the course of the debenzylations of L-PBA and of L-PBG. Perhaps such solvent effects have a counterpart in the reactions of enzymes, where amino acid side-chains of residues near the active site may exert an influence upon reactions at the active site by determining the environment at the site.

[CONTRIBUTION FROM THE GORGAS LABORATORY, ROHM & HAAS COMPANY, REDSTONE ARSENAL RESEARCH DIVISION, HUNTSVILLE ALA.]

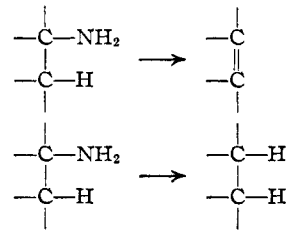
Deamination Reactions of Difluoroamine

BY CARL L. BUMGARDNER, KENNETH J. MARTIN AND JEREMIAH P. FREEMAN

RECEIVED SEPTEMBER 7, 1962

Difluoroamine (HNF_2) converts primary aliphatic amines to alkanes. Nitrogen and alkylammonium fluorides constitute the other major products. The secondary amines, aziridine, azetidine and dibenzylamine react with difluoroamine to yield, respectively, ethylene, cyclopropane and bibenzyl. Butene-1 is obtained from reaction of difluoroamine and cyclopropylcarbinylamine and from treatment of N-cyclopropylmethyl-*p*-toluenesulfonamide with hydroxylamine-O-sulfonic acid in aqueous base. Difluoroamine induces fragmentation of 3,5,5-trimethylpyrazoline into acetonitrile, isobutylene and nitrogen. These transformations are rationalized by postulating the formation of fluorazene (NF), which subsequently leads to intermediates of the type RN=NH and $R_2\overset{+}{N}=\overset{-}{N}$.

Removal of an amino group from an aliphatic carbon atom may be accomplished by applying one of several E_1 or E_2 olefin-forming elimination reactions[1,2], eq. 1, or by a reductive deamination process which results in a saturated hydrocarbon,[3] eq. 2. The only general method for effecting this latter transformation involves



(1)

(2)

conversion of a primary amine to a sulfonamide derivative which is then treated with hydroxylamine-O-sulfonic acid in aqueous base to generate the alkane.[3]

We have observed that difluoroamine[4] functions as an efficient and direct deaminating reagent for aliphatic and aromatic primary amines and certain secondary amines. The over-all reaction with primary amines may be represented by eq. 3.

$$3RNH_2 + HNF_2 \longrightarrow 2R\overset{+}{N}H_3\overset{-}{F} + N_2 + R\text{-}H \quad (3)$$

Representative examples are collected in Table I.

TABLE I

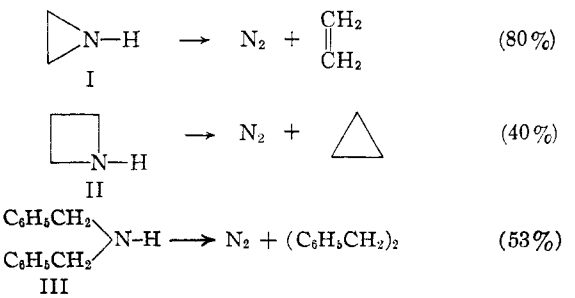
$$RNH_2 \xrightarrow{HNF_2} RH$$

Nature of R	Yield of alkane,[a] %
n-Butyl	61
sec-Butyl	40
t-Butyl	22
Cyclopropyl	77
Cyclopropylmethyl	46[b]
Phenyl	20

[a] Based on HNF_2. Yields are not necessarily the optimum obtainable; see Experimental. [b] Product is butene-1; see Discussion.

The reactions were conducted in a glass vacuum system by condensing difluoroamine into an excess of amine. Volatile products were purified by bulb-to-bulb distillation and identified by infrared and mass spectrometry. Elemental analyses, infrared and F^{19} n.m.r. spectra showed the solid product obtained to be alkylammonium fluoride. Examination of the infrared spectra of the less volatile liquid fractions revealed that small amounts of alkyl azide were usually present. In the case of *t*-butylamine, traces of isobutylene and ammonia were also detected.

When treated with difluoroamine, aziridine (I), azetidine (II) and dibenzylamine (III) released nitrogen and the remaining fragments coupled to form ethylene, cyclopropane and bibenzyl, respectively.



(80%)

(40%)

(53%)

Discussion

The primary amine transformations may be rationalized in terms of intermediate IV, which, in turn, may arise by the sequence

R—N=N—H

IV

Amine-promoted α-elimination of the elements of hydrofluoric acid from difluoroamine can yield fluorazene,[5] NF, reminiscent of the formation of NH by elimination of sulfuric acid from hydroxylamine-O-sulfonic acid[6] and formation of dihalocarbene from haloforms.[7] Attack by the electrophilic azene on nucleophilic amine,[8] followed by a proton shift and loss of the elements of hydrofluoric acid, would produce structure IV. This intermediate, identical to that proposed by Nickon and Sinz[3] to arise from elimination of sulfinic acid from alkyl sulfonhydrazides, would be expected to proceed readily to hydrocarbon and nitrogen. A portion, however, may also act as a trap for fluorazene and, after loss of HF, yield azide.

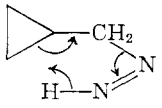
$$RN_3 \longleftarrow IV \longrightarrow N_2 + R\text{—}H$$

The ammonia and isobutylene observed from reaction of *t*-butylamine and difluoroamine probably arise from direct elimination of ammonia from the aliphatic amine. Ammonia and isobutylene were also obtained when

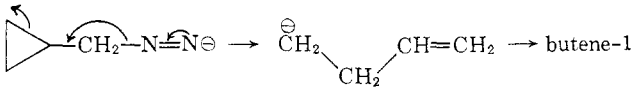
(1) E. H. White and H. Scherrer, *Tetrahedron Letters*, 758 (1961).
(2) A. C. Cope and E. R. Trumbull, *Org. Reactions*, **11**, 317 (1960).
(3) A. Nickon and A. Sinz, *J. Am. Chem. Soc.*, **82**, 753 (1960).
(4) J. P. Freeman, A. Kennedy and C. B. Colburn, *ibid.*, **82**, 5304 (1960).
(5) For a discussion of nomenclature, see P. A. S. Smith and J. H. Hall, *ibid.*, **84**, 480 (1962).
(6) For examples of this type of reaction, see C. L. Bumgardner and R. L. Lilly, *Chemistry and Industry*, 559 (1962).
(7) J. Hine and R. J. Rosscup, *J. Am. Chem. Soc.*, **82**, 6115 (1960).

t-butylamine and hydrogen chloride gas were allowed to react under conditions similar to those used in the difluoroamine experiments. These results are consistent with the view that difluoroamine is acting as an acid toward the amine reactants.[8]

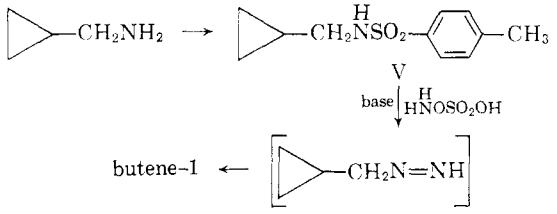
To learn something of the nature of the decomposition of structure IV to nitrogen and hydrocarbon, we investigated the products derived from IV when R = cyclopropylmethyl. The only hydrocarbon detected was butene-1. The absence of cyclobutane rules out heterolytic cleavage of the C–N bond to give a carbonium ion[9] and failure to observe methylcyclopropane argues against homolytic breakage. Photochlorination of methylcyclopropane, for example, yields a mixture of cyclopropylcarbinyl chloride (from $\triangleright$—CH_2·) and allylcarbinyl chloride (from CH_2=CH—CH_2—CH_2·) in which the former predominates.[10] Still consistent is a concerted breakdown or possibly a carbanoid de-



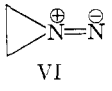
composition. Carbanions generated next to a cyclopropane ring are known to interact with the ring.[11]



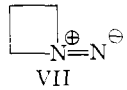
Application of the Nickon-Sinz deamination, eq. 4, using sulfonamide V resulted in the same hydrocarbon, butene-1, underscoring the general relationship between this deamination process and the HNF_2–amine procedure.[12]



The intermediates corresponding to IV for the secondary amines I and II are represented by structures VI and VII, respectively. Ejection of nitrogen and



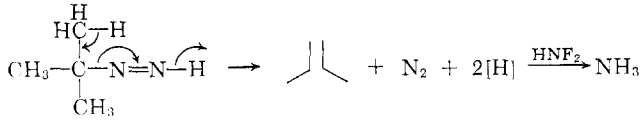
VI



VII

collapse to ethylene by VI would be anticipated in view of the action of certain nitrosating agents on aziridine.[13]

(8) An attractive alternative for IV when R = *t*-butyl involves reductive fragmentation yielding isobutylene, nitrogen and ammonia, the last product resulting from reduction of difluoroamine.



This type of collapse, which may be sterically assisted, resembles the reducing action of diimide, HN=NH. For example, see S. Hünig, H. R. Müller and W. Thier, *Tetrahedron Letters*, 353 (1961).

(9) M. S. Silver, M. C. Caserio, H. E. Rice and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 3673 (1961).

(10) E. Renk, P. R. Shafer, W. H. Graham, R. H. Mazur and J. D. Roberts, *ibid.*, **83**, 1989 (1961).

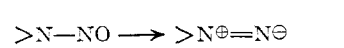
(11) C. L. Bumgardner, *ibid.*, **85**, 73 (1963).

(12) D. J. Cram, J. S. Bradshaw, W. Lwowski and G. R. Knox, *ibid.*, **84**, 2832 (1962), have just published a report describing the results of applying the Nickon–Sinz and related procedures to optically active amine derivatives. These authors conclude that intermediates similar to IV are formed and that these decompose into carbanions and radicals, the partitioning depending on solvent and other reaction conditions.

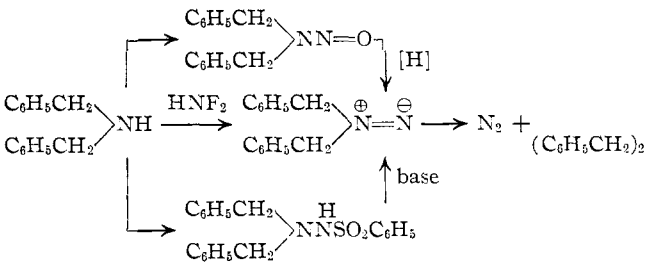
(13) C. L. Bumgardner, K. S. McCallum and J. P. Freeman, *ibid.*, **83**, 4417 (1961).

Intermediate VII behaves in the same manner as VI and gives nitrogen and the ring contraction product, cyclopropane.

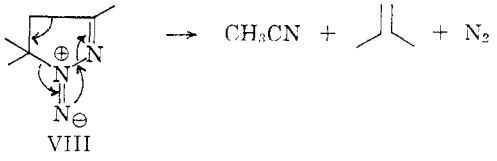
If intermediates such as VII are involved, other methods of generating these structures should yield the same end products. Thus, cyclopropane was observed from reaction of N-nitrosoazetidine with sodium hydrosulfite in base, a reagent Overberger, Lombardino and Hiskey[14] believe forms intermediates analogous to VII.



The supposition that such structures are involved in the reactions of difluoroamine with amines was strengthened by the observation that dibenzylamine upon treatment with difluoroamine, gave nitrogen and bibenzyl, the same products which come from reaction of 1,1-dibenzyl-2-benzenesulfonhydrazide with base[15] and from reduction of N-nitrosodibenzylamine with sodium hydrosulfite.[14]



A more complicated fragmentation[16] occurred when 3,5,5-trimethylpyrazoline was subjected to difluoroamine. Since isobutylene, acetonitrile and nitrogen were observed, intermediate formation of structure VIII seems plausible.



VIII

Experimental

CAUTION: DIFLUOROAMINE SHOULD BE HANDLED WITH CARE; SEE REF. 4 FOR PRECAUTIONS

Primary Amines and Difluoroamine.—The reaction of cyclopropylamine with difluoroamine is described as a typical example.

Cyclopropylamine (Aldrich Chemical Co.; 1.14 g., 20 mmoles) was introduced into a vacuum system and degassed. After the amine was transferred to a round-bottom flask equipped with a magnetic stirrer and manometer, difluoroamine[4] (4.8 mmoles) was condensed in by means of a methylcyclohexane slush bath. While the stirred mixture was allowed to warm to room temperature, gas (N_2 and cyclopropane) was evolved. After the pressure became constant at 25°, the products were fractionated by pumping through three traps in series, the first cooled in a Dry Ice–acetone-bath, the second in a methylcyclohexane slush, and the third in liquid nitrogen. A total of 3.7 mmoles (77%) of cyclopropane, identified by its infrared and mass spectrum, was obtained. According to its infrared spectrum, the liquid fraction which collected in the Dry Ice–acetone trap was composed of recovered starting amine and alkyl azide (band at 2140 cm.$^{-1}$), presumably cyclopropyl azide.

The solid residue, which analysis, infrared and n.m.r. spectra showed was cyclopropylammonium fluoride, weighed 0.76 g. (99%).

Anal. Calcd. for C_3H_8FN: N, 18.2. Found: N, 17.1.

Secondary Amines and Difluoroamine.—Freshly distilled aziridine (Chemirad Corp.; 30 mmoles) was treated with 5

(14) C. G. Overberger, J. G. Lombardino and R. G. Hiskey, *ibid.*, **80**, 3011 (1958).

(15) L. A. Carpino, *ibid.*, **79**, 4427 (1957).

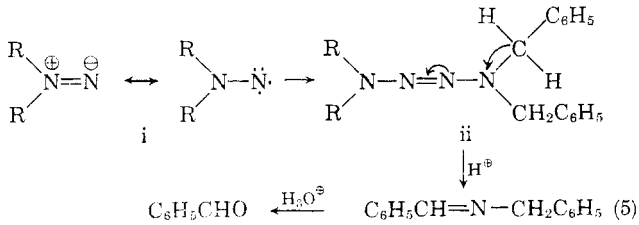
(16) For a similar reaction in this system see J. P. Freeman, *Tetrahedron Letters*, 749 (1961).

mmoles of difluoroamine as described above. Ethylene was isolated in 80% yield. Similar treatment of azetidine[17] gave cyclopropane in 40% yield. Dibenzylamine (30 mmoles) reacted with difluoroamine (4.4 mmoles) under similar conditions giving N_2 (3.5 mmoles) as the only gaseous product. Bibenzyl, m.p. 50–51° (uncor.), identified by its infrared spectrum, was isolated in 53% yield by extracting the semi-solid residue with ether, removing unconverted amine with aqueous hydrochloric acid solution, and chromatographing over silica gel. Benzaldehyde was also obtained as a by-product.[18]

N-Cyclopropylmethyl-*p*-toluenesulfonamide (V) was prepared from 4.0 g. of cyclopropylcarbinylamine,[19] 10.8 g. of *p*-toluenesulfonyl chloride and 25 ml. of pyridine by the general procedure outlined by Vogel.[20]

(17) W. R. Vaughan, R. S. Klonowski, R. S. McElhinney and B. B. Millward, *J. Org. Chem.*, **26**, 138 (1961).

(18) This aldehyde probably arises by the sequence shown in eq. 5, R = benzyl. Dimerization of intermediate i could produce tetrazene ii which



would be expected to undergo decomposition during acid work-up. Formation of tetrazene ii could also account for the failure to observe quantitative N_2 evolution. See G. G. Overberger, *Rec. Chem. Progr. (Kresge–Hooker Sci. Lib.)*, **21**, 40 (1960), and W. R. McBride and H. W. Kruse, *J. Am. Chem. Soc.*, **79**, 572 (1957).

(19) J. D. Roberts and R. M. Mazur, *ibid.*, **73**, 2509 (1951).

N-Cyclopropylmethyl-*p*-toluenesulfonamide was obtained in 76% yield, m.p. 57–58° (uncor.)

Anal. Calcd. for $C_{11}H_{15}NSO_2$: C, 58.64; H, 6.71; N, 6.22. Found: C, 59.05; H, 6.95; N, 6.20.

Decomposition of N-Cyclopropylmethyl-*p*-toluenesulfonamide with Hydroxylamine-O-sulfonic Acid.—The general procedure described by Nickon and Sinz[3] was followed with the exception that a gas trap, cooled in liquid nitrogen and protected by drying tubes, was connected to the exit end of the reflux condenser. After completion of the reaction, which was conducted with 2.25 g. of sulfonamide V and 28.3 g. of hydroxylamine-O-sulfonic acid (Eastman Kodak Co.), the contents of the gas trap were fractionated on a vacuum line, giving 0.8 mmole of butene-1, identified by its infrared and mass spectrum.

Reduction of N-Nitrosoazetidine.—N-Nitrosoazetidine[13] was reduced with sodium hydrosulfite by the method described for reduction of N-nitrosodibenzylamine.[14] Cyclopropane was identified in the escaping gases by its mass spectrum.

3,5,5-Trimethylpyrazoline and Difluoroamine.—Addition of 5 mmoles of difluoroamine to 2.24 g. (20 mmoles) of 3,5,5-trimethylpyrazoline[16] in the manner described above for cyclopropylamine liberated 2.7 mmoles of N_2 and vacuum line fractionation yielded 2.1 mmoles of isobutylene and 0.7 mmole of acetonitrile, identified by their infrared and mass spectra. Only that acetonitrile in the gas phase was measured. According to the infrared spectrum, additional acetonitrile was present in the liquid fraction which collected in the Dry Ice–acetone trap.

Acknowledgments.—This investigation was supported by the Advanced Research Projects Agency under Army Ord. Contract DA–01–021 ORD–11909. We are grateful to Mr. Kirt Keller for technical assistance and to Dr. Grover Paulett for mass spectral analyses.

(20) A. I. Vogel, "Practical Organic Chemistry," second edition, Longmans, Green and Co., London, 1951, p. 625.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF CHICAGO, CHICAGO 37, ILL.]

Carbenes from Alkyl Halides and Organolithium Compounds. V. Formation of Alkylcyclopropenes by Ring Closure of Alkenyl Substituted Carbenoid Intermediates[1,2]

BY GERHARD L. CLOSS AND LISELOTTE E. CLOSS

RECEIVED JULY 23, 1962

Reactions of 1,2-dimethylpropenyllithium and 2-methylpropenyllithium with methylene chloride give 1,3,3-trimethylcyclopropene and 3,3-dimethylcyclopropene, respectively. Product formation is conveniently accounted for in terms of a mechanism invoking alkenyl substituted intermediates. This hypothesis is strengthened by the observation that α-dehydrochlorination on 1-chloro-2,3-dimethyl-2-butene and α-debromination on 1,1-dibromo-2,3-dimethyl-2-butene with alkyllithium compounds give 1,3,3-trimethylcyclopropene, as well. Other possible mechanisms are discussed.

Introduction

The chemistry of alkylcarbenes has attracted considerable interest in recent years.[3] Although rigorous proof for the intermediacy of free carbenes has not yet been brought forth in all cases, the following three reaction types are generally assumed to lead to alkyl substituted carbenoid species: (a) Photolysis or pyrolysis of diazoalkanes is probably the most versatile method for the formation of these intermediates. Frequently, the diazoalkane is produced *in situ via* the base-catalyzed decomposition of *p*-toluenesulfonylhydrazones of aldehydes and ketones in aprotic solvents.[4] (b) Alkyl halides may be converted to carbenes through α-dehydrohalogenation with such strong bases as organoalkali metal compounds.[5a–e] A preparative valuable variation of this method is the reaction of gemina polyhalides with organolithium compounds. Here one halogen atom, preferentially a bromine atom undergoes the halogen–metal exchange reaction while a remaining one serves as the anionic leaving group.[6a,b] (c) Finally, the product distribution in the reaction of organolithium compounds with methylene chloride is conveniently interpreted by invoking alkylcarbenes as intermediates.[7]

$$\mathrm{RLi} + :\mathrm{CHCl} \longrightarrow \mathrm{R{-}CHClLi}$$
$$\mathrm{R{-}CHClLi} \longrightarrow \mathrm{R{-}CH{:}} + \mathrm{LiCl} \qquad (1)$$

In this reaction (sequence 1) the initially formed chlorocarbene can be thought to insert between the carbon–lithium bond of the lithium reagent to form the hypothetical α-chloroalkyllithium. The free carbene may then be formed by elimination of lithium chloride.[8]

Previous work carried out on the latter reaction led us to explore the possibilities of extending this scheme to the synthesis of carbenes with unsaturated substituents. Particularly, since alkenyllithium compounds are

(1) Supported in part by a grant (NSF-G19927) from the National Science Foundation.

(2) Part of this work was reported in preliminary communications; G. L. Closs and L. E. Closs, *J. Am. Chem. Soc.*, **83**, 1003, 2015 (1961).

(3) For a recent review, see, W. Kirmse, *Angew. Chem.*, **73**, 161 (1961).

(4) J. W. Powell and M. C. Whiting, *Tetrahedon*, **7**, 305 (1959); L. Friedman and H. Shechter, *J. Am. Chem. Soc.*, **81**, 5512 (1959); **82**, 1002 (1960); **83**, 3159 (1961).

(5) (a) G. L. Closs and L. E. Closs, *ibid.*, **81**, 4996 (1959); **82**, 5723 (1960); (b) W. Kirmse and W. v. E. Doering, *Tetrahedron*, **11**, 266 (1960); W. v. E. Doering and W. Kirmse, *ibid.*, **11**, 272 (1960); (c) L. Friedman and J. G. Berger, *J. Am. Chem. Soc.*, **82**, 5758 (1960); **83**, 492, 500 (1961); (d) G. L. Closs and L. E. Closs, *Tetrahedron Letters*, **24**, 26 (1960); (e) P. S. Skell and A. P. Krapcho, *J. Am. Chem. Soc.*, **83**, 754 (1961).

(6) (a) W. T. Miller, Jr., and C. S. Y. Kim, *ibid.*, **81**, 5008 (1959); (b) W. R. Moore and H. R. Ward, *J. Org. Chem.*, **25**, 2073 (1960); W. R. Moore, H. R. Ward and R. F. Merritt, *J. Am. Chem. Soc.*, **83**, 2019 (1961).

(7) G. L. Closs, *ibid.*, **84**, 809 (1962).

(8) Although intermediacy of a free carbene explains the available data best, it has not been excluded that the α-chloroalkyllithium is the direct precursor of the resulting products[7] (see also footnote 18).