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INTRAMOLECULAR CYCLIZATIONS OF ORGANOMETALLIC COMPOUNDS. I. THE THERMAL REARRANGEMENT OF 4-LITHIO-1,7-OCTADIENE

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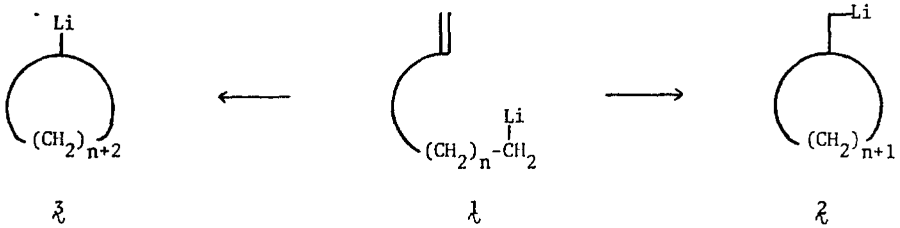
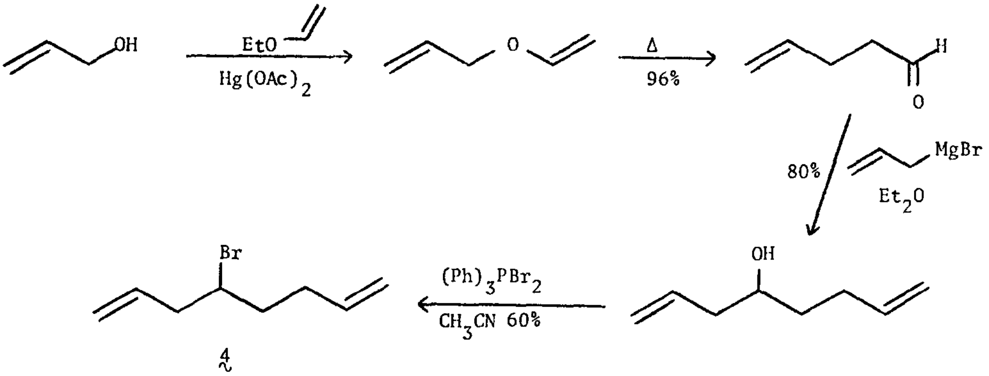
Any reaction that results in ring formation can be of considerable potential use in organic synthesis. It has been recognized for several years that a carbon-carbon double bond can experience insertion into a carbon-lithium bond resulting in the formation of a new carbon carbon σ linkage.[1] If the double bond were incorporated in the lithium reagent (1), such an intramolecular reaction would result in ring formation.[2] In those systems which have been studied, structural type 2 is formed with few exceptions.[3] This communication reports on the thermal rearrangement of 4-lithio-1,7-octadiene which is mechanistically interpreted in terms of reaction 1 $\rightleftarrows$ 2.

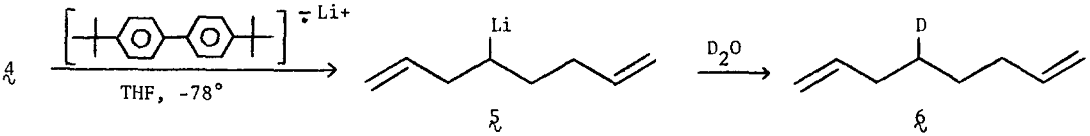


Scheme I

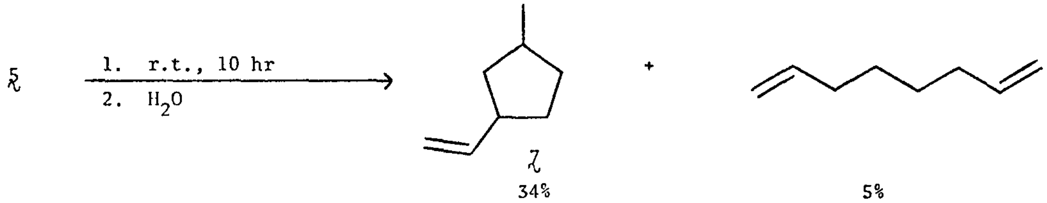


The straightforward preparation of 4-bromo-1,7-octadiene (4) is given in Scheme I. Bromodiene 4 exhibited the following nmr spectrum: $\delta_{\mathrm{TMS}}^{\mathrm{CCl}}$ 5.55-6.07 (2H,m), 4.90-5.30 (4H,m), 3.96 (1H, quintet) and 1.73-2.80 (6H,m).

Conventional methods of preparing organolithium reagents from the halide and lithium metal did not prove very successful in the case of compound **4**. Preparation of 4-lithio-1,7-octadiene was accomplished by adding the bromide to an excess of lithium *p p'*-di-*t*-butylbiphenyl in THF at -78°C.[4] Preparation of the lithium reagent in this fashion ensured that subsequent cyclization at higher temperature reflected the behavior of the lithium reagent and not a radical intermediate formed in the process of preparing the lithium reagent.[5] Quenching the reaction at low temperature with water relinquished 1,7-octadiene in 71% yield based on **4**. When deuterium oxide was employed in the quench the 1,7-octadiene was monodeuterated (90 ± 2%) at the most interior methylene position (**6**) as readily determined by nmr spectroscopy.[6]

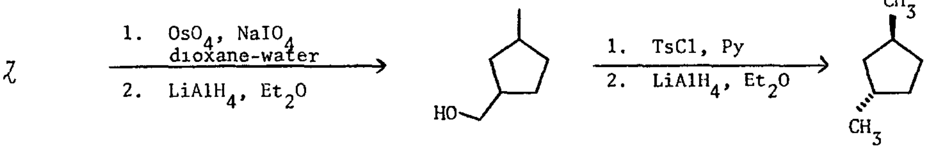


As the solution containing **5** warmed to room temperature rearrangement took place producing 1-methyl-3-vinylcyclopentane (**7**) after water quench. A small amount of 1,7-octadiene was also isolated. The percentage yields are based on starting bromide **4**.



An attempt was made to determine the stereochemistry of **7** by conversion into 1,3-dimethylcyclopentane as shown in Scheme II. The product that was isolated displayed an nmr spectrum nearly identical to that of authentic *trans*-1,3-dimethylcyclopentane. However, the authentic samples of *cis* and *trans* isomers proved resistant to resolution using the gas chromatography at our disposal, and the degradation product may have contained up to 15% *cis* isomer. The contention that **7** is mainly one isomer is supported by a clean methyl doublet (J = 6.5) observed at 0.97δ in its nmr spectrum.[7,8]

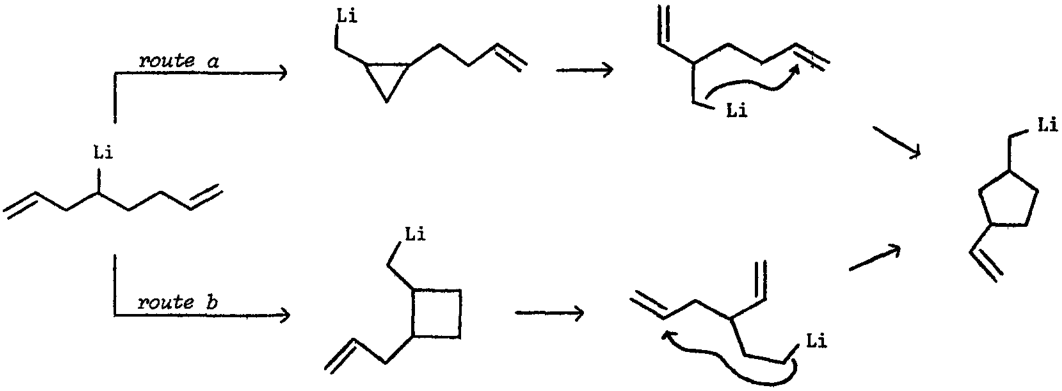
Scheme II



Alkene **7** could be formed by two distinct pathways involving insertion of a double bond intc a carbon-lithium bond as delineated in Scheme III. The experiment capable of differentiating *route a* from *route b* would also reveal the preferred closure to form a 3- or 4-membered ring. Both of these closures are reversible processes which thermodynamically favor the open form.

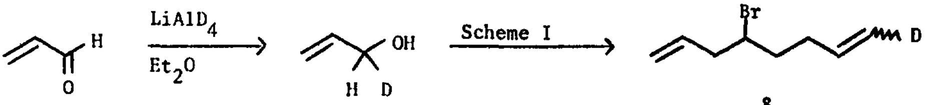
Route a and *route b* can be differentiated by deuterium labelling. Scheme IV follows the

Scheme III



path of a deuterium label using the synthetic approach previously found successful in the preparation of 4. Subjection of the lithium reagent prepared from 8 to reaction conditions liberated compound 9 with deuterium residing exclusively at the methyl position *(route a)* and not at the vinyl position *(route b)* as readily determined from its nmr spectrum. This evidence strongly supports *route a* and a more facile formation of the 3-membered ring.

Scheme IV



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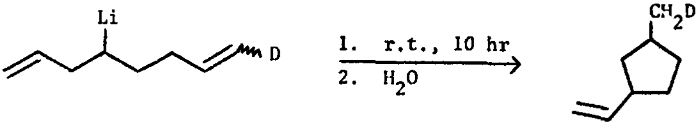

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The behavior of 5-lithio-1,9-decadiene has also been studied in our laboratory. It has been found that cyclization to form the 5-membered ring occurs readily even at -78°C in THF solution.[9] It would appear, therefore, that the relative rates of cyclization to form various sized rings follow the order 5>3>4 when all other factors, such as substitution patterns, are equal.

Acknowledgments

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References

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2. (a) J. St. Denis, T. Dolzine and J. P. Oliver, *J. Amer. Chem. Soc.*, 94, 8260 (1972); (b) P. T. Lansbury and F. J. Caridi, *Chem. Commun.*, 714 (1970); (c) V. N. Drozd, Yu a Ustynyjuk, M. A. Tsel'eva and L. B. Bmitriev, *Zh. Obshch. Khim.*, 38, 2114 (1968); (d) E. A. Hill, H. G. Richey, Jr., and T. C. Rees, *J. Org. Chem.*, 28, 2161 (1963); (e) P. T. Lansbury, V. A. Pattison, W. A. Clement, and J. D. Sidler, *J. Amer. Chem. Soc.*, 86, 2247 (1965).
3. A possible exception involving a strained double bond is found in a paper by Wittig: G. Wittig and J. Otten, *Tetrahedron Lett.*, 601 (1963).
4. This procedure follows work originally performed by L. L. Hutchinson at Oregon State University. For a similar reaction using lithium naphthalene see: C. G. Screttas, *J. Chem. Soc. Chem. Comm.*, 752 (1972).
5. M. Julia, *Accounts of Chem. Res.*, 4, 386 (1971).
6. The nmr spectrum of 1,7-octadiene displayed vinyl, allylic methylene, and interior methylene regions. All of the regions were completely resolved on the nmr which made location of the deuterium an easy matter.
7. The methyl doublet of *cis*-1,3-dimethylcyclopentane falls at 0.95δ, and of *trans*-1,3-dimethylcyclopentane at 0.93δ in CCl_4 solution. In a 50-50 mixture the two sets of doublets are readily discernible.
8. Acceptable elemental analyses were obtained for 1,7-octadien-4-ol, **4**, and **7**.
9. More detailed results on this and related systems will be published at a later date.