The Rearrangement of *N*-Chloro-1-methyl-1-aminocyclopentane in the Presence of Alkyllithiums

LeRoy W. Haynes (1b) and Richard A. Amos (1c)

Department of Chemistry, The College of Wooster, Wooster, Ohio 44691

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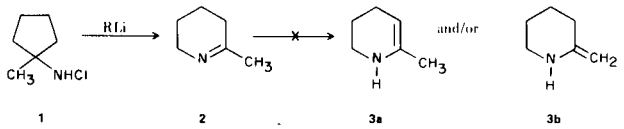
Stieglitz reported the first example of a rearrangement involving an *N*-haloamine by converting *N*-chlorotritylamine to the anil of benzophenone in the presence of a base (2). A related reaction, the conversion of *N*-chloro-9-aryl or alkyl-9-fluorylamines to 9-aryl or alkylphenanthridienes using sodium methoxide as a base, has also been demonstrated (3). However, in both cases, only migration of aryl groups has been noted. The work of Gassman and his co-workers provides examples of migration of alkyl groups. For example, 2-chloro-2-azabicyclo[2.2.2.]octane underwent alkyl migration in the presence of methanolic silver nitrate to give 2-methoxy-1-azabicyclo[3.2.1.]octane (4). In addition to bicyclic systems, Gassman has also demonstrated similar rearrangements in cyclopropyl and cyclobutyl compounds (5). In each case, he proposes a nitrenium ion, a positive, divalent, electron deficient nitrogen, as the intermediate involved.

This note reports the first case of an alkyl migration using 1-methyl-1-aminocyclopentane, a primary amine, as the starting material (Gassman's rearrangements involved secondary amines). Recently Wilkie and Dimmel (6) demonstrated that the reaction of *N*-chloroaniline and *n*-butyllithium led to the formation of azobenzene, a product most likely arising from the formation of *N*-chloro-*N*-lithioaniline, a nitrenoid. These authors propose, as we do, that the first step is the abstraction of the hydrogen on nitrogen by the alkyllithium (Scheme 2). In our study *N*-chloro-1-methyl-1-aminocyclopentane (**1**) plus an alkyllithium gave 2-methyl-1-azacyclohex-1(2)ene (**2**) in a maximum yield of 35%. Related ring expansions are the formation of 1-azacyclohex-1(2)ene from cyclopentanol in the presence of hydrogen azide (7) and the formation of 2-ethyl-1-azacyclohex-1(2)ene from 1-ethyl-1-nitrosocyclopentane and trialkyl phosphites (8).

The product (**2**) was identified by its ir spectrum (strong -C=N-absorption at 1650 cm^{-1}), elemental analysis, and pmr spectra (9). The pmr spectra were quite complex but double resonance experiments did reveal a singlet at 1.5 ppm consistent with an allylic methyl group. The pmr spectra displayed no peaks downfield from 3 ppm which rules out the isomeric enamines (**3a**), (**3b**), products which could be formed by base catalyzed isomerization of the imine (**2**). The vinyl protons of an enamine would appear at or downfield from 3.9 ppm (10). To establish with certainty the ring size, a sample of (**2**) was hydrogenated. The resulting product gave ir and pmr spectra identical to those of 2-methylpiperidine.

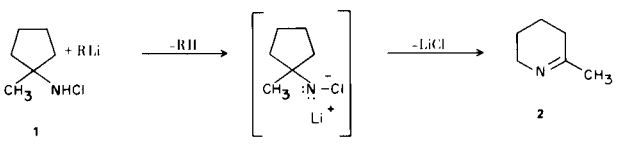
A number of different dehydrochlorination agents were tried. Sodium hydride in three different solvents (ether, tetrahydrofuran, and benzene) gave absolutely no reaction at room temperature as measured by hydrogen evolution. Elevated reaction temperatures were precluded because of thermal degradation of the *N*-chloroamine (**1**) (4). Potassium hydroxide and sodium methoxide, in ethanol and methanol respectively, gave only 1-methyl-1-aminocyclopentane as the product. Following the procedures by Gassman (4), silver nitrate in ethanol was used, but no reaction products could be isolated.

SCHEME 1



1 2 3a 3b

SCHEME 2



1 2

To overcome the problems associated with heterogeneous reaction mixtures and protic solvents, ethyllithium in benzene and *n*-butyllithium in cyclohexane were employed. Both of these alkyllithiums gave an apparent immediate reaction with the *N*-chloroamine (**1**) as evidenced by color changes, evolution of ethane (no butane was detected apparently because of its solubility in the reaction mixture), and precipitation of lithium chloride.

The first step appears to be removal of the acidic amine hydrogen by the base. The presence of the

resulting ethane was confirmed by comparison of ir spectra. Although we have not definitive evidence, we consider the most likely pathway to the observed product to be a concerted reaction involving migration of one of the secondary carbons *alpha* to the nitrogen as chloride ion is lost. The possibility of methyl migration also exists. However, we obtained no spectral evidence indicating the presence of cyclopentanone methylimine nor of its reduction product, *N*-methyl-1-aminocyclopentane.

EXPERIMENTAL

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. Pmr spectra were obtained on Varian A-60 and HA-100 spectrometers (9). Infrared spectra were obtained on Perkin-Elmer 21 and 700 spectrometers. All thin layer chromatography was done using alumina as the solid support, benzene as solvent, and iodine for visualization. All boiling points are uncorrected. The ethyllithium in benzene was purchased from Alfa Inorganics, Inc., and the *n*-butyllithium from the Foote Mineral Company.

1-Methyl-1-aminocyclopentane.

The amine was synthesized using the Ritter synthesis (11) (best yield 51%) or by the amination (12) of 1-methylcyclopentane (best yield 35%).

N-Chloro-1-methyl-1-aminocyclopentane (**1**).

1-Methyl-1-aminocyclopentane, 5.0 g. (0.06 mole), was added to 30 ml. of diethyl ether, and the mixture was placed in an ice bath over a magnetic stirrer. A calcium hypochlorite solution, 1.580 *M* in hypochlorite, was added dropwise with stirring until 38 ml. (0.060 mole) had been added. The reaction mixture was stirred for 40 minutes, and then the organic layer was drawn off and washed with 2 x 50 ml. of cold water. The ether extract was dried over sodium sulfate. Benzene and cyclohexane were also successfully used as solvents in this reaction. Due to the instability of the product, it was rarely isolated. Tlc analysis showed that none of the *N,N*-dichloroamine was formed when this procedure was used and also that only a trace of the starting amine was present.

Anal. Calcd. for $C_6H_{12}ClN$: C, 53.93; H, 9.05. Found: C, 53.81; H, 8.80.

Dehydrochlorination of *N*-Chloro-1-methyl-1-aminocyclopentane (**1**). General Procedure.

The dried extract from the chlorination of 10.0 g. (0.10 mole) of the starting primary amine was placed in a 500 ml. 3-necked flask, equipped with a thermometer, gas collection apparatus and an addition funnel. In a glove bag under nitrogen, about 0.11 mole of the alkyllithium was measured out and placed in the addition funnel. The alkyllithium was added to the stirred, cooled (ice-bath) reaction solution at such a rate as to maintain an internal temperature of 10-20°. At or somewhat beyond the calculated equivalence point the solution became dark brown and potassium iodide starch indicator paper showed that no *N*-chloroamine remained. 2-Propanol was used to destroy excess alkyllithium. The reaction mixture was filtered to remove lithium chloride and the solvent(s) removed by distillation through a 9″ glass helices column. The residue was distilled at atmospheric pressure to give the imine (**2**), b.p. 124-130°. Using benzene as the solvent for the *N*-chloroamine and ethyllithium in benzene the yield was 35%.

Anal. Calcd. for $C_6H_{11}N$: C, 74.23; H, 11.34; N, 14.43. Found: C, 74.41; H, 11.60; N, 14.08.

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