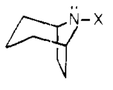
Silver Ion Induced Rearrangement of *N*-Chloramines. Isolation of an Ionic Product in High Yield

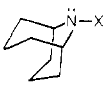
Summary: Treatment of *N*-chlorogranatanine with silver tetrafluoroborate in benzene followed by hydride reduction provides δ-coniceine in high yield. Similarly, *N*-chloro derivatives of nortropane and *trans*-decahydroquinoline provided pyrrolizidine and 1-azabicyclo[5.3.0]decane, respectively. Under these reaction conditions, only small amounts of secondary amines are found in the product. The rearrangement product of *N*-chlorogranatanine was isolated without hydride reduction and shown to be the expected immonium ion product.

Sir: Recently we initiated a study of silver ion induced rearrangements of chloramines **1–3** as a model study for the synthesis of alkaloids containing a bridgehead nitrogen.[1] At the outset we anticipated several problems with respect to eventual application of the rearrangement to complex molecules. First, silver ion treatment of chloramines has not always resulted in the generation of electron-deficient nitrogen species.[2,3] Second, even when rearrangement can and does occur, mixtures are usually obtained, and the yields of rearrangement products are sometimes low.[4] Third, the desired rearrangement products may be too reactive to be isolated or usefully trapped.



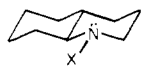
1 X = Cl

4 X = H



2 X = Cl

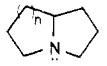
5 X = H



3 X = Cl

6 X = H

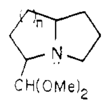
Indeed, during our initial studies of **1–3**, significant difficulties were encountered with respect to yield and reactivity of rearrangement products.[1] Treatment of **1** with methanolic silver nitrate followed by sodium cyanoborohydride provides a 35% yield of pyrrolizidine (**7**) and a 45% yield of **4**. However, when **2** was exposed to similar reaction conditions, acetal **10** and amine **5** were obtained in 25% and 50% yields, respectively. Likewise, **3** provided **11** and **6** in 26% and 45% yields, respectively. Neither of the expected products **8** or **9** was observed in the reactions of **2** or **3**. It appears that the intermediates **12** and **13**, or their enamine counterparts, are very susceptible to oxidation under these reaction conditions.



7 n = 1

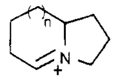
8 n = 2

9 n = 3



10 n = 1

11 n = 2



12 n = 1

13 n = 2

We now report a methodology which not only prevents oxidation of the immonium ion rearrangement products but also minimizes the production of secondary amines. In an attempt to protect immonium ion **12** by precipitation as it formed, **2** was exposed to silver tetrafluoroborate in benzene at room temperature, and precipitation of silver chloride was complete in only 4 h. After the precipitate was filtered and washed,[5] the organic solutions were combined, and the solvent was removed. The resulting material was immediately reduced with sodium borohydride to produce δ-coniceine (**8**)[6] in 92% isolated yield. Gas chromatographic analysis of the crude reduction product indicated the presence of 2–3% of secondary amine **5**.[7,8] In a similar fashion, **1** and **3** were converted to **7** and **9**[9] in equally high yields along with small amounts of secondary amines.[7]

Since chloramines are normally assumed to rearrange via nitrenium ions,[4] we were surprised to find the reaction faster and higher yielding in the less polar solvent. We were also somewhat surprised to find that the rearrangement product was fairly soluble in benzene; hence, its further characterization seemed worthwhile. The ^{13}C NMR chemical shifts of the only observable product of silver ion treatment of **2** (CH carbons at δ 174.9 and 62.1 and CH_2 carbons at δ 54.9, 29.6, 27.1, 24.7, 20.2, and 15.4) leave little doubt that the expected immonium ion **12** is produced. *This represents the first ionic rearrangement product isolated from a silver ion induced reaction of a chloramine.*

The facile production of ionic rearrangement products in benzene raises questions concerning the nature of the rearranging species. In an attempt to trap an intermediate nitrenium ion, anisole was employed as the solvent for rearrangement of **2**. No new products were obtained, and the product composition was the same as that with benzene. Thus, it is assumed that chloride is lost with σ-bond participation; however, a very tight ion pair cannot be ruled out.

The very low amount of secondary amine production in benzene is worthy of comment. Secondary amine formation has been attributed to hydrogen atom abstraction by triplet nitrenium ions[9] and by neutral amino radicals.[2,3] Clearly, in benzene solution there are not as many readily abstracted hydrogens as in methanol, although the rearrangement products should be excellent hydrogen atom donors. In view of the evidence for radical formation in many other systems,[2,3] it might be suspected that amino radicals are undergoing oxidation by silver ion.[10] Two observations are in conflict with this hypothesis: there is no silver produced in the reactions of **1–3** in benzene,[11] and there is no increase in secondary amine production when the reaction of **2** is carried out in anisole which should be an excellent hydrogen atom donor. Thus it appears that the chloramines are undergoing direct reaction to ionic materials.

The high yields of rearrangement products from **1–3** in benzene imply that the reorganization process is relatively

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[1] Schell, F. M.; Ganguly, R. N.; Percell, K. S.; Parker, J. E. *Tetrahedron Lett.* **1979**, 4925.

[2] Transannular cyclization of medium-ring chloramines in the presence of silver ion has been shown to be a radical process. Edwards, O. E.; Vocelle, D.; ApSimon, J. W. *Can. J. Chem.* **1972**, *52*, 1167.

[3] Several studies have shown that cyclization of various olefinic chloramines, with or without silver ion, is a homolytic process; e.g.: (a) Bastable, J. W.; Hobson, J. D.; Riddell, W. D. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2205. (b) Edwards, O. E.; Bernath, G.; Dixon, J.; Paton, J. M.; Vocelle, D. *Can. J. Chem.* **1974**, *52*, 2123. (c) Furstoss, R.; Tadayoni, R.; Waegell, B. *Nouv. J. Chim.* **1977**, *1*, 167.

[4] Gassman, P. G. *Acc. Chem. Res.* **1970**, *3*, 26 and references therein.

[5] Significantly lower yields are obtained if the precipitate is not washed well.

[6] The spectroscopic data for this material were in complete accord with literature values. Wenkert, E.; Bindra, J. S.; Chang, C.-J.; Cochran, D. W.; Schell, F. M. *Acc. Chem. Res.* **1974**, *7*, 46.

[7] The amount of secondary amine formed in these reactions was variable but was never more than 5%. It is probably present in the chloramine which is routinely used without purification.

[8] Satisfactory IR, NMR, and mass spectra were obtained for this compound.[2] The ^{13}C NMR chemical shifts are as follows: δ 64.8, 57.3, 55.0, 34.6, 33.1, 27.8, 25.8, 25.6, 22.4.

[9] Gassman, P. G.; Cryberg, R. L. *J. Am. Chem. Soc.* **1969**, *91*, 5176.

[10] A previous attempt to demonstrate the oxidation of amino radicals to nitrenium ions by silver ion failed.[2]

[11] This alone does not rule out a radical oxidation process. If amino radicals are generated by traces of silver metal[2] or by other means, the following chain process could occur: (1) $R_2N\cdot + Ag^+ \rightarrow Ag^0 + R_2N^+$; (2) $R_2NCl + Ag^0 \rightarrow R_2N\cdot + AgCl$.

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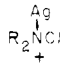
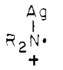
easy, yet in methanol yields of rearranged materials are low while secondary amine formation is high. It is thus difficult to accept a triplet nitrenium ion explanation[9] for the formation of secondary amines in these three cases. Homolytic reaction of **1**–**3** in methanol followed by hydrogen atom abstraction could provide the observed amines. However, neutral amino radicals have been shown to generate substantial amounts of imine products by loss of a hydrogen atom from the amino carbon.[12] Of course, amino radicals derived from **1** or **2** would not have this option since the imines produced would violate Bredt's rule.[13] Amino radicals derived from **3** could produce imine products; however, there is no evidence for such materials in the methanol–silver ion reactions of **3**. Workup of the reaction with and without hydride reduction produces the same ratio of **11** and **6**.

We can only speculate at this time, but it may be that chloramine–silver ion complexes **14** and/or radical cations **15** have been too readily dismissed.[14] Is is very suspicious that amino radicals generated in the presence of silver ion[2,3,15] do not yield the same products as those generated without silver ion.[12] Radical cation **15**, generated by homolysis of **14** or possibly by reactions of an amino radical with silver ion, should be an excellent hydrogen atom abstractor.[16] On the other hand, loss of silver from **15** would provide an alternate route to triplet nitrenium ions.


$R_2\overset{Ag}{\underset{+}{N}}Cl$

14


$R_2\overset{Ag}{\underset{+}{N}}\cdot$

15

The reason for the dramatic change in products when the chloramine rearrangement is carried out in aprotic media rather than the traditional hydroxylic solvents is not clear at this time. However, investigation of chloramine–silver ion interactions and alkaloid synthesis by using the high-yielding conditions reported herein are continuing.

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Registry No. **1**, 74327-95-0; **2**, 73322-95-9; **3**, 74364-91-3; **4**, 280-05-7; **5**, 280-97-7; **6**, 767-92-0; **7**, 643-20-9; **8**, 13618-93-4; **9**, 5715-05-9; **11**, 74763-56-7; **12**, 74779-50-3; silver tetrafluoroborate, 14104-20-2.

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(12) Gassman, P. G.; Uneyama, K.; Hahnfeld, J. L. *J. Am. Chem. Soc.* **1977**, *99*, 647.

(13) Buchanan, G. L. *Chem. Soc. Rev.* **1974**, *3*, 41.

(14) Gassman, P. G.; Cryberg, R. L. *J. Am. Chem. Soc.* **1969**, *91*, 2047.

(15) In Edwards' extensive investigation of silver ion and silver metal reactions of chloramines, he reports the formation of imines in several reaction mixtures containing silver ion.[2] These reactions employed added amine or were carried out with silver oxide. In either case, the chloramine would not be expected to compete effectively with the more basic ligands in the complexation of silver ion. Hence, it is quite reasonable that neutral amino radical products were produced.

(16) For reviews of nitrogen radical and radical-cation chemistry, see: (a) Sosnovsky, G.; Rawlinson, D. J. *Adv. Free-Radical Chem.* **1972**, *4*, 203; (b) Nelsen, S. F. In "Free Radicals"; Kochi, J. K., Ed.; Wiley-Interscience: New York, 1973; 527; (c) Neale, R. S. *Synthesis* **1971**, 1; (d) Chow, Y. L. *Acc. Chem. Res.* **1973**, *6*, 354; (e) Minisei, F. *Synthesis* **1973**, 1.