Synthesis of Optically Active Grandisol

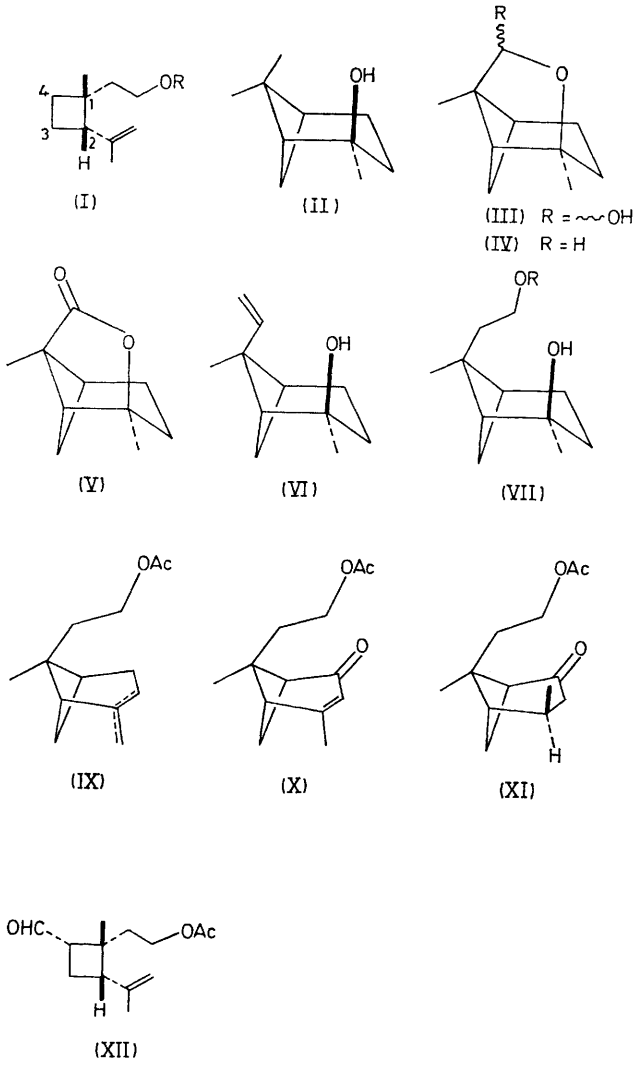
By PETER D. HOBBS and PHILIP D. MAGNUS*
(*Chemistry Department, Imperial College, South Kensington, London* SW7 2AY)

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



(1 : 2) in CH_2Cl_2 gave the enone (X) (48%), ν_{max} 1750, 1690 cm^{-1}. Hydrogenation (20% Pd–C in EtOH) of the enone (X) gave the ketone (XI) (90%), ν_{max} 1750 and 1720 cm^{-1}, τ 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%), ν_{max} 1735, 1705, and 1645 cm^{-1}, τ, 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%), τ, 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), α_D^{25} + 12·7° (*c*, 3% in n-hexane) α_D^{25} + 5·5 (*c*, 3% in $CHCl_3$), α_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*, 8*th 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]

[1] J. H. Tumlinson, D. D. Hardee, R. C. Gueldner, A. C. Thompson, P. A. Hedin, and J. P. Minyard, *Science*, 1969, **166**, 1010.
[2] (a) J. H. Tumlinson, R. C. Gueldner, D. D. Hardee, A. C. Thompson, P. A. Hedin, and J. P. Minyard, *J. Org. Chem.*, 1971, **36**, 2616; (b) R. L. Zurfluh, L. L. Durham, V. L. Spain, and J. B. Siddall, *J. Amer. Chem. Soc.*, 1970, **92**, 425; (c) R. C. Gueldner, A. C. Thompson, and P. A. Hedin, *J. Org. Chem.*, 1972, **37**, 1854.
[3] (a) W. D. Burrows and R. H. Eastman, *J. Amer. Chem. Soc.*, 1959, **81**, 245; (b) W. Huckel and E. Gelchscheimer, *Annalen*, 1959, 625, 12.
[4] (a) T. W. Gibson and W. F. Erman, *J. Amer. Chem. Soc.*, 1969, **91**, 4771; (b) A. G. Hortmann and R. E. Youngstrom, *J. Org. Chem.*, 1969, **34**, 3392; (c) N. Bosworth and P. D. Magnus, *J.C.S. Perkin I*, 1972, 943.
[5] D. H. R. Barton, J. M. Beaton, L. E. Geller, and M. M. Pechet, *J. Amer. Chem. Soc.*, 1960, **82**, 2640.
[6] (a) A. G. Fallis, *Tetrahedron Letters*, 1972, 4573; (b) T. Matsui, *ibid.*, 1967, 3761; (c) G. W. Schaffer, A. B. Doerr, and K. L. Purzycki, *J. Org. Chem.*, 1972, **37**, 25.