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THE CHAIR-BOAT EQUILIBRIUM IN 3-α-GRANATANOL

C.-Y. Chen and R.J.W. Le Fèvre
School of Chemistry, University of Sydney, Sydney,
New South Wales, Australia

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The high energy difference (1) between chair and boat forms prevents the contribution from non-chair conformations in possible chair-boat equilibria of cyclohexane derivatives from becoming appreciable. Only few authenic cases are known (2) in which the combinations of steric and/or other interactions force the six-membered ring to adopt conformations other than that of a chair. If we accept the general assumption (3) that the principles of conformational analysis as applied to cyclohexane derivatives can be carried over to six-membered rings containing nitrogen and/or oxygen, we would anticipate that boat forms in piperidine derivatives should also be very rare. So far, only 1,2,2,6,6-pentamethyl-4-phenyl-4-piperidinol (4), phenyl 3α-phenyl-3β-tropanyl ketone (5), and α-1,3,5-trimethyl-2,6-diphenyl-4-piperidinol (I) (6a,b) are known to show intramolecular hydrogen bonding and, therefore, in these compounds some participation of boat conformations must be occurred. In this note, we wish to report that 3-α-granatanol (II) also undergoes a chair-boat equilibrium, and provides the first instance where the contribution of the boat form to the equilibrium is more important than that of the chair.

Catalytic hydrogenation (7) and lithium aluminium hydride ($LiAlH_4$) reduction (8) of ψ-pelletierine yield almost exclusively 3-α-granatanol (II), m.p. 62-4°(Lit. 65°(9); however, the compound is highly hygroscopic and has been reported (7) with a b.p. of 90-95° at 0.04 mm Hg). The proton magnetic resonance (p.m.r.) spectrum of (II) is reproduced here as FIG. 1.

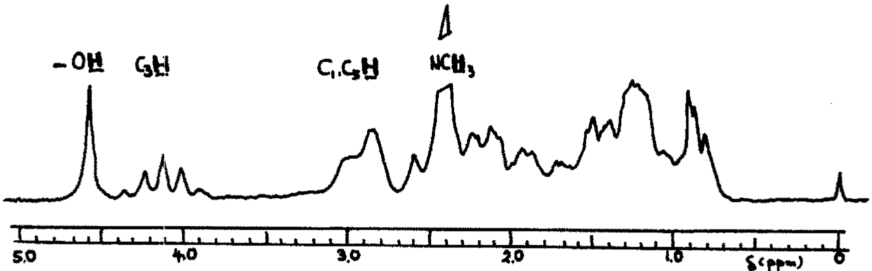
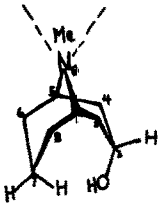


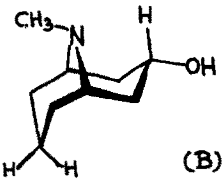
FIG. 1. The 60 Mc p.m.r. Spectrum of 3-α- granatanol (II) in deuteriochloroform (Ca. 10% wt./vol.).

Pertinent information in FIG. 1. is: (i) the quintet (intensity ratio 1:4:6:4:1) centered at τ = 5.86 p.p.m. with spacings equal to 6.8 c/s.; this, no doubt, arises from the C_3 proton; and (ii) a poorly resolved signal centered at τ = 7.08 p.p.m. due to two protons from C_1 and C_5, with a half-height width of 16 c/s. and base line width of ca. 28 c/s..

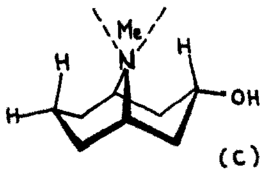
Chemical evidence (7) has proven that the configuration of 3-α-granatanol (II) must be represented by (A) although the conformational equilibrium has not been established. Theoretically,



(A)



(B)



(C)

3-α-granatanol (II) could exist in a number of conformations, such as (A), (B), and (C). (Flexible forms which are more stable in cyclohexane than a classical boat are not considered here owing to the presence of ring fusion). Consideration of non-bonded interactions disfavours (C) relatively to (A) and (B) in the equilibrium even though (A) and (B) are not free from severe steric interactions themselves. If the molecules of (II) exist mainly as (A), then, the signal from the C_3 proton (taken as the X-part of an A_2B_2X system (10)) should appear as a pseudo-triplet with a separation between terminal lines of 9.8 c/s. which is approximately equal to 2($J_{AX}+ J_{BX}$) and a base line width of 16.8 c/s. as in tropine (10,11). Since ($J_{AX}+ J_{BX}$) is 2x6.8 or 13.6 c/s. in compound (II), 3-α-granatanol (II) cannot exist exclusively as (A).

For the conformer (B), ($J_{AX}+ J_{BX}$) can be expected to be in the order of 15 c/s. (11 c/s. allowed for axial-axial coupling and 4 c/s. for axial-equatorial coupling (11)). Using ($J_{AX}+ J_{BX}$) = 5 c/s. for the conformer (A) and 15 c/s. for (B), we calculate the percentage contribution of the chair-boat conformer (B) in the equilibrium (at a probe temperature of approximately 35°) to be in the vicinity of 86%- a figure much larger than that in compound (I), where the contribution from the boat form is less than 20% (6b). The increases in the half-height and base line widths of the signal from the C_1,C_5 protons when compared with those of ψ-pelletierine (which has been shown (12) to have a chair-chair conformation) are also compatible with increasing contribution from the boat form of one of the rings- in this case, the 4-piperidinol ring.

The p.m.r. spectrum of (II) in benzene is essentially the same as in deuteriochloroform which seems to suggest that the quintet arising from the C_3 proton is the result of a dynamic equilibrium, and not of an accidental equivalence of the chemical shifts of the two pairs of the C_2,C_4 protons.

We, therefore, conclude that 3-α-granatanol (II) as a solute exists in chair-boat equilibration with the chair-boat conformer (B) predominating.

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