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STEREOSELECTIVE SYNTHESIS OF (4RS, 7RS)-7-METHYLTETRACYCLO[6.2.1.$0^{2,7}$.$0^{2,10}$]UNDECAN-4-OL. A TRACE CONSTITUENT OF LAVENDER OIL

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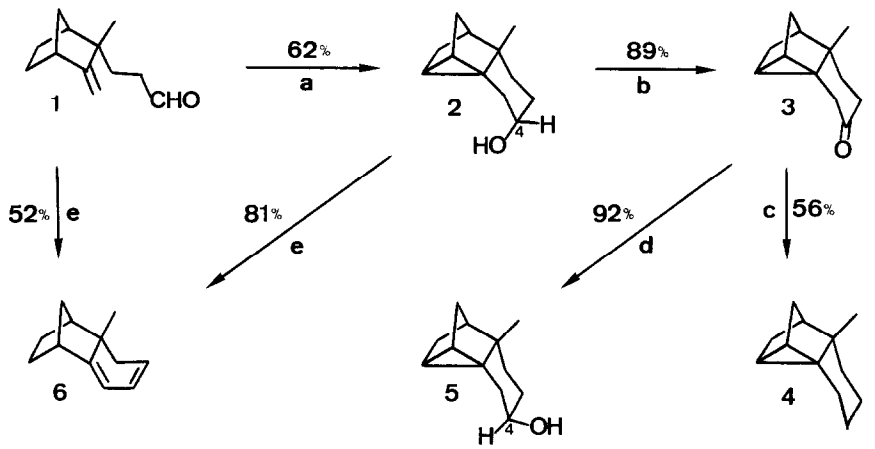
Abstract: Treatment of the bicyclic aldehyde 1 with a catalytic amount of BF_3-etherate in CH_2Cl_2 affords stereoselectively the title compound 2 in 62% yield.

During an analysis of Lavender oil[1] we identified the known bicyclic aldehyde 1[2] as a minor constituent by means of capillary GC/MS coupling experiments. Also present in the natural oil were trace amounts of a more polar substance whose strong patchouli odour encouraged further investigation. We subsequently discovered that the racemate of this latter compound, mp 80-81°C, assigned the tetracyclic structure 2[3] after analysis of its spectroscopic data, was formed on treatment of synthetic 1 with catalytic amounts of a *Lewis* acid; optimum reaction conditions were found to involve stirring 1 with BF_3-etherate (0.02 mole equiv.) in CH_2Cl_2 at -10°C.

Scheme 1

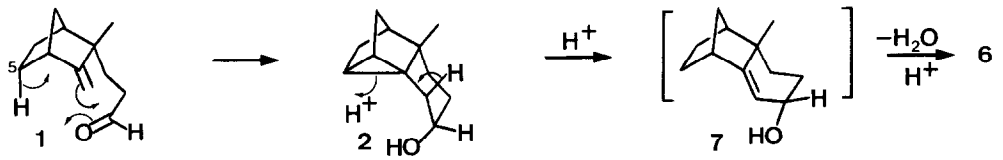


a) $BF_3 \cdot Et_2O$(cat.)/CH_2Cl_2, -10°C; b) PCC/NaOAc(anhyd.)/CH_2Cl_2, 25°C; c) $H_2N \cdot NH_2$/KOH/ethylene glycol, 190°C; d) Na/1-propanol, reflux; e) *p*·TsOH(cat.)/toluene, 25°C.

Structural confirmation was obtained by oxidation of 2 to the ketone 3 (mp 57-58°C, 89%) followed by Wolff-Kishner reduction to the known tetracyclic hydrocarbon 4[4] (mp 40-41°C, 56%). In addition, reduction of 3 with sodium in refluxing 1-propanol afforded 5 (mp 47-48°C, 92%), the C(4)-epimer of 2, with ≥95% stereoselectivity (*cf. Scheme 1*).

The excellent stereoselectivity (≥99%[5]) of the transformation 1 → 2 may be rationalised by an intramolecular Type II ene reaction mechanism[6,7] in which the C(5) *endo* hydrogen atom is transferred to the carbonyl oxygen atom with concomitant formation of a cyclopropane ring[8] (*cf. Scheme 2*).

Scheme 2



In contrast treatment of either 1 or 2 with a catalytic amount of a *Brönsted* acid (e.g. *p*TsOH) afforded the tricyclic diene 6[9] as the major product (52% and 81% yields respectively), possibly *via* the tricyclic allylic alcohol 7 (*cf. Scheme 2*).

References and Notes

1) For other analyses of Lavender oil, see: R. Kaiser & D. Lamparsky, *Helv. Chim. Acta 66*, 1835 (1983) and references cited therein.
2) To our knowledge 1 has not previously been reported as naturally occurring; for syntheses, see: a) B.J. Willis & P.A. Christenson, *J. Org. Chem. 45*, 3068 (1980); b) R.L. Snowden, P. Sonnay & G. Ohloff, *Helv. Chim. Acta 64*, 25 (1981).
3) All synthetic compounds reported here are racemic and have been fully characterised spectroscopically (IR, NMR, MS). NMR (^{1}H(360 MHz) / ^{13}C(90.5 MHz)) spectral data (δ, in $CDCl_3$):
2: ^{1}H-NMR: 0.87 (*s*,3H); 0.80-2.20 (13H); 2.10 (*s*,1H,OH); 4.06 (*m*,1H,H-C(4)). ^{13}C-NMR: 67.9 (*d*); 42.7 (*s*); 40.8 (*d*); 31.5 (*t*); 30.7 (*t*); 30.0 (*t*); 29.2 (*t*); 24.9 (*t*); 24.0 (*s*); 18.5 (*d*); 16.6 (*q*); 13.5 (*d*).
3: ^{1}H-NMR: 1.08 (*s*,3H); 0.80-2.90 (13H). ^{13}C-NMR: 211.5 (*s*); 42.4 (*s*); 40.4 (*d*); 40.2 (*t*); 38.3 (*t*); 33.0 (*t*); 30.4 (*t*); 30.2 (*t*); 30.1 (*s*); 18.4 (*d*); 16.7 (*q*); 16.2 (*d*).
4: ^{1}H-NMR: 0.71 (*d*,*J*=5Hz,1H); 0.84 (*s*,3H); 0.97 (*d*,*J*=5Hz,1H); 0.80-1.70 (13H). ^{13}C-NMR: 42.8 (*s*); 40.9 (*d*); 31.7 (*t*); 31.2 (*t*); 30.4 (*t*); 28.7 (*s*); 26.2 (*t*); 24.2 (*t*); 22.5 (*t*); 17.9 (*d*); 17.2 (*q*); 16.8 (*d*).
5: ^{1}H-NMR: 0.87 (*s*,3H); 0.70-2.10 (13H); 2.03 (*s*,1H,OH); 3.60 (*dddd*,*J*=10,10,5 and 5Hz,1H, H-C(4)). ^{13}C-NMR: 71.4 (*d*); 42.3 (*s*); 40.4 (*d*); 33.4 (*t*); 32.6 (*t*); 32.1 (*t*); 30.2 (*t*); 28.9 (*t*); 28.0 (*s*); 18.0 (*d*); 17.2 (*q*); 15.8 (*q*).
6: ^{1}H-NMR: 1.01 (*s*,3H); 1.20-1.80 (6H); 1.84 (*ddd*,*J*=17,6 and 0.5Hz,1H,αH-C(6)); 2.04 (*m*,1H-H-C(8)); 2.42 (*ddd*,*J*=17,3.5 and 2.5Hz,1H,βH-C(6)); 2.75 (*m*,1H,H-C(1)); 5.58 (*ddd*,*J*=9.5,6 and 2.5Hz,1H,H-C(5)); 5.58 (*d*,*J*=4.5Hz,1H,H-C(3)); 5.87 (*dddd*,*J*=9.5,4.5,3.5 and 0.5Hz,1H, H-C(4)). ^{13}C-NMR: 154.5 (*s*); 125.3 (*d*); 124.3 (*d*); 111.4 (*d*); 46.7 (*d*); 42.7 (*d*); 40.0 (*s*); 34.6 (*t*); 32.2 (2*t*); 22.0 (*t*); 19.7 (*q*).
4) D. Heissler & J.J. Riehl, *Tetrahedron Lett.*, 4711 (1980).
5) The absence of 5 (≤1%) in the reaction mixture was ascertained by chromatographic (TLC/GC) and spectroscopic (^{1}H-NMR) analysis.
6) For a review of the *Lewis* acid-catalysed ene reaction, see: B.B. Snider, *Acc. Chem. Res. 13*, 426 (1980).
7) For recent examples of intramolecular *Lewis* acid-catalysed ene reactions of alkenals, see: a) L.A. Paquette & Y.-K. Han, *J. Am. Chem. Soc. 103*, 1835 (1981); b) M. Bertrand, M.L. Roumestant & P. Sylvestre-Panthet, *Tetrahedron Lett. 22*, 3589 (1981); c) B.B. Snider & E.A. Deutsch, *J. Org. Chem. 47*, 745 (1982); d) B.B. Snider, M. Karras, R.T. Price & D.J. Rodini, *J. Org. Chem. 47*, 4538 (1982).
8) For an intermolecular analogy of 1 → 2, the *Lewis* acid-catalysed *Prins* reaction between camphene and formaldehyde, see: A.T. Blomquist & R.J. Himics, *Tetrahedron Lett.*, 3947 (1967).
9) The structure of 6 was confirmed by ^{1}H-NMR nuclear Overhauser enhancement experiments.

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