# Synthesis of Optically Active Grandisol

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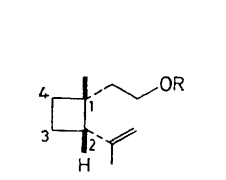
*Summary.* (−)-β-Pinene is converted stepwise into (+)-(1*R*,2*S*)-1-methyl-1-(2-hydroxy)ethyl-2-isopropenylcyclobutane (grandisol) (I; R = H).

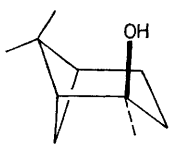
GRANDISOL (I; R = H) is the major component of the four synergistic compounds of the male boll weevil pheromone.[1] The synthesis of racemic grandisol (I; R = H) has been reported by a number of groups, all utilising a (2 + 2)-cycloaddition to construct the cyclobutane ring.[2]

Our approach is to start from an optically active starting material containing a cyclobutane ring, namely (−)-β-pinene. (−)-β-Pinene was converted into pinan-2β-ol[3] (II) by standard procedures.[4] Photolysis[5] of the nitrite ester of (II) followed by pyrolysis of the initially formed nitroso-dimer gave a mixture of *syn*- and *anti*-hydroxyoximes, which on hydrolysis (ether–acetone–2% aqueous HCl) gave the lactol (III) (51%), m.p. 58—60°. The lactol (III) was also prepared from pinan-2β-ol *via* the ether (IV).[4] Oxidation of the ether (IV) with hydrated $RuO_2$ (1 mol)–$KIO_4$ (1 mol) in aqueous $CCl_4$ gave the lactone (V)[4] (76% from pinan-2β-ol), m.p. 37—38°. Reduction of the lactone (V) with $Li(EtO)_3AlH$ at −20° gave the lactol (III) (97%). Whilst this route to the lactol (III) is longer the overall yield (74%) is higher.

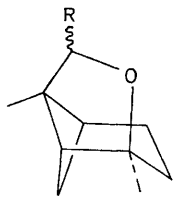
The lactol (III) was treated with $CH_2 = PPh_3$ in $Me_2SO$ to give the olefin (VI) (67%), m.p. 50·5—51·5°. Treatment of the olefin (VI) with bis(1-isopropylethyl)borane followed by oxidative work-up ($H_2O_2$–NaOH) gave the diol (VII; R = H) (95%), m.p. 110—111°. Acetylation ($Ac_2O$–pyridine) of the diol (VII; R = H) gave the monoacetate (VII; R = Ac) (95%) which on treatment with $POCl_3$ in pyridine at 0° gave the olefin acetate (IX) (59%; 2:1 mixture of α- and β- isomers). Oxidation of (IX) with $CrO_3$–pyridine



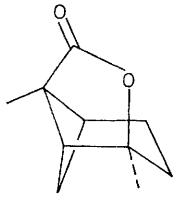

(I)



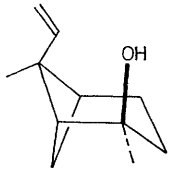

(II)



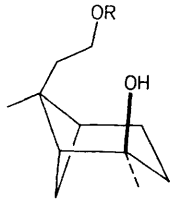

(III) R = ~~OH
(IV) R = H



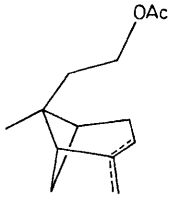

(V)



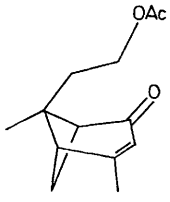

(VI)



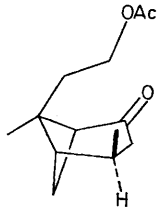

(VII)



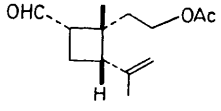

(IX)




(X)




(XI)




(XII)

(1 : 2) in $CH_2Cl_2$ gave the enone (X) (48%), $\nu_{max}$ 1750, 1690 $cm^{-1}$. Hydrogenation (20% Pd–C in EtOH) of the enone (X) gave the ketone (XI) (90%), $\nu_{max}$ 1750 and 1720 $cm^{-1}$, $\tau$ 8·77 (3H, *J* 10 Hz), 8·58 (3H, s), 7·92 (3H, s), 8·50—7·08 (9H, m), and 5·90 (2H, t, *J* 10 Hz). A 1% solution of the ketone (XI) in MeOH containing $NaHCO_3$ (1 mg/ml) was photolysed[6] (Hanovia 500 W medium-pressure lamp) to give the aldehyde (XII)(60%), $\nu_{max}$ 1735, 1705, and 1645 $cm^{-1}$, $\tau$, 8·58 (3H, s), 8·30 (3H, s), 8·07 (3H, s), 9·13—7·07 (6H, m), 6·08 (2H, m), 5·23br (1H, s), 5·08br (1H, s), and 0·28 (1H, d, *J* 3 Hz) (containing *ca.* 10% of a cyclobutene compound[6]). The aldehyde (XII), in refluxing $CH_2Cl_2$, was treated with $(PPh_3)_3RhCl$ (1·5 equiv.) to give grandisol acetate (I; R = Ac)[2], (75%), $\tau$, 8·80 (3H, s), 8·33 (3H, s), 8·05 (3H, s), 7·45 (1H, t), 6·01 (2H, t, *J* 8 Hz), 5·38br (1H, s), and 5·18br (1H, s). Grandisol acetate (I; R = Ac) was reduced with $LiAlH_4$ to give grandisol (I; R = H), 8·82 (3H, s), 8·33 (3H, s), 8·28br (2H, s), 7·93 (1H, s, exchanged by $D_2O$), 7·48 (1H, t *J* 8 Hz), 6·46 (2H, t, *J* 7·5 Hz), 5·40br (1H, s), and 5·22br (1H, s).† Purification was achieved through the *p*-nitrobenzoate (I; R = $COC_6H_4NO_2$-*p*) (recryst. 5 times), m.p. 73—74°, hydrolysis (KOH–MeOH–$H_2O$) and distillation. A sample purified this way had $\alpha_D^{21.5}$ + 14·7° (*c*, 1% in n-hexane), $\alpha_D^{25}$ + 12·7° (*c*, 3% in n-hexane) $\alpha_D^{25}$ + 5·5 (*c*, 3% in $CHCl_3$), $\alpha_D^{25}$ + 9·8° (*c*, 3% in EtOH) (lit.,[1] +50 ± 10°, measured on a crude sample).‡ This value is exceptionally high when compared with other monoterpene alcohols.

This particular synthesis offers the possibility of preparing analogues *via* Wittig reactions on the lactol (III). The unusual photochemical transformation (XI) → (XII), generating the isopropenyl group and exposing the cyclobutane ring with the quaternary centre in the correct absolute configuration is a novel and quite general reaction for these particular pinane derivatives.

All new compounds gave satisfactory spectral and microanalytical data.

(*Received, 8th August* 1974; *Com.* 1019.)

† Comparison with spectral data kindly supplied by Dr. C. A. Henrick (Zöecon) of (±)-grandisol showed them to be identical (i.r. and n.m.r.).

‡ All formulae are written in their correct absolute configuration.[4c]

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