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ACID-CATALYZED THERMOLYSIS OF DICYCLOPROPYL KETIMINES. SUBSTITUENT EFFECTS ON THE COURSE OF THE REARRANGEMENT

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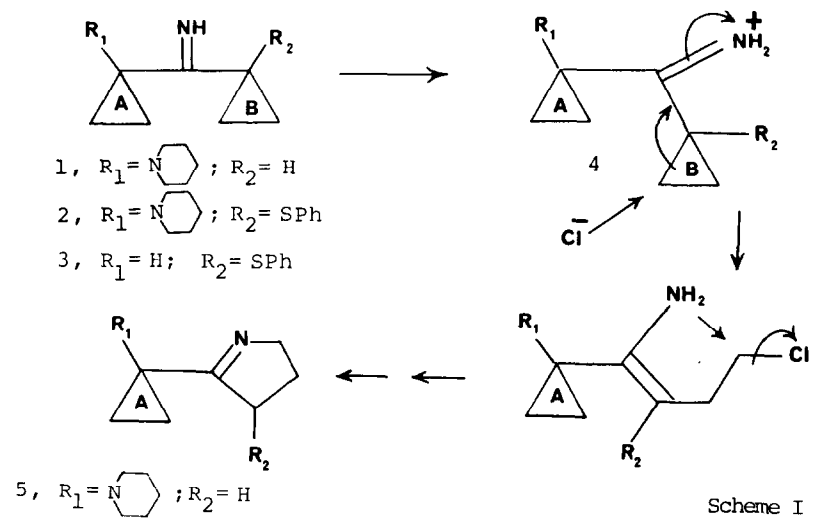
Summary: On thermolysis with ammonium halides, dicyclopropyl ketimines yield cyclopropyl pyrrolines resulting from S_N2 ring-opening by the nucleophilic halide. In the absence of a nucleophilic counterion, the acid-catalyzed thermolyses lead to pyrroles if there can be stabilization of cationic intermediates by an electron-releasing substituent.

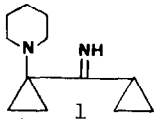
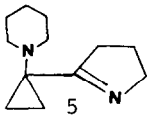
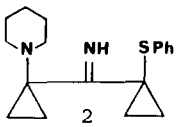
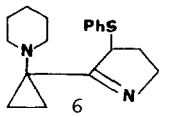
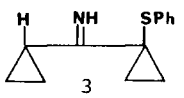
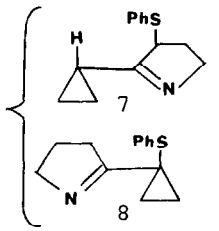
In a recent communication[1] we reported that the dicyclopropyl-ketimine (1) undergoes rearrangement on heating with ammonium chloride to form the pyrroline (5) (Scheme I). We have now carried out further studies on this acid-catalyzed thermolysis in which we have examined the effects of substituents in determining the preferred opening (A vs. B) of the cyclopropyl rings in the presence of both nucleophilic and non-nucleophilic counterions.



Scheme I

Table I summarizes the results obtained with ammonium chloride. The thermolyses were all carried out in refluxing xylene at 140° for 1.5-5 hr. No reaction took place in the absence of NH_4Cl (or other acid) as shown by the recovery of the starting ketimine from reaction vessels which were previously washed with base.

Table I

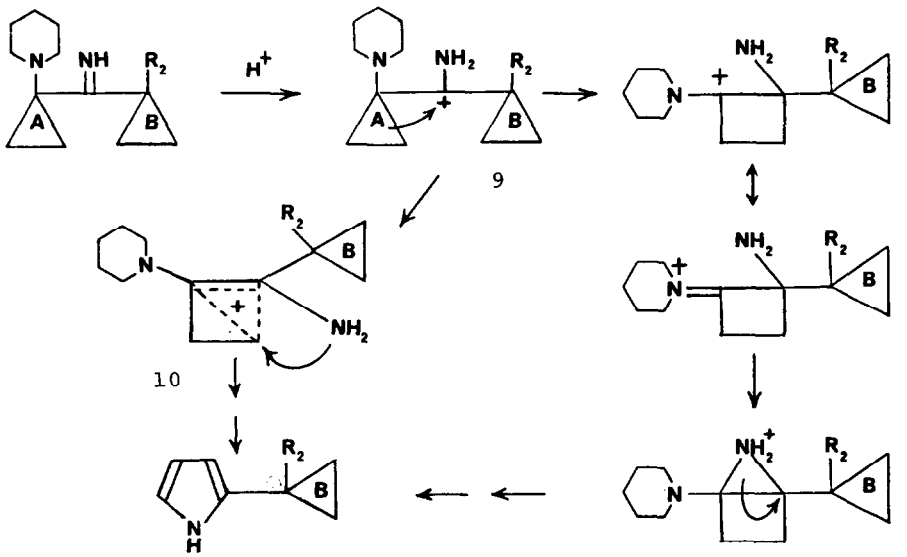
dicyclopropylketimine[2]	pyrroline	yield,%[6]
 1	 5	78
 2	 6	69
 3	 7	28
	8	22

The findings in Table I are in accord with the mechanism proposed earlier[7] by Stevens for related rearrangements of monocyclopropyl ketimines.[7,8,9] Thus, attack of halide ion on the protonated ketimine derived from 1 appears to take place *via* 4 at the less-substituted cyclopropane ring (B) leading, through intermediate 4, to pyrroline (5) as shown. In the case of 2, containing a thiophenyl group, attack on ring (B) (yielding 6) is again favored, most probably by the participation of the sulfur atom in stabilizing the negative charge developing in the transition state. With substrate (3), it might be expected that the combination of steric and electronic factors operating at stage (4) would yield a mixture of products, (7) and (8) as is, in fact, observed.

A completely different result was obtained when the dicyclopropyl ketimines were subjected to acid-catalyzed thermolysis in the presence of a non-nucleophilic counterion. On heating 1 and 2 in xylene with the dimethyl ether complex of fluoroboric acid, both substrates underwent rearrangement to pyrrole derivatives (12) (32%) and (13) (42%).[10] In these instances, the only products isolated[11] resulted from ring-opening of cyclopropyl ring (A) (containing the electron-releasing piperidino group). These findings are in disagreement with previous reports in which it is proposed that a cyclopropyl ketimine rearrangement does not occur in the presence of an acid with a non-nucleophilic counterion.[7,8] One may now conclude that, even without the attack of a nucleophile, cyclopropyl ketimines undergo acid-catalyzed rearrangement if there can be sufficient

stabilization of the positive charge formed during the ring-opening process.

Formation of the pyrrole derivative by expansion of ring (A) may occur by initial protonation of the imine to form the bis-cyclopropyl carbinyl cation (9).[12] Ring-expansion of 9 to a 5-membered ring could then take place either through the bridged ion (10) or the bicyclic intermediate (11).[13] Scheme II outlines two possible pathways for this transformation.[13,14,15]



Scheme II

The application of this rearrangement to the synthesis of α-substituted pyrroles is under investigation. We are also exploring the mechanism of the ring-expansion.

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REFERENCES AND NOTES

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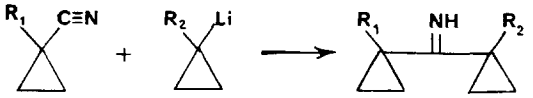
2. The dicyclopropyl ketimines were prepared as previously described by reaction of the cyclopropyl nitrile component[1,3,4] with the cyclopropyllithium derivative[5] in ether at -78°.



3. H. Dressler and J.E. Graham, J. Org. Chem., 32, 985 (1967).

4. M. Makosza, E. Bialecka and M. Ludwiko, Tetrahedron Lett., 2391, (1972).

5. W.E. Truce, K.R. Hollister, L.B. Lindy and J.E. Parr, J. Org. Chem., 33, 43 (1968).

6. All new products exhibited spectroscopic properties (NMR and IR) in accord with the assigned structures. Satisfactory elemental analyses or high resolution mass spectra were obtained for all new compounds.

7. R.V. Stevens, Accts. Chem. Res., 10, 193 (1977), and references therein.

8. R.V. Stevens and J.T. Shen, J. Chem. Soc., Chem. Commun., 682 (1975).

9. H.W. Pinnick and Y.-H. Chang, Tetrahedron Lett., 837 (1979).

10. Isolated, homogeneous products purified by column chromatography.

11. The remainder of the reaction mixture consisted of unidentified material resembling pyrrole decomposition products.

12. For a recent discussion of the chemistry of cyclopropyl carbinyl cations, see G.A. Olah, G.K. Surya Prakash and T. Nakajima, J. Amer. Chem. Soc., 104, 1031 (1982) and references therein.

13. For a recent example of pyrrole formation through bicyclo[2.1.0]azapentanes, see G. L'abbe, P. Van Stappen and J.-P. Dekerk, J. Chem. Soc., Chem Commun., 784 (1982).

14. For ring expansion of a cyclopropyl ring to a pyrrolidine by what appears to be an acid-catalyzed cyclopropyl ketimine rearrangement, see K.W. Blake, I. Gillies and R.C. Denney, J. Chem. Soc., Perkin Trans. 1, 700 (1981).

15. An example of a vinylcyclopropane type of rearrangement leading to pyrrole formation has been reported; H. Quast, W. von der Saal and J. Stawitz, Angew. Chem. Int. Ed. Engl., 20, no. 6/7, 588 (1981).

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