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DIRECT SYNTHESIS OF SESQUICARENE FROM *cis,trans*-FARNESOL

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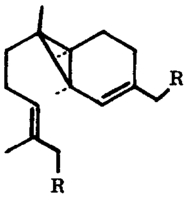
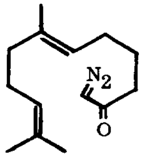
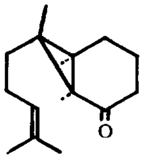
A stereospecific synthesis of the terpenoid hydrocarbon sesquicarene (I, R = H) (1) has recently been reported in which the key step was the transformation of the diazoketone II to the bicyclic ketone III (2). This approach has also been used for the total synthesis of the allomyces female sex attractant sirenin, I, R = OH (3, 4).



I

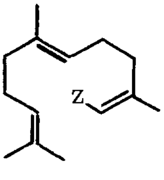


II



III

We describe herein a simple and fairly efficient four-step synthesis of sesquicarene from *cis,trans*-farnesol (IV), which is readily available by fractional distillation of commercial farnesol (5). Oxidation of the alcohol IV with excess activated manganese dioxide in hexane at 0° for 1 hr. afforded farnesal V, which was converted into the hydrazone VI by reaction with 6 equiv. of hydrazine and 6 equiv. of triethylamine in ethanol at 25° for 15 hr. (6). The hydrazone VI was isolated by removal of volatile solvent and excess reactants at 1 mm. and room temperature. The orange diazo compound VII was prepared directly from VI by oxidation with excess (sixfold) activated manganese dioxide in methylene chloride at 0° for 2 hr. and isolated simply by evaporation of solvent. The infrared spectrum of VII exhibited a strong sharp band at 4.88 μ confirming the presence of the diazo function. Slow addition of the unsaturated diazo compound VII (0.1 M) in tetrahydrofuran to a suspension of cuprous iodide (2 equiv.) in tetrahydrofuran (1 volume) at 35° afforded *dl*-sesquicarene in 25% yield based on IV. The product so obtained was completely identical with a sample of *dl*-sesquicarene previously synthesized (2) and natural sesquicarene (1, 7) by v.p.c. (8), n.m.r., and infrared analysis.



IV, Z = CH_2OH
V, Z = CHO
VI, Z = $CH{=}NNH_2$
VII, Z = $CH{=}N_2$

Sesquicarene could also be obtained in fair yield from the diazo compound VII using cupric fluoborate in cyclohexane at 35° (*ca.* 16% yield). Cuprous chloride, copper powder, and lithium bromide were less satisfactory as catalysts for the internal cyclization (9, 10).

REFERENCES

1. For the isolation and structure of sesquicarene, see Y. Ohta and Y. Hirose, *Tetrahedron Letters* 1251 (1968).
2. E. J. Corey and K. Achiwa, *Tetrahedron Letters* 1837 (1969).
3. For structure see L. Machlis, W. H. Nutting, and H. Rapoport, *J. Am. Chem. Soc.* **90**, 1674, 6434 (1968).
4. E. J. Corey, K. Achiwa, and J. A. Katzenellenbogen, *J. Am. Chem. Soc.* **91**, In press.
5. Commercial farnesol was obtained from the Givaudan Corporation, Clifton, N. J., as a mixture of 70% *trans,trans* isomer and 28% *cis,trans* isomer. Fractionation was carried out using an 18-in. spinning band (Teflon) column (Nester/Faust) at 0.2 mm. with the *cis,trans* isomer distilling first (b.p. 95°).
6. See D. H. R. Barton, R. E. O'Brien, and S. Sternhell, *J. Chem. Soc.* 470 (1962).
7. We are indebted to Dr. Hirose for providing n.m.r. and infrared spectra of natural sesquicarene and a generous sample.
8. V.p.c. analysis was performed using a 6-ft. x 0.125-in. column of 5% Carbowax 20M on silanized support at 120°, the observed retention time of the various samples being 2.5 min. at 60 ml./min. N_2 flow.
9. For an earlier example of an intramolecular addition reaction of an unsaturated diazo compound, see G. Büchi and J. D. White, *J. Am. Chem. Soc.* **86**, 2884 (1964).
10. This work was supported by the National Science Foundation.

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