The Structure of Sideritol, a Diterpenoid of the *ent*-Atisane Class

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Sideritol, $C_{20}H_{32}O_3$, diterpenoid isolated from *Sideritis angustifolia* Lag., has been shown to be *ent*-13-atisen-1β,16α,17-triol (**1**). Sideritol is the first reported oxygenated diterpenoid of the *ent*-atisane class which does not contain nitrogen. The transformation of sideritol into *ent*-17-noratisane (**11**), previously prepared from atisine, rigorously defines the skeleton and absolute stereochemistry of sideritol.

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Le sidéritol, diterpène de formule brute $C_{20}H_{32}O_3$, isolé du *Sideritis angustifolia* Lag., est l'*ent*-antisen-13 triol-1β,16α,17 (**1**). Le sidéritol est le premier diterpène oxygéné ne contenant pas d'azote que l'on mentionne dans la classe de l'*ent*-atisane. On définit rigoureusement le squelette et la stéréochimie absolue du sidéritol par sa transformation en *ent*-nor-17 atisane (**11**) qui a déjà été préparé à partir de l'atisine. [Traduit par le journal]

Although numerous diterpene alkaloids of the atisane-type have been isolated from natural sources (1), only two nitrogen free diterpenoids of this skeleton, atisirene and isoatisirene, have been reported (2). We report herein the structure of the first oxygenated nitrogen-free diterpenoid of the *ent*-atisane type.

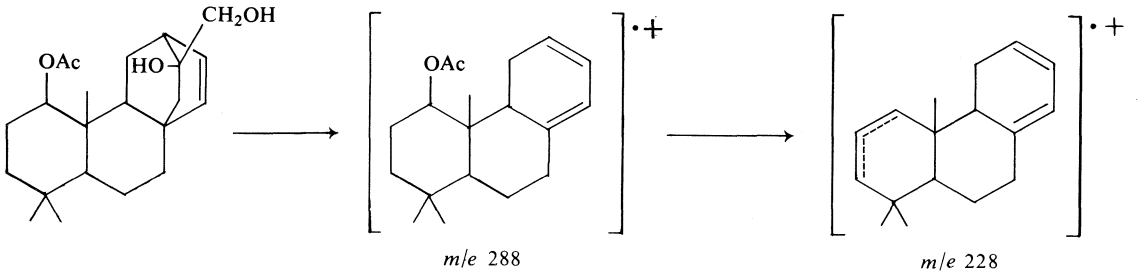
Plants of the genus *Sideritis* (family *Labiatae*) have proven to be a rich source of diterpenoids of the kaurene–isokaurene, labdane (3, and refs. therein), rimuene (4), and stachene (5) types. The isolation and separation of the diterpenoids of *Sideritis angustifolia* Lag. have been reported (5). Among the compounds isolated after acetylation of the crude diterpenoid fraction is the oily triacetate of a triol[1] $C_{20}H_{32}O_3$. Saponification of the triacetyl derivative with alcoholic potassium hydroxide yields a nicely crystalline monoacetyl derivative $C_{22}H_{34}O_4$ (monoacetylsideritol) which has been the starting point for our structural studies. In order to facilitate the discussion we will use the structure **1** derived for sideritol throughout.

Inspection of the i.r. and n.m.r. spectra (see Experimental) of sideritol monoacetate (**2**, prepared by saponification of the triacetate), triacetate (**3**), and diacetate (**4**, prepared by acetylation of **2** in the cold) reveals that the oxygen functions of sideritol are present as a primary, a secondary, and a tertiary alcohol and that it is the secondary hydroxyl function which is acetylated in the monoacetate **2**. The spectra also reveal the presence of a disubstituted olefinic linkage. Sideritol is thus a tetracyclic compound. The n.m.r. spectra also show the presence of three quaternary methyl groups.

The mass spectrum of the monoacetyl compound **2** (M^+ 362) was especially informative. A strong metastable ion peak at *m/e* 229 corresponds to the fragmentation of the molecular ion to the intense *m/e* 288 ion (362 − $C_3H_6O_2$, $C_{19}H_{28}O_2$).[2] A metastable peak at 180.5 corresponds to the loss of acetic acid from the *m/e* 288 ion to give the intense 228 ion ($C_{17}H_{24}$).[2] The facile loss of the fragment $C_3H_6O_2$ *in one step* shows that the primary hydroxyl and the tertiary hydroxyl are located on three contiguous carbons. This was confirmed by the finding that **2** readily forms an acetonide (**5**). Periodate cleavage of **2** gave the norketone **6**, absorbing

[1]We have no direct proof that the triol, for which we suggest the name sideritol, does not occur in a partially acetylated form in the plant. Triacetylsideritol is referred to as "the fourth component" in the previously described (5) isolation procedure.

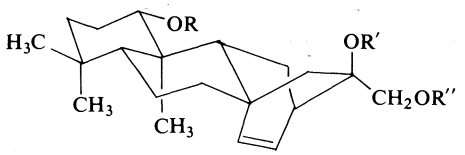
[2]Formulas of fragment ions determined by high resolution mass spectrometry.

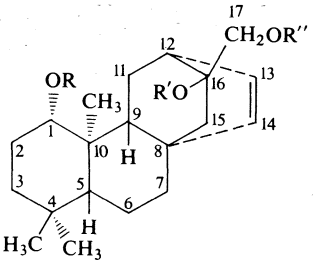


SCHEME 1

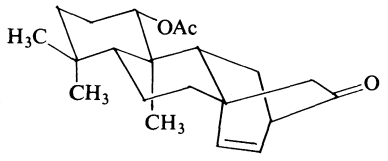
at 1720 cm^{-1} in the i.r., showing that **2** is a vicinal diol. The fragmentation may be rationalized in terms of a retro-Diels–Alder cleavage as shown in Scheme 1, and first suggested the presence of the bicyclo[2.2.2]octene system, and thus the atisene skeleton, in sideritol. In bicyclo-[2.2.2]octene systems $J_{olefinic}$ = 8.0–8.8 Hz (6) and $J_{1,2}$ = 6.6 Hz (7). The values found in the sideritol series for $J_{13,14}$ and $J_{12,13}$ agree (see Experimental) with this formulation.

The circular dichroism (c.d.) spectrum of ketone **6** shows a strongly positive Cotton effect at 294 nm ($\Delta\varepsilon$ +4.97) and a negative Cotton effect at 222 nm ($\Delta\varepsilon$ − 3.73), consistent (8) with the absolute stereochemistry of the bicyclo-[2.2.2]octenone system in **6**. However, the c.d. spectrum is also consistent with structure **7** and it was important to determine whether sideritol is an atisane derivative (ketone **7**) or an *ent*-atisane derivative (ketone **6**). It has been shown (9) that in atisene derivatives the presence of a C-13,C-14 double bond causes an abnormal shielding of the C-10 methyl so that it shows a chemical shift in the range δ 0.4–0.6. In none of the sideritol derivatives mentioned thus far is this the case. However, none of the model compounds has an oxygen substituent at C-1. In order to assess the effect of the C-1 substituent the acetonide **5** (highest field methyl at δ 0.79) was transformed to the alcohol **8** (highest field methyl at δ 0.62) by lithium aluminum hydride reduction (the C-1 ester function is extremely difficult to hydrolyze). Alcohol **8** was oxidized to ketone **9** (i.r. 1695 cm^{-1}, highest field methyl





1 R = R′ = R″ = H
2 R = Ac; R′ = R″ = H
3 R = R′ = R″ = Ac
4 R = R″ = AcR′ = H
5 R = Ac; R′ + R″ = $C(CH_3)_2$
8 R = H; R′ = R″ = $C(CH_3)_2$



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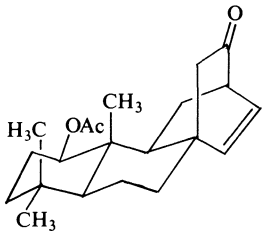

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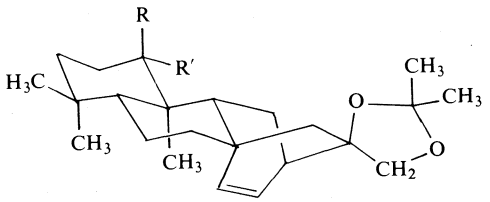
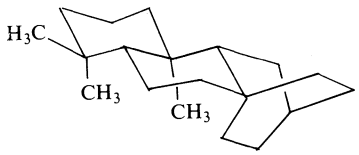


9 R, R′ = Carbonyl
10 R = R′ = H



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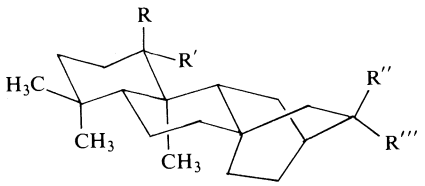
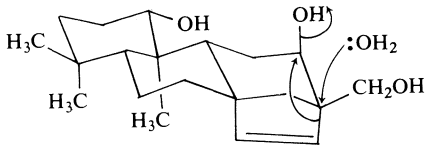


12 R = H; R′ = OAc, R″; R‴ = Carbonyl
13 R = H; R′ = OH; R″ = R‴ = H
14 R, R′ = Carbonyl; R″ = R‴ = H



15

δ 0.97) and this was reduced (10) to **10**. The highest field methyl signal in **10** appears at δ 0.57, suggesting that the C-10 methyl *is* shielded by the C-13,C-14 double bond and that sideritol is an *ent*-atisane derivative. Since this argument is subject to some ambiguity the absolute stereochemistry was rigorously established by direct correlation of sideritol with a compound of known absolute stereochemistry.

Both *ent*-17-noratisane (**11**) and its enantiomer 17-noratisane are known compounds of established absolute stereochemistry (11). We have therefore converted sideritol into *ent*-17-noratisane (**11**) in the following manner: catalytic hydrogenation of ketone **6** gave **12** and the latter upon Wolff–Kishner reduction afforded alcohol **13**. As expected (12) ketone **12** shows a negative Cotton effect at 290 nm in its c.d. spectrum. Alcohol **13** was transformed to the ketone **14** by Sarett oxidation and this was reduced (10) to *ent*-17-noratisane (**11**), identical in all respects, including o.r.d. spectrum, with an authentic sample prepared from atisine (11).

There remains to justify the positioning of the secondary hydroxyl group at C-1 and the assignment of stereochemistry at C-16. The latter point will be dealt with first. Catalytic hydrogenation of the olefinic double bond in sideritol derivatives is accompanied by a significant downfield shift of the protons geminal to the primary hydroxy group (δ 3.23 in **2**, 3.75 in dihydro **2**), thus the hydroxymethylene group appears to be *syn* to the olefinic linkage (13).

The location of the secondary hydroxyl group at C-1 is based on the following arguments: the signal for the proton geminal to this oxygen function invariably appears as a doublet of doublets, $J = 5$ and 10 Hz, indicative of an axial proton flanked by one axial and one equatorial proton. This restricts the location of the hydroxyl to C-1, C-3, or C-7. The extreme resistance to saponification (the monoacetates **2***a*, **5***a*, and **6** are resistant to hydrolysis with hot alcoholic KOH) of an equatorial acetoxyl group is best rationalized if it is located at C-1 (*peri* interaction with C-11). The effect of the functionality on the chemical shift of the C-10 methyl group (*vide supra*) also supports its location at C-1. The c.d. spectra of ketones **9** and **14** both show weakly positive Cotton effects associated with the $n \rightarrow \pi^*$ transition of the carbonyl group as expected for a C-1 ketone (14). If the carbonyl group were located at C-7 a strongly positive ($\Delta\varepsilon > +2.0$) Cotton effect would be expected in both cases (15).

In conclusion it should be noted that sideritol may be biogenetically related to jativatriol (**15**), a compound occurring in *S. angustifolia* (5). Rearrangement of jativatriol as indicated by the arrows in **15** would lead to sideritol (**1**). A laboratory analogy for the transformation of the *ent*-beyerene skeleton to the *ent*-atisene skeleton

has recently been reported (16). Attempts to correlate sideritol with jativatriol utilizing the reported method are in progress.

Experimental

Solutions were dried over anhydrous magnesium sulfate unless otherwise specified.

Melting points were determined on a Fischer-Johns hot-stage melting point apparatus and are uncorrected.

Infrared spectra were recorded on a Unicam SP1000 grating infrared spectrophotometer or a Perkin-Elmer Model 421 dual grating infrared spectrophotometer.

Nuclear magnetic resonance spectra were measured using a Varian Model HR-100 spectrometer with tetramethylsilane as internal standard and are quoted as δ (number of protons, description of signal assignment). Only significant signals are quoted.

Mass spectra including high resolution measurements (h.r.m.s.), were recorded on an A.E.I. Model MS-9 mass spectrometer and are reported as *m/e* (relative intensity). Unless diagnostically significant only peaks over *m/e* 40 and over 20% as intense as the base peak are recorded. Because of the small quantities of pure material available, most of the molecular formulas of transformation products have been determined by h.r.m.s.

Woelm silica gel (less than 0.08 mm) was used for column chromatography.

Isolation of Triacetylsideritol (3)

Triacetylsideritol was isolated as previously described (5). A crystalline sample was prepared by acetylation of purified monoacetylsideritol. The acetylation was accomplished by refluxing a solution of monoacetylsideritol (20 mg), isopropenyl acetate (11 mg), and *p*-toluenesulfonic acid (trace) in benzene (2 ml) for 1 h, then removing the acetone under reduced pressure. The benzene solution (after being washed with saturated $NaHCO_3$ and water, dried, and concentrated) gave triacetylsideritol (13 mg). After crystallization from acetone–ether it melted at 121–124 °C; i.r. (CCl_4) cm^{-1}: 3010 medium (olefinic CH), 2940, 2850 medium (C—H stretching vibrations), 1745 strong, 1730 shoulder, 1715 shoulder (C=O), 1250 strong (C—O of ester); n.m.r. ($CDCl_3$) δ: 5.96 (2H, multiplet, H-13 and H-14), 4.50 (1H, apparent doublet of doublets, H-1α), 4.27 (2H, quartet, —CH_2—OAc), 2.83 (1H, multiplet, $w_{1/2}$ 12 Hz, H-12), 1.97 (3H, singlet, —OCOCH_3), 1.94 (3H, singlet, —OCOCH_3), 1.92 (3H, singlet, —OCOCH_3), 0.82 (3H, singlet, quaternary methyl), 0.78 (3H, singlet, quaternary methyl), 0.72 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 446 (M^+ 3), 386.2457 calcd. for $C_{24}H_{34}O_4$, 386.2461 measured (M^+ − CH_3COOH, 4), 265 (21), 228 (34), 200 (20), 173 (20), 172 (23), 157 (26), 142 (20), 131 (21), 124 (100), 123 (26), 122 (26), 121 (26), 119 (28), 118 (29), 117 (28), 109 (76), 107 (24), 105 (38), 104 (36), 95 (34), 93 (22), 91 (63), 81 (72), 79 (38).

Monoacetylsideritol (2)

Crude triacetylsideritol in ethanol was added to a cooled (0°) solution of KOH in ethanol (2.5%). The solution was allowed to stir at room temperature for 1½ h. It was then acidified (10% HCl) to p*H* 5 and extracted with $CHCl_3$. Column chromatography on silica gel (eluent ethyl acetate) affords monoacetylsideritol **2**, m.p. 181–182 °C (from acetone–pentane); i.r. (Nujol) cm^{-1}: 3400 medium, 3220 broad (OH), 1737 strong (C=O), 1240 (C—O of ester); n.m.r. ($CDCl_3$, 220 MHz) δ: 6.07 (1H, doublet of doublets, $J_{12,13}$ = 6.5 Hz, $J_{13,14}$ = 8 Hz, H-13), 5.82 (1H, doublet, $J_{13,14}$ = 8 Hz, H-14), 4.58 (1H, doublet of doublets, *J* = 6 and 10 Hz, H-1α), 3.23 (2H, quartet *J* = 12 Hz, —CH_2—OH), 2.50 (1H, multiplet $w_{1/2}$ 13 Hz, H-12), 2.00 (3H, singlet, —OCOCH_3), 0.91 (3H, singlet, quaternary methyl), 0.85 (3H, singlet, quaternary methyl), 0.81 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 362 (M^+ 2), 344 (2), 302.2246 calcd. for $C_{20}H_{30}O_2$, 302.2244 measured (3), 288.2089 calcd. for $C_{19}H_{28}O_2$, 288.2097 measured (20), 228.1878 calcd. for $C_{17}H_{24}$, 288.1875 measured (58), 213 (23), 171 (45), 125 (26), 124 (100), 123 (20), 118 (25), 109 (57), 105 (21), 104 (37), 95 (27), 92 (22), 91 (53), 81 (47), 55 (20), 42 (40), 41 (22).

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.89; H, 9.46. Found: C, 73.10; H, 9.60.

Monoacetylsideritol (**2**, 100 mg) in ethanol solution was hydrogenated over 10% Pd–C during 8 h; n.m.r. ($CDCl_3$) δ: 4.58 (1H, multiplet, —C*H*OAc), 3.70 (2H, quartet, *J* = 9 Hz, —CH_2—OH), 1.80 (3H, singlet, —OCOCH_3), 1.10 (3H, singlet, quaternary methyl), 0.80 (6H, singlet, 2 quaternary methyls).

Sideritol (1)

To monoacetylsideritol (**2**, 20 mg) in ether (15 ml) was added an excess of a 1 *M* ether solution of $LiAlH_4$. The solution was allowed to stir at room temperature overnight (under nitrogen). Excess $LiAlH_4$ was then destroyed by addition of water and ether extraction gave sideritol (12 mg), m.p. 174–176 °C (from acetone–pentane); i.r. ($CHCl_3$) cm^{-1}: 3590 weak, 3420 broad (—OH), 3015 strong (olefinic C—H), 2930, 2850 strong (C—H stretching vibrations); n.m.r. ($CDCl_3$) δ: 5.95 (2H, multiplet, H-13 and H-14), 3.56 (2H, quartet, *J* = 10 Hz, —CH_2—OH), 3.25 (1H, multiplet, H-1α), 2.52 (1H, multiplet, $w_{1/2}$ 6 Hz, H-12), 0.87 (3H, singlet, quaternary methyl), 0.82 (3H, singlet, quaternary methyl), 0.80 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 302 (M^+ − H_2O, 4), 247 (22), 246 (100), 228 (29), 213 (29), 172 (28), 157 (20), 137 (23), 131 (22), 125 (21), 124 (100), 123 (44), 122 (31), 119 (22), 118 (71), 117 (20), 109 (100), 107 (33), 106 (21), 105 (37), 104 (56), 96 (43), 93 (25), 92 (35), 91 (77), 83 (20), 81 (57), 79 (25), 69 (33), 55 (33), 43 (24), 41 (38).

Diacetylsideritol (4)

A mixture of monoacetylsideritol (20 mg), pyridine (1 ml), and acetic anhydride (0.5 ml), was allowed to stand at 0 °C for 48 h. The reaction mixture was then taken up in benzene (~5 ml) and evaporated under reduced pressure. The residue was taken up in benzene (~2 ml) and washed with one drop of water. The benzene layer was removed and evaporated to afford a crude mixture of the triacetyl and diacetyl derivatives. Chromatography over silica gel (eluent, ethyl acetate) gave diacetylsideritol **4**, (11 mg); i.r. (Nujol) cm^{-1}: 3480 medium (OH), 1740, 1708 strong (C=O's), 1645 very weak (C=C); n.m.r. ($CDCl_3$) δ: 5.95 (2H, multiplet, H-13 and

H-14), 4.52 (1H, doublet of doublets, $J = 6$ and 8 Hz, H-1α) 3.76 (2H, quartet, CH_2—OAc), 2.42 (1H, multiplet, $w_{1/2}$ 7 Hz, H-12), 2.06 (3H, singlet, CH_2—$OCOCH_3$), 1.94 (3H, singlet, CH—$OCOCH_3$), 0.87 (3H, singlet, quaternary methyl), 0.81 (3H, singlet, quaternary methyl), 0.77 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 344 (3), 288 (10), 228 (68), 172 (46), 157 (30), 131 (22), 124 (94), 118 (26), 117 (24), 109 (60), 105 (33), 95 (26), 91 (100), 81 (76), 79 (36), 77 (25), 74 (32).

*ent-1β-Acetoxyatis-13-en-16α,17-acetonide (**5**)*

To a solution of monoacetylsideritol (20 mg) in acetone (2 ml) was added 1 drop of $HClO_4$ (70%). The solution was then allowed to stir at room temperature for 1 h. One drop of pyridine was added and the acetone evaporated under reduced pressure. Water was added to the residue. Extraction with ether gave the acetonide derivative **5** (18 mg), m.p. 152–154 °C, (from acetone–pentane); i.r. ($CHCl_3$) cm^{-1}: 1725 strong (C=O), 1150 medium (C—O—C), 1260 strong (C—O of ester); n.m.r. ($CDCl_3$) δ: 5.98 (2H, multiplet, H-13 and H-14) 4.54 (1H, doublet of doublets, $J = 6$ and 8 Hz, H-1α), 3.57 (2H, quartet, —CH_2—O—), 2.45 (1H, multiplet, $w_{1/2}$ 12 Hz, H-12), 2.00 (3H, singlet, —$OCOCH_3$), 1.40 (3H, singlet —O—C—CH_3), 1.32 (3H, singlet, —O—C—CH_3), 0.90 (3H, singlet, quaternary methyl), 0.85 (3H, singlet, quaternary methyl), 0.79 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 402 (M^+ 4), 288 (6), 228 (14), 124 (16), 91 (26), 79 (23), 43 (100), 41 (32).

The acetonide derivative (**5**, 100 mg) in ethanol solution was hydrogenated over 10% Pd–C during 8 h; n.m.r. ($CDCl_3$) δ: 4.55 (1H, multiplet, —CH—OAc), 3.70 (2H, quartet, $J = 7$ Hz, —CH_2—O), 2.00 (3H, singlet, —$OCOCH_3$), 1.10 (3H, singlet, quaternary methyl), 0.80 (6H, singlet, 2 quaternary methyls).

Mol. wt. Calcd. for $C_{25}H_{38}O_4$: 402.2770. Found (h.r.m.s.): 402.2773.

*ent-1β-Acetoxy-17-noratis-13-en-16-one (**6**)*

Periodic acid (380 mg) in water (4 ml) was added to a solution of monoacetylsideritol (**2**, 170 mg) in methanol (15 ml). The solution was stirred at room temperature for 24 h, diluted with water, and methanol removed under reduced pressure. Extraction with ether and chromatography over silica gel (eluent ethyl acetate) gave the crystalline ketone **6** (88 mg), m.p. 126–127.5 °C (from acetone–pentane); i.r. (Nujol) cm^{-1}: 1735 shoulder, 1720 strong (C=O), 1240 strong (C—O of ester); n.m.r. ($CDCl_3$) δ: 6.12 (2H, apparent doublet, separation 3.5 Hz, H-13 and H-14), 4.60 (1H, doublet of doublets $J = 6$ and 9 Hz, H-1α), 3.02 (1H, multiplet $w_{1/2}$ 8 Hz, H-12), 1.98 (3H, singlet, —$OCOCH_3$), 0.91 (3H, singlet, quaternary methyl), 0.88 (3H, singlet, quaternary methyl), 0.86 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 330 (M^+ 3), 288 (7), 228 (13), 124 (70), 109 (30), 91 (53), 81 (35), 55 (15), 43 (100), 41 (34); circular dichroism (*c* 0.0034 *M*, methanol): $\Delta\varepsilon_{294}$ +4.97, $\Delta\varepsilon_{225}$ −3.73.

Mol. wt. Calcd. for $C_{21}H_{30}O_3$: 330.2195. Found (h.r.m.s.): 330.2200.

*ent-1β-Hydroxyatis-13-en-16α,17-acetonide (**8**)*

The acetonide (**5**, 15 mg) was taken up in ether and treated with $LiAlH_4$ (20 drops of a 1 *M* ether solution) under nitrogen for ½ h. Work-up in the usual manner gave the crystalline alcohol **8** (10 mg), m.p. 129–132 °C (from acetone); i.r. (Nujol) cm^{-1}: 3515 weak, 3400 broad (OH), 1150 medium (C—O—C); n.m.r. ($CDCl_3$) δ: 5.94 (2H, multiplet, H-13 and H-14), 4.00 (2H, quartet, $J = 12$ Hz, —CH_2—O—), 4.23 (1H, multiplet, H-1α), 2.46 (1H, multiplet, H-12), 2.36 (3H, singlet —O—C—CH_3), 2.28 (3H, singlet, O—C—CH_3), 0.62 (3H, singlet, quaternary methyl), 0.74 (3H, singlet, quaternary methyl), 0.81 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 360 (M^+ 4), 246 (42), 228 (8), 124 (100), 118 (36), 109 (65), 105 (20), 104 (30), 95 (20), 92 (20), 91 (64), 81 (42), 79 (20), 69 (32), 57 (30), 55 (50), 43 (74), 41 (65).

Mol. wt. Calcd. for $C_{23}H_{36}O_3$: 360.2665. Found (h.r.m.s.): 360.2677.

*ent-1-Oxoatis-13-en-16α,17-acetonide (**9**)*

To pyridine (18 mg) in methylene chloride was added CrO_3 (30 mg). The resulting dark solution was stirred for 15 min, then alcohol **8** (10 mg) in methylene chloride was added. After 15 min the solution was filtered and evaporated. The residue was distributed between water and ether, and the ether extracts dried and evaporated to give the ketone **9** (7 mg), i.r. (Nujol) cm^{-1}: 1696 strong (C=O), 1145 medium (C—O—C); n.m.r. ($CDCl_3$) δ: 6.00 (2H, multiplet, H_{13} and H_{14}), 3.57 (2H, quartet, $J = 9$ Hz, —CH_2—O), 2.50 (1H, multiplet, H-12), 1.42 (3H, singlet, —O—C—CH_3), 1.35 (3H, singlet, —O—C—CH_3), 1.04 (3H, singlet, quaternary methyl), 0.98 (6H, singlet, quaternary methyls); mass spectrum *m/e*: 358 (M^+ 4), 244 (27), 188 (33), 139 (100), 91 (33), 43 (34), 41 (22); circular dichroism (*c* 0.0028 *M*, methanol) $\Delta\varepsilon_{280}$ −0.09, $\Delta\varepsilon_{310}$ +0.07, $\Delta\varepsilon_{320}$ +0.06.

Mol wt. Calcd. for $C_{23}H_{34}O_3$: 358.2508. Found (h.r.m.s.): 358.2522.

*ent-Atis-13-en-16α,17-acetonide (**10**)*

Anhydrous hydrazine was distilled into a solution of sodium (0.2 g) in diglyme (15 ml) until the solution refluxed freely at 180 °C. The ketone **9** (7 mg) was then added and refluxing continued for 18 h. The temperature was then raised to 210 °C by distilling hydrazine out of the reaction vessel. Refluxing was continued at this temperature for 18 h. The reaction mixture was then cooled and diluted with water. Continuous extraction with pentane (24 h) gave the crystalline compound **10** (3 mg), m.p. 134–136 °C (from acetone); i.r. (CCl_4) cm^{-1}: 2920, 2850 strong (C—H stretching), 1655 very weak (), 1385, 1375, 1365 sharp (methyls), 1150 medium (C—O—C); n.m.r. ($CDCl_3$) δ: 0.87 (3H, singlet, quaternary methyl), 0.78 (3H, singlet, quaternary methyl), 0.57 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 344 (M^+ 6), 230 (100), 137 (82), 106 (88), 105 (20), 104 (24), 95 (22), 94 (22), 92 (50), 91 (58), 81 (26), 69 (40), 67 (20), 57 (21), 55 (40), 43 (36), 41 (44).

Mol. wt. Calcd. for $C_{23}H_{36}O_2$: 344.2715. Found (h.r.m.s.): 344.2721.

*ent-1β-Acetoxy-17-noratisan-16-one (**12**)*

Ketone **6** (116 mg) in methanol was hydrogenated, at atmospheric pressure, over 5% Pd–C for ~3 h. The reaction mixture was then filtered and concentrated to give the crystalline ketone **12** (115 mg), m.p. 166–169 °C (from acetone); i.r. (Nujol) cm^{-1}: 1720 strong, 1698 shoulder (C=O), 1240 (C—O of ester); n.m.r. ($CDCl_3$)

δ: 4.50 (1H, doublet of doublets $J = 6$ and 8 Hz H-1α), 1.92 (3H, singlet, —O—CO—CH_3), 1.14 (3H, singlet, quaternary methyl), 0.82 (6H, singlet, quaternary methyls); mass spectrum *m/e*: 332 (M^+ 6), 272 (25), 230 (50), 106 (30), 93 (20), 81 (25), 79 (20), 55 (30), 53 (31), 43 (100), 41 (40); circular dichroism (*c* 0.0045 *M*, methanol), $\Delta\varepsilon_{290}$ −0.073.

Mol. wt. Calcd. for $C_{21}H_{32}O_3$: 332.2352. Found (h.r.m.s.): 332.2336.

*ent-17-Noratisan-1β-ol (**13**)*

The ketone **12** (115 mg) was reduced as described for the reduction of **9**. Pentane extraction gave the crystalline alcohol **13** (74 mg) purified by sublimation at 88 °C/0.5 mm Hg, m.p. 155.5–156.5 °C; i.r. (Nujol) cm^{-1}: 3370 medium, broad (OH); n.m.r. ($CDCl_3$) δ: 3.32 (1H, doublet of doublets, $J = 6$ and 7 Hz, H-1α), 1.01 (3H, singlet, quaternary methyl), 0.81 (3H, singlet, quaternary methyl), 0.80 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 276 (M^+ 11), 258 (60), 243 (28), 134 (40), 123 (27), 121 (26), 109 (26), 107 (22), 95 (38), 93 (40), 91 (32), 83 (32), 81 (68), 79 (40), 69 (56), 66 (46), 57 (90), 55 (86), 44 (94), 43 (100), 41 (90).

Mol. wt. Calcd. for $C_{19}H_{32}O$: 276.2453. Found (h.r.m.s.): 276.2459.

*ent-17-Noratisan-1-one (**14**)*

The alcohol **13** (65 mg) was oxidized as described above for alcohol **8**, to give the crystalline ketone **14** (40 mg), m.p. 79–81 °C (from methanol – Skelly B); i.r. (CCl_4) cm^{-1}: 1708 strong (C=O); n.m.r. ($CDCl_3$) δ: 2.73 (1H, 8 lines, $J_{2\alpha,2\beta} = 14$ Hz, $J_{2\beta,3\alpha} = 11.5$ Hz, $J_{2\beta,3\beta} = 6$ Hz, H-2β), 1.32 (3H, singlet, quaternary methyl), 1.05 (3H, singlet, quaternary methyl), 0.93 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 274 (M^+ 40), 259 (40), 256 (57), 175 (26), 139 (46), 105 (20), 95 (20), 93 (30), 91 (42), 81 (46), 79 (48), 77 (20), 69 (26), 67 (48), 56 (61), 53 (22), 41 (100); circular dichroism (*c* 0.009 *M*, *iso*-octane) $\Delta\varepsilon_{301}$ +0.11, $\Delta\varepsilon_{311}$ +0.22, $\Delta\varepsilon_{324}$ +0.15; (*c* 0.007 *M*, methanol) $\Delta\varepsilon_{300}$ +0.32.

Mol. wt. Calcd. for $C_{19}H_{30}O$: 274.2297. Found (h.r.m.s.) 274.2293.

*ent-17-Noratisane (**11**)*

The ketone **14** (30 mg) was reduced as described above for **9**. Continuous pentane extraction (2 days) followed by column chromatography of the residue over alumina (eluent pentane) and sublimation (atmospheric pressure, 150 °C) gave the crystalline hydrocarbon **11** (13 mg) m.p. 83–85 °C, identical in i.r., n.m.r., o.r.d., and mass spectra with an authentic sample (11); i.r. (CCl_4) cm^{-1}: 2920, 2855 strong (C—H stretching vibration), 1450 medium (methylene scissoring and asymmetrical methyl bending vibrations), 1380 sharp (—CH_3), 1360 sharp, 1355 shoulder (*gem* dimethyl group); n.m.r. ($CDCl_3$) δ: 1.05 (3H, singlet, quaternary methyl), 0.90 (3H, singlet, quaternary methyl), 0.80 (3H, singlet, quaternary methyl); mass spectrum *m/e*: 261 (M^+ +1, 23), 260 (M^+ 100), 245 (73), 175 (36), 137 (27), 136 (30), 135 (21), 125 (21), 124 (47), 123 (100), 111 (21), 109 (45), 107 (23), 105 (27), 95 (48), 93 (36), 91 (33), 82 (33), 81 (54), 79 (45), 77 (23), 75 (57), 69 (51), 67 (48), 55 (51), 45 (100), 43 (24), 41 (66); optical rotatory dispersion (*c* 0.03, methanol) 25°: $[\alpha]_{240}$ − 370°, $[\alpha]_{260}$ − 270°, $[\alpha]_{280}$ − 200°, $[\alpha]_{300}$ − 130°, $[\alpha]_{350}$ − 100°, $[\alpha]_{400}$ − 80°.

Mol. wt. Calcd. for $C_{19}H_{32}$: 260.2504. Found (h.r.m.s.): 260.2514.

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