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Bridged Spiropentanes: Ring Expansion

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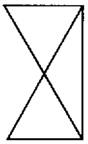
Abstract: Diazomethane ring expansion of tricyclo[4.1.0.0^{1,3}]heptan-4-one provides a convenient route to three carbon-bridged spiropentanes. The relative rates of reaction and the migratory preferences of cyclopropyl vs methylene were examined for several cyclopropyl alkyl ketones, and were correlated with the results of HF/6-31G* MO calculations.

We have been interested in examining the structures and reactions of the series of bridged spiropentanes, **1**-**4**.[1] We have recently reported the preparation of **1**, but its high thermal reactivity precludes a detailed examination of its reactions.[2] It is relatively easy to obtain **3** and its derivatives via the internal carbene ring closure developed by Skattebøl.[3] However, no derivative of **2** has been reported, and there has only been one report of the formation of **4**.[4] The ready availability of **3** and its derivatives made it desirable to see if compounds related to **2** and **4** might be prepared from it.



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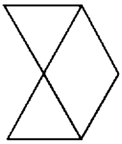

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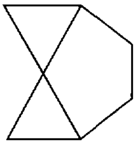

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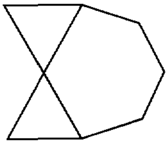
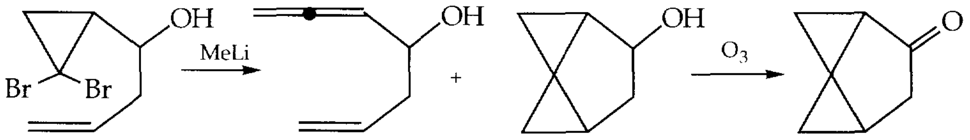


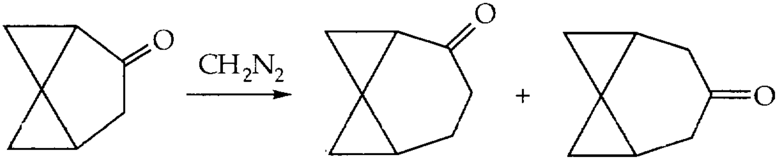
4

The ketone **5** has previously been reported,[5] and we have improved the procedure by finding that the hydroxy group in **6** need not be protected before the carbene ring closure, and that the alcohol **7** is oxidized to **5** along with the destruction of the allene by-product when the reaction mixture is treated with ozone. The conversion of **7** to **5** proceeded with a 6% overall yield.



6 **7** **5**

Treatment of **5** with diazomethane led to ring expansion giving mainly one ketone. The ring expansion could have occurred in two ways, giving either **8** or **9**. The latter has the higher symmetry and would give only 5 signals in the ^{13}C nmr spectrum. The observed spectrum of the major product had 8 different chemical shifts (δ = 13.0, 17.1, 18.6, 22.7, 23.2, 30.6, 38.5, 212.4) and therefore corresponds to **8**. The IR carbonyl band was at 1700 cm^{-1}, whereas that of **5** was at 1721 cm^{-1}. A small amount (~5%) of **9** also was found, with ^{13}C chemical shifts δ = 11.5, 14.3, 15.8, 41.1, 214.9, and a carbonyl band at 1715 cm^{-1}.

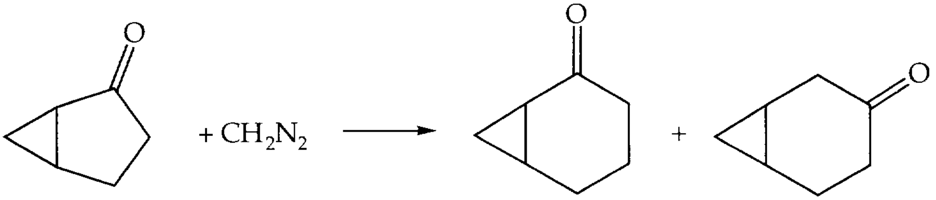


5 **8** **9**

20:1

There were two interesting aspects to the reaction. First, why was **8** formed in preference to **9**? Second, why does the reaction proceed rapidly in ether solution at room temperature whereas most ketones react relatively slowly, and often require catalysis by methanol or other reagents?[6]

In trying to answer the first question, it was necessary to establish the relative migratory preference of a cyclopropyl group vs a methylene group in a relatively unstrained molecule. Therefore the following compounds were examined:



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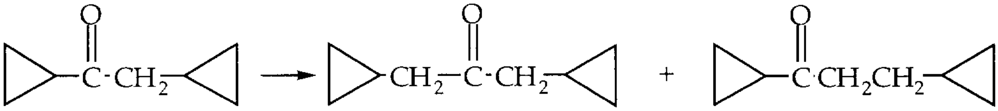
3:1



10

2:1

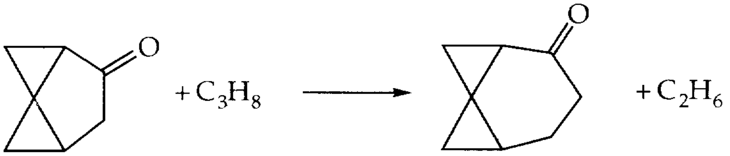
In each case, the products were identified by comparison with authentic samples. It can be seen that in the open chain case, cyclopropane migrates in preference to methylene, whereas in the bicyclic and tricyclic cases, methylene migrates in preference to cyclopropyl. Since the migratory preference is quite small in the open chain case, the change in preference with the cyclic ketones might be due to a difference in the energies of the two possible product ketones. This possibility was examined by calculating the energies of **8** and **9** at the RHF/6-31G* theoretical level.[7] Here, **8** was calculated to have a 1.2 kcal/mol lower energy than **9**, which could lead to an 8:1 preference for the formation of **8**. Thus, much of the preference for **8** may simply result from the difference in energy between the two product ketone. The small difference in migratory aptitude between alkyl and cyclopropyl has also been seen in Baeyer-Villiger oxidations.[8] However, in the pinacol rearrangement, cyclopropyl has a considerably higher migratory aptitude than alkyl.[9]

The relative reactivities of the ketones toward diazomethane was determined by competition reactions. A mixture of two ketones in ether/methanol was treated with diazomethane, and samples were withdrawn and analyzed by gc at different times. The ratio of products was extrapolated to zero time, and this ratio divided by the ratio of the reactant ketones gave the relative reactivities shown in Table I. The high reactivity of **5** is striking. What is its origin?

Table I Relative reactivities of ketone

Compound	krel
10	1
11	3.5
5	275

Again, it is possible that the reactivity is controlled by strain relief. This hypothesis could be tested by calculating the energy of the following reaction:



At the HF/6-31G* theoretical level, the reaction was calculated to be exothermic by -13 kcal/mol. This is clearly sufficient strain relief to account for a rapid reaction.

The ring expansion reaction provides for the first time a convenient route to compounds related to **4**, and will allow their reactions to be examined. Investigations of the thermal and protolytic reactions of **4**, and of the solvolysis of the alcohols derived from both **5** and **8** are in progress and will be reported subsequently.

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