Ring c Functionalised Diterpenoids. Part VII.[1] Formolysis of (16*S*)-*ent*-12α-*p*-Tolylsulphonyloxykaurane

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Buffered formolysis of the title tosylate (1b) at room temperature followed by mild hydrolysis gave chiefly the corresponding alcohol (1a), smaller amounts of the epimeric *ent*-atisan-13- (6a and c) and -16-ols (7a and c), together with traces of the *ent*-kauranol (1d) and the *ent*-14(13→12)*abeo*-kauranol (5a). The product distribution is rationalised in terms of the relative stabilities of intermediate carbocations. Formolysis of the deuteriated tosylate (1g) demonstrated that the *ent*-atisan-13-ols are formed mainly *via* a classical ion [(B) in the Scheme]. A mechanism involving formation of *ent*-trachylobane (9a) and a corner-protonated cyclopropane (H) is proposed to account for the loss of deuterium associated with the conversion of (1g) into the *ent*-atisan-16-ols.

CONTINUING our investigations [1] of the rearrangements of the bicyclo-octane unit in tetracyclic diterpenoids, we have now examined the formolysis of (16*S*)-*ent*-12α-*p*-tolylsulphonyloxykaurane (1b). Two possible rearrangement routes (outlined in the Scheme) were anticipated. Rearrangement with concerted bond migration *via* species (A) involves formation of a *cis*-perhydroindane system (D). The greater strain in the latter than in the starting decalin system was expected to increase the likelihood of rearrangement *via* the classical cation (B) [contrast the fate [1] of the *ent*-beyeran-12β-yl tosylate (2)] in comparison with the parent bicyclo-octyl system.† Transformation of (B) into (C), which we have generated [3] from (16*S*)-*ent*-12β-*p*-tolylsulphonyloxykaurane (1e), would lead to products derived from (C) and (F). Of course the same products could arise by rearrangement *via* (D) and (E).

RESULTS

Formolysis of (16S)-ent-12α-p-*Tolylsulphonyloxykaurane* (1b).—Formolysis of the tosylate (1b) followed by hydrolysis gave a mixture of olefins and alcohols which was separated by preparative t.l.c. Analytical t.l.c. on silver nitrate–silica gel of the olefin fraction (10% of mixture) showed the presence of at least four components, only two of which, (16*S*)-*ent*-atis-13-ene (3) and (16*S*)-*ent*-kaur-11-ene (4), were identified. The least polar alcohol fraction (6%) contained several components, two of which predominated. The R_F values of these two alcohols were identical with those of (16*S*)-*ent*-kauran-12β-ol (1d) and the sole product (5a) of reduction of (16*S*)-*ent*-14(13→12)*abeo*-kauran-13-one (5c) [3] with lithium aluminium hydride. The n.m.r. spectra of (5a) and its epimer (5b) are almost identical, but the compounds differ in t.l.c. mobility. Extensive preparative t.l.c. was required to effect separation of the more polar alcohols which were identified (in order of increasing polarity) as (16*S*)-*ent*-atisan-13β-ol (6a) [3] (12%), (16*S*)-*ent*-kauran-12α-ol (1a) [3] (40%), *ent*-atisan-16β-ol (7a) [3] (6%), *ent*-atisan-16α-ol (7c) (6%), and (16*S*)-*ent*-atisan-13α-ol (6c) [3] (12%).

Stereochemistry of the ent-*Atisan*-16-*ols* (7a *and* c).—The products (7a and c) were identified as *ent*-atisan-16-ols by conversion of each with thionyl chloride–pyridine into a mixture in which the only hydrocarbon components were *ent*-atis-15-ene (8a) and *ent*-atis-16-ene (8b). These olefins were accompanied by further products, presumably chlorides, which were transformed into a *ca.* 1 : 1 mixture of (8a) and (8b) during preparative t.l.c. on silver nitrate–silica gel. There are only two reports [3,4] of the *ent*-atisan-16-ols (7a and c). The m.p. (108°) of the less polar epimer (7a) corresponds closely with that of a product obtained [3] from the solvolysis of the tosylate (1e). However, the m.p. (174—176°) of the more polar alcohol (7c) does not correspond with that (145°) reported for a product of acid-catalysed opening of trachylobane (9a) and assigned [4] the structure of a tertiary atisanol (stereochemistry at C-16 undefined). We are unable to explain this discrepancy, but we have shown by direct comparison that

† Acetolysis of *endo*-bicyclo[3.2.1]octan-2-yl tosylate gives [2] *ca.* 10% of products resulting from 'leakage' *via* the classical carbocation.

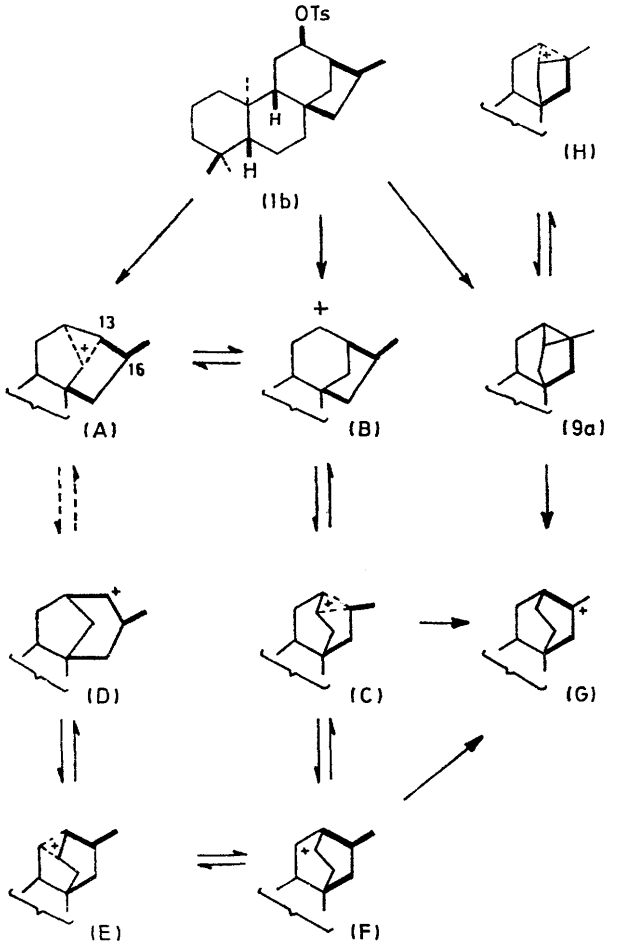
[1] Part VI, A. J. McAlees, R. McCrindle, and S. T. Murphy, *J.C.S. Perkin I*, 1975, 1641.

[2] H. L. Goering and G. N. Fickes, *J. Amer. Chem. Soc.*, 1968, **90**, 2848.

[3] A. J. McAlees and R. McCrindle, *J.C.S. Perkin I*, 1975, 861.

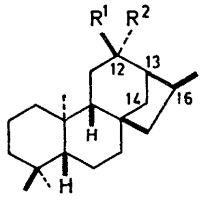
[4] G. Hugel, L. Lods, J. M. Mellor, and G. Ourisson, *Bull. Soc. chim. France*, 1965, 2894.

another product * formulated [4] as *ent*-kauran-16α-ol (10) is identical with (7c).

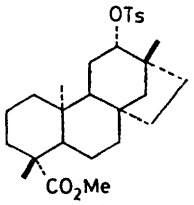


SCHEME

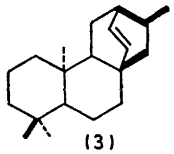
The production of *both* tertiary atisanols from (11b), which would be expected if the classical carbocation(G) (Scheme) were an intermediate in the formolysis, led us to re-examine the products of formolysis [3] of (6b and and d). Previously only the less polar epimer (7a) was isolated.[3] We have now found (see Experimental section) that the (16*S*)-*ent*-atisan-13α-ol (6c) recovered from these solvolyses contains (7c). We also turned our attention to the two other reports [4,5] of tertiary atisanols, in both of which *apparently* only one epimer was isolated. The first of these,[4] involving acid-catalysed opening of the cyclopropane ring in trachylobane, has been mentioned above. We have examined the reaction of methyl *ent*-trachyloban-19-oate (9b) with acetic, formic, and aqueous mineral acids. In each case (after hydrolysis of acetates or formates) the resulting mixtures contained approximately equal amounts of (7b and d) in addition to other products. Both tertiary alcohols (7b and d) gave a mixture of the olefins (8c and d) when treated with thionyl chloride–pyridine. Coates and Bertram have reported [5] obtaining *an* atisan-16-ol from brief trifluoroacetolysis of methyl *ent*-12α-*p*-tolylsulphonyloxybeyeran-19-oate (11b) followed by hydrolysis. However, repetition of this reaction and a careful re-examination of Coates' and Bertram's sample† showed that the two tertiary alcohols (7b and d) were produced in approximately equal proportions together with small amounts of the *ent*-beyeran-12α-ol (11a) and the *ent*-atisenes (8c and d). Coates and Bertram [6] had also obtained an *ent*-atisan-16-ol from brief formolysis of the tosylate (12). Re-examination of this product† showed that it was indeed one compound which proved to be identical with the more polar, higher melting tertiary *ent*-atisanol (7d) from the acid-induced opening of methyl



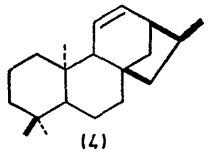
(1) a; R^1=OH, R^2=H
b; R^1=OTs, R^2=H
c; R^1 R^2=O
d; R^1=H, R^2=OH
e; R^1=H, R^2=OTs
f; R^1=OH, R^2=^{2}H
g; R^1=OTs, R^2=^{2}H



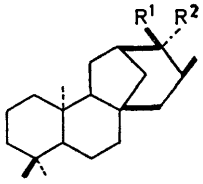
(2)



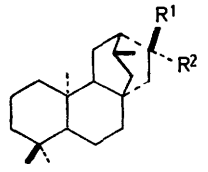
(3)



(4)



(5) a; R^1=OH, R^2=H
b; R^1=H, R^2=OH
c; R^1 R^2=O



(6) a; R^1=H, R^2=OH
b; R^1=H, R^2=OTs
c; R^1=OH, R^2=H
d; R^1=OTs, R^2=H
e; R^1 R^2=O

* We thank Professor Ourisson for supplying the '(−)-kauranol-16*S*' (m.p. 170—172°). Unfortunately, the '16-atisanol' (m.p. 145°) was no longer available.

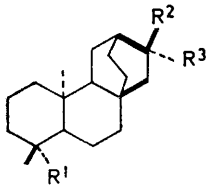
† We thank Professor Coates for samples and n.m.r. spectra of the atisan-16-ol mixture from trifluoroacetolysis [5] of (11b), the *ent*-atisan-16α-ol (7d) from the formolysis [6] of (12), and the *ent*-kauran-16β-ol (13a).

ent-trachyloban-19-oate (9b). In our experience the procedures employed [6] to isolate this product would not have

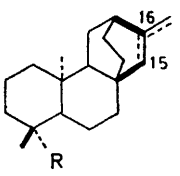
[5] R. M. Coates and E. F. Bertram, *J. Org. Chem.*, 1971, **36**, 3722.

[6] R. M. Coates and E. F. Bertram, *J. Org. Chem.*, 1971, **36**, 2625.

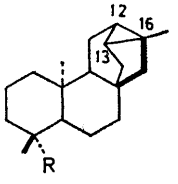
separated the epimeric *ent*-atisanols and thus it was presumably the major (if not the only) one formed. Since the tertiary *ent*-atisanol derived from formolysis of (12) under conditions of kinetic control would be expected to have the stereochemistry depicted in (7d), we could now confidently assign the stereochemistry of the *ent*-atisanols derived from the acid-catalysed opening of (9b) and, by analogy, those obtained from solvolysis of (1b). Thus the less polar, lower melting, alcohols have the structures (7a and b) and the more polar, higher melting epimers are (7c and d).



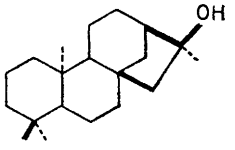
(7) a; R^1 = Me, R^2 = Me, R^3 = OH
b; R^1 = CO_2Me, R^2 = Me, R^3 = OH
c; R^1 = Me, R^2 = OH, R^3 = Me
d; R^1 = CO_2Me, R^2 = OH, R^3 = Me



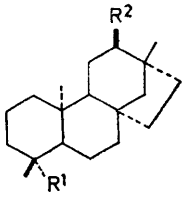
(8) a; Δ^{15}, R = Me
b; Δ^{16}, R = Me
c; Δ^{15}, R = CO_2Me
d; Δ^{16}, R = CO_2Me



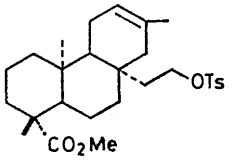
(9) a; R = Me
b; R = CO_2Me



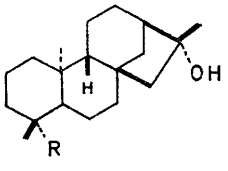
(10)



(11) a; R^1 = CO_2Me, R^2 = OH
b; R^1 = CO_2Me, R^2 = OTs
c; R^1 = Me, R^2 = OH

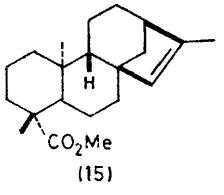


(12)



(13) a; R = CO_2Me
b; R = Me

(14)



(15)

Solvolysis of the Deuteriated Tosylate (1g).—As indicated in our introduction, it was envisaged that the products of the solvolysis of the tosylate (1b) could arise *via* two possible pathways: (A)→(D)→(E)→(F)→(G) or (A)→(B)→(C)→(F)→(G) (Scheme). To allow distinction between these alternatives, formolysis of the deuteriated tosylate (1g) was undertaken. The position of the label in the resulting *ent*-atisan-13-ols (6a and c) is different for each pathway (13- and 12-^{2}H, respectively) and is readily determinable from the mass spectrum of the corresponding ketone (6e). Formolysis of (1g) [the parent alcohol (1f) contained ⩾98% deuterium], followed by hydrolysis and preparative t.l.c., gave a band containing the deuteriated analogues of *ent*-atisan-13α-ol (6c) and *ent*-atisan-16α-ol (7c) and a less polar band containing deuteriated *ent*-kauran-12α-ol (1a), *ent*-atisan-13β-ol (6a), and *ent*-atisan-16β-ol (7a). The two mixtures were separately oxidised and the resulting ketones, (6e) and (1c), were separated from the tertiary alcohols (7a and c) by preparative t.l.c. Mass spectral examination of the *ent*-atisan-13-one (6e) samples derived from (6c and a) showed deuterium *retentions* of 75 and 89%, respectively, indicating that in both alcohols most of the label must be at C-12. Thus the *ent*-atisan-13-ols (6a and c) arise predominantly *via* the ions (A)→(B)→(C)→(F).

As expected, the ketone (1c) contained no deuterium. Surprisingly, only 55 and 46% deuterium retention was measured in the deuteriated analogues of the *ent*-atisan-16-ols (7a and c) respectively (see Discussion section).

Control Experiments.—Under our formolysis conditions, *ent*-kaur-11-ene (4) did not react, *ent*-atis-13-ene (3) reacted only to a small extent, and *ent*-atis-15-ene (8a) and *ent*-atis-16-ene (8b) were completely converted into formates. The formates of the *ent*-atisan-13-ols (6a and c) were stable to the formolysis conditions.

No deuterium loss was observed when the partially deuteriated *ent*-atisan-16-ols (7a and c) obtained from the solvolysis of (1g) were re-subjected to the solvolysis conditions (see Discussion section), but a *mixture* of the two epimers (7a and c) was recovered in each case after work-up. As expected (6a), (6c), and (11c) were not detected in the products

DISCUSSION

The products from formolysis of the tosylate (1b) can be accounted for by reference to the Scheme. Return of the starting system (1a) in high yield reflects the relatively long life of the ion (A) (or equivalent species). Very little product (⩽3%) derived from solvent attack at C-13 in (A) [or (D)] is observed, since this would require the formation of a strained *cis*-perhydroindane system (see below) and since attack at C-13 on the β-face of (A) is hindered by the C-16 methyl group.

As shown by the results obtained from the solvolysis

of the deuteriated tosylate (1g) the *ent*-atisan-13-ols (6a and c) are derived chiefly by rearrangement *via* the ion (B) to (C) and thence to (F). Thus, as anticipated, rearrangement of (A) to the *cis*-perhydroindane system (D) is less favoured than transformation into (B), which incorporates the less strained *cis*-decalin unit. This result is in contrast to that observed in the solvolysis [1] of the tosylate (2), where rearrangement to the *trans*-perhydroindane system is preferred because of the tertiary nature of the resulting cation.

The classical ion (B) apparently has a short life since the product (1d) of solvent attack on the relatively unhindered α-face was obtained in low yield (≤3%) and at least some of (1d) must derive from attack [3] on (C). The formate of the secondary alcohol (1d) would not be expected [1,7] to re-ionise under the solvolytic conditions.

The formolysis [3] of the *ent*-12β-tosylate (1e) yielded the *ent*-atisan-13-ols (6a and c) in the ratio *ca.* 5 : 8. The rather high proportion of the *ent*-13β-isomer (6a) in comparison with ratios (*ca.* 1 : 5) obtained for the solvolysis of the *ent*-atisan-13-yl tosylates (6b and d) was rationalised by suggesting that in the solvolysis of (1e) solvent capture from the α-side at C-13 was almost synchronous with migration of the 13,16-bond. In the present case equal amounts of the epimeric *ent*-atisan-13-ols were obtained. It is suggested that the same mechanism applies here but, since the departing anion is leaving from the β-face, solvent attack on the α-side is even more favoured.

In the solvolysis [3] of the *ent*-atisan-13-yl tosylates (6b and d), a 1,3-hydride shift from C-16 to C-13 in the secondary cation (F) [or (C)] to form the tertiary classical ion (G) followed by solvent capture could account for the formation of the esters of the tertiary *ent*-atisanols (7a and c). However, two observations suggest that this simple explanation may not be adequate in the present case. First, the yield of these *ent*-atisan-16-ols is much higher (total 12%) than that obtained from the solvolysis of the epimeric tosylate (1e) (total yield of *ent*-atisanes <1%).* Secondly, the large loss of deuterium (average 50%) in the tertiary *ent*-atisanols (7a and c) derived from solvolysis of the deuteriated tosylate (1g) cannot be explained by the first two pathways outlined in the Scheme since (G) is formed *via* (F) [or (C)], the products from which contained an average of 82% deuterium. The possibility that deuterium loss occurs after formation of (G) (by protonation–deprotonation of rearranged olefins) can be discounted since no further loss of deuterium occurred when either of the partially deuteriated *ent*-atisan-16-ols was resubjected to the formolysis conditions. Isolation of both epimers from each sample showed that reionisation to (G) had occurred. Thus apparently the cation (G) is not derived exclusively from (F) and at least one other mechanism is operating.

We suggest that the major pathway to the tertiary *ent*-atisanols involves formation (distorted *endo*-S geometry [8]) of the cyclopropane intermediate, *ent*-trachylobane (9a), which subsequently opens† under the solvolysis conditions. Deuterium at C–12 in (9a) could be removed by exchange *via* a corner-protonated cyclopropane (H). This mechanism is not of importance (distorted W geometry [8] would be involved) in the solvolysis [3] of (1e) since migration of the 13,16-bond is probably almost synchronous with departure of the anion leading to (C) and (F). Therefore the yield of *ent*-atisan-16-ols (or related olefins) is very low in this case.

Corner-protonated cyclopropanes have been invoked to account for multiple incorporation and scrambling of deuterium in acid-induced cleavages [9] of simple cyclopropanes and nortricyclene. A significant amount of 6-*exo*-deuteriation observed [10] in deuteriated acid-induced opening of 1-methylnortricyclene (14) could be explained by corner protonation of the cyclopropane ring. It was noted in this case [10] that deuterium was not incorporated into recovered substrate (14). However, in this symmetrical double bicyclo[3.1.0]hexyl system relief of strain [11] associated with cleavage of either of the two 0 bridges [1,2- and 1,6-bonds in (14)] is so great that deprotonation back to the cyclopropane cannot compete with solvent attack and rearrangement. This argument might apply to protonation, *via* an edge-protonated species, of *ent*-trachylobane (9a) at C-13 (in fact, cleavage of the 13,16-bond leads to the major products) but not to protonation at C-12 since cleavage of the 12,16-bond, which is the 0 bridge of the bicyclo-[4.1.0]heptyl system, should give a smaller relief [12] of strain.

Coates and Bertram [5] ruled out significant intervention of the *ent*-trachylobane (9b) as an alternative to hydride shift between C-16 and C-12 in the trifluoroacetolysis of (11b) and in related reactions. However, careful examination of their results shows that it could play a minor role. Thus treatment of (9b) with trifluoroacetic [^{2}H]acid gave a small (3%) incorporation of *seven* deuterium atoms in the major product (11a). The seventh deuterium atom may have been introduced *via* exchange in a corner-protonated *ent*-trachylobane intermediate.

Appropriate experiments to test our conclusions are in

* In the solvolysis [3] of (1e) only *ent*-atis-15-ene (8a) and *ent*-atis-16-ene (8b) were detected. From (1b) only alcohols (7a and c) were obtained. Control experiments (see Experimental section) show that (8a and b) are converted into (7a and c) under the present much longer reaction times (48 *versus* 7 h).

† Acid-catalysed opening of (9a) should also give a 5—10% yield of *ent*-kauran-16β-ol (13b) under these conditions, but the amount expected here (*ca.* 0.1%) would be below our limit of detection (*ca.* 1%).

[7] J. C. Fairlie, A. J. McAlees, R. McCrindle, and E. Neidert, *Canad. J. Chem.*, 1974, **52**, 706.

[8] A. Nickon and N. H. Werstiuk, *J. Amer. Chem. Soc.*, 1967, **89**, 3914, 3915, 3917.

[9] N. C. Deno, D. La Vietes, J. Moekus, and P. C. Schiff, *J. Amer. Chem. Soc.*, 1968, **90**, 6457; A. Nickon and J. H. Hammons, *ibid.*, 1964, **86**, 3322; R. L. Baird and A. Aboderin, *ibid.*, p. 252.

[10] J. H. Hammons, E. K. Probasco, L. A. Sanders, and E. J. Whalen, *J. Org. Chem.*, 1968, **33**, 4493.

[11] R. T. LaLonde and L. S. Forney, *J. Amer. Chem. Soc.*, 1963, **85**, 3767.

[12] R. J. Ouellette, A. South, and D. L. Shaw, *J. Amer. Chem. Soc.*, 1965, **87**, 2602.

progress. The possibility of demonstrating the occurrence of proton exchange in a corner-protonated cyclopropane would be of major significance in the classical–non-classical ion controversy.

EXPERIMENTAL

General details have been outlined previously.[1,3]

Preparation of (16S)-ent-12α-p-*Tolylsulphonyloxykaurane* (1b).—Reduction of the ketone (1c) (230 mg) with lithium aluminium hydride as described previously [3] gave, after separation, the *ent*-kauran-12α-ol (1a) (165 mg) and a mixture of (1d and a) (51 mg). Treatment of (1a) (165 mg) with toluene-*p*-sulphonyl chloride (700 mg) in pyridine (10 ml) for 20 h at room temperature, followed by aqueous acidic work-up and crystallisation from cold light petroleum, afforded the *tosylate* (1b) (210 mg, 83%), prisms, m.p. 85—87° (Found: C, 72.6; H, 8.75. $C_{27}H_{40}O_3S$ requires C, 72.95; H, 9.05%).

Buffered Formolysis of the Tosylate (1b).—Formic acid (50 ml) containing anhydrous sodium carbonate (1.0 g) was added to a solution of the tosylate (1b) (210 mg) in chloroform (10 ml) and the mixture was stirred vigorously for 2.5 days. (Chloroform achieves and maintains solubility; *cf.* ref. 3.) The chloroform and formic acid were evaporated off *in vacuo* (≤50°) and the residue was heated (reflux) with M-sodium hydroxide [4 g in water (20 ml) and methanol (80 ml)] for 3 h. Work-up afforded the crude product (130 mg), which was subjected to preparative t.l.c. (light petroleum–ethyl acetate, 9 : 1), to yield four bands which are discussed in order of increasing polarity.

The least polar band (13 mg, 10%) was subjected to preparative t.l.c. (silver nitrate–silica gel; light petroleum) to give, in order of decreasing polarity, *ent*-atis-13-ene (3) (1 mg), *ent*-kaur-11-ene (4) (1 mg) (both identified by t.l.c. and mass spectral comparison with authentic samples), and two unidentified non-polar compounds (0.7 and 4 mg). The mass spectra of these last two had significant peaks at *m/e* 272 (63%), 257 (80), 217 (88), and 123 (100), and *m/e* 272 (60%), 257 (100), 217 (57), 205 (35), and 123 (100), respectively.

The next more polar band (9 mg, 6%) contained several components, two of which were equally predominant. Analytical t.l.c. in different solvents [light petroleum–ethyl acetate (9 : 1), light petroleum–acetone (24 : 1), run four times, and benzene, run four times] showed that these two major components had R_F values identical with those of the *ent*-kauran-12β-ol (1d) (more polar) and the alcohol (5a) (less polar) obtained from reduction of the ketone (5c) with lithium aluminium hydride (see below). The epimeric alcohol (5b) was no longer available for comparison.[3]

The second most polar band (77 mg) was subjected to preparative t.l.c. (benzene, run 4 times) to yield, in order of increasing polarity, the *ent*-atisan-13β-ol (6a) (16 mg, 12%), the *ent*-kauran-12α-ol (1a) (54 mg, 40%), and the *ent*-atisan-16β-ol (7a) (8 mg, 6%). Use of light petroleum–ethyl acetate or light petroleum–acetone mixtures as developing solvents for t.l.c. failed to separate these alcohols satisfactorily.

The most polar band (25 mg) when subjected to preparative t.l.c. [light petroleum–acetone (24 : 1) run four times] gave the *ent*-atisan-16α-ol (7c) (8 mg, 6%) and the more polar *ent*-atisan-13α-ol (6c) (16 mg, 12%). Use of benzene as developing solvent for t.l.c. reversed the order of polarity of these two alcohols.

All the alcohols in these two polar bonds [except (7c)] were identified by direct comparison (t.l.c. and n.m.r. spectra) with authentic samples.[3] *ent*-Beyeran-12α-ol was not detected in any of the formolysis products by analytical t.l.c. in a variety of solvent mixtures. *ent*-Atisan-16β-ol (7a) had m.p. 107—109° (plates from acetonitrile) (*cf.* ref. 3, sublimed, m.p. 106—109°); δ(100 MHz; $CDCl_3$) 1.275 (s, 17-H_3), and 0.96, 0.85, and 0.82 (all 3 H, all s); δ(100 MHz; C_6D_6) 1.145 (s, 17-H_3), 0.885 (6 H, s), and 0.85 (3 H, s). ent-*Atisan*-16α-*ol* (7c) had m.p. 174—176° (needles from light petroleum); δ (100 MHz; $CDCl_3$) 1.29 (s, 17-H_3), and 0.955, 0.85, and 0.825 (all 3 H, all s); δ(100 MHz; C_6D_6) 1.165 (s, 17-H_3), and 0.89, 0.875, and 0.84 (all 3 H, all s) (Found: C, 82.65, H, 11.9. $C_{20}H_{34}O$ requires C, 82.7; H, 11.8%).

This alcohol (7c) was detected by analytical t.l.c. [light petroleum–acetone (24 : 1) run four times] in the samples of *ent*-atisan-13α-ol derived from formolysis of (6b and d),[3] being *ca.* 20—30% of the total. Also, (7c) was identical (n.m.r. spectra, m.p. and mixed m.p.) with the (−)-kauranol-16*S*,[4] a sample of which was supplied by Professor Ourisson.

Reduction of the Ketone (5c) *to the Alcohol* (5a).—The ketone (5c) [3] (9 mg) was stirred with lithium aluminium hydride (100 mg) in dry ether (10 ml) for 3 h. Work-up afforded a gum, which from analytical t.l.c. (light petroleum–ethyl acetate, 9 : 1) appeared to contain only one major product. Preparative t.l.c. gave the pure compound (5a) (5 mg), which was crystalline but could not be recrystallised; δ(CCl_4) 3.75 (C*H*OH, m, $W_{1/2}$ 8 Hz), 1.15 (3 H, d, *J* 6.5 Hz), and 0.91, 0.86, and 0.82 (all 3 H, all s). The n.m.r. spectrum is virtually identical with that reported for the epimer (5b),[3] which was no longer available for direct comparison.

Dehydration of Tertiary ent-*Atisanols* (7a *and* c).—Thionyl chloride (0.2 ml; freshly distilled from *p*-mentha-1,8-diene) was added to separate solutions (3 ml) in pyridine of the tertiary alcohols (7a and c) (10 mg each) at 0 °C, and after 1 h at 0 °C the mixtures were worked up. Analytical t.l.c. (silica gel–silver nitrate; light petroleum–ethyl acetate, 98 : 2) of the crude products showed the presence of *ent*-atis-16-ene (8b) and the less polar *ent*-atis-15-ene (8a), with the latter predominating, as the only olefinic components in each case. Each mixture also contained more polar material. Preparative t.l.c. under the same conditions gave pure (8a and b), whose identities were confirmed by comparison of their mass spectra with those of authentic samples,[3] and in each case a *ca.* 1 : 1 mixture of the tertiary *ent*-atisanols (7a and c) (from hydrolysis of chlorides on the silver nitrate–silica gel chromatoplates).

Treatment of Methyl ent-*Trachyloban*-19-*oate* (9b) *with Acids.*—(i) Methyl *ent*-trachyloban-19-oate (9b) (632 mg) was dissolved in acetic acid (50 ml) containing anhydrous sodium carbonate (1.0 g) and the mixture was kept at 85—90 °C for 5 days. The acetic acid was evaporated off *in vacuo* to yield an oil, which was heated to reflux in M-sodium hydroxide [4 g in water (20 ml) and methanol (80 ml)] for 3 h. Work-up afforded the product (617 mg), which upon column chromatography over alumina (50 g) gave an olefin fraction (415 mg) and an alcohol fraction (203 mg). Analytical t.l.c. (light petroleum–ethyl acetate, 3 : 1) and n.m.r. spectra ($CDCl_3$ and C_6D_6) of the alcohol fraction revealed the presence of only the tertiary *ent*-atisanols (7b and d) in approximately equal proportions. Analytical t.l.c. (silver nitrate–silica gel; light petroleum–ethyl acetate, 9 : 1) and n.m.r. spectra showed that the olefin fraction consisted mainly of the methyl *ent*-atiseno-

ates (8c and d), with a smaller amount of methyl *ent*-kaur-15-en-19-oate (15) and a trace of substrate (9b). The n.m.r. spectrum showed the ratio (8c) : (8d) : (15) to be 65 : 25 : 10.

(ii) Methyl *ent*-trachyloban-19-oate (9b) (316 mg) in tetrahydrofuran (20 ml) was stirred with concentrated hydrochloric acid (3 ml) and water (3 ml) at room temperature for 5 days. T.l.c. of the crude product after work-up showed mainly substrate (9b) with small amounts of (8c and d), a trace of (15), and small amounts of the tertiary *ent*-atisanols (7b and d) (*ca.* 1 : 1) and the slightly more polar tertiary *ent*-kauranol (13a) (same R_F value as a sample supplied by Professor Coates [5]).

(iii) Methyl *ent*-trachyloban-19-oate (9b) (102 mg) in chloroform (2 ml) was added to formic acid (12.5 ml) containing anhydrous sodium carbonate (250 mg) and the mixture was stirred vigorously for 40 h. Evaporation of the solvent *in vacuo* (≤50°) and mild hydrolysis of the residue [potassium hydroxide (2.8 g) in water (10 ml) and methanol (40 ml); 3 h reflux] gave the product mixture (94 mg). T.l.c. showed that the major products were the *ent*-atisanols (7b and d) (*ca.* 1 : 1); a small amount of the *ent*-kauranol (13a) and traces of the olefins (8c), (8d), and (15) were also present. A trace of an unidentified alcohol [slightly less polar than (7b)] was also evident.

Trifluoroacetylolysis of the Tosylate (11b).—As previously described,[5] the tosylate (11b) (123 mg) was dissolved in trifluoroacetic acid (12.5 ml) containing anhydrous sodium carbonate (250 mg); the mixture was kept for 5 min at room temperature, then the trifluoroacetic acid was evaporated off *in vacuo*. The residue was subjected to mild hydrolysis [sodium hydroxide (1 g) in water (5 ml) and methanol (20 ml); 3 h reflux] to yield the product mixture (96 mg). Preparative t.l.c. (light petroleum–ethyl acetate, 3 : 1) afforded the tertiary *ent*-atisanols [the less polar (7b) (31 mg) and the more polar (7d) (40 mg)] as well as a mixture of the olefins (8c and d) and the parent alcohol (11a) (total 22 mg). The identities of the last three were confirmed by t.l.c. and n.m.r. spectral comparison with authentic samples. T.l.c. examination of the ' 16-atisanol ' previously obtained from the same reaction,[5] supplied by Professor Coates, showed that it contained (7b), (7d), and (11a) in a similar ratio to the above. *Methyl* ent-16β-*hydroxyatisan*-19-*oate* (7b) had m.p. 134.5—137° (prisms from hexane); δ($CDCl_3$; 60 MHz) 3.65 (s, $CO_2{\cdot}CH_3$), and 1.28, 1.17, and 0.79 (all s, 17-, 18-, and 20-H_3); δ(C_6D_6; 60 MHz) 3.38 (s, $CO_2{\cdot}CH_3$), and 1.16, 1.13, and 0.86 (all s, 17-, 18-, and 20-H_3) (Found: C, 75.2; H, 10.2. $C_{21}H_{34}O_3$ requires C, 75.4; H, 10.25%). *Methyl* ent-16α-*hydroxyatisan*-19-*oate* (7d) had m.p. 149.5—151.5° (prisms from hexane); δ($CDCl_3$; 60 MHz) 3.65 (s, $CO_2{\cdot}CH_3$), and 1.29, 1.17, and 0.79 (all s, 17-, 18-, and 20-H_3); δ(C_6D_6; 60 MHz) 3.37 (s, $CO_2{\cdot}CH_3$), and 1.19, 1.13, and 0.86 (all s, 17-, 18-, and 20-H_3) (Found: C, 75.55; H, 10.1. $C_{21}H_{34}O_3$ requires C, 75.4; H, 10.25%). This alcohol was identical (t.l.c., m.p., and mixed m.p.) with the sample obtained [6] from the formolysis of the tosylate (12) and supplied by Professor Coates.

Dehydration of the Tertiary ent-*Atisanols* (7b *and* d).—Separate samples of (7b and d) (10 mg each) in pyridine (3 ml) at 0 °C were treated with thionyl chloride (0.2 ml; freshly distilled from *p*-mentha-1,8-diene). The mixture was kept at 0 °C for 1 h then subjected to aqueous acidic work-up. T.l.c. analysis of the products (silver nitrate–silica gel; light petroleum–ethyl acetate, 9 : 1) showed that in each case the *ent*-atisenoates (8c and d) had been produced. In the case of the *ent*-atisan-16β-ol (7b) another olefin (?), slightly more polar than (8d), was also evident. More polar products, presumably alcohols, were also present.

Preparation and Formolysis of the Tosylate (1g).—Reduction of the ketone (1c) (72 mg) by the method previously described,[3] but with lithium aluminium deuteride (300 mg) (Stohler Isotope Chemicals, d_4, 99% D) gave a mixture of alcohols which was separated by preparative t.l.c. [light petroleum–ethyl acetate (19 : 1) run three times] to give the deuteriated *ent*-kauran-12α-ol (1f) (55.5 mg) and its epimer (5.5 mg). The mass spectrum of (1f) showed the deuterium content to be ≥98%.

The deuteriated alcohol (1f) (55 mg) was converted as described above into the crude tosylate (1g) (70 mg), which was not purified but dissolved directly in chloroform (5 ml) to which formic acid (12.5 ml) containing anhydrous sodium carbonate (250 mg) was then added. The mixture was stirred vigorously at room temperature for 40 h. The solvents were evaporated off *in vacuo* (≤50 °C) and the residue was heated at reflux for 3 h with M-sodium hydroxide [2 g in water (10 ml) and methanol (40 ml)]. Preparative t.l.c. (light petroleum–ethyl acetate, 9 : 1) of the hydrolysis product (48 mg) gave a polar band (8 mg) containing the deuteriated analogues of *ent*-atisan-13α-ol (6c) and *ent*-atisan-16α-ol (7c) and a less polar band containing the deuteriated *ent*-atisan-13β-ol (6a), the *ent*-kauran-12α-ol (1a), and the *ent*-atisan-16β-ol (7a).

Oxidation of the more polar band by the method [13] of Ratcliffe and Rodehorst [chromic oxide (26 mg), pyridine (32 mg), and dichloromethane (total 3 ml)] followed by work-up and preparative t.l.c. (light petroleum–ethyl acetate, 9 : 1) gave the *ent*-atisan-13-one (6e) (4.4 mg) and the *ent*-atisan-16α-ol (7c) (3.6 mg). Mass spectra showed that the *ent*-atisan-13-one (6e) contained 75% deuterium and the *ent*-atisan-16α-ol (7c) 46% deuterium (data obtained from parent peaks after correction for $P + 1$ peaks).

Oxidation of the less polar band [chromic oxide (60 mg), pyridine (95 mg), and dichloromethane (total 4 ml)] followed by work-up and preparative t.l.c. (light petroleum–ethyl acetate, 9 : 1) gave the *ent*-kauran-12-one (1c) (20 mg), the *ent*-atisan-13-one (6e) (4.0 mg), and the *ent*-atisan-16β-ol (7a) (3.9 mg). Mass spectra showed that the *ent*-kauran-12-one (1c) contained no deuterium, the *ent*-atisan-13-one (6e) 89% deuterium, and the *ent*-atisan-16β-ol (7a) 55% deuterium.

Control Experiments.—(i) Small amounts of *ent*-kaur-11-ene (4), *ent*-atis-15-ene (8a), *ent*-atis-16-ene (8b), and *ent*-atis-13-ene (3) (*ca.* 2 mg each) were separately dissolved in chloroform (0.5 ml). Formic acid (2.5 ml) containing anhydrous sodium carbonate (50 mg) was added to each sample and the mixtures were shaken for 2 days at room temperature. The solvents were evaporated off *in vacuo* (≤50 °C). T.l.c. analysis showed that *ent*-kaur-11-ene (4) had not reacted (no formates present), *ent*-atis-13-ene (3) had reacted only to a very small extent, while *ent*-atis-15-ene (8a) and *ent*-atis-16-ene (8b) had reacted completely to produce compounds corresponding in R_F value to formates.

(ii) *ent*-Atisan-13α-ol (6c) and *ent*-atisan-13β-ol (6a) (15 mg each) were separately dissolved in chloroform (2 ml). Formic acid (10 ml) containing anhydrous sodium carbonate (200 mg) was added to each sample and the mixtures were stirred vigorously for 2 days at room temperature. T.l.c.

[13] R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, 1970, **35**, 4000.

after 24 h showed that more than half of each alcohol had been converted into a formate. The solvents were evaporated off *in vacuo* (≤50 °C) and the residues were hydrolysed in refluxing M-sodium hydroxide [1 g in water (5 ml) and methanol (20 ml)] for 3 h. Analytical t.l.c. and n.m.r. spectra of the products showed only starting material in each case.

(iii) The partially deuteriated tertiary alcohols, *ent*-atisan-16β-ol (7a) (55% $^2H_1$) and *ent*-atisan-16α-ol (7c) (46% $^2H_1$) (*ca.* 3 mg each) obtained from the formolysis of the tosylate (1g) (see above) were dissolved separately in chloroform (1 ml). Formic acid (5 ml) containing anhydrous sodium carbonate (100 mg) was added to each sample and the mixtures were stirred vigorously for 2 days at room temperature. The solvents were evaporated off *in vacuo* (≤50 °C) and the residues were hydrolysed in refluxing M-sodium hydroxide [0.5 g in water (2.5 ml) and methanol (10 ml)] for 3 h. T.l.c. of the products showed that in each case a *ca.* 1 : 1 mixture of both epimers (7a and c) had been produced. The *ent*-atisan-13-ols (6a and c) and *ent*-beyeran-12α-ol (11c) were absent. Mass spectra of each crude product showed that no deuterium loss had occurred.

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