times. Recrystallization from methanol afforded 0.53 g of colorless crystals of **2**. TLC of the mother liquor indicated some starting material. Preparative TLC (six plates) was employed to obtain an additional 0.69 g of **2**, total yield 1.2 g (6.12 mmol), 43%, mp 234–235.5°.

Synthesis of Longimammine Hydrochloride (8). A Houben–Hoesch condensation of anisole with *N*-methylaminoacetonitrile hydrochloride afforded a 29% yield of 4-methoxy-ω-methylaminoacetophenone hydrochloride, mp 229–230.5°, lit.[24] mp 229–231°. This compound was reduced with sodium borohydride to give optically inactive **8** which was converted to the hydrochloride (mp 116–117°, lit.[20] mp 117–118°).

Synthesis of Longimammatine Hydrochloride (7). The condensation of *m*-methoxybenzaldehyde with nitromethane afforded *m*-methoxy-ω-nitrostyrene (mp 90–91°, lit.[25] mp 91–92°). A lithium aluminum hydride reduction of *m*-methoxy-ω-nitrostyrene afforded *m*-methoxy-β-phenethylamine which was converted to the hydrochloride, mp 129–130.5°. Following slight modification of the procedure described by Helfer,[15] the *m*-methoxy-β-phenethylamine hydrochloride cyclized with formaldehyde to yield **7** (mp 244–245.5°, lit[10] mp 238–239°).

Registry No.—**1**, 34222-77-0; **1** free base, 14788-32-0; **2**, 57196-60-8; **2** free base, 14097-39-3; **3**, 57286-92-7; **3** free base, 57236-57-4; **4**, 582-84-3; **6**, 57196-61-9; **7**, 57196-62-0 **8**, 57286-93-8; **8** HCl, 57236-58-5; **9**, 41136-36-1; L-phenylephrine hydrochloride, 61-76-7; anisole, 100-66-3; *N*-methylaminoacetonitrile, 5616-32-0; *m*-hydroxybenzaldehyde, 100-83-4; nitromethane, 75-52-5.

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Protonated Cyclopropane Intermediates from the Deamination of 3-Methyl-2-aminobutane

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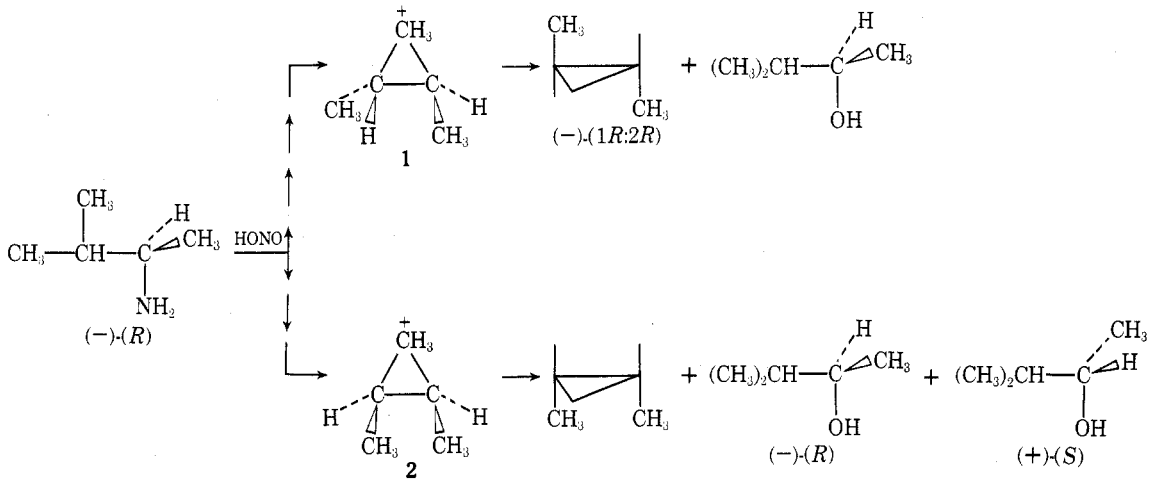
Received August 20, 1975

The formation of 1,2-dimethylcyclopropanes in the aqueous deamination of 3-methyl-2-aminobutane suggests that the 3-methyl group of the amine plays a role in the reaction. The extent of this role has now been established. Deamination of optically active amine provides *trans*-1,2-dimethylcyclopropane with 57 ± 2% net inversion and 3-methyl-2-butanol with a remarkable 37 ± 3% net *retention* of configuration. Study of the products obtained by deamination of 3-methyl-2-aminobutane-*1,1,1,3-d*$_4$ proves that 37 ± 4% of the 3-methyl-2-butanol formed but essentially none of the 2-methyl-2-butanol has undergone 1,2-methyl rearrangement. A scheme postulating the intervention in the deamination reactions of corner-protonated (methylene carbon) *cis*- and *trans*-1,2-dimethylcyclopropane intermediates adequately rationalizes all the observations. This mechanism cannot be distinguished from one implicating rapidly equilibrating edge-protonated cyclopropane intermediates.

Several carbonium ion reactions apparently generate[1,2] the protonated cyclopropane cation, c-$C_3H_7^+$. For example, postulation that deamination of 1-aminopropane-*1*-^{14}C produces a trace of c-$C_3H_7^+$ provides a simple explanation for the fact that the C_3H_6 fraction obtained contains 10% cyclopropane and that positions 2 and 3 of the 1-propanol formed each contain 2% of the ^{14}C label. Whether c-$C_3H_7^+$ is best represented as edge- or corner-protonated remains undecided.[1,3]

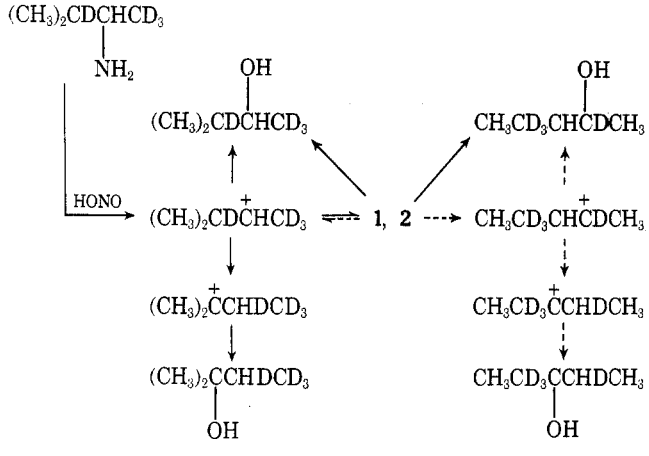
Protonated cyclopropane intermediates seemingly are less important in the deamination of higher alkylamines. The hydrocarbon fraction obtained from deamination of *n*-, *sec*-, or isobutylamine, 1-aminopentane, 2-aminopentane, isopentylamine, or 2-methyl-1-aminobutane contained only 1–5% of the pertinent alkylcyclopropane derivatives.[4,5] Likewise deamination of suitably deuterium-labeled *n*-, *sec*-, or isobutylamine afforded butanols and methylcyclopropane which revealed almost none of the

Scheme I[a]



[a] Illustration of how the intervention of protonated cyclopropanes 1 and 2 in the deamination of optically active 3-methyl-2-aminobutane could result in the formation of *trans*-1,2-dimethylcyclopropane with net inversion and 3-methyl-2-butanol with net retention of configuration.

Scheme II[a]



[a] Simplified representation of the deamination of 3-methyl-2-aminobutane-*1,1,1,3-d*$_4$. The appearance of CH_3 protons at the 1 position of 3-methyl-2-butanol and the 4 position of 2-methyl-2-butanol reveal the extent of participation by 1 and 2. The dotted arrows describe potential reaction paths which we were unable to detect.

deuterium rearrangement expected if protonated cyclopropanes had been formed.[6-8] This diminished contribution of alkyl-substituted protonated cyclopropane intermediates has been attributed to the destabilizing influence of alkyl–hydrogen eclipsing interactions.[6,7,9]

The deamination of 3-methyl-2-aminobutane (hereafter RNH_2) significantly differs from the deaminations just cited, for it yields a C_5H_{10} fraction of which 13–18% are 1,2-dimethylcyclopropanes.[4,10a] Protonated cyclopropane intermediates approximating 1 and 2 (Scheme I) may therefore be of significance in the deamination of RNH_2. If so, they could reveal their presence in three other ways: (1) optically active RNH_2 should yield *trans*-1,2-dimethylcyclopropane with inversion of configuration (Scheme I);[10b] (2) optically active RNH_2 might provide 3-methyl-2-butanol with net retention of configuration (Scheme I); and (3) 3-methyl-2-aminobutane-*1,1,1,3-d*$_4$ could afford 3-methyl-2-butanol and/or 2-methyl-2-butanol in which the CD_3 group had undergone a 1,2 shift (Scheme II). Results for all three experiments, presented below, establish that protonated cyclopropanes 1 and 2 are major intermediates in the deamination of 3-methyl-2-aminobutane.[11]

Experimental Section

Instrumental Methods. Most of the polarimetric data were obtained with a Perkin-Elmer 141 polarimeter; a few were obtained with a Zeiss 0.01° circular scale instrument. NMR spectra were run on a Varian A-60 instrument at room temperature; integrations of spectra employed either the device incorporated into the spectrometer or a Keuffel and Esser Compensating Polar planimeter. Eu(dpm) [tris(2,2,6,6-tetramethylheptanedionato)europium(III)] was an Alfa-Ventron product. Both Aerograph 90-P and 1520 gas–liquid chromatographs were used; peak areas were determined with either the planimeter or a Vidar 6300 digital integrator. Studies with solutions of known composition established that peak areas accurately reflected percent composition in determining both the amount of *trans*-1,2-dimethylcyclopropane in the C_5H_{10} mixture and the amount of 3-methyl-2-butanol in the $C_5H_{12}O$ mixture. VPC analysis of alcohol or alcohol–acetate fractions typically employed a 5 ft × 0.25 in. column packed with 10% Carbowax on 80–100 Chromosorb W operated at 75°. For the hydrocarbons, we used a 8 ft × 0.25 in. silver nitrate–ethylene glycol column in series with a nonylphenoxypolyoxyethyleneethanol on Firebrick column of the same size, both operated at room temperature. Under these conditions, *trans*-1,2-dimethylcyclopropane had the lowest retention time of the hydrocarbons present. Infrared spectroscopy (Perkin-Elmer 137 Infracord) confirmed the VPC-determined composition of several alcohol reaction mixtures.

Aqueous Deamination Reactions. The reaction apparatus consisted of a 2-l. three-necked round-bottomed flask immersed in a 55° bath and equipped with magnetic stirrer, combination pH electrode, pressure-equalizing dropping funnel, and a gas outlet tube attached to a trap filled with KOH pellets (cooled in ice) which in turn was attached to two empty dry ice cooled traps. Combination of a solution of sodium nitrite (41.5 g, 0.60 mol) in 370 ml of water with a solution of 3-methyl-2-aminobutane [21.9 g, 0.25 mol, $[\alpha]^{23}D$ +2.90° (neat)][12] in aqueous perchloric acid (22 ml of 70% $HClO_4$ plus 200 ml of water) produced the initial reaction mixture, pH 4.6. Addition of 70% $HClO_4$ from the dropping funnel adjusted the pH to 4.0; periodic further additions of acid maintained the pH at 4.0 ± 0.1 until reaction had ceased (~70 min). When the apparatus was disassembled, the first dry ice trap contained the bulk of the hydrocarbon. This material was dried over KOH and transferred to a precooled 25-ml distilling flask. The flask was immersed in an oil bath at room temperature and the hydrocarbon distilled into ice-cold 3-in. test tubes as the temperature of the oil bath was gradually increased. Normally we collected a single fraction. In the run described here four fractions of ~0.3 ml each were obtained, at the following bath temperatures: ≤27°, 28–34°, 34–41°, and 41–47°. Determination of the *trans*-1,2-dimethylcyclopropane content (6.1–6.6%) and optical rotation of each fraction provided the specific rotations entered in lines 5–8 of columns 4–6 of Table II. The higher "% net inversion" found for the highest boiling fraction must be caused by a trace impurity (contaminating nitrite?) whose nature was revealed by neither VPC nor infrared.

Table I
Stereochemistry of 3-Methyl-2-butanol from the Deamination of Optically Active 3-Methyl-2-aminobutane at 55°

	3-Methyl-2-aminobutane[a]		$(CH_3)_2CHCHOHCH_3$[b]		
Reaction conditions	$[\alpha]^{23}D$, deg	% optical purity	$[\alpha]^{27}D$, deg	% optical purity	% net retention[c]
H_3O^+– $NaNO_2$[d]	+2.69	77	+1.39	28	36
	−1.34	39	−0.84	17	44
	−2.09	60	−1.25	25	42[e]
	+3.14	90	+1.31	26	29
	+2.09	60	+1.12	21[f-h]	35
			+1.08	20[f]	34
	+2.90	83	+1.54	31[g,i]	37
			+1.66	33	40
			+1.60	32	39
HOAc– $NaNO_2$	−0.94	27	−0.26	4.8[f]	18
	−2.37	68	−0.48	9.6[g,j]	14
			−0.57	11.5	17
			−0.58	11.7	17

[a] Rotations are for neat amine, which when optically pure has $[\alpha]^{24}D \pm 3.5°$ (ref 13, 16). Experiments for each set of reaction conditions are listed in order of performance. [b] For deamination in acetic acid, the rotation is for the alcohol obtained from saponification of an alcohol–acetate mixture, primarily derived from the acetate portion. Data are for a neat mixture of 3-methyl-2-butanol and 2-methyl-2-butanol containing 30–70% of the former. Neat optically pure 3-methyl-2-butanol has $[\alpha]^{27}D \pm 5.0°$ (ref 16). [c] See text for references to absolute configurations. [d] Aqueous perchloric acid, pH 4.0. [e] Data for this run unaffected by redistillation of the alcohol mixture. [f] Rotations measured on a 20–40% solution of the C_5 alcohol mixture in ethanol. Optically pure 3-methyl-2-butanol has $[\alpha]D \pm 5.34°$ (c 5, EtOH) (ref 17). [g] Collected fractions were of approximately equal size; they are listed in order of increasing boiling point. [h] Two fractions. [i] Three fractions with bp 104–107, 107–108, and 108–109°, respectively. [j] Three fractions with bp 88–100, 100–107.5, and 107.5–108°, respectively.

Steam distillation of the deamination mixture in the reaction vessel gave a two-phase distillate to which several grams of KOH pellets were added. The separated organic layer was washed with water, dilute HCl, and water and dried over sodium sulfate. The decanted alcohol mixture was distilled through a small distillation apparatus. Normally a single fraction was collected; it was suitable for either optical rotation determination or NMR analysis. In the run described here, four fractions were collected, bp 91–104° (1.2 ml, 41.6%), 104–107° (2.2 ml, 46.8%), 107–108° (2.5 ml, 54.0%), and 108–109° (1.7 ml, 70.0%), where the percentage of 3-methyl-2-butanol in each fraction is specified. The calculated $[\alpha]^{27}D$'s for 3-methyl-2-butanol in the last three fractions were identical [+1.60 ± 0.04° (neat); lines 7–9, columns 4–6, Table I] but in the fraction of lowest boiling point it had $[\alpha]^{27}D$ +1.19°, corresponding to 29% net retention. Both the infrared spectrum and VPC indicated that fraction 1 contained small amounts of nitrites.

Deaminations in Acetic Acid. The reaction was carried out in a thermostated 2-l. three-necked round-bottomed flask equipped with magnetic stirrer, cork, gas outlet tube connected as described above, and a piece of rubber tubing to which was attached a flask containing 35 g (0.51 mol) of $NaNO_2$. The reaction vessel held 22 g [0.25 mol, $[\alpha]^{23}D$ −2.37° (neat)] of amine dissolved in 200 ml of acetic acid. Cautious addition of the $NaNO_2$ required ~60 min. Soon thereafter the apparatus was disassembled. The dry ice traps held a plentiful amount of hydrocarbon which, when treated as usual, gave four fractions with identical calculated $[\alpha]^{15}D$'s (lines 12–15, columns 4–6, Table II): bp 38° (1.5 ml); 38–42° (1.5 ml); 42–43° (1.0 ml); 43–44° (1.5 ml) (each contained 9.9–10.2% *trans*-1,2-dimethylcyclopropane). Addition of 20% NaOH raised the pH of the mixture in the reaction flask to 6.

In polarimetric experiments, the pH 6 material was steam distilled. The separated top layer (~15 ml) consisted of 19% 2-methyl-2-butyl acetate, 60% 3-methyl-2-butyl acetate, 5.5% 2-methyl-2-butanol, and 15.5% 3-methyl-2-butanol. Saponification of 7 ml of the mixture by heating it for 60 min under reflux with a solution of 6.5 g of KOH in 5 ml of water plus 25 ml of triethylene glycol was followed by steam distillation. The alcohol layer was separated, dried, and analyzed by VPC. It was then distilled and the three fractions obtained (usually only one) showed nearly identical values of $[\alpha]^{27}D$ for 3-methyl-2-butanol (last three entries, columns 4–6, Table I): bp 88–100° (1.2 ml, 60.0%); 100–107.5° (2.0 ml, 70.0%); 107.5–108° (1.5 ml, 78.2%). These calculated specific rotations primarily reflect the stereochemistry characterizing formation of 3-methyl-2-butyl acetate.

Table II
Stereochemistry of *trans*-1,2-Dimethylcyclopropane from the Deamination of Optically Active 3-Methyl-2-aminobutane at 55°

	3-Methyl-2-aminobutane[a]		*trans*-1,2-Dimethylcyclopropane[b]		
Reaction conditions	$[\alpha]^{23}D$, deg	% optical purity	$[\alpha]^{15}D$, deg	% optical purity	% net inversion
H_3O^+– $NaNO_2$[c]	−2.09	60	−15.9	35	58
	+3.24	90	+21.3	46	52
	+2.09	60	+15.8	34	57[d,e]
			+19.6	43	71
	+2.90	83	+20.7	45	54[d,f]
			+20.1	44	53
			+23.7	52	62
			+28.2	61	73
HOAc– $NaNO_2$	−1.94	55	−15.2	33[g]	59
	+2.53	72	+18.2	40[g]	55
	+2.53	72	+18.9	41[g]	57
	−2.37	68	−18.4	40	59[d,f]
			−17.4	38	56
			−17.9	39	57
			−17.6	38	56

[a] See footnote a, Table I. [b] Rotations measured on a diglyme solution containing 5–20% of a mixture of C_5H_{10} hydrocarbons of which 6–12% was *trans*-1,2-dimethylcyclopropane. Observed rotations were 0.04–0.66°. Optically pure material has $[\alpha]^{20}D \pm 46°$ and the absolute configuration is known (ref 22). [c] Aqueous perchloric acid, pH 4.0. [d] Collected fractions were of approximately equal size; they are listed in order of increasing boiling point. [e] Two fractions. [f] Four fractions. [g] Rotations measured at 5°.

Experiments with deuterioamine were performed on a much smaller scale. The pH 6 material was extracted with CCl_4 and the CCl_4 solution was washed with dilute HCl and water, dried over Na_2SO_4, filtered, and concentrated to a small volume, suitable for NMR analysis. Such a sample was primarily a mixture of 3-methyl-2-butyl and 2-methyl-2-butyl acetate, and contained a little CCl_4 and only traces of 3-methyl-2-butanol plus 2-methyl-2-butanol. NMR analysis established the deuterium distribution in only the secondary acetate.

Synthesis and Deamination of 3-Methyl-2-aminobutane-*1,1,1,3-d*$_4$. Repeated base-catalyzed exchanges[14] of 3-methyl-2-butanone with D_2O provided 3-methyl-2-butanone-*1,1,1,3-d*$_4$. Reduction of the corresponding ketoxime with sodium in ethanol supplied the desired amine. NMR analysis established that the ketone, oxime, and amine held >98% deuterium in the 3 position and that the first two held >95%, but the amine seemingly only 85 ± 3% deuterium in the 1 position [analysis of the deuterium content of RNH_2 required the use of $Eu(dpm)_3$, 0.171 mol/mol RNH_2]. Deuterium may have been lost during the sodium reduction or a trace impurity may have fortuitously caused the amine to show a spuriously large CH_3CHNH_2 peak. The data presented at the end of this section for the deuterium distribution in the 2-methyl-2-butanol isolated from aqueous deamination suggest that the second explanation is probably correct.

Studies with synthetic mixtures established that addition of $Eu(dpm)_3$ to a solution of 20–25 mg of a mixture of 3-methyl-2-butanol and 2-methyl-2-butanol in 0.5 ml of $CDCl_3$ (containing 1% Me_4Si) make it possible to integrate accurately the *gem*-dimethyl and single methyl resonances of each alcohol. The $Eu(dpm)_3$ to alcohol mole ratio was 0.3–0.5:1 and filtration of the NMR sample through glass wool removed insoluble matter and greatly improved the quality of the NMR spectra. In a typical experiment a ratio of 0.46:1 caused the $(CH_3)_2C$ resonance of secondary alcohol to ap-

Table III
Extent of Methyl Rearrangement in the 3-Methyl-2-butyl Product Formed by Deamination of $(CH_3)_2CDCHNH_2CD_3$ at 55°

Reaction conditions[a]	No. of samples[b]	% shift[c] Minimum[d]	% shift[c] Maximum[e]
H_3O^+–$NaNO_2$	2	33	40
	1	34	40
HOAc–$NaNO_2$	4	23	30
	2	23	32

[a] Two runs were performed in each solvent. Aqueous deamination (perchloric acid, pH 4.0) provided 3-methyl-2-butanol; acetic acid yielded 3-methyl-2-butyl acetate. [b] Multiple integrations were performed on each sample. [c] The error for each value is ±3%. [d] Based on the assumption that starting amine contained 85% deuterium in the CD_3 group. [e] Based on the assumption that starting amine contained 95% deuterium in the CD_3 group.

pear at τ 5.61 and the single CH_3 peak at τ 3.62. For tertiary alcohol, the corresponding peaks appeared at τ 4.83 and 6.80. The remaining proton resonances of the two alcohols did not interfere with any of the four peaks of interest. Analysis of the mixture of 3-methyl-2-butyl and 2-methyl-2-butyl acetates from deamination in acetic acid employed a similar technique but an accurate integration was only possible for the former.

$$\% \text{ shift} = 100(6.0 - 0.45R)/2.55(1 + R) \quad (1)$$

Table III records the data obtained in the deuterioamine studies. If it is assumed that d_4 amine contained 85% deuterium in the 1 position (0.45 protons/molecule) and if R = (dimethyl intensity)/(single methyl intensity), eq 1 defines the "minimum" percent methyl shift accompanying formation of 3-methyl-2-butyl product. A similar calculation which assumes 95% deuterium content in the 1 position provides the "maximum" values of Table III. These two estimates undoubtedly bracket the true value for percent methyl shift. The calculations make the valid assumption[11,15] that no loss of deuterium accompanied protic deamination of RNH_2-d_4.

Evaluation of the amount of methyl migration characterizing formation of 2-methyl-2-butanol proved difficult with the available NMR equipment. In theory the mixture of deuterated alcohols should exhibit weak adsorption at the CH_3CH_2 resonance in the absence of any methyl rearrangement because of incomplete deuteration in starting amine; an increase in this peak signifies methyl-shifted tertiary alcohol. Experimentally the CH_3CH_2 resonance, relative to the $(CH_3)_2C$ peak for tertiary alcohol, was smaller than expected if the starting amine contained 85% deuterium at the 1 position and *no* rearrangement had occurred. The best estimate for the area of the CH_3CH_2 peak derived from a comparison of the size of this peak relative to that of the *gem*-dimethyl peak for a weighed sample of deuterioalcohols [with $(Eu(dpm)_3$] before and after the addition of a weighed amount of 3-methyl-2-butanol. This experiment suggested that the *tert*-pentyl alcohol from the deamination reaction contained ≥95% deuterium in the CH_3CH_2 position. It therefore appears that the RNH_2-d_4 held ≥95% deuterium in its CH_3CHNH_2 position and that essentially no methyl-rearranged 2-methyl-2-butanol is present. Our data are insufficiently accurate to prove the absence of methyl-rearranged tertiary alcohol, but we can confidently assert that ≤5% of the tertiary alcohol formed had undergone methyl rearrangement, far less than the corresponding figure for secondary alcohol (Table IV) (see also ref 11).

Miscellaneous Details. The experimental procedures described above were dictated by our concern to obtain the purest material possible. No effort was made to maximize yields.

We sought to determine if 2-methyl-1-butanol, 2-pentanol, or 3-pentanol were present in the alcohol mixtures. No satisfactory separation of 3-pentanol from 3-methyl-2-butanol was achieved. No 2-pentanol could be detected so <0.5% was present. A small VPC peak indicated that a trace of 2-methyl-1-butanol (≲1%) may have been produced in aqueous deamination only. The maximum effect of the presence of 0.5% 2-pentanol plus 1% 2-methyl-1-butanol would be to cause the "% net retention" data of Table I to be 3% too high or low.

The percentage of 2-methyl-2-butanol in the alcohol mixtures was as follows: H_2O, 54 ± 3% ($C_5H_{13}N$) vs. 47 ± 1% ($C_5H_9D_4N$), k_H/k_D = 1.3 ± 0.1; HOAc, 25 ± 1% ($C_5H_{13}N$) vs. 15.5 ± 1% ($C_5H_9D_4N$), k_H/k_D = 1.8 ± 0.2. Calculation of k_H/k_D for the 3,2-hydride shift assumes that the four deuterium atoms present have altered the composition of the alcohol fraction solely by reducing the rate of this shift, which is probably nearly true.

It seemed possible that methyl-shifted 3-methyl-2-butanol could derive from solvolysis of 1,2-dimethylcyclopropane. If so, 1,1-dimethylcyclopropane should undergo solvolysis still more rapidly, since it directly yields the *tert*-pentyl cation. We were unable to detect any *tert*-pentyl alcohol among the reaction products from the aqueous deamination of *tert*-butylamine in the presence of 1,1-dimethylcyclopropane.

The ratio of *trans*- to *cis*-1,2-dimethylcyclopropane was 3.5:1 in water and 2.5:1 in acetic acid.

Results[5]

The reaction products from aqueous deamination of 3-methyl-2-aminobutane are readily separated into a high- and low-boiling fraction. The former is a mixture of 3-methyl-2-butanol and 2-methyl-2-butanol. Since only 3-methyl-2-butanol is chiral and since the absolute configuration and specific rotation of optically pure 3-methyl-2-aminobutane and 3-methyl-2-butanol are known,[13,16-21] determination of the composition and rotation of the alcohol mixture obtained from deamination of optically active amine defines the stereochemistry governing 3-methyl-2-butanol formation (Scheme I and Table I). Because the lower boiling fraction also contains only one chiral component, *trans*-1,2-dimethylcyclopropane, of known absolute configuration and maximum specific rotation,[22] the same technique permitted ready evaluation of the stereochemistry characterizing *trans*-1,2-dimethylcyclopropane formation (Scheme I and Table II).

We believe that the quantitative stereochemical data of Tables I and II, based on the measured optical rotations of purified mixtures of alcohols or hydrocarbons, are reliable. The products formed by deamination of RNH_2 have been extensively characterized (ref 10a). The tabulated data exhibit good reproducibility and are identical, within experimental error, whether based on the measured rotation for an unfractionated or fractionated reaction mixture. Only in the case of *trans*-1,2-dimethylcyclopropane from aqueous deamination did the fractionation procedure cause the stereochemical result to show a trend. In this instance we decided that refinement of the data of Table II did not justify the effort required if we were to determine accurately the specific rotation of isolated pure *trans*-1,2-dimethylcyclopropane from aqueous deamination of optically active amine. The yield of the hydrocarbon in the reaction is only ~0.25%.

In another series of experiments we employed NMR to measure the deuterium distribution in the alcohols isolated from deamination of 3-methyl-2-aminobutane-*1,1,1,3-d*$_4$ and thus to determine the amount of methyl rearrangement accompanying production of 3-methyl-2-butanol and 2-methyl-2-butanol. As Scheme II illustrates, such rearrangement causes, for each alcohol, the growth of the single methyl resonance at the expense of the *gem*-dimethyl peak. Table III shows that the secondary alcohol is extensively rearranged; in marked contrast, less than 5% of the tertiary alcohol from aqueous deamination had undergone methyl rearrangement.

Discussion

The four paragraphs which follow assess the significance of our experimental findings, as summarized in Table IV, and establish that the 3-methyl group participates to an extraordinary extent in the deamination of 3-methyl-2-aminobutane.

(1) Formation of *trans*-1,2-dimethylcyclopropane with 57% net inversion shows that methyl rearrangement in the deamination of RNH_2 closely follows loss of nitrogen from

Table IV
Description of the Reaction Products from the Protic Deamination of 3-Methyl-2-aminobutane at 55°

Property	H_2O[a]	HOAc[b]
trans-/*cis*-1,2-Dimethylcyclopropane	3.5	2.5
$(CH_3)_2CHCHXCH_3$/$(CH_3)_2CXCH_2CH_3$	0.85	3.0
Percent net inversion in *trans*-1,2-dimethylcyclopropane	57 ± 2	57 ± 2
Percent net retention in $(CH_3)_2CHCHXCH_3$	37 ± 3	17 ± 3
Percent methyl migration in $(CH_3)_2CHCHXCH_3$	33–40	23–32
Percent methyl migration in $(CH_3)_2CXCH_2CH_3$	<5	Not determined

[a] X = OH. [b] X = OAc.

Table V
Predicted Stereochemistry of $(CH_3)_2CHCHXCH_3$ Formed by the Deamination of 3-Methyl-2-aminobutane If Scheme I Is Correct[a]

Step of calculation[b]	H_2O	HOAc
1. % of RX derived from 1 + 2	73 (2 × 36.5)	55 (2 × 27.5)
2. % of RX derived from 1	57 (73 × 3.5/4.5)	39 (55 × 2.5/3.5)
3. % net retention in RX because of 1 pathway	32 (57 × 0.57)	22 (39 × 0.57)
4. % net inversion in RX because of non-1, 2 pathway	6 (27 × 0.23)	13 (45 × 0.28)
5. Predicted % retention in RX[c]	26	9
6. Observed % retention in RX	37 ± 3	17 ± 3

[a] X = OH (H_2O) or OAc (HOAc). [b] The numbers refer to statements in the text where the calculation is explained. The data employed may be found in Table IV or the text. [c] Line 3 minus line 4.

the alkyldiazonium ion (see Scheme I). Methyl rearrangement in the deamination of optically active neopentylamine-*1-d*, which resembles the methyl migration of Scheme I, causes at least 85% net inversion at the migration terminus.[23]

(2) The process just described can also explain the observed net *retention* of configuration in 3-methyl-2-butanol, particularly if ion **1** is the intermediate from which much of the alcohol derives. This unexpected retention of configuration cannot be attributed to micelle phenomena, given the molecular weight of RNH_2 and the reaction conditions employed.[24,25] By contrast deamination of a secondary alkylamine generally yields *inverted* substitution product; for example, 2-aminobutane affords 2-butyl alcohol (or acetate) with 23 (H_2O)–28% (HOAc) net inversion.[24,26]

(3) The stereochemical experiment of 2 only reveals 3-methyl-2-butanol originating from **1**, but the deuterioamine experiment counts rearrangements occurring via both **1** and **2**. If **1** and **2** are intermediates, they are the source of a remarkable 66–80% of the 3-methyl-2-butanol formed by the aqueous deamination of RNH_2. While <1% of the 3-methyl-2-butyl acetate obtained from acetolysis of 3-methyl-2-butyl tosylate has undergone methyl rearrangement (hydrogen participation dominates),[27,28] the corresponding figure is >23% for acetic acid deamination of RNH_2.

(4) The absence of an appreciable amount of methyl-shifted 2-methyl-2-butanol, $CH_3CD_3COHCHDCH_3$, from among the products of aqueous deamination of deuterioamine eliminates $CH_3CD_3C^+CHDCH_3$ as an important intermediate in the reaction (Scheme II). Deaminative ions **1** and **2**, like their relatives in strongly acidic media,[3,29] therefore cannot open directly to the *tert*-pentyl cation. Moreover, the absence of $CH_3CD_3C^+CHDCH_3$ renders highly unlikely the intervention of $CH_3CD_3CHC^+DCH_3$ in the deamination of deuterioamine, for there is no reason to suspect that the pedigree of this 3-methyl-2-butyl cation would render it, once formed, incapable of undergoing extensive favorable hydride shift to $CH_3CD_3C^+CHDCH_3$. Certainly in other deaminations a cation formed by prior rearrangement exhibits no impaired ability to undergo still further rearrangement. The 3-methyl-2-butyl cation generated by a 1,2-hydride shift in the deamination of 3-methyl-1-aminobutane gives a higher ratio of *tert*-pentyl to 3-methyl-2-butyl product than does that obtained directly from 3-methyl-2-aminobutane.[10,30] Similarly the extent of isoenergetic 1,2-hydride shift by the 2-butyl cation is approximately the same when the cation is formed by deamination of 2-aminobutane, 1-aminobutane (prior 1,2-hydride shift), or 2-methyl-1-aminopropane (prior 1,2-methide shift).[6,7]

Scheme I qualitatively accommodates the above observations on the deamination of 3-methyl-2-aminobutane. It postulates that cations **1** and **2** are intermediates which undergo either deprotonation to form 1,2-dimethylcyclopropane or nucleophilic attack with inversion by solvent[31] to yield 3-methyl-2-butanol of retained configuration, but which do not open to either the 3-methyl-2-butyl or 2-methyl-2-butyl cation. Since the scheme posits an intimate relationship between cyclopropane formation and the methyl rearrangement and stereochemistry characterizing formation of 3-methyl-2-butanol, it can be quantitatively tested for internal consistency. If it is assumed that secondary product derives only from Scheme I or a competitive, "normal" substitution process which affords material of net inverted configuration (4 below), the available data permit us to calculate the stereochemistry expected for 3-methyl-2-butanol without reference to the measured value for the quantity. The calculation, outlined in Table V, requires five steps: (1) the percent of $(CH_3)_2CHCHXCH_3$ derived from (**1** + **2**) is set at twice the percent methyl migration in $(CH_3)_2CHCHXCH_3$; (2) ions **1** and **2** are assumed to give the same $(CH_3)_2CHCHXCH_3$/1,2-dimethylcyclopropane ratio, so that the amount of $(CH_3)_2CHCHXCH_3$ obtained from **1** relative to that obtained from **2** is taken as identical with the ratio of *trans*- to *cis*-1,2-dimethylcyclopropane; (3) the net retention in that $(CH_3)_2CHCHXCH_3$ derived from **1** is set equal to the net inversion in *trans*-1,2-dimethylcyclopropane, while **2** affords only racemic alcohol or ester; (4) the stereochemistry of $(CH_3)_2CHCHXCH_3$ not originating from **1** and **2** is assumed to be the same[32] as that of $CH_3CH_2CHXCH_3$ produced by deamination of 2-aminobutane (see above); (5) the result is that, in water, deamination of RNH_2 is predicted to afford 3-methyl-2-butanol with 26% net retention of configuration (37 ± 3% observed) while in acetic acid it should yield 3-methyl-2-butyl acetate with 9% net retention (17 ± 3% observed).

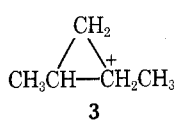
Given the simplicity of Scheme I, the approximations made in the calculation, and the experimental uncertainty in the numerical data employed, the agreement between expectation and observation is quite reasonable.

Mechanistic alternatives to Scheme I which assume that **1** and **2** represent transition states seem far more ad hoc.

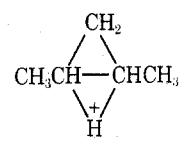
Such mechanisms must introduce an additional reaction sequence to explain 1,2-dimethylcyclopropane formation. The rearranged 3-methyl-2-butyl cation, $CH_3CD_3CHC^+DCH_3$, might react with solvent to provide $(CH_3)_2CHCHXCH_3$ of some net retained configuration;[33] the failure of this cation to undergo 1,2-hydride shift would have to be attributed to conformational factors. While our data offer no evidence for this open, rearranged 3-methyl-2-butyl cation, such a species might be the source of the 3-methyl-1-butene-*2-d* obtained[11] by deamination of 3-methyl-2-aminobutane-*3-d*. To explain formation of this olefin in the context of Scheme I, we must allow **1** and **2** to undergo deprotonation directly to 3-methyl-1-butene.

Edge- or Corner-Protonated? Neither edge- nor corner-protonated cyclopropanes appear capable of rationalizing all the reactions in which such intermediates have been implicated. With regard to the parent ion, $c\text{-}C_3H_7^+$, the edge-protonated species best explains[1] the isotopic distribution in (a) 1-propanol obtained from solvolysis of cyclopropane in deuteriosulfuric acid; (b) 1-propyl formate produced by formolysis of 1-propyl-*1*-^{14}C tosylate; and (c) unreacted 1-bromopropane recovered after treating 1-bromopropane-*1*-^{13}C with aluminum bromide. However, corner-protonated $c\text{-}C_3H_7^+$ seemingly is the essential intermediate[3] in rearrangements of the isopropyl cation in SbF_5–SO_2ClF. We wish to inquire whether edge- or corner-protonated dimethylcyclopropane intermediates better account for the data in Table IV.

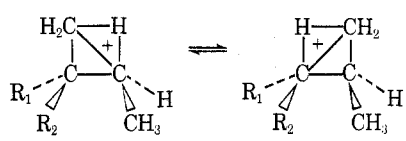
Let us assume that **1–6** represent the complete set of protonated 1,2-dimethylcyclopropanes. Kramer's report[29] that protonated cyclopropanes in SbF_5–HSO_3F generally possess a single exchangeable hydrogen is compatible with either the edge- or a somewhat unsymmetrical[31] corner-protonated formulation. For the case at hand complete equilibration of **5a** with **5b** and **6a** with **6b** before product formation is indistinguishable from Scheme I, but a mechanism postulating partial equilibration is worth exploring.[34,35]



3



4 (cis and trans)



	R_1	R_2	
5a	CH_3	H	**5b**
6a	H	CH_3	**6b**

In this mechanism only **5a** and **6a** are initially formed by deamination of RNH_2. Each could be the source of the trace of 2-methyl-1-butanol detected. Each, prior to equilibration with its tautomer, would afford 3-methyl-2-butanol of *retained configuration* but *unrearranged* methyl groups. Since the calculation of Table V recognizes as retention events only those reactions passing through **1** (or equilibrations of **5a** with **5b**), it should underestimate (as may well be the case) the extent of net retention attending formation of 3-methyl-2-butanol if the edge-protonated mechanism is correct. Can the same edge-protonated intermediates explain certain aspects of the deamination of 2-methyl-1-aminobutane?[33]

This deamination produces 9.5% 2-pentanol and 0.5% 3-methyl-2-butanol. An attractive edge-protonated mechanism to explain these observations[36] is $CH_3CH_2CH(CH_3)CH_2N_2^+ \rightarrow$ **5a, 6a** $\rightarrow [3]^\ddagger \rightarrow$ **4** $\rightarrow$ 2-pentanol, with **5a, 6a** $\rightarrow$ 3-methyl-2-butanol. Thus both the small yield of 3-methyl-2-butanol from 2-methyl-1-aminobutane and the failure of RNH_2 to afford any 2-pentanol are incompatible with **5a, 6a** as the sole initial protonated cyclopropane intermediates common to the deamination of the two amines. If the edge-protonated mechanism for deamination of RNH_2 is preferred, we must postulate that deamination of 2-methyl-1-aminobutane forms **5a, 6a** and $[3]^\ddagger$ in competitive reactions: $(CH_3)_2CHCHOHCH_3 \leftarrow$ **5a, 6a** $\leftarrow CH_3CH_2CH(CH_3)CH_2N_2^+ \rightarrow [3]^\ddagger \rightarrow CH_3C^+HCH_2CH_2CH_3 \rightarrow$ 2-pentanol.

The corner-protonated intermediates explain all but one of the cited observations, if it is assumed that **1** and **2** are more stable than **3**.[3] Deamination of 2-methyl-1-aminobutane initially provides **3**, which primarily affords 2-pentanol but to a small extent isomerizes to **1, 2,** ultimately yielding 3-methyl-2-butanol. Deamination of 3-methyl-2-aminobutane proceeds according to Scheme I. The failure of the isomerization **1, 2** $\rightarrow$ **3** to occur explains the lack of 2-pentanol, but the origin of the trace of 2-methyl-1-butanol remains obscure.

Acknowledgments. A.G.M. held an NSF undergraduate summer fellowship and Z.Z.M. was the John F. White summer fellow in 1974. Most of the data reported here derive from the B.A. Theses of A.G.M. (1970) and H.A.N. (1974).

Registry No.—(−)-(*R*)-3-Methyl-2-aminobutane, 34701-33-2; (−)-(*R*)-3-methyl-2-butanol, 1572-93-6; (+)-(*S*)-3-methyl-2-butanol, 1517-66-4; (−)-(1*R*:2*R*)-1,2-dimethylcyclopropane, 20520-64-3; *cis*-1,2-dimethylcyclopropane, 930-18-7; (−)-(*R*)-3-methyl-2-butanol acetate, 57274-06-3; (+)-(*S*)-3-methyl-2-butanol acetate, 56640-64-3; 3-methyl-2-aminobutane-*1,1,1,3-d*$_4$, 57274-07-4; 3-methyl-2-butanone, 563-80-4; D_2O, 7789-20-0.

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(33) Deamination of optically active 2-methyl-1-aminobutane gives 2-pentanol with 38% net inversion. See W. Kirmse and H. Arold, *Chem. Ber.*, **103**, 23 (1970).
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(35) No attempt will be made to distinguish between partial equilibration of **5a** with **5b** and **6a** with **6b** and initial formation of **5a, 6a** with subsequent isomerization to **1,2**.
(36) Other protonated cyclopropane intermediates are responsible for the partial racemization of the isolated 2-methyl-1-butanol (ref 33).

Thermal Fragmentation of β-Halo Esters via Chain Halogenolysis–Decarboxylation–Elimination[1]

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Received April 14, 1975

Solution pyrolysis (240°) of dimethyl 1,2-dibromocyclobutane-1,2-dicarboxylate gives CO_2 and methyl bromide (2 mol) in good yield in lieu of cracking or geometrical isomerization. According to their behavior under pyrolysis conditions, methyl 3-bromocyclobutene-2-carboxylate and methyl 3-bromobutadiene-2-carboxylate are permissible intermediates in the cyclobutane decomposition. Elimination–debromocarbomethoxylation of β-halo esters appears to be quite general since derivatives of the methyl 3-halopropenoates and methyl 3-bromopropanoate also decompose to CO_2 and methyl halide at elevated temperatures. Elimination products, unstable under high temperature pyrolysis conditions, are not obtained in significant yield. The kinetics for these fragmentations appear complex, exhibiting in some cases autocatalytic behavior. Substituent and solvent effect data and the results of gas phase decomposition rule out pericyclic or ion pair mechanistic possibilities. The effects of additives on the course of pyrolysis reveal that a chain decomposition is important, more likely involving halide ion displacement on the ester group followed by decarboxylation–elimination than a similar free-radical chain mechanism. Catalysis of halo ester fragmentation by halide ion is quite effective, and in some cases moderate yields of elimination product are obtained. The use of halogenolysis–decarboxylation–elimination in synthetic and degradative schemes is discussed.

In search for heavy-atom effects in thermal reactions which in principle involve diradicals, we have examined the pyrolysis of halogen substituted cyclobutanes. In one series a surprising fragmentation took place in lieu of expected ring opening. We report now the generality of this halogenolytic degradation of β-halo esters along with data that suggest a mechanism.

Results and Discussion

Neither cracking to methyl 2-bromopropenoate nor geometrical isomerization[2] were observed on static pyrolysis of the stereoisomeric dimethyl 1,2-dibromo-1,2-cyclobutanedicarboxylates (**1**)[3] in diphenyl ether (DPE), diphenylmethane (DPM), or nitrobenzene (NB). Decomposition at 240° produced in nearly quantitative yield methyl bromide (2 mol), identified by GLC and NMR comparison with authentic material. No other volatile organic material was obtained in significant amount, but CO_2 (60% of the theoretical 2 mol) was trapped from pyrolysis solutions using Ascarite.

Cyclobutene **2**, the product of a suspected eliminative debromocarbomethoxylation of **1**, was prepared independently and pyrolyzed. At 160° smooth first-order ring opening to **3** ($k = 5.1 \times 10^{-4}$ sec^{-1}) occurred, followed by slow decomposition to nonvolatile, presumably polymeric material. Butadiene **3** from preparative GLC of a pyrolysate of **2** polymerized as a neat sample at room temperature. Characterization involved ir, NMR, and tandem VPC–mass spectral analysis of a CCl_4 solution of **3** obtained by collection of a GLC injector port pyrolysis of **2**. Remarkably, heating a sample of **2**, after ring opening at 160°, briefly at 240° gave methyl bromide and CO_2.

With the novel eliminative degradation of **1** a strong possibility, we examined other halo esters expecting that the fragmentation might be general. Indeed, solution pyrolysis of **4–7** gave methyl bromide and CO_2 (about 60% each). The halomaleates, obtained from commercially available bromo- and chloromaleic anhydride, were the starting materials for **4–6**. Preequilibrium of maleates and fumarates (about 40:60), which was rapidly established at the onset temperatures for fragmentation to methyl bromide (300, 290, and 250°, respectively), was indicated by GLC and the appearance in the NMR of new signals assignable to olefinic (lower field for the fumarates) and OMe resonances. Dimethyl bromofumarate (**5**),[4] obtained by preparative GLC of a partial pyrolysate, was identified from spectral data and pyrolyzed separately. Brief pyrolysis of the *Z* and *E* diastereomers of **7**, obtained separately from the HBr addition products of methyl phenylpropiolate,[5] allowed the approach to preequilibrium (63 ± 4% *Z*, 290°, DPE) from both sides. The nature of the pyrolytic isomerization for **4–7** which accompanied fragmentation to methyl bromide was not established, and heterogeneous as well as molecular mechanisms are possible.[6]