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STEREOCHEMISTRY AND MECHANISM OF THE FORMATION OF 1,2-DIMETHYLCYCLOPROPANE IN THE DEAMINATION OF OPTICALLY ACTIVE 3-METHYL-2-BUTYLAMINE[1a]

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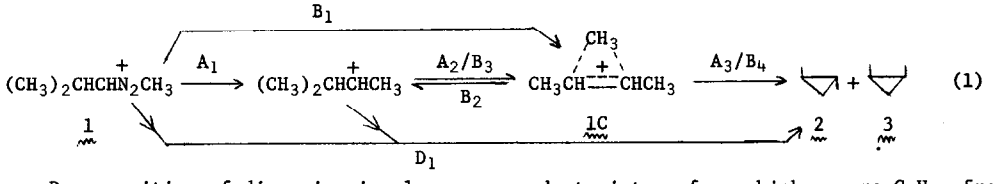
Speculation continues on the role of protonated cyclopropanes, "free" or "hot" cations, ion-pairs, *et al.* as intermediates in the deamination of primary aliphatic amines.[2-4] A belief that knowledge of the stereoselectivity characterizing the formation[5] of *trans*-1,2-dimethylcyclopropane (2) in the deamination of optically active 3-methyl-2-butylamine should provide insight into these questions prompted the experiments described below.



(1)

Decomposition of diazonium ion 1 gave a product mixture from which a pure C_5H_{10} fraction, bp 25-40°, was obtained.[5] VPC analysis established the presence of 2, *cis*-1,2-dimethylcyclopropane (3), 2-methyl-1-butene, 2-methyl-2-butene and 3-methyl-1-butene and quantitatively determined 2. Measurement of the optical rotation of a diglyme solution of the C_5H_{10} fraction obtained from optically active 1 defined the specific activity of 2 and hence the stereochemistry of the conversion 1 → 2, since 2 is the sole chiral component of the hydrocarbon fraction and the absolute configuration and rotation of optically pure 3-methyl-2-butylamine[7-9] and 2[6] are known. The fact that the same specific rotation for optically pure 2 is deduced from the observed rotation of a diglyme solution of either pure 2 or a hydrocarbon mixture containing 13% 2 confirms our experimental procedure.[6]

Table I. Stereochemistry of *Trans*-1,2-Dimethylcyclopropane from the Deamination of Optically Active 3-Methyl-2-butylamine

Reaction Conditions	Amine[a,b]		*Trans*-1,2-dimethylcyclopropane[a,c]			% Net Inversion[d]
	$[\alpha]^{23}_D$	% Optical Purity	α^5_D	$[\alpha]^5_D$	% Optical Purity	
$HClO_4/H_2O/NaNO_2$[e]	+2.69	78	+.21	+3.6	7.8	10
$HOAc/NaNO_2$	-1.94	55	-.36	-15	33	59
	+2.53	72	+.60	+18	40	55
	+2.53	72	+.66	+19	41	57
$CHCl_3/RONO$[f]	-1.17	33	-.71	-10	21	64
	-1.17	33	-.34	-10	22	66

[a]All rotations measured in a 2 dm tube. [b]Rotations refer to neat material which when optically pure has $[\alpha]^{24}_D \pm 3.5°$. [c]Rotations refer to diglyme solutions containing 10-20% of a hydrocarbon mixture whose composition was solvent independent and which contained ~10% of 2. Optically pure 2 has $[\alpha]^{20}_D \pm 46°$. [d](-)-2 is *R:R* and (-)-amine is *R*. [e]pH = 4. [f]Contained 1 mole HOAc/mole RNH_2.

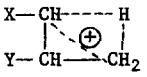
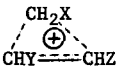
The data of Table I establish that 2 is formed with a high degree of stereoselectivity in acetic acid and chloroform but with nearly total racemization in water. As expected, our observed stereoselectivity for intramolecular alkyl migration toward a potential secondary carbocation is lower than that for the same process when a primary carbocation is involved. Net inversion exceeds 85% for methyl migration in the deamination of optically active neopentylamine-1-d (HOAc).[3b,10] Intermolecular S_N displacements are similarly less stereoselective for *sec*-alkyl diazonium ions: 28%(HOAc)-23%(H_2O) net inversion for 2-butylamine *versus* 69%(HOAc) for 1-butylamine.[12,13] These differences in stereoselectivity for *sec*- and *prim*-alkyldiazonium ions are minimum differences, since diazoalkane formation and its concomitant racemization are more significant for the latter.[3c]

The available data justify three generalizations about the transformation of 1 into 2:

(1) The 3-methyl-2-butyl cation probably intervenes, at least in aqueous solution. It best accounts[2] for the production of highly racemic 2 in H_2O and of trace amounts of 2 and 3 in the deamination of isopentylamine.[5] Mechanism A_{1-3} of eq 1 introduces this cation in a simple manner. Mechanism B_{1-4}, with direct conversion of 1 to 1C and subsequent opening of and reclosing to 1C, or a racemization process involving equilibrating methyl-bridged ions, cannot be excluded.

Mechanisms A and B equally well rationalize the higher net inversion encountered in $CHCl_3$ and HOAc since these less polar solvents should give shorter-lived cations.[3c] In A,

Table II. Protonated Cyclopropanes from the Deamination of Alkylamines in HOAc

Diazonium Ion	% Cyclopropanes in Alkane Fraction[a]	Structure of Possible Protonated Cyclopropanes						
								
		Name	X	Y	Name	X	Y	Z
4 = $CH_3CH_2CH_2N_2^+$	10	4E	H	H	4C	H	H	H
5 = $(CH_3)_2CHCH_2N_2^+$	5	5E	H	Me	5C	H	Me	H
6 = $CH_3(CH_2)_3N_2^+$	1	6E	Me	H	6C	Me	H	H
7 = $CH_3CH_2CHN_2^+CH_3$	1	7E	Me	H	7C	H	Me	H
1 = $(CH_3)_2CHCHN_2^+CH_3$	18	1E	Me	Me	1C	H	Me	Me

[a]From refs. 3, 5 or references therein.

cyclization of the initial cation will be more rapid while in B deprotonation *via* B_4 will compete more favorably with B_2. Neither A or B explains why net inversion in $CHCl_3$ does not exceed that in HOAc to a larger extent,[3c] but a suitable blend of A,B, conformational[12] and counterion[2] effects, and stereospecific front-side rearrangements[14] seem adequate to account for this[1a] or any[3] observation.

(2) Introduction of a protonated cyclopropane (such as 1C) as the immediate precursor of 2,3 offers the best rationalization for a) the large amount of 2,3 produced by 1; b) the data of Tables I and II; c) the tentative observation[1a] that aqueous decomposition of 1 yields 3-methyl-2-butanol of net retained configuration. Definitive evidence for any protonated cyclopropane other than $C_3H_7^+$ is lacking,[3,4] except possibly in the work of Kirmse and Arold.[11]

The most obvious alternative mechanism for formation of 2,3 is D_1, a 1,3-elimination by 1 and/or the 3-methyl-2-butyl cation. If D holds, we expect the yield of methylcyclopropane from the 2-butyldiazonium ion (7) to surpass that of 2,3 from 1, since the latter reaction competes against a more advantageous 1,2-hydride shift (2° → 3° cation)[5,15] and results in a more highly strained cyclopropane derivative.[16] We also expect the counterion to play a prominent role in D in $CHCl_3$ and HOAc, especially in the former, and to promote production of 2 with retained configuration. Since neither expectation is fulfilled (Table I,II) mechanism D cannot predominate.

(3) Decomposition of the *n*-propyldiazonium ion, 4, leads to edge-protonated ion 4E,[4] but we believe 1 gives the corner-protonated ion 1C,[17] if it yields a protonated cyclopropane at all. Ion 1C offers the best opportunity for charge stabilization by the two methyl groups.

Although edge-protonated ions 4E → 7E appear capable of rationalizing the trend in yields of cyclopropane derivatives from 4 - 7 (Table II), there is no obvious reason why 1E should afford so much 2 and 3. In fact a unique class of intermediate cannot explain why 5 produces slightly less cyclopropane derivative than 4 while 1 gives far more than 7, since the relationship between 5 and 4 is the same as that between 1 and 7.

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17) 1E, a "tautomer" of 1C, could be an intermediate in the formation of 1,2-dimethylcyclopropane[5] and 3-methyl-2-butanol[11] from the deamination of 2-methyl-1-butylamine.