Hydrochlorides described in Tables I and II were precipitated from ethereal solutions of the amines with ethereal hydrogen chloride (ice bath) and were crystallized (with the exception of VIIIa HCl, Table II) from mixtures of ethyl acetate and absolute ethanol. Compound VIIIa HCl decomposed even on gentle heating in attempts to crystallize and hence was analyzed in the crude form.

Acknowledgment.—The authors wish to express their thanks to Air Reduction Chemical Company, New York, for generous samples of 3-methyl-1-butyn-3-ol; to Messrs. H. L. Hunter, David Cline, G. M. Maciak, and Charles Ashbrook of the Lilly Research Laboratories, Indianapolis, Indiana, for the analytical determinations; to Dr. E. C. Kornfeld and R. Spangler for the pK_a determinations; and to Eli Lilly and Company for the support of this work. Special thanks are also due to Dr. D. J. Pasto for his invaluable services in interpreting n.m.r. spectra.

Sterically Crowded Amines. V. Hydrogen Chloride Elimination with Rearrangement in Some β-Chloroamines[1]

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Received February 15, 1965

Hydrogen chloride elimination from β-chloroamines, $R^1CH_2C(CH_2R^2)(NR^3R^4)CH(Cl)CH_3$, yielding rearranged allylic amines, $R^1CH{=}C(CH_2R^2)CH(NR^3R^4)CH_3$, was studied. A mechanism, involving an aziridinium ion, is proposed. Solvent effects, product studies, and hydrogenation of the allylic amines gave evidence supporting the mechanism and helped define the scope and limitations of the reaction. A competing side reaction with probable intermediacy of an alkylideneaminium ion (or enamine) was discovered.

Discussion

An earlier paper[3] in this series reported that 3-methyl-3-isopropylamino-2-chlorobutane hydrochloride was converted to 2-methyl-3-isopropylamino-1-butene hydrochloride by thermal elimination of hydrogen chloride with rearrangement. The same product was also obtained from either 2-methyl-3-isopropylamino-2-chlorobutane hydrochloride or 1-isopropyl-2,2,3-trimethylaziridinium chloride. This rearrangement reaction has now been examined in greater detail to determine its mechanism, scope, and limitations.

The chloroamine hydrochlorides used in this work were prepared by the action of thionyl chloride on the hydrochlorides of the corresponding β-amino alcohols as previously reported.[3] In most cases the crude product of the thionyl chloride reaction was not purified, but was simply heated *in vacuo* to effect the rearrangement.

$$R^1CH_2C(CH_2R^2)(NR^3R^4)CH(OH)CH_3 \xrightarrow[2.\ SOCl_2]{1.\ HCl(g)}$$

$$R^1CH_2C(CH_2R^2)(NR^3R^4)CH(Cl)CH_3\cdot HCl \xrightarrow[2.\ NaOH(aq)]{1.\ \Delta} R^1CH{=}C(CH_2R^2)CH(NR^3R^4)CH_3$$

The resulting mixture was then made alkaline and steam distilled. The distillate was extracted with ether and the ethereal solution was dried and distilled to give the allylic amine. Some reactions (discussed below) were performed using purified chloroamine hydrochlorides[3] as starting materials.

The physical properties and yields of the allylic amines, with supporting analytical data for the corresponding hydrochloride salts, are found in Table I. The structures of the final products were established by their infrared spectra, in some cases also by their n.m.r. spectra, and by comparison of the melting points of the hydrochloride salts with those of the hydrochlorides of the isomeric "unrearranged" allylic amines previously prepared[4] by semihydrogenation of propargylic amines.

$$R^1CH_2C(CH_2R^2)(NR^3R^4)C{\equiv}CH \xrightarrow{H_2\text{-}Pd} R^1CH_2C(CH_2R^2)(NR^3R^4)CH{=}CH_2$$

Low-pressure catalytic hydrogenation of the products also gave evidence supporting the proposed structures. The hydrogenation products and the analytical data for the hydrochloride salts are found in Table II. The "unrearranged" isomers of these saturated compounds had been prepared and described previously.[4a] Melting points of the rearranged product hydrochlorides, both saturated and allylic, were different from the unrearranged isomers so that it was easily possible to demonstrate that rearrangement, rather than 1,2 elimination of hydrogen chloride from the β-chloroamines, had occurred. Repeated attempts to hydrogenate compounds VI–VIII with nickel, platinum oxide, and palladium catalysts consistently met with failure, however, presumably for steric reasons.

The previously mentioned facts served not only to show that the allylic amines were indeed products of rearrangement, but also that no 1,2 elimination products had formed. This was also borne out by g.l.c. examination of compounds III and IX which showed only one peak and by the sharp melting points of the hydrochloride salts of the butene and cyclohexene products. The melting points of the pentene hydrochlorides (compounds VI and VII) covered a wide range, as was expected, since these rearranged allylic amines could exist as mixtures of *cis* and *trans* isomers.

The rearrangement was not limited to monoalkylamino groups since both pyrrolidino and dimethylamino also migrated (compounds V and VIII). Alkyl groups attached to the tertiary carbon atom had little effect on the outcome of the reaction as shown by the

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[1] Paper No. 80 on substituted acetylenes. Previous paper: G. F. Hennion and C. V. DiGiovanna, *J. Org. Chem.*, **30**, 2645 (1965).

[2] Eli Lilly Co. Fellow, 1962–1964. Abstracted from a portion of the Ph.D. Dissertation of A. C. H.

[3] G. F. Hennion and P. E. Butler, *J. Org. Chem.*, **27**, 2088 (1962).

[4] (a) G. F. Hennion and R. S. Hanzel, *J. Am. Chem. Soc.*, **82**, 4908 (1960); (b) G. F. Hennion and A. C. Perrino, *J. Org. Chem.*, **26**, 1073 (1961).

Table I

Allylic Amines

$R^1CH{=}C(CH_2R^2)CH(NR^3R^4)CH_3$

								Hydrochlorides							
										Carbon, %		Hydrogen, %		Nitrogen, %	
Compd.	R¹	R²	R³	R⁴	B.p., °C. (mm.)	$n^{25}D$	Yield, %	Formula	M.p., °C.	Calcd.	Found	Calcd.	Found	Calcd.	Found
I	H	H	H	CH_3	93–96	1.4148	17	$C_6H_{14}ClN$	95–97	53.13	53.32	10.40	10.33	10.33	10.18
II	H	H	H	C_2H_5	107–113	1.4141	44	$C_7H_{16}ClN$	138–140	56.17	56.23	10.78	11.00	9.36	9.21
III[a]	H	H	H	i-C_3H_7	121–126	1.4163	80	$C_8H_{18}ClN$	188–190	58.70	58.92	11.08	11.01	8.56	8.44
IV	H	H	H	t-C_4H_9	139–142	1.4212	77	$C_9H_{20}ClN$	170–172	60.82	60.99	11.34	11.55	7.88	7.66
V[b]	H	H	$-CH_2(CH_2)_2CH_2-$		85–86 (63)	1.4513	6	$C_{15}H_{20}N_4O_7$[b]	201–203	48.91	48.99	5.47	5.82		
VI	CH_3	H	H	i-C_3H_7	85–87 (90)	1.4299	85	$C_9H_{20}ClN$	163–169	60.82	61.08	11.34	11.41	7.88	7.58
VII	CH_3	CH_3	H	i-C_3H_7	68–69 (21)	1.4347	75	$C_{10}H_{22}ClN$	129–139	62.64	62.84	11.57	11.76	7.31	6.95
VIII	$-CH_2CH_2CH_2-$		CH_3	CH_3	78–80 (16)	1.4649	61	$C_{10}H_{20}ClN$	204–206	63.30	63.60	10.62	10.83	7.38	7.47
IX	$-CH_2CH_2CH_2-$		H	i-C_3H_7	93–94 (20)	1.4619	80	$C_{11}H_{22}ClN$	226–228	64.84	65.10	10.88	11.03	6.87	6.70

[a] Analytical sample prepared by Hennion and Butler.[3] [b] Picrate salt used for analysis instead of the hydrochloride.

Table II

Saturated Amines

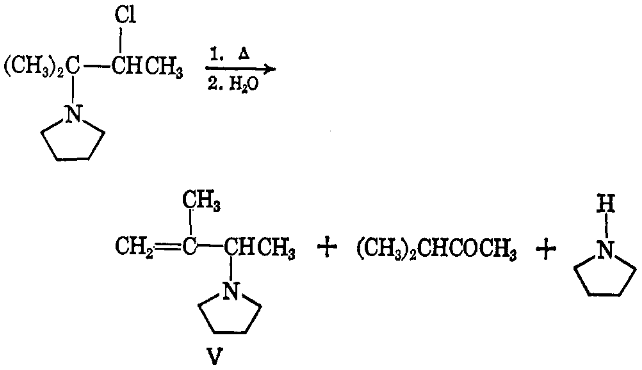
$R^1CH_2CH(CH_2R^2)CH(NR^3R^4)CH_3$

						Hydrochlorides							
								Carbon, %		Hydrogen, %		Nitrogen, %	
Compd.	R¹	R²	R³	R⁴	Yield, %	Formula	M.p., °C.	Calcd.	Found	Calcd.	Found	Calcd.	Found
X	H	H	H	CH_3	94[a]	$C_6H_{16}ClN$	106–108	52.35	52.15	11.72	12.05	10.18	9.73
XI	H	H	H	C_2H_5	52[b]	$C_7H_{18}ClN$	163–165	55.43	55.26	11.96	12.06	9.24	9.00
XII[c]	H	H	H	i-C_3H_7	85	$C_8H_{20}ClN$	125–126	57.98	58.17	12.17	12.10	8.45	8.39
XIII	H	H	H	t-C_4H_9	67	$C_9H_{22}ClN$	239–240	60.14	60.38	12.34	12.59	7.79	7.50
XIV	$-CH_2CH_2CH_2-$		H	i-C_3H_7	71[a]	$C_{11}H_{24}ClN$	181–183	64.20	64.41	11.76	11.83	6.81	6.63

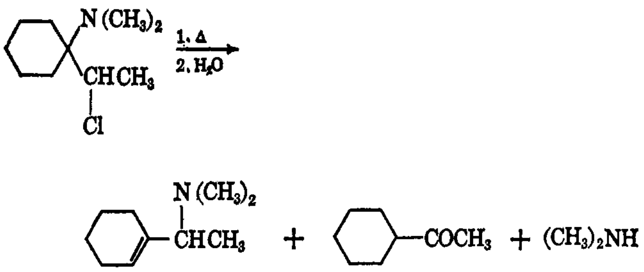
[a] Yield of hydrochloride salt. [b] Combined yield of distilled base and hydrochloride salt precipitated from forefraction of distillation. [c] See ref. 3.

small variance in yields of compounds III, VI, VII, and IX in which the migrating group was isopropylamino and only the groups on the tertiary carbon atom were varied. Best yields of allylic amines were obtained when the migrating group was a large monoalkylamino group such as isopropylamino or *t*-butylamino. The smaller monoalkylamino groups gave much poorer yields (compounds I and II).

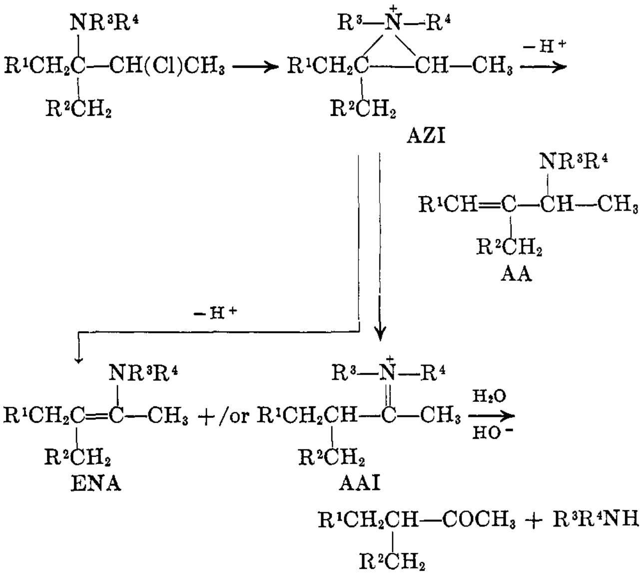
A competing side reaction which resulted in formation of ketone and saturated amine occurred in most, if not all, cases of the rearrangement. Preparation of 2-methyl-3-pyrrolidino-1-butene (V), for example, gave also methyl isopropyl ketone and pyrrolidine. Similarly, acetylcyclohexane was isolated during the preparation of 1-(1-dimethylaminoethyl)cyclohexene (VIII). This type of side reaction appears to have been involved in each case of rearrangement although the extent of ketone formation varied considerably from case to case. Preparation of 2-methyl-3-*t*-butylamino-1-butene (IV), for example, showed no evidence of ketone formation, although trace quantities might have been lost. The other extreme was observed during the attempted preparation of 2-methyl-3-dimethylamino-1-butene which gave no rearrangement product but did give methyl isopropyl ketone. This competitive side reaction seems to be at least partially responsible for the variable yields of rearrangement products. The fact that fragmentation to ketone and saturated amine occurred as a side reaction during alkaline steam distillation suggests the intermediacy of the enamine (ENA)



V

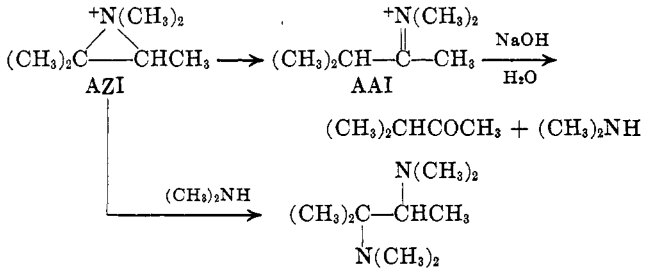


VIII

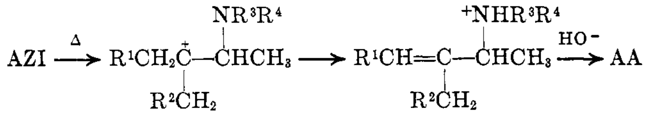


or alkylideneaminium ion[5] (AAI) to account for these products. As was pointed out to us,[5] rearrangement of the aziridinium ion (AZI) to AAI should be favored relative to allylamine formation (AA) when both R^3 and R^4 are alkyl groups. The intermediates AZI and AAI thus account for all of the products isolated from the various experiments.

The only rearrangement which failed to give any allylic amine was the attempted preparation 2-methyl-3-dimethylamino-1-butene from 3-dimethylamino-3-methyl-2-chlorobutane hydrochloride. It appears that reaction did proceed to the aziridinium ion stage (AZI) with partial conversion to the aminium ion (AAI). The latter was subsequently hydrolyzed to methyl isopropyl ketone and dimethylamine and the liberated dimethylamine then combined with the remaining aziridinium ion to form 2-methyl-2,3-bis(dimethylamino)butane as shown. The diamine was identical with a sample prepared by treating 3-dimethylamino-3-methyl-2-chlorobutane with excess of 40% aqueous dimethylamine.



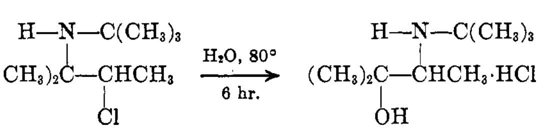
The mechanism of elimination with rearrangement (→ AA) appears to be well established as involving a transition state having a high degree of tertiary carbonium ion character. The aziridinium ion (AZI) has long been recognized[6] as an intermediate in reactions of β-chloroamines. Lack of any 1,2-elimination indicates that the secondary carbon atom, which contained the chlorine atom, acquired very little carbonium ion character since such an ion would have been expected to eliminate a proton from the adjacent carbon to form the unrearranged allylic amine. That the reaction was intramolecular was shown by an experiment in which 3-methyl-3-*t*-butylamino-2-chlorobutane hydrochloride was rearranged in the presence of dimethylamine hydrochloride. No crossover product, 2-methyl-3-dimethylamino-1-butene, could be found.



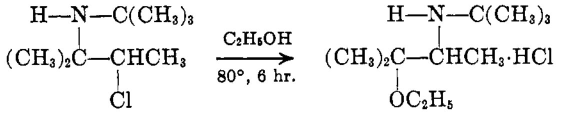
$$\mathrm{AZI} \xrightarrow{\Delta} \mathrm{R^1CH_2}\underset{\mathrm{R^2CH_2}}{\overset{+}{\mathrm{C}}}\mathrm{-}\overset{\mathrm{NR^3R^4}}{\mathrm{C}}\mathrm{HCH_3} \longrightarrow \mathrm{R^1CH{=}}\underset{\mathrm{R^2CH_2}}{\mathrm{C}}\mathrm{-}\overset{\mathrm{^+NHR^3R^4}}{\mathrm{C}}\mathrm{HCH_3} \xrightarrow{\mathrm{HO^-}} \mathrm{AA}$$

The tertiary carbonium ion like intermediate was indicated also by the fact that the elimination followed a Saytzeff rather than a Hofmann pattern when 3-methyl-3-isopropylamino-2-chloropentane hydrochloride was the starting material. In this case the trisubstituted ethylene, 3-methyl-4-isopropylamino-2-pentene, was the major product and the terminal olefin, 2-ethyl-3-isopropylamino-1-butene, was formed to a much smaller extent. This was shown by the n.m.r. spectrum which fits a mixture of 86% pentene and 14% butene (based on relative intensities of the peaks due to each). G.l.c. examination also showed two peaks with relative areas of approximately 9 to 1. Also, repeated attempts to hydrogenate this mixture failed to produce any isolable saturated amine, indicating that the major component was sterically hindered to low-pressure catalytic hydrogenation.

Supporting evidence for the mechanism was obtained by examination of reactions of purified 3-methyl-3-*t*-butylamino-2-chlorobutane hydrochloride. In inert solvents rearrangement proceeded slowly at 140° but was not observed at 80°. No reaction was observed when an aqueous solution was maintained for 6 hr. at 80°, but when the free chloroamine (liberated by aqueous potassium carbonate) was treated with water in the same fashion, 2-methyl-3-*t*-butylamino-2-butanol hydrochloride was obtained. Failure of the chloroamine hydrochloride to react with water indicated that the nitrogen must be deprotonated for the rearrangement to occur. Solvolysis of the chloroamine in ethanol gave 2-methyl-2-ethoxy-3-*t*-butylaminobutane hydrochloride. Attack by the solvent molecules at the tertiary carbon atom of the intermediate also reveals the tertiary carbonium ion character of the various reactions.



$$\mathrm{(CH_3)_2}\overset{\mathrm{H{-}N{-}C(CH_3)_3}}{\mathrm{C}}\mathrm{-}\underset{\mathrm{Cl}}{\mathrm{C}}\mathrm{HCH_3} \xrightarrow[\mathrm{6\ hr.}]{\mathrm{H_2O,\ 80^\circ}} \mathrm{(CH_3)_2}\underset{\mathrm{OH}}{\mathrm{C}}\mathrm{-}\overset{\mathrm{H{-}N{-}C(CH_3)_3}}{\mathrm{C}}\mathrm{HCH_3{\cdot}HCl}$$



$$\mathrm{(CH_3)_2}\overset{\mathrm{H{-}N{-}C(CH_3)_3}}{\mathrm{C}}\mathrm{-}\underset{\mathrm{Cl}}{\mathrm{C}}\mathrm{HCH_3} \xrightarrow[\mathrm{80^\circ,\ 6\ hr.}]{\mathrm{C_2H_5OH}} \mathrm{(CH_3)_2}\underset{\mathrm{OC_2H_5}}{\mathrm{C}}\mathrm{-}\overset{\mathrm{H{-}N{-}C(CH_3)_3}}{\mathrm{C}}\mathrm{HCH_3{\cdot}HCl}$$

Similar reactions were performed on 3-methyl-3-dimethylamino-2-chlorobutane. Treatment of the free base with water gave 2-methyl-3-dimethylamino-2-butanol hydrochloride. This salt was converted to the methiodide for comparison with the isomeric 3-methyl-3-dimethylamino-2-butanol methiodide, described previously.[4b] The melting points were sufficiently different to show that rearrangement had occurred.

Reaction of 3-dimethylamino-3-methyl-2-chlorobutane hydrochloride with excess 40% aqueous dimethylamine resulted in formation of 2-methyl-2,3-bis(dimethylamino)butane, one of the products isolated from the attempted rearrangement of the chloroamine hydrochloride. Other reactions performed previously[7] by Cromwell, Cram, and co-workers were also found to involve a similar rearrangement.

Experimental

The amino alcohols used in this work were prepared by sodium borohydride reduction[4b,8] of the corresponding ketones which were prepared by hydration of the acetylenic amines.[4]

3-Methyl-3-methylamino-2-butanol was prepared in 79% yield from 3-methyl-3-methylamino-2-butanone[9] and sodium

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[5] The authors are grateful to a referee for suggestion of the alkylideneaminium ion intermediate and for calling attention to similarities in our findings with those of N. J. Leonard, J. V. Paukstelis, and L. E. Brady [*J. Org. Chem.*, **29**, 3383 (1964)]. It is significant that thermal rearrangement of 1,1,2,2-tetramethylaziridinium perchlorate found by them gave N-isobutylidenedimethylaminium perchlorate.

[6] A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 105.

[7] N. Cromwell, C. Harris, and D. Cram, *J. Am. Chem. Soc.*, **66**, 134 (1944); see also earlier papers.

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

[9] N. R. Easton and R. D. Dillard, *ibid.*, **28**, 2465 (1963).

borohydride in isopropyl alcohol, b.p. 77–79° (50 mm.), lit.[10] b.p. 95° (70 mm.).

1-Dimethylamino-1-(1-hydroxyethyl)cyclohexane (new) was similarly prepared from 1-dimethylamino-1-acetylcyclohexane in 90% yield, b.p. 112–113° (11 mm.), $n^{25}\text{D}$ 1.4868.

The **hydrochloride** had m.p. 200–201°.

Anal. Calcd. for $C_{10}H_{22}ClNO$: C, 57.81; H, 10.68; N, 6.74. Found: C, 57.55; H, 10.72; N, 6.68.

The chloroamine hydrochlorides used in this work were prepared according to the procedure of Hennion and Butler[3] with slight modification.

3-Dimethylamino-3-methyl-2-chlorobutane Hydrochloride.—A solution of 46.1 g. (0.35 mole) of 3-dimethylamino-3-methyl-2-butanol[4b] in 175 ml. of anhydrous chloroform was stirred, cooled (ice bath), and saturated with dry hydrogen chloride. To this was added 52.4 g. (0.44 mole) of thionyl chloride over a 15-min. period. The resulting mixture was stirred at room temperature for 30 min., then heated to reflux for 5 hr. Solvent and volatiles were removed by distillation *in vacuo*, leaving a tan solid. This solid was washed with three 50-ml. portions of anhydrous ether (ether decanted) yielding 142 g. of tan (wet) solid, m.p. 96–103° dec. An 80-g. portion gave 23.6 g. of once-crystallized (ethanol-ethyl acetate) material, m.p. 121–125° dec. The yield of crystallized product (based on the return from the 80-g. portion of crude material) was 64%. Two recrystallizations (same solvent) gave an analytical sample, m.p. 124-125° dec.

Anal. Calcd. for $C_7H_{17}Cl_2N$: C, 45.17; H, 9.21; N, 7.52. Found: C, 45.10; H, 9.33; N, 7.28.

3-Pyrrolidino-2-methyl-1-butene (V).—A solution of 45.3 g. (0.29 mole) of 3-pyrrolidino-3-methyl-2-butanol[4b] in 70 ml. of anhydrous chloroform was saturated with dry hydrogen chloride. The cold solution was treated with 41.3 g. (0.35 mole) of thionyl chloride and stirred for 1 hr. at room temperature. The mixture was then heated to reflux for 6 hr. (until gas evolution ceased). Solvent and volatiles were removed by distillation, leaving a black residue. Vacuum (water aspirator) was applied and the temperature was raised to 160° (frothing visible at 120°) and maintained for 1 hr. (until frothing ceased). The resulting tar was cooled and treated with 200 g. of cold 40% aqueous sodium hydroxide. The mixture was steam distilled and the distillate was treated with 10 g. of sodium hydroxide pellets, then extracted with three 50-ml. portions of ether. The ether extracts were combined and dried overnight with anhydrous potassium carbonate. Previous work had shown that this procedure gave 3-methyl-2-butanone and pyrrolidine as major products (the ketone 2,4-dinitrophenylhydrazone had m.p. 116–117°, no depression when mixed with authentic sample; pyrrolidine picrate had m.p. 110–112°, mixture with authentic sample had m.p. 110–112°). G.l.c. examination of the dried ethereal solution showed three poorly resolved peaks (excluding ether) with relative intensities of 1:5:3 and retention times of 2.8, 3.4, and 4.0 min., respectively (using Carbowax 20M on Chromosorb W, 95°, with flow rate of 35 cc. of helium/min.). The central peak increased in size upon the addition of 3-methyl-2-butanone and the third peak increased when pyrrolidine was added. The ethereal solution was treated with 100 ml. of 6 *N* hydrochloric acid and the aqueous layer was extracted with three 50-ml. portions of ether (ether discarded). The acidic solution was made strongly alkaline by addition of 40% aqueous sodium hydroxide and then extracted with four 50-ml. portions of ether. The ether extracts were combined and dried overnight with anhydrous potassium carbonate. G.l.c. analysis now gave two peaks (relative intensities of 1:2 with retention times of 2.6 and 4.0 min., respectively). Addition of pyrrolidine caused the second peak to grow and addition of 3-methyl-2-butanone gave three peaks as in the original mixture. Distillation through a 15-cm. Vigreux column gave 4.3 g. of pyrrolidine, b.p. 88–90°, and 2.2 g. (6% yield) of product V, b.p. 85–86° (63 mm.), $n^{25}\text{D}$ 1.4513. The infrared spectrum (neat) had bands at 3.28 ($=CH_2$ stretch), 6.08 ($C=C$ stretch), 11.14 ($C=CH$ out-of-plane deformation), and 5.61 μ (overtone of out-of-plane deformation).

The **picrate** was prepared by treating the amine in ethanol with a saturated ethanolic solution of picric acid. The solution was boiled for 5 min., then allowed to stand overnight, giving yellow crystals, m.p. 192–196° dec. Two crystallizations from ethanol gave an analytical sample, m.p. 201–203° dec.

Anal. Calcd. for $C_{15}H_{20}N_4O_7$: C, 48.91; H, 5.47. Found: C, 48.99; H, 5.82.

3-Methyl-4-isopropylamino-2-pentene and 2-Ethyl-3-isopropylamino-1-butene.—The above procedure was employed with 129.1 g. (0.81 mole) of 3-isopropylamino-3-methyl-2-pentanol, 400 ml. of anhydrous chloroform, and 119 g. (1.0 mole) of thionyl chloride. After removal of solvent and volatiles, vacuum (water aspirator) was applied and the temperature was raised to 140° and maintained for 1 hr. (until frothing ceased). The resulting black solid was treated with 200 g. of cold 40% aqueous sodium hydroxide and the mixture was steam distilled. The distillate was extracted with three 100-ml. portions of ether and the combined ether extracts were dried overnight with anhydrous potassium carbonate. Distillation gave 97.3 g. (85% yield) of colorless oil, b.p. 85–87° (90 mm.), $n^{25}\text{D}$ 1.4299. The infrared spectrum (neat) had the ordinary olefin bands at 6.00 and 6.10 μ, a medium-intensity band at 11.1 μ typical of 1,1-disubstituted ethylenes, and a strong band at 12.0 μ attributed to trisubstituted ethylene. G.l.c. analysis (10-ft. column, Carbowax 20M on firebrick, column temperature 120°, 30 cc. of helium/min.) gave two poorly resolved peaks in approximately 1:9 ratio with retention times of 6.0 and 6.4 min., respectively. The n.m.r. spectrum was consistent with a mixture containing 86% of the pentene and 14% of the butene.

The **hydrochloride** salt, precipitated from ether and crystallized three times from ethanol–ethyl acetate, had m.p. 163–169°.

Anal. Calcd. for $C_9H_{20}ClN$: C, 60.82; H, 11.34; N, 7.88. Found: C, 61.08; H, 11.41; N, 7.58.

2-Methyl-3-methylaminobutane Hydrochloride (X).—A mixture containing 0.04 g. of platinum oxide, 4.7 g. (0.035 mole) of 2-methyl-3-methylamino-1-butene hydrochloride, and 25 ml. of absolute ethanol was shaken with hydrogen at an initial pressure of 50 p.s.i.g. until the theoretical uptake of 3 p.s.i.g. was achieved (3 hr.). The catalyst was removed by filtration and the filtrate was stripped of solvent on a flash evaporator. The solid residue was crystallized from ethyl acetate to give 4.5 g. (94% yield) of white crystals, m.p. 95–100°. Two crystallizations (same solvent) gave an analytical sample, m.p. 106–108°. The infrared spectrum (chloroform) had no bands in the 6-μ region.

Anal. Calcd. for $C_6H_{16}ClN$: C, 52.35; H, 11.72; N, 10.18. Found: C, 52.15; H, 12.05; N, 9.73.

(1-Isopropylaminoethyl)cyclohexane hydrochloride (XIV) was prepared using the above procedure. All other saturated amines listed in Table II were prepared by the method of Hennion and Butler.[3]

2-Methyl-3-*t*-butylamino-2-butanol Hydrochloride.—To a cold suspension of 4.28 g. (20 mmoles) of 3-methyl-3-*t*-butylamino-2-chlorobutane hydrochloride[3] in 50 ml. of ether was added 2.76 g. (20 mmoles) of potassium carbonate in 15 ml. of water. The ether layer was dried by shaking with 2 g. of anhydrous potassium carbonate. Distillation through a Claisen column removed the ether and left a colorless oil which was treated with 50 ml. of water and heated to 80° for 6 hr. Removal of solvent on a flash evaporator left 3.35 g. (86% yield) of white solid, m.p. 188–190° dec. The infrared spectrum (chloroform) had bands at 3 (O–H stretch) and 8.5 μ (tertiary C–O stretch). Two crystallizations from ethanol–ethyl acetate gave an analytical sample, m.p. 190–191° dec.

Anal. Calcd. for $C_9H_{22}ClNO$: C, 55.22; H, 11.33; N, 7.16. Found: C, 55.03; H, 11.26; N, 7.08.

3-Dimethylamino-2-methyl-2-butanol methiodide was prepared from 3.7 g. of 3-dimethylamino-3-methyl-2-chlorobutane hydrochloride by treatment with potassium carbonate and then with water at 80° as described above. The oil remaining after removal of the water was treated with aqueous sodium hydroxide and the alkaline mixture was extracted with three 15-ml. portions of ether. The ether extracts were combined, dried by shaking for 3 min. with anhydrous potassium carbonate, then filtered. The filtrate was treated with methyl iodide and allowed to stand at room temperature overnight. Filtration gave 0.32 g., m.p. 234–235°. One crystallization from ethanol–ethyl acetate gave an analytical sample, m.p. 238–239°.

Anal. Calcd. for $C_8H_{20}INO$: C, 35.17; H, 7.38; N, 5.13. Found: C, 35.44; H, 7.64; N, 4.99.

2-Methyl-2-ethoxy-3-*t*-butylaminobutane hydrochloride was prepared from 3-methyl-3-*t*-butylamino-2-chlorobutane (liberated from the hydrochloride[3] by aqueous potassium carbonate) by boiling an ethanolic solution for 6 hr., followed by removal of the

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[10] N. R. Easton, D. R. Cassady, and R. D. Dillard, *J. Org. Chem.*, **29**, 1851 (1964).

solvent on a flash evaporator. This procedure gave an 85% yield of white crystals, m.p. 219–220° dec. Two crystallizations from ethanol–ethyl acetate gave an analytical sample, m.p. 221–222° dec.

Anal. Calcd. for $C_{11}H_{26}ClNO$: C, 59.03; H, 11.71; N, 6.26. Found: C, 58.90; H, 11.73; N, 6.12.

2-Methyl-2,3-bis(dimethylamino)butane.—A mixture of 15.9 g. (0.085 mole) of 3-dimethylamino-3-methyl-2-chlorobutane hydrochloride and 60 g. (0.53 mole) of 40% aqueous dimethylamine was shaken mechanically for 16 hr. The mixture was then warmed to 50° for 1 hr. after which the temperature was raised to 80° and maintained for 1 hr. The resulting mixture was treated with 8.4 g. (0.21 mole) of sodium hydroxide pellets, then extracted with three 15-ml. portions of ether. The ether extracts were combined and dried with anhydrous potassium carbonate. Distillation from glass wool through a 50-cm. Vigreux column gave 10.1 g. (75% yield) of colorless oil, b.p. 95° (54 mm.), n^{20}_{D} 1.4482. Redistillation gave an analytical sample, b.p. 93° (52 mm.), n^{20}_{D} 1.4482.

Anal. Calcd. for $C_9H_{22}N_2$: C, 68.29; H, 14.01; N, 17.70. Found: C, 68.28; H, 14.20; N, 17.3 (average).

The **methiodide** was precipitated from an ethyl acetate solution of the amine and had m.p. 155°. Attempts to crystallize the sample from ethanol plus ethyl acetate resulted in partial decomposition.

Acknowledgment.—The authors express their thanks to Air Reduction Chemical Company, New York, for generous samples of tertiary acetylenic carbinols; to Messrs. H. L. Hunter, David Cline, G. M. Maciak, and Charles Ashbrook of the Lilly Research Laboratories, Indianapolis, Indiana, for the analytical determinations; and to Eli Lilly and Company for support of this work. Special thanks are also due to Dr. D. J. Pasto for his assistance in interpreting many n.m.r. spectra.

Optically Active Amines. IV. The Dissymmetric Chromophore in the N-Salicylidene Derivatives of α- and β-Arylalkylamines[1]

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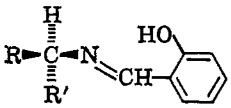
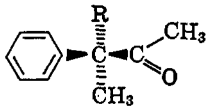
Received April 20, 1965

The degradative conversion of (+)-α-phenylneopentylamine to D-α-benzamido-β,β-dimethylbutyric acid definitively establishes the (*R*) configuration for this amine. This supports the suggestion made earlier that for the N-salicylidene derivatives of α- and β-arylalkylamines, a dissymmetric chromophore, arising from the interaction of the aryl group and the salicylidenimino moiety, is responsible for the observed Cotton effect near 315 mμ in their optical rotatory dispersion curves. In addition, an assessment of the steric requirements for this interaction is now possible. As borne out by optical rotatory dispersion and circular dichroism measurements with (*S*)-(−)-N-salicylidene-α,β-diphenylethylamine, consideration of these requirements may allow the assignment of the absolute configuration of an optically active α- or β-arylalkylamine from the sign of the Cotton effect near 315 mμ in the optical rotatory dispersion curve of its N-salicylidene derivative.

In the two previous papers in this series,[1b,2] the optical rotatory dispersion curves of a number of N-salicylidene-α- and -β-arylalkylamines (Ia–h) were reported. With the exception of Ih, these Schiff bases in ethanol display Cotton effects near 410 and 315 mμ. With dioxane or hexane as the solvent, only the Cotton effect near 315 mμ was observed, usually enhanced in amplitude. On the basis of a comparison of these curves with those of the N-salicylidene derivatives of (*S*)-(+)-*sec*-butylamine and a number of optically active aliphatic α-amino acid esters, for which no complete Cotton effect could be observed, it was suggested that, for the α- and β-arylalkylamine derivatives, the relatively strong Cotton effects may be due to a dissymmetric chromophore.[3] The latter is thought to arise from an interaction of the π-electrons of the aryl group and the salicylidenimino moiety. It was also suggested that this interaction may be analogous to that between the carbon–carbon π-electrons and the carbonyl group in an optically active β,γ-unsaturated or α-phenyl ketone[4] (II) which sometimes results in a Cotton effect near 300 mμ of much greater amplitude than those displayed by saturated analogs.





(*S*)-(+)-Ia, R = 1-$C_{10}H_7$; R′ = CH_3
(*S*)-(+)-Ib, R = C_6H_5; R′ = CH_3
(*R*)-(−)-Ic, R = C_2H_5; R′ = C_6H_5
(*R*)-(−)-Id, R = $CH_2CO_2C_2H_5$; R′ = C_6H_5
(*R*)-(−)-Ie, R = $C(CH_3)_3$; R′ = C_6H_5
(*S*)-(+)-If, R = $C_6H_5CH_2$; R′ = CH_3
L-(−)-Ig, R = CO_2CH_3; R′ = *p*-$HOC_6H_4CH_2$
(*S*)-(−)-Ih, R = C_6H_5; R′ = $C_6H_5CH_2$

(*S*)-(+)-IIa, R = H
(*R*)-(−)-IIb, R = C_2H_5

For these unsaturated ketones, the rotatory power depends principally on the spatial arrangement of the interacting carbon–carbon double bonds with respect to the carbonyl group. The conformational arrangements for which the interactions arise have been discussed in detail.[4a,b,d] For (*S*)-(+)-3-phenyl-2-butanone (IIa), the Cotton effect near 300 mμ is positive,[4b] whereas, for (*R*)-(−)-3-phenyl-3-methyl-2-pentanone (IIb), the effect is negative,[4b] the sign and the amplitude depending on the relative effective size of the R group in II with respect to that of methyl.

For the N-salicylidene derivative of an optically active α-arylalkylamine such as Ia–e, it was suggested that a similar analysis may allow a correlation between its absolute configuration and its rotatory dispersion

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(1) (a) Presented at the 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965, Abstracts of Papers, p. 21P. (b) Paper III: M. E. Warren, Jr., and H. E. Smith, *J. Am. Chem. Soc.*, **87**, 1757 (1965).

(2) H. E. Smith, S. L. Cook, and M. E. Warren, Jr., *J. Org. Chem.*, **29**, 2265 (1964).

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(4) (a) R. C. Cookson and J. Hudec, *J. Chem. Soc.*, 429 (1962); (b) A. Moscowitz, K. Mislow, M. A. W. Glass, and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 1945 (1962); (c) K. Mislow and J. G. Berger, *ibid.*, **84**, 1956 (1962); (d) K. Mislow, *Ann. N. Y. Acad. Sci.*, **93**, 459 (1962); (e) S. F. Mason, *J. Chem. Soc.*, 3285 (1962); *Mol. Phys.*, **5**, 343 (1962).