Mechanism of the Isomerization of 1-(Arylthiocarbonyl)aziridines to 2-(Arylthioalkyl) Isocyanates

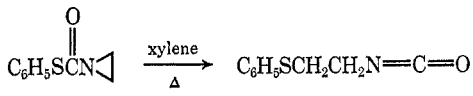
DONALD A. TOMALIA,[1] DAVID P. SHEETZ, AND G. E. HAM

Edgar C. Britton Research Laboratory, The Dow Chemical Company, Midland, Michigan 48640, and Texas Amines Research Laboratory, The Dow Chemical Company, Freeport, Texas 77541

Received March 14, 1969

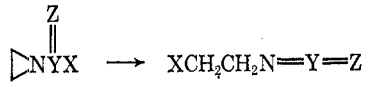
It has been shown that the isomerization of 1-(arylthiocarbonyl)aziridines to 2-(arylthioalkyl) isocyanates is catalyzed by triethylamine or thiophenolate ion and may occur under relatively mild conditions (25–77°). 1-(Arylthiocarbonyl)-2-methylaziridines rearranged to their isomeric isocyanates by selective ring fission at the unsubstituted aziridine ring carbon, thus indicating the SN2 character of these rearrangements. Kinetic experiments have shown that these isomerizations are first order in 1-(arylthiocarbonyl)aziridine, with the first-order rate constant being proportional to thiophenolate concentration. A cross-over experiment demonstrated that the isomerization is an *intermolecular* process.

Heine described the thermal rearrangement of 1-phenylthiocarbonylaziridine (**1**) into the isomeric 2-phenylthioethyl isocyanate[2] (**2**). This may be the



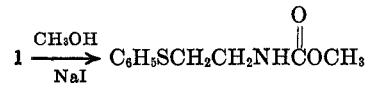
1 **2**

first example of a general class of aziridine rearrangements which one of us has described recently, involving a 1,4 migration of X accompanied by the formation of an —N=Y=Z function.[3] This rearrangement has



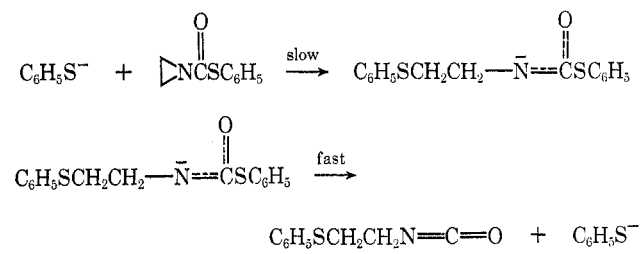
been shown to be useful for the preparation of sulfinyl amines,[3] isothiocyanates,[4] and isocyanates.[5] Since the skeletal changes occurring in these isomerizations resemble the well-known homoallylic rearrangements which have been observed in the cyclopropane series,[6] it was of interest to see if there were any mechanistic similarities.

Heine has reported that **1** can be isomerized to its isomeric isocyanate, 2-phenylthioethyl isocyanate, by heating in xylene (200°) for 3 days. He also found that **1** produced N-(2-phenylthioethyl)-O-methylcarbamate at room temperature when allowed to react with methanol containing sodium iodide. This reaction did not



occur in neat methanol without sodium iodide. The reaction was presumed to proceed *via* **2**. Heine has compared each of the above reactions to *intramolecular* alkylation processes analogous to those which have been postulated for the thermal isomerization of 1-benzoylaziridine[7,8] and the iodide ion catalyzed rearrangement of 1-aziridinecarboxanilides,[9,10] respectively.

We wish to report data which show that triethylamine, which is used in the preparation of **1**, is actually a catalyst which can effect the isomerization of **1** → **2** by the production of thiophenolate ion. Kinetic experiments have shown that this rearrangement is first order in aziridine **1**, with the first-order rate constant proportional to thiophenolate concentration. A "cross-over" experiment demonstrated that the isomerization is *intermolecular* in the presence of catalytic amounts of triethylamine. We propose the following as an accommodating mechanism for these data.

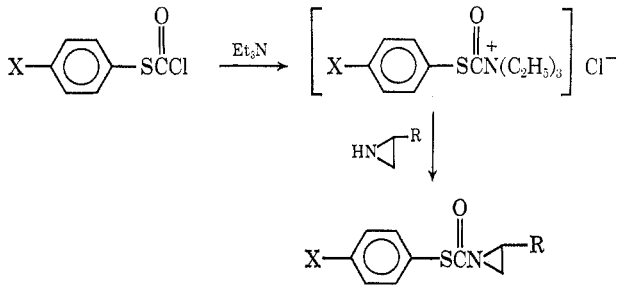


Results and Discussion

It was observed that the order of combining aziridine and triethylamine with the aryl thiochloroformates was critical. Adding aziridine plus triethylamine to the thiochloroformates, as described by Heine,[2] consistently assured good yields of the desired 1-(arylthiocarbonyl)-aziridines. Alternatively, it was found that these materials could be obtained in good yields by the addition of aziridines to the preformed triethylamine–arylthiochloroformate complexes. In this manner, yields of 70–86% were observed for compounds **1**, **3**, **4**, and **5**. Only compounds **1** and **3** could be isolated as crystalline solids at room temperature. Compounds **4** and **5** were obtained as thermolabile oils which could not be purified by distillation without decomposition into rearrangement products. Pure **1** and **3** could be stored at reduced temperature (0 to −5°) for several weeks without deterioration. Allowing unpurified, neat samples to stand at room temperature for several hours usually resulted in conversion to oils consisting of polymer, isomeric isocyanate, and isocyanate-derived products. By reversing the order of addition and adding the thiochloroformates to the aziridines plus

(1) To whom correspondence should be addressed: Physical Research Laboratory, The Dow Chemical Co., Midland, Mich. 48640.
(2) H. W. Heine, *J. Amer. Chem. Soc.*, **85**, 2743 (1963).
(3) D. A. Tomalia, *Tetrahedron Lett.*, **27**, 2559 (1967).
(4) D. A. Tomalia, *J. Heterocycl. Chem.*, **3**, 384 (1966).
(5) (a) D. A. Tomalia and J. N. Paige, *ibid.*, **4**, 178 (1967); (b) C. K. Johnson, *J. Org. Chem.*, **32**, 1508 (1967).
(6) R. Breslow in "Molecular Rearrangements," Vol. 1, P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1967, p 259.
(7) S. Gabriel and R. Stelzner, *Ber.*, **28**, 2929 (1895).
(8) A. A. Goldberg and W. Kelley, *J. Chem. Soc.*, 1919 (1948).
(9) H. W. Heine, W. G. Kenyon, and E. M. Johnson, *J. Amer. Chem. Soc.*, **83**, 2570 (1961).
(10) H. Najer, R. Giudicelli, J. Menin, and C. Morel, *Compt. Rend.*, **253**, 2369 (1961).

triethylamine, the reaction gave impure compounds (**1**, **3**, **4**, and **5**) accompanied by the corresponding

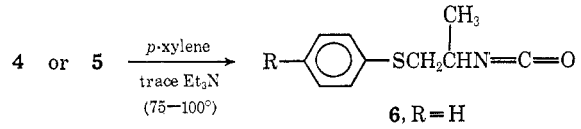


1, X = H; R = H
3, X = Cl; R = H
4, X = H; R = CH_3
5, X = Cl; R = CH_3

2-arylthioethyl isocyanates and isocyanate-derived products. The unexpected formation of these isocyanates under such mild conditions seemed to implicate the involvement of either uncomplexed aziridine or triethylamine. Further examination revealed that no rearrangement to the isomeric isocyanate was observed when pure **1** was maintained at 77° (*p*-xylene solvent) for several hours either in the presence or absence of catalytic amounts of aziridine. Upon adding a catalytic amount of triethylamine under these conditions, complete isomerization to 2-phenylthioethyl isocyanate was observed in *ca.* 1 hr.

The isomerization of **1** was easily monitored by infrared and nmr spectroscopy. Compound **1** displayed an infrared absorption band at 5.90 μ which decreased as a band at 4.42 μ (—N=C=O) developed during the course of the isomerization. Prolonged reaction times led to a substantial amount of base-catalyzed trimerization of the isocyanate to isocyanurate.[11] This consecutive reaction complicated kinetic experiments which will be described later. Trimerization was accompanied by the development of an absorption band at 4.89 μ. Isomerization of **1** was also followed by nmr spectroscopy, wherein a singlet at −2.27 ppm (CCl_4) for the aziridine protons diminished as a multiplet centered at −3.18 ppm (—SCH_2CH_2N) was enhanced a commensurate amount.

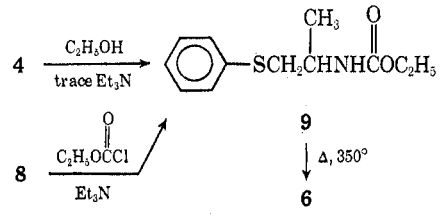
Aziridines **4** and **5** could be obtained only as a thermolabile oil and a low-melting solid, respectively. Isomerization of these materials was accomplished by heating for several hours with a catalytic amount of triethylamine in an inert solvent (*p*-xylene or benzene) at 75–100°. The rearrangement proceeded in a selective manner to give the isomeric isocyanates **6** or **7**. The selectivity of this reaction was determined by



6, R = H
7, R = Cl

glpc and by the subsequent structure proof of the sole product of this rearrangement. Structure **6** was confirmed by an independent synthesis which involved the phosgenation of 1-phenylthio-2-propylamine (**8**).

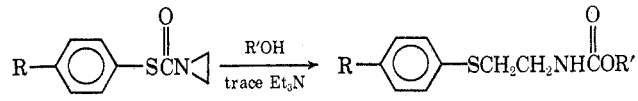
Aziridine **4** underwent a selective reaction with ethanol, containing a trace of triethylamine, to produce N-(1-phenylthio-2-propyl)-O-ethylcarbamate (**9**). Compound **9** was found to be identical with the product



obtained from the reaction of **8** with ethyl chloroformate and triethylamine. Furthermore, the crude product from **4** and ethanol pyrolyzed cleanly on a glpc instrument at an injection port temperature of 350° to yield 1-phenylthio-2-propyl-isocyanate (**6**) and ethanol.

The aforementioned selective ring-opening reactions of aziridines **4** and **5**, which involve ring fission at the unsubstituted aziridine ring carbon, strongly suggest that these reactions are SN2 in character. This clearly distinguished these rearrangements as being mechanistically different from cyclopropyl carbinyl halide rearrangements[6] and perhaps the related 1-(aziridine)-thiocarbonyl chloride,[4] 1-(aziridinyl)sulfinyl chloride,[3] and 1-(aziridinyl)carbonyl chloride[5a,b] rearrangements, which have thus far implicated carbonium ion type intermediates in the ring-opening process.

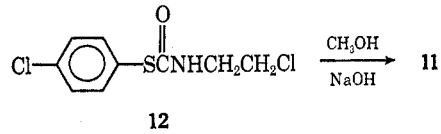
Triethylamine functioned much as sodium iodide in that it transformed **1** or **3** into their corresponding urethans in the presence of either ethanol or methanol.



1 or 3

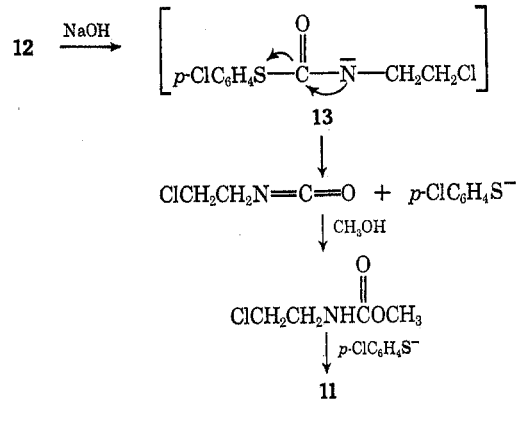
10, R = H; R′ = C_2H_5
11, R = Cl, R′ = CH_3

Proof of structure for compound **10** was garnered by allowing 2-phenylthioethylamine to react with equivalent amounts of ethyl chloroformate and triethylamine. Structure **11** was confirmed by the reaction of 2-(*p*-chlorophenyl)thioethyl isocyanate with methanol and also by the dehydrochlorination of N-(2-chloroethyl)-S-(*p*-chlorophenyl)thiocarbamate (**12**) with methanolic sodium hydroxide. Transformation of **12** presumably



12

involves the intermediacy of 2-chloroethyl isocyanate as shown below.



(11) The tertiary amine catalyzed reaction of 1-(aryloxycarbonyl)aziridines led to exclusive formation of isocyanurates [*e.g.*, G. E. Ham, H. L. Hairston, and D. A. Tomalia, U. S. Patent 3,409,618 (1968)].

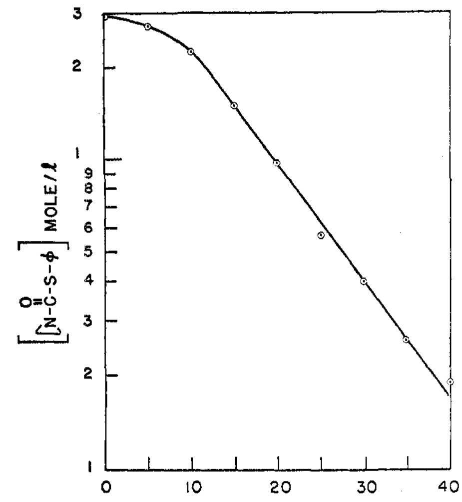


Figure 1.

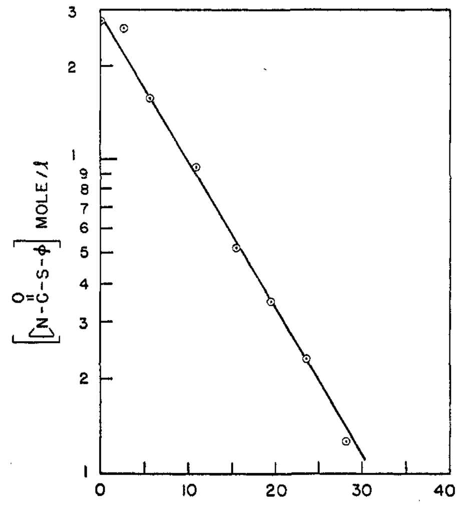


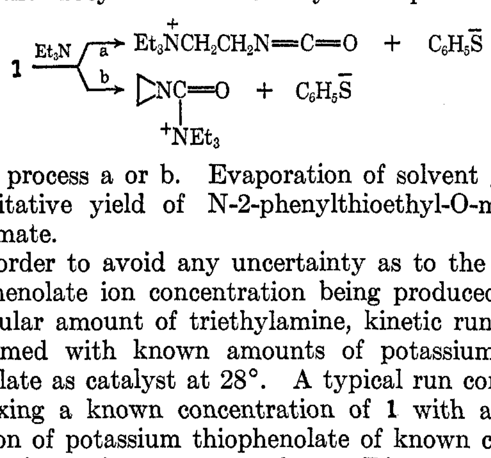
Figure 2.

This speculation is in agreement with work reported by Niemann and coworkers[12,13] on a related N-alkyl-S-arylthiocarbamate system, wherein isocyanates are postulated as transient intermediates in base-catalyzed reactions which lead to urea formation.

It should be noted that anion **13** resembles the anionic intermediate postulated by Heine for the reaction of **1** with methanolic sodium iodide. However, by simulating Heine's reaction conditions, using shorter reaction times, it was hoped that, according to the above process, it would be possible to detect the intermediate N-2-iodoethyl-O-methylcarbamate (**14**). At room temperature and a reaction time of 1 hr, it was found that **1** was completely converted into N-2-phenylthioethyl-O-methylcarbamate without any spectroscopically detectable amounts of N-2-iodoethyl-O-methylcarbamate being present. This result indicates that either the reaction was indeed intramolecular or the displacement of iodide ion from **14** by thiophenolate was very rapid under these conditions even after 1 hr. In order to test the latter hypothesis, N-2-iodoethyl-O-ethylcarbamate was allowed to react with potassium thiophenolate under the same conditions. Conversion into N-2-phenylthioethyl-O-ethylcarbamate was complete in 1 hr. This clearly shows that the 1,2-heteroatomic elimination of thiophenolate ion as described above (*e.g.*, **13**) cannot be excluded.

A kinetic examination of the isomerization was even more revealing. Since triethylamine catalyzed a consecutive trimerization of isocyanate in neat acetonitrile or *p*-xylene, leading to heterogeneous reaction mixtures, it was necessary to use a solvent system (90:10 v/v) of acetonitrile and methanol. Methanol scavenged the isocyanate produced *in situ*, thus yielding homogeneous systems and reproducible kinetic data. Kinetic measurements were made by observing the disappearance of an infrared absorption band of **1** which appeared at 11.75 μ.

Aziridine **1** was allowed to react with a catalytic amount of triethylamine at 50° in the above solvent system and yielded the data in Figure 1, which shows a plot of aziridine concentration as a function of time. A definite induction period was noted during the first 10 min of the reaction. This suggested to us that triethylamine was generating thiophenolate ion in a slow step, which then went on to catalyze rearrangement of **1** to the isocyanate. This may be represented by



either process a or b. Evaporation of solvent gave a quantitative yield of N-2-phenylthioethyl-O-methylcarbamate.

In order to avoid any uncertainty as to the actual thiophenolate ion concentration being produced by a particular amount of triethylamine, kinetic runs were performed with known amounts of potassium thiophenolate as catalyst at 28°. A typical run consisted of mixing a known concentration of **1** with a stock solution of potassium thiophenolate of known concentration in a nitrogen atmosphere. Disappearance of the infrared absorption band for **1** at 11.75 μ was followed. It should be mentioned that no change in concentration of **1** was observed over a period of 5 hr, in the absence of potassium thiophenolate in this solvent system. The longest reaction time for the kinetic experiments was 2 hr. A first-order plot of these data gives the linear relationship shown in Figure 2. The first-order rate constant was determined in the usual manner from the slope of this line. In this manner rate constants (k_1) were determined for seven different concentrations of potassium thiophenolate. A plot of k_1 *vs.* potassium thiophenolate concentration was linear (Figure 3). From this plot the overall second-order rate constant (k_2) was determined as follows.

$$\text{over-all rate} = k_1 \left[\triangleright\text{N}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{SC}_6\text{H}_5 \right]$$

$$k_1 = k_2 \left[\text{C}_6\text{H}_5\text{SK} \right]$$

$$\text{over-all rate} = k_2 \left[\text{C}_6\text{H}_5\text{SK} \right] \left[\triangleright\text{N}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{SC}_6\text{H}_5 \right]$$

$$k_2 = 21.7 \text{ l. mol}^{-1} \text{ min}^{-1}$$

(12) C. Niemann and W. H. Schuller, *J. Amer. Chem. Soc.*, **75**, 3425 (1953).
(13) C. Niemann and D. G. Crosby, *ibid.*, **76**, 4458 (1954).

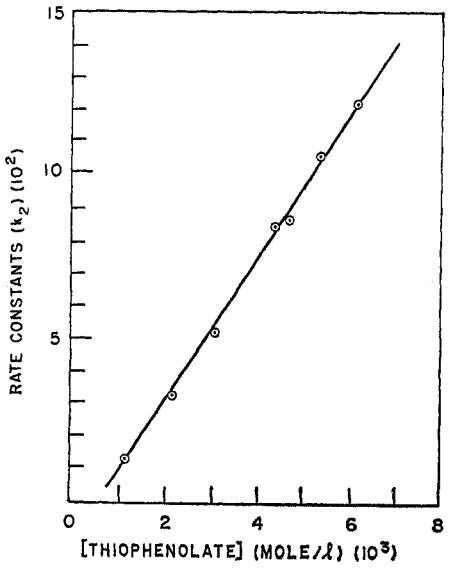
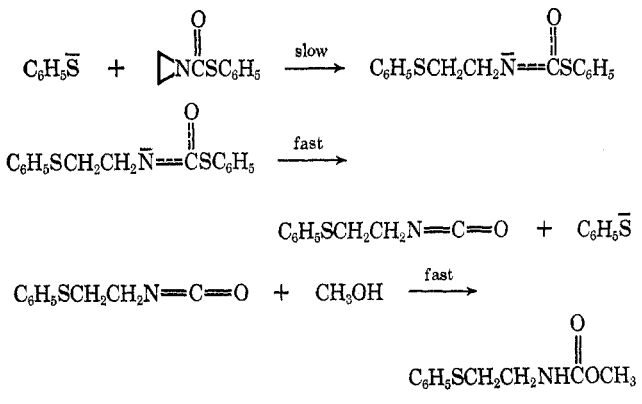
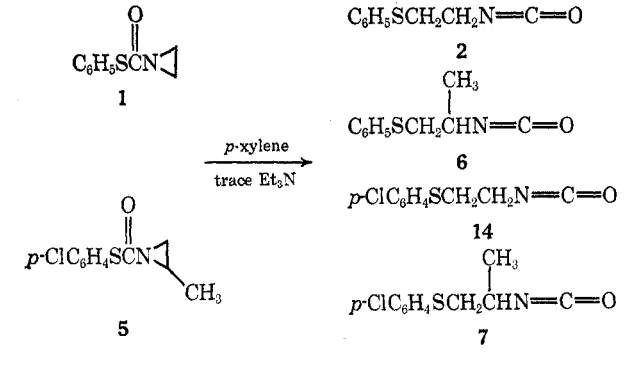


Figure 3.

This kinetic expression is consistent with the following proposed mechanism.



The above mechanism implies intermolecular transfer of the thiophenolate moiety from carbonyl attachment in **1** to attachment at an alkyl carbon, as seen in the isocyanate product. This hypothesis was tested by means of a "cross-over" experiment. Equivalent amounts of 1-(phenylthiocarbonyl)aziridine, (**1**) and 1-(*p*-chlorophenylthiocarbonyl)-2-methylaziridine (**5**) were refluxed for 1 hr in *p*-xylene containing a catalytic amount of triethylamine. A sample of this crude reaction mixture was analyzed by glpc and resolved into four components. A synthetic mixture consisting of authentic samples of isocyanates **2**, **6**, **14**, and **7** gave essentially the same chromatogram, with identical retention times for the individual components. Infrared and nmr spectroscopy also corroborated the identification of these isocyanates.

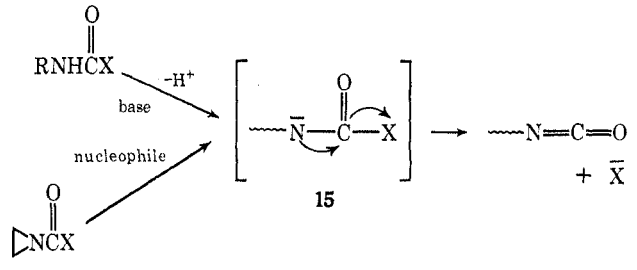


Process a (see earlier text) is preferred as the mode by which thiophenolate anion is generated in the triethylamine-catalyzed reactions for at least two reasons. First, Heine[14] and Ham[15] have shown that activated aziridines usually undergo ring opening as described by process a. Second, it has been shown that N,N-dialkyl-S-arylthiocarbamates are resistant to hydrolysis by basic reagents,[12,16] thus diminishing the possibility that process b would be an important source for thiophenolate ion.

Process a is very much like an SN2′ reaction,[17] wherein the nucleophilic attack occurs at a site which is remote to the departing group (*i.e.*, thiophenolate ion).

It seems that this isomerization cannot be generalized as a simple unimolecular-type pyrolysis, as previously described by Heine.[2] Since Heine's more rigorous conditions were not tested, one cannot dismiss the occurrence of an intramolecular mechanism at high temperatures. On the other hand, it would also be difficult to exclude the possibility of trace amounts of adventitious nucleophiles under his conditions.

In conclusion, the rearrangement of 1-(arylthiocarbonyl)aziridines to their isomeric isocyanates appears to be related to the well-known 1,2-heterolytic elimination of a good departing group from a carbonyl moiety as shown below. The primary difference seems to be the mode by which anion **15** is generated. To our knowledge, all other previous 1,2 eliminations of this type have involved a proton loss[18] or abstraction,[12,13,19] whereas anion **15** arises from the 1-(arylthiocarbonyl)aziridines by a simple nucleophilic ring opening of the aziridine ring.



Experimental Section

The aryl chlorothioformates were obtained from Stauffer Chemical Co.

Nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 spectrometer. Chemical shifts are reported as parts per million relative to tetramethylsilane. Infrared spectra were scanned on a Perkin-Elmer 337 spectrometer. Melting points were determined in a capillary and are uncorrected unless otherwise noted.

Vapor phase chromatography work was conducted on an F & M Model 500 unit.

1-(Arylthiocarbonyl)aziridines (1, 3, 4, and 5).—These compounds were obtained in good yield according to Heine's method.[2] Alternatively, they were prepared by the following general procedure.

A solution of arylthiochloroformate (0.1 mol) in 150 ml of anhydrous ether and protected from atmospheric moisture was vig-

(14) H. W. Heine, D. C. King and L. A. Portland, *J. Org. Chem.*, **31**, 2662 (1966).
(15) G. E. Ham, *J. Org. Chem.*, **29**, 3052 (1964).
(16) H. Rivier, *Bull. Soc. Chim.*, [4] **1**, 733 (1907).
(17) R. H. deWolfe and W. G. Young, *Chem. Revs.*, **56**, 769 (1956).
(18) C. Scholtissek, *Chem. Ber.*, **89**, 2562 (1956).
(19) Y. Iwakura and A. Nabeya, *J. Org. Chem.*, **25**, 1118 (1960); **26**, 4384 (1961).

orously stirred at 0–5° while a solution of triethylamine (0.1 mol) in 50 ml of dry ether was added dropwise over a period of 20 min. Under these same conditions, a solution of aziridine or 2-methylaziridine (0.1 mol) was then added to this vigorously stirred slurry over a period of 20 min. The reaction mixture was stirred at room temperature for 20 min and then filtered. Evaporation of the etheral filtrate gave either an oil or a crystalline product with physical properties as indicated below.

Compound **1** was obtained from petroleum ether (bp 30–60°) in 86% yield as a white crystalline material, mp 40–41° (lit.[2] mp 39–41°). The infrared spectrum (Nujol) showed carbonyl absorption at 5.88 and 5,91 μ. The nmr spectrum (CCl_4) consisted of a multiplet centered at −7.36 and a singlet at −2.27 ppm in a ratio of 5:4.

Compound **3** was obtained from petroleum ether in 81% yield as glittering white crystals, mp 64.5–66°. The infrared spectrum (Nujol) showed carbonyl absorption at 5.98 μ. The nmr spectrum ($CDCl_3$) consisted of a singlet at −7.39 and a singlet at −2.36 ppm in a ratio of 1:1.

Anal. Calcd for C_9H_8ClNOS: C, 50.58; H, 3.77; N, 6.55. Found: C, 50.49; H, 3.66; N, 6.41.

Compound **4** was obtained from petroleum ether (bp 50–60°) as a low-melting solid, mp 28–29°, in 71% yield. The infrared spectrum (neat) showed carbonyl absorption at 5.90 μ.

Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.14; H, 5.73; N, 7.24. Found: C, 61.87; H, 5.52; N, 6.98.

Compound **5** was obtained as a nearly colorless, thermolabile oil in 82% yield. Attempts to distil this material resulted in the formation of the isomeric isocyanate and polymers. The infrared spectrum (neat) showed carbonyl absorption at 5.87 μ.

Anal. Calcd for $C_{10}H_{10}ClNOS$: C, 52.74; H, 4.42; N, 6.15. Found: C, 52.43; H, 4.31; N, 5.82.

Rearrangement of Unpurified 1-(*p*-Chlorophenylthiocarbonyl)-aziridine (3) at Room Temperature.—A sample of unpurified aziridine **3**, which melted at 61–63° (glittering white plates), was allowed to stand at room temperature in a stoppered bottle for 1.25 hr. During that time, the solid transformed into a colorless oil which was found by infrared spectroscopy to be nearly all isocyanate. Over a period of 6 days, the oil resolidified to a white solid. Recrystallization from an acetone–methanol mixture gave a white powder melting at 115–116°. The yield was essentially quantitative. Infrared and nmr analysis identified the solid product as N,N′,N″-tris-2-(*p*-chlorophenylthioethyl) isocyanurate. The infrared spectrum showed carbonyl absorption at 5.90 μ. The nmr spectrum consisted of a singlet at −7.30 ppm and two sets of triplets centered at −4.07 and −3.10 ppm ($CDCl_3$). Proton integration revealed a ratio of 2:1:1 for the resonances as reported above.

Anal. Calcd for $C_{27}H_{24}Cl_3N_3O_3S_3$: N, 6.55. Found: N, 6.32.

1-Phenylthio-2-propyl Isocyanate (6). Method A.—Dry hydrogen chloride was bubbled through a stirred solution of 1-phenylthio-2-propylamine[20] (47.0 g, 0.282 mol) in 250 ml of anhydrous *p*-xylene until 18.3 g (0.5 mol) had been taken up. The reaction mixture was heated to 100° and maintained at that temperature while phosgene was bubbled through. After a total of 111 g (1.12 mol) had been taken up, the reaction mixture was allowed to stir for 1 hr at 100° and then refluxed for 3 hr. Solvent was removed by distillation at atmospheric pressure, leaving an amber-colored oil residue which distilled at 155–157° (18 mm) and weighed 43.9 g (79%).

Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.14; H, 5.74; N, 7.25. Found: C, 61.98; H, 5.78; N, 7.14.

Method B.—1-(Phenylthiocarbonyl)-2-methylaziridine (21.2 g, 0.11 mol) and 60 μl of triethylamine in 150 ml of dry benzene were refluxed for 14.25 hr under anhydrous conditions. Solvent was removed under vacuum at room temperature, leaving a light amber-colored liquid residue. Distillation of this material gave a colorless fraction boiling at 142–143° (10 mm) which weighed 12.1 g. This product was spectroscopically identical with the material obtained by method A. Then mr spectrum (CCl_4) consisted of a multiplet centered at −7.27 ppm, a quintuplet at −3.57 ppm, a doublet at −2.95 ppm, and a doublet at −1.30 ppm. The protons were present in a ratio of 5:1:2:3, respectively.

N-(1-Phenylthio-2-propyl)-O-ethylcarbamate (9). Method A.—To a vigorously stirred solution of 33.4 g (0.2 mol) of 1-phenylthio-2-propylamine[20] and 20.2 g (0.2 mol) of triethylamine dissolved in 75 ml of dry benzene was added 21.2 g (0.2 mol) of ethyl chloroformate in 25 ml of benzene. The dropwise addition was conducted at such a rate that the temperature did not exceed 45°. The solution was stirred at room temperature for 20 min, triethylamine hydrochloride was filtered off, and solvent was evaporated to give a heavy yellow oil which weighed 21.05 g (44%). The crude product distilled at 159–160° (4.5 mm); however, it was invariably accompanied by isocyanate **6** as a minor impurity. Pyrolysis appears to occur during the course of distillation.

The infrared spectrum (neat) contained a medium-intensity absorption at 3.00 μ (NH) and a high-intensity carbonyl absorption at 5.88 μ.

Method B.—A solution of 1-(phenylthiocarbonyl)-2-methylaziridine, (**4**), mp 26–28°, and 15 μl of triethylamine in 50 ml of absolute ethanol was refluxed for 3 hr. Solvent was removed under reduced pressure, leaving an amber-yellow oil. Infrared and nmr analysis of this material showed that it was identical with the product obtained by method A. Distillation of this material gave a major fraction boiling at 140–153° (2.5 mm) which, according to infrared analysis, contained substantial amounts of 1-phenyl-2-propyl isocyanate (intense absorption band at 4.42 μ).

Pyrolysis of 9 from Method B.—A 0.6-μl sample of the crude **9** obtained by method B was injected onto a 10-ft silicone gum rubber column with an injection port temperature of 350°. Complete pyrolysis to **6** and ethanol was observed. The chromatogram consisted of two clean peaks with retention times of 1.0 and 7.1 min. A synthetic solution consisting of 25 μl of 1-phenylthio-2-propyl isocyanate in 10 drops of absolute ethanol was chromatographed under the same conditions. The chromatogram of this sample consisted of two peaks with retention times of 1.0 and 7.0 min. Nmr and infrared analyses also corroborated the identities of the pyrolysates.

Reaction of 1 with Methanolic Sodium Iodide.—Sodium iodide (4.0 g, 0.0267 mol) was dissolved in 20 ml of anhydrous methanol and to that solution was added 1.0 g (0.0056 mol) of 1-(phenylthiocarbonyl)aziridine (**1**). The reaction mixture was allowed to stand at room temperature for 1 hr and was then extracted with 200 ml of benzene. The benzene layer was washed with two 100-ml portions of distilled water, dried with anhydrous sodium sulfate, and filtered, and the benzene was removed under vacuum. A white solid weighing 0.80 g (mp 56–61°) was obtained which had an infrared spectrum identical with that obtained for authentic N-(2-phenylthioethyl)-O-methylcarbamate. No N-(2-iodoethyl)-O-methylcarbamate could be detected by infrared spectroscopy.

Reaction of N-(2-Iodoethyl)-O-ethylcarbamate with Potassium Thiophenolate in the Presence of Sodium Iodide.—Sodium iodide (3.1635 g, 0.0211 mol) and potassium thiophenolate (0.8294 g, 0.00559 mol) were dissolved in 20 ml of anhydrous methanol. To this solution was added 1.3566 g (0.00558 mol) of N-(2-iodoethyl)-O-ethyl carbamate. After 1 hr at room temperature, the reaction mixture was worked up exactly as described in the previous experiment. A low-melting solid weighing 1.00 g was isolated which had an infrared spectrum identical with authentic N-2-(phenylthioethyl)-O-ethylcarbamate. Recrystallization from *n*-hexane gave 0.48 g of white crystals, mp 39–41°. An admixture melting point with authentic carbamate was undepressed.

N-(2-*p*-Chlorophenylthioethyl)-O-methylcarbamate (11). Method A. Reaction of 3 with Methanol Containing Triethylamine Catalyst.—To 25 ml of absolute methanol was added 2.0 g (0.0093 mol) of 1-(*p*-chlorophenylthiocarbonyl)aziridine and 25 μl of triethylamine. The homogeneous solution was allowed to stand at room temperature for 22 hr. Evaporation of solvent gave a white solid residue melting at 74–78°. This crude material was slurried in petroleum ether (bp 30–60°) and filtered to give 2.1 g (93%) of a white powdery product, mp 76–81°. Recrystallization from diethyl ether yielded white crystals, mp 82.5–83.5°. The infrared spectrum (Nujol) contained an NH stretching absorption at 3.03 μ and a strong carbonyl absorption at 5.93 μ.

Anal. Calcd for $C_{10}H_{12}ClNO_2S$: N, 5.70. Found: N, 5.59.

Method B. Dehydrohalogenation of 12 with Methanolic Sodium Hydroxide.—N-(2-Chloroethyl)-S-(*p*-chlorophenyl)thiocarbamate (12.45 g, 0.05 mol) was added to a solution of sodium hydroxide (2.0 g, 0.05 mol) in 100 ml of absolute ethanol. The reaction mixture was refluxed for 1 hr, sodium chloride was

(20) L. Clapp and G. Mequerian, *J. Amer. Chem. Soc.*, **75**, 2121 (1951).

filtered, and evaporation of the filtrate gave a white solid residue. This crude material was slurried in two 15-ml portions of cold water and dried. The product weighed 10.3 g (74%), mp 73–76°. Recrystallization from diethyl ether raised the melting point to 81–82°. An admixture melting point with material prepared by method A was undepressed. Infrared and nmr spectra were also identical with those obtained by Method A.

N-(2-Chloroethyl)-S-(*p*-chlorophenyl)thiocarbamate (12). Method A.—A solution of *p*-chlorophenyl thiochloroformate (0.5 mol) in 200 ml of chloroform was stirred at 5–10° while a solution of 0.5 mol of aziridine in 20 ml of chloroform was added dropwise over a period of 40 min. The reaction temperature was maintained at 10–17° during the addition period. The solution was stirred for 1 hr at room temperature and then refluxed for 3 hr, and the solvent was evaporated to give a 96% yield of white crystalline product. Recrystallization from diethyl ether gave glittering white needles melting at 98–99°.

Anal. Calcd for $C_9H_9Cl_2NOS$: C, 67.49; H, 5.66; N, 8.75. Found: C, 67.41; H, 5.55; N, 8.63.

N-(2-chloroethyl)-S-phenylthiocarbamate was also prepared by the above method in 95% yield as white needles from diethyl ether; it had mp 82–83.5°.

Method B.—A 0.015-mol quantity of either **1** or **3** was added in one portion, with stirring, to 25 ml of concentrated (36%) hydrochloric acid. The suspension was allowed to stir for 20 min at room temperature and then warmed on a steam bath for 10 min. A white precipitate remained; after the suspension had cooled, it was filtered. The infrared spectra of these products were identical with those obtained for carbamates prepared by method A.

Kinetic Measurements.—Stock solutions of **1** and potassium thiophenolate were made up with a solvent consisting of 90% acetonitrile–10% methanol (v/v). Under anhydrous conditions and in a nitrogen atmosphere, various quantities of each stock solution and solvent were mixed to obtain desired concentrations. The "zero" time was recorded as the time at mixing. These reaction mixtures were placed in a vial equipped with a rubber serum cap and kept in a constant-temperature bath at 28 ± 0.5°. Samples were withdrawn at various time intervals with a needle syringe and charged into a fixed-volume NaCl cell. Times were recorded during the scan at the peak of the 11.75-μ band. The same cell was used for all the kinetic runs. The temperature of the sample in the infrared beam did not vary significantly from the reaction bath temperature. At 100% conversion the base line is completely flat in the 11.75-μ region. Completely clear, homogeneous solutions were obtained after 100% conversion.

"Cross-Over" Reaction.—To 25 ml of sodium-dried and redistilled *p*-xylene was added 300 mg of aziridine **1**, 300 mg of aziridine **5**, and 15 μl of anhydrous triethylamine. This reaction mixture was refluxed under anhydrous conditions for 1 hr. A 15-μl sample of this reaction mixture was injected onto a 10-ft silicone gum rubber column under the following conditions: flow rate, 60 ml/min; inlet pressure, 35 lb/in.^{2}; detector temperature, 350°; injection port temperature, 200°. The column temperature was programmed from 200 to 275° at a rate of 11°/min. The chromatogram consisted of four peaks, in addition to the solvent peak, with retention times of 6.7, 7.0, 8.9, and 9.1 min. These peaks were identified as isocyanates **2**, **6**, **14**, and **7**, respectively, by comparison with the chromatogram obtained for a synthetic mixture containing authentic samples of each of the above isocyanates.

Registry No.—**1**, 22040-27-3; **3**, 22040-28-4; **4**, 22039-86-7; **5**, 22039-87-8; **6**, 22039-88-9; **9**, 22039-89-0; **11**, 22103-89-5; **12**, 22039-90-3; N,N′,N″-tris-2-(*p*-chlorophenylthioethyl) isocyanurate, 21252-94-8.

Mass Spectrometric Studies. I. The Fragmentation of Methyl Cyclohexyl Ether[1]

GERALD W. KLEIN[2] AND VINCENT F. SMITH, JR.

Department of Chemistry, University of Wyoming, Laramie, Wyoming 82070

Received May 2, 1969

The electron impact induced mass spectra of methyl cyclohexyl ether (**1a**) and six deuterated analogs have been obtained. With the aid of high-resolution techniques, the range of available deuteriated analogs has permitted a very thorough understanding of the spectrum of **1a**. The major decomposition modes of the molecular ion of **1a** have been found to parallel closely the reported fragmentations of cyclohexyl alcohol and methyl cyclobutyl ether, and, just as was found for these compounds, it is initial β cleavage which accounts for the major portion of ions in the spectrum of **1a** and renders this spectrum, too, substantially different from the spectra of acyclic ethers. The base peak in the spectrum, found at *m/e* **71** $(CH_2O{=}CHCH{=}CH_2)^+$, arises *via* β cleavage of the molecular ion followed by hydrogen transfer and carbon–carbon bond homolysis. One of the features common to the spectra of cyclic and acyclic ethers, 1,3 and 1,4 elimination of the elements of ROH, is discussed as a potentially powerful analytical technique for the measurement of the stereochemistry of deuterium incorporation reactions in ring compounds. The synthetic procedures by which the deuteriated analogs of **1a** have been prepared are described in detail.

A considerable body of data has been amassed from the electron impact induced mass spectra of aliphatic ethers and alcohols.[3] From these data the more significant fragmentation processes undergone by aliphatic ethers and alcohols have been determined and are found to be similar in many ways. The usefulness of the data compiled on these and other classes of compounds in the elucidation of organic structures is great and needs no discussion here. However, owing to the lack of analogy between cyclic and acyclic spectra, difficulties are encountered when attempts are made to use mass spectrometric data from acyclic compounds in structure proofs of ring-containing compounds. The differences between the spectra of these classes of compounds may arise because of higher symmetry and uniquely restricted intramolecular interactions imposed by the rings. The resulting spectra, more often than not, possess few of the features of acyclic analogs. For example, the mass spectra of two cyclic methyl ethers, cyclobutyl and cyclopropyl carbinyl, have recently been reported,[4] and both show base peaks at *m/e* 58, an ion not found to be of significance for acyclic ethers and quite obviously an ion arising as a consequence of the presence

(1) Acknowledgment is made to the Research Corporation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

(2) To whom inquiries should be addressed: Department of Chemistry, Columbia University, New York, N. Y. 10027.

(3) For general discussions and leading references, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, Chapters 2 and 6.

(4) W. G. Dauben, J. H. Smith, and J. Saltiel, *J. Org. Chem.*, **34**, 261 (1969).