Tetrahedron Letters No. 21, pp. 1807-1810, 1971. Pergamon Press. Printed in Great Britain.

OLEFIN PARTICIPATION IN THE ACID-CATALYZED OPENING OF ACYLCYCLOPROPANES. IV. CYCLIZATION OF 5-METHYL-6-ENDO-(TRANS-3-PENTENYL)BICYCLO(3.1.0)HEXAN-2-ONE.[1]

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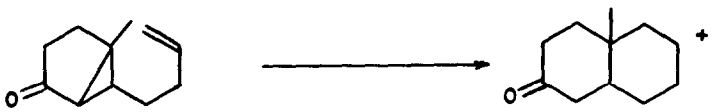
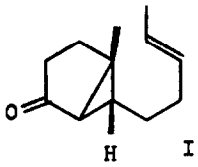
(Received in USA 30 March 1971; received in UK for publication 20 April 1971)

Previous studies have shown that acylcyclopropanes can undergo acid-catalyzed transformation with participation of a suitably placed double bond and formation of a new ring(cf. A→B).[2-4] We now report on a case(endo-bicyclo(3.1.0)hexanone, I) in which the double bond undergoes 90% olefin participation generating a cyclohexyl cationic species which experiences either simple proton loss or hydride transfer leading to a new cation which either undergoes angular methyl migration or gets trapped by the enol.

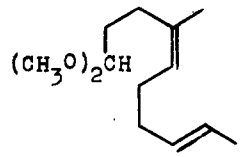


A B

The endo-bicyclo(3.1.0)hexanone I was synthesized from the dienic acetal IV(vide infra) by the usual sequence via the aldehyde V, R=H, λ(film) 3.70, 5.81, 10.35μ; acid V, R=OH(silver oxide oxidation), λ(film) 2.80-4.20, 5.85, 10.35μ; δ($CDCl_3$) 11.08(s, 1H); acid chloride V, R=Cl(thionyl chloride/carbon tetrachloride), λ(film) 5.53, 10.35μ; and diazoketone V, R=CHN_2, λ(film) 3.25, 4.74, 6.05, 10.35μ. Cyclization of the latter(reflux with copper bronze in cyclohexane) afforded the desired ketone I. I was homogeneous by glpc(DEGS, 190°,



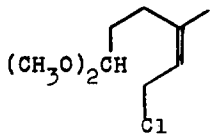
I



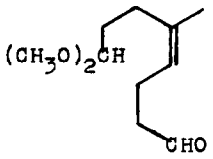
IV

10 ft. x 0.25 in., 90 ml/min., retention time 6 min.) and tlc(benzene/ethyl acetate, 95:5) after chromatography on silica gel. I exhibited the anticipated spectral features: λ (film) 5.80, 10.32μ ; δ ($CDCl_3$) 1.30(s, 3H), 5.40(m, 2H).

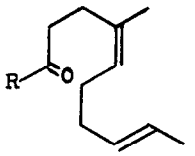
The dienic acetal IV was prepared from the readily available acetal chloride II.[5] Alkylation of acetoacetic ester with a molar equivalent of II afforded the alkylated product which was cleanly deacetylated with sodium ethoxide-ethanol.[6] Reduction of the ester group with lithium aluminum hydride followed by Collins oxidation[7] provided the acetal aldehyde III. Construction of the trans disubstituted olefin in IV was accomplished by the Schlosser modification[8] of the Wittig reaction, employing the ylide derived from ethyl iodide.



II



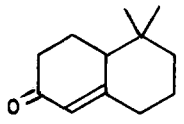
III



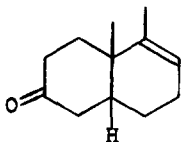
V

A pure sample of I(250 mg), obtained by preparative glpc(DEGS, 190°) was cyclized by keeping its solution in 10 ml of benzene and 2ml of stannic chloride for 18 hours at room temperature under nitrogen. Glpc analysis (SE 30, 155°) after 18 hours showed no starting ketone and three major peaks X, Y and Z(retention times 9, 10 and 14 minutes respectively in a ratio of 7:7:5). These three substances totaled 90% of the reaction products. Preparative glpc(DEGS, 190°) furnished pure fractions of X, Y and Z. Product Z was assigned the 5,5-dimethyl-$\Delta^{1(9)}$-2-octalone structure VI on the basis of its spectral characteristics: λ (film) 5.98, 6.18μ ; no trans olefin; δ ($CDCl_3$) 1.08 (s, 3H), 0.85(s, 3H), 5.78(s, broad, 1H). This assignment was substantiated

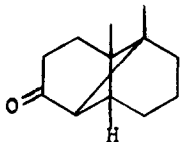
by comparison of the nmr and ir spectra of VI with those of an authentic sample.[2] Product Y had spectral data consistent with the product of cyclopropane cleavage accompanied by cyclization, followed by loss of a proton: λ(film) 5.80μ ; δ($CDCl_3$) 1.20(s, 3H), 1.70(d, J~2Hz, 3H), 5.45(s, broad, 1H). Accordingly, Y was assigned the cis-dimethyloctalone structure VII which was confirmed by synthesis from the commercially available diketone IX. Product X showed no olefinic protons in the nmr spectrum and the infrared exhibited an unconjugated carbonyl: λ(film) 5.80μ; δ($CDCl_3$) 0.79(s, 3H), 0.95(s, 3H), 2.65(s, 1H). Mass spectral data indicated a molecular ion at m/e 178. Consideration of structures consistent with these data, together with mechanistic considerations led to the tricyclic ketone VIII. Further proof for this structure came from the demonstration that treatment of the cis-dimethyloctalone VII with a solution of methylene chloride saturated with boron trifloride furnished VIII in 90% yield.



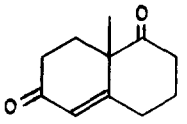
VI



VII

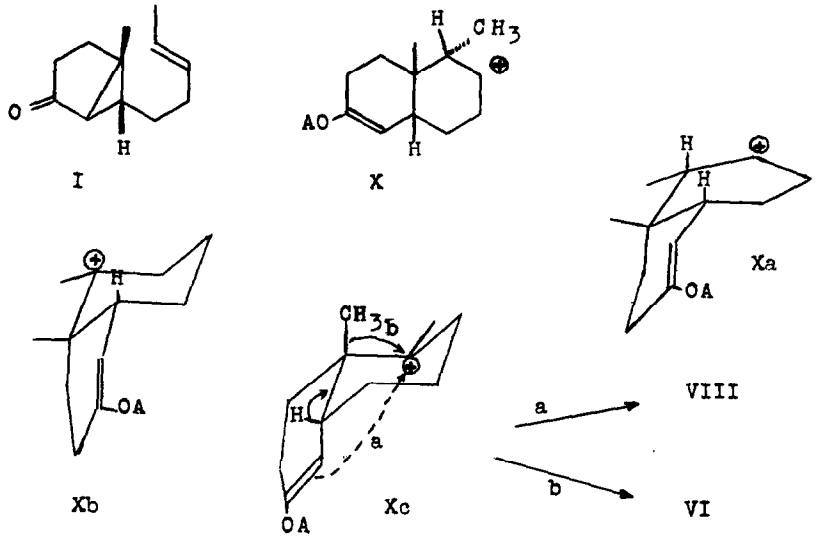


VIII



IX

We have shown that VI and VIII are not formed by way of VII, as the latter did not form either VI or VIII when submitted to the cyclization conditions. The formation of VI, VII and VIII, in yields of 20, 35 and 35 percent respectively, shows again that an external double bond can become involved in a concerted fashion in the cyclopropane opening of I since all the products arise from the initially formed cyclohexyl cation X which should initially be in conformation Xa, assuming a reasonably concerted reaction for the formation of the new ring. The cyclohexyl cation Xa has the proper geometry for elimination affording the octalone VII, and secondly for a 1,2 hydride transfer producing a tertiary carbonium Xb. This new carbonium ion after flipping to the other cis conformer Xc, as shown, can partition between two possible pathways, namely rearrangement (Xc → VI) and trapping of the cation by the enol(Xc → VIII). We have thus demonstrated the initial formation of the cis bicyclic cation X from the endo



substituted bicyclo(3.1.0)hexanone series. It remains to be seen whether the cation can be trapped by a suitably disposed nucleophilic carbon, thus forming a further ring, sufficiently rapidly to prevent the rearrangement we have just demonstrated in the absence of such a center.[9]

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1. Presented, in part, by one of us(P.A.G.) at the 7th International Symposium on the Chemistry of Natural Products held in Riga, USSR, in June, 1970.
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9. Support of this work by the National Science Foundation and the National Institutes of Health is gratefully acknowledged.