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INTRAMOLECULAR CYCLIZATIONS OF ACETYLENIC GRIGNARD REAGENTS

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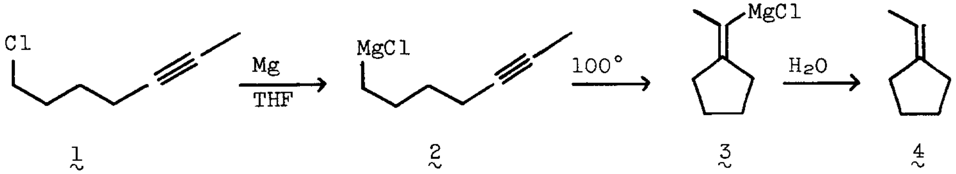
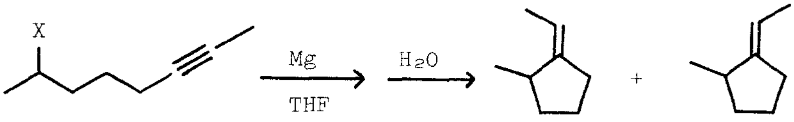
Intramolecular additions of Grignard reagents to unconjugated carbon-carbon triple bonds in aliphatic systems are mechanistically interesting and produce synthetically useful vinyl Grignard reagents. These reactions are an extension to alkynes of previously reported intramolecular additions of Grignard reagents to alkenes (2). Cyclization of an acetylenic Grignard reagent has been reported previously only for a system in which the triple bond is activated by a phenyl substituent and the configurational possibilities are few compared to those of the aliphatic reagents studied here (7).

Hydrolysis of a tetrahydrofuran solution of Grignard reagent prepared from 7-chloro-2-heptyne (1) and heated for 6 days at 100° furnished ethylidenecyclopentane (4) in ~90% yield. In contrast, hydrolysis immediately after preparation of the Grignard reagent in refluxing tetrahydrofuran furnished only a few percent of 4, the remainder of the product being 2-heptyne. Therefore, cyclization occurred after formation of the Grignard reagent. The relative amounts of 2-heptyne and 4 in aliquots removed at different times indicated that $t_{\frac{1}{2}}$ of the



cyclization was ∼50 hours at 100°. The formation of 4 is explained readily by assuming that 2 cyclizes to 3. The product, 1-methylcyclohexene, that would have resulted from cyclization to the other end of the triple bond was not observed, though as little as 1% would have been detected.

Similar experiments with 7-chloro- and 7-bromo-2-octyne (5) furnished a mixture of 6 and 7 in good yield. The cyclization of the Grignard reagent prepared from the bromide had $t_{\frac{1}{2}}$ of ∼15 hours at 100°.



5 6 7

The formation of ethylidenecyclopentanes in preference to more stable methylcyclohexenes in in accord with observations (2) that intramolecular Grignard additions to 3,4-, 4,5-, and 5,6-double bonds also form the smaller of the two possible rings (8). The mechanisms of Grignard cyclizations will not be discussed until a later publication. However, these observations can be rationalized by assuming that the addition is a concerted process that involves formation of a C-Mg bond at the same time that the new C-C bond is being formed (5). However, an assumption that bond formation in these reactions involves preferential approach of the reactive carbon along the axis of an atomic p-orbital at a carbon of the double or triple bond provides an alternative rationalization (5); examination of models suggests that such approach to the nearer carbon of 3,4-, 4,5-, and 5,6- and perhaps even 6,7-double and triple bonds may be less strained than approach to the more distant carbon. A requirement for this approach in radical cyclizations would rationalize such observations as the more rapid cyclization of the 5-hexen-1-yl radical to the cyclopentylmethyl than to the more stable cyclohexyl radical (9). In similar cyclizations that involve carbonium ions, however, formation of the larger of two possible rings is sometimes noted, at least when substituents are favorably placed (10). Transition states for carbonium ion cyclizations may have geometries qualitatively different from those for carbanion or radical cyclizations. The transition state for a carbonium ion cyclization is predicted to gain stabilization by a bonding (and therefore approach) of the reactive carbon to both carbons of the double or triple bond (11). However, in carbanion or radical cyclizations, bonding to both carbons of the double or triple bond is predicted to be unfavorable (13) and cyclization may involve approach specifically to only one of the carbons.

The more rapid cyclization of secondary than primary Grignard reagents was noted also with olefinic Grignard reagents. Comparisons of the rates of the acetylenic cyclizations to those of related olefinic cyclizations and the significance of these kinetic observations will be discussed in a fuller publication.

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