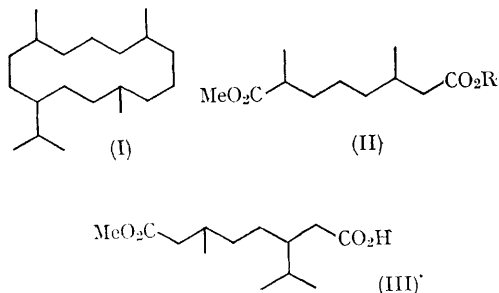


Synthesis of 1,5,9-Trimethyl-12-isopropylcyclotetradecane (Cembrane)

By I. D. ENTWISTLE and R. A. W. JOHNSTONE

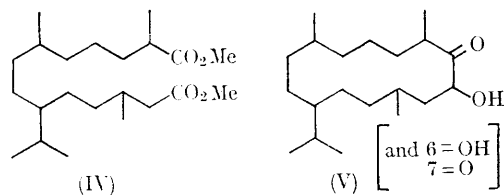
[*M.R.C. Unit, Exeter University (I.D.E.), and The Robert Robinson Laboratories, Liverpool University (R.A.W.J.)*]

A FEW macrocyclic terpenes containing fourteen-membered rings have been reported. Thus, the duvatriene diols were isolated from Turkish tobacco¹ and cembrene from pine trees.² We have now synthesised the parent hydrocarbon, 1,5,9-trimethyl-12-isopropylcyclotetradecane (I, cembrane or duvane). Methyl hydrogen $\alpha\alpha'$ -dimethylpimelate was converted by the Arndt-Eistert method into 6-benzyloxycarbonyl-1-methoxycarbonyl-1,5-dimethylhexane (II; R = benzyl) after hydrogenolysis of the benzyl group, the resulting half-ester was electrolysed with 1-carboxy-6-methoxycarbonyl-2-isopropyl-5-methylhexane (III). On preparative scale gas chromatography, the mixture of di-esters from the electrolysis afforded the required long-chain di-ester (IV, m.w. 370, by mass spectrometry), which was cyclised by the acyloin method³ to a mixture of keto-alcohols (V).



Clemmensen reduction of the mixed acyloins gave the saturated hydrocarbon (I), b.p. 136—138°/0.35 mm., ν_{\max} 2900, 1450, 1365, 725 cm^{-1} , τ 9.18, 9.12, 8.75, 8.38, 8.30 (little fine structure even at 100 Mc./sec.), m.w. 280 (mass spectrometry). In gas-chromatographic behaviour, and

infrared, nuclear magnetic resonance, and mass spectra, the hydrocarbon (I) and cembrene obtained by catalytic reduction of cembrene, were identical. Gas chromatography of the cycloalkane (I, from cembrene or by synthesis) on a 150 ft. capillary column coated with a silicone, SE-30, showed only a single peak although diastereoisomeric forms undoubtedly exist in the material as synthesised here.



(Received, January 24th, 1966; Com. 044.)

¹ D. L. Roberts and R. L. Rowland, *J. Org. Chem.*, 1962, **27**, 3989.

² W. G. Dauben, W. E. Thiessen, and P. R. Resnick, *J. Amer. Chem. Soc.*, 1962, **84**, 2015.

³ V. Prelog, L. Frenkiel, M. Kobelt, and P. Barman, *Helv. Chim. Acta*, 1947, **30**, 1741.