"Abnormal" Isomers by Amine Cleavage of Basic Uncharged 1-*t*-Butylaziridines

V. R. Gaertner

Research Department, Organic Chemicals Division,
Monsanto Company, St. Louis, Missouri 63166

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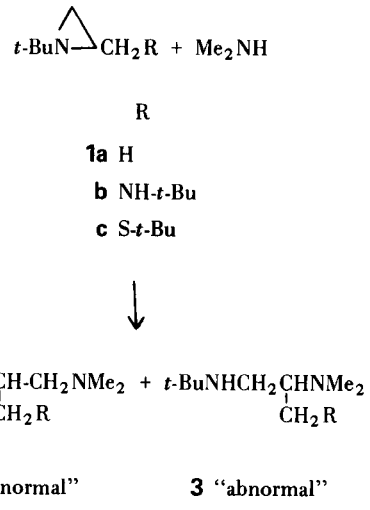
Sir:

We wish to report that three uncharged basic aziridines (1) and the corresponding aziridinium acid cations were opened by dimethylamine to give, in addition to the "normal" products, minor amounts of the "abnormal" isomers. The effects of solvents and an acid catalyst on the product ratios supported the S_N2 mechanism alone, rather than duality with any S_N1 process, as the genesis of the "abnormal" products.

Openings of unsymmetrically-substituted basic aziridines (such as **1**) by strong nucleophiles, especially amines and sulfur anions (2), form "normal" products (3), *e.g.*, **2**, by S_N2 attack at the less-substituted ring carbon atom.



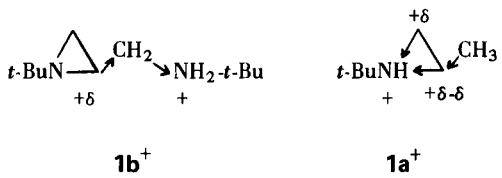
With weaker nucleophiles and activated aziridines, dual S_N2-S_N1 mechanisms are generally accepted, "abnormal" attack at the more-substituted ("S_N1-susceptible") carbon being attributed to the S_N1 route (4).

Evidence for the latter pathway includes the fact that acid catalysts and more polar solvents favor formation of the isomer. However, mechanistic studies have involved quaternization (5), acid catalysis, or activation by negative *N*- or *C*-substituents.

Recently we reported the alkylation of *t*-butylamine by aminomethylaziridine **1b** under moderate aprotic conditions in the presence of an acid scavenger (6). This apparent exception to the rule that a basic aziridine is opened by nucleophiles only *via* the aziridinium cation (7) suggested a comparison of the uncharged bases (1,8) **1a** (9), **1b** (6) and **1c** (9) with their aziridinium acid cations in solvents of varying polarity to determine the effect of the ring system unperturbed by a charge on nitrogen or other activation.

"Abnormal" isomers (**3**) were formed in minor amounts. In two series, **a** and **c**, the mixtures were completely resolved by gas chromatography (gc) and for **b** the nmr spectra provided both identification and quantification. Alternative syntheses gave mixed isomers **2a** and **3a**, by *t*-butylamine addition (11) to the 2,*N*,*N*-trimethylaziridinium ion from 1-dimethylamino-2-propyl chloride (12), and pure **2b** and **3b**, by opening (8) 3-*t*-butylamino-1-*t*-butylazetidine (6) with dimethylamine and 1-*t*-butyl-3-dimethylaminoazetidine (6) with *t*-butylamine. Finally, the mixture of isomers **2c** and **3c** was desulfurized with Raney nickel catalyst to a corresponding mixture of **2a** and **3a**.

In the Table are listed the results of varying the reaction conditions. Most striking is the fact that 1-*t*-butyl-2-methylaziridine (**1a**) opened to form *less* of the "abnormal" isomer (**3a**) as solvent polarity and acidity *increased* in the order: dioxane, dimethylamine, water, aqueous trifluoroacetic acid (runs 1-4). The methyl group stabilizes an electrophilic center to which it is bonded. Since its effect here was to *decrease* nucleophilic attack at C-2, under conditions which increasingly favored the S_N1 mechanism, this result is clearly inconsistent with any S_N1 process.



TABLE

Opening of 1-*t*-Butylaziridines by Dimethylamine at 110°.

Run (a)	Substituent	Medium	Time, days	Ratio of "Normal" to "Abnormal" Isomers, 2:3 (10, d)
1	2-CH_3 (**1a**)	dioxane	15	91.1: 8.9 **a** (e)
2	2-CH_3 (**1a**)	Me_2NH	6	93.4: 6.6 **a**
3	2-CH_3 (**1a**)	water	4	95.4: 4.6 **a**
4	2-CH_3 (**1a**)	water (TFA, b)	1	96.4: 3.6 **a**
5	2-*t*-$BuNHCH_2$ (**1b**)	Me_2NH	7	94.2: 5.8 **b** (f)
6	2-*t*-$BuNHCH_2$ (**1b**)	Me_2NH (TFA, c)	2	93.5: 6.5 **b**
7	2-*t*-$BuNHCH_2$ (**1b**)	water	3	93.7: 6.3 **b**
8	2-*t*-$BuNHCH_2$ (**1b**)	water (TFA, c)	1	89.9:10.1 **b**
9	2-*t*-$BuSCH_2$ (**1c**)	Me_2NH	13	95.7: 4.3 **c** (g)
10	2-*t*-$BuSCH_2$ (**1c**)	water (TFA, c)	1	94.6: 5.4 **c**

Footnotes: (a) General procedure: Purified aziridine (0.01-0.02 mole) was charged to a glass-lined 25-ml. stainless steel bomb (being flushed with nitrogen). About 5 ml. of redistilled anhydrous dimethylamine was added to the cooled bomb, which was sealed and heated in the oven. Samples were checked by gc for completion. Runs in water used 10 ml. of 25% aqueous amine. (b) About 20 mole % trifluoroacetic acid added (caution: exothermic), based on aziridine. (c) About 100 mole % trifluoroacetic acid added. (d) As percentage of total isomers, **2** and **3**. Yields of distilled products were 80-85% (runs 1-4), 84-94% (runs 5-8), and 85-88% (runs 9, 10). (e) B.p. 55-56° at 10 mm. Analyses (area %) were by gc at 110° on column C (6). Residual dioxane (run 1) was poorly resolved from **2a** on this column but was determined separately on column A (6) at 70°. (f) B.p. 65-67° at 1 mm. Mole percentages were determined from nmr spectra. The expanded *t*-butyl region was recorded on the Varian HA-100 at 100 MHz in carbon tetrachloride (locksignal internal tetramethylsilane), then the curves were accurately simulated on the DuPont 310 Curve Resolver. The writer thanks Mr. Pierre A. Berger and Mrs. Claudette Deatherage for these determinations. Triamines **2b** and **3b** were not resolved on several gc columns. The two equal *t*-butyl singlets of **2b** were found 64.5 and 66.8 Hz downfield from internal TMS at 60 MHz, and the one of **3b**, 65.3 Hz, in chloroform-*d*. (g) B.p. 87-88° at 1 mm. Analyzed (area %) on column C (6) at 170°. Isomers **2c** and **3c** were also completely desulfurized with Raney nickel catalyst in boiling ethanol to give **2a** and **3a**, which were identified by nmr and gc as in (e).

The *t*-butylaminomethyl group in **1b** led to appreciably more "abnormal" isomer, **3b**, only with added acid (run 8), indicating that the acid cation (**1b**+, or dication **1b**++) activates the 2 position inductively as shown. This is supported by the small change seen for **1c** carrying the *t*-butylthiomethyl group (runs 9,10).

The data are consistent with the S_N2 mechanism. Tentatively, we suggest the methyl group deactivates the 2-position in the aziridinium cation, **1a**+ (relative to the 3 position), although both carbons are more electrophilic than in the uncharged aziridine.

These results imply that the S_N2-S_N1 duality usually invoked for activated aziridines and weaker nucleophiles is not significantly involved for a strong nucleophile. A broader experimental search for "abnormal" products in other S_N2 openings seems indicated.

REFERENCES

(1) H. Bestian, *Ann. Chem.*, 556, 219 (1950), claimed slow uncatalyzed addition of amines to ethylenimine at open reflux. It is reasonable to assume (2, p. 237) that adventitious acids such as carbon dioxide were catalysts. In the present work, precautions were taken to exclude such catalysts but minute traces may have been present; see the Table, footnote (a).

(2) O. C. Dermer and G. E. Ham, "Ethylenimine and Other Aziridines", Academic Press, New York, N. Y., 1969, pp. 230-240. This monograph contains an exhaustive bibliography.

(3) However, see, for example, L. B. Clapp, *J. Am. Chem. Soc.*, 70, 184 (1948), for isomers isolated from acid-catalyzed amine openings; "abnormal" structures were assumed.

(4) Ref. 2, pp. 206-219.

(5) D. R. Crist and N. J. Leonard, *Angew. Chem. Intern. Ed. Engl.*, 8, 962 (1969).

(6) V. R. Gaertner, *J. Org. Chem.*, 35, 3952 (1970).

(7) Ref. 2, p. 206.

(8) See V. R. Gaertner, *J. Heterocyclic Chem.*, 6, 273 (1969), concerning the use of hindering *N*-*t*-alkyl groups to promote clean alkylations by azetidines.

(9) Aziridines **1a** and **1c** were prepared from 1-*t*-butylamino-2-propanol and 1-*t*-butylamino-3-*t*-butylthio-2-propanol (8), respectively, by cyclization (6) of the unstable crude *O*-mesylates: **1a** (10, distilled from potassium), 24% yield, b.p. 38-39° at 80 mm.; **1c** (10), 76% yield, b.p. 62-63° at 1 mm.

(10) Consistent elemental analyses and nmr spectra were obtained for new compounds and for cleavage product mixtures.

(11) It is interesting that this reaction (69% yield) gave **2a** and **3a** in 12.9:87.1 ratio (area %) reversing the ratio of run 1 but preserving the relation of "normal" to "abnormal" attack.

(12) E. M. Schultz and J. M. Sprague, *J. Am. Chem. Soc.*, 70, 48 (1948).