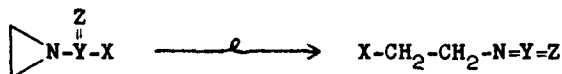


1-(AZIRIDINE)SULFINYL CHLORIDES
ISOMERIZATION TO 2-CHLORO-N-SULFINYLALKYLAMINES

Donald A. Tomalia
Edgar C. Britton Research Laboratory
The Dow Chemical Company
Midland, Michigan 48640

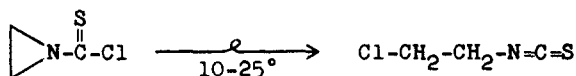
(Received 14 April 1967)

In 1963 Heine (1) found that 1-(phenylthiocarbonyl)-aziridine undergoes isomerization to 2-(phenylthioethyl)-isocyanate upon heating at 200° for three days. This appears to be the first reported example of what has recently been found to be a general class of aziridine isomerizations involving a 1,4 shift of X accompanied by the formation of an -N = Y = Z group as shown below:

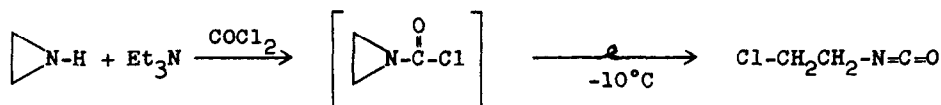


This class of isomerizations represents the first example of a heteroatomic homoallylic rearrangement. The skeletal changes occurring in these isomerizations resemble the well known homoallylic rearrangements that have been observed in the cyclopropane series (2).

Recently we reported on a second example of this type of aziridine rearrangement in which case it was found that 1-(aziridine)thiocarbonyl chloride isomerizes to 2-chloroethyl isothiocyanate under extremely mild conditions, i.e. 10 to 25°C (3). Since then we have found that the oxygen analogue isomerizes

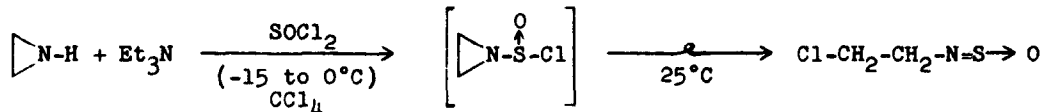


in a similar manner. This latter rearrangement is so facile that 1-aziridine carbonyl chloride cannot be observed spectroscopically even at -10°C (4).



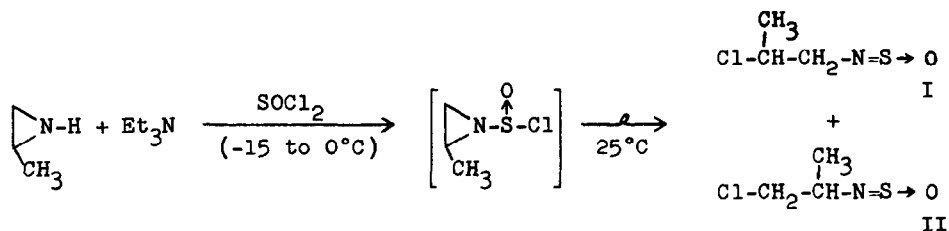
We now wish to report on the first example of a non-carbonyl type of aziridine derivative which undergoes this kind of isomerization under relatively mild conditions.

By reacting equimolar amounts of aziridine and triethylamine with thionyl chloride at reduced temperature (c.a. -15 to 0°C) it was possible to trap and characterize the new class of aziridine derivatives, 1-(aziridine) sulfinyl chlorides. 1-(Aziridine)sulfinyl chloride was obtained as a light yellow

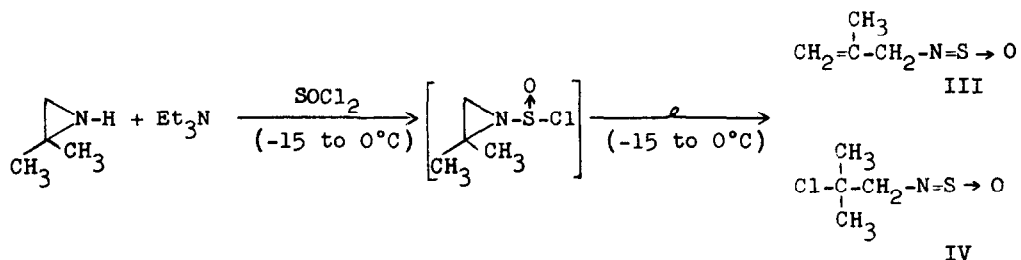


solution in CCl_4 . This solution was examined by n.m.r. at a probe temperature of -15°C and found to give a spectrum which consisted of only a singlet at -2.65 p.p.m. Allowing the sample to stand at room temperature (c.a. 25°C) for several hours caused slight decolorization of the sample and n.m.r. analysis of the sample at this point showed that the singlet was disappearing while an A_2M_2 pattern was developing concurrently at a downfield position. After the sample had stood at 25°C for ~ 20 hours the singlet was completely gone and the spectrum was found to be identical to that obtained for an authentic sample of 2-chloro-N-sulfinylethylamine (5). The product was isolated in 48% yield as a colorless liquid, b.p. $62-64^{\circ}/33$ mm. Anal. Calcd. for $\text{C}_2\text{H}_4\text{ClNOS}$: C, 19.13; H, 3.21. Found: C, 19.03; H, 3.18. An infrared spectrum of this product contained bands at $581\text{ cm}^{-1}(\text{m})$, $1123\text{ cm}^{-1}(\text{s})$ and $1260\text{ cm}^{-1}(\text{s})$ (6), whereas, the n.m.r. spectrum consisted of an A_2M_2 pattern with triplets centered at -3.70 and -4.85 p.p.m. (CHCl_3).

In a similar manner, 1-(2-methylaziridine)-sulfinyl chloride was prepared under identical conditions. The n.m.r. spectrum of this derivative (probe temperature, -15°C) consisted of a doublet at -1.51 p.p.m., a doublet at -2.38 p.p.m. and a multiplet at -2.66 to -3.16 p.p.m. (CCl_4). Integration showed that these protons were present in a ratio of 3:1:2. Warming the sample up to 25°C resulted in isomerization to a mixture of 2-chloro-N-sulfinylpropylamine (I) and 2-chloro-1-methyl-N-sulfinylethylamine (II). The reaction was complete after a period of 8-10 hours. N.m.r. analysis of the crude isomer mixture indicated that the ratio of I to II was 44:56 (7). The product was obtained in 54% yield as an isomer mixture, b.p. $68-69^{\circ}/45$ mm. Anal. Calcd. for $\text{C}_3\text{H}_6\text{ClNOS}$: C, 25.81; H, 4.33; Cl, 25.40. Found: C, 25.68; H, 4.50; Cl, 25.08.



1-(2,2-Dimethyl aziridine)-sulfinyl chloride could not be observed spectroscopically under the same conditions. Immediate isomerization to a mixture



of methallyl-N-sulfinylamine (III) and 2-chloro-2-methyl-N-sulfinylpropylamine (IV) occurred even at -15 to 0°C. Compound (III) gave an n.m.r. spectrum consisting of a finely split multiplet centered at -4.96 p.p.m. ($\text{CH}_2=\overset{1}{\text{C}}$), a singlet at -4.50 p.p.m. ($-\text{CH}_2-$) and a broad singlet at -1.86 p.p.m. (CH_3-) (CCl_4). These protons were present in a ratio of 2:2:3, respectively. Compound (IV) gave an n.m.r. spectrum containing a singlet at -4.12 p.p.m. ($-\text{CH}_2-$) and a singlet at -1.62 p.p.m. ($\text{CH}_3-\overset{1}{\text{C}}-\text{CH}_3$) (neat). Proton integration showed they were present in a ratio of 1:3, respectively. N.m.r. examination of the crude reaction mixture indicated that compounds (III) and (IV) were formed in a ratio of ~33:67 mole % from this reaction.

The exclusive formation of (III) and (IV) from 2,2-dimethyl aziridine is a general reaction common to the phosgene and thiophosgene systems since the reaction of 2,2-dimethyl aziridine with phosgene or thiophosgene also gave the isocyanate and isothiocyanate analogues, respectively, of (III) and (IV) (8).

It was interesting to note that the reaction of equimolar amounts of aziridines and thionyl chloride in the absence of an external acid acceptor, such as triethylamine, also led to 2-chloro-N-sulfinylalkylamines in 33-51% yields. In these cases the aziridine absorbs two equivalents of hydrogen

chloride to produce 2-chloroalkylamine salts as the accompanying product. These reactions parallel the thiophosgene system; however, in the phosgene system these reactions led to a predominance of bis-2-(chloroalkyl) urea and a smaller amount of the corresponding 2-chloroalkyl carbamoyl chloride (4).

REFERENCES

1. H. W. Heine, J. Am. Chem. Soc., 85, 2743 (1963).
2. P. De Mayo, Molecular Rearrangements, Interscience Publishers, New York, Vol. I, p. 259 (1964).
3. D. A. Tomalia, J. Heterocyclic Chem., 3, 384 (1966).
4. D. A. Tomalia, ibid., (in press).
5. The authentic sample was prepared according to the method of W. T. Smith, Jr., W. Y. Chen and M. Linfield, J. Med. Chem., 8, 718 (1965).
6. N-Alkyl sulfinylamines are reported to exhibit these characteristic infrared absorption bands. See G. Kresze, et.al., Angew. Chem. Internat. Edit. Engl., 1, 89 (1962).
7. This ratio is based on a comparison of both methyl and methylene proton integrations for the respective isomers.
8. D. A. Tomalia, unpublished results.