

A VERSATILE CIS-DECALIN-2,6-DIONE SYNTHESIS

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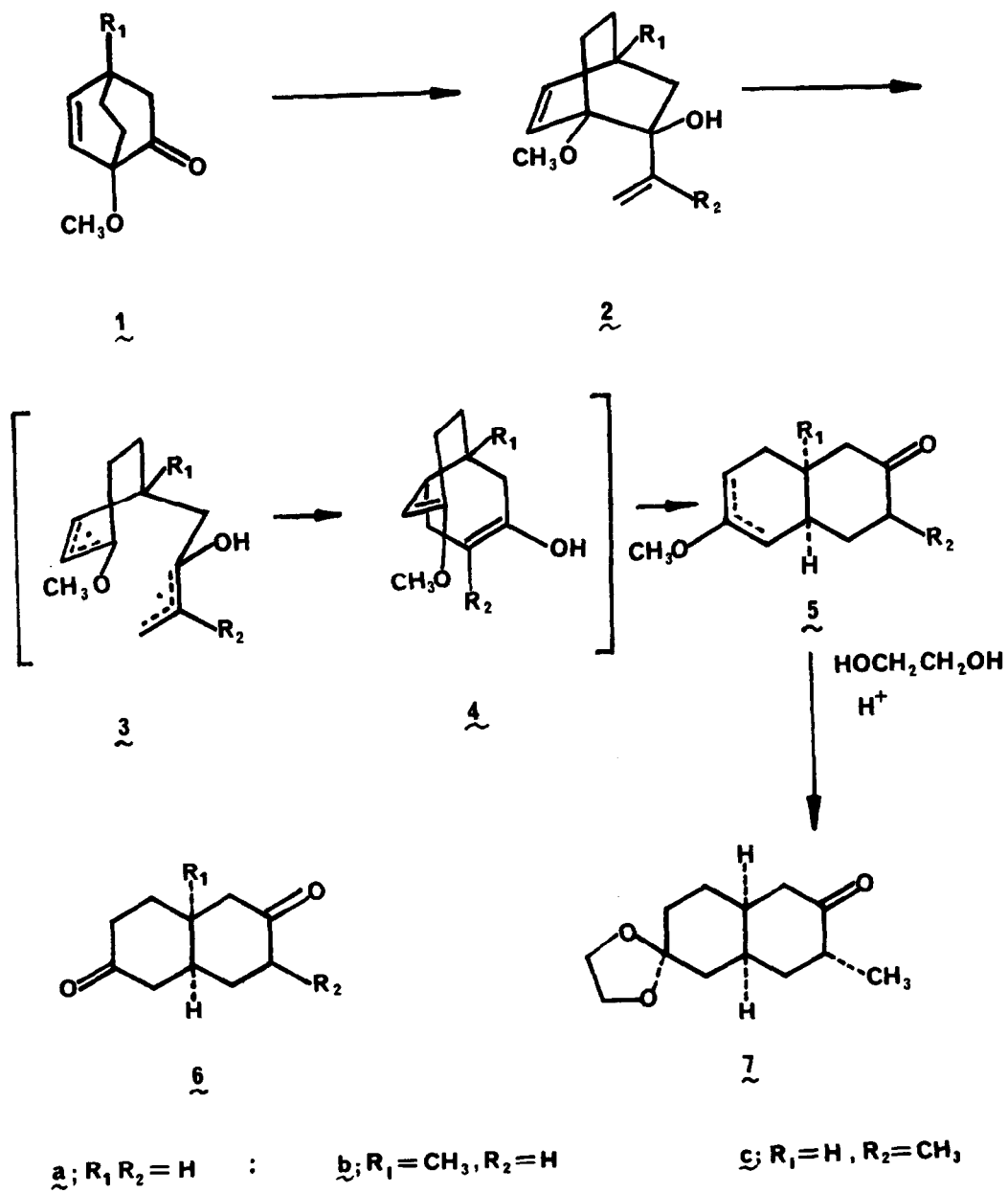
There are currently available in the literature a number of different approaches to the synthesis of oxygenated cis-fused decalin ring systems. Two frequently used routes involve either hydrogenation¹ or the addition of organocuprates to $\Delta^{1(9)}$ -2-octalone derivatives.² An equally versatile and widely used concept which provides cis-decalin carbocycles having an array of functionality not readily obtainable by the aforementioned routes has involved the use of the Diels-Alder reaction between substituted dienes and either quinones³ or cyclohexenone derivatives.⁴

As a result of our need for an efficient stereoselective synthesis of the cis-fused ketal ketone 7 which did not appear to be readily obtainable by any of the previously discussed routes, we have investigated the viability of the approach⁵ outlined in Scheme I as a solution to our problem. At the outset the convergent nature of this ring synthesis with its inherent flexibility had attracted our attention. Contingent upon the success of this approach are both the availability of bicyclooctenones 1⁶ and the high-yield requirement in the oxy-Cope step (2 \rightarrow 5). As delineated in this and the preceding communication,⁶ both of these criteria have been met.

In analogy with earlier work,^{5a} we have found that vinylmagnesium bromide and isopropylmagnesium bromide add to ketone 1 (R=H) to give 2:1 and 3:1 ratios of allylic alcohols respectively in which the desired endo adducts 2a and 2c constitute the major isomers in the mixture.^{7,8}

As summarized in Table I, the liquid-phase pyrolyses of alcohols 2a-c proceed cleanly to the 2-decalone enol ethers 5a-c which were obtained as mixtures of double bond isomers. For purposes of characterization the enol ethers were transformed in aqueous acid to the crystalline diketones 6a-c.⁹ For further synthetic structural changes requiring stabilization of one of the cis-decalin conformations the enol ether at C-6 in 5 may be selectively transformed into the corresponding C-6 ketal function (Scheme I). Thus, rearrangement of 2c for 4 hr at 250° followed by treatment of the crude oxy-Cope product 5c with 5 equiv of ethylene glycol in dry

SCHEME I

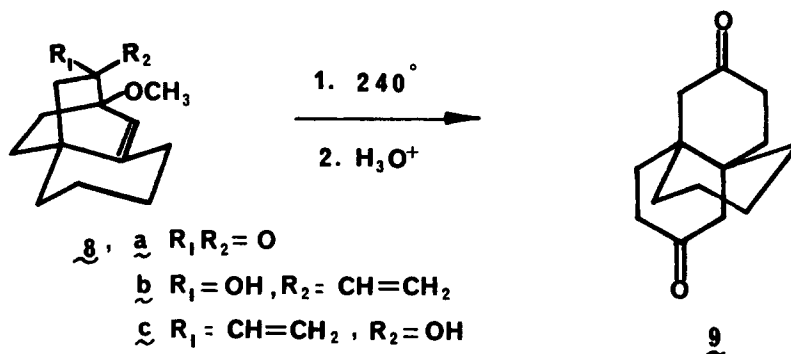


THF in the presence of a catalytic amount of *p*-toluenesulfonic acid resulted in a 70% overall yield of the monoketal 7, mp 117-118°. ⁸ The success of this transesterification step was surprising in that under the conditions of this reaction ketal exchange could be completely suppressed.

Table I - *cis*-Decalin-2,6-dione (9) Synthesis ⁸

Alcohol <u>2</u>	Conditions ^a	Yield, % ^b <u>6a-2c</u>	Mp. °C,
<u>2a</u>	195°, 26 hr	74	69-70
<u>2b</u>	195°, 26 hr	78	74-76
<u>2c</u>	250°, 4 hr	75	56-68 ^c

^a, Rearrangements were carried out in sealed ampoules on the neat alcohol; ^b, yields reported on chromatographed material; ^c, epimeric mixture at C-3.



In a structurally related system we have studied the thermal rearrangement of alcohols 8b and 8c, ⁸ readily synthesized from the known ketone 8a. ¹⁰ In contrast to the characteristically clean pyrolyses observed in our previous systems, rearrangement of 8b at 240° for 2 hr resulted in several products which, on aqueous acid treatment, afforded the crystalline diketone 9, mp 180-181° in 27% yield after column chromatography. ⁸ In keeping with the proposed intermediacy of diradicals in these oxy-Cope processes, ^{5b} we have found that both 8b and 8c and the corresponding trimethylsilyl ethers rearrange at comparable rates. However, less than two percent of 9 was observed in the pyrolysis of 8c. This route to the [4.4.4]propellane ring system is noteworthy in its brevity. It is unfortunate that the yield in the pyrolysis step is not greater. One factor contributing to the decreased yield in the oxy-Cope step could be due to the increased steric congestion as a result of alkyl substitution at the 1-5 diene terminus. In

this regard the results of Viola and coworkers clearly demonstrate that both the steric and electronic effects of methyl substitution on the diene terminus play a substantial role in suppressing the oxy-Cope pathway in aliphatic systems.¹¹ At this time it is not clear whether the results obtained on the pyrolysis of **8b** can be generalized to the point where C-5 substitution in other bicyclo[2.2.2]octene derivatives will also result in lower yields during the oxy-Cope step.

With the exception indicated, this ring synthesis offers a flexible, stereoselective route to a variety of oxygenated cis-decalin carbocycles. The application of this chemistry to natural products synthesis is currently in progress.

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