strong tendency to sublime even at room temperature. Hence, it was further purified by sublimation at room temperature under vacuum.

Anal. Calcd.: C, 22.87; H, 0.48; N, 13.37; F, 63.31. Found: C, 22.64; H, 0.39; N, 13.19; F, 63.36.

Acknowledgment.—The author wishes to thank Dr. R. A. Henry, Dr. W. P. Norris, and Dr. W. G. Finnegan for numerous helpful suggestions concerning this research.

Sterically Crowded Amines. III. β-Chloroamines and Aziridines[1]

G. F. HENNION AND PETER E. BUTLER[2]

Chemical Laboratories of the University of Notre Dame, Notre Dame, Ind.

Received December 18, 1961

Tetra-substituted aziridines, $R^1R^2\overline{C\text{—}CH(CH_3)\text{—}N}\text{—}R^3$, were prepared by cyclization of β-chloroamines, $R^1R^2C(NHR^3)\text{—}CHCl\text{—}CH_3$. The chloroamines of indicated structure were obtained by treatment of the corresponding β-amino alcohols with thionyl chloride. Methods are described for the preparation of sterically crowded aziridines.

Mention was made in a previous paper[3] that 1,2,2,3-tetra-substituted aziridines may be prepared from certain sterically crowded β-amino alcohols *via* the intermediate β-chloroamines. The synthesis involves the steps A→B→C→II→XI shown in Fig. 1. These transformations and the nature of the various products were studied in detail in the case of 1-isopropyl-2,2,3-trimethylaziridine (XI) and related compounds correlated as shown. The fact that the amines A,D,E, and XVIII and their hydrochlorides were already known aided significantly in the assignment of the structures II, XI, XVI, and XVII.

Treatment of 3-isopropylamino-3-methyl-2-butanol[3] (preferably as the hydrochloride[3] in chloroform) with thionyl chloride yielded a chloroamine

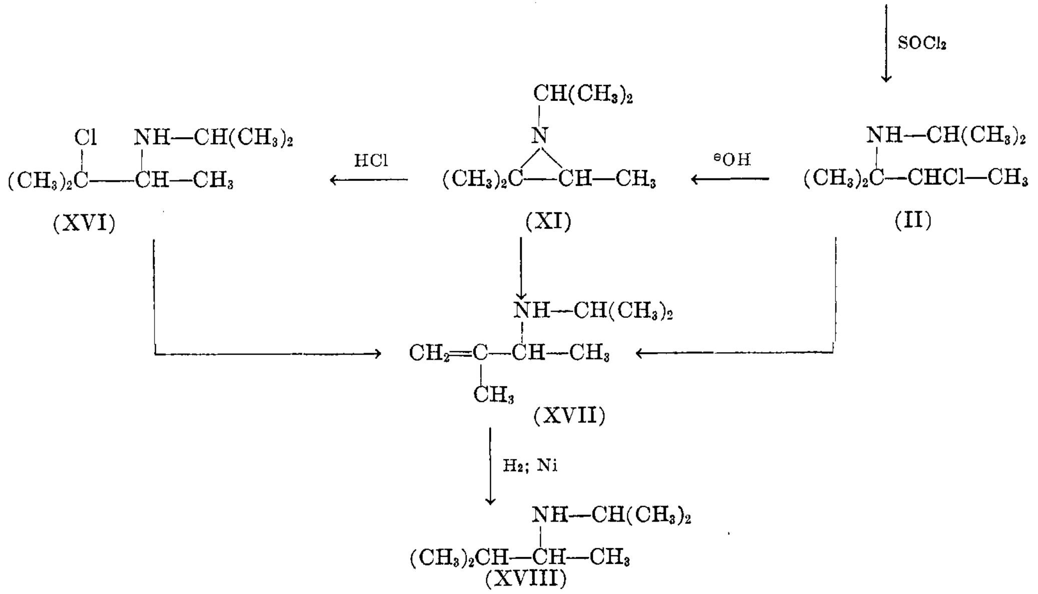


Fig. 1.—1-Isopropyl-2,2,3-trimethylaziridine and related compounds.

---

[1] Paper no. 78 on substituted acetylenes; previous paper, G. F. Hennion and Leonard Price, *J. Org. Chem.*, **27**, 1587 (1962).

[2] Eli Lilly Company Fellow, 1959-1961. Abstracted in part from the Ph.D. dissertation of P. E. B.

[3] G. F. Hennion and P. E. Butler, *J. Org. Chem.*, **26**, 3341 (1961).

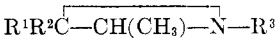
TABLE I

β-CHLOROAMINE HYDROCHLORIDES, $R^1R^2C(NHR^3)—CHCl—CH_3 \cdot HCl$

Compd.	R^1	R^2	R^3	Yield,[a] %	M.P.[b]	Mol. Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
I	CH_3—	CH_3—	C_2H_5—	51	165–166[c]	$C_7H_{17}Cl_2N$	45.17	45.42	9.21	9.01	7.53	7.23
II	CH_3—	CH_3—	i-C_3H_7—	73	157–158	$C_8H_{19}Cl_2N$	48.00	48.18	9.57	9.74	7.00	7.19
III	CH_3—	CH_3—	t-C_4H_9—	69	166–167	$C_9H_{21}Cl_2N$	50.46	50.30	9.88	9.96	6.54	6.62
IV	CH_3—	C_2H_5—	C_2H_5—	35	156–158	$C_8H_{19}Cl_2N$	48.00	48.33	9.57	9.43	7.00	7.10
V	CH_3—	C_2H_5—	i-C_3H_7—	60	126–127	$C_9H_{21}Cl_2N$	50.46	50.78	9.88	9.99	6.54	6.75
VI	CH_3—	C_2H_5—	t-C_4H_9—	28	135–136	$C_{10}H_{23}Cl_2N$	52.63	52.71	10.16	10.27	6.14	6.01
VII	C_2H_5—	C_2H_5—	i-C_3H_7—	48	147–148	$C_{10}H_{23}Cl_2N$	52.63	52.41	10.16	9.85	6.14	5.88
VIII	—$CH_2(CH_2)_3CH_2$—		i-C_3H_7—	55	138[d]	$C_{11}H_{23}Cl_2N$	55.00	54.80	9.65	9.40	5.83	6.08
IX	—$CH_2(CH_2)_3CH_2$—		t-C_4H_9—	47	142–143	$C_{12}H_{25}Cl_2N$	56.69	57.07	9.91	9.94	5.51	5.53

[a] Yields are for once crystallized products. [b] Melting points are for analytical samples. [c] Softened at 158°. [d] Softened, then melted over wide range.

TABLE II

TETRASUBSTITUTED AZIRIDINES, 

$R^1R^2\overset{}{C}—CH(CH_3)—N—R^3$

Compd.	R^1	R^2	R^3	Yield,[a] %	B.P.[b]	Mm.	$n^{25}D$[b]	Mol. Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
X	CH_3—	CH_3—	C_2H_5—	69	97–98		1.4069	$C_7H_{15}N$	74.27	74.21	13.36	13.22	12.37	12.45
XI	CH_3—	CH_3—	i-C_3H_7—	73	112		1.4062	$C_8H_{17}N$	75.52	75.56	13.47	13.33	11.01	11.14
XII	CH_3—	CH_3—	t-C_4H_9—	69	129		1.4158	$C_9H_{19}N$	76.52	77.28	13.56	13.38	9.92	9.76
XIII	CH_3—	C_2H_5—	i-C_3H_7—	73	139		1.4170	$C_9H_{19}N$	76.52	76.73	13.56	13.56	9.92	10.06
XIV	—$CH_2(CH_2)_3CH_2$—		i-C_3H_7—	59	98	35	1.4522	$C_{11}H_{21}N$	78.97	78.77	12.65	12.67	8.37	8.56
XV	—$CH_2(CH_2)_3CH_2$—		t-C_4H_9—	56	107	35	1.4569	$C_{12}H_{23}N$	79.49	78.83	12.78	12.82	7.73	7.91

[a] Yields correspond to once or twice distilled material of 3° boiling range or less. [b] Analytical fraction.

hydrochloride in good yield. The structure II was assigned to this product on the basis of the mode of preparation, infrared spectrum, and NMR spectrum.[4] Ring closure to the aziridine (XI) occurred readily in aqueous sodium hydroxide. Treatment of the aziridine with cold ethereal hydrogen chloride (minimum amount) gave the hydrochloride; with excess hydrochloric acid (in aqueous ethanol) the aziridine ring opened and yielded a chloroamine (XVI) isomeric with II. The three hydrochlorides (of II, XI, and XVI) evolved hydrogen chloride gas on melting and were transformed in this way to the same unsaturated amine hydrochloride, XVII. This fact, along with the infrared and NMR spectral data, served to confirm the assigned structures. It may be assumed safely that the hydrochlorides of II, XI, and XVI rearrange thermally to XVII by way of the same cyclic immonium ion.[5] The structure of XVII, indicated immediately by the infrared and NMR spectra, was confirmed by hydrogenation to XVIII, previously described by Bewad.[6]

A considerable number of β-amino alcohol hydrochlorides previously prepared[3] were converted to the corresponding β-chloroamine hydrochlorides by reaction with thionyl chloride. The products are described in Table I. Preliminary work indicates that all of these compounds undergo rearrangement with elimination of hydrogen chloride as discussed above. Further work is in progress.

Ease of ring closure to the aziridines proved dependent on steric features of the β-chloroamine. The least crowded compounds—*e. g.*, I and II—appeared to yield the aziridines rapidly by treatment with base. On the other hand, the formation of XIII from VI, XIV from VIII, and XV from IX required stirring with aqueous sodium hydroxide at room temperature for periods of twenty-four hours or more in order to obtain satisfactory yields. The aziridines (Table II) appeared to be of excellent purity. The infrared spectra had no bands indicative of N—H or of unsaturation; gas liquid chromatography indicated substantial homogeneity in all instances.

Experimental

3-Isopropylamino-3-methyl-2-chlorobutane Hydrochloride (II).—To 23.8 g. (0.13 mole) of 3-isopropylamino-3-methyl-2-butanol hydrochloride[3] dissolved in 125 ml. of dry chloroform was added dropwise at ice bath temperature 20 g. (0.17 mole) of freshly distilled thionyl chloride dissolved in 50 ml. of dry chloroform. The mixture was stirred for 30 min. at ice bath temperature and then boiled gently with stirring for 2 hr. The solvent and volatiles were removed *in vacuo* (steam bath), leaving a solid residue which was crystallized from absolute ethanol–ethyl acetate; weight, 21.2 g. (73% yield), m.p. 154–157°.

1-Isopropyl-2,2,3-trimethylaziridine (XI).—A concentrated aqueous solution of 20.2 g. (0.1 mole) of 3-isopropylamino-3-methyl-2-chlorobutane hydrochloride (II) was added dropwise with stirring to a cold solution of sodium hydroxide (40 g., 1 mole) in water (125 ml.). The mixture was distilled, while stirring, until a test portion of distillate showed no oil. The total distillate was treated with 5 g. of

---

[4] The NMR spectra of the hydrochlorides of compounds II, XVI, XVII, and XVIII were taken on solutions in deuterium oxide containing one drop of water and were compatible with the assigned structures. The NMR spectrum of XI was taken as the free base with tetramethylsilane as an internal standard and was in accord with the aziridine structure. Details of the work and discussion of the spectra are given in the Ph.D. dissertation of P. E. B.

[5] A. Streitwiesser, *Chem. Rev.*, **56**, 677–680 (1956).

[6] I. Bewad, *Ber.*, **40**, 3069 (1907); Beilstein, "Handbuch der Organische Chemie," 4th ed., Vol. IV, p. 180.

solid potassium hydroxide (allowed to dissolve) and extracted with two 50-ml. portions of ether. The combined ether extract was dried over anhydrous potassium carbonate and then with potassium hydroxide pellets. Distillation gave 13.9 g. of product (73% yield), b.p. 110–112°, $n^{25}\text{D}$ 1.4064–1.4070. After redistillation, gas liquid chromatography (Silicone SF-96 column at 117° and helium flow of 34 ml./min.) revealed a peak, retention time 25 min., indicating 99% purity or better. The infrared spectrum showed no bands indicative of unsaturation.

The **hydrochloride** was precipitated from 2.0 g. dissolved in 30 ml. of cold ethyl acetate by slow addition of cold ethereal hydrogen chloride. The product was crystallized from absolute ethanol–ethyl acetate; yield 2.2 g., m.p. 131–133° dec. (turned red at 127°). After three recrystallizations the m.p. was 130.5–131° dec. (red at 127°).

Anal. Calcd. for $C_8H_{18}ClN$: C, 58.70; H, 11.08; N, 8.56. Found: C, 58.62; H, 11.03; N, 8.46.

2-Chloro-2-methyl-3-isopropylaminobutane Hydrochloride (XVI).—A 2.2-g. portion of the aziridine (XI) described above was dissolved in 50 ml. of ethanol, chilled in ice, and made acidic by addition of 5 ml. of concentrated aqueous hydrochloric acid. The solvents and volatiles were removed *in vacuo* (steam bath). The residue was crystallized from absolute ethanol–ethyl acetate; weight 2.6. g. (77% yield), m.p. 147.5–148.5°. Two recrystallizations raised the m.p. to 149.5–150°. A mixture of the isomeric hydrochlorides II and XVI melted at 139–147°.

Anal. Calcd. for $C_8H_{19}Cl_2N$: C, 48.00; H, 9.57; N, 7.00. Found: C, 48.17; H, 9.64; N, 7.06.

2-Methyl-3-isopropylamino-1-butene Hydrochloride (XVII). A. From 3-Isopropylamino-3-methyl-2-chlorobutane Hydrochloride (II).—A 30-g. portion (0.15 mole) of 3-isopropylamino-3-methyl-2-chloro-butane hydrochloride (II) was heated *in vacuo* at 175° (oil bath temp.) for 30 min. The compound melted with evolution of hydrogen chloride gas and then resolidified while still at 175°. The product was allowed to cool and was crystallized from absolute ethanol–ethyl acetate; weight, 20.4 g. (82% yield); m.p. 186–189°. Three recrystallizations of a small portion from the same solvent mixture gave the analytical sample with m.p. 187–189°.

Anal. Calcd. for $C_8H_{18}ClN$: C, 58.70; H, 11.08; N, 8.56. Found: C, 58.92; H, 11.01; N, 8.44.

B. From 1-Isopropyl-2,2,3-trimethylaziridine Hydrochloride (XI).—The aziridine hydrochloride (XI; 250 mg.) was heated for 10 min. at 150°. The sample melted and turned dark red. After cooling, the dark solid was broken up with a spatula and was washed with 5 ml. of ethereal hydrogen chloride, then with anhydrous ether; weight 210 mg. (84% yield), m.p. 160–178°. After two crystallizations the m.p. was 187–189°, not depressed by mixture with a sample described under A, above.

C. From 2-Chloro-2-methyl-3-isopropylaminobutane Hydrochloride (XVI).—A 750-mg. portion of the hydrochloride (XVI) was heated *in vacuo* at 175° for 30 min. The product was crystallized from absolute ethanol–ethyl acetate; weight 530 mg., m.p. 183–186°. One recrystallization raised the m.p. to 187–189°, not depressed by mixture with a sample described under A, above.

2-Methyl-3-isopropylamino-1-butene.—The hydrochloride (20.3 g.; 0.124 mole) was dissolved in 50 ml. of water and cooled in an ice bath. The amine was released by addition of 10 g. of sodium hydroxide dissolved in 25 ml. of water and was taken up in ether. The ethereal solution was dried with anhydrous potassium carbonate and then with potassium hydroxide pellets. Distillation gave 12.1 g., b.p. 124–124.5°. The infrared spectrum had bands at 3.02, 3.28, 6.11, 6.92, and 11.2 μ consistent with the assigned structure. A portion of the free base was reconverted to the hydrochloride, m.p. 187–189°.

2-Isopropylamino-3-methylbutane (XVIII).—A solution of 10.6 g. of 2-methyl-3-isopropylamino-1-butene in 50 ml. of 95% ethanol containing 3 g. of Raney nickel (wet with water) was hydrogenated at room temperature, initial pressure 60.0 p.s.i.g. (Parr machine). The theoretical amount of hydrogen was taken up in 1 hr. The catalyst was removed by filtration and the filtrate was acidified with 12 ml. of concd. hydrochloric acid. The solvent and volatiles were then removed *in vacuo* (steam bath). The residue was dissolved in 50 ml. of water and the amine was released by addition of solid potassium hydroxide. The oil so liberated was taken up in ether; the solution, dried and distilled. Two distillate fractions were retained: (a), b.p. 124–127°, $n^{25}\text{D}$ 1.4041, 1.9 g.; (b), b.p. 127–128°, $n^{25}\text{D}$ 1.4069, 7.2 g. (lit.,[6] b.p. 129–131°). The infrared spectrum had no bands indicative of unsaturation.

The **hydrochloride** was precipitated with ethereal hydrogen chloride and crystallized from absolute ethanol–ethyl acetate; m.p. 125–126.5° (lit.,[6] m.p. 124–125°).

Anal. Calcd. for $C_8H_{20}ClN$: C, 57.98; H, 12.17; N, 8.45. Found: C, 58.17; H, 12.10; N, 8.39.

Acknowledgment.—The authors gratefully express their thanks to Messrs. W. L. Brown, G. M Maciak, H. L. Hunter, R. M. Hughes, Alfred Brown, and David Cline of the Lilly Research Laboratories, Indianapolis, Ind., for the analytical determinations; to Drs. E. L. Eliel, H. M. Gianni, D. J. Pasto, and Mr. Bernard Nowak, all of this department, and Drs. L. M. Jackman, C. H. DePuy, and R. W. King, Iowa State University, Ames, Iowa, for assistance in the NMR studies; to the National Science Foundation for the gas chromatography unit (Model A-90) used in the work; and to Eli Lilly and Co. for financial support.