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FACILE INTRAMOLECULAR CYCLIZATION OF AN OLEFINIC GRIGNARD REAGENT (1)

Herman G. Richey, Jr., (3) and Thomas C. Rees
Department of Chemistry
The Pennsylvania State University
University Park, Pennsylvania 16802

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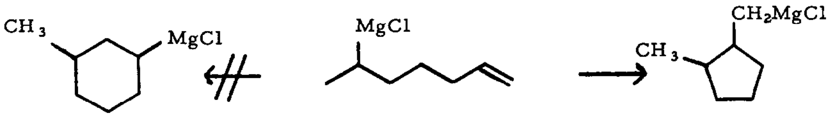
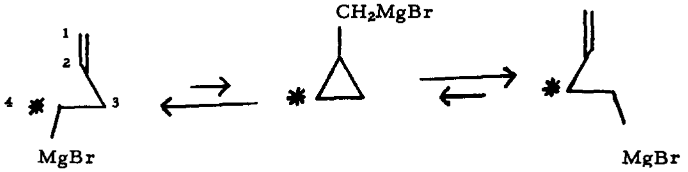
Intramolecular addition of a Grignard reagent to an unconjugated carbon-carbon double bond to form a cyclic product occurs readily in a system that we have studied. A tetrahydrofuran solution of 6-chloro-1-heptene (4) was refluxed with magnesium for 5 hours. The product obtained in 88% yield from hydrolysis of the solution consisted mostly of _cis_- and _trans_-1,2-dimethylcyclopentane (5) in a ratio of about 1:4. This reaction presumably proceeds by cyclization of Grignard reagent I to form _cis_ and _trans_ II. This ready cyclization suggests that formation of rings from intramolecular Grignard additions to carbon-carbon multiple bonds will be feasible in a variety of other systems.



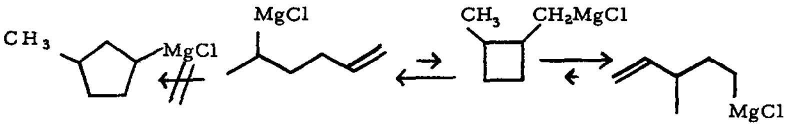
III I II

The mild conditions needed for this cyclization are surprising since intermolecular additions of Grignard reagents to unconjugated carbon-carbon double bonds are unknown (6). However, the cyclization of I to II must be related to some known rearrangements (7). For example, cyclic Grignard reagent V is presumably an intermediate in the equilibration of



IV V VI

labeled IV and VI studied by Roberts and his coworkers (8), though reactions of the equilibrium mixture do not furnish detectable amounts of cyclic products (9). The isomerization of VII to IX that we found to

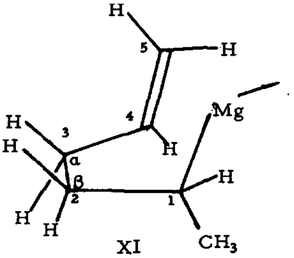


X VII VIII IX

occur under much more stringent conditions (rate≃ 3 x 10^{-6} $\sec^{-1}$ at 110° in tetrahydrofuran) must also be due to a cyclization followed by ring opening (10). The cyclic isomer (VIII) is less stable than IX and cyclic products are not observed.

Formation of small rings instead of less strained larger rings is a striking feature of the cyclizations of I and VII. It might have been expected that the difference in ring strain between VIII and X of ~20 kcal/mole (11) and between II and III of about 7 kcal/mole (11) would be reflected in relative energies of transition states for cyclization that would greatly favor formation of the larger rings. Cyclization to form the smaller rings might be favored to the extent that the energies of the transition states reflect the greater stability of primary than of secondary Grignard reagents. However, a recent study (12) indicates that this difference should not exceed a few kcal/mole.

Therefore, some additional factor, perhaps the necessity of achieving a particular geometry in the transition state for cyclization, must favor formation of the smaller rings. For example, the results can be rationalized by assuming that the addition to a double bond is a concerted process (13) that involves formation of a C-Mg bond at the same time that the new C-C bond is being formed. Structure XI shows a conformational isomer of VII, free of angle strain, that should approximate the geometry of a concerted transition state for formation of VIII if angles α and β are decreased. It is much more difficult to achieve the geometry



XI

requisite for a concerted addition of C-1 to C-5 and of Mg to C-4 that would lead to X. Though the significance of this factor in favoring formation of smaller rings should decrease as chain length increases, it may be responsible for the formation of II instead of III. Alternatively, the ring sizes obtained may be due to a stringent requirement for approach of C-1 along the axis of a p-orbital even though a new C-Mg bond is not forming simultaneously (14). In system XI, for example, it may be easier to achieve such approach to C-4 than to C-5.

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REFERENCES

1. The work described in this communication is taken from ref. 2.
2. T. C. Rees, Ph. D. Thesis, The Pennsylvania State University, March, 1966.
3. Alfred P. Sloan Foundation Research Fellow.
4. A satisfactory elemental analysis and the expected nmr and infrared spectra were obtained for this new compound.
5. These compounds were identified by comparison of their infrared spectra, nmr spectra, and glc retention times with those of authentic samples. Small amounts of 1-heptene and of two unidentified compounds were the only other products detected.

6. Possible exceptions have been reported recently [J. J. Eisch and G. R. Husk, *J. Am. Chem. Soc.*, **87**, 4194 (1965); M. Chérest, H. Felkin, C. Frajerman, C. Lion, G. Roussi, and G. Swierczewski, *Tetrahedron Letters*, 875 (1966)]. However, these additions may be intramolecular mechanistically; since each olefin involved contains a hydroxyl group, it is possible for RMg- to become attached to the olefin by means of the oxygen before addition to the double bond occurs.

7. R. E. Dessy has kindly informed us of a publication in press [S. A. Kandil and R. E. Dessy, *J. Am. Chem. Soc.*, **88**, 0000 (1966)] that describes an intramolecular Grignard addition to a carbon-carbon triple bond.

8. This work is reviewed in D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N.Y., 1965, Chapter 6.

9. Cyclic products are obtained if a vinyl or two phenyl substituents are placed at C-1 (8).

10. A preliminary report has appeared [E. A. Hill, H. G. Richey, Jr., and T. C. Rees, *J. Org. Chem*, **28**, 2161 (1963)]. A detailed study (2) has shown that this rearrangement is nearly quantitative.

11. E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1965, Chapter 4.

12. R. E. Dessy, W. Kitching, T. Psarras, R. Salinger, A. Chen, and T. Chivers, *J. Am. Chem. Soc.*, **88**, 460 (1966).

13. E. A. Hill and J. A. Davidson, *ibid.*, **86**, 4663 (1964).

14. The organolithium and organosodium compounds corresponding to VII apparently also cyclize to form four- rather than five-membered rings (2).