

STEREOCHEMISTRY OF ISOLONGIFOLENE ALCOHOLS

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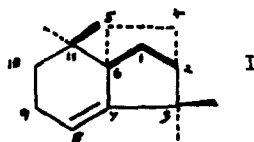
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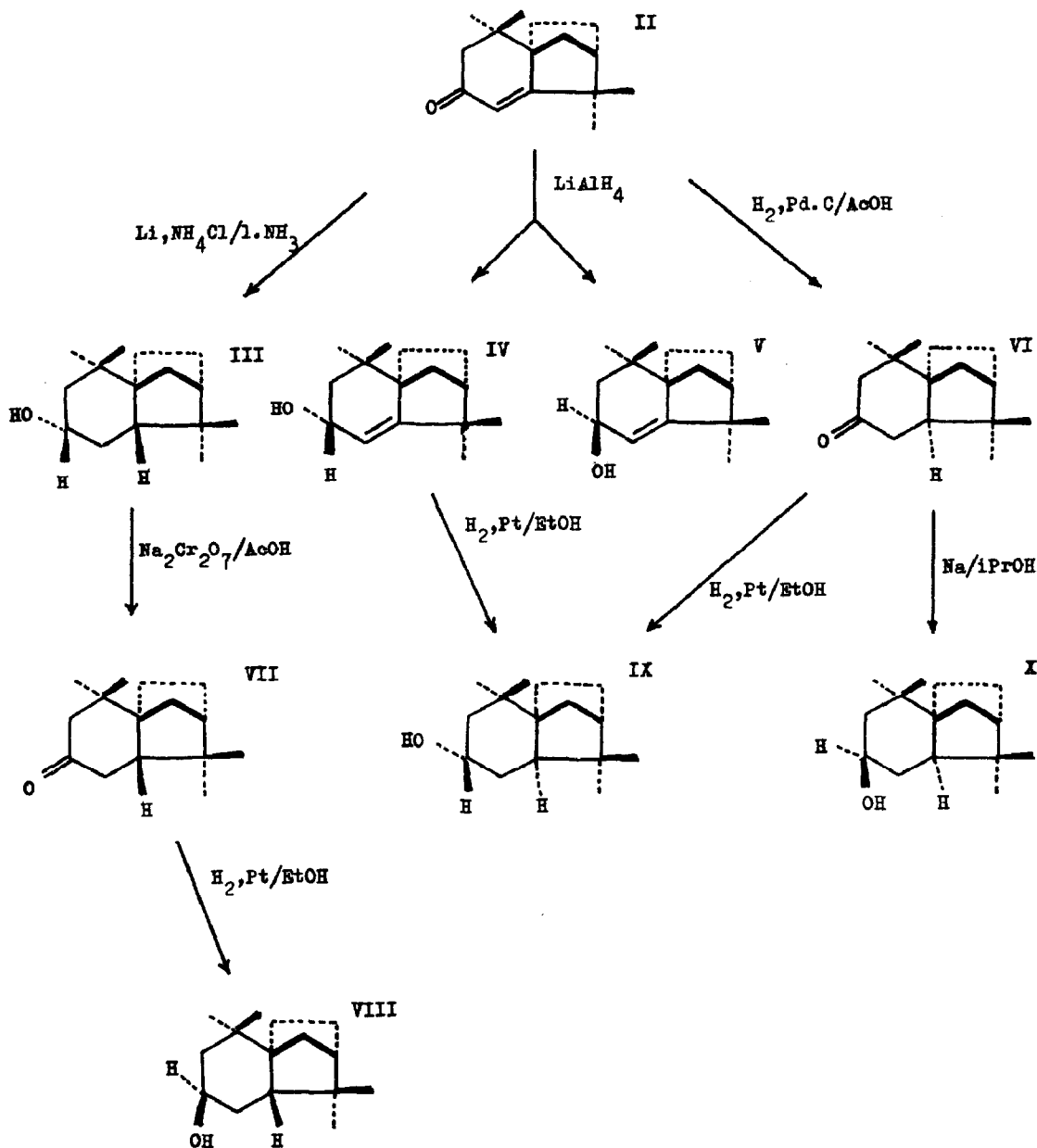
(Received in UK 26 July 1972; accepted for publication 8 August 1972)

Recent studies of the conversion of isolongifolene epoxide (isolongifolene, I) into 8-oxo-isolongifolene disagree on the assignment of the stereochemistry at C(7) . The epoxide has been assigned ^{1,2} the β configuration but this conclusion has been contested as a result of degradation of this compound to a fenchol derivative and spectral investigation of this ³ .



We have prepared all the structural isomers of 9-hydroxy-isolongifolene , 9-hydroxy-isolongifolane , and 9-oxo-isolongifolane by methods precluding skeletal rearrangements , and our conclusions as to the stereochemistry of addition to the C(7) - C(8) double bond have relevance to this dispute .

Dreiding models suggest that 9- α -hydroxy-isolongifolene in its more stable conformation has a C(9) - H bond that makes dihedral angles of about 90 , 180 , and 60° with the planes occupied by the C(8) - H and the two C(10) - H bonds . The alternative conformation is less favoured as it introduces a gauche-butane interaction at the α face , in addition to a 1,3-interaction between the pseudo-axial C(9) - OH group and the α -methyl group at C(11).



9- β -Hydroxy-isolongifolene can exist in two conformations ; one has the plane containing C(6) , C(1) , and C(2) approximately bisecting the angle between the methyls linked to C(11) , as in 9-oxo-isolongifolene ; but this conformation is destabilised by 1,3-interactions between the pseudo-axial C(9) - OH and the methyl at C(11) . The other conformation has two rear gauche -butane interactions between the methyls linked at C(11) and the C(1) - C(6) and C(5) - C(6) bonds , but the transannular 1,3 interaction is now relieved as the OH group becomes pseudo-equatorial .

Reduction of 9-oxo-isolongifolene (II) with LiAlH_4 gave two α - β unsaturated alcohols (24 : 76 w/w). The major product (m.p. 94° , i.r. bands at 3,300 , 1,668 cm^{-1} , molecular weight from mass spectra 220 ; all compounds also had satisfactory elemental analyses) had an n.m.r. signal for CHOH as an eight-line multiplet (centred at δ 4.00 ; J ($\beta\text{9H} - \alpha\text{10H}$) , 9.3 Hz ; J ($\beta\text{9H} - \beta\text{10H}$) , 6.0 Hz ; J ($\beta\text{9H} - \text{8H}$) , 2.4 Hz). This represents vicinal dihedral angles of 170° , 30° , and 55° respectively . The C(8) - $\underline{\text{H}}$ signal is a doublet (centred at δ 5.00 ; J ($\text{8H} - \beta\text{9H}$) , 2.4 Hz). These measurements are consistent with 9- α -hydroxy-isolongifolene (IV) in the conformation with the C(9) - OH bond pseudo-equatorial . The minor product (m.p. 71° , i.r. bands 3,400 , 1668 cm^{-1} ; molecular weight from mass spectra 220) has an n.m.r. signal for CHOH as an eight-line multiplet (centred at δ 3.97 , J ($\alpha\text{9H} - \text{8H}$) , 4.5 Hz ; J ($\alpha\text{9H} - \alpha\text{10H}$) , 4.0 Hz and J ($\alpha\text{9H} - \beta\text{10H}$) 3.0 Hz). These represent dihedral angles of 35° , 45° , and 55° respectively . The C(8) - $\underline{\text{H}}$ signal is a doublet at δ 5.12 , J ($\text{8H} - \alpha\text{9H}$) , 4.5 Hz . These results are consistent with 9- β -hydroxy-isolongifolene (V) with the C(9) - OH bond pseudo-axial . Reduction with NaBH_4 , both alone and with added triethylamine⁴ gave the same proportions of products , but reduction with $\text{NaAlH}_2(\text{OCH}_2\text{CH}_2\text{OCH}_3)_2$ gave the reverse (82 : 18 w/w) ratio . It is likely that the product proportions in the LiAlH_4 and NaBH_4 reductions are governed by eclipsing effects⁵ whereas those in the last reduction are governed by bulk steric effects ; this is consistent with the preferred approach of the last bulky reagent from the least hindered side to give the main product . In support , equilibration of the alcohol (V) with base in the presence of benzophenone gave α,β alcohols (94 : 6 w/w) .

Lithium - ammonia reduction of (II) gave a saturated alcohol with n.m.r. signal for C(9) - $\underline{\text{H}}$ as a broad multiplet (centred at δ 3.70). Dichromate oxidation of this and hydrogenation (Pt/EtOH) resulted in an axial alcohol (m.p. $99\text{--}100^\circ$) with a n.m.r. signal for C(9) - H as a narrow multiplet (centred at δ 4.05) .

Hydrogenation of (II) (Pd.C/AcOH) gave a saturated ketone (m.p. 60°) ; further hydrogenation (Pt/EtOH) of this formed a saturated alcohol (m.p.) . The latter had a n.m.r. signal for C(9) - $\underline{\text{H}}$ as a narrow multiplet (centred at δ 4.10) . Reduction of the above saturated ketone (Na/iPrOH) gave the corresponding equatorial alcohol with n.m.r. signal for C(9) - $\underline{\text{H}}$ as a broad multiplet (centred at δ 3.70) .

The four 9-hydroxy-isolongifolanes were all different (i.r. , n.m.r. , m.p. , m.s. , and g.c. characteristics. Hydrogenation of (IV) (Pt/EtOH) gave a saturated alcohol (A) identical with the axial alcohol prepared by hydrogenation of (II) with Pd.C/AcOH and the reduction of the resulting saturated ketone with hydrogen over Pt. The C(7) - H bond (α or β) in all isolongifolanes must be axial to the ring

containing the C(7) - C(8) bond (from Dreiding models) , and from the previous discussion the configuration at C(9) of the unsaturated alcohol is known ; the configuration at C(7) must therefore be α , and so the saturated alcohol (A) must be 9- α -hydroxy-7- α -H-isolongifolane. The stereochemistry of the series of reductions may thus be written as in the diagram . These assignments are consistent with results from independent crystallographic studies on glycols formed from nor-C(11)-methyl-isolongifolenes⁶ .

Our results indicate that cis-addition to the C(7) - C(8) double bond in hydrogenation occurs from the α face (of structure II)⁺ and so support the revised conclusions³ as to the stereochemistry of the isolongifolene epoxides .

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Note The projection of isolongifolene in Dev's publications is the reverse of the projection used in this paper .

ACKNOWLEDGMENTS

We thank the Directors of Bush Boake Allen Ltd. for permission to publish this paper . We wish to thank Mr. R. Duprey , Mr. J. Janes , Mr. V. Skeels , and Mr. P. Steer for analytical assistance .

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