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REARRANGEMENTS OF 1-t-BUTYL-3-CHLOROAZETIDINE AND 1-t-BUTYL-2-CHLOROMETHYLAZIRIDINE

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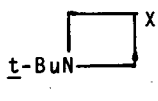
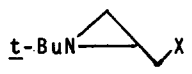
The title heterocycles, 1a and 2a, are analogs of cyclobutyl and cyclopropylmethyl halides, rearrangements of which have been widely considered to involve nonclassical carbonium ions, with delocalization as the driving force for ionization (1). However, recent studies indicated that such ring-strained ions are distinct species (2), and the cyclobutyl cation was termed "completely classical" (3).



1a. Cl
1b. CN
1c. OAc
1d. OTs



2a. Cl
2b. CN
2c. OAc

Ring expansion and cleavage have been observed in the few known reactions of related heterocycles. Both 2-chloromethylthiirane and 3-chlorothietane were reported to ionize with sulfur participation to the classical bicyclic sulfonium ion,  , which alkylated nucleophiles with cleavage of the cross-ring bond, yielding only 3-substituted thietanes (4). The 1-benzenesulfonyl-2-aziridinylmethyl carbonium ion expanded to the -2-azetidinyl cation, or a nonclassical intermediate, and then cleaved, during Friedel-Crafts alkylation of benzene by the bromide (5).

We report here examples of ring contraction, expansion, and cleavage in reactions of 1a and 2a* The chloroazetidine partially isomerized thermally to aziridine 2a, either in solution, or in gas chromatography (gc) on a

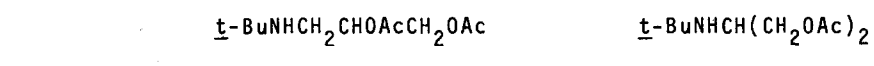
*1-t-Butylamino-3-chloro-2-propanol was converted (i) to 1-t-butyl-3-azetidinol (6), which with the triphenylphosphine-CCl_4 reagent (7) gave chloride 1a, and, (ii) via the O-mesylate, cyclized with aqueous alkali carbonate, to 2a. All other numbered compounds were also synthesized by unequivocal methods and had consistent properties, including pmr and ir spectra, and were resolved (gc) from their isomers on a 2-m. x 1/4 in. column of 10% poly(neopentyl glycol succinate) on acid-washed Chromosorb W. Details will be described later.

mercuric chloride-Carbowax 20M column eluting the isomers at 165-175°, conditions under which the aziridine did not isomerize. In acetonitrile at 90° (64 hrs. in a bomb), 1a gave a mixture of 1a and 2a in 63:37 ratio (41% recovery*). Aziridine 2a was again more stable (77% recovery) and generated only a small proportion of the azetidine (1a:2a ratio, 4:96). This contraction of the azetidine ring to an aziridine, apparently the first recorded, contrasts with rearrangements of strainless beta-amino primary halides to the secondary halides via aziridinium ions (8).

A change in reagent and solvent favored ring expansion. With potassium cyanide in methanol at 100°, chloroazetidine 1a gave only the expected 1-t-butyl-3-cyanoazetidine (1b, 9); but 1b also arose in 8% yield from aziridine 2a, along with the internal return product, chloroazetidine 1a (5% yield), and at least seven other unidentified compounds formed in more than traces. 1-t-Butyl-2-cyanomethylazirídine (2b) was not present, in either case.

The initial first order ionization rate constants were determined in buffered anhydrous acetic acid: 1a, 0.0100 hr^{-1} at 100.0°; 2a, 0.088 hr^{-1} at 50.0°.** The acetolyses presumably involved ion pairs, but internal return was not detectáble since 1a reacted very slowly at 50° and 2a was 94% ionized in twenty min. at 100°. These rates are about double and eighty-fold, respectively, the published combined acetolysis-rearrangement constants for cyclobutyl and cyclopropylmethyl chlorides (10). The latter are typical of enhanced rate data supporting delocalization as the driving force for ionization.

The final acetolysis products at 100° were amino diacetates 3 and 4,



3 4

* At least six less volatile uncharacterized products were also formed. They were poorly resolved by gc as shown by rapid-scan mass spectrometry.

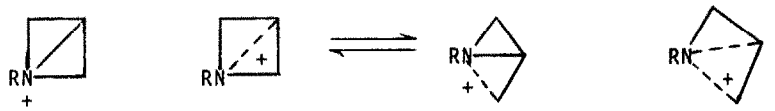
** Rates were measured by potentiometric titration of liberated chloride. Data are listed for about 0.04 M solutions of both the halide and buffer (KOAc) with 1% excess acetic anhydride. The rates showed a small salt effect.

formed by acetic acid opening of the cyclic acetates 1c (6) and 2c.* The ratios of 3 and 4 from 1a (49:51) and 2a (5:95) were not clearly diagnostic of ionic intermediates, since competitive acetic acid opening of 1a and 2a interfered, the resulting chloro acetates recyclizing to 2c.

Evidence for ionic ring contraction was found in the acetolysis at 60° of the azetidinyl tosylate, 1d (9). The only products were the azetidinyl acetate (1c) and 1,3 diacetate 4 (ratio, 95:5); unchanged 1d was recovered. Since 1c was stable under these conditions, we believe that 1d also was not opened by acetic acid. Thus 4 must have been formed by direct ionization and ring contraction to give 2c, followed by ring opening of the aziridine.

A mechanism must explain the ionic rearrangements, i.e., both ring contraction and expansion, as well as the enhanced ionization rates. Dissociation with nitrogen participation to the bicyclic quaternary ion, I, seems unlikely because analogy with the sulfur cases (4) and bicyclobutane chemistry suggests that I should yield only azetidines by cross-ring bond cleavage. Simple ionization to classical carbonium ions does not explain the rates, especially in view of the smaller ring strain energies of the heterocycles (aziridine, 14 kcal/mole, 11), compared to the carbocycles (cyclopropane, 25 kcal/mole). These facts also seem to bear against a common nonclassical heterocyclic ion, as do the differing courses of the rearrangements.

While the present evidence is not conclusive, the writer suggests that these results are most simply rationalized in terms of relatively slowly equilibrating paired carbonium ions stabilized by partial overlap of the empty carbon orbital and the electron-pair orbital on nitrogen, as indicated by the dotted line in II and III (12). The transition state for rearrangement is then IV, in which the partial bonds are essentially equivalent.



I II III IV

* The stepwise reactions mentioned in this paragraph were confirmed separately under acetolysis conditions.

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