Tetrahedron Letters No. 28, pp. 1949-1951, 1963. Pergamon Press Ltd.
Printed in Great Britain.

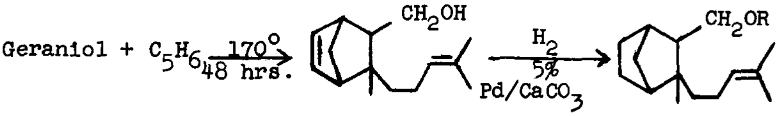
A NEW SYNTHESIS OF d,ℓ-β-SANTALENE AND d,ℓ-epi-β-SANTALENE[1]

Gottfried Brieger

Department of Chemistry, University of California
Berkeley 4, California

(Received 30 September 1963)

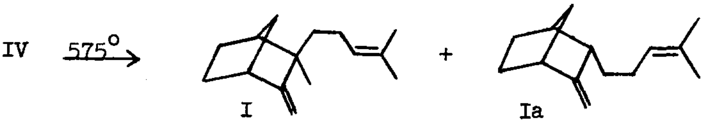
A recent paper[2] has described one approach to the synthesis of d,ℓ-β-santalene (I), and d,ℓ-epi-β-santalene (Ia). We wish to report herein a new and particularly simple synthesis of the same compounds.



II

III R=OH

IV R=



I

Ia

Little is known about the Diels-Alder reactions of dienophiles containing trisubstituted double bonds without activating groups. Presumably, steric effects retard the reaction greatly. Nevertheless, we have been able to demonstrate the reaction between geraniol and cyclopentadiene. When these components are heated at 170°C for

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[1] Part II. Synthetic Transformation of Natural Products.

[2] E. J. Corey, R. Hartmann, and P. A. Vatakenchery, J. Am. Chem. Soc., 84, 2611 (1962).

48 hours, adducts of structure II are formed in ca. 4% yield. Some addition to the terminal double bond was also noted. The adducts were separated from starting materials and polymer by distillation. The liquid adducts were then chromatographed on alumina. Final purification was effected by vapor-phase chromatography.

The structure of adducts II is supported by the elemental analysis (Calc. for $C_{15}H_{24}O$: C, 81.81; H, 10.90. Found: C, 81.56; H, 10.92.) and by pyrolysis to the starting materials, geraniol and cyclopentadiene. The infra-red spectrum had bands at 6.05 μ and 6.40 μ, indicative of the exocyclic and endocyclic double bonds, respectively. There is also a characteristic band at 13.55 μ. The n.m.r. spectrum (taken in CS_2 with tetramethylsilane internal standard) is also in accord with these structures, having a broad peak at 3.85 τ arising from the endocyclic olefinic protons and a triplet centered about 4.85 τ assigned to the alicyclic vinyl proton. A doublet at 8.35 τ is assigned to the side-chain methyl-groups while the angular methyl appears at 9.21 τ. The assignment of stereochemistry is presently under investigation.

Conversion to the santalenes was effected as follows: Selective hydrogenation of the endocyclic double bond with 5% Pd/$CaCO_3$ gives the dihydro-adducts III. (Anal. calc. for $C_{15}H_{26}O$: C, 81.08; H, 11.71. Found: C, 81.02; H, 11.91.) The infra-red bands at 6.40 and 13.55 μ as well as the absorption at 3.85 τ in the n.m.r. were no longer present in the saturated adducts. The alcohols III were converted to the corresponding acetates IV by treatment with acetic anhydride and pyridine. Pyrolysis of the acetates at 575°C gave d,ℓ-β-santalene (I) and d,ℓ-epi-β-santalene (Ia) in a ratio of approximately 6:4. (Anal. calc. for $C_{15}H_{24}$: C, 88.24; H, 11.76. Found: C, 87.84; H, 11.96.) The products were analyzed by vapor-phase chromatography (10' 25% tricyanoethoxypropane on 60/80 Chromosorb W[2]). Their retention times corresponded to those from a sample of the natural mixture.[3] Furthermore, the infra-red spectra and n.m.r. spectra were identical with those of the natural materials.

We are continuing to explore this approach to the synthesis of natural products.

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[3] Kindly supplied by Professor Sukh Dhev.