Notes

Competitive Amide *vs.* Thioamide Cyclization. Cyclization of *N*-Allylrhodanine in Strong Acid Media[1]

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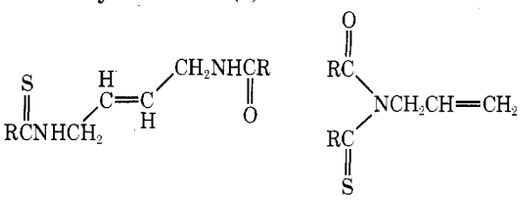
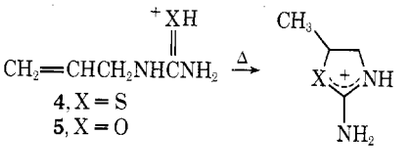
In a previous report[3] we commented on the relative sluggishness of the cyclization of *N*-allylthiourea as compared to *N*-allylurea. This observation prompted our investigation of the competitive cyclization of an amide group *vs.* a thioamide group. The unavailability of symmetrical model derivatives such as 1 or 2 led us to study the readily available *N*-allylrhodanine (3).



1 2

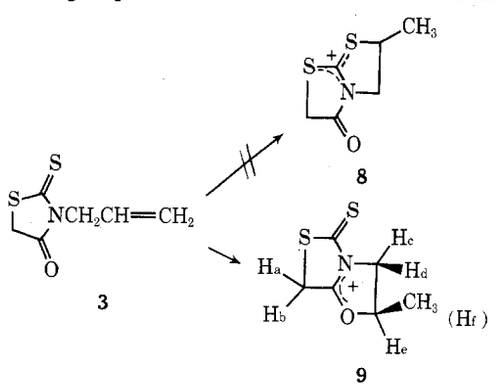
In sulfuric acid solutions (60–96%) at room temperature, *N*-allylthiourea and *N*-allylurea exist in the S-protonated (4) and O-protonated (5) forms, respectively.[3] Cyclization of 4 and 5 to the respective thiazolinium (6) and oxazolinium (7) cations occurs, in competition with polymerization, only upon heating of the acid solutions to 70–90°.[3] Usually excellent cyclization yields are achieved.[3]



4, X = S
5, X = O

6, X = S
7, X = O

Unlike 4 and 5, *N*-allylrhodanine (3) cyclized rapidly and quantitatively upon dissolving in concentrated sulfuric acid at 15°. The proton nmr spectrum of the yellow solution revealed a single species which we assumed to be either 8 or



3 8 9

J_{cd} = 12.5 Hz, J_{ce} = 6.5 Hz, J_{de} = 8.5 Hz

9. The 100-MHz spectrum consisted of peaks at δ 2.32 (H_f, 3 protons, doublet), 4.68 (H_c, 1 proton, quartet), 5.08 (H_d, 1 proton, quartet), 5.27 (H_a and H_b, 2 protons, singlet), and 5.58 (H_e, 1 proton, multiplet). Decoupling experiments established that the methyl doublet (H_f, δ 2.32) was coupled with the multiplet (H_e) at δ 5.58. The δ 5.58 multiplet must then be either the proton on carbon bonded to sulfur in 8 or the proton on carbon bearing oxygen in 9. The chemical shift of this proton is consistent only with its assignment as H_e in 9. The chemical shift of protons on carbon bonded to sulfur in thiazolinium cations (C-5 in simple cases) has been reported in the region δ 4.17–4.60 while the chemical shift of protons on carbon bonded to oxygen in oxazolinium cations is in the range of δ 4.79–6.30 depending on other substituents.[3–8] Since H_e appears at δ 5.58, a region farther downfield than any known case for C—H adjacent to sulfur in a thiazolinium cation, we are confident that cyclization to oxygen and not sulfur has obtained in the case of 3.

Since we were somewhat surprised to find only cyclization to oxygen occurring in the presence of the more nucleophilic sulfur, we sought to examine more carefully the cyclization process.

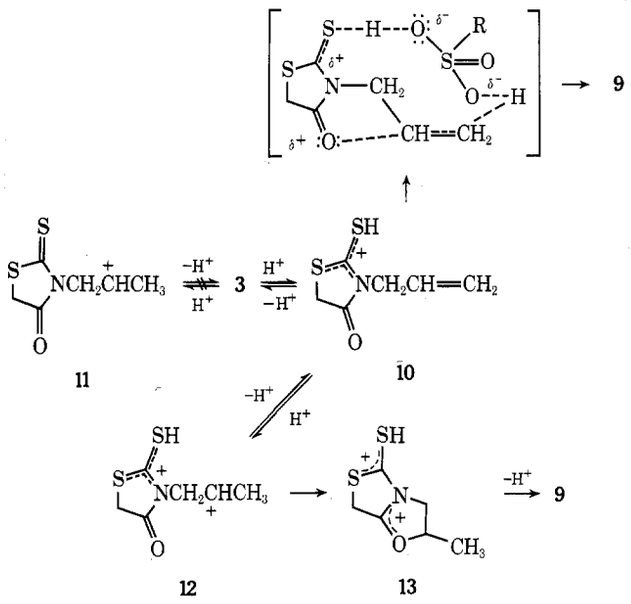
In FSO_3H, a stronger acid than H_2SO_4, cyclization occurred more slowly. Initially, the nmr spectrum contains peaks consistent with C=S protonated allylrhodanine (10), with the S–H resonance at δ 6.45.[9] With time the peaks due to 10 decreased (and finally disappeared) and those due to 9 increased. Again, 9 was the sole product of cyclization. In the strongest acid of the series, CF_3SO_3H, the cyclization was slowest. Thus, in both FSO_3H and CF_3SO_3H, C=S protonation is occurring to form 10 and further protonation, if it occurs with 10, is fast and reversible.

While our experiments do not definitively dissect this complex kinetic process, the results suggest two possible mechanisms for the formation of 9. First of all, we assume that cation 11 is not involved in this process since it would be difficult to explain why the less nucleophilic oxygen attacks the carbocation, especially in view of the apparent greater resonance stabilization afforded 8 by a second sulfur atom. Additionally, protonation of the C=S bond, even in sulfuric acid must be important; thus 10 or a more highly protonated form is involved. If 12 were the species leading to cyclization, the correct cyclic product would result, but one might expect that cyclization would be faster and not slower in stronger acids. If, however, the formation of the dication 13 were sluggish, then the rate of conversion of 10 into 9 might be dependent of sulfur deprotonation concurrent with cyclization. A possible explanation of how this may occur is shown in Scheme I. This type of proton transfer has many precedents especially where water acts as the bimolecular component.[10,11]

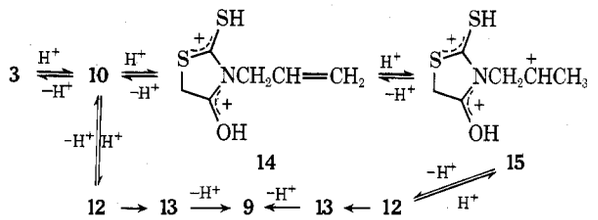
The second possibility is that 10 cyclizes through cation 12. The observed results could be explained if C=O protonation to form dication 14 occurs more readily than C=C protonation to form 12. In acids stronger than H_2SO_4, the formation of 9 would then occur more slowly since more and more of 10 is reversibly converted to 14 with that equilibrium slowing formation of 12; or formation of 9 may require rate-limiting deprotonation of 15 to 12.[12] These possibilities are shown in Scheme II.

There is no assurance that a single mechanism accounts for the cyclization in all acids, but it appears certain that

Scheme I



Scheme II



the initial protonation of the C=S is the primary reason that cyclization to oxygen rather than sulfur occurs.[13]

Experimental Section

N-Allylrhodanine was purchased from Aldrich Chemical Co., Inc. The acids were used without prior purification. Nmr spectra were determined with a Varian HA-100 MHz or a HFX-10 90 MHz instrument. The decoupling experiments were performed on the latter instrument. Tetramethylsilane was used as the reference (internal capillary) standard for all nmr measurements.

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Registry No.—**3**, 1457-47-2; **9**, 52123-50-9.

References and Notes

(1) Part XI of the series Acid-Catalyzed Cyclization Reactions; for the previous paper see S. P. McManus, C. U. Pittman, Jr., and P. E. Fanta, *J. Org. Chem.*, **37**, 2353 (1972).
(2) Abstracted, in part, from the M.S. Thesis of K. Y. L., The University of Alabama in Huntsville, May 1973.
(3) S. P. McManus, J. T. Carroll, and C. U. Pittman, Jr., *J. Org. Chem.*, **35**, 3768 (1970); corrections: *ibid.*, **37**, 3752 (1972); *ibid.*, **38**, 4217 (1973).
(4) C. U. Pittman, Jr., S. P. McManus, and J. W. Larsen, *Chem. Rev.*, **72**, 457 (1972).
(5) D. A. Tomalia and J. N. Paige, *J. Org. Chem.*, **38**, 422 (1973).
(6) M. A. Weinberger and R. Greenbalgh, *Can. J. Chem.*, **41**, 1038 (1963).
(7) Tomalia and Paige [*J. Org. Chem.*, **38**, 3949 (1973)] have incorrectly assigned the ring protons of their thiazolinium cation in their recent paper by apparently misreading the assignments of thiazolinium cations in ref 6. The assignments should be reversed. These assignments in no way affect the interesting results presented in that paper.
(8) R. A. Wohl, *J. Org. Chem.*, **38**, 3099 (1973).
(9) G. A. Olah, A. M. White, and D. H. O'Brien, *Chem. Rev.*, **70**, 561 (1970).
(10) M. L. Bender, "Mechanisms of Homogeneous Catalysis from Protons to Proteins," Wiley-Interscience, New York, N. Y., 1971, Chapter 9.
(11) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969.
(12) Formation of the trication **15** is a possibility in very strong acids (see ref 9), but **15** is not expected to be important in H_2SO_4.
(13) The coordination of sulfur by acidic reagents may explain the relatively low yields of cyclic products obtained from *N*-alkenylthioamides; *cf.* P. A. S. Smith and J. M. Sullivan, *J. Org. Chem.*, **26**, 1132 (1961).

Reaction of Hexamethylphosphoric Triamide with Alkyllithiums. *In Situ* Formation of *N*-Methylmethylenimine

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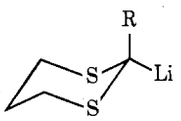
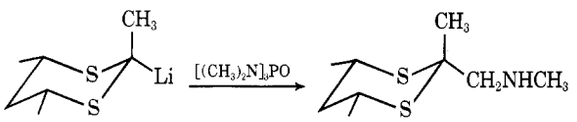
Hexamethylphosphoric triamide (HMPTA) is a useful solvent of high polarity and low nucleophilic character. We have employed it as a medium for nmr spectral study of 2-dithianyllithium (**1**) and 2-Phenyl-2-dithianyllithium (**2**).[1] When we tried to dissolve *r*-2-lithio-2,*cis*-4,*cis*-6-trimethyl-1,3-dithiane (**3**)[2] in the same solvent, we noted that a reaction occurred; the product, according to elemental analysis and nmr spectral evidence, was *r*-2-methylaminomethyl-2,*cis*-4,*cis*-6-trimethyl-1,3-dithiane (**4**).



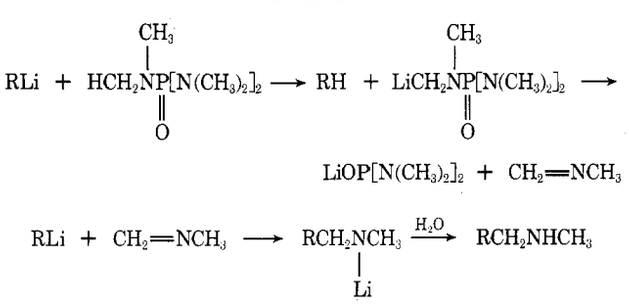
1, R = H
2, R = C_6H_5



3 **4**

About the time we carried out this experiment, a report appeared[3] describing the reaction of dialkoxyphosphoric amides with alkyllithiums to give lithium dialkoxyphosphites and Schiff bases which then react with a second mole of alkyllithium to give the lithium derivative of a secondary amine. It appeared that the reaction we had observed followed a path similar to that postulated by Savignac and Leroux[3] (Scheme I).

Scheme I



In accordance with expectations based on this scheme, we found that *n*-butyllithium, *sec*-butyllithium, and phenyllithium, when allowed to react with hexamethylphospho-