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Unusual Reactions of the Tricyclo[5.3.1.0^{5,11}]undecane Ring System of the Decipiane Diterpenes†

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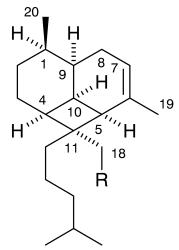
The tricyclo[5.3.1.0^{5,11}]undecane ring system of the decipiane diterpenes has been converted to the 1,4-disubstituted tetralin system of the serrulatane diterpenes in two steps.

Members of the serulatane **1** and decipiane **2** classes of diterpenes have been encountered frequently as metabolites of species of the plant genus *Eremophila* (Myoporaceae).[1]



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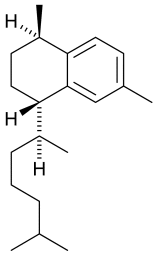
3 R = OAc



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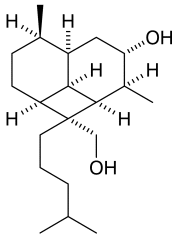

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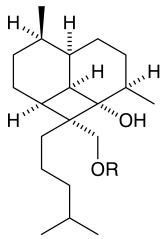
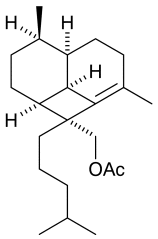


5 R = H
10 R = Ac



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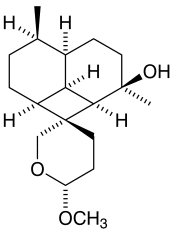

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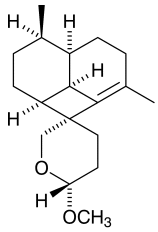

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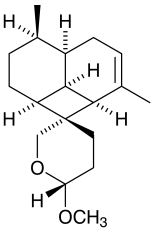

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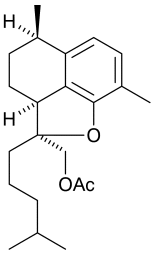

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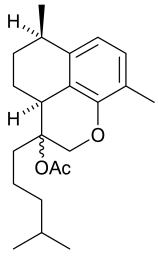

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Determination of their absolute stereochemistry has shown that they share the same absolute configuration at C1 but are epimeric at C4.[1,2] In attempts to convert the decipiane skeleton to the 4-*epi*-serrulatane skeleton, we have uncovered two unusual reactions of the decipiane skeleton, details of which are described in this report.

Hydroboration of the acetate **3**, a compound readily derived from a metabolite of *Eremophila decipiens*,[3] afforded mainly two compounds in addition to trace amounts of the dihydro derivative. The minor component could be assigned the expected structure **4** on the basis of spectroscopic analysis. The major compound on the other hand lacked a secondary hydroxy group and was shown to be the tertiary alcohol **5** as follows. The ^{1}H NMR spectrum included a doublet for a secondary methyl (δ 1.00) which replaced the vinyl methyl at δ 1.61 in the spectrum of **3**. The signals for the protons at C10 and C5, observed at δ 2.59 (appar. q, J 9.3 Hz) and 2.45 (d, J 9.1 Hz) in **3**, were replaced by a doublet of doublets at δ 2.29 (J 11.9 and 8.6 Hz; H-10). The ^{13}C NMR spectrum included a singlet for an oxygenated carbon at δ 80.0 (C5).

An explanation for the formation of **5** requires the isomerisation of the double bond at C6, under the influence of diborane, to give the compound **6** with a tetrasubstituted double bond at C5. Such isomerisations have been reported before[4] and are known to occur even at low temperature.[5] Nevertheless, the formation of **5** is surprising in view of the fact that dehydration of the tertiary alcohol **7** has been reported[6] to provide mainly the compound with a tetrasubstituted double bond **8** which could be completely isomerised with sulfur dioxide to the less strained trisubstituted counterpart **9**. Molecular mechanics energy minimization techniques[7] indeed show that **8** is less stable than **9** (74.5 kcal mol^{-1} compared to 70.6 kcal mol^{-1}; 1 cal = 4.184 J) due, in part, to an extra close contact interaction between C5–C8 (2.805 Å). In contrast, similar minimization techniques on **3** and **6**, the acetate derivative of **5** show that the former (78.5 kcal mol^{-1}) is less stable than the latter (74.4 kcal mol^{-1}) with an extra close contact interaction between C6–C9 (2.848 Å).

The tertiary alcohol **10**, obtained by acetylation of **5**, on treatment with Pb(OAc)$_4$–CaCO$_3$ at room temperature yielded a new compound **11** which was shown by HRMS to have the molecular formula $C_{22}H_{32}O_3$. The presence of the 1,2,3,4-tetrasubstituted benzene ring was evident from the NMR spectral data (4 singlets and 2 doublets for sp^2 carbons; δ_H 6.62 and 6.68, AB system, J 7.7 Hz), which also indicated the presence of an oxygen substituent (δ_C 154.9) and an aromatic methyl group (δ_H 2.15). The appearance of two multiplets at δ_H 3.26 and 2.96 were reminiscent of the signals observed for the benzylic hydrogens at C1 and C4 in the serrulatane system **2**,[8] and homonuclear COSY techniques confirmed the connectivity of the isolated system C20–C1 to C4. Signals for the C12–C17 side chains and an acetoxy group could also be identified, thus leaving two carbons to be assigned. Both of these carried an oxygen substituent, and comprised a fully substituted carbon (δ_C

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93.0 s) and a methyleneoxy carbon (δ_C 67.0, t; δ_H 4.38 and 4.43, AB system, J 11.6 Hz). This information leads to two possible structures **11** and **12** and a choice in favour of **11** could be made since the ^{1}H NMR spectrum of the hydrolysis product showed the AB system of the methyleneoxy group at δ_H 3.46, a consequence of the conversion of the C18-acetate to a primary hydroxy group. The stereochemistry at C11 was tentatively assigned from the observation that the C4 methine proton had undergone a downfield shift to δ_H 3.48, presumably a result of the removal of the shielding effect of a *syn*-acetate. The near identity of the chemical shift for the protons at C18 and C4 precluded confirmation of this through NOE measurements.

The formation of **11** and **10** can be rationalised by assuming that the ketone produced from fragmentation of the C5–C11 bond undergoes aromatization through α-acetoxylation, a process for which there are precedents.[8] The apparent formation of a single diastereoisomer, explainable by involvement of the 18-acetoxy group in stabilizing a developing radical or carbocation at C11, is probably a consequence of the purification process. Smaller amounts of a C11-stereoisomer could have been lost in the chromatographic steps.

Experimental

^{1}H and ^{13}C NMR spectra were measured for $CDCl_3$ solutions at either 300 MHz (Bruker AM-300) or 500 MHz (Bruker AMX-500). J values are in Hz.

Hydroboration of the acetate **3**.—The acetate **3** (900 mg, 2.7 mmol) in dry diethyl ether was mixed with an excess of $BH_3.(CH_3)_2S$ (2.0 ml) at 0 °C under N_2. The solution was allowed to warm to room temperature for 3 h. After cooling to 0 °C, ethanol (0.3 ml) was added followed by 30% NaOH (4 ml) and 35% H_2O_2 (3.5 ml) solutions. The mixture was stirred at 40 °C for 1 h, diluted with water and extracted with diethyl ether. Separation by radial chromatography (Si gel; EtOAc–light petroleum, 1:9) of the residue gave the 6,7-dihydro alcohol (34 mg, 4%), the 7,18-diol **4** (105 mg, 13%) and the 5,18-diol **5** (340 mg, 41%) as oils.

Decipiane-6,7-*dihydroalcohol*.—Oil, δ_H (300 MHz, $CDCl_3$), 3.64 and 3.48 (each 1 H, d, J 10.6, H_2-18), 2.45 (1 H, m, H-10); 2.20 (1 H, dd, J 10, 4.5, H-5); 0.97 (3 H, d, J 6.7, H_3-20), 0.88 (3 H, d, J 6.6, H_3-19), 0.84 (6 H, d, J 6.6, H_3-16 and H-17); δ_C (75 MHz, $CDCl_3$): 71.2, d; 48.6, s; 43.9, d; 40.2 t; 34.3, d; 32.6, d; 30.5, t; 30.2, d; 28.8, d; 28.0, d; 27.4, t; 25.7, d; 23.0, t; 22.7, q; 22.6, q; 21.1, q; 20.2, d; 18.8, q. m/z 292 (M^+) (41), 261 (33), 189 (46), 163 (59), 135 (29), 122 (100).

Decipiane-7,18-*diol* **4**.—Oil, δ_H (300 MHz, $CDCl_3$), 3.64 and 3.45 (each 1 H, d, J 10.6, H_2-18), 1.09 (3 H, d, J 7.1, H_3-20), 0.88 (3 H, d, J 6.6, H_3-19), 0.84 and 0.83 (each 3 H, d, J 6.6, H_3-16 and H_3-17); δ_C (75 MHz, $CDCl_3$): 71.8, d; 71.1, t; 48.5, s; 45.3, d; 40.1, t; 38.7, d; 33.9, t; 31.8, d; 29.9, d; 29.6, d; 29.2, t; 28.0, d; 25.4, t; 23.0, t; 22.7, q; 22.5, q; 20.2, q; 18.6, d; 17.1 q.

Decipiane-5,18-*diol* **5**.—Oil, δ_H (300 MHz, $CDCl_3$); 3.90 and 3.87 (each 1 H, d, J 11.1, H_2-18), 2.55 (br s, OH), 2.33 (1 H, dd, J 10.8, 8.3, H-17), 1.06 (3 H, d, J 6.9, H_3-20), 0.85 (3 H, d, J 6.6, H_3-19), 0.84 (6 H, d, J 6.6, H_3-16 and H_3-17); δ_C (75 MHz, $CDCl_3$): 80.0, s; 67.7, t; 53.2, s; 44.6, d; 40.4, d; 40.2, t; 29.9, d; 29.4, d; 29.0, t; 28.8, d; 28.0, d; 28.0, t; 25.4, t; 23.3, t; 22.7, q; 22.5, q; 20.0, q; 19.5, t; 18.2, t; 16.4, q; EIMS, m/z 308 (M^+) (3), 290 (50), 205 (97), 171 (62), 149 (100).

Lead tetraacetate treatment of **10**.—The diol **5** was acetylated with Ac_2O–pyridine and the monoacetate alcohol **10** (170 mg, 0.48 mmol) was treated with $Pb(OAc)_4$ (0.49 mmol) in the presence of $CaCO_3$ for 20 h. Radial chromatography (Si gel, EtOAc–light petroleum; 1:19 to 1:4) of the reaction product afforded the 4-*epi*-serrulatane 5,11-ether **11** (40 mg) as an oil; ν_{max}/cm^{-1} 1748, 1604, 1227; δ_H (500 MHz, $CDCl_3$): 0.82 (6 H, d, J 6.6, H_3-16 and H_3-17), 1.05 (2 H, m, H_2-14), 1.18 (3 H, d, J 7.2, H_3-20), 1.50 (1 H, m, H-15), 1.55 (1 H, m, H_a-3), 1.74 (1 H, m, H_b-3), 2.12 (3 H, s, OAc), 2.15 (3 H, br s, H_3-19), 2.96 (1 H, dq, J 7.2, 7.2, H-1), 3.26 (1 H, dd, J 4.7, 11.9, H-4), 4.38 (1 H, d, J 11.6, H_a-18), 4.43 (1 H, d, J 11.6, H_b-18), 6.62 (1 H, d, J 7.7, H-8), 6.88 (1 H, d, J 7.7, H-7); assignments were aided by COSY techniques; δ_C (75 MHz, $CDCl_3$): 14.7 (C19), 19.2 (C3), 20.7 (C2), 20.9 (CH_3CO), 22.4, 22.5 (C16, C17), 23.9 (C20), 27.7 (C15), 29.3 (C1), 31.2, 31.1 (C13, C14), 39.3 (C12), 45.6 (C4), 67.0 (C18), 93.0 (C11), 116.3 (C6), 119.1 (C8), 127.3 (C10), 129.6 (C7), 138.0 (C9), 154.9 (C5), 170.9 (CH_3CO) (FABMS: found: M^++H, 345.2407. $C_{22}H_{33}O_3$ requires: M^++H, 345.2430); CIMS, m/z: 345 (M^++H), 285 (51), 205 (10), 175 (11), 121 (100).

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