.90 (m, H-12) and 4.48 (t, J=7 Hz, H-15a and H-15b).

Reduction of 5 mg of *11* with LAH yielded 4 mg of a product, which was indistinguishable from the sample of (12*R*,13*S*)-8,12-epoxy-13-labdanol (*12*) prepared by catalytic hydrogenation of (12*R*,13*S*)-8,12-epoxy-14-labden-13-ol (*4*). Compound *12* had IR (CCl_4) bands at 3590 and 3450 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.85 (s)/0.85 (s)/0.87 (s) (H-18/H-19/H-20), 0.92 (t, J=7 Hz, H-15), 1.13 (s, H-16), 1.13 (s, H-17) and 3.91 (m, H-12); MS [*m/z* (%)]: 293 (M-15, 2), 275 (2), 235 (14), 221 (10), 217 (13), 192 (100), 191 (73), 177 (71), 163 (3), 149 (13), 137 (29), 123 (29), 109 (26), 95 (30), 81 (31), 73 (50), 55 (32) and 43 (33).

*Conversion of (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanol (2) to (12*S*,13*R*)-8,12-epoxy-13-labdanol (15).* Reduction of 80 mg of *2* with LAH afforded 35 mg of (12*S*,13*R*)-8,12-epoxy-13,15-labdanediol (*13*), which had ^1H NMR ($CDCl_3$): δ 0.82 (s)/0.85 (s)/0.87 (s) (H-18/H-19/H-20), 1.17 (s, H-17), 1.29 (s, H-16) and 3.8 (overlapping signals, H-12, H-15a and H-15b).

Treatment of 35 mg of (*13*) with 20 µl methanesulfonyl chloride in pyridine at room temperature for 2 h gave 37 mg of (12*S*,13*R*)-8,12-epoxy-13-hydroxy-15-labdanoyl methanesulfonate (*14*), which had IR ($CHCl_3$) bands at 3590 and 3440 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.82 (s)/0.85 (s)/0.87 (s) (H-18/H-19/H-20), 1.17 (s, H-17), 1.25 (s, H-16), 3.01 (s, OSO_2CH_3), 3.73 (m, H-12) and 4.45 (t, J=7 Hz, H-15a and H-15b).

An ethereal solution of 35 mg of *14* was refluxed with excess LAH for 3 h. Work-up and chromatography over silica gel gave 24 mg of a product which was identical in all respects to the sample of (12*S*,13*R*)-8,12-epoxy-13-labdanol (*15*) obtained by catalytic hydrogenation of (12*S*,13*R*)-8,12-epoxy-14-labden-13-ol (*5*). Compound *15* had IR (CCl_4) bands at 3590 and 3440 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.83 (s)/0.85 (s)/0.87 (s) (H-18/H-19/H-20), 0.93 (t, J=7 Hz, H-15), 1.18 (s)/1.20 (s) (H-16/H-17) and 3.75 (m, H-12); MS [*m/z* (%)]: 293 (M-15, 6), 275 (2), 257 (1), 235 (21), 221 (9), 217 (18), 192 (81), 191 (100), 177 (73), 161 (7), 149 (13), 137 (38), 123 (31), 109 (36), 95 (40), 81 (44), 73 (72), 55 (47) and 43 (59).

Treatment of (12Z)-abienol (22) with lead tetraacetate (LTA). I. To a solution of 1.5 g of (12*Z*)-abienol (*22*) in 30 ml of benzene was added 2.2 g of LTA. The reaction mixture was refluxed for 1 h, diluted with ether, filtered, washed with aqueous sodium bicarbonate (5 %) and water, dried and evaporated. The residue was separated by HPLC using a column packed with Spherisorb/CN and hexane–ethyl acetate (90:10) as an eluent to give (12*R*,13*S*)-8,12-epoxy-14-labden-13-oyl acetate (*23*, 29 %), (12*S*,13*R*)-8,12-epoxy-14-labden-13-oyl acetate (*24*, 37 %), (12*R*,13*E*)-8,12-epoxy-13-labden-15-oyl acetate (*25*, 15 %) and (12*S*,13*E*)-8,12-epoxy-13-labden-15-oyl acetate (*26*, *19 %*).

(12*R*,13*S*)-8,12-Epoxy-14-labden-13-oyl acetate (*23*) was an oil and had $[\alpha]_D$ −15.6° (*c* 1.47, $CHCl_3$); IR (CCl_4) bands at 3090, 1740, 1640 and 1250 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.82 (s)/0.82 (s)/0.87 (s) (H-18/H-19/H-20), 1.13 (s, H-17), 1.56 (s, H-16), 2.03 (s, $OCOCH_3$), 4.17 (m, H-12), 5.21 (d, J=17.5 Hz, H-15a), 5.24 (d, J=11 Hz, H-15b) and 6.05 (dd, J=11 and 17.5 Hz, H-14); MS [*m/z* (%)]: 288 (M-60, 11), 273 (8), 255 (1), 235 (16), 217 (12), 205 (26), 191 (100), 175 (17), 163 (10), 149 (18), 137 (30),123 (21), 109 (40), 95 (30), 83 (41), 69 (39), 55 (59) and 43 (51).

(12*S*,13*R*)-8,12-Epoxy-14-labden-13-oyl acetate (*24*) had m.p. 107–109 °C and $[\alpha]_D$ −21.9° (*c* 1.44, $CHCl_3$); IR (CCl_4) bands at 3090, 1735, 1635 and 1245 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.82 (s)/0.84 (s)/0.86 (s) (H-18/H-19/H-20), 1.16 (s,

H-17), 1.63 (s, H-16), 2.03 (s, OCOCH_3), 3.83 (m, H-12), 5.14 (d, J=17.5 Hz, H-15a), 5.20 (d, J=11 Hz, H-15b) and 5.95 (dd, J=11 and 17.5 Hz, H-14); MS [*m/z* (%)]: 288 (M−60, 22), 273 (11), 255 (2), 235 (12), 217 (9), 205 (28), 191 (100), 175 (21),163 (12), 149 (20), 137 (30), 123 (25), 109 (40), 95 (32), 83 (68), 69 (40), 55 (69) and 43 (61).

(12*R*,13*E*)-8,12-Epoxy-13-labden-15-oyl acetate (*25*) was an oil and had $[\alpha]_D$ +2.17°(*c* 1.15, $CHCl_3$); IR (CCl_4) bands at 1745, 1675 and 1235 cm^{-1}: ^1H NMR ($CDCl_3$): δ 0.83 (s)/0.83 (s)/0.88 (s) (H-18/H-19/H-20), 1.15 (s, H-17), 1.67 (s, H-16), 2.05 (s, OCOCH_3), 4.41 (m, H-12), 4.63 (d, J=7 Hz, H-15a and H-15b) and 5.64 (t, J=7 Hz, H-14); MS [*m/z* (%)]: 288 (M-60, 29), 273 (11), 255 (3), 233 (2), 219 (5), 205 (13), 191 (100), 175 (11), 163 (10), 149 (15), 137 (31), 123 (49), 109 (40), 95 (45), 81 (38), 69 (46), 55 (45) and 43 (65).

(12*S*,13*E*)-8,12-Epoxy-13-labden-15-oyl acetate (*26*) was an oil and had IR (CCl_4) bands at 1740, 1680, and 1235 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.83 (s)/0.83 (s)/0.87 (s) (H-18/H-19/H-20), 1.12 (s, H-17), 1.68 (s, H-16), 2.04 (s, OCOCH_3) 4.32 (m, H-12), 4.64 (d, J=7 Hz, H-15a and H-15b) and 5.72 (t, J=6.5 Hz, H-14); MS [*m/z* (%)]: 288 (M-60, 26), 273 (13), 255 (3), 233 (2), 215 (2), 205 (10), 191 (100), 175 (8), 163 (6), 149 (13), 137 (31), 123 (27), 109 (31), 95 (33), 83 (40), 69 (45), 55 (48) and 43 (82).

II. A solution of 60 mg of *20* and 20 mg of $CaCO_3$ in 3 ml of benzene and 32 mg of pyridine was refluxed with 98 mg of LTA for 2 h. Work-up and examination and separation by HPLC yielded *23, 24, 25* and *26* in the ratio 32:38:14:16.

*Hydrolysis of the (12*R,*13*S*)- and (12*S,*13*R*)-8,12-epoxy-14-labden-13-oyl acetates* 23 *and* 24. A solution of 23 mg of *23* and 3 drops of aqueous potassium hydroxide (45 %) in 1 ml of ethanol was refluxed under nitrogen for 2 h. The reaction mixture was diluted with water, acidified and extracted with ether. The residue obtained after removal of the solvent was purified by HPLC (μ-Porasil, hexane–ethyl acetate 95:5) to yield 13 mg of (12*R*,13*S*)-8,12-epoxy-14-labden-13-ol (*4*).

Hydrolysis using the conditions described above converted *24* into (12*S*,13*R*)-8,12-epoxy-14-labden-13-ol (*5*).

*Conversion of (12*R,*13*S*)-8,12-epoxy-14-labden-13-oyl acetate (23) to (12*R,*13*E*)-8,12-epoxy-13-labden-15-ol (18).* A solution of 66 mg of *23* in 5 ml of tetrahydrofuran was stirred with 15 mg of bis(acetonitrile)palladium(II) chloride under nitrogen and at room temperature for 1 h. The reaction mixture was diluted with water, extracted with ether, washed with water, dried and evaporated. The residue was purified by HPLC using a column packed with Spherisorb/CN and hexane–ethyl acetate (90:10) as an eluent to give 45 mg of (12*R*,13*E*)-8,12-epoxy-13-labden-15-oyl acetate (*25*).

A solution of 45 mg of *25* in 5 ml of ethanol and 20 μl of aqueous potassium hydroxide (45 %) was stirred under nitrogen and at room temperature for 3 h. Work-up and purification by HPLC [Spherisorb/CN; hexane–ethyl acetate (60:40)] afforded 35 mg of (12*R*,13*E*)-8,12-epoxy-13-labden-15-ol (*18*), which had m.p. 84−85 °C and $[\alpha]_D$ −3.1° (*c* 0.45, $CHCl_3$); IR (CCl_4) bands at 3610, 3400 and 1670 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.83 (s)/0.83 (s)/0.88 (s) (H-18/H-19/H-20), 1.16 (s, H-17), 1.66 (s, H-16), 4.20 (d, J=6.5 Hz, H-15a and H-15b), 4.41 (m, H-12) and 5.72 (dt, J=1.2 and 6.8 Hz, H-14): ^1H NMR (CCl_4): δ 0.82 (s)/0.82 (s)/0.88 (s) (H-18/H-19/H-20), 1.10 (s, H-17), 1.60 (s, H-16), 4.04 (d, J=6.6 Hz, H-15a and 15b), 4.28 (m, H-12) and 5.57 (t, J=6.8 Hz, H-14); MS [*m/z* (%)]: 306 (M, 0.4), 291 (3), 275 (40), 206 (18), 191 (100), 150 (12), 137 (35), 123 (65), 109 (40), 95 (49), 82 (49), 69 (64), 55 (45) and 43 (55).

*Conversion of (12*S,*13*R*)-8,12-epoxy-14-labden-13-oyl acetate (24) to (12*S,*13*E*)-8,12-epoxy-13-labden-15-ol (19).* Treatment of 103 mg of *24* with 20 mg of bis(acetonitrile)palladium(II) chloride in 10 ml of tetrahydrofuran for 1 h afforded, after work-up and purification by HPLC [Spherisorb/CN; hexane–ethyl acetate (90:10)], 90 mg of (12*S*,13*E*)-8,12-epoxy-13-labden-15-oyl acetate (*26*).

Hydrolysis of 85 mg of *26* using 20 μl of aqueous potassium hydroxide (45 %) in 10 ml of ethanol, followed by work-up and purification by HPLC [Spherisorb/CN; hexane–ethyl acetate (60:40)] yielded 20 mg of (12*S*,13*E*)-8,12-epoxy-13-labden-15-ol (*19*), which was an oil and had $[\alpha]_{589}$ −13.9°; $[\alpha]_{578}$ −14.7°; $[\alpha]_{546}$ −17.5°; $[\alpha]_{436}$ −29.0° (*c* 0.57, $CHCl_3$); IR (CCl_4) bands at 3620, 3420 and 1670 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.83 (s)/0.83 (s)/0.88 (s) (H-18/H-19/H-20), 1.14 (s, H-17), 1.66 (s, H-16), 4.21 (d, J=6 Hz, H-15a and H-15b), 4.31 (m, H-12), and 5.79 (dt, J=1.5 and 7 Hz, H-14); ^1H NMR (CCl_4): δ 0.82 (s)/0.82 (s)/0.88 (s) (H-18/H-19/H-20), 1.07 (H-17), 1.61 (s, H-16), 4.05 (d, J=6.6 Hz, H-15), 4.18 (m, H-12) and 5.66 (t, J=6.6 Hz, H-14); MS [*m/z* (%)]: 306 (M, 0.3), 291 (4), 275 (37), 206 (7), 191 (100), 137 (30), 123 (34), 109 (30), 95 (38), 81 (36), 69 (53), 55 (41) and 43 (53).

*Preparation of (12*R,*13*E*)- and (12*S,*13*E*)-8,12-epoxy-13-labden-15-al (27, 28).* A solution of 4.5 mg of *18* in 1 ml of diethyl ether was stirred with 100 mg of manganese dioxide on activated charcoal at room temperature for 5.5 h. The reaction mixture was filtered and concentrated to

give 2.5 mg of (12*R*,13*E*)-8,12-epoxy-13-labden-15-al (*27*), which had IR (CCl_4) bands at 2740, 1678, 1645 and 1618 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.83 (s)/0.84 (s)/0.88 (s) (H-18/H-19/H-20), 1.18 (s, H-17), 2.13 (d, J=0.85 Hz, H-16), 4.49 (m, H-12), 6.20 (d of quintets, J=1.3 and 8.1 Hz, H-14) and 10.05 (d, J=8.1 Hz, H-15); ^1H NMR (CCl_4): δ 0.83 (s)/0.83 (s)/0.88 (s) (H-18/H-19/H-20), 1.13 (s, H-17), 2.09 (d, J=1.2 Hz, H-16), 4.41 (m, H-12), 6.03 (d of quintets, J=1.3 and 7.4 Hz, H-14) and 9.95 (d, J=7.4 Hz, H-15); MS [*m/z* (%)]: 304 (M, 5), 289 (46), 275 (12), 206 (30), 191 (65), 137 (40), 123 (58), 109 (40), 95 (62), 81 (63), 69 (87), 55 (60) and 41 (100).

Treatment of 3.9 mg of *19* in 1 ml of diethyl ether with 100 mg of manganese dioxide on activated charcoal at room temperature for 12 h furnished 1.5 mg of (12*S*,13*E*)-8,12-epoxy-13-labden-15-al (*28*), which had IR (CCl_4) bands at 2740, 1675, 1642 and 1618 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.82 (s)/0.82 (s)/0.88 (s) (H-18/H-19/H-20), 1.11 (s, H-17), 2.12 (d, J=1.1 Hz, H-16), 4.44 (m, H-12), 6.29 (d of quintets, J=1.4 and 8.1 Hz, H-14) and 10.05 (d, J=8.1, H-15); ^1H NMR (CCl_4): δ 0.82 (s)/0.82 (s)/0.88 (s) (H-18/H-19/H-20), 1.08 (s, H-17), 2.09 (s, H-16), 4.34 (m, H-12), 6.14 (d of quintets, J=1.4 and 7.4 Hz, H-14) and 9.95 (d, J=7.4 Hz, H-15); MS [*m/z* (%)]: 304 (M, 9), 289 (21), 275 (11), 206 (11), 191 (82), 137 (21), 121 (20), 109 (31), 95 (58), 81 (45), 69 (100), 55 (61) and 41 (93).

*Epoxidation of (12*R*,13*E*)- and (12*S*,13*E*)-8,12-epoxy-13-labden-15-ols (*18, 19*).* A solution of 30 mg of *18* in 5 ml of chloroform was stirred with 24 mg of *m*-chloroperbenzoic acid at room temperature for 1 h. The reaction mixture was washed with aqueous sodium bicarbonate and water, dried and evaporated. The residue was purified by HPLC using a column packed with Spherisorb and hexane–ethyl acetate (60:40) as an eluent to give 12 mg of (12*R*,13*R*,14*R*)-8,12-13,14-diepoxy-15-labdanol (*1*).

Epoxidation of 20 mg of *19* using 15 mg of *m*-chloroperbenzoic acid in 5 ml of chloroform for 0.5 h afforded, after work-up and purification by HPLC, 8 mg of (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanol (*2*).

*Treatment of (12*E*)-abienol (3) with* m-*chloroperbenzoic acid in a buffered system.* To a stirred solution of 65 mg of *3* in 8 ml of diethyl ether and 4 ml of 0.5 M aqueous sodium bicarbonate was added a solution of 79 mg of *m*-chloroperbenzoic acid in 1 ml of ether. The reaction mixture was stirred at 20 °C for 4 h. The ether phase was washed with water, dried and concentrated. The residue was examined by HPLC using a column packed with Spherisorb/CN and hexane–ethyl acetate (60:40) as an eluent. Polar fractions, which contained (12*R*,13*E*)-8,12-epoxy-13-labden-15-ol (*18*, 1.3 mg), (12*S*,13*E*)-8,12-epoxy-13-labden-15-ol (*19*, 2.6 mg), (12*R*,13*R*,14*R*)-8,12-13,14-diepoxy-15-labdanol (*1*, 0.3 mg) and (12*S*,13*S*,14*S*)-8,12-13,14-diepoxy-15-labdanol (*2*, 2.0 mg), were collected.

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