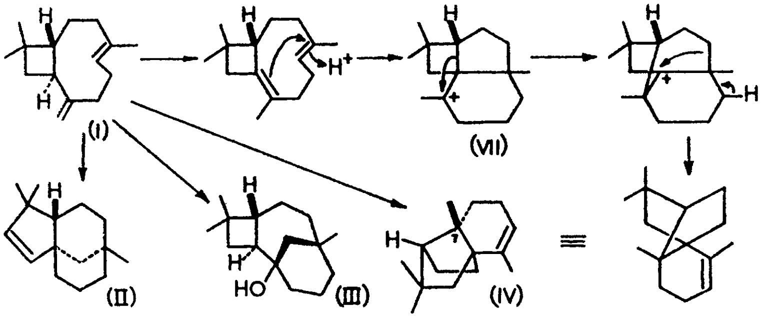
The Synthesis of Neoclovene[1]

By T. F. W. McKillop, J. Martin, W. Parker, and J. S. Roberts
(*Chemistry Department, The University of Glasgow, Glasgow, W.2*)

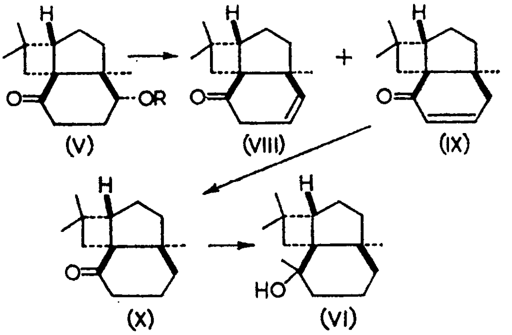
On treatment with acidic reagents, caryophyllene (I) undergoes ring closure to give a mixture of clovene (II), caryolan-1-ol (III), and neoclovene (IV).[2] The mode of formation and final stereochemistry of (II) and (III) have been fully rationalised by Barton,[3] but it is impossible to accommodate neoclovene within this mechanistic framework. Accordingly, the mechanism shown below was suggested[2] for this conversion of (I) into (IV).



In the light of this suggestion, it became apparent that a specific transformation of the ketol (V, R = H) into the tertiary alcohol (VI) would permit access to the cation (VII), which is involved in the suggested mechanism for the transformation of (I) into (IV). Hence a brief series of experiments might well achieve three objectives, *viz.*, (a) a test of the feasibility of the suggested mechanism, (b) a synthesis of neoclovene, and (c) additional confirmation* of the relative stereochemistry of the methyl group at C-7.

The crystalline carbonate† (V; R = CO_2Et) of the ketol (V; R = H), a known degradation product[4] of caryophyllene, was converted into a mixture (5 : 1) of the nonconjugated and conjugated ketones (VIII) and (IX) by pyrolysis at 350°. Catalytic hydrogenation of this mixture produced a homogeneous tricyclic ketone (X) which was converted by treatment with methylmagnesium iodide into a single tertiary carbinol (VI) whose stereochemistry at the carbinyl carbon is as yet undefined. When the carbinol was treated with a solution of concentrated sulphuric acid in anhydrous ether, simulating the conditions used in the rearrangement of caryophyllene, an olefinic product was isolated in 75% yield. The major component (>99%) of this material was homogeneous in terms of successive mass-spectral examination through the single g.l.c. peak and was identical in all respects with authentic neoclovene (optical rotation, mass spectrum, n.m.r., and infrared spectra, and capillary g.l.c.).

With the stereochemistry of the ketol (V; R = H)[5] established, this rearrangement can only proceed to neoclovene with the C-7 methyl group *syn* to the *gem*-dimethyl grouping.



(*Received, December 29th,* 1966; *Com.* 1043.)

---

* The stereochemistry of (IV) as depicted has been established from o.r.d. studies to be reported in a full Paper.

† Satisfactory analytical and spectroscopic data have been obtained for all new compounds.

[1] Preliminary experiments towards the synthesis of this hydrocarbon have been reported by H. J. E. Loewenthal, *Israel J. Chem.*, 1966, **4**, 31.

[2] W. Parker, R. A. Raphael, and J. S. Roberts, *Tetrahedron Letters*, 1965, 2313.

[3] A. Aebi, D. H. R. Barton, A. W. Burgstahler, and A. S. Lindsey, *J. Chem. Soc.*, 1954, 4659.

[4] D. H. R. Barton and A. S. Lindsey, *J. Chem. Soc.*, 1951, 2988.

[5] D. H. R. Barton and A. Nickon, *J. Chem. Soc.*, 1954, 4665; A. Horeau and J. K. Sutherland, *J. Chem. Soc.* (*C*), 1966, 247.