Factors Affecting the Formation and Stability of the Equilibrating Protonated Cyclopropane[1]

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Abstract: Deamination of *n*-propyl-3,3,3-d_3-amine and *n*-propyl-2,2-d_2-amine gave hydrocarbon mixtures containing cyclopropane and propene. The deuterium content of the cyclopropane varied with the reaction medium and this is attributed to solvent dependency on the extent of equilibration of the intermediate protonated cyclopropane. Routes for propene formation are also suggested.

An equilibrating protonated cyclopropane has been postulated to account for scrambling observed in the *n*-propyl alcohol obtained from deamination of labeled *n*-propylamine[3] and to explain the products obtained from cyclopropane ring opening reactions.[4] However, the possible intermediacy of a protonated cyclopropane in cyclopropane *formation* has been studied in only one system, *n*-propyl-3,3,3-d_3-amine.[5] Direct insertion into C-3 concurrent with deuterium loss would give cyclopropane-d_2. When diazotization was effected in 35% perchloric acid the deuterium content of cyclopropane was 43 ± 1% d_2 and 57 ± 1% d_3. An equilibrating protonated cyclopropane was proposed to account for the extensive retention of deuterium.[5]

We would now like to report on the effect of solvent on the stability of the equilibrating protonated cyclopropanes obtained from diazotization of *n*-propylamine.

Results and Discussion

Diazotization of *n*-propyl-3,3,3-d_3-amine–HOAc in chloroform gave a hydrocarbon mixture containing 10% cyclopropane and 90% propene.[6] Limited scrambling of deuterium in the cyclopropane (84% d_2, 16% d_3) occurred relative to that observed in 35% $HClO_4$ (43% d_2, 57% d_3).[5] An intermediate amount of scrambling occurred in aqueous acetic acid (Table I). These results strongly indicate that an equilibrating protonated cyclopropane does indeed occur in the diazotization of *n*-propylamine (Scheme I), and that the extent of equilibration is markedly solvent dependent. Since protium–deuterium exchange between solvent and the equilibrating protonated cyclopropane does not occur,[7] these solvent-dependent results require further explanation.

Table I. Diazotization of *n*-Propylamine-3,3,3-d_3[a,b]

	—Deuterium content,[c] mol %—			
	△			
Acid–solvent	d_2	d_3	d_2	d_3
HOAc–$HCCl_3$	84	16	5	95
HOAc–H_2O[d]	52	48	10	90
35% $HClO_4$–H_2O[d,e]	41	59	14	86

[a] Amine (4.4% d_2, 95.6% d_3; 1 equiv), HOAc (1 equiv), and OcONO (1.1 equiv) and solvent at reflux. [b] Duplicate runs unless otherwise stated. [c] The deuterium content corrected for d_2 in starting amine. [d] Sodium nitrite used as diazotizing agent; reaction carried out at room temperature. [e] Single run.

It has been pointed out that anions in polar aprotic solvents (DMSO, DMF) are much more reactive toward hydrogen than in protic solvent.[8] For example, sodium methoxide catalyzed H–D exchange, on carbon α to a cyano group, was 10^9 times faster in dimethyl sulfoxide than in methanol.[9] Similarly, tetraethylammonium fluoride decomposes to ethylene and hydrogen fluoride when warmed in aprotic solvents.[10]

Deuterium–hydrogen isotope effects are to a limited degree dependent upon the polarity of solvent[11] and temperature.[12] However, the magnitude of these effects[13] would be too small to account for the extent to which deuterium scrambling occurs.

The results can best be rationalized by considering the effect of solvent on the extent to which equilibration of the protonated cyclopropanes (A, B, C, D, and E) can occur prior to deprotonation to cyclopropane (or collapse to propyl alcohol[3]). In aprotic media deprotonation would be expected to occur more rapidly than in protic media, *i.e.*, less equilibration (hence greater loss of deuterium) would be expected to occur in chloroform than in aqueous acetic acid or 35% perchloric acid. In addition, while the difference in

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[1] (a) Financial support (Grant No. GP-3976) from the National Science Foundation is gratefully acknowledged. (b) For the preceding paper in this series, see L. Friedman, A. T. Jurewicz, and J. H. Bayless, *J. Am. Chem. Soc.*, **91**, 1795 (1969).

[2] Taken from the Ph.D. Thesis of A. T. J., Case Institute of Technology, June 1967.

[3] (a) G. J. Karabatsos, C. E. Orzech, and S. Meyerson, *J. Am. Chem. Soc.*, **87**, 4394 (1965); (b) C. C. Lee, J. E. Kruger, and E. W. C. Wong, *ibid.*, **87**, 3985 (1965); (c) C. C. Lee and J. E. Kruger, *ibid.*, **87**, 3986 (1965).

[4] (a) R. L. Baird and A. A. Aboderin, *ibid.*, **86**, 252 (1964); (b) N. C. Deno and D. N. Lincoln, *ibid.*, **88**, 5328 (1966); (c) H. Hart and R. H. Schlosberg, *ibid.*, **88**, 5030 (1966).

[5] A. A. Aboderin and R. L. Baird, *ibid.*, **86**, 2300 (1964).

[6] The hydrocarbon composition (10 ± 2% cyclopropane, 90 ± 2% propene) from diazotization of *n*-propylamine is solvent independent.

[7] Cyclopropane obtained from diazotization of *n*-propylamine-d_2 in D_2O–DOAc (1:1) contained only 1% deuterium.

[8] A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962); A. J. Parker, *Advan. Org. Chem.*, **5**, 16 (1965).

[9] D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Haberfield, *J. Am. Chem. Soc.*, **83**, 3688 (1961).

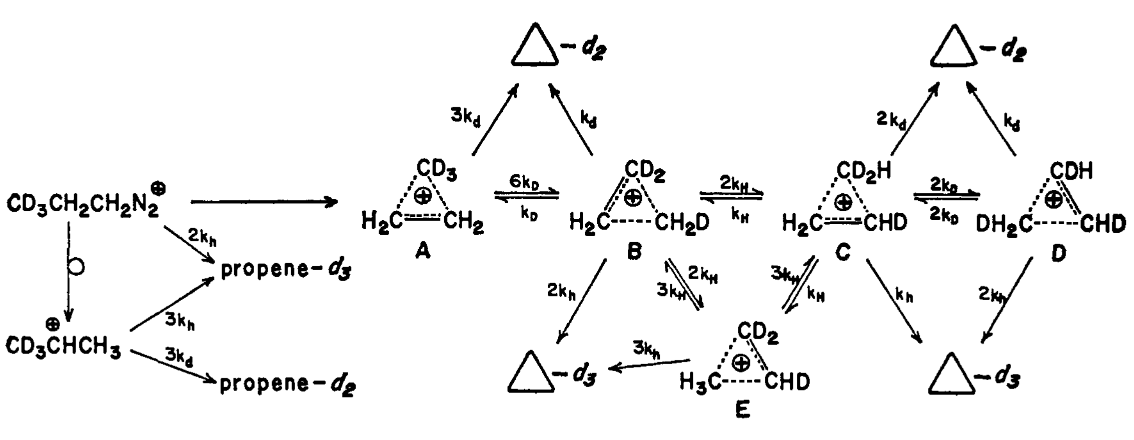
[10] W. T. Miller, J. Fried, and H. Goldwhite, *ibid.*, **82**, 3091 (1960).

[11] W. H. Saunders, Jr., and D. H. Edison, *ibid.*, **82**, 138 (1960), footnote 15.

[12] J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 72.

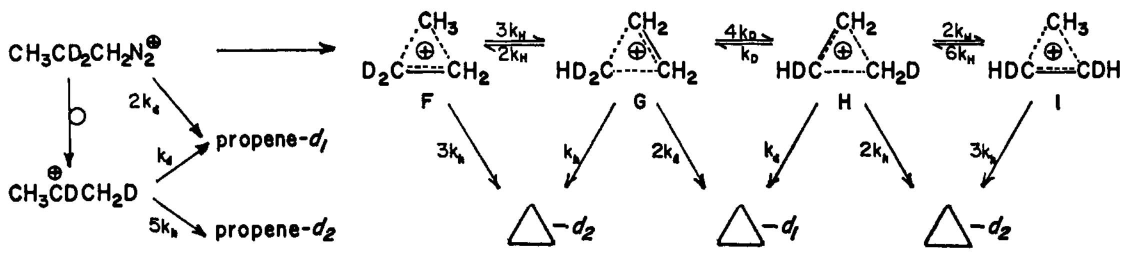
[13] Diazotization in protic media was carried out at room temperature (25–30°), whereas in aprotic solvents diazotization was effected at the solvent reflux temperature (61° for chloroform).

Scheme I



At equilibrium [A]:[B]:[C]:[D]:[E] = 1:6:12:12:4

Scheme II



At equilibrium [F]:[G]:[H]:[I] = 2:3:12:4

basicity of the gegenion is a factor affecting the equilibration of the ions in aprotic and protic media, it is probably the major factor responsible for the differences observed in aqueous acetic acid and 35% perchloric acid. If total equilibration is reached (A:B:C:D:E = 1:6:12:12:4) the deuterium content of the cyclopropane would be 43% d_2, 57% d_3 ($k_H/k_D = 1$). If a k_H/k_D of 1.1–1.2 per deuterium atom is assumed, then the extent of equilibration reached in chloroform, aqueous acetic acid, and 35% perchloric acid is 16–22%, 61–72%, and 80–90%, respectively.

The explanation used to rationalize the observations obtained from *n*-propyl-3,3,3-d_3-amine involved the participation of C-2 hydrogens, *i.e.*, an equilibrating protonated cyclopropane.[6] Since this assumption was based on isotopic rearrangements observed in the *n*-propyl alcohol,[3] *n*-propyl-2,2,-d_2-amine (Table II) was diazotized to determine if the C-2 hydrogens were involved in cyclopropane formation. Thus diazotization in chloroform gave cyclopropane (9% d_1, 91% d_2) and propene (73% d_1, 27% d_2). An *increase* in deuterium loss in the cyclopropane occurred when the reaction was carried out in aqueous acetic acid. These results substantiate the participation of C-2 hydrogens and the protonated cyclopropane concept (Scheme II). Here again, the larger amount of scrambling in aqueous systems can be attributed to the greater degree of equilibration of the ions F, G, H, and I. The extent of equilibration (assuming a k_H/k_D of 1.1–1.2 per deuterium atom) is about 35–42% in chloroform and 60–67% in aqueous acetic acid. While the same degree of equilibration is reached from both diazonium ions in aqueous acetic acid, in chloroform more equilibration apparently occurs from F than from A. This is probably a result of the kinetic isotope effect on the initial rearrangement. Thus the two amines studied show that the stability of the protonated cyclopropane is solvent dependent. The lifetime of these species is longest in aqueous strongly acidic media (35% $HClO_4$), intermediate in aqueous acetic acid, and shortest in chloroform (aprotic media).

It was implied (Schemes I and II) that only *n*-propyldiazonium ion and/or the isopropyl cation gave propene. However, the observed deuterium contents of the propenes (Tables I and II) are inconsistent with this postulate. The extent of deuterium retention in propene from *n*-propyl-3,3,3-d_3-amine is larger than expected. If it is assumed that *all* the propene arises from either *n*-propyldiazonium ion or isopropyl cation in aprotic deamination of *n*-propyl-2,2-d_2-amine (Table II),[14] calculations using these data predict that the

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[14] Diazonium ions have been postulated as the primary reactive intermediates in aprotic media to account for the limited amounts of rearrangement observed in these solvents: J. H. Bayless, A. Jurewicz, and L. Friedman, *J. Am. Chem. Soc.*, **90**, 4466 (1968).

Table II. Diazotization of *n*-Propyl-2,2-d_2-amine[a,b]

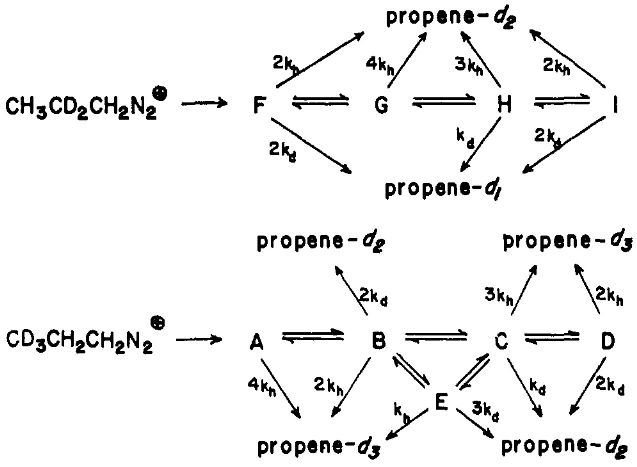
	Deuterium content[c]			
	△		/=	
Acid–solvent	d_1	d_2	d_1	d_2
HOAc–$HCCl_3$	9	91	73	27
HOAc–H_2O[d]	15	85	61	39

[a] Amine (7% d_1, 93% d_2; 1 equiv), HOAc (1 equiv), and OcONO (1.1 equiv) and solvent at reflux. [b] Single runs. [c] The deuterium content corrected for d_1 in starting amine. [d] Sodium nitrite used as diazotizing agent; reaction carried out at room temperature.

deuterium content of propene from aprotic deamination of *n*-propyl-3,3,3-d_3-amine would be 16% d_2 and 84% d_3.[15] However, experimentally a larger amount of deuterium retention occurred (Table I). Although most of the propene is probably derived from either *n*-propyldiazonium ion or isopropyl cation some other route to propene is needed to explain the apparent ambiguities in the deuterium content from the two *n*-propylamine precursors.

Thus some propene formation from an equilibrating protonated cyclopropane is suggested.[16] Loss of protium (deuterium) from the original C-2 position could give propene, whereas propene formation by protium (deuterium) abstraction from the original C-3 position could only occur after further equilibration (Scheme III). Scrambled propene could be formed directly from the equilibrating protonated cyclopropanes (A–E or F–I) or from the scrambled primary propyl cation derived from them. Propene arising *via* this mode could account for differences in deuterium content from aprotic media.[17]

Scheme III



Thus it appears that the *n*-propyldiazonium ion can react with solvent to give *n*-propyl alcohol, deprotonate to give propene, rearrange to isopropyl cation which then can give isopropyl alcohol and propene, and form an equilibrating protonated cyclopropane which can either react with solvent to give isotopically rearranged *n*-propyl alcohol[3] or deprotonate to give cyclopropane[5, 18] and propene.

Experimental Section[19]

Ethyl-2,2,2-d_3 Alcohol. Tetradeuterioacetic acid (64 g, 1 mol) was added dropwise at 5° to a stirred solution of lithium aluminum hydride (38 g, 1 mol) in diethyl Carbitol[20] (500 ml). The mixture was heated for 1 hr at 100°. Hydrolysis with *n*-butoxyethyl alcohol (360 g, 3 mol) was effected at 0°. A yield of 80% was obtained by direct distillation of the ethyl-2,2,2-d_3 alcohol (44.2 g, 0.9 mol), bp 75–79° (lit.[21] bp of d_0 compound 78.5°), from the reaction flask.

Ethyl-2,2,2-d_3 *p*-toluenesulfonate was prepared from ethyl-2,2,2-d_3 alcohol (44.2 g, 0.9 mol), *p*-toluenesulfonyl chloride (210 g, 1.1 mol), and pyridine (158 g, 2 mol), according to the procedure used to prepare dodecyl *p*-toluenesulfonate.[22] The yield of crude material, mp 29–33° (lit.[23] mp of d_0 compound 32°), was 95%.

Propionitrile-3,3,3-d_3 was prepared from ethyl-2,2,2-d_3 tosylate (173 g, 0.85 mol) and sodium cyanide (53 g, 1.08 mol) in dimethyl sulfoxide (250 ml) according to the procedure[24] used to convert alkyl halides into nitriles. The yield of propionitrile-3,3,3-d_3 (17.3 g, 0.85 mol), bp 97° (lit.[25] bp of d_0 compound 97°), was 63%.

Product isolation is somewhat more difficult with low molecular weight nitriles due to their solubility in water. Isolation can be accomplished by steam distillation of the nitrile from the reaction flask, followed by liquid–liquid ether extraction.

***n*-Propyl-3,3,3-d_3-amine.** Reduction[26] of propionitrile-3,3,3-d_3 (31 g, 0.64 mol) with lithium aluminum hydride (38 g, 1 mol) gave *n*-propyl-3,3,3-d_3-amine (19 g, 0.31 mol), bp 49°, $n^{25}D$ 1.4282 (lit.[25b] bp of d_0 compound 49°; $n^{20}D$ 1.4428), in 50% yield.

The nmr spectra showed a trace methyl signal and two triplets. Deuterium analysis by low-voltage mass spectrometry showed the composition to be 4.4% d_1 and 95.6% d_3.

Ethyl Methylcyanoacetate. Alkylation of ethylcyanoacetate (98 g, 1 mol) with methyl iodide (143 g, 1 mol), according to the procedure used to prepare pelargonic acid,[27] gave ethyl methylcyanoacetate (89.5 g, 0.79 mol), bp 195–200°, $n^{28}D$ 1.4099 (lit.[28,29] bp 197–198°, $n^{28.5}D$ 1.4104), in 79% yield.

Propionitrile-2,2-d_3. The hydrolysis of the ethyl methylcyanoacetate was accomplished by heating a mixture of the ester (25.4 g 0.2 mol), deuterium oxide (12 g, 0.6 mol), acetic acid-d_1, and DCl (2 ml of 5 *N* in D_2O), and distilling out the ethyl acetate[30] formed in the reaction. The excess deuterium oxide and acetic acid-d_1 was then stripped off. Exchange[31] with deuterium oxide gave 2-cyanopropionic-2-d_1 acid-d_1. Decarboxylation[32] of the 2-cyano-2-d_1-

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[15] (a) The calculation was based on the assumption that the deuterium content of propene would be d_1 by direct formation of *n*-propyl-2,2-d_2-diazonium ion, and would be d_1 and d_2 from the isopropyl cation. No deuterium isotope effects were employed in the calculation. In order to make the calculations agree with the results obtained from aprotic diazotization a k_H/k_D (per deuterium atom) of 1.5 would have to be employed. This is larger than the k_H/k_D (1.3) that would be needed to adjust the calculations to fit the data from protic media. (b) Isotope effects for olefin formation have been determined for solvolysis[15c,d] (k_H/k_D = 1.15–1.19 per deuterium atom) of *t*-pentyl chloride and deamination[15d] (k_H/k_D = 1.08 per deuterium atom) of *t*-pentylamine in 75% aqueous acetic acid. A value of 2 has been estimated[5] to account for the deuterium content in the cyclopropane formed by deprotonation of the equilibrating protonated cyclopropane. (c) V. J. Shiner, *J. Am. Chem. Soc.*, **75**, 2925 (1953); (d) M. S. Silver, *ibid.*, **83**, 3487 (1961).

[16] Since the deuterium contents from protic deaminations could be reconciled if a k_H/k_D of 1.3 is employed for the loss of deuterium from isopropyl cation, propene formation still requires alternate routes in protic media.

[17] Acylation of cyclopropane gave a 33% yield of 3-methyl-3-buten-2-one. Deprotonation of a protonated cyclopropane intermediate to give this olefin was postulated (ref 4c).

[18] P. S. Skell and I. Starer, *J. Am. Chem. Soc.*, **82**, 2971 (1960).

[19] Boiling points and melting points are uncorrected. Mass spectra were recorded on a General Electric analytical mass spectrometer.

[20] The diethyl Carbitol used was first distilled over calcium hydride and then passed through a column of alumina.

[21] "Dictionary of Organic Compounds," G. Harris, Ed., Vol. III, Oxford University Press, New York, N. Y., 1965, p 1361.

[22] E. S. Marvel and V. C. Sekera, "Organic Syntheses," Coll. Vol. III, John Wiley & Sons, Inc., New York, N. Y., 1955, p 366.

[23] R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

[24] L. Friedman and H. Shechter, *ibid.*, **25**, 877 (1960).

[25] (a) Reference 21, Vol. V, p 2786; (b) *ibid.*, p 2790.

[26] L. Friedman and A. T. Jurewicz, *J. Org. Chem.*, **33**, 1254 (1968).

[27] E. Reid and J. R. Ruhoff, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, p 474.

[28] C. C. Steele, *J. Am. Chem. Soc.*, **53**, 286 (1931).

[29] M. A. Pollack, *ibid.*, **65**, 1335 (1943).

[30] Ethyl acetate (70% of the theoretical amount) was collected.

[31] P. Holemann and K. Clasius, *Chem. Ber.*, **70**, 819 (1937).

[32] C. S. Marvel and V. DuVigneaud, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, p 93.

propionic acid-d_1 gave propionitrile-2,2-d_2 (6 g, 0.11 mol), bp 95–99°, $n^{27}\mathrm{D}$ 1.3652 (lit.[25] bp of d_0 compound 97°; $n^{25}\mathrm{D}$ 1.3659), in 53% yield.

n-Propylamine-2,2-d_2. Reduction[26] of propionitrile-2,2-d_2 (6 g, 0.11 mol) with lithium aluminum hydride (5 g, 0.13 mol) afforded a 55% yield of n-propylamine-2,2-d_2 (3.5 g, 0.06 mol), bp 50–54° (lit.[26] bp of d_0 compound 49°). The amine was purified through its hydrochloride, mp 156–158° (lit.[26] mp of d_0 compound 157–158°). Low-voltage mass spectrometry showed the deuterium composition to be 7% d_1 and 93% d_2.

Reaction Procedure. The procedure developed earlier[33] was employed in the diazotization reactons. A solution of the amine (0.01 mol), acetic acid (0.01 mol), and octyl nitrite (0.011 mol)[34] in chloroform (10 ml) was heated to reflux.[35] The olefins were trapped in heptane and glpc analyzed. The samples used for deuterium analysis were directly glpc trapped.

Acknowledgment. The authors are deeply indebted to Professor C. J. Collins for his most helpful comments and suggestions in interpreting the data.

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[33] L. Friedman and J. H. Bayless, *J. Am. Chem. Soc.*, **91**, 1790 (1969).

[34] Sodium nitrite was used when the reactions were effected in aqueous acetic acid and 35% perchloric acid.

[35] Reactions in aqueous acetic acid and 35% perchloric acid were carried out at room temperature.

Hydrocarbon Forming Pathways from Amine Diazotizations[1]

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Contribution from the Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106. Received July 22, 1968

Abstract: Diazotization of several deuterium-labeled isobutyl- and *sec*-butylamines in protic and aprotic solvents gave hydrocarbon mixtures containing methylcyclopropane. The deuterium contents of the methylcyclopropanes suggest that a minor amount (~2%) of the methylcyclopropane arises *via* a partially equilibrating protonated methylcyclopropane. From the deuterium content of isobutylene it is possible to calculate the extent of hydride shift to *t*-butyl cation in its formation. Rearrangement (1,2-hydride shift) of *sec*-butyl cation obtained from isobutylamine *via* a 1,2-methyl shift was found to be solvent dependent. Possible explanations for this phenomenon are considered.

It has been recently demonstrated[3] that protic diazotization of methyl-substituted deuterium-labeled propylamines gave alcohols without involving the intermediacy of protonated cyclopropanes. This conclusion was based upon the positions of the deuterium label in the products. Furthermore, it was stated that there was no evidence for an edge-protonated methylcyclopropane and that the "methyl bridged species, if present, can be detected only by formation of methylcyclopropane."[3a]

In an attempt[4] to elucidate the processes occurring *prior* to loss of nitrogen from alkyldiazonium ions it was found that some of the reactions *following* loss of nitrogen from isobutyl-1,1-d_2-amine (**1**) could be interpreted as going *via* a *partially* equilibrating protonated methylcyclopropane.[5] A more thorough investigation of the isobutyl system was thus warranted to verify this interpretation. In principle, this could be accomplished by determining the deuterium contents of the hydrocarbon products formed *via* the protic and aprotic diazotization of 2-methyl-d_3-propyl-2,3,3,3-d_4-amine (**2**) and isobutyl-2-d_1-amine (**3**). In addition, it was of interest to see the effect that such isotopic labeling would have on hydrocarbon product composition.

Results and Discussion

Diazotization of **2** and **3** gave essentially the same hydrocarbon composition (Table I) as that obtained from unlabeled isobutylamine when identical reaction conditions were employed. The absence of a significant deuterium isotope effect is somewhat surprising in light of the results obtained from deuterated *t*-pentylamine[6] and from partially deuterated neopentyldiazonium ion.[7,8]

The deuterium contents of the hydrocarbon products from the diazotization of **2** are given in Table II. The slight retention (2–4%) of deuterium in methylcyclopropane corresponds with the small difference in deuterium between 1-butene and methylcyclopropane obtained from **1**.[4] This can also be attributed to the limited involvement of a partially equilibrating protonated methylcyclopropane or less likely carbenic intermediates.[9]

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[1] (a) Financial support (Grant No. GP-3976) from the National Science Foundation is gratefully acknowledged. (b) A preliminary account of portions of this work have been published: J. H. Bayless, A. T. Jurewicz, and L. Friedman, *J. Am. Chem. Soc.*, **90**, 4466 (1968). (c) For the preceding paper in this series, see L. Friedman and A. T. Jurewicz, *ibid.*, **90**, 1800 (1968).

[2] Taken from the Ph.D. thesis of A. T. J., Case Institute of Technology, June 1967.

[3] (a) G. J. Karabatsos, N. Hsi, and S. Meyerson, *J. Am. Chem. Soc.*, **88**, 5649 (1966); (b) G. J. Karabatsos, R. A. Mount, D. O. Rickter, and S. Meyerson, *ibid.*, **88**, 5651 (1966).

[4] (a) A. T. Jurewicz and L. Friedman, *ibid.*, **89**, 149 (1967); (b) J. H. Bayless and L. Friedman, *J. Am. Chem. Soc.*, **89**, 147 (1967).

[5] We have been studying the diazotization of aliphatic amines under widely varying reaction conditions and our results from several deuterium-labeled iso- and *sec*-butylamines are generally in good agreement with the conclusions of Karabatsos, Hsi, and Meyerson.[3a] The differences are mainly concerned with minor reaction pathways.

[6] M. S. Silver, *J. Am. Chem. Soc.*, **83**, 3487 (1961).

[7] J. H. Bayless, Ph.D. Thesis, Case Institute of Technology, June 1967.

[8] The small variations in product composition (Table I) could be attributed to deuterium isotope effects. Since five hydrocarbons are formed wide variations in product composition are not anticipated.

[9] Carbenes are not expected to be intermediates in media such as glacial and aqueous acetic acid because of the highly acidic nature of these solvents. This expectation is in good agreement with minor amounts of deuterium pickup in glacial acetic acid and the absence of deuterium pickup in aqueous acetic acid in the products from diazotization of isobutyl-d_2-amine: J. H. Bayless and L. Friedman, *J. Am. Chem. Soc.*, **89**, 147 (1967). By analogy, carbenoid involvement is not expected to be a major pathway in aprotic diazotization.