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π-ROUTE TO AZABICYCLICS III. THE SOLVOLYSIS OF PROTONATED N-CHLORAMINES[1]

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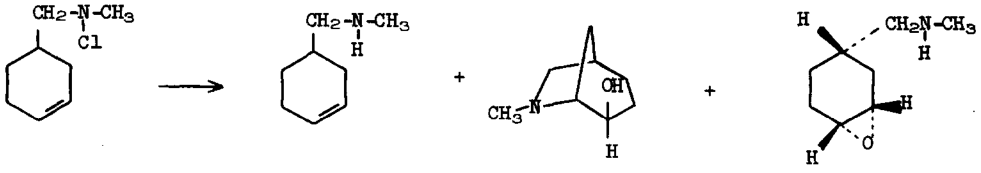
Recently, we demonstrated that nitrenium ions generated solvolytically from N-chloramines add intramolecularly to available double bonds to produce substituted azabicyclics.[1,2] As part of our overall interest in the chemistry of N-chloramines in general and in their use in the synthesis of nitrogen containing polycyclics in particular, we have now studied the solvolytic behavior of protonated N-chloramines in aqueous acid. We wish to report that the solvolysis of 1 in 1 M sulfuric acid or 1 M phosphoric acid differs considerably from the solvolysis of 1 in aqueous tetrahydrofuran.[1] Similarly, the solvolysis of 2, which gave 3 as the only major product in methanol, gave good yields of a bicyclic product when ionized in 1 M sulfuric acid.

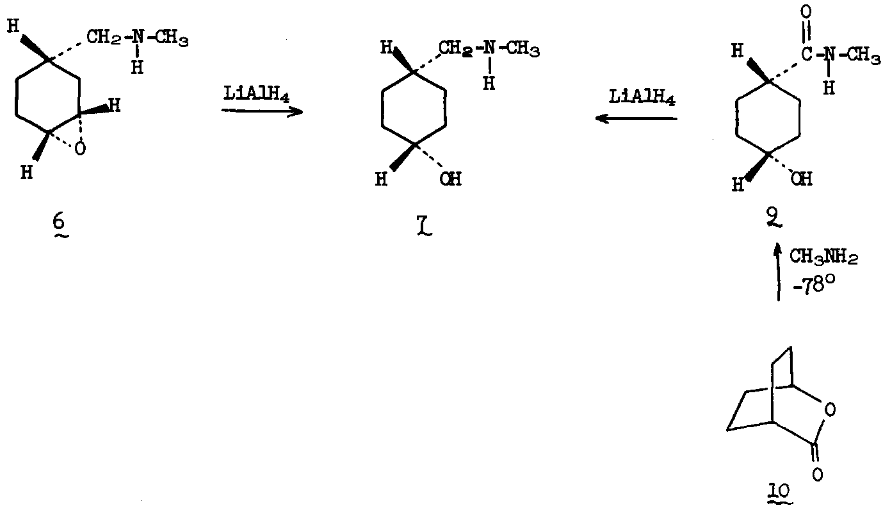
When 1 was refluxed in either 1 M sulfuric acid or 1 M phosphoric acid we obtained a mixture of 4, 5, and 6, which were present in the ratio of 1:13:8, respectively. The starting amine 4 and the bicyclic alcohol, 5, were readily identified by comparison with authentic samples.[1] The epoxide, 6, was extremely unstable and decomposed extensively during both



1 4 5 6

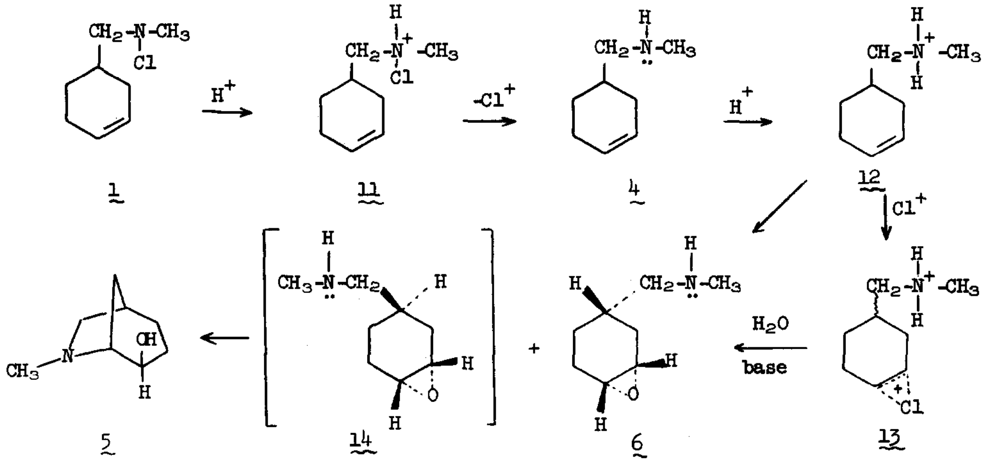
vapor phase chromatography and column chromatography. However, very rapid chromatography on basic alumina gave a sample of 6 which was 90% pure. The infrared spectrum of 6 showed an

N-H stretching vibration, but no hydroxyl absorption. The mass spectrum of 6 had a parent peak at m/e 141 indicating that 6 was isomeric with 5. Lithium aluminum hydride reduction of 6 gave 7 which was independently synthesized *via* the hydride reduction of 9. The amide,



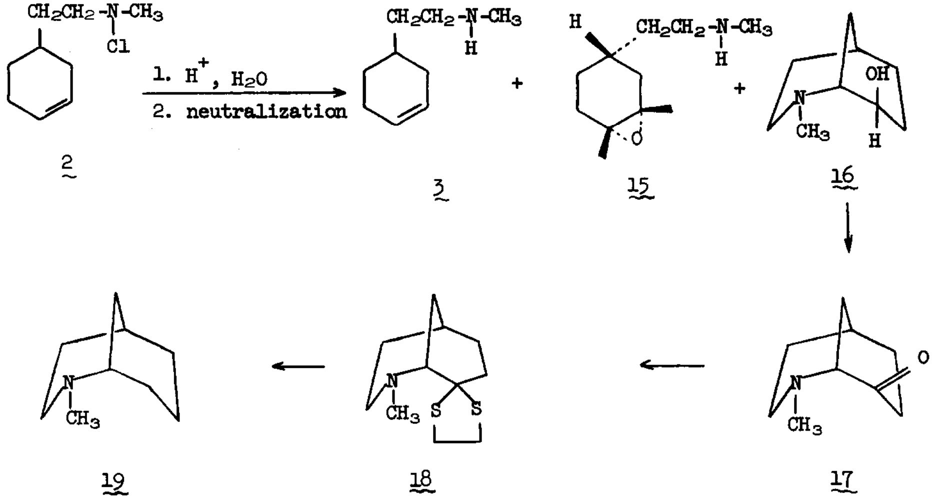
9, was readily prepared through the reaction of 10 with methylamine at -78°.

The formation of 5 and 6 in the acid catalyzed solvolysis of 1 indicated that the mechanism of solvolysis of 1 in the presence of strong acid was very different from that in methanol or tetrahydrofuran-water. We suggest that 1 is protonated to give 11 which ionizes to give 4 and positive chlorine. Protonation of 4 followed by addition of the chloronium ion to the double bond would produce 13 *via* 12. Addition of water to 13 followed by epoxide



formation during the neutralization of the acidic reaction mixture would give 6 and 14. Intramolecular opening of the epoxide ring of 14 would yield 5. In order to demonstrate the plausibility of this mechanistic rationale, 12 was treated with trifluoroperacetic acid. This epoxidation gave a mixture of 5 and 6. No trace of 14 could be detected.

As noted above, the solvolysis of 2 in methanol was unsatisfactory for the synthesis of azabicyclics. However, when 2 was solvolyzed in 1 M sulfuric acid, vpc analysis indicated a 1:2:4 mixture of 3, 15, and 16, respectively. The identity of 3 was established by comparison with the authentic sample which served as the precursor of 2. The epoxide 15 was similar in stability to 6. It could not be obtained pure in our hands. The infrared and nmr spectra of 15 were very similar to those of 6. The mass spectrum of 15 showed a parent ion at m/e 155 indicating that 15 was isomeric with 16.



The structure proof of 16, which was obtained in 37% yield after rigorous purification, was based on the conversion of 16 to 19. Oxidation of the hydrochloride of 16 with Jones' reagent gave 17, which was converted to the thioketal 18. Raney nickel reduction of 18 gave 19 which was identical in all respects to an authentic sample of 19.[3]

The results discussed above demonstrate the dramatic effect which the presence of strong acid can have on the solvolytic behavior of N-chloramines. The acid-catalyzed π-route to azabicyclics outlined in this communication indicates that the solvolysis of suitable N-chloramines in acidic media may be the preferred method of synthesis for a variety of substituted azabicyclics.

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References

1. Paper XIV in a series on The Chemistry of Nitrenium Ions. For the previous paper in this series see the preceeding communication.
2. P. G. Gassman, F. Hoyda, and J. Dygos, J. Am. Chem. Soc., **90**, 2716 (1968).
3. An authentic sample of **19** was prepared *via* a six step synthetic sequence starting with *m*-nitrophenylacetic acid. The details of this synthesis will be presented in a full paper on this subject.