The Reaction of Aziridine with Perhalogenated Nitriles

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Reaction of one or two molecules of aziridine with the cyano groups of trichloroacetonitrile and trifluoroacetonitrile was observed. The resulting aziridinyl amino derivatives represent novel functional groups. Intramolecular cyclization of a bis-aziridinyl structure involving one aziridinyl group was observed. New synthetic routes to imidazolines and imidazolidines are a result of these rearrangments.

Introduction.

The reaction of aziridine with halogenated acetonitriles was investigated. It had been demonstrated earlier that the perfluoroalkyl group increases the reactivity of the cyano group in perfluoroalkyl cyanides and that the addition of amines leads to *N*-alkylperfluoroamidines of the type **1** (Eq. 1) (1). At the same time, the fluoroboric acid catalyzed addition of aziridine to aryl and alkyl cyanides was shown to lead to imidazolines (Eq. 2) (2). In no instance was addition of a second molecule of amine observed.

Eq. 1 $R_f \cdot CN + HNR_2 \longrightarrow R_f \cdot C(=NH)NR_2$ $R_f = CF_3, C_2F_5, C_3F_7$; $R = H$ or CH_3

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Eq. 2 $R \cdot CN + H_2N^+(CH_2)_2 \; BF_4^- \longrightarrow R\text{-}C(=N^+H_2)\text{-}N(CH_2)_2 \; BF_4^-$ $R = CH_3$

We have now observed that this addition reaction is not restricted to perfluoroalkyl cyanides but that it can also be achieved on trichloroacetonitrile (**3**), and that the addition of a second molecule of amine to structures of the type **1** can be achieved when aziridine (**2**) is used as the amine. Thus, a 1,1-diaziridinyl-1-aminomethyl derivative is synthetically available.

Results.

Reaction of **2** and **3** at -20° in methylene chloride led to the amidine **4** in a yield of 72% (Scheme I). The structure of **4** was unambiguously demonstrated by two signals in the nuclear magnetic resonance spectrum at 2.43 and 9.82 ppm in a proportion of 4:1. The singlet resonance pattern for the aziridinyl protons at 2.43 ppm indicates that the temperature of coalescence of these protons is below ambient temperature in agreement with the observation on *N*-substituted aziridine derivatives containing electron withdrawing substituents (3). Additional proof for structure **4** is evident from its infrared spectrum (potassium bromide) which shows aziridinyl ring absorptions at 3005 cm^{-1} and absorptions due to the imino group at 1625 cm^{-1} and 3310 cm^{-1} (1% w/w) in carbon tetrachloride.

The addition of excess aziridine to **3** occurs readily at -20° to give 1,1,1-trichloro-2,2-diaziridinyl-2-aminoethane (**5**) in a yield of 59%. However, several repeated reactions gave inconsistent yields of this product. In fact, in one reaction, the rearranged product **6** was isolated in a yield of 55% as a consequence of minor changes in the reaction conditions, for example, when the crude reaction product was allowed to stand at ambient temperature for periods of several days.

On attempts to obtain a derivative of **5** in a reaction with allylisocyanate, product **4** was isolated in a yield of 52%, accompanied by the addition product **8**, indicating

$CH_2{=}C\text{-}CH_2\text{-}NCO + 5 \longrightarrow CH_2{=}CH\text{-}CH_2\text{-}N(H)\text{-}C(=O)\text{-}N\langle + 4$

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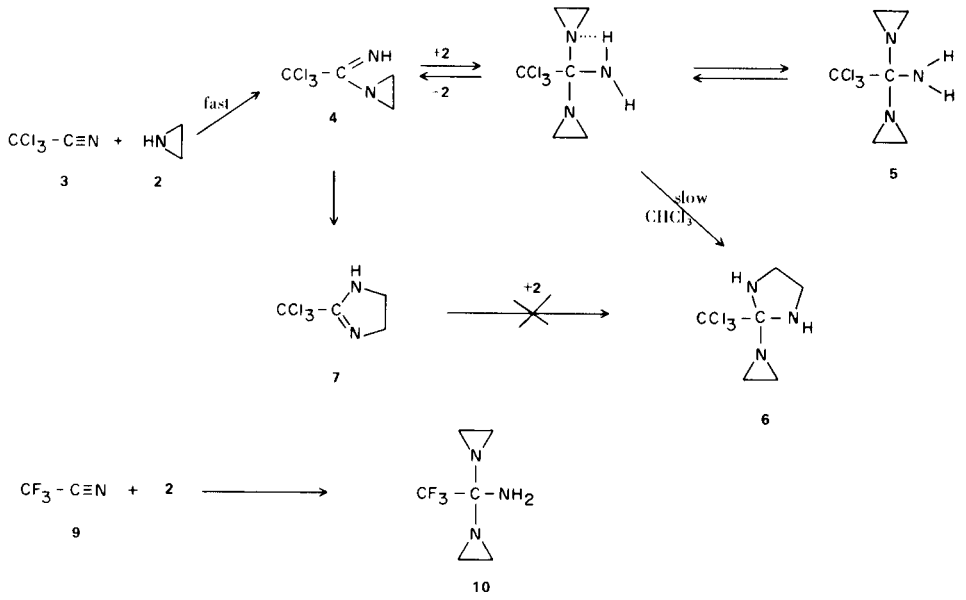
a tendency for dissociation of **5** into aziridine which is also evidenced by the formation of 2-trichloromethyl-4,5-dihydroimidazole (**7**) on repeated sublimations of **5** and was apparent in several instances when the infrared spectrum of **5** was recorded in potassium bromide pellets.

The structure of **5** was evident from spectroscopic characteristics. In the infrared spectrum of a potassium bromide pellet, carbon-hydrogen stretching frequencies at 3080 and 3005 cm^{-1} as well as the absence

Scheme 1



of "normal" frequencies in the range of 2800 to 2950 cm^{-1} suggested the exclusive presence of aziridinyl groups. Two absorption bands at 3370 and 3285 cm^{-1} indicated the presence of a primary amino group. A solution of **5** in pyridine showed a nuclear magnetic resonance spectrum in which the imino group, arising from the presence of **4**, was clearly separated as a single peak at 2.43 ppm (half-width 3 cps) (Fig. 1) whereas the protons of the aziridinyl and amino-groups showed an asymmetric pattern centred at approximately 1.44 ppm.

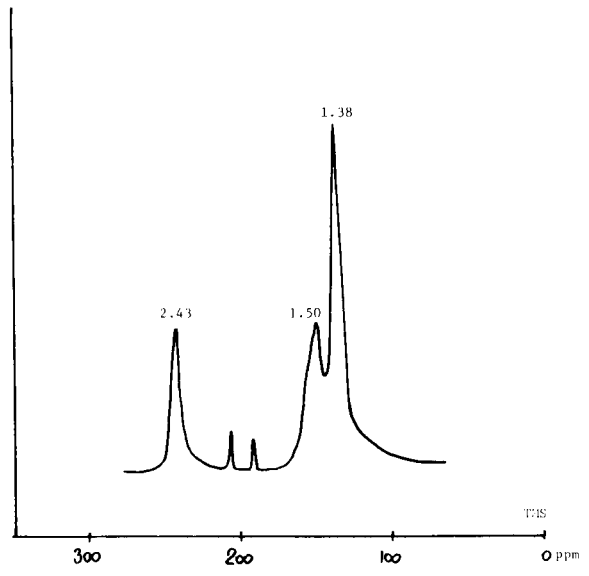


Fig. 1. The NMR Spectrum of **5** in Pyridine at 25°.

The nmr spectrum of **5** in deuteriochloroform was essentially identical with a spectrum of an equimolar solution of **4** and aziridine, (Fig. 2a) with characteristic signals at 2.43 and 1.61 ppm, respectively, in addition to a complex pattern for the remaining aziridinyl and amino-protons due to **5** at ~ 2 ppm, indicating the dissociation of **5** into **4** and **2**. The position of this equilibrium **2** + **4** ⇌ **5** was found to vary from 1:1.3 to 1:3.6. For example, a solution of **5** in deuteriochloroform at 21° exhibited values in the range of 1:2.5 to 1:3.6 and mixtures of **4** and aziridine under the same conditions show values of 1:1.37 and 1:3.5.

A solution of **5** in deuteriochloroform changed to a mixture containing 30% of **6** upon standing at room temperature for 5 days. Less than 5% of **6** was observed in an equimolar mixture of **4** and aziridine after 24 hours at 21°.

The structure of **6** is evident from its nmr spectrum which showed two multiplets for the aziridinyl protons at 1.19 and 1.75 ppm, indicating a significantly higher temperature of coalescence for the aziridinyl protons in **6** than in **5**. In addition, two multiplets of equal intensity were observed for the protons of the five membered ring at 2.45 and 3.48 ppm. The protons of both secondary amino groups are represented by a very wide signal at 6.25 ppm.

The formation of the imidazoline **7** was achieved readily from **5**. Treatment of **5** with sodium iodide led to **7** in a yield of 70%. The structure of **7** was demonstrated by an nmr signal for the amino proton at 5.62 ppm and a multiplet for the methylenic protons centred at 3.83 ppm (Fig. 3).

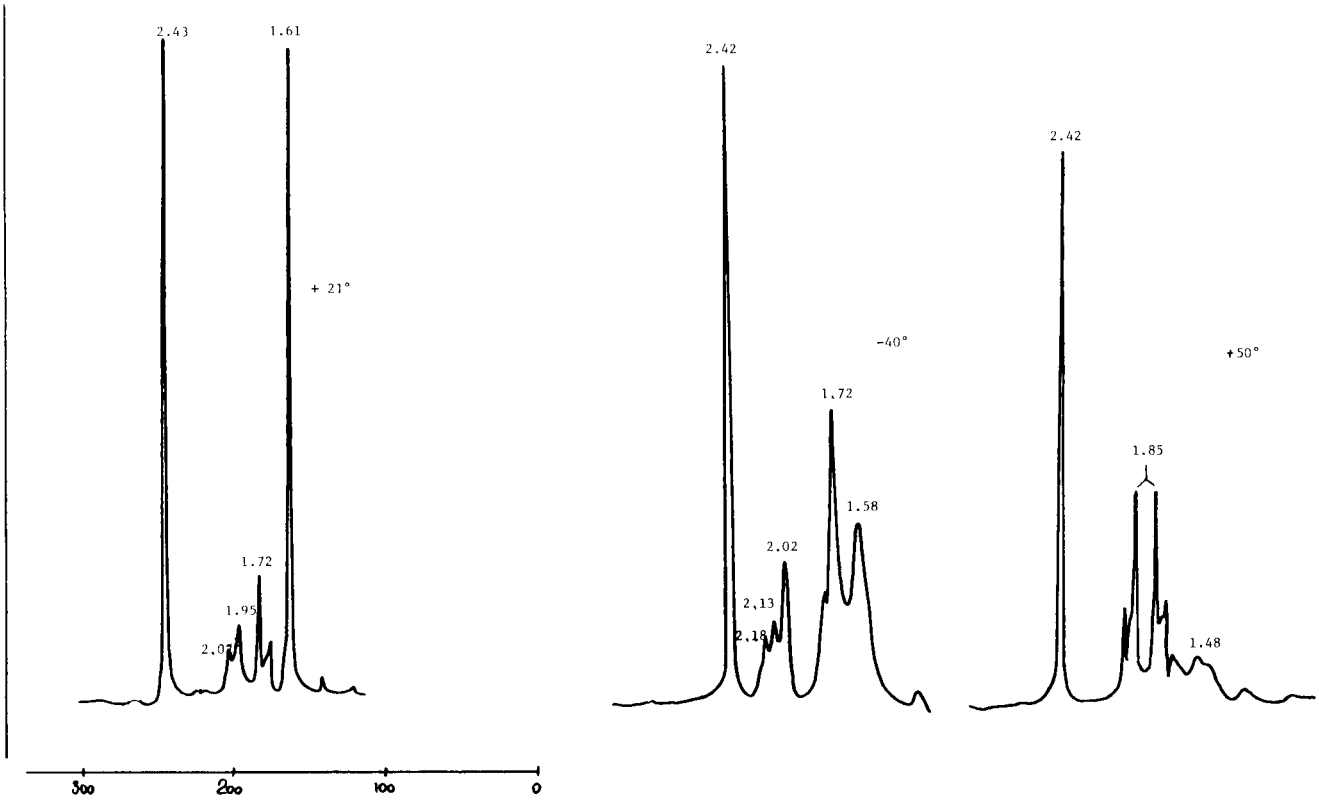


Fig. 2a. The NMR spectra of equimolar proportions of **4** and **2** in deuteriochloroform. The spectra were recorded in the order **2a** to **2c** with 30 minute intervals between recordings for temperature adjustment.

Fig. 2b.

Fig. 2c.

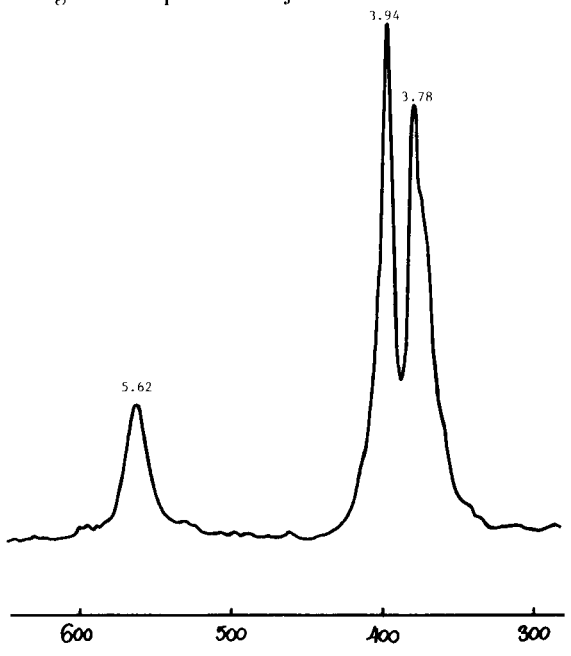


Fig. 3. The NMR Spectrum of **7** in Deuteriochloroform at 25°.

In order to decide whether the imidazoline **7** could represent the precursor the the "rearranged" structure **6**, the nuclear magnetic resonance spectrum of mixtures of **7** and aziridine was observed. On addition of an equimolar proportion of aziridine to **7**, a significant change in the spectrum of **7** was observed (Fig. 4). The spectrum showed collapse of the splitting pattern for the CH_2 groups at 3.83 ppm as it was observed in **7** to a single signal of a half-width of 5 cps. Broadening of this signal was observed at -40° (half-width 20 cps) without evidence for splitting, and in addition, a broad signal at 7.35 became apparent. This change was found to be reversible on heating to +20°. Addition of a second molar equivalent of aziridine caused a further narrowing of the signal at 3.83 ppm (half-width ~ 2.5 cps) at 21° and on cooling of this solution to -40°, splitting of the signal, which is not identical with the splitting pattern of **7** at 20°, was observed (Fig. 5). This is accompanied by the appearance of a sharp signal for the downfield proton (NH). Even on observing the solution for a period of twelve days, no indication for the formation of **6** was observed under these conditions. Furthermore, on evaporation only **7** was obtained. Further evidence for the absence of a reaction between **7** and aziridine was provided by the infrared spectrum of a mixture of both components in

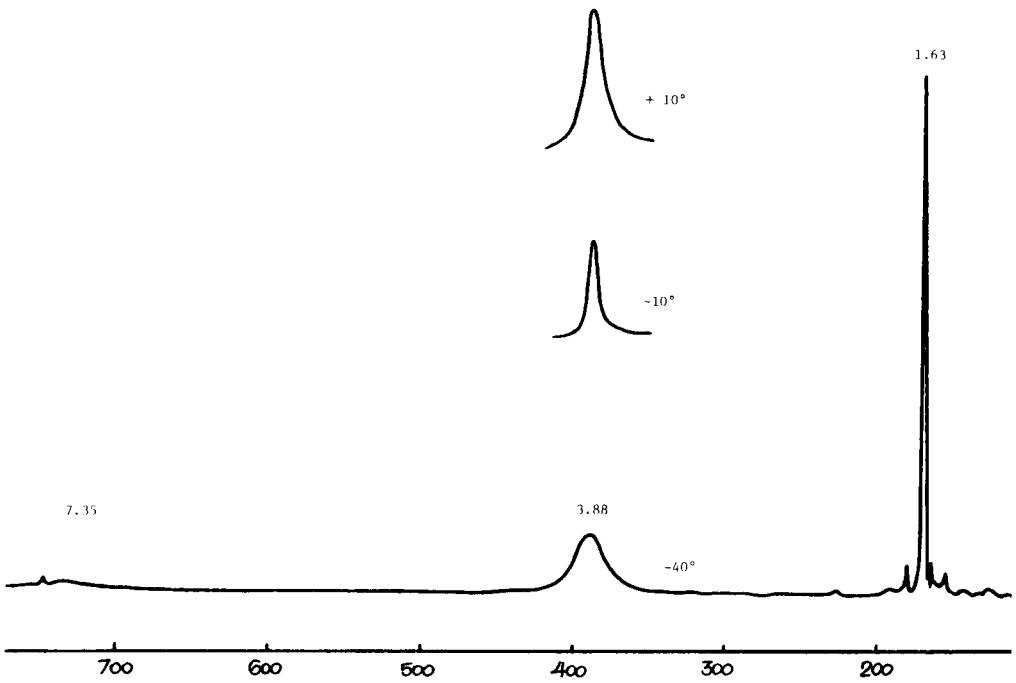


Fig. 4. The NMR spectrum of a solution of **7** in deuteriochloroform containing one molar equivalent of aziridine.

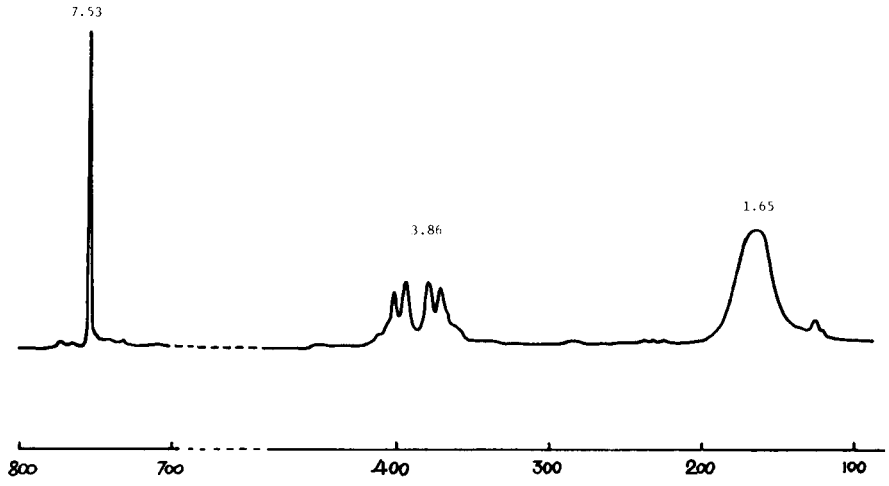


Fig. 5. The NMR spectrum of a solution of **7** in deuteriochloroform at -40° containing two molar equivalents of aziridine.

chloroform, which showed the absence of bands other than those arising from the components. The conversion of **7** to **6** was also not achieved in a more polar solvent such as pyridine, as evidenced by the nuclear magnetic resonance spectrum of that solution.

In analogy to the addition of aziridine to **1**, addition to trifluoroacetonitrile (**9**) leads to the addition product **10** in a yield of 98% (Scheme 1). The structure of **10** was again evident from spectroscopic characteristics. In the infrared spectrum, recorded in a potassium bromide pellet, high frequency carbon-hydrogen stretching bands at 3080 and 3005 cm^{-1} as well as the absence of absorption bands in the region of 2800 to 2950 cm^{-1} suggested the exclusive presence of aziridinyl groups. The nuclear magnetic resonance spectrum of **10** again showed partial dissociation. No detailed investigation of the dissociation and

rearrangement behavior of **10** was carried out.

The rearrangement of the initial addition product **5** to **6** can either proceed directly or involve dissociation of **5** into **2** and **4** with subsequent rearrangement of **4** to **7** and final reaction of **7** with aziridine. However, the failure to achieve a reaction between **7** and aziridine excludes this reaction path and supports an intramolecular reaction. This rearrangement would be favoured by intramolecular hydrogen bonding between the amino group and the aziridinyl nitrogen and would release molecular crowding in **5**, which arises from rotation or inversion of its aziridinyl groups. The absence of dissociation products in solutions of **6** is in contrast to the dissociation of **5** and emphasizes that **6** represents the thermodynamically favoured product in the reaction sequence of aziridine with trichloroacetonitrile.

The rearrangement of **4** to **7** is analogous to the rearrangement of *N*-acylaziridines and *N*-thioacylaziridines and represents an extension of this type of ring expansion to iminoaziridines. Thus, a novel route to imidazolines by the addition of aziridine to perhalogenated nitriles is provided.

EXPERIMENTAL

Nuclear magnetic resonance spectra of 10% (w/w) solutions were recorded on a Joel HR-100 instrument using tetramethylsilane as internal standard. Melting points were recorded on a Hallenkamp block and infrared spectra on a Perkin-Elmer 521 grating instrument, either in potassium bromide for solids or neat for liquids.

Aziridine was distilled before use and stored over potassium hydroxide pellets. Trichloroacetonitrile was fractionated before use. Trifluoroacetonitrile was commercial grade as supplied by Pierce Chemical Co., Rockford, Illinois, U.S.A.

The Reaction of Trichloroacetonitrile with Excess Aziridine. 1,1,1-Trichloro-2,2-diaziridinyl-2-aminoethane (**5**).

To a solution of 25.5 g. of trichloroacetonitrile in 100 ml. of methylene chloride was added 86 g. (2 moles) of aziridine at an internal temperature of -20° with stirring over a period of 30 minutes. After that time, gas chromatographic analysis indicated the absence of unreacted trichloroacetonitrile. The cold suspension was filtered to give 24.2 g. (59%) of **5**, m.p. 128-129°. The residual filtrate was analyzed by infrared spectroscopy after evaporation of volatile components and found to consist largely of product **5**. Sublimation of 1.0 g. yielded 0.8 g. of an analytical sample of **5**, m.p. 129-131° (vac.).

The infrared spectrum showed characteristic absorptions for the amino group at 3370, 3280 and 1623 cm^{-1} and C–H stretching frequencies at 3090, 3070 and 3000 cm^{-1}.

Anal. Calcd. for $C_6H_{10}Cl_3N_3$: C, 31.26; H, 4.37; N, 18.23; Cl, 46.14. Found: C, 31.22; H, 4.38; N, 17.93; Cl, 46.30.

The Reaction of Trichloroacetonitrile with Aziridine. 2-Trichloromethyl-2-aziridinylimidazolidine (**6**).

To a solution of 125 g. (0.864 mole) of trichloroacetonitrile in 500 ml. of methylene chloride was added 86 g. (2 moles) of azirdine at an internal temperature of -20°. The solution was then allowed to stand at +20° for 3 days and partially evaporated on a rotary evaporator to give, after filtration, 109.5 g. (55%) of crystalline **6**, m.p. 101-110°. The infrared spectrum shows the absence of isomer **5**.

An analytical sample of **6**, m.p. 107-109°, was obtained by sublimation or recrystallization from chloroform. Product **6** is distinguished from product **5** by infrared absorption peaks at 3365, 1655, 1633, 1310 and 1010 cm^{-1} with additional broad absorption bands at 3320 and 3090 cm^{-1}. Absorption bands between 2820 and 2950 cm^{-1} indicate the presence of CH_2 groups other than in an aziridinyl ring structure. Fractional crystallization of the mother liquor of the crude product **6** gives various proportions of additional **6** as well as both **5** and **7**.

Anal. Calcd. for $C_6H_{10}Cl_3N_3$: C, 31.26; H, 4.37; N, 18.23; Cl, 46.14. Found: C, 31.63; H, 4.17; N, 18.20; Cl, 46.00.

The Reaction of Trifluoroacetonitrile with Aziridine. 1,1,1-Trifluoro-2,2-diaziridinyl-2-aminoethane (**10**).

To a solution of 49.5 g. (0.52 mole) of trifluoroacetonitrile in 100 ml. of methylene chloride was added 70.3 g. (1.63 moles) of aziridine at an internal temperature of -20° over a period of 10 minutes. After standing for 12 hours at -20°, the solution was completely evaporated and 91.6 g. of product (97.1%) was obtained, m.p. 46-49.5°. Recrystallization from hexane increased the m.p. to 50-51.5° (80% recovery).

The structure **10** is evident from the high frequency of the carbon-hydrogen stretching in the infrared spectrum between 3000 and 3100 cm^{-1} and the absence of absorptions between 2970 and 2800 cm^{-1}.

Anal. Calcd. for $C_6H_{10}F_3N_3$: C, 39.78; H, 5.57; F, 31.49; N, 23.20. Found: C, 39.48; H, 5.50; F, 31.75; N, 23.28.

The Reaction of Aziridine with Trichloroacetonitrile. 1-Imino-1-aziridinyltrichloroethane (**4**), and 2-Trichloromethyl-4,5-dihydroimidazole (**7**).

To a solution of 13.6 g. (0.094 mole) of trichloroacetonitrile in 60 ml. of methylene chloride was added 4.3 g. (0.1 mole) of aziridine at an internal temperature of -20°. The solution was then allowed to warm up to ambient temperature and after 48 hours, the solvent was evaporated on a rotary evaporator to leave 18.0 g. of an oily residue. Distillation through a 10 cm Vigreux column gave 13.0 g. (72%) of **4**, b.p. 37-39°/0.5 mm Hg; $n_D^{25} = 1.5180$.

The crystalline distillation residue (1.5 g.) was identified as **7** by its infrared spectrum and, after sublimation, by a mixture melting point with the product obtained by treatment of **5** with potassium iodide.

Rearrangement of **5** with Potassium Iodide. 2-Trichloromethyl-4,5-dihydroimidazole (**7**).

To a solution of 2 g. of **5** in 20 ml. of acetone was added 0.9 g. of potassium iodide and the suspension was refluxed for 8 hours. After evaporation to dryness on a rotary evaporator, the residue was extracted with benzene, the solution evaporated to dryness to give 1.4 g. (70%) of crude **7**, m.p. 122-124°. Sublimation yielded an analytical sample. The infrared spectrum showed major absorptions at 3130 (NH), 1608, 1488, 1461, 1282, 1043, 980, 820 and 785 cm^{-1}.

Anal. Calcd. for $C_4H_5Cl_3N_2$: C, 25.63; H, 2.69; N, 14.94. Found: C, 25.52; H, 2.63; N, 15.33.

The Reaction of Allylisocyanate with Aziridine.

To a solution of 8.6 g. of distilled aziridine in 25 ml. of methylene chloride was added dropwise, a solution of 16.6 g. of

allylisocyanate in 25 ml. of methylene chloride at 25°. A slight temperature rise to ~35° was observed during the addition. After one hour, the volatile components were removed by distillation and a fraction of **8**, m.p. 82-84°/0.7 mm Hg, 10.1 g. was collected.

The infrared spectrum of **8** indicates the presence of aziridinyl hydrogens by absorptions at 3065 and 2995 cm^{-1}, vinylic unsaturation (985 and 917 cm^{-1}) in addition to strong absorption bands at 3280 and 1650 (broad) cm^{-1} due to the NH–CO– group.

Anal. Calcd. for $C_6H_{10}N_2O$: C, 57.12; H, 7.98; N, 22.21. Found: C, 56.99; H, 8.04; N, 22.06.

The Reaction of **5** with Allylisocyanate.

To a solution of 10 g. (0.04 mole) of **5** in 20 ml. of methylene chloride was added 3.6 g. (0.035 mole) of allylisocyanate at an internal temperature of 0°. After keeping the solution at 25° for 12 hours, the product was distilled to give 4.2 g. of **4**, m.p. 33-35°/0.1 mm Hg; 4.6 g. of **8**, b.p. 71.5-73°/0.1 mm and a crystalline residue which was identified to be **7** by mixture melting point and infrared analysis.

Product **4** is characterized as an isomer of **7** by its infrared and nuclear magnetic resonance spectra.

Product **8** was identified by comparison of its infrared spectrum with an authentic sample prepared from allylisocyanate and aziridine.

Anal. Calcd. for $C_4H_5Cl_3N_2$: C, 25.63; H, 2.69; N, 14.94; Cl, 56.74. Found: C, 25.44; H, 2.67; N, 14.95; Cl, 56.35.

Attempted Addition of Aziridine to **7**.

Equimolar proportions of **7** and **2** in both chloroform and pyridine (10% by weight) were allowed to stand at ambient temperature for a total of 7 days. Both infrared and nuclear magnetic resonance spectra showed no indication for product formation and **7** was recovered from that chloroform solution after evaporation and sublimation of the crystalline residue.

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