CHEMISTRY OF N-BROMAMINES AND N-CHLORAMINES*

PETER KOVACIC, MICHAEL K. LOWERY, AND KURT W. FIELD

Departments of Chemistry, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin 53201, and Case Western Reserve University, Cleveland, Ohio 44106

Received October 3, 1968 (Revised Manuscript Received July 8, 1970)

Contents

I. Introduction

The chemistry of N-halamines is a very broad area which has received considerable attention through the years, resulting in substantial advances both in the synthetic and mechanistic categories. Mellor[1] and Gmelin,[2] in their coverage of inorganic chemistry, treat the subject of halogen derivatives of nitrogen. Later, because of the importance in water purification, Berliner[3] wrote about the chloro derivatives of ammonia, with most of the emphasis placed on chloramine. Snelders[4] has reviewed the discovery and early chemistry of nitrogen trichloride. Probably the best described N-halamine in the literature, chloramine was also reviewed more recently by Drago,[5] Colton and Jones,[6] and Theilacker and Wegner.[7] A compilation by Schmitz[8] illustrates the use of N-halamines as precursors for the preparation of various classes of organic compounds. Wolff[9] presented a comprehensive survey of the Hofmann-Löffler reaction through the middle of 1961.

This review article attempts to present an over-all, up-to-date discussion of the chemistry of N-bromo and N-chloro derivatives of ammonia and alkylamines. However, N-halamides are excluded. We have not duplicated the material, particularly the early literature, treated in the inorganic summaries[1,2] of more than 40 years ago. In general, the present article includes publications appearing until the beginning of 1970. Only when there is special pertinence are N-fluor-[10] and N-iodamines mentioned. Rather than endeavor to cite every previous reference, we have provided a selective representation. The usefulness and drawbacks of various syntheses are discussed and, whenever possible, the mechanistic aspects are treated.

II. Hazards

It is important for anyone working in the N-halamine area to be cognizant of the real and potential hazards, namely,

---

* Several sections of this review are also treated in a forthcoming review by G. Sosnovsky and D. J. Rawlinson, "Advances in Free Radical Chemistry."

(1) J. W. Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Vol. VIII, Longmans, Green and Co., New York, N. Y., 1928, p 598 ff; Vol. VIII, Suppl. II, Part II, 1967, p 409 ff.

(2) "Gmelin's Handbuch der anorganischen Chemie," 8th ed, R. J. Meyer, Ed., No. 6, Verlag Chemie, Berlin, 1927, p 410 ff and p 334.

(3) J. F. T. Berliner, *J. Amer. Water Works Assoc.*, 23, 1320 (1931).

(4) H. A. M. Snelders, *Chem. Tech. Rev.*, 22, 457 (1967); *Chem. Abstr.*, 68, 9212 (1968).

(5) R. S. Drago, *J. Chem. Educ.*, 34, 541 (1957).

(6) E. Colton and M. M. Jones, *ibid.*, 32, 485 (1955).

(7) W. Theilacker and E. Wegner, *Angew. Chem.*, 72, 127 (1960); "Newer Methods of Preparative Organic Chemistry," Vol. III, Wilhelm Foerst, Ed., Academic Press, New York, N. Y., 1963, p 303 ff.

(8) E. Schmitz, *Angew. Chem.*, 73, 23 (1961); *Chem. Abstr.*, 55, 11384 (1961).

(9) M. E. Wolff *Chem. Rev.*, 63, 55 (1963).

(10) J. K. Ruff, *ibid.*, 67, 665 (1967).

toxicity and explosiveness.[10a] Some members of this class, such as nitrogen trichloride, are highly unstable in the pure form and have caused serious injury, particularly to some of the early investigators.[1] In general, the explosion hazard is eliminated or greatly diminished when an inert solvent is employed. On the other hand, others, *e.g.*, N,N-dichloro-*t*-butylamine,[11] can be safely distilled. Nitrogen trichloride showed promise as a bleaching agent for flour until its adverse effect on body functions was recognized.[12]

III. Analysis

The analysis of N-halamines for halogen content is usually accomplished titrimetrically. Iodine, liberated from an acidified solution of potassium iodide and the N-halo compound, is titrated with a standard thiosulfate solution.[13] Conversion to ammonia[13,14] and the Dumas method[13] serve as means for ascertaining nitrogen content. The concentration of chloramine in aqueous solution can be determined colorimetrically with *p*-aminodimethylaniline.[15] Aqueous chloramine solutions have been found to obey Beer's law, thus forming the basis for spectrophotometric determination.[16] The infrared and ultraviolet absorption spectra of various N-bromo- and N-chloroalkylamines are reported.[17] Absorption in the 500–670-cm^{-1} region is indicative of the N–Cl or N–Br structure, and ultraviolet absorption between 250 and 320 mμ is attributed to these same functionalities. Those N-haloalkylamines which possess the N–H grouping display bands at 3212–3306 cm^{-1}. The half-wave potentials in aqueous solution at the dropping mercury electrode with a saturated calomel reference are known for certain N-chloramines:[18] chloramine is reduced at −0.65 V, dichloramine is not reduced, and nitrogen trichloride is reduced at the half-wave potential of hypochlorite, +0.08 V.

IV. Synthetic Methods

The formation of N-halo derivatives of amines has been accomplished principally by (1) treatment of a solution of the amine with positive halogen or (2) gas-phase reaction of the amine and molecular halogen. The simplest chlorine member of the series, chloramine, has received considerable attention as attested by the availability of several review articles.[5-7] Aqueous solutions of chloramine are prepared by reaction of ammonia with sodium hypochlorite[19,20] (eq 1).

$$NH_3 + NaOCl \longrightarrow NH_2Cl + NaOH \qquad (1)$$

The gas-phase reaction of ammonia and chlorine, which has been studied extensively,[21,22] requires a large excess of ammonia for good yields, 75–90% (eq 2); a recent simplification affords high yields.[23] Anhydrous chloramine, mp −66°, was found to decompose at −50° with formation of nitrogen, chlorine, and nitrogen trichloride.[24] Dichloramine is the least characterized species among the N-chloro derivatives of ammonia because of its instability and difficulty of preparation.[25] At pH 4.5–5.0 it is essentially the only product in the reaction of chlorine with excess ammonium ions.[26] Further investigation revealed that chlorine must be converted to hypochlorous acid in order for the reaction to take place.[27] The fully chlorinated derivative of ammonia can be obtained from appropriate ratios of ammonia and chlorine.[28] Careful studies of the system over a period of years culminated in a convenient method of preparation.[29-31] Another synthesis of nitrogen trichloride, employing commercial "HTH" (calcium hypochlorite) with ammonium chloride,[13] involves extraction by organic solvent: benzene, toluene, *o*-dichlorobenzene, methylene chloride, or ethylene dichloride. In formation of the various N-chloramines, the pH of the solution was found to be extremely important.[25] From the reaction of ammonia with chlorine or hypochlorous acid, the product in solution at pH <3 is nitrogen trichloride, at pH 3–5, dichloramine, and at pH >8, chloramine, If the solution is strongly basic, nitrogen is generated.[32]

$$2NH_3 + Cl_2 \longrightarrow NH_2Cl + NH_4Cl \qquad (2)$$

Bromamine has been prepared by treatment of ammonia with bromine in ether solution.[33] Both mono- and dibromamine are formed in aqueous solution when bromine combines with ammonium salts at neutral pH.[34] A convenient synthesis of dibromamine in ether has been disclosed.[35] Nitrogen tribromide has been observed at −78° when bromine is allowed to react with liquid ammonia.[36] Although bromamine is also present, the equilibrium is shifted toward nitrogen tribromide at low temperatures and high concentrations. There is no evidence for existence of nitrogen tribromide in aqueous solution.[34]

Mixed halogen derivatives of ammonia have also been prepared, *e.g.*, chlorodifluoramine and dichlorofluoramine. Chlorodifluoramine can be synthesized in a number of ways: (1) by reaction of difluoramine with boron trichloride,[37] phosgene, hydrogen chloride,[38] or chlorine and a metal fluo-

---

(10a) P. Kovacic and S. S. Chaudhary, *Org. Syn.*, **48**, 4 (1968).

(11) H. Zimmer and L. F. Audrieth, *J. Amer. Chem. Soc.*, **76**, 3856 (1954).

(12) G. H. Pollock, *J. Appl. Physiol.*, **1**, 802 (1949); *Chem. Abstr.*, **44**, 8011 (1950).

(13) P. Kovacic, C. T. Goralski, J. J. Hiller, Jr., J. A. Levisky, and R. M. Lange, *J. Amer. Chem. Soc.*, **87**, 1262 (1965).

(14) C. T. Dowell and W. C. Bray, *ibid.*, **39**, 896 (1917).

(15) A. Palin, *Analyst*, **70**, 203 (1945); *Chem. Abstr.*, **39**, 4172 (1945).

(16) J. Kleinberg, M. Tecotzky, and L. F. Audrieth, *Anal. Chem.*, **26**, 1388 (1954).

(17) V. L. Heasley, P. Kovacic, and R. M. Lange, *J. Org. Chem.*, **31**, 3050 (1966).

(18) K. Heller and E. N. Jenkins, *Nature*, **158**, 706 (1946).

(19) F. Raschig, *Chem. Ber.*, **40**, 4580 (1907).

(20) G. H. Coleman and H. L. Johnson, *Inorg. Syn.*, **1**, 59 (1939).

(21) H. H. Sisler, F. T. Neth, R. S. Drago, and D. Yaney, *J. Amer. Chem. Soc.*, **76**, 3906 (1954).

(22) H. H. Sisler and G. M. Omietanski, *Inorg. Syn.*, **5**, 91 (1957).

(23) R. G. Laughlin, *Chem.-Ztg., Chem. App.*, **92**, 383 (1968); *Chem. Abstr.*, **69**, 51465 (1968).

(24) W. Marckwald and M. Wille, *Chem. Ber.*, **56**, 1319 (1923); *Chem. Abstr.*, **17**, 3301 (1923).

(25) R. E. Corbett, W. S. Metcalf, and F. G. Soper, *J. Chem. Soc.*, 1927 (1953).

(26) R. M. Chapin, *J. Amer. Chem. Soc.*, **51**, 2112 (1929).

(27) R. M. Chapin, *ibid.*, **53**, 912 (1931).

(28) W. A. Noyes and A. C. Lyon, *ibid.*, **23**, 460 (1901).

(29) W. A. Noyes, *ibid.*, **42**, 2173 (1920).

(30) W. A. Noyes and A. B. Haw, *ibid.*, **42**, 2167 (1920).

(31) W. A. Noyes, *Inorg. Syn.*, **1**, 65 (1939).

(32) W. C. Bray and C. T. Dowell, *J. Amer. Chem. Soc.*, **39**, 905 (1917).

(33) W. Moldenhauer and M. Burger, *Chem. Ber.*, **62**, 1615 (1929); *Chem. Abstr.*, **23**, 3869 (1929).

(34) J. K. Johannesson, *J. Chem. Soc.*, 2998 (1959).

(35) G. H. Coleman and G. E. Goheen, *Inorg. Syn.*, **1**, 62 (1939).

(36) J. Jander and E. Kurzbach, *Z. Anorg. Allg. Chem.*, **296**, 117 (1958); *Chem. Abstr.*, **53**, 109 (1959).

(37) R. C. Petry, *J. Amer. Chem. Soc.*, **82**, 2400 (1960).

(38) E. A. Lawton and J. Q. Weber, *ibid.*, **85**, 3595 (1963).

ride,[39] and (2) from gaseous fluorine and a mixture of sodium azide and sodium chloride at low temperature.[40] The best preparation appears to be the quantitative reaction of difluoramine with *t*-butyl hypochlorite under mild conditions.[41] Another good procedure involves the photolysis of tetrafluorohydrazine (commercially available) mixed with thionyl chloride.[42] A variation of the sodium azide reaction entailing chlorine monofluoride generated dichlorofluoramine.[43]

A large number of halogenated alkylamines are reported, mainly as precursors in the Hofmann–Löffler reaction. Representative of these preparations are (1) treatment of a solution of alkylamine and sodium bicarbonate with chlorine to form the alkyldichloramine,[44] (2) use of *t*-butyl hypochlorite with an amine which leads to the corresponding N-chloro derivative,[11,45–47] and (3) the interaction of an amine with N-chlorosuccinimide.[48] A novel method involves the cleavage of trimethylsilylamines with chlorine gas (eq 3);[49] yields range from 40 to 90%. N-Bromo- and N-iododialkylamines

$$R_2NSiR_3 + Cl_2 \longrightarrow R_2NCl + R_3SiCl \qquad (3)$$

were also prepared in this fashion.

Kinetic studies revealed that the formation of N-chloramines from hypochlorous acid and ammonia, primary amine, or secondary amine was second order.[50,51] In aqueous solutions of pH 2–6 the reaction between ammonia and bromine, which entails hypobromite ion as the active oxidant, is also second order.[52] In contrast, the exchange of chlorine between dimethylchloramine and succinimide takes place directly and not through the intermediate formation of hypochlorous acid.[53]

V. Physical Properties

Various thermodynamic properties of mono- and dichloramine and nitrogen trichloride have been calculated, namely the acidities, free energy of formation, and the oxidation potentials in both aqueous and liquid ammonia solutions.[54] The basic ionization constants of chloramine and dialkylchloramines were obtained from the ultraviolet absorption spectra.[55] From measurements of the absorption spectra of mono- and dichloramine, nitrogen trichloride, and some alkyl derivatives, the frequency of maximum absorption was shown to be inversely proportional to the polarizability of the group attached to N-Cl.[56] With mono- and dibromamine, the opposite was found in that bromamine absorbs at greater wavelength than dibromamine.[57] The physical chemical constants,[58] including bond angles and internuclear distances,[59] have been determined for chlorodifluoramine.

The infrared spectra of the chlorine derivatives of ammonia were studied, permitting calculation of structural parameters, such as $\angle$Cl–N–Cl = 106° and r_{N-Cl} = 1.76 Å for $NHCl_2$.[60] Recent infrared[61] and Raman[61–64] spectral studies of nitrogen trichloride established its structure as pyramidal. All the fundamental frequencies have been identified and observed combination bands assigned. An electron diffraction investigation of dimethylchloramine and methyldichloramine revealed N–Cl bond distances of 1.77 ± 0.02 and 1.74 ± 0.02 Å, respectively.[65] The deviation from that predicted from the covalent radius table[66] is attributed to the high electronegativity of both nitrogen and chlorine. Infrared spectral investigations are reported for the NF, NCl, and NBr entities.[67–70] The mixed halamine, chlorodifluoramine, shows six fundamentals in the infrared, five of which were assigned.[71]

The polar nature of halogen in N-halo compounds has been debated for a long time without resolution. As early as 1901, the halogen portion was postulated to exist in positive and negative forms.[28,72] Nitrogen trichloride has been designated as the most covalent molecule in the unsymmetrical category because the electronegativities of chlorine and nitrogen are essentially the same.[73] However, several reports concerning the direction of polarization in a variety of N-halo compounds classify nitrogen as the positive partner, $N^+–X^-$.[74–77]

VI. Chemical Reactions

A. AMINATING AGENT

1. *Alkane Structures*

Except for the Hofmann–Löffler reaction,[9] the interaction of N-halamines with saturated functionalities was virtually

---

(39) W. C. Firth, Jr., *Inorg. Chem.*, **4**, 254 (1965).

(40) T. A. Austin and R. W. Mason, *ibid.*, **2**, 646 (1963).

(41) K. O. Christe, *ibid.*, **8**, 1539 (1969).

(42) L. M. Zaborowski, K. E. Pullen, and J. M. Shreeve, *ibid.*, **8**, 2005 (1969).

(43) B. Sukornick, R. F. Stahl, and J. Gordon, *ibid.*, **2**, 875 (1963).

(44) L. K. Jackson, G. N. R. Smart, and G. F. Wright, *J. Amer. Chem. Soc.*, **69**, 1539 (1947).

(45) J. S. Chalsty and S. S. Israelstam, *Chem. Ind. (London)*, 1452 (1954).

(46) W. E. Bachmann, M. P. Cava, and A. S. Dreiding, *J. Amer. Chem. Soc.*, **76**, 5554 (1954).

(47) G. H. Alt and W. S. Knowles, *Org. Syn.*, **45**, 16 (1965).

(48) H. Ruschig, W. Fritsch, J. Schmidt-Thomé, and W. Haede, *Chem. Ber.*, **88**, 883 (1955).

(49) K. Seppelt and W. Sundermeyer, *Z. Naturforsch. B*, **24**, 774 (1969).

(50) C. R. Edmond and F. G. Soper, *J. Chem. Soc.*, 2942 (1949).

(51) I. Weil and J. C. Morris, *J. Amer. Chem. Soc.*, **71**, 1664 (1949).

(52) K. C. Grover and R. C. Mehrotra, *Z. Phys. Chem.* (Frankfurt am Main), **14**, 357 (1958).

(53) T. Higuchi and J. Hasegawa, *J. Phys. Chem.*, **69**, 796 (1965).

(54) W. L. Jolly, *ibid.*, **60**, 507 (1956).

(55) I. Weil and J. C. Morris, *J. Amer. Chem. Soc.*, **71**, 3123 (1949).

(56) W. S. Metcalf, *J. Chem. Soc.*, 148 (1942).

(57) J. K. Johannesson, *Chem. Ind.* (London), 97 (1958).

(58) T. V. Kuznetsova, L. F. Egorova, and A. V. Pankratov, *Zh. Neorg. Khim.*, **13**, 2304 (1968); *Chem. Abstr.*, **69**, 110074 (1968).

(59) L. V. Vilkov and I. I. Nazarenko, *Zh. Strukt. Khim.*, **8**, 346 (1967); *Chem. Abstr.*, **67**, 77019 (1967).

(60) G. E. Moore and R. M. Badger, *J. Amer. Chem. Soc.*, **74**, 6076 (1952).

(61) J. C. Carter, R. F. Bratton, and J. F. Jackovitz, *J. Chem. Phys.*, **49**, 3751 (1968).

(62) P. J. Hendra and J. R. Mackenzie, *Chem. Commun.*, 760 (1968).

(63) M. Delhaye, N. Durrieu-Mercier, and M. Migeon, *C. R. Acad. Sci., Ser. B*, **267**, 135 (1968).

(64) L. Bayersdorfer, U. Engelhardt, K. Höhne, J. Fischer, and J. Jander, *Z. Naturforsch. B*, **23**, 1602 (1968).

(65) D. P. Stevenson and V. Schomaker, *J. Amer. Chem. Soc.*, **62**, 1913 (1940).

(66) L. Pauling and M. L. Huggins, *Z. Kristallogr.*, **87**, 205 (1934).

(67) D. E. Milligan and M. E. Jaycox, *J. Chem. Phys.*, **40**, 2461 (1964).

(68) D. E. Milligan, *ibid.*, **35**, 372 (1961).

(69) E. R. V. Milton, H. B. Dunford, and A. E. Douglas, *ibid.*, **35**, 1202 (1961).

(70) A. Elliott, *Proc. Roy. Soc., Ser. A*, **169**, 469 (1939).

(71) R. Ettinger, *J. Chem. Phys.*, **38**, 2427 (1963).

(72) J. Stieglitz, *J. Amer. Chem. Soc.*, **23**, 797 (1901).

(73) L. Pauling, *ibid.*, **54**, 3570 (1932).

(74) E. Allenstein, *Z. Anorg. Allg. Chem.*, **308**, 1 (1961); *Chem. Abstr.*, **55**, 18224 (1961).

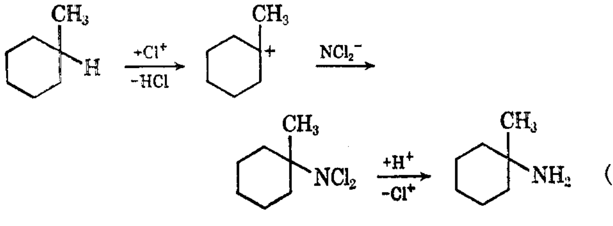
(75) H. Lumbroso, *Bull. Soc. Chim. Fr.*, 373 (1961); *Chem. Abstr.*, **55**, 18224 (1961).

(76) H. Lumbroso, *Bull. Soc. Chim. Fr.*, 2519 (1963); *Chem. Abstr.*, **60**, 6298 (1964).

(77) H. Lumbroso, *Bull. Soc. Chim. Fr.*, 887 (1959); *Chem. Abstr.*, **55**, 16055 (1961).

unknown until the aminating system, nitrogen trichloride and aluminum chloride, was applied.[78,79] An extensive study of reaction variables enabled 1-amino-1-methylcyclohexane to be obtained in synthetically useful yields (70–80%) from methylcyclohexane. The most practical procedure involves addition of nitrogen trichloride to a mixture of methylcyclohexane and aluminum chloride in a molar ratio of 1:2:2.[10a] Amination is postulated to occur as in eq 4 and 5. Hydride

$$Cl_3N + AlCl_3 \rightleftharpoons Cl_3N\cdots AlCl_3 \rightleftharpoons Cl^{\delta+}(Cl_2NAlCl_3)^{\delta-} \quad (4)$$

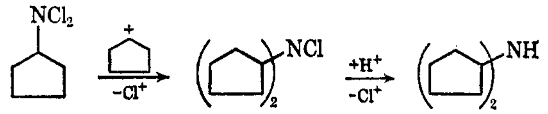


(5)

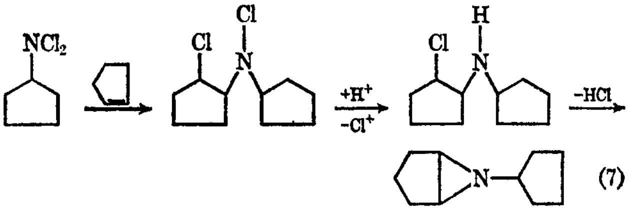
abstraction is apparently effected by Cl^+. Attack by dichloramide ion followed by an exchange reaction affords the product, 1-amino-1-methylcyclohexane. Although the exact nature of the nitrogenous nucleophile is not known, isolation of N,N-dichlorocyclohexylamine from cyclohexane[80] and N,N-dichloro-1-adamantylamine from adamantane[81] suggests involvement of dichloramide ion. Evidence has been presented for the analogous combination of N-fluoramines with carbonium ions.[82–84]

Relative rate data obtained for secondary *vs.* tertiary alkanes gives good evidence for the involvement of *t*-alkyl cations in the rate determining step of amination.[80] The scope of this novel amination reaction was investigated with a variety of cycloalkanes[80] and bicyclic[85] and tricyclic[81] compounds (Table I).

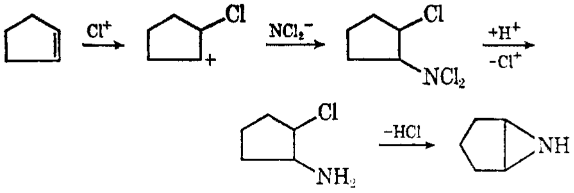
Most bicyclic and tricyclic hydrocarbons proved amenable to amination. Adamantane and alkyladamantanes gave excellent yields of the corresponding bridgehead amines.[81] Various tricyclic alkanes (precursors of adamantanes) underwent rearrangement and amination to adamantylamines in one step with nitrogen trichloride under Friedel–Crafts conditions.[81] Similarly, *cis*- and *trans*-decalin and hydrindan suffered attack at the tertiary position yielding amines of *cis* configuration.[80] With some substrates skeletal rearrangement proved to be the favored reaction path. Cycloheptane gave 1-amino-1-methylcyclohexane,[80] and the reaction with cyclohexane produced temperature-dependent products. At low temperatures cyclohexylamine was formed, while at higher temperatures 1-amino-1-methylcyclopentane predominated. With cyclopentane several simultaneous reactions gave rise to various types of amines. Dicyclopentylamine and N-cyclopentyl-6-azabicyclo[3.1.0]hexane are believed to arise *via* the indicated transformations (eq 6 and 7). 6-Azabicyclo[3.1.0]hexane presumably forms from the addition of the nitrogenous nucleophile to a 2-chlorocyclopentyl cation (eq 8). Cyclopentene was detected in the neutral portion of the reaction mixture from amination of cyclopentane.



(6)



(7)



(8)

Side-chain amination was effected in a similar fashion with *p*-cymene.[86,87] Optimum conditions, resulting in an 80% yield of 8-amino-*p*-cymeme based on nitrogen trichloride, entailed introduction of *t*-butyl bromide which eliminated nuclear amination. Apparently the derived *t*-butyl cation acts as an efficient hydride abstractor to give *p*-methyl-α,α-dimethylbenzyl cation. Isolation of isobutane from the reaction supports this hypothesis. The method was applied successfully to a number of other aryldialkylmethines:[88] *p*-alkyl- and *p*-halocumenes, and *p*-cyclohexyltoluene. Amination of 3-(*p*-tolyl)pentane took place with rearrangement forming 2-(*p*-tolyl)-2-pentylamine, the same product as was obtained from 2-(*p*-tolyl)pentane.

This method possesses synthetic utility since few attractive methods are available which provide tertiary carbinamines. In addition, alkanes represent a novel precursor for the direct synthesis of amines in this class. The Ritter reaction, which is generally the preferred, classical technique, usually, employs alcohols or olefins.

2. *Alkyl Halides*

The reaction of alkyl halides with nitrogen trichloride–aluminum chloride produces primary and secondary amines, and aziridines, depending upon the substrate used.[89,90] An extensive investigation was carried out with *t*-butyl chloride affording a 90% yield of *t*-butylamine based on nitrogen trichloride. Of pertinence to the nature of the nucleophile, N,N-dichloro-*t*-butylamine was isolated suggesting involvement of dichloramide ion (eq 4 and 9). Chlorinated derivatives

$$(CH_3)_3CCl \xrightarrow[-Cl^-]{AlCl_3} (CH_3)_3C^+ \xrightarrow{NCl_2^-} (CH_3)_3CNCl_2 \xrightarrow[-Cl^+]{+H^+} (CH_3)_3CNH_2 \quad (9)$$

---

(78) P. Kovacic, R. J. Hopper, S. S. Chaudhary, J. A. Levisky, and V. A. Liepkalns, *Chem. Commun.*, 232 (1966).

(79) P. Kovacic and S. S. Chaudhary, *Tetrahedron*, **23**, 3563 (1967).

(80) K. W. Field, P. Kovacic, and T. Herskovitz, *J. Org. Chem.*, **35**, 2146 (1970).

(81) P. Kovacic and P. D. Roskos, *J. Amer. Chem. Soc.*, **91**, 6457 (1969).

(82) T. E. Stevens, *J. Org. Chem.*, **33**, 2664 (1968).

(83) W. H. Graham and J. P. Freeman, *J. Amer. Chem. Soc.*, **89**, 716 (1967).

(84) J. P. Freeman, W. H. Graham, and C. O. Parker, *ibid.*, **90**, 121 (1968).

(85) P. Kovacic, M. K. Lowery, and P. D. Roskos, *Tetrahedron*, **26**, 529 (1970).

(86) P. Kovacic and R. J. Hopper, *ibid.*, **23**, 3965 (1967).

(87) P. Kovacic and R. J. Hopper, *ibid.*, **23**, 3977 (1967).

(88) P. Kovacic, J. F. Gormish, R. J. Hopper, and J. W. Knapczyk, *J. Org. Chem.*, **33**, 4515 (1968).

(89) P. Kovacic and M. K. Lowery, *Chem. Commun.*, 651 (1966).

(90) P. Kovacic and M. K. Lowery, *J. Org. Chem.*, **34**, 911 (1969).

Table I

Amination Products from Cycloalkanes and Bicyclic and Tricyclic Compounds with Nitrogen Trichloride–Aluminum Chloride

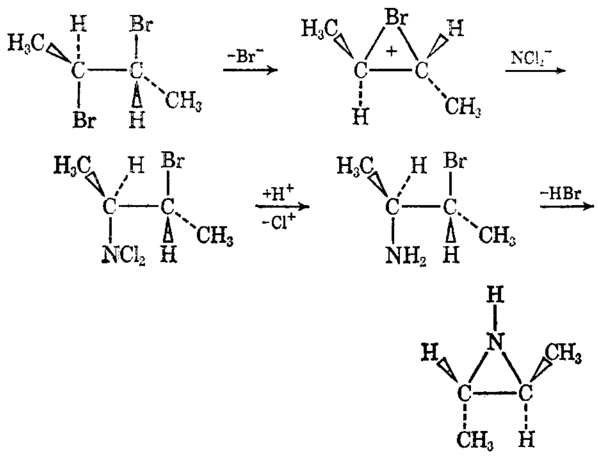
Substrate	*Amine products*	*Yield,[a] %*
Adamantane	1-Aminoadamantane	95[b]
Trimethylenenorbornane	1-Aminoadamantane	75[b]
1-Methyladamantane	3-Methyl-1-aminoadamantane	93[b]
Tetramethylenenorbornane	3-Methyl-1-aminoadamantane	85[b]
1,3-Dimethyladamantane	3,5-Dimethyl-1-aminoadamantane	73[b]
Perhydroacenaphthene	3,5-Dimethyl-1-aminoadamantane	73[b]
Dimethyltrimethylenenorbornane	3,5-Dimethyl-1-aminoadamantane	73[b]
1,3,5-Trimethyladamantane	3,5,7-Trimethyl-1-aminoadamantane	90[b]
Norbornane	*exo*-2-Aminonorbornane	39[c]
Decalin[d]	*cis*-9-Aminodecalin	50[e]
Hydrindan	*cis*-8-Aminohydrindan	70[e]
Methylcyclopentane	1-Amino-1-methylcyclopentane	61[e]
Cycloheptane	1-Amino-1-methylcyclohexane	65[e]
Cyclooctane	1,3- and 1,4-dimethyl-1-aminocyclohexane	50[e]
Methylcycloheptane	1,3- and 1,4-dimethyl-1-aminocyclohexane	50[e]
cis-1,3-Dimethylcyclohexane	1,3- and 1,4-dimethyl-1-aminocyclohexane	55[e]
1,4-Dimethylcyclohexane	1,3- and 1,4-dimethyl-1-aminocyclohexane	50[e]
Cyclohexane	Cyclohexylamine	41[e,f]
Cyclohexane	1-Amino-1-methylcyclopentane	49[e,f]
Cyclopentane	Cyclopentylamine	3[e]
	6-Azabicyclo[3.1.0]hexane	36[e]
	N-Cyclopentyl-6-azabicyclo[3.1.0]hexane	13[e]
	Dicyclopentylamine	2[e]

[a] Yield based on nitrogen trichloride; molar ratio, $NCl_3:AlCl_3$:hydrocarbon = ~1:2:1.5. [b] Reference 81. [c] Reference 85. [d] Mixture of isomers. The same product was formed from the pure *cis* or *trans* isomer. [e] Reference 80; molar ratio, $NCl_3:AlCl_3$:hydrocarbon = 1:2:5. [f] See text discussion.

of isobutane were detected among the neutral products, which is taken as evidence for participation of $Cl^{\delta+}$. A minor product, 2,2-dimethylaziridine, was accounted for by a scheme similar to the one proposed for cyclopentenimine (eq 8).

When isobutyl chloride was treated with nitrogen trichloride–aluminum chloride, three products were found: *t*-butylamine (major), *sec*-butylamine, and 2,2-dimethylaziridine. The first two can be rationalized by initial polarization of the isobutyl chloride accompanied by a hydrogen or methyl shift, respectively. In this aminating system, secondary alkyl halides gave secondary amines and N-alkylaziridines (*cf.* eq 6 and 7) in addition to primary amines.

The diastereomeric 2,3-dibromobutanes were similarly subjected to amination. The *meso* form gave *trans*-2,3-dimethylaziridine in 40% yield, while the *dl* diastereomer gave no basic organic product. A stereospecific scheme is suggested (eq 10).



(10)

The reaction of nitrogen trichloride–aluminum chloride with *t*-alkyl halides provides a novel method of synthesis of *t*-alkylamines. The interesting specificity of the nucleophile is emphasized by the easy elimination which occurs on treatment of *t*-alkyl halides with amines. With few exceptions, *e.g.*, the Ritter reaction, the classical routes to tertiary carbinamines are characterized by a multiplicity of steps.[91]

3. Grignard Reagents

The reaction of Grignard reagents with various N-halamines has been investigated quite extensively. Depending on the Grignard reagent and N-halamine chosen, primary, secondary, and tertiary amines are formed. Table II lists the results from *n*-butyl Grignard reagent and different types of N-halamines. Chlor- and bromamine form primary amines.[92–94] Dibromamine and nitrogen trichloride produce primary, as well as secondary, amines.[95,96] When treated with the same Grignard reagent, the following pathways were observed: N,N-dichloroalkylamines yielded primary, secondary, and tertiary amines; N-chlorodialkylamines provided secondary and tertiary amines; and N-chloroalkylamines gave primary and secondary amines.[97] Several years later it was discovered that the use of dialkylmagnesium compounds with chloramine

---

[91] R. B. Wagner and H. D. Zook, "Synthetic Organic Chemistry," Wiley, New York, N. Y., 1953, Chapter 24.

[92] G. H. Coleman and C. R. Hauser, *J. Amer. Chem. Soc.*, **50**, 1193 (1928).

[93] G. H. Coleman and C. B. Yager, *ibid.*, **51**, 567 (1929).

[94] G. H. Coleman, H. Soroos, and C. B. Yager, *ibid.*, **55**, 2075 (1933).

[95] G. H. Coleman, C. B. Yager, and H. Soroos, *ibid.*, **56**, 965 (1934).

[96] G. H. Coleman, M. A. Buchanan, and W. L. Paxson, *ibid.*, **55**, 3669 (1933).

[97] G. H. Coleman, *ibid.*, **55**, 3001 (1933).

Table II

Amination Products from *n*-Butyl Grignard Reagent and N-Halamines

Grignard reagent	*N-Halamine*	*Products: yield, %*			*Ref*
		RNH_2	*R_2NH*	*R_3N*	
RMgCl	NH_2Cl	59			92
RMgBr	NH_2Cl	27			
RMgI	NH_2Cl	15			
RMgCl	NH_2Br	29			94
RMgBr	NH_2Br	9			
RMgI	NH_2Br	3			
RMgCl	$NHBr_2$	15	5		95
RMgBr	$NHBr_2$	5	1		
RMgI	$NHBr_2$	2	0.4		
RMgCl	NCl_3	37	5		96
RMgBr	NCl_3	21	2		
RMgI	NCl_3	4	1		
RMgCl	CH_3NCl_2	43[a]	22[a]	5[a]	97
RMgCl	$(n\text{-}C_4H_9)_2NCl$		85[a]	4[a]	
RMgCl	CH_3NHCl	72[a]	14[a]		
R_2Mg	NH_2Cl	90[a]			98

[a] R's may be different.

generated optimum amounts of primary amines.[98] The yields of primary amines from primary, secondary, tertiary, and benzyl Grignard reagents are usually between 55 and 85%, while dialkylmagnesium compounds give values near 90% (Table II). The experimental procedure involves the addition of an ether solution of chloramine to an excess of the Grignard reagent at 0°, followed by isolation of the amine.

Unlike their alkyl analogs, phenyl Grignard reagents gave low yields of amine.[92] A similar reaction was attempted with phenylmagnesium bromide and several N-chlorodialkylamines, namely, 1-chloropiperidine and dimethyl- and diethylchloramine, but no aniline derivatives were obtained.[99] A competing reaction, replacement of MgX by chlorine, was favored. Benzylmagnesium chloride was found to produce *o*-tolylcarbinol when treated with formaldehyde.[100] Similarly, in an attempt to form *o*-toluidines from benzylmagnesium chloride and chloramine, benzylamine was obtained instead in good yield.[101] Cinnamylmagnesium chloride also reacted with chloramine in a straightforward manner to give the unrearranged primary amine.

From Table II the yield order of amine from RMgX with variation in X was Cl > Br > I for a given N-halamine, which may be a reflection of steric factors and the carbanionic character of R. Formation of amines presumably involves the halogen of the amine leaving as a negative entity through SN2 attack. Equations 11 and 12 were presented by Coleman and Hauser.[92] The alteration in yield of primary amine when

$$RMgX + NH_2Cl \longrightarrow RNH_2 + MgXCl \qquad (11)$$

$$RMgX + NH_2Cl \longrightarrow RCl + MgXNH_2 \qquad (12)$$

the N-halo atom is changed can also be rationalized. Substitution of bromine for chlorine in monohalamine increases the basicity of the nitrogen, thereby discouraging nucleophilic attack at that site (Table II). The absence of aniline derivatives when phenyl Grignard reagents are treated with dialkylchloramines is apparently due to steric factors and the inductive effect of the alkyl substitutents.

These observations are very interesting because they illustrate the dual nature of the halogen in N-halamines, exhibiting either anionic or cationic character. During the generation of amines (eq 11) the halogen functions as the leaving entity, whereas when the alkyl halide is obtained (eq 12) the amino group is displaced. Equations 11 and 12 were shown to be interdependent since ammonia production was found to be inversely proportional to amine formation.

In conjunction with the over-all study of organometallic compounds with N-halamines, organolithium and organozinc precursors have also been used.[102] Chloramine combines with these reagents to form primary amines. Primary and secondary amines are obtained upon treatment of zinc alkyls with nitrogen trichloride. The yields in these reactions are slightly lower than those from the Grignard reagent. Another modification of the N-halamine–organometallic reaction has been reported.[103] Isopropylpotassium, prepared from the corresponding Grignard reagent, was added to N-chlorodiisopropylamine, resulting in the generation of triisopropylamine (3%) and tetraisopropylhydrazine (4.5%).

There is little similarity in the reaction of N-halamines with Grignard reagents and with alkyl halides–aluminum chloride, other than the nature of the end products. With Grignard reagents the success of the reaction presumably depends on the halogen of the N-halamine acting as an anion, while in the latter system cationic halogen appears to participate. Synthetically, the preparation of amines from chloramine and Grignard reagents deserves mention. One advantage is that this technique is not plagued by rearrangements. The nitrogen trichloride–aluminum chloride procedure seems to be the method of choice for certain *tertiary* carbinamines. However, the Grignard system can be used for carbinamines in general.

4. *Organoboranes*

In connection with an extensive study of organoboranes, a convenient synthesis of amines from olefins and chloramine *via* hydroboration was found.[104] The yields are good, 60%, considering that only two of the alkyl groups of the organoborane (R_3B) undergo reaction. The third alkyl group was found in the monoalkylboronic acid by-product which reacted very slowly with choramine. Representative results with tetrahydrofuran as solvent were *n*-octylamine (51%), cyclopentylamine (50%), and *cis*-myrtarylamine (48%) from 1-octene, cyclopentene, and β-pinene, respectively. Hydroxylamine-O-sulfonic acid can be used in place of chloramine as the aminating agent with little change in yields.

5. *Unsaturated Aliphatic Materials*

The reaction of N-halamines with various unsaturated compounds, such as olefins, acetylenes, α,β-unsaturated ketones and acids, and ketenes involves addition to the double bond.

---

(98) G. H. Coleman and R. F. Blomquist, *J. Amer. Chem. Soc.*, **63**, 1692 (1941).

(99) R. J. W. Le Fèvre, *J. Chem. Soc.*, 1745 (1932).

(100) M. Tiffeneau and R. Delange, *C. R. Acad. Sci.*, **137**, 573 (1903).

(101) G. H. Coleman and R. A. Forrester, *J. Amer. Chem. Soc.*, **58**, 27 (1936).

(102) G. H. Coleman, J. L. Hermanson, and H. L. Johnson, *ibid.*, **59**, 1896 (1937).

(103) F. Kuffner and W. Siefried, *Monatsh. Chem.*, **83**, 748 (1952); *Chem. Abstr.*, **48**, 5077 (1954).

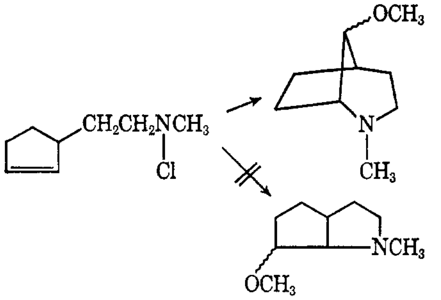
(104) H. C. Brown, W. R. Heydkamp, E. Breuer, and W. S. Murphy, *J. Amer. Chem. Soc.*, **86**, 3565 (1964).

a. Alkenes

Coleman and coworkers have made significant contributions to the chemistry of N-halamines, including an extensive study of the reaction of nitrogen trichloride with carbon–carbon double bonds.[105–107] Nitrogen trichloride underwent addition to the following olefins: 1- and 2-butene, ethylene, propylene, 2-pentene, isobutylene, and cyclohexene. The products were β-chloroalkylamines which presumably were derived from the corresponding N,N-dichloro derivatives as the primary adducts. Treatment with concentrated hydrochloric acid effected conversion to the amine salt. With unsymmetrical olefins, Markovnikov's rule was followed with chlorine adding to the least substituted carbon atom, and nitrogen becoming affixed to the other position. However, trimethylethylene, 1,1-diphenylethylene, triphenylethylene, and tetraphenylethylene gave no organic amine products. The data do not permit a meaningful discussion of the mechanism; the position of the chlorine suggests initial attack by either $Cl\cdot$ or $Cl^{\delta+}$. Whether the addition is a stepwise or concerted process is not known. The stereochemistry is also unknown, *i.e.*, *cis*, *trans*, or nonstereospecific addition. The use of *cis*- and *trans*-2-butene should aid in elucidating the nature of the addition.

Treatment of isobutylene with nitrogen trichloride–aluminum chloride gave 2,2-dimethylazirdine as the sole basic material in 10% yield.[90] The pathway is believed to entail addition of nitrogen trichloride across the double bond, replacement of chlorine on nitrogen with hydrogen, and subsequent internal nucleophilic displacement (*cf.* eq 8).

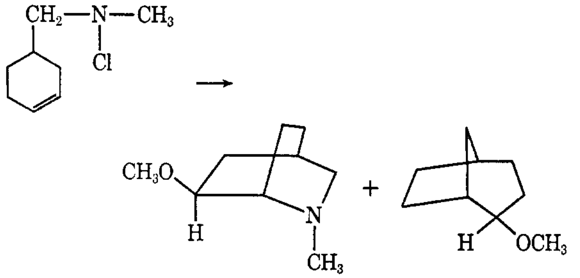
A novel route to azabicyclics is the conversion of a monocyclic olefinic N-chloramine into a bicyclic amino ether under solvolytic conditions[108] (eq 13). Ionization of the chlorine leads to an electron-deficient nitrogen which adds intramolecularly to the double bond. Of the two possible modes of addition, only the route leading to 8-methoxy-2-methyl-2-azabicyclo[3.2.1]octane is followed. A similar cyclization gave two major bicyclic products[109] (eq 15). The stereochemistry of **1** indicated over-all *trans* addition.



(13)

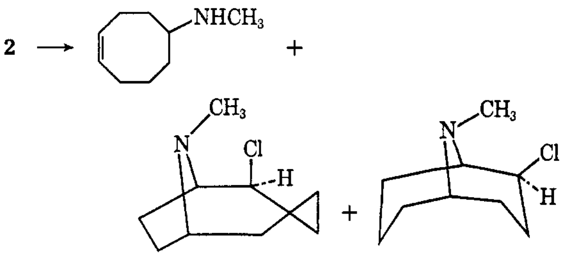
(14)

Another study dealt with interaction of N-chloro-N-methyl-4-cyclooctenamine (**2**) with silver perchlorate in refluxing acetone to give N-methyl-4-cyclooctenamine (71% yield) and minor quantities of two azabicyclics[110] (eq 16). The bicyclic products arise from stereospecific *cis* addition. A rationalization was presented involving coordination of the catalyst on nitrogen. Alternatively, perhaps structure **4** is applicable in view of the evidence (ref 109) for internal return of chlorine during solvolysis by silver ion.

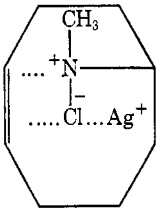


1

(15)



(16)

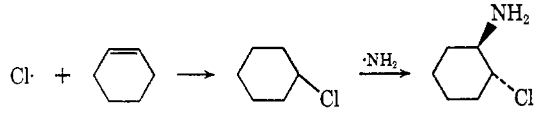


3

One interpretation of eq 15 comprises *cis* addition of nitrogen and chlorine to the double bond followed by attack of solvent with displacement of chloride ion to produce the bicyclic amino ether, **1**. This approach provides a common rationale for the results depicted in eq 15 along with those of eq 16.

A considerable amount of work has been carried out on addition of halamines to olefins by means of radical intermediates. The photochemical addition of chloramine to cyclohexene results in the production of *trans*-2-chlorocyclohexylamine (8%) and neutral products.[111] A radical mechanism was postulated (eq 17 and 18). Since lowering of the temperature increases radical lifetime and enhances the yield of amine, a coupling of radicals was proposed. N-Bromobistrifluoromethylamine formed 1:1 adducts with various olefins in high yield, apparently by way of a homolytic mechanism.[111a]

$$NH_2Cl \rightleftarrows NH_2Cl^* \rightleftarrows NH_2\cdot + Cl\cdot \qquad (17)$$



(18)

---

[105] G. H. Coleman, G. M. Mullins, and E. Pickering, *J. Amer. Chem. Soc.*, **50**, 2739 (1928).

[106] G. H. Coleman and H. P. Howells, *ibid.*, **45**, 3084 (1923).

[107] G. H. Coleman and A. W. Campbell, *ibid.*, **50**, 2754 (1928).

[108] P. Gassman, F. Hoyda, and J. Dygos, *ibid.*, **90**, 2716 (1968).

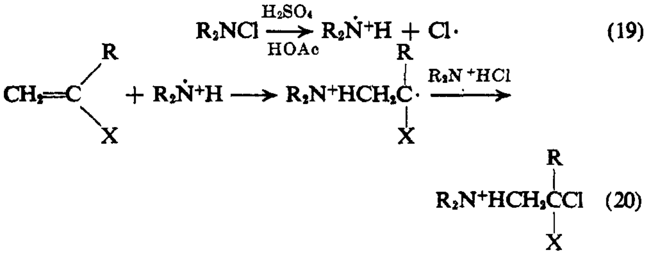
[109] P. G.Gassman, *Accounts Chem. Res.*, **3**, 26 (1970).

[110] J. D. Hobson and W. D. Riddell, *Chem. Commun.*, 1178 (1968).

[111] Y. Ogata, Y. Izawa, and H. Tomoika, *Tetrahedron*, **23**, 1509 (1967).

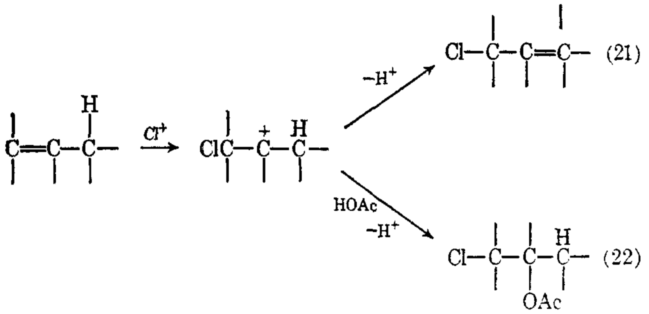
[111a] R. N. Haszeldine and A. E. Tipping, *J. Chem. Soc.*, 6141 (1965).

Radical addition of N-chlorodialkylamines was found to occur with terminal olefins in acid media.[112] Two competing


(19)

(20)

X = F, Cl, Br, Si(CH$_3$)$_3$


(21)

(22)

reactions are involved: (1) free-radical addition of the ion radical, $R_2\dot{N}^+H$, in a chain process (eq 19 and 20) and (2) attack by ionic chlorine (eq 21 and 22). The presence of oxygen inhibited the radical route. It is interesting that the aminium radical displayed little inclination to participate in intermolecular hydrogen abstraction reactions (*cf.* ref 237).

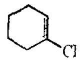
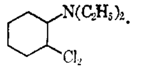
The use of various substituted olefins was studied to determine which groups would facilitate radical participation of the N-chloramine *vs.* electrophilic attack by chlorine. Substituents which are electron withdrawing and do not place a π electron system in conjugation with the olefinic double bond enhance radical addition, and at the same time destabilize the potential carbonium ion (*cf.* ref 118). When X = Br, Cl, Si(CH$_3$)$_3$, CH$_2$CN, or CH$_2$C$_6$H$_5$, synthetically useful yields of the radical adducts were obtained, whereas when X = OCH$_3$, OCOC$_2$H$_5$, or 4-pyridinyl, no isolable products of this type were found. The synthetic utility of the method should be emphasized since the β-chloramines are not readily available by any other one-step reaction involving unsaturated hydrocarbons. Representative additions of N-chlorodiethylamine to terminal, substituted vinyl and allylic olefins are listed[112] in Table III. Other N-chlorodialkylamines also proved effective. The experimental procedure usually involves the addition of olefin to a 4 *M* sulfuric acid–acetic acid mixture containing the chloramine at 30°.

Monoalkyl-N-chloramines add to olefins substituted in the vinylic and allylic positions in the sulfuric acid–acetic acid medium.[113] The yields of β-chloramines range from 40 to 70%, in general lower than those obtained from dialkylchloramines. Interestingly, several olefins which gave good yields of adducts with dialkylchloramines gave no analogous product with monoalkyl-N-chloramines.

During this same period of time, the discovery was made that radical addition of N-chloramines to olefins takes place in oxidation–reduction systems.[114–117] Styrene, cyclohexene, and 1-hexene participate according to eq 23–25. The yield

Table III

Addition of N-Chlorodiethylamine to Olefins

Olefin	*Adduct*	*Yield, %*
CH$_2$=CHCH$_3$	(C$_2$H$_5$)$_2$NCH$_2$CHClCH$_3$	42
CH$_2$=C(CH$_3$)$_2$	...	0
CH$_2$=CHCl	(C$_2$H$_5$)$_2$NCH$_2$CHCl$_2$	82
		60
CH$_2$=CHF	(C$_2$H$_5$)$_2$NCH$_2$CHClF	80
CH$_2$=CBrCH$_3$	(C$_2$H$_5$)$_2$NCH$_2$CBrClCH$_3$	46
CH$_2$=CHSi(CH$_3$)$_3$	(C$_2$H$_5$)$_2$NCH$_2$CHClSi(CH$_3$)$_3$	65
CH$_2$=CHCH$_2$Cl	(C$_2$H$_5$)$_2$NCH$_2$CHClCH$_2$Cl	83
CH$_2$=CHCH$_2$C$_6$H$_5$	(C$_2$H$_5$)$_2$NCH$_2$CHClCH$_2$C$_6$H$_5$	57

$$R_2NCl + M^+ \longrightarrow R_2N\cdot + MCl^+ \qquad (23)$$

M = Cu or Fe

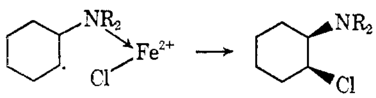
$$R_2N\cdot + C_6H_{12} \longrightarrow R_2NC_6H_{12}\cdot \qquad (24)$$

$$R_2NC_6H_{12}\cdot + MCl^+ \longrightarrow R_2NC_6H_{12}Cl + M^+ \qquad (25)$$

of chloramination adduct was 30–40% based on N-chloramine. The oxidation–reduction pairs, Cu^{2+}–Cu$^+$ or Fe^{3+}–Fe^{2+}, were used with N-chlorodiethylamine or N-chloropiperidine.

Modification by the introduction of sulfuric acid changed the attacking species to the dialkylamino radical ion, $R_2\dot{N}^+H$.[118] Addition of N-chloropiperidine occurs with cyclohexene (54%), styrene (58%), *cis*-2-pentene, and 1-hexene. The experimental procedure usually consisted of the addition under nitrogen of a solution of the N-chloramine in concentrated sulfuric acid to a 65% sulfuric acid–ferrous sulfate solution containing the olefin. An equimolar amount of salt is employed relative to the N-chloramine. It seems that appropriate conditions have been found for generalized radical addition of protonated N-chloramines to simple olefins.

An interesting stereochemical result from the reaction of protonated and unprotonated N-chloropiperidine with cyclohexene provides a clue to the mechanism of chlorine transfer. Unprotonated N-chloropiperidine adds to cyclohexene stereoselectively to generate the *cis* isomer,[119] whereas the protonated N-halamine gives rise to both the *cis* and *trans* forms. The *cis* stereoselectivity may be correlated with coordination of the unprotonated amino group with ferric salt which is apparently responsible for the chlorine transfer (eq 26). In sulfuric acid, the reaction probably occurs by a


(26)

radical chain (eq 27).

---

(112) R. S. Neale and N. L. Marcus, *J. Org. Chem.*, 32, 3273 (1967).

(113) R. S. Neale and N. L. Marcus, *ibid.*, 33, 3457 (1968).

(114) F. Minisci and R. Galli, *Tetrahedron Lett.*, 167 (1964).

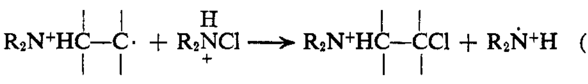
(115) F. Minisci and R. Galli, *Chim. Ind. (Milan)*, 45, 1400 (1963); *Chem. Abstr.*, 60, 10497 (1964).

(116) F. Minisci and R. Galli, *Chim. Ind. (Milan)*, 46, 546 (1964); *Chem. Abstr.*, 61, 4308 (1964).

(117) F. Minisci, *Chim. Ind. (Milan)*, 49, 705 (1967).

(118) F. Minisci, R. Galli, and M. Cecere, *Tetrahedron Lett.*, 3163 (1966).

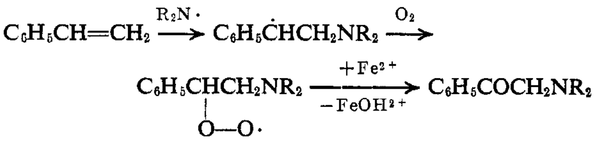
(119) F. Minisci, R. Galli, and M. Cecere, *Chim. Ind. (Milan)*, 48, 347 (1966).



$$R_2N^+H\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}\cdot + R_2\overset{H}{\underset{+}{N}}Cl \longrightarrow R_2N^+H\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}Cl + R_2\dot{N}^+H \quad (27)$$

On the basis that oxygen is inert toward amino radicals, but very reactive toward the alkyl counterparts, a new synthesis of α-amino ketones was developed.[120] Mixtures of olefins and N-chloramines were exposed to ferrous or cuprous salt and oxygen. In most cases the yields ranged from 41 to 76%. Conjugated olefins, *e.g.*, styrene, which also possess relatively low steric hindrance gave the best results. A plausible pathway is presented in eq 28 and 29.

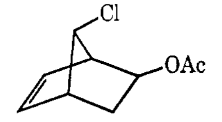
$$R_2NCl + Fe^{2+} \longrightarrow R_2N\cdot + FeCl^{2+} \quad (28)$$



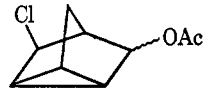
$$C_6H_5CH{=}CH_2 \xrightarrow{R_2N\cdot} C_6H_5\dot{C}HCH_2NR_2 \xrightarrow{O_2}$$
$$\underset{\displaystyle O\!-\!O\cdot}{C_6H_5CHCH_2NR_2} \xrightarrow[-FeOH^{2+}]{+Fe^{2+}} C_6H_5COCH_2NR_2 \quad (29)$$

In a 4 *M* sulfuric acid–acetic acid medium in the presence of 1,3-dienes, the Hofmann–Löffler reaction is suppressed and 1,4 addition of the N-chloramine occurs.[121] Use of a variety of N-chlorodialkylamines and butadiene gave 1,4 adducts with yields ranging from 42 to 60%. Similarly, 1,3-cyclooctadiene and N-chlorodiethylamine gave the 1,4-adduct in 68% yield.[122] However, when 1,1-diphenylethylene was treated with N-chlorodibutylamine, only dibutylamine and 1,1-diphenyl-2-chloroethylene were isolated.[121] The addition of N-chloromorpholine, N-chloropiperidine, N-chlorodiethylamine, and N-chlorodibutylamine to 1,3-butadiene in redox systems was reported to proceed in yields of 35–62%.[123]

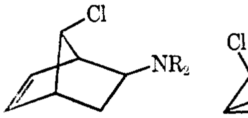
Reaction of N-chlorodiethylamine with norbornadiene in strong acid was carried out in an attempt to elucidate the dual nature of the N-chloramine.[124] Approximately equal amounts of neutral and basic materials were obtained, **4**–**7**. All products can be accounted for by an ionic pathway in which the first step is postulated as *exo* fixation of chloronium ion to norbornadiene, giving rise to a common intermediate, **8**. Evidently there is insufficient homoconjugation in norbornadiene to induce a radical addition of N-chlorodiethylamine. The method for chloramination which employs a reducing salt might be the best choice for norbornadiene since ionic reactions would be eliminated.[118]



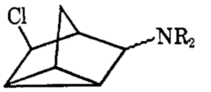
4



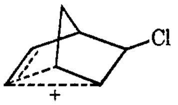
5



6

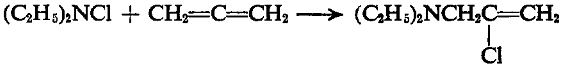


7

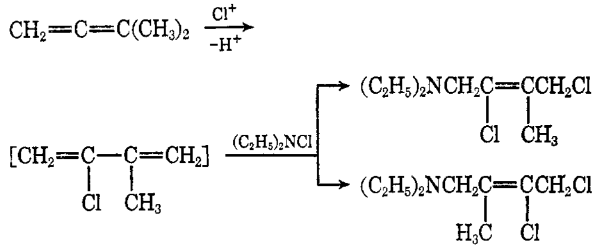


8

In keeping with the behavior of simple olefins, allenes undergo 1,2-radical addition with N-chlorodialkylamines in sulfuric acid and acetic acid. Aminium radical attack results in nitrogen becoming affixed to the least substituted carbon atom[122,125] (eq 30). This constitutes a useful method for the preparation of 2-chloroallylamines. Substituted allenes apparently suffer initial ionic attack by Cl^+ for the most part, followed by 1,4 addition of halamine to the resultant 1,3-diene (eq 31 and 32).



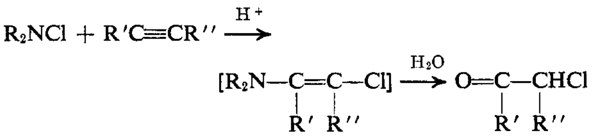
$$(C_2H_5)_2NCl + CH_2{=}C{=}CH_2 \longrightarrow (C_2H_5)_2NCH_2\underset{Cl}{\underset{|}{C}}{=}CH_2 \quad (30)$$



$$CH_2{=}C{=}C(CH_3)_2 \xrightarrow[-H^+]{Cl^+}$$
$$[CH_2{=}\underset{Cl}{\underset{|}{C}}-\underset{CH_3}{\underset{|}{C}}{=}CH_2] \xrightarrow{(C_2H_5)_2NCl} (C_2H_5)_2NCH_2\underset{Cl}{\underset{|}{C}}{=}\underset{CH_3}{\underset{|}{C}}CH_2Cl \quad (31)$$
$$\phantom{[CH_2{=}C-C{=}CH_2]}\longrightarrow (C_2H_5)_2NCH_2\underset{H_3C}{\underset{|}{C}}{=}\underset{Cl}{\underset{|}{C}}CH_2Cl \quad (32)$$

b. Alkynes

When acetylenes are treated with N-chloramines in acidic media, α-chlorocarbonyl compounds are generated in a procedure which appears synthetically attractive.[122,125] One mechanistic possibility entails formation of an enamine *via* participation of aminium radical (eq 33) (the enamine has not been isolated). N-Chlorodiethylamine and 2-hexyne gave both possible isomeric α-chloro ketones in similar amounts.[122] A drawback to this system is that long-chain chloramines give significant amounts of Hofmann–Löffler product, as they did with terminal olefins.



$$R_2NCl + R'C{\equiv}CR'' \xrightarrow{H^+}$$
$$[R_2N-\underset{R'}{\underset{|}{C}}{=}\underset{R''}{\underset{|}{C}}-Cl] \xrightarrow{H_2O} O{=}\underset{R'}{\underset{|}{C}}-\underset{R''}{\underset{|}{C}}HCl \quad (33)$$

R = Et, R′ = H, R″ = n-C_4H_9 (45%)

R = R′ = R″ = Et (59%)

R = Et, R′ = H, R″ = $(CH_3)_3C$ (60%)

The acid systems and the metal ion–acid systems are similar in many respects. The reaction of protonated amino radicals with olefins give adducts, with no significant intermolecular free-radical hydrogen abstraction. The metal ion–N-chloramine reactions are postulated as involving free neutral amino radicals. However, a metal ion–amino radical complex might be involved, which could account for its similarity to the acid system.[112] The differences in yield and stereochemistry can be explained by the different conditions employed.

Synthetically, the techniques are quite useful. The metal ion–acid system gives good yields of adducts from simple olefins. The acid system provides a simple one-step method for obtaining addition products from vinyl and allyl olefins, as well as from many substituted alkenes.

c. α,β-Unsaturated Carbonyl Compounds

Addition of nitrogen trichloride in carbon tetrachloride solution to benzalacetophenone and to benzalacetone in the cold generated 1-amino-2-chloro-1,3-diphenylpropanone-3

---

(120) F. Minisci and R. Galli, *Tetrahedron Lett.*, 3197 (1964).

(121) R. S. Neale and R. L. Hinman, *J. Amer. Chem. Soc.*, **85**, 2666 (1963).

(122) R. S. Neale, *J. Org. Chem.*, 32, 3263 (1967).

(123) F. Minisci, R. Galli, and G. Pollina, *Chim. Ind. (Milan)*, **47**, 736 (1965); *Chem. Abstr.*, **64**, 691 (1966).

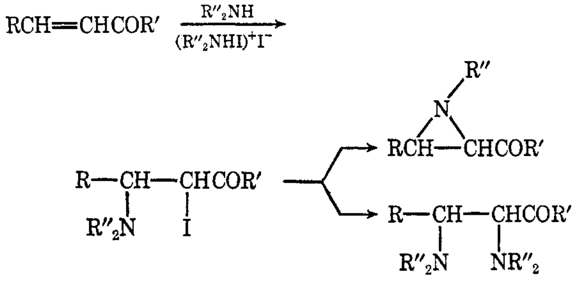
(124) R. S. Neale and E. B. Whipple, *J. Amer. Chem. Soc.*, **86**, 3130 1964).

(125) R. S. Neale, *ibid.*, **86**, 5340 (1964).

and 1-amino-2-chloro-1-phenylbutanone-3, respectively,[126,127] in low yields, along with neutral products and large amounts of nitrogen and ammonium chloride. The corresponding, N,N-dichloro derivatives are postulated as intermediates. The carbonyl group apparently governs the orientation. On the assumption of a polar pathway, by analogy with conjugate addition, nitrogen trichloride would then be exhibiting the indicated character, $Cl^{\delta+}–NCl_2^{\delta-}$. Because of the meager amount of evidence at hand, no definitive statement can be made regarding details of the reaction course.

The behavior of benzalacetophenone and benzalacetone toward iodine–amine complexes in the presence of excess amine has been investigated.[128] Benzalacetophenone reacts with complexes of iodine and ammonia (57% yield) or primary amines (benzylamine, 73% yield; cyclohexylamine, 46% yield) to form 2-phenyl-3-benzoylethylenimines, whereas with secondary amines (morpholine, 87% yield; piperidine, 59% yield) α,β-diaminobenzylacetophenones are obtained. In a similar manner benzalacetone yields α,β-diaminobenzylacetones with secondary amine complexes (morpholine, 55% yield, and piperidine, 12% yield), but ethylenimine ketones are not produced from ammonia or primary amine complexes. The scope of the reaction of unsaturated compounds with the iodine–morpholine reagent was explored further.[129] Of the compounds investigated, *trans*-1,2-dibenzoylethylene and *trans*-β-benzoylacrylic acid participated readily at room temperature to form α,β-dimorpholino derivatives, whereas with β-nitrostyrene, 1-iodo-1-nitro-2-morpholino-2-phenylpropane was obtained. α-Phenylbenzalacetone, ethyl cinnamate, cinnamonitrile, cyclohexene, and *trans,trans*-1,4-diphenyl-1,3-butadiene did not react noticeably under these conditions.

Mechanistically, it appears that functional groups capable of withdrawing electrons from double bonds facilitate reaction with iodine–morpholine. The initial step is visualized as the net addition of R''_2NI to the double bond (eq 34 and 35). The existence of the α-iodo-β-amino ketone as an intermediate was not rigorously demonstrated; however, benzalacetophenone dibromide yields the corresponding dimorpholino ketone when treated with morpholine.[130]



$$RCH{=}CHCOR' \xrightarrow[(R''_2NHI)^+I^-]{R''_2NH}$$

(34)

(35)

R'' = alkyl or H

N-Bromomorpholine was found to add to *trans*-benzalacetophenone, producing α-bromo-β-morpholinobenzylacetophenone.[131] Hydrolysis and methanolysis of this product yielded, respectively, α-morpholino-β-hydroxybenzylacetophenone and a compound thought to be α-morpholino-β-methoxybenzylacetophenone. Evidence, admittedly not definitive, is presented that the α-bromo-β-morpholinobenzylacetophenone is an *erythro* form. On this assumption, *trans* addition of N-bromomorpholine to *trans*-benzalacetophenone occurred. The formation of the hydroxy, methoxy, and dimorpholino compounds would then result from an initial internal displacement giving the intermediate ethyleniminonium salt which then undergoes attack with final inversion. The generation of ethylenimine ketones from α,β-unsaturated ketones and complexes of iodine with ammonia or primary amines would follow the same reaction pathway initially. Internal nucleophilic displacement of iodide from the intermediate β-iodoamine would give rise to the observed end product. Later it was found that the reaction of N-bromocyclohexylamine and *p*-phenylcrotonophenone produced the *cis*-ethylenimine ketone as the major product.[132] Only the *trans*-ethylenimine ketones were obtained from treatment of cyclohexylamine–iodine complexes with α,β-unsaturated ketones.

Several explanations have been offered for the steric control of conjugate addition of N-bromamines and iodine–amine complexes (eq 34) to α,β-unsaturated carbonyl compounds, ultimately leading to ethylenimine ketones. The conformation of the intermediate enol may well be controlled by the steric interaction of substituents.[133] The nature of the solvent can have a decisive influence on determining the product configuration.[134,135] For example, substitution of methanol for benzene increased the amount of *trans*-ethylenimine ketone formed during the reaction of *trans*-benzalacetophenone or *trans*-4-nitrobenzalacetophenone with cyclohexylamine and its iodine complex or with N-bromocyclohexylamine. Similarly, changing the solvent from benzene to methanol doubled the amount of *cis*-ethylenimine ketone obtained from the interaction of cyclohexylamine and α-bromobenzalacetophenone. The configuration can be correctly predicted in both reactions by assuming the formation of chelated amino enol intermediates, whose halogenation or protonation is governed by asymmetric steric hindrance.

Nitrogen trichloride will also add to α,β-unsaturated acids.[136] With crotonic and cinnamic acids, extended periods were required for complete reaction; the products were β-amino-α-chlorobutyric acid (12%) and β-amino-α-chloro-β-phenylpropionic acid (8%), respectively. Unlike the reactions of other unsaturated compounds with nitrogen trichloride, only a small amount of ammonium chloride is formed, with a corresponding increase in the amounts of nitrogen and chlorine. The hydrogen chloride produced in the reaction converts the N,N-dichloro derivative to the amine form.

d. Ketenes

A number of N-halamines have been studied in their behavior toward ketene and diphenylketene[137] (Table IV). In all cases except for combination of chloramine with ketene, the electropositive halogen adds to the aliphatic carbon farthest from oxygen. For the exception, eq 36 appears

---

[126] G. H. Coleman and D. Craig, *J. Amer. Chem. Soc.*, **49**, 2593 (1927).

[127] G. H. Coleman and D. Craig, *ibid.*, **50**, 1816 (1928).

[128] P. L. Southwick and D. R. Christman, *ibid.*, **74**, 1886 (1952).

[129] P. L. Southwick and D. R. Christman, *ibid.*, **75**, 629 (1953).

[130] N. H. Cromwell, *ibid.*, **62**, 2897 (1940).

[131] P. L. Southwick and W. L. Walsh, *ibid.*, **77**, 405 (1955).

[132] N. H. Cromwell, R. P. Cahoy, W. E. Franklin, and G. D. Mercer, *ibid.*, **79**, 922 (1957).

[133] N. H. Cromwell, *ibid.*, **81**, 4702 (1959).

[134] P. L. Southwick and R. J. Shozda, *ibid.*, **82**, 2888 (1960).

[135] P. L. Southwick and R. J. Shozda, *ibid.*, **81**, 5435 (1959).

[136] G. H. Coleman and G. M. Mullins, *ibid.*, **51**, 937 (1929).

[137] G. H. Coleman, R. L. Peterson, and G. E. Goheen, *ibid.*, **58**, 1874 (1936).

Table IV

Products from Ketene or Diphenylketene with N-Halamines

Ketene	*N-Halamine*	*Product*	*Yield, %*
CH_2CO	NH_2Cl	$CH_3CONHCl$	73
	$NHBr_2$	$BrCH_2CONH_2$	18
	NCl_3	$ClCH_2CONH_2$	14
	$(CH_3)_2NCl$	$ClCH_2CON(CH_3)_2$	..
$(C_6H_5)_2CCO$	NH_2Cl	$(C_6H_5)_2CClCONH_2$	51
	NCl_3	$(C_6H_5)_2CClCONCl_2$	..
	$(CH_3)_2NCl$	$(C_6H_5)_2CClCON(CH_3)_2$	100

$$NH_2Cl \longrightarrow H^{\delta+}(NHCl)^{\delta-} \xrightarrow{CH_2=C=O} CH_3CONHCl \quad (36)$$

relevant. In some cases, the N-haloamide serves as precursor to the amide under the reaction conditions. With a different procedure, the adduct of diphenylketene and nitrogen trichloride is transformed to 1,1-diphenylmethylenimine hydrochloride.[107] This reaction is discussed elsewhere in more detail (see Rearrangement, section VI).

e. Miscellaneous

Several miscellaneous reactions can also be fitted into this category. The addition of N-bromobistrifluoromethylamine to unsaturated compounds proceeds readily.[138] The products are consistent with the initial formation of a bistrifluoromethylamino radical (Table V). Photolysis of N-bromobistrifluoromethylamine gave perfluorotetramethylhydrazine, supporting the radical process.

Table V

Addition Products of N-Bromobistrifluoromethylamine with Unsaturated Compounds

Compound	*Product*	*Compound*	*Product*
NO_2	$(CF_3)_2NONO$	C_2H_4	$(CF_3)_2NC_2H_4Br$
NO	$(CF_3)_2NNO$	C_2H_2	$(CF_3)_2NC_2H_2Br$
CO	$(CF_3)_2NCOBr$	C_2F_4	$(CF_3)_2NC_2F_4Br$

N-Nitrosamines are formed from N-chloramines and nitric oxide in methanol solution containing $Fe_2SO_4 \cdot 7H_2O$ (*cf.* Table V, entry 2).[139] N-Chlorodibutylamine afforded N-nitrosodibutylamine (65% yield); also prepared were N-nitrosomorpholine, N-nitrosopiperidine, and N-nitrosodiethylamine.

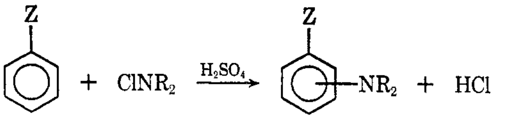
6. Arenes

N-Halamines can serve as agents for direct amination of the aromatic nucleus under a variety of conditions. In a number of cases, the procedures appear to be synthetically useful. Various mechanistic pathways are followed, including polar and radical categories.

The earliest disclosure of aromatic amination with N-halamines was apparently the report describing the reaction of benzene with N-chloropiperidine in the presence of aluminum chloride.[140] A small amount of N-phenylpiperidine was detected in the reaction product. The amination of aromatic compounds with hydroxylamine hydrochloride and aluminum chloride was claimed to proceed through chloramine as an intermediate.[141] Chloramine reacts with phenol yielding small amounts of *p*-aminophenol, along with 4,4′-dihydroxydiphenylamine and the iminoquinone.[142] Phenols containing a free *ortho* position were aminated by heating with sodium hydroxide and chloramine,[7] whereas with 2,6-disubstituted phenols, rearrangement involving ring expansion to dihydroazepinone derivatives occurred,[143,144] affording a one-step method for their synthesis in moderate yields. An N-chloramidine was postulated as an intermediate in the formation of benzimidazoles from N-arylamidines and hypochlorite in the presence of base.[145] Chloramine reacts with pyridine to give 2-aminopyridine (low yield),[146] in contrast with an earlier study[147] which revealed only ammonium chloride and decomposition of the heterocycle. Similarly, quinoline is converted to 2-aminoquinoline in 40% yield.[146] Although the mechanism was not discussed, several possibilities appear plausible: nucleophilic substitution, radical substitution, or addition–elimination.

Three groups have dominated the recent work on amination of aromatic compounds with N-halamines: Bock and Kompa, Minisci and coworkers, and Kovacic and coworkers. The results from each laboratory will be discussed separately and then compared.

Nuclear amination with N-chlorodialkylamines has been investigated extensively by three principal techniques.[148–151] With 96% sulfuric acid, N-chlorodimethylamine, and various aromatic substrates (benzene, toluene, chlorobenzene, naphthalene), N,N-dimethylarylamines were obtained in yields of 20–80%, generally (eq 37).[150]



(37)

Relative rate constants for the amination reaction closely resembled those obtained for electrophilic nitration and acetylation, rather than radical phenylation, thus supporting an electrophilic substitution mechanism. Furthermore, on addition of ferric chloride, a carbon radical scavenger,[152] to the benzene reaction mixture there was little decrease in yield of basic product and no formation of chlorobenzene. The isomer distribution was determined for dimethylamination of toluene, *ortho*:*meta*:*para* = 9:53:38. No rationalization of the high *meta* content was offered. Two possibilities were suggested for the aminating species depending on the site of protonation (eq 38 and 39).

---

(138) H. J. Emeleus and B. W. Tattershall, *Z. Anorg. Allg. Chem.*, **327**, 147 (1964).

(139) F. Minisci and R. Galli, *Chim. Ind. (Milan)*, **46**, 173 (1964); *Chem. Abstr.*, **61**, 1861 (1964).

(140) E. Lellman and W. Geller, *Chem. Ber.*, **21**, 1921 (1888).

(141) M. I. Boeseken, *Recl. Trav. Chim. Pays-Bas*, **24**, 6 (1905).

(142) F. Raschig, *Z. Angew. Chem.*, **20**, 2065 (1907).

(143) L. A. Paquette, *J. Amer. Chem. Soc.*, **85**, 3288 (1963).

(144) L. A. Paquette and W. C. Farley, *ibid.*, **89**, 3595 (1967).

(145) V. J. Grenda, R. E. Jones, G. Gal, and M. Sletzinger, *J. Org. Chem.*, **30**, 259 (1965).

(146) M. E. Brooks and B. Rudner, *J. Amer. Chem. Soc.*, **78**, 2339 (1956).

(147) G. M. Omietanski and H. H. Sisler, *ibid.*, **78**, 1211 (1956).

(148) H. Bock and K. Kompa, *Chem. Ber.*, **99**, 1357 (1966).

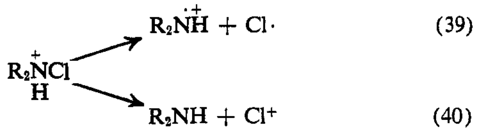
(149) H. Bock and K. Kompa, *ibid.*, **99**, 1361 (1966).

(150) H. Bock and K. Kompa, *ibid.*, **99**, 1347 (1966).

(151) H. Bock and K. Kompa, *Angew. Chem., Int. Ed. Engl.*, **4**, 783 (1965).

(152) J. K. Kochi, *J. Amer. Chem. Soc.*, **78**, 4815 (1956).

$$R_2NCl\overset{+}{H} \longrightarrow R_2N^+ + HCl \qquad (38)$$



$$R_2\overset{+}{\underset{H}{N}}Cl \longrightarrow R_2\overset{\cdot +}{NH} + Cl\cdot \qquad (39)$$

$$R_2\overset{+}{\underset{H}{N}}Cl \longrightarrow R_2NH + Cl^+ \qquad (40)$$

According to the second technique, photolysis of a mixture of N-chlorodialkylamine, cold sulfuric acid, and aromatic substrate gave nuclear amination products in essentially the same yield as for the thermal decomposition.[148] The identical orientation (toluene), *ortho*:*meta*:*para* = 9:53:38, from the two routes intimates that the same reaction pathway is involved. Neither formation of chlorine nor side-chain halogenation of toluene was noted. The same isomer distribution was obtained from the amination of toluene with N-chlorodimethylamine in a redox system; $R_2\dot{N}^+H$ was proposed as the attacking species (*cf.* eq 39).[153]

The third method of nuclear amination involves N-chlorodialkylamine, excess aluminum chloride, substrate, and nitroalkane solvent.[149] With benzene, the 90% yield of N,N-dimethylaniline surpasses that obtained by the thermal and photolytic processes. There is also a difference in the orientation for toluene, an increase in the *para* isomer at the expense of *meta*, *ortho*:*meta*:*para* = 14:27:59. A complex between the nitroalkane and aluminum chloride is invoked, but its mechanistic role is not specified. Nuclear chlorination was observed in certain cases for the three procedures.

Recently, aromatic aminations which likely proceed by way of radical intermediates have been disclosed. Results are reported for dialkylhalamines, hydroxylamines, and hydroxylamine-O-sulfonic acid in redox systems;[153] the orientation figures are set forth in Table VI.[153,154]

Table VI

Orientation in Amination with Redox Systems[a]

Substrate	*Aminating species*	*Amine product, % ortho*	*meta*	*para*
Toluene	NH_2OSO_3H	37	21.5	41.5
	NH_2OH	41.2	19.5	39.3
	$(CH_3)_2NCl$	9	53	38
Anisole	NH_2OSO_3H	34	...	66
	NH_2OH	52	...	48
	$C_5H_{10}NCl$	9.3	...	90.7
Chlorobenzene	NH_2OSO_3H	10	<8	>75
	NH_2OH	4.5	<8	>86
	$(CH_3)_2NCl$	17	<5	>68
Bromobenzene	NH_2OSO_3H	7	<8	>77
	NH_2OH	3.5	<8	>87
	$(CH_3)_2NCl$	19	3	67
Iodobenzene	NH_2OSO_3H	7.7	<8	>76
	$(CH_3)_2NCl$	5	8	80
		2,6	*2,4*	*3,5*
m-Xylene	NH_2OSO_3H	10.8	78.3	10.9
	NH_2OH	21.6	68.2	10.2
	$(CH_3)_2NCl$	0.5	28	71.5
		α	β	
Naphthalene	NH_2OSO_3H	76.8	23.2	
	NH_2OH	40.4	59.6	
	$(CH_3)_2HCl$	97	3	

[a] Yields: NH_2OSO_3H (10–40%), NH_2OH (5–15%), and $(CH_3)_2NCl\cdot H_2SO_4$ (60–80%).

The working hypothesis in the case of N-chlorodialkylamines–sulfuric acid is illustrated for generation of the radicals (eq 41)[153] involved in subsequent substitution (*cf.* eq 42).

$$R_2\overset{+}{N}HCl + Fe^{2+} \longrightarrow R_2\overset{+}{N}H\cdots Cl\cdots Fe^{2+} \longrightarrow R_2\underset{\cdot}{\overset{+}{N}}H + FeCl^{2+} \qquad (41)$$

Factors affecting the orientation, as well as the extent of side-chain attack, in amination of alkylbenzenes include the size of the side-chain, solvent, and inductive effects.[155] In addition, positional selectivity was influenced by reaction temperature and the nature of the catalyst.[156] Relative rates were determined for the three aminating species[153,154] (Table VII). A scrutiny of the entire data indicates varying degrees of electrophilic character associated with the attacking radicals. Differences between H_2NOH and H_2NOSO_3H are ascribed to involvement of $NH_3\cdot^+$ in the latter case.

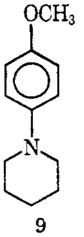
Table VII

Relative Reaction Rates for Amination in Redox Systems

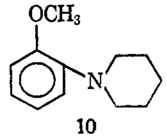
$k_x/k_{C_6H_6}$

x	*NH_2OSO_3H*	*NH_2OH*	*$(CH_3)_2NCl$*
m-Xylene	...	...	5.5
Toluene	3.1	2.4	4.6
Chlorobenzene	0.13	0.19	0.10
Bromobenzene	0.12	0.18	0.10
Iodobenzene	0.09	...	...

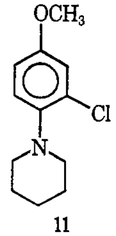
High selectivity can be achieved in homolytic nuclear dialkylamination with certain aromatic components.[157] Anisole was converted to the indicated products (11% yield), **9**:**10**:**11** = 90.5:4.5:5, in methanol. With neat ansiole and ferrous lactate, there was alteration in both the yield (19.5%) and orientation, **9**:**10**:**11** = 37.6:4.4:58. Use of 1,3-dimethoxybenzene afforded 26% of basic products. A radical-ionic sequence, initiated by a charge transfer phenomenon, was invoked to rationalize the anisole data (*cf.* eq 41 and 42).



9



10



11

Chlorination (see section VI.C) occurs as a competing pathway and, in fact, prevails with certain substrates[157] (Table VIII). The kinetic aspects of amination *vs.* chlorination[158] have been measured for a number of dialkylchloramines. With increasing bulk of the alkyl groups, amination decreases and benzylic chlorination increases. The low amount

---

(153) F. Minisci, R. Galli, and M. Cecere, *Tetrahedron Lett.*, 4663 (1965).

(154) F. Minisci, R. Bernardi, L. Grippa, and V. Trabucchi, *Chim. Ind. (Milan)*, **48**, 264 (1966); *Chem. Abstr.*, **64**, 19360 (1966).

(155) F. Minisci, R. Galli, A. Galli, and R. Bernardi, *Chim. Ind. (Milan)*, **49**, 252 (1967); *Chem. Abstr.*, **67**, 43119 (1967).

(156) F. Minisci, R. Galli, R. Bernardi, and A. Galli, *Chim. Ind. (Milan)*, **49**, 368 (1967); *Chem. Abstr.*, **68**, 95410 (1968).

(157) F. Minisci and R. Galli, *Tetrahedron Lett.*, 433 (1965).

(158) F. Minisci, R. Galli, and R. Bernardi, *ibid.*, 699 (1966).

Table VIII

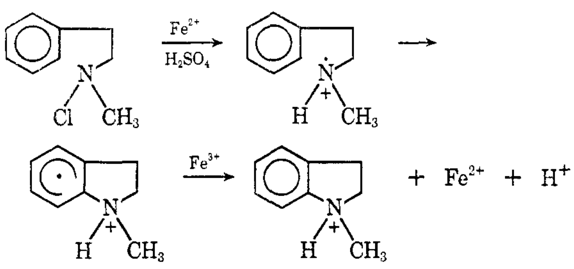
Competition between Chlorination and Amination of Toluene

N-Haloamine/redox salt	*Benzyl chloride* (%)	*Toluidines* (%)
N-Chlorodimethylamine/Fe^{2+}	23	52
N-Chlorodimethylamine/Ti^{2+}	13	65
N-Chloropiperidine/Fe^{2+}	20	41
N-Chlorodiethylamine/Fe^{2+}	35	7
N-Chlorodi-*n*-butylamine/Fe^{2+}	12	..
N-Chlorodiisobutylamine/Fe^{2+}	61	..

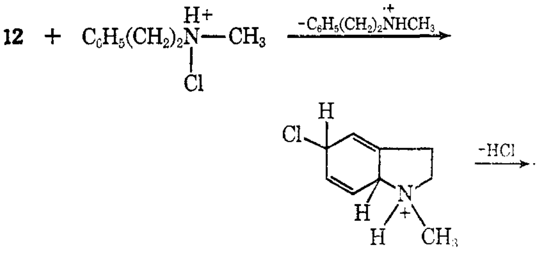
of benzyl chloride formed with N-chlorodi-*n*-butylamine reflects preference for the intramolecular route (Hofmann–Löffler reaction).

1-Substituted naphthalenes gave aminated products on exposure to N-chlorodimethylamine in the metal ion–acid system. The 1,5 and 1,8 isomers were formed with electron-withdrawing substituents (Cl, Br, NO_2) whereas the 1,4 isomer was favored with 1-methylnaphthalene.[159] Similarly, biphenyl provided N,N,N′,N′-tetramethyl-4,4′-diaminobiphenyl together with some N,N-dimethyl-4-aminobiphenyl; fluorene afforded N,N-dimethyl-2-aminofluorene and N,N,N′,N′-tetramethyl-2,7-diaminofluorene.[160]

Homolytic aromatic amination has been applied to the synthesis of indolines (27%) *via* intramolecular attack. Two possible mechanisms were offered (eq 42 or 43).[161] The first



12 13 (42)



$$12 + C_6H_5(CH_2)_2\overset{H+}{\underset{Cl}{N}}—CH_3 \xrightarrow{-C_6H_5(CH_2)_2\dot{N}HCH_3}$$

13 (43)

step in the formation of N-methylindoline is apparently the intramolecular addition of the aminium radical leading to a σ-complex radical which subsequently can (1) be oxidized by ferric salt or (2) add chlorine in a radical-chain sequence followed by rearomatization with elimination of hydrogen chloride. Benzyl chloride, a product of β scission, is also generated in a competing process (eq 44 and 45). Formation of a benzyl radical should favor the cleavage reaction. When no β scission occurs, as with N-methyl-3-phenylpropyl-N-chloramine, the cyclized product, N-methyltetrahydroquinoline, is obtained in 81% yield. This type of degradation is analogous to the photochemical fragmentation of certain N-chloramines (see Rearrangement section).

$$C_6H_5CH_2CH_2\dot{N}^+HCH_3 \longrightarrow C_6H_5CH_2\cdot + CH_2{=}N^+HCH_3 \quad (44)$$

$$C_6H_5CH_2\cdot + C_6H_5CH_2CH_2N^+HClCH_3 \longrightarrow C_6H_5CH_2Cl + C_6H_5CH_2CH_2\dot{N}^+HCH_3 \quad (45)$$

Aromatic amination can also be effected with various N-chloroalkylamines and N,N-dichloroalkylamines. However, the yields (7–45%) were lower than the optimum values obtained from N-chlorodialkylamines.[162]

From the reaction of nitrogen trichloride with benzene and toluene, mainly chlorinated aromatic hydrocarbons, along with small amounts of chloroanilines, were found.[163] Later, the system consisting of aromatic substrate–nitrogen trichloride–aluminum chloride was selected for investigation.[13,164] With toluene, almost exclusive formation of *m*-toluidine occurred in 42% yield. Studies of other alkylated benzenes revealed the same orientation[165] (Table IX). The unusual selectivity with alkylbenzenes and *m*-dialkylbenzenes makes for synthetic usefulness in the case of certain members.[165,166] A competing reaction, affording products from side-chain amination, occurs with dialkylbenzenes containing a tertiary benzylic hydrogen.[86,87]

Table IX

Amination of Alkylbenzenes with Nitrogen Trichloride–Aluminum Chloride

Substituted benzene	*Aniline product*	*Yield, %*[a]
Parent	Parent	20
Methyl	*m*-Methyl	36
Ethyl	*m*-Ethyl	31
n-Propyl	*m*-*n*-Propyl	28
Isopropyl	*m*-Isopropyl	23[b]
n-Butyl	*m*-*n*-Butyl	18
sec-Butyl	*m*-*sec*-Butyl	29
t-Butyl	*m*-*t*-Butyl	8
1,2-Dimethyl	2,3-Dimethyl	16
	3,4-Dimethyl	12
1,3-Dimethyl	3,5-Dimethyl	24[c]
1,4-Dimethyl	2,5-Dimethyl	22
1,2,4-Trimethyl	2,3,5-Trimethyl	13

[a] Yield based on nitrogen trichloride. [b] Reference 88. [c] Reference 166.

In an investigation of the mechanistic pathway of this novel type of substitution, the relative rates of amination by nitrogen trichloride–aluminum bromide were ascertained for benzene, monoalkylbenzenes, and the xylenes.[167] With

---

(159) F. Minisci, V. Trabucchi, R. Galli, and R. Bernardi, *Chim. Ind.* (*Milan*), **48**, 845 (1966); *Chem. Abstr.*, **65**, 15289 (1966).

(160) F. Minisci, V. Trabucchi, and R. Galli, *ibid.*, **48**, 716 (1966); *Chem. Abstr.*, **66**, 10785 (1967).

(161) F. Minisci and R. Galli, *Tetrahedron Lett.*, 2531 (1966).

(162) F. Minisci, R. Galli, and M. Cecere, *Chim. Ind.* (*Milan*), **48**, 725 (1966); *Chem. Abstr.*, **66**, 10669 (1967).

(163) G. H. Coleman and W. A. Noyes, *J. Amer. Chem. Soc.*, **43**, 2211 (1921).

(164) P. Kovacic, R. M. Lange, J. L. Foote, C. T. Goralski, J. J. Hiller, Jr., and J. A. Levisky, *ibid.*, **86**, 1650 (1964).

(165) P. Kovacic, J. A. Levisky, and C. T. Goralski, *ibid.*, **88**, 100 (1966).

(166) P. Kovacic, K. W. Field, P. D. Roskos, and F. V. Scalzi, *J. Org. Chem.*, **32**, 585 (1967).

(167) P. Kovacic and J. A. Levisky, *J. Amer. Chem. Soc.*, **88**, 1000 (1966).

toluene as reference, the reactivity order determined in *o*-dichlorobenzene or ethylene dichloride is listed in Table X.

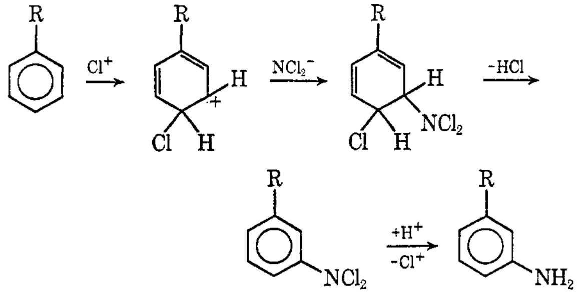
Table X

Relative Rates of Aromatic Amination with Nitrogen Trichloride–Aluminum Bromide

ArH	$k_{ArH}/k_{C_6H_5CH_3}$
Benzene	0.005
Ethylbenzene	0.8
Isopropylbenzene	0.6
o-Xylene	6
p-Xylene	8
m-Xylene	48

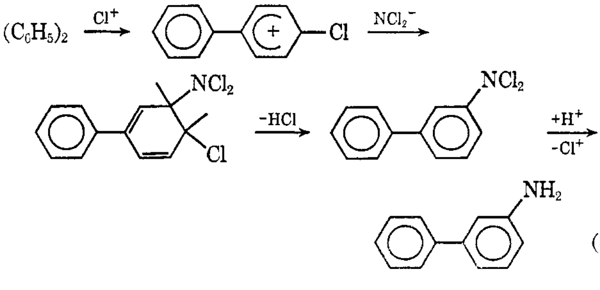
Logarithmic plots of the relative rates of amination *vs.* basicity, bromination, and chlorination show linear relationships which suggest σ-complex formation as the rate-determining step. On the basis of the experimental findings, a mechanistic scheme entailing addition–elimination (σ substitution) was proposed (eq 46 and 47). Electrophilic attack by Cl$^{\delta+}$ generates a chlorarenonium ion which then undergoes attack by the nitrogenous nucleophile, presumably dichloramide ion. Elimination of hydrogen chloride followed by exchange of H for Cl constitute the final steps. No simple addition products were obtained apparently owing to facile rearomatization accompanied by loss of hydrogen chloride.

$$Cl_3N + AlCl_3 \rightleftharpoons Cl_3N\cdots AlCl_3 \rightleftharpoons Cl^{\delta+}(Cl_2NAlCl_3)^{\delta-} \quad (46)$$

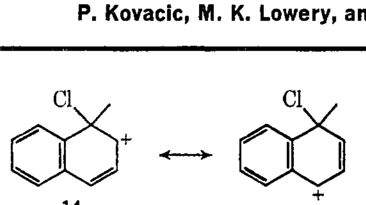


(47)

Further evidence for a σ-substitution mechanism was provided by the amination of biphenyl and naphthalene.[168] In the biphenyl reaction, 3-aminobiphenyl was obtained almost exclusively (eq 48). Naphthalene produced both α- and β-naphthylamines which can be accommodated mechanistically as illustrated by **14** and **15**. Subsequent attack by the nucleophile at either the α or β position would lead to the observed products. Analysis of the neutral fraction showed only α-chloronaphthalene to be present.

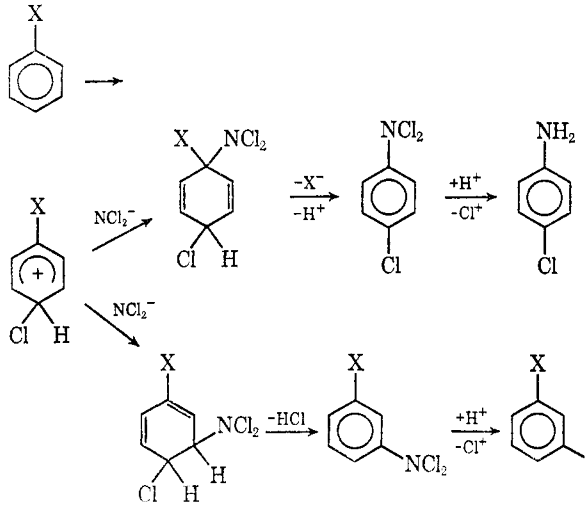


(48)



14 **15**

When a haloaromatic or anisole was used as substrate, nucleophilic σ substitution (eq 49) competed with the σ-substitution process[169,170] (eq 50). With fluorobenzene, the amination products were *m*-fluoroaniline and *o*- and *p*-chloroanilines. The ratio of nucleophilic σ substitution to σ substitution varied depending on the nature of the substrate, being highest with fluorobenzene and *m*-fluorotoluene and lowest with *o*-chlorotoluene. Formation of *o*- and *p*-chloroanilines from halobenzenes and anisole is further evidence for generation of σ complex *via* attack by Cl$^{\delta+}$.



(49)

(50)

The reaction of toluene–aluminum chloride with N-haloalkylamines and N,N-dihaloalkylamines was not as successful as with nitrogen trichloride.[17] Yields of aromatic amines were much lower and the extremely high degree of *meta* orientation was not observed in all cases. Three rationalizations are offered for the low yields: (1) destruction of N-haloalkylamine *via* intramolecular elimination of hydrogen halide or by homolytic decomposition, (2) adverse steric effect of the alkyl group, and (3) increased coordination of aluminum chloride on nitrogen. The decrease in *meta* orientation was attributed to electrophilic amination or free radical reactions competing with σ substitution.

Comparison and critical scrutiny of the work from the three laboratories are in order. The high *meta* content in the amination of toluene with N-chlorodialkylamines found by Minisci and Galli and Bock and Kompa is to be compared to the almost exclusive *meta* orientation found by Kovacic and coworkers. Perhaps rearrangement occurs in the sulfuric acid system, but not with aluminum chloride because of the moderating influence of the nitroalkane (Bock and Kompa). Minicsi and Galli attribute the high percentage

---

(168) P. Kovacic and A. K. Harrison, *J. Org. Chem.*, **32**, 207 (1967).

(169) P. Kovacic, J. J. Hiller, Jr., J. F. Gormish, and J. A. Levisky, *Chem. Commun.*, 580 (1965).

(170) P. Kovacic and J. F. Gormish, *J. Amer. Chem. Soc.*, **88**, 3819 (1966).

of *meta* product to a steric factor of the attacking ion radical, $R_2\dot{N}^+H$. The Minisci group point out that the same orientation for toluene is obtained in the redox system as in the thermal and photochemical aminations catalyzed by sulfuric acid, and hence conclude that the same radical processes are involved. Perhaps there is a competition between electrophilic, radical, and σ-substitution pathways in some instances.[17] Marked differences have been noted for the aromatic substrate–R_2NCl system in sulfuric acid–acetic acid depending on the nature of the promoter (irradiation or redox metal salt).[171] It is clear that, although considerable progress has been made in a relatively short time, the theoretical portion of aromatic amination contains many unanswered questions.

7. Aldehydes and Ketones

The reaction of formaldehyde with chloramine has been investigated (eq 51).[172] Although analysis of the product

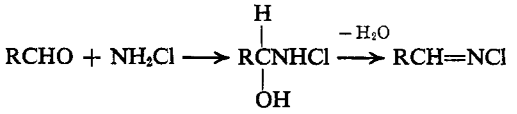
$$n\mathrm{CH_2O} + n\mathrm{NH_2Cl} \longrightarrow (\mathrm{CH_2{=}NCl})_n + n\mathrm{H_2O} \qquad (51)$$

for nitrogen and chlorine suggested the formula CH_2NCl, the molecular weight value, about which there was some question concerning reliability, pointed to a dimer. A compound, $(CH_2NCl)_3$, is formed from formaldehyde, ammonia, and hypochlorous acid[173] or, alternatively, on treatment of hexamethylenetetramine with hypochlorite in the presence of acetic acid.[174] A reinvestigation substantiated the earlier results concerning the trimeric nature.[175] The rate of formation of methylenechloramine and the subsequent trimerization were followed cryoscopically (eq 52 and 53). The formation

$$3\mathrm{NH_2Cl} + 3\mathrm{CH_2O} \longrightarrow 3\mathrm{CH_2{=}NCl} + 3\mathrm{H_2O} \qquad (52)$$

$$3\mathrm{CH_2{=}NCl} \longrightarrow (\mathrm{CH_2NCl})_3 \qquad (53)$$

of ald-chlorimines is merely an example of a Schiff base reaction (eq 54).


$$\mathrm{RCHO} + \mathrm{NH_2Cl} \longrightarrow \mathrm{R}\overset{\mathrm{H}}{\underset{\mathrm{OH}}{\mathrm{C}}}\mathrm{NHCl} \xrightarrow{-\mathrm{H_2O}} \mathrm{RCH{=}NCl} \qquad (54)$$

Studies of the properties of ald-chlorimines formed from chloramine and an aldehyde have been carried out;[176,177] *e.g.*, primary amines are generated by reduction[178] (eq 55).

$$\mathrm{RCH{=}O} + \mathrm{NH_2Cl} \xrightarrow{-\mathrm{H_2O}} \mathrm{RCH{=}NCl} \xrightarrow{[\mathrm{H}]} \mathrm{RCH_2NH_2{\cdot}HCl} \qquad (55)$$

Keto-chlorimines are prepared by the action of chlorine or alkyl hypochlorites on compounds of the type $RR'C{=}NMgX$, obtained from nitriles and Grignard reagents[179] (eq 56).

$$\mathrm{RR'C{=}NMgX} \xrightarrow[\mathrm{R''OCl}]{\mathrm{Cl_2\ or}} \mathrm{RR'C{=}NCl} \qquad (56)$$

8. Nitrogenous Substrates

Most of the material in this category is concerned with synthesis of hydrazines which will be treated first, followed by a discussion of diazoalkane formation from oximes, and finally treatment of several miscellaneous categories.

The reaction of chloramine with ammonia and amines to form hydrazines has received much attention in the literature. The reviews of chloramine provide extensive coverages of the reactions which are briefly summarized in Table XI.

Table XI

Reactions of Chloramine with Amines[6]

$NH_2Cl + 2NH_3 \longrightarrow NH_2NH_2 + NH_4Cl$
$NH_2Cl + 2RNH_2 \longrightarrow RNHNH_2 + RNH_3Cl$
$NH_2Cl + 2R_2NH \longrightarrow R_2NNH_2 + R_2NH_2Cl$
$NH_2Cl + R_3N \longrightarrow R_3NNH_2^+Cl^-$
$NH_2Cl + 2NH_3(aq) \longrightarrow N_2H_4 + 2NH_4Cl$
$NH_2Cl + NH_3(aq) + OH^- \longrightarrow N_2H_4 + Cl^- + H_2O$
$NH_2Cl + RNH_2(aq) + OH^- \longrightarrow RNHNH_2 + Cl^- + H_2O$
$NH_2Cl + R_2NH(aq) + OH^- \longrightarrow R_2NNH_2 + Cl^- + H_2O$

Hydrazine can also be formed from bromamine and potassium amide in liquid ammonia.[180]

From a conductometric study of the kinetics of hydrazine formation from chloramine–ammonia in liquid ammonia, the reaction was found to be pseudo first order.[181] In aqueous solutions, the system is first order in both chloramine and ammonia from pH 10 to 14, and follows a base-independent path.[182] At high alkalinities the base-catalyzed reaction is proportional to the rise in acidity function H_-. There are two mechanisms involved in the hydrazine synthesis, a base-catalyzed and a base-independent path; nucleophilic attack of ammonia on chloramine is used to explain the latter route (eq 57). Substitution of alkyl groups for hydrogen

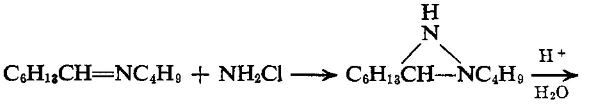
$$\mathrm{NH_3} + \mathrm{NH_2Cl} \longrightarrow \mathrm{N_2H_4} + \mathrm{HCl} \qquad (57)$$

in ammonia increases the rate constant, as would be expected for an SN2 type reaction, thus giving rise to alkylhydrazines in a similar manner. Tertiary amines and chloramine also follow second-order kinetics in organic solvents.[183] The base-catalyzed scheme is envisaged as a rapid preequilibrium formation of chloramide ion which is subsequently attacked by ammonia (eq 58 and 59).

$$\mathrm{OH^-} + \mathrm{NH_2Cl} \longrightarrow \mathrm{NHCl^-} + \mathrm{H_2O} \qquad (58)$$

$$\mathrm{NH_3} + \mathrm{NHCl^-} \longrightarrow \mathrm{N_2H_4} + \mathrm{Cl^-} \qquad (59)$$

Schiff bases undergo reaction with chloramine in ether to give diaziridines which are cleaved by dilute acid to an aldehyde and alkylhydrazine (eq 60). Diaziridines are also


$$\mathrm{C_6H_{13}CH{=}NC_4H_9} + \mathrm{NH_2Cl} \longrightarrow \mathrm{C_6H_{13}CH{-}NC_4H_9}\ (\mathrm{N{-}H\ bridge}) \xrightarrow[\mathrm{H_2O}]{\mathrm{H^+}} \mathrm{C_6H_{13}CHO} + \mathrm{C_4H_9NHNH_2} \qquad (60)$$

---

(171) R. S. Neale and E. Gross, *J. Amer. Chem. Soc.*, **89**, 6579 (1967).
(172) C. F. Cross, E. J. Bevan, and W. Bacon, *J. Chem. Soc.*, 2404 (1910).
(173) M. Delepine, *C. R. Acad. Sci.*, **128**, 105 (1899).
(174) M. Delepine, *Bull. Soc. Chim. Fr.*, **9**, 1025 (1911).
(175) M. Lindsay and F. G. Soper, *J. Chem. Soc.*, 791 (1946).
(176) C. R. Hauser and M. L. Hauser, *J. Amer. Chem. Soc.*, **52**, 2050 (1930).
(177) C. R. Hauser, M. L. Hauser, and A. G. Gillaspie, *ibid.*, **52**, 4158 (1930).
(178) C. R. Hauser, *ibid.*, **52**, 1108 (1930).
(179) C. R. Hauser, H. A. Humble, and G. J. Haus, *ibid.*, **54**, 2476 (1932).
(180) J. Jander and E. Kurzbach, *Angew. Chem.*, **72**, 919 (1960).
(181) F. N. Collier Jr., H. H. Sisler, J. G. Calvert, and F. R. Hurley, *J. Amer. Chem. Soc.*, **81**, 6177 (1959).
(182) G. Yagil and M. Anbar, *ibid.*, **84**, 1797 (1962).
(183) G. L. Braude and J. A. Cogliano, *J. Chem. Soc.*, 4172 (1961).

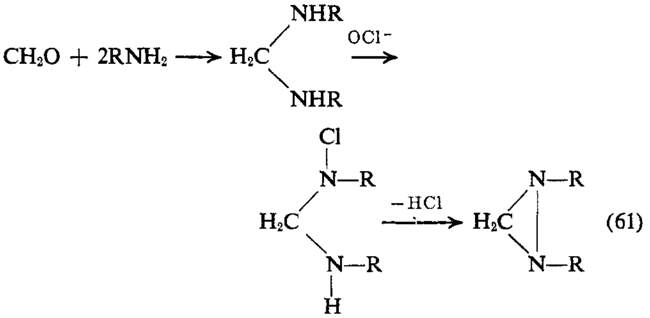
formed from the interaction of hypochlorite with alkylamines and formaldehyde in 2 *N* sodium hydroxide solution (Table XII) (eq 61;[184] *cf.* eq 57).

Table XII

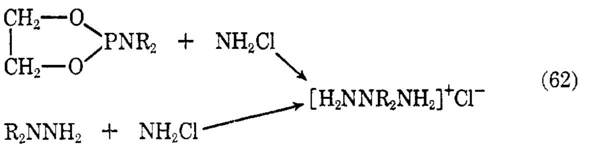
Diaziridines from Formaldehyde, Alkylamines, and Hypochlorite

Alkylamine	*Yield, %*	*Alkylamine*	*Yield, %*
Methylamine	48	Butylamine	72
Ethylamine	31	Isobutylamine	45
Propylamine	53	Benzylamine	27
Isopropylamine	28	1,3-Diaminobutane[a]	93

[a] Product, 2-methyl-1,5-diazabicyclo[3.1.0]hexane.

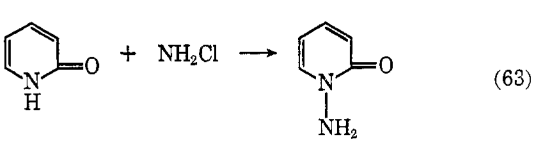


Triazanium salts are generated from a gaseous mixture of ammonia and chloramine with either 2-dialkylamino-1,3,2-dioxophospholane or 1,1-dialkylhydrazine[185] (eq 62). Further investigation revealed that 1,1-dimethylhydrazine

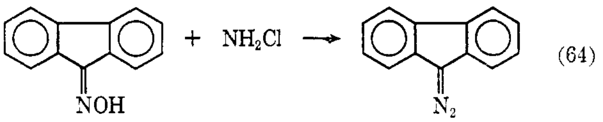


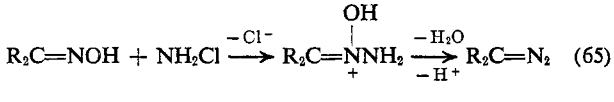
gave 2,2-dimethyltriazanium chloride[186,187] and tetramethyl-2-tetrazene, $(CH_3)_2NN{=}NN(CH_3)_2$,[187] when treated with chloramine. Chloramination of $(CH_3)_2NNHCH_3$ and $(CH_3)_2NN{=}CH_2$ yields $[(CH_3)_2N(NH_2)_2]^+Cl^-$, based on preliminary results.[185]

Chloramine reacts with α-pyridone in the presence of base to form a hydrazine derivative in 28% yield (eq 63).[188]



Although one reported try to prepare diazofluorene by the Forster reaction[189] failed,[190] a later attempt met with success[191] (eq 64). The corresponding diazo compounds were also prepared from the oximes of acetophenone, benzophenone, and benzaldehyde. Hydroxylamine-O-sulfonic acid, used in place of chloramine, also proved to be effective. Application to the purely aliphatic series is illustrated by conversion of a mixture of formaldehyde oxime and chloramine to diazomethane in about 75% yield.[192] Mechanistically, a sequence of steps initiated by nucleophilic displacement at the chloramine nitrogen was considered to be most likely[191] (eq 65.)





$$R_2C{=}NOH + NH_2Cl \xrightarrow{-Cl^-} R_2C{=}\overset{OH}{\underset{+}{N}}NH_2 \xrightarrow[-H^+]{-H_2O} R_2C{=}N_2 \qquad (65)$$

The first dialkylamine azide was generated by treatment of N-chloramines with metal azide in methylene chloride solvent at room temperature (eq 66).[193] By this procedure dimethylamine azide was obtained in 25% yield.

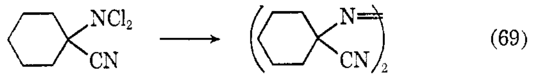
$$R_2NCl + MN_3 \longrightarrow R_2NN_3 + MCl \qquad (66)$$

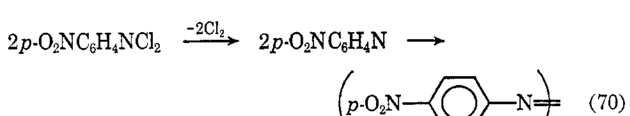
The alkaline decomposition of chloramine, which affords hydroxylamine as an intermediate,[194-196] apparently occurs through an SN2 mechanism in the initial step (eq 67). Hydroxylamine further reacts with chloramine to form diimide, a hydrogenating agent[196,197] (eq 68).

$$NH_2Cl + OH^- \longrightarrow NH_2OH \qquad (67)$$

$$NH_2OH + NH_2Cl \longrightarrow HN{=}NH \qquad (68)$$

Symmetrical azo compounds with the general formula NCRR′CN=NCR′RCN, in which R and R′ are low molecular weight alkyl groups or RR′ is a cycloalkyl group, have been prepared by coupling 2 mol of N,N-dichloramine (eq 69).[198] The yields are approximately 85%. The experimental procedure consists of stirring a methanol solution of the halamine with 50% sodium hydroxide for 0.5 hr at −10 to 10°. In order to rationalize the formation of 4,4′-dinitroazobenzene from thermal decomposition of N,N-dichloro-*p*-nitroaniline, a nitrene intermediate was suggested[199] (eq 70).





---

(184) R. Ohme, E. Schmitz, and P. Dolge, *Chem. Ber.*, **99**, 2104 (1966).

(185) K. Utvary and H. H. Sisler, *Inorg. Chem.*, **5**, 1835 (1966).

(186) K. Utvary and H. H. Sisler, *ibid.*, **7**, 698 (1968).

(187) H. H. Sisler, R. M. Kren, and K. Utvary, *ibid.*, **8**, 2007 (1969).

(188) K. Hoegerle and H. Erlenmeyer, *Helv. Chim. Acta*, **39**, 1203 (1956).

(189) M. O. Forster, *J. Chem. Soc.*, **107**, 260 (1915).

(190) L. A. Carpino, C. A. Giza, and B. A. Carpino, *J. Amer. Chem. Soc.*, **81**, 955 (1959).

(191) J. Meinwald, P. G. Gassman, and E. G. Miller, *ibid.*, **81**, 4751 (1959).

(192) W. Rundel, *Angew. Chem., Int. Ed. Engl.*, **1**, 403 (1962).

(193) H. Bock and K. L. Kompa, *Z. Anorg. Allg. Chem.*, **332**, 238 (1964).

(194) M. Anbar and G. Yagil, *J. Amer. Chem. Soc.*, **84**, 1790 (1962).

(195) R. E. McCoy, *ibid.*, **76**, 1447 (1954).

(196) W. J. LeNoble, *Tetrahedron Lett.*, 727 (1966).

(197) E. Schmitz, R. Ohme, and G. Kozakiewicz, *Z. Anorg. Allg. Chem.*, **339**, 44 (1965); *Chem. Abstr.*, **63**, 14362 (1965).

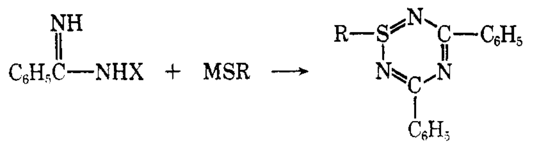
(198) J. J. Fuchs, U. S. Patent 3346554 (1967); *Chem. Abstr.*, **68**, 2593 (1968).

(199) S. Goldschmidt and L. Strohmenger, *Chem. Ber.*, **55**, 2450 (1922).

Other nitrogenous substrates are treated in sections VI. C and G.

9. *Sulfur Compounds*

The behavior of sulfur compounds toward N-halamines has received little attention. Of the reactions studied, the most common process appears to be nucleophilic substitution on halamine nitrogen by the sulfur compound. For example, sulfenamides are formed in high yield from the reaction of N-monochloro derivatives of primary amines with metal mercaptides.[200] A new ring compound, named sulfinetriazine, was prepared by treatment of N-bromo- or N-iodobenzamidine with a metal salt of a thiol[201] (eq 71). The mixed condensation proceeds in 40–50% yield.


(71)

More extensively investigated is the reaction of thioethers with N-chloramines. Early work[202] demonstrated that when dialkyl sulfides were treated with chloramine in ether solution, the dialkylsulfilimine hydrochloride precipitated (eq 72).

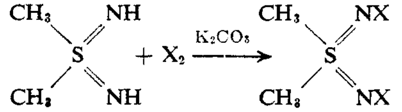
$$R_2S + NH_2X \longrightarrow [R_2SNH_2]^+X^- \qquad (72)$$

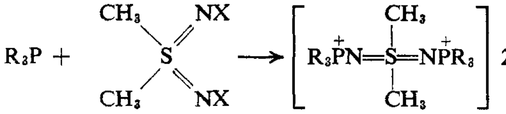
In alcoholic solvent, 2 mol of chloramine reacted with 1 mol of sulfide to form the hydrochloride of bis(iminodialkylsulfilimine)[203] (eq 73). The dialkylsulfilimine was shown to be an intermediate by independent synthesis and reaction with chloramine. The authors visualized the dimers as containing two betaine-type monomeric units held together either by electrostatic attraction or by resonance stabilization. A reinvestigation of the reaction of thioethers and chloramine in alcohols yielded the same substances, $[(R_2S^+NH\bar{N}H)_2]$-HCl.[204] Nitrogen trichloride reacts with diphenyl thioether to give a product, designated as bis(diphenyl sulfide)nitride trichloride, which loses chlorine upon recrystallization[205] (eq 74).

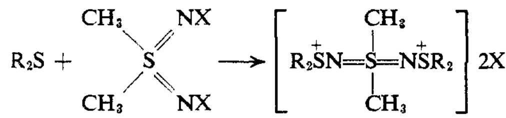
$$2R_2S + 4NH_2Cl \longrightarrow [(R_2\overset{+}{S}NH\overset{-}{N}H)_2]HCl + 3HCl \qquad (73)$$

$$(C_6H_5)_2S + NCl_3 \longrightarrow [(C_6H_5)_2SNS(C_6H_5)_2]^+Cl_3^- \qquad (74)$$

A new type of N-halo compound, N,N-dihalogeno-S,S-dimethylsulfur diimide, was prepared by halogenation of dimethylsulfur diimide in a buffered aqueous solution (eq 75).[206] These compounds underwent nucleophilic substitution with phosphines and sulfides (eq 76 and 77).


(75)


(76)


(77)

Various amino thiocyanates were generated by Bock and Kompa who treated N-chloramines with ammonium thiocyanate (eq 78).[193]

$$RNCl_2 + 2NH_4SCN \longrightarrow RN(SCN)_2 + 2NH_4Cl \qquad (78)$$

10. *Phosphorus Compounds*

Phosphorus compounds and N-halamines combine in a variety of ways. When an aryl phosphite is treated with N-chlorodialkylamine, an addition compound is generated[207] (eq 79),

$$(C_6H_5O)_3P + Et_2NCl \longrightarrow (C_6H_5O)_3P(NEt_2)Cl \qquad (79)$$

whereas an alkyl phosphite reacts further (eq 80).

$$(EtO)_3P + Et_2NCl \longrightarrow Et_2NPO(OEt)_2 \qquad (80)$$

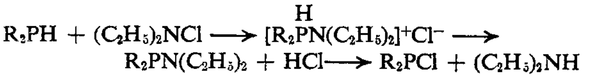
Trisubstituted phosphines and chloramine give quaternary aminophosphonium chlorides in high yield, which in some cases are hard to isolate because of facile hydrolysis[208] (eq 81 and 82). Trishydroxymethylphosphine with diethylchloramine forms the corresponding aminophosphonium chloride in 95% yield (eq 83), which loses a molecule of formaldehyde and of hydrogen chloride upon treatment with triethylamine[209] (eq 84). Phenylphosphine and diphenylphosphine failed to give the analogous addition products with diethylchloramine, which was attributed to decomposition of the initially formed adducts (eq 85). Phenylphosphine and diphenylphosphine produced tetraphenylphosphetane and tetraphenylbiphosphine, respectively, when treated with dimethylchloramine or chloramine (eq 86 and 87).[210]

$$R_3P + NH_2Cl \longrightarrow [R_3PNH_2]^+Cl^- \qquad (81)$$

$$[R_3PNH_2]Cl + H_2O \longrightarrow R_3PO + NH_4Cl \qquad (82)$$

$$P(CH_2OH)_3 + (C_2H_5)_2NCl \longrightarrow [(CH_2OH)_3PN(C_2H_5)_2]^+Cl^- \qquad (83)$$

$$[(CH_2OH)_3PN(C_2H_5)_2] \xrightarrow{(C_2H_5)_3N} (HOCH_2)_2PN(C_2H_5)_2 + CH_2O + (C_2H_5)_3N\cdot HCl \qquad (84)$$



$$R_2PH + (C_2H_5)_2NCl \longrightarrow [R_2\overset{H}{P}N(C_2H_5)_2]^+Cl^- \longrightarrow R_2PN(C_2H_5)_2 + HCl \longrightarrow R_2PCl + (C_2H_5)_2NH \qquad (8\ 5)$$

$$4C_6H_5PH_2 + 4R_2NCl \longrightarrow (C_6H_5P)_4 + 4R_2NH_2Cl \qquad (86)$$

$$2(C_6H_5)_2PH + R_2NCl \longrightarrow (C_6H_5)_2PP(C_6H_5)_2 + R_2NH_2Cl \qquad (87)$$

$$R = CH_3 \text{ or } H$$

Phosphine gave elemental phosphorus with dimethylchloramine (eq 88), and polymeric phosphorus hydride with chlor-

$$2PH_3 + 3(CH_3)_2NCl \longrightarrow 2P + 3(CH_3)_2NH_2Cl \qquad (88)$$

---

(200) G. Alliger, U. S. Patent 2495085 (1950); *Chem. Abstr.*, **45**, 177 (1951).

(201) J. Goerdeler and D. Loevenich, *Chem. Ber.*, **87**, 1079 (1954); *Chem. Abstr.*, **49**, 13259 (1955).

(202) R. Appel and W. Büchner, *Chem. Ber.*, **95**, 849 (1962); *Chem. Abstr.*, **57**, 5785 (1962).

(203) J. A. Cogliano and G. L. Braude, *J. Org. Chem.*, **29**, 1397 (1964).

(204) R. Appel, H. W. Fehlhaber, D. Haenssgen, and R. Schöellhorn, *Chem. Ber.*, **99**, 3108 (1966); *Chem. Abstr.*, **66**, 18491 (1967).

(205) R. Appel and G. Büchler, *Ann. Chem.*, **684**, 112 (1965); *Chem. Abstr.*, **63**, 8184 (1965).

(206) R. Appel and D. Hänssgen, *Angew. Chem., Int. Ed. Engl.*, **6**, 91 (1967).

(207) K. A. Petrov and G. A. Sokol'skii, *J. Gen. Chem. USSR*, **26**, 3378 (1956); *Chem. Abstr.*, **51**, 8029 (1957).

(208) H. H. Sisler, A. Sarkis, H. S. Ahuja, R. J. Drago, and N. L. Smith, *J. Amer. Chem. Soc.*, **81**, 2982 (1959).

(209) K. A. Petrov, V. A. Parshina, B. A. Orlov, and G. M. Tsypina, *J. Gen. Chem. USSR*, **32**, 3944 (1962).

(210) R. E. Highsmith and H. H. Sisler, *Inorg. Chem.*, **7**, 1740 (1968).

amine. With nitrogen trichloride and triphenylphosphine as precursors, bis(triphenylphosphine)nitride trichloride has been synthesized[211] (eq 89).

$$(C_6H_5)_3P + NCl_3 \longrightarrow [((C_6H_5)_3P)_2N]Cl_3 \qquad (89)$$

Diphenylchlorophosphine combines with a mixture of chloramine and ammonia to form compounds which on heating are converted to trimers and tetramers of the empirical formula $(C_6H_5)_2PN$.[212] The reaction of ammonia-free chloramine and diphenylchlorophosphine[213] proceeds as illustrated in eq 90. Pyrolysis of the product yielded the trimer

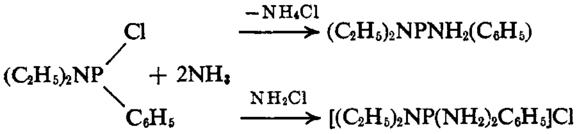
$$(C_6H_5)_2PCl + NH_2Cl \longrightarrow [(C_6H_5)_2P(Cl)NH_2]Cl \xrightarrow{-HCl} (C_6H_5)_2P(NH_2)(Cl)NHP(Cl)_2(C_6H_5)_2 \qquad (90)$$

and tetramer $[(C_6H_5)_2PN]_3$ and $[(C_6H_5)_3PN]_4$, respectively.

Although, theoretically, reaction between aminophosphines and chloramine presents the possibility of either a nitrogen–nitrogen or a phosphorus–nitrogen bond being formed,[214,215] amination always occurs at the phosphorus site (eq 91). A similar pathway was followed with $(R_2N)_2PC_6H_5$ or $(R_2N)_3P$. The yields of aminophosphonium chlorides ranged from 43 to 79%. Amination was shown to occur on phosphorus from an examination of the products obtained on basic hydrolysis of amino-*t*-butylaminodiphenylphosphonium chloride (eq 92). If amination had occurred on nitrogen, *t*-butylhydrazine would have been generated instead of *t*-butylamine. On the basis of the result from the mixed phosphine, $(C_2H_5)_2NP(Cl)(C_6H_5)$, and a mixture of chloramine and ammonia, eq 93 was proposed since P–Cl bonds are subject to rapid ammonolysis. Dimethylaminophosphines and dimethylchloramine behave analogously giving phosphonium salts.[216]

$$R_2NP(C_6H_5)_2 + NH_2Cl \longrightarrow [R_2NPNH_2(C_6H_5)_2]Cl \qquad (91)$$

$$\{(H_2N)[(t\text{-}C_4H_9)NH](C_6H_5)_2P\}^+ + H_2O + OH^- \longrightarrow (C_6H_5)_2P(O)OH + NH_3 + t\text{-}C_4H_9NH_2 \qquad (92)$$



$$(C_2H_5)_2NP(Cl)(C_6H_5) + 2NH_3 \xrightarrow{-NH_4Cl} (C_2H_5)_2NPNH_2(C_6H_5); \quad \xrightarrow{NH_2Cl} [(C_2H_5)_2NP(NH_2)_2C_6H_5]Cl \qquad (93)$$

Chloramine also aminates on the phosphorus of hydrazinophosphines[217] (eq 94). The amination of aminophosphines and hydrazinophosphines on phosphorus by chloramine demonstrates that electron density on phosphorus is enhanced with respect to the attached amino nitrogen, probably through pπ–dπ bonding. Furthermore, the other nitrogen of the hydrazino group is a less preferred site for reaction.

$$(C_6H_5)_2PN(CH_3)N(CH_3)_2 + NH_2Cl \longrightarrow [(C_6H_5)_2P(NH_2)N(CH_3)N(CH_3)_2]Cl \qquad (94)$$

Phosphines generally react with chloramine in the same manner as their nitrogen counterparts. Chloramine participates in such a way that the chlorine atom assumes the role of a negative species. The formation of hydrazines is postulated to take place in an analogous fashion.

11. Arsenic and Antimony Compounds

The chloramination of substituted arsines with chloramine[218,219] and dimethylchloramine[219,220] has been reported. Triphenyl- and diphenylarsine react with chloramine to give aminoarsonium chlorides[219] (eq 95), analogous to the behavior toward triphenylphosphines (*cf.* eq 81). The fission of some arsenic–phenyl bonds with the production of chlorobenzene in the chloramination of phenylarsine is observed under some conditions.[218]

$$(C_6H_5)_3As \xrightarrow{NH_2Cl} [(C_6H_5)_3AsNH_2]Cl \qquad (95)$$

The reaction of chloramine and dimethylchloramine with arsine, primary arsines, and secondary arsines gave elemental arsenic, diarsines, and tetrasubstituted cyclopolyarsines, respectively (Table XIII).[221] The halamine abstracts hydrogen from As–H bonds, indicating that the process differs from that postulated for trisubstituted phosphines and arsines. Several feasible mechanisms were presented.

Table XIII

Reaction of Chloramine and Dimethylchloramine with Arsines Containing As–H Bonds

Arsine	*N-Halamine*	*Products*	*Yield, %*
AsH_3	NH_2Cl	As	77
		NH_4Cl	77
AsH_3	$(CH_3)_2NCl$	As	66
		$(CH_3)_2NH_2Cl$	66
CH_3AsH_2	NH_2Cl	$(CH_3As)_5$	94
		NH_4Cl	100
CH_3AsH_2	$(CH_3)_2NCl$	$(CH_3As)_5$	85
		$(CH_3)_2NH_2Cl$	96
$(CH_3)_2AsH$	NH_2Cl	$(CH_3)_2AsAs(CH_3)_2$	96
		NH_4Cl	100
$(CH_3)_2AsH$	$(CH_3)_2NCl$	$(CH_3)_2AsAs(CH_3)_2$	45
		$(CH_3)_2NH_2Cl$	46

Various substituted stibines combine with chloramine (eq 96 and 97) to produce compounds of the type $[R_3Sb(Cl)]_2NH$[222] (Table XIV). The iminobis(trialkylchlorostibanes) are readily hydrolyzed to the corresponding anhydrides, $[R_3Sb(Cl)]_2O$, and ammonia.

$$R_3Sb + NH_2Cl \longrightarrow R_3Sb(NH_2)Cl \qquad (96)$$

$$2R_3Sb(NH_2)Cl \longrightarrow [R_3Sb(Cl)]_2NH + NH_3 \qquad (97)$$

12. Silicon, Germanium, and Tin Compounds

The reaction of chloramine and dimethylchloramine with tris(trimethylsilyl)phosphine (eq 98) and certain silyl-, germyl-,

---

(211) R. Appel and G. Büchler, *Z. Naturforsch.*, **17b**, 422 (1962); *Chem. Abstr.*, 57, 12530 (1962).

(212) H. H. Sisler, H. S. Ahuja, and N. L. Smith, *Inorg. Chem.*, **1**, 84 (1962).

(213) I. T. Gilson and H. H. Sisler, *ibid.*, **4**, 273 (1965).

(214) W. A. Hart and H. H. Sisler, *ibid.*, **3**, 617 (1964).

(215) D. F. Clemens and H. H. Sisler, *ibid.*, **4**, 1222 (1965).

(216) S. R. Jain, L. K. Krannich, R. E. Highsmith, and H. H. Sisler, *ibid.*, **6**, 1058 (1967).

(217) R. P. Nielsen, J. F. Vincent, and H. H. Sisler, *ibid.*, **2**, 760 (1963).

(218) H. H. Sisler and C. Stratton, *ibid.*, **5**, 2003 (1966).

(219) H. H. Sisler and S. R. Jain, *ibid.*, **7**, 104 (1968).

(220) H. J. Vetter and H. Nöth, *Z. Anorg. Allg. Chem.*, **330**, 233 (1964).

(221) L. K. Krannich and H. H. Sisler, *Inorg. Chem.*, **8**, 1032 (1969).

(222) R. L. McKenney and H. H. Sisler, *ibid.*, **6**, 1178 (1967).

Table XIV

Products from Chloramination of Substituted Stibines

Stibine	*Product*	*Yield, %*
$(CH_3)_3Sb$	$[(CH_3)_3Sb(Cl)]_2NH$	71
	$(CH_3)_3SbCl_2$	16
$(C_2H_5)_3Sb$	$[(C_2H_5)_3Sb(Cl)]_2NH$	87
$(n\text{-}C_3H_7)_3Sb$	$[(n\text{-}C_3H_7)_3Sb(Cl)]_2NH$	76.5
$(n\text{-}C_4H_9)_3Sb$	$[(n\text{-}C_4H_9)_3Sb(Cl)]_2NH$	51
$(C_6H_5)_3Sb$	$[(C_6H_5)_3Sb(Cl)]_2NH$	55-71
	$(C_6H_5)_3SbCl_2$	25-43

$$[(CH_3)_3Si]_3P + 3NH_2Cl \longrightarrow 3(CH_3)_3SiCl + (NH_2)_3P \quad (98)$$

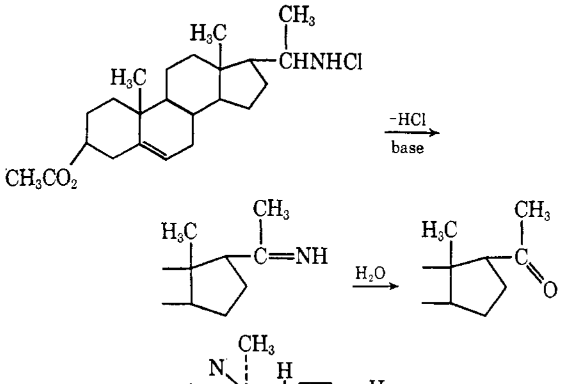
and stannylamines gave products derived from cleavage of the metal to nitrogen or phosphorus bond.[223] No stable addition compounds were formed as found with chloramine and phosphines (*cf.* eq 81). The products from combination with dimethyl(trialkylmetal)amines can be described by eq 99 and 100 (M = Si, Ge, or Sn). Other examples of halamines as aminating agents may be found in section VI.G.

$$3R_3MN(CH_3)_2 + 3NH_2Cl \longrightarrow 3R_3MCl + 3(CH_3)_2NH + NH_3 + N_2 \quad (99)$$

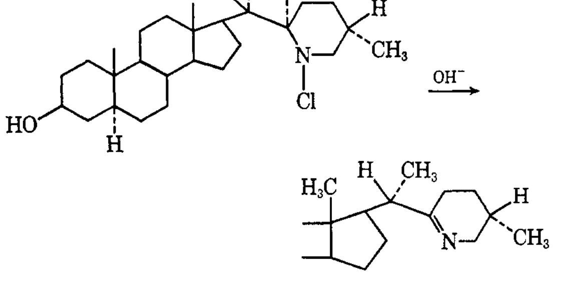
$$3(R_3M)_2NH + 6NH_2Cl \longrightarrow 6R_3MCl + 5NH_3 + 2N_2 \quad (100)$$
$$M \neq Si$$

B. DEHYDROHALOGENATION

N-Chloramines have been used to synthesize carbonyl compounds *via* dehydrohalogenation and hydrolysis.[46] This method was applied successfully in the conversion of the N-chloro derivative of 3β-acetoxy-20-amino-5-pregnene to 5-pregnenolone (eq 101).[224] The initially formed imino moiety[224a] was isolated in a similar transformation (eq 102).[225]



(101)



(102)

The reaction, which is rather broad in scope, usually affords carbonyl compounds in good yields[226] (Table XV). The procedure has been generalized to include both primary and secondary amines.[227]

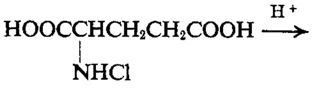
Table XV

Carbonyl Compounds from Amines

Amine	*Carbonyl compound*	*Yield, %*
9-Aminofluorene	Fluorenone	98
Benzylamine	Benzaldehyde	80
Cyclohexylamine	Cyclohexanone	73
3β-Acetoxy-20-amino-5-pregnene acetate	5-Pregnenolone	71
β-Phenylethylamine	Phenylacetaldehyde	39

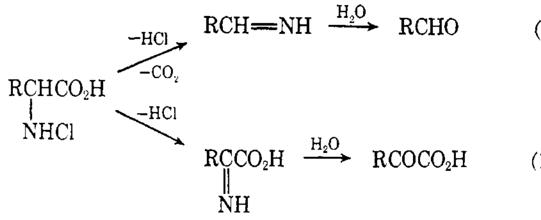
When α-amino acids combine with N-bromosuccinimide, an aldehyde containing one less carbon is obtained.[228] A possible pathway is shown in eq 103. Analogously, the decomposition of α-N-chloroaminoglutaric acid under acidic conditions to succinaldehydic acid and α-ketoglutaric acid was observed in the synthesis of indoleacetic acid from glutamic acid[229] (eq 104). Aldehyde formation comprised the principal route. The postulated mechanism is consistent with the original proposal of Langheld[230] concerning formation of aldehydes from α-amino acids (eq 105 and 106).

$$R'N{=}CRCO_2H \xrightarrow{H_2O} CO_2 + R'NH_2 + RCHO \quad (103)$$



$$\underset{\displaystyle NHCl}{HOOC\underset{|}{C}HCH_2CH_2COOH} \xrightarrow{H^+}$$

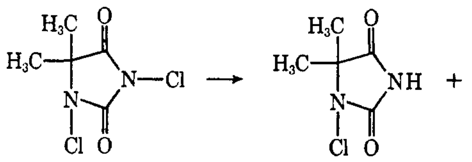
$$CHOCH_2CH_2COOH + HOOCCOCH_2CH_2COOH \quad (104)$$



$$RCHCO_2H\ (NHCl) \xrightarrow{-HCl,\ -CO_2} RCH{=}NH \xrightarrow{H_2O} RCHO \quad (105)$$

$$RCHCO_2H\ (NHCl) \xrightarrow{-HCl} R\underset{\displaystyle NH}{\underset{\|}{C}}CO_2H \xrightarrow{H_2O} RCOCO_2H \quad (106)$$

The decomposition of 1,3-dichloro-5,5-dimethylhydantoin in water at pH 9 gives 2-chloro-5,5-dimethylhydantoin, N-chloroisopropylamine, chloride ion, nitrogen, and carbon dioxide[231] (eq 107). Hydrolysis of N-chloroisopropylamine



$$(CH_3)_2CHNHCl + CO_2 + N_2 + Cl^- \quad (107)$$

---

(223) R. E. Highsmith and H. H. Sisler, *Inorg. Chem.*, **8**, 1029 (1969).

(224) H. Ruschig, *Med. Chem.*, **4**, 327 (1942).

(224a) G. F. Wright, *J. Amer. Chem. Soc.*, **70**, 1958 (1948).

(225) G. Adam and K. Schreiber, *Angew. Chem.*, **76**, 752 (1964).

(226) W. E. Bachmann, P. Cava, and A. S. Dreiding, *J. Amer. Chem. Soc.*, **76**, 5554 (1954).

(227) A. L. Comen, *Diss. Abstr.*, **25**, 828 (1964).

(228) A. Schönberg, R. Moubasher, and M. Z. Barakat, *J. Chem. Soc.*, 2504 (1951).

(229) S. W. Fox and M. W. Bullock, *J. Amer. Chem. Soc.*, **73**, 2754 (1951).

(230) K. Langheld, *Chem. Ber.*, **42**, 2360 (1909).

(231) R. C. Petterson and U. Grzeskowiak, *J. Org. Chem.*, **24**, 1414 (1959).

generates acetone and ammonia, probably through the intermediacy of isopropylimine (eq 108). Treatment of N,N-

$$(CH_3)_2CHNHCl \xrightarrow{-HCl} (CH_3)_2C{=}NH \xrightarrow{H_2O} (CH_3)_2CO + NH_3 \quad (108)$$

dichloroisopropylamine with aluminum chloride furnished acetone after hydrolysis[90] (eq 109). Analogously, N,N-di-

$$(CH_3)_2CHNCl_2 \xrightarrow[-HCl]{AlCl_3} (CH_3)_2C{=}NCl \xrightarrow{H_2O} (CH_3)_2CO + NH_2Cl \quad (109)$$

chloramines containing only one α hydrogen provided N-chloroimines on exposure to cesium fluoride, *e.g.*, N,N-dichlorocyclohexylamine afforded N-chlorocyclohexylimine in 90% yields,[232] or when subjected to potassium acetate, *e.g.*, N,N-dichlorocyclohexylamine gave N-chlorocyclohexylidenimine (48–69% yield).[47]

Nitriles are formed from ald-chlorimines of the type in eq 110 by thermal decomposition or exposure to base.[233,234]

$$RCH{=}NCl \xrightarrow{-HCl} RC{\equiv}N \quad (110)$$

Reaction of seven different ring-substituted benzalchlorimines with sodium ethoxide led to the corresponding nitriles in good yield (60–96%).[235] With ring-substituted benazlchlorimines, the ease of removal of hydrogen chloride by base follows the same relative order as the ionization constants of the corresponding acids and phenols.[235]

N,N-Dihaloamines of the type RCH_2NX_2 produce nitriles when subjected to caustic[236] (*cf.* eq 111). A novel method

$$RCH_2NCl_2 \xrightarrow[40^\circ]{CsF} RC{\equiv}N \quad (111)$$

for the preparation of nitriles involves treatment of the same type of precursor with cesium fluoride in acetonitrile (eq 111).[232] N,N-Dichloro-*n*-butylamine gave the nitrile in 90% yield.

C. HALOGENATING AGENT

N-Halamines are known to act as agents for the halogenation of aliphatic and aromatic compounds. Recently, alkanes, as well as esters, alkyl halides, and ethers, were found susceptible to facile chlorination[155,237–242] or bromination[155,238] (Table XVI) with $(CH_3)_2NX$ in the presence of sulfuric acid, usually with Fe^{2+} or light as the initiator. The proposed mechanism is essentially the same as for the Hofmann–Löffler reaction except that intermolecular hydrogen abstraction takes place (eq 112).[237] The observed selectivity

$$(CH_3)_2\overset{+}{N}HX \xrightarrow[-FeCl^{2+}]{+Fe^{2+}} (CH_3)_2\dot{N}^{+}H \xrightarrow[-(CH_3)_2\overset{+}{N}H_2]{+RH} R\cdot \xrightarrow[-(CH_3)_2\dot{N}^{+}H]{+(CH_3)_2\overset{+}{N}HX} RX \quad (112)$$

X = Cl or Br

(Table XVI) was attributed to the sensitivity of protonated amino radicals to the inductive effect of the ester residue and the differing reactivities of methylene and methyl hydrogens.

Table XVI

Isomer Distributions in Halogenation of Methyl Heptanoate[238]

Halogenating agent	*Isomer distribution, %* *CH_3O_2C*	— *CH_2*	— *CH_2*	— *CH_2*	— *CH_2*	— *CH_2*	— *CH_3*
$(CH_3)_2\overset{+}{N}HCl/Fe^{2+}$	..	..	..	1.2	14.7	80.4	3.7
$(CH_3)_2\overset{+}{N}HBr/Fe^{2+}$	..	..	..	1	13.4	82.2	3.5

A reinvestigation suggested that halogenation proceeded *via* the chlorine atom as the chain-propagating species (eq 113).[243] The hypothesis was based on the fact that the isomer

$$X\cdot + RH \longrightarrow HX + R\cdot$$
$$R_2\overset{+}{N}HX + HX \longrightarrow X_2 + R_2\overset{+}{N}H_2 \quad (113)$$
$$R\cdot + X_2 \longrightarrow RX + X\cdot$$

distributions from various metal-ion-initiated chlorinations of 1-chloropropane with different N-chloramines were similar. Also, the orientation was identical with that obtained from photochlorination, a process which must involve chlorine atoms in the chain propagation.

A recently published study lends support to the original mechanism.[244] From an extensive investigation of the N-halamine halogenation of 1-chlorobutane in sulfuric acid–acetic acid, chlorination was found to occur by a radical-chain process in which aminium radicals are the principal hydrogen abstracting species. Evidence was also presented which implicated impurities (molecular chlorine, hydrogen chloride, or chloride ion) in the N-halamine as promoters of a concurrent chlorine atom chain. This new evidence may account for the results observed by Tanner and Mosher.[243]

The kinetics have been investigated for radical chain chlorination of decanoic acid by N-chlorodimethylamine and N-chloropiperidine in sulfuric acid–acetic acid.[245] The rate of the reaction was found to be proportional to the decanoic acid concentration and to the square root of the rate of chain initiation, but independent of the N-halamine concentration. The rate-controlling step in propagation involves attack of an aminium radical on the acid, and termination consists of the combination of two nitrogen radicals. The absolute rate constants for propagation and termination, determined by the rotating sector method, were 7×10^2 to 1×10^4 and $5 \times 10^7\ M^{-1}\,sec^{-1}$, respectively.

The combined data from several studies indicate that aminium radicals function as the primary hydrogen-abstracting

---

(232) C. M. Sharts, *J. Org. Chem.*, **33**, 1008 (1968).

(233) C. R. Hauser and A. G. Gillaspie, *J. Amer. Chem. Soc.*, **52**, 4517 (1930).

(234) C. R. Hauser, A. G. Gillaspie, and J. W. LeMaistre, *ibid.*, **57**, 567 (1935).

(235) C. R. Hauser and E. Moore, *ibid.*, **55**, 4526 (1933).

(236) P. A. S. Smith, "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. I, W. A. Benjamin, Inc., New York, N. Y., 1965, p 194.

(237) F. Minisci, R. Galli, A. Galli, and R. Bernardi, *Tetrahedron Lett.*, 2207 (1967).

(238) F. Minisci, R. Galli, R. Bernardi, and M. Perchinunno, *Chem. Ind. (Milan)*, **51**, 280 (1969); *Chem. Abstr.*, **71**, 112362 (1969).

(239) F. Minisci, G. P. Gardini, and F. Bertini, *Can. J. Chem.*, **48**, 544 (1970).

(240) R. Bernardi, R. Galli, and F. Minisci, *J. Chem. Soc. B*, 324 (1968).

(241) F. Minisci, R. Galli, and R. Bernardi, *Chim. Ind. (Milan)*, **49**, 594 (1967); *Chem. Abstr.*, **68**, 28914 (1968).

(242) F. Minisci, R. Galli, M. Perchinunno, and R. Bernardi, *Chem. Ind. (Milan)* **50**, 453 (1968); *Chem. Abstr.*, **69**, 26646 (1968).

(243) D. D. Tanner and M. W. Mosher, *Can. J. Chem.*, **47**, 715 (1969).

(244) J. Spanswick and K. U. Ingold, *ibid.*, **48**, 546 (1970).

(245) J. Spanswick and K. U. Ingold, *ibid.*, **48**, 554 (1970).

species in the metal-ion-initiated N-halamine halogenation of alkyl residues in sulfuric acid–acetic acid.

Benzylic chlorination results when ring-substituted toluenes are exposed to N-chloropiperidine in sulfuric acid–acetic acid under photolytic conditions.[171] From a plot of the relative reactivities against σ^+ substituent constants, a ρ value of -1.36 was obtained (*cf.* $\rho = 0.66$ for chlorine atoms). Good evidence was presented to support the contention that hydrogen abstraction was effected by the aminium radical.

Another example in the general category of halogenation of alkane structures may be cited. Although allylic bromination is usually accomplished with N-bromosuccinimide,[246] the same over-all transformation can also be brought about by N-bromo-*t*-butylamine.[247]

The interaction of N-halamines and olefins has received considerable attention in relation to the synthesis of β-chloramines (see section VI.A.5a). Much less emphasis has been placed on the use of N-halamines as halogenating agents for olefins. Chloramine and cyclohexene produce low yields of *vic*-dichloride and other products under photolytic conditions.[111] Similarly, olefins combine with nitrogen trichloride to give β-chloramines in low yield and unspecified amounts of dichloride.[105–107] The interaction of cyclohexene with nitrogen trichloride is reported to give the dichloride (82%).[248] In a more recent investigation, nitrogen trichloride has been shown to provide a simple means for the preparation of *vic*-dichlorides in excellent yield from certain types of olefins (eq 114) (Table XVII).[249] Experimentally, the procedure

$$3RCH{=}CH_2 + 2NCl_3 \longrightarrow 3RCCHClCH_2Cl + N_2 \qquad (114)$$

involves the dropwise addition of the olefin in methylene chloride solvent to nitrogen trichloride solution at 0°. Nitrogen is generated almost quantitatively. From a synthetic standpoint, the procedure deserves mention because most of the alternate methods are limited owing to the occurrence of side reactions.[251,252] The scope of the procedure is under investigation.

Table XVII

vic-Dichloride Formation from Olefins and Acetylenes with Nitrogen Trichloride

Unsaturate	*Product*	*Yield, %[a]*
1-Hexene	1,2-Dichlorohexane	93–97
1-Octene	1,2-Dichlorooctane	93
Cyclopentene	*trans*-1,2-Dichlorocyclopentane	89
Cyclohexene	*trans*-1,2-Dichlorocyclohexane	91
1-Hexyne[b]	1,2-Dichloro-1-hexene	54

[a] Yield based on nitrogen trichloride. [b] Reference 250, carbon tetrachloride solvent.

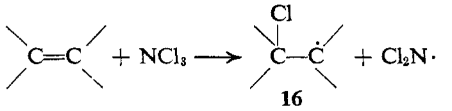
Mechanistically, the findings lead to the conclusion that a radical process pertains. Product distributions from *cis*- and *trans*-2-butene resembled literature data[253] for radical chlorination with chlorine gas, rather than polar halogenation (Table XVIII). The pathway apparently does not involve chlorine gas or free chlorine atoms since the by-products associated with the molecular chlorine procedure are largely absent. As described in eq 115 initiation may be of the molecule-induced type. The unstable tetrachlorohydrazine has been tentatively assigned the role of a key intermediate (eq 116). **16** could then abstract a chlorine atom from NCl_3,

$$2Cl_2N\cdot \longrightarrow Cl_2NNCl_2 \qquad (116)$$

Cl_2NNCl_2, or the Cl_2NNCl_3 complex (eq 117). Nitrogen

$$Cl_2N\cdot + NCl_3 \longrightarrow Cl_2N\cdots NCl_3 \qquad (117)$$

would be generated by complete loss of chlorine from the hydrazine derivative. Since these studies are only in the early stages, the designations should be regarded as quite hypothetical (NCl might also be involved).



16

(115)

Table XVIII

Halogenation of *cis*- and *trans*-2-Butene

2-Butene	*Chlorinating agent*	*1,2-Dichlorobutane isomers, %* meso	dl
cis	Cl_2 (polar)	0	100
	Cl_2 (radical)	33	67
	NCl_3	28	72
trans	Cl_2 (polar)	100	0
	Cl_2 (radical)	88	12
	NCl_3	86	14

Chlorinated alkanes were isolated from the interaction of cycloalkanes with nitrogen trichloride–aluminum chloride.[79,80] With this same reagent, the neutral products from *t*-butyl chloride contained highly chlorinated alkanes.[89,90] These processes may well take place with participation of alkene intermediates.

Acetylenes undergo chlorination with nitrogen trichloride to give *vic*-dichloroalkenes, predominantly.[250]

The interaction of N-chloramines and different types of aliphatic amines affords some interesting results.[254] The primary and secondary types merely participate in an exchange reaction (H and X), whereas tertiary amines give rise to an aldehyde and dialkylchloramine.[255] Tertiary amines also form aldehydic products on interaction with halogen, apparently *via* $(R_3NX)^+X^-$.[256,257]

In the aromatic category, when benzene or toluene was treated with nitrogen trichloride, nuclear chlorination oc-

---

(246) H. J. Dauben, Jr., and L. L. McCoy, *J. Amer. Chem. Soc.*, **81**, 4863 (1959).

(247) C. E. Boozer and J. W. Moncrief, *J. Org. Chem.*, **27**, 623 (1962).

(248) N. Stoll, *Bull. Soc. Chim. Belg.*, **38**, 71 (1929); *Chem. Abstr.*, **23**, 4456 (1929).

(249) K. W. Field and P. Kovacic, *Synthesis*, 135 (1969).

(250) P. Kovacic and M. Nazareno, unpublished data.

(251) P. B. D. de la Mare and R. Bolton, "Electrophilic Additions to Unsaturated Systems," Elsevier, New York, N. Y., 1966, p 105.

(252) M. L. Poutsma, *J. Amer. Chem. Soc.*, **87**, 2161 (1965).

(253) M. L. Poutsma, *ibid.*, **87**, 2172 (1965).

(254) S. N. Danilov and O. P. Kozmina, *J. Gen. Chem. USSR*, **19**, 269 (1949).

(255) A. J. Ellis and F. G. Soper, *J. Chem. Soc.*, 1750 (1954).

(256) C. W. Crane, J. Forrest, O. Stephenson, and W. A. Waters, *ibid.*, 827 (1946).

(257) H. Böhme and W. Krause, *Chem. Ber.*, **84**, 170 (1951).

curred, as well as side-chain attack on toluene.[163,248,258] The formation of bromobenzene was observed from the reaction of benzene, N-bromodimethylamine, and aluminum chloride.[259] Chlorophenol has been found in chlorination of phenol with N-chloromorpholine[260] or N-chlorodiethylamine.[261] Protonated N-chloromorpholine is reported to be the actual agent involved.[260] Similarly, the kinetics of halogenation of phenol by N-chlorodiethylamine can be interpreted in terms of interaction of phenoxide ions and diethylchlorammonium cations.[261] Sodium phenoxide underwent chlorination on exposure to chloramine.[259] Recently, it was reported that treatment of anilines and N-alkylanilines with N-chlorosuccinimide gave *o*- and *p*-chloroanilines in very good yields.[262] The high *ortho*: *para* ratio of >2 suggested involvement of an intramolecular rearrangement. Support for the hypothesis was provided from the rearrangement of the intermediate N-chloro-N-methylaniline, which afforded *o*-chloro-N-methylaniline (67%), *p*-chloro-N-methylaniline (3%), and dichloro-N-methylaniline (17%).[263] Primary arylamines undergo ring chlorination unless there is an excess of N-chloramine, in which case an azo compound is also formed[251] (see section VI.A.8). In aromatic amination with N-halamines under various conditions chlorination was noted as a significant, accompanying reaction (see section VI.A.6). Although not treated here, halogenation of the aromatic nucleus with N-haloanilides has been studied extensively, including the mechanistic aspects.[264]

D. PHOTOLYSIS

The photochemistry of N-halamines has been limited for the most part to simple molecules such as chloramine and nitrogen trichloride. The photolysis of chloramine at −190° with ultraviolet light generates NH, nitrogen monohydride.[265] The same labile entity was proposed as an intermediate in the thermal decomposition of NH_2Cl at 500° in the presence of carbon monoxide, which afforded hydrogen cyanate as the end product.[265] Chloramine and cyclohexene gave *trans*-1-amino-2-chlorohexane, *trans*-1,2-dichlorohexane, and other products under photolytic conditions.[111] On exposure to light, nitrogen trichloride in organic solvent leads to chlorination of the solvent. In carbon tetrachloride the decomposition was of a simple type,[266] first order with an energy of activation of 32 kcal, giving rise to nitrogen and chlorine.[267] In the presence of an alcohol, the corresponding carbonyl compound was formed along with ammonium chloride and hydrogen chloride.[266]

An extensive study of the photodecomposition of nitrogen trichloride in the presence of chlorine established that chlorine was acting as a photosensitizer.[268–270] The chain mechanism of eq 118–122, which is zero order, was suggested. The

$$Cl_2 + h\nu \longrightarrow 2Cl \tag{118}$$

$$NCl_3 + Cl \longrightarrow NCl_2 + Cl_2 \tag{119}$$

$$NCl_3 + NCl_2 \longrightarrow N_2 + 2Cl_2 + Cl \tag{120}$$

$$Cl + NCl_3 + X \rightleftharpoons NCl_4 + X \tag{121}$$

$$2NCl_4 \longrightarrow N_2 + 4Cl_2 \tag{122}$$

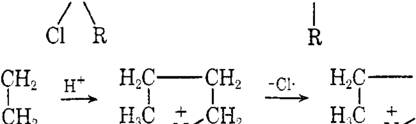
presence of nitrogen trichloride causes an induction period in the hydrogen–chlorine reaction.[270] About 30 years later a reinvestigation of these same reactions involving flash photolysis[271] resulted in the assignment of two transient absorptions at 2400 and 2950 Å to NCl and NCl_2, respectively. The NCl is a photolysis product of NCl_2 when radiation below 3100 Å is used. Since the earlier work employed the 4360- and 3650-Å Hg lines, there was apparently no formation of NCl. No induction period in the hydrogen–chlorine reaction in the presence of nitrogen trichloride was detected under the conditions of the later work.

The explosive decomposition of mixtures of hydrogen, chlorine, and nitrogen trichloride has been discussed.[272] In such a breakdown entailing chlorine azide and nitrogen trichloride, a continuous spectrum from the ultraviolet to red with a maximum intensity at 5000–5500 Å was observed.[273] Also, see section VI.E.1.

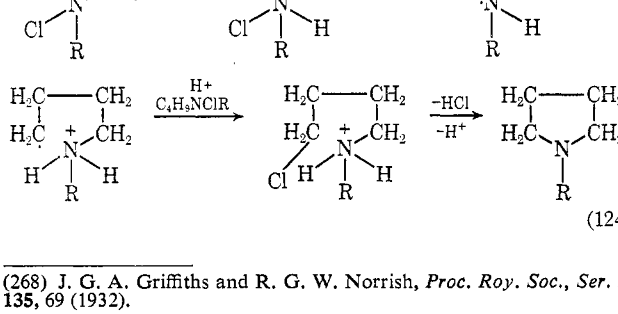
E. REARRANGEMENT

1. *Hofmann–Löffler Reaction*

Probably the best known transformation involving N-halamines is the Hofmann–Löffler reaction which provides an elegant synthesis of certain cyclic amines (an example is illustrated in eq 123). A comprehensive review by Wolff[9] covers the literature through the first half of 1961. The mechanism of eq 124 was proposed to rationalize existing data.[274] The salt of the N-chloramine is homolytically cleaved under



(123)



(124)

---

(258) W. Hentschel, *Ber.*, **30**, 1434 (1897).

(259) G. N. Dorofeenko, *Nauchn. Zap. Lugansk. Sel'skokhoz, Inst.*, **7**, 203 (1961); *Chem. Abstr.*, **58**, 2393 (1963).

(260) M. D. Carr and B. C. England, *Proc. Chem. Soc. London*, 350 (1958).

(261) L. O. Brown and F. G. Soper, *J. Chem. Soc.*, 3576 (1953).

(262) R. S. Neale, R. G. Schepers, and M. R. Walsh, *J. Org. Chem.*, **29**, 3390 (1964).

(263) P. Haberfield and D. Paul, *J. Amer. Chem. Soc.*, **87**, 5502 (1965).

(264) F. G. Soper, *J. Phys. Chem.*, **31**, 1192 (1927).

(265) J. Jander and J. Fischer, *Z. Anorg. Allg. Chem.*, **313**, 37 (1961); *Chem. Abstr.*, **56**, 15124 (1962).

(266) V. A. Shushunov and L. Z. Pavlova, *Russ. J. Inorg. Chem.*, **2**, 446 (1957).

(267) E. H. Bowen, *J. Chem. Soc.*, 1199 (1923).

(268) J. G. A. Griffiths and R. G. W. Norrish, *Proc. Roy. Soc., Ser. A*, **135**, 69 (1932).

(269) J. G. A. Griffiths and R. G. W. Norrish, *ibid., Ser. A*, **130**, 591 (1931).

(270) J. G. A. Griffiths and R. G. W. Norrish, *Trans. Faraday Soc.*, **27**, 451 (1931).

(271) A. G. Briggs and R. G. W. Norrish, *Proc. Roy. Soc., Ser. A*, **278**, 27 (1964).

(272) P. G. Ashmore, *Nature*, **172**, 449 (1953).

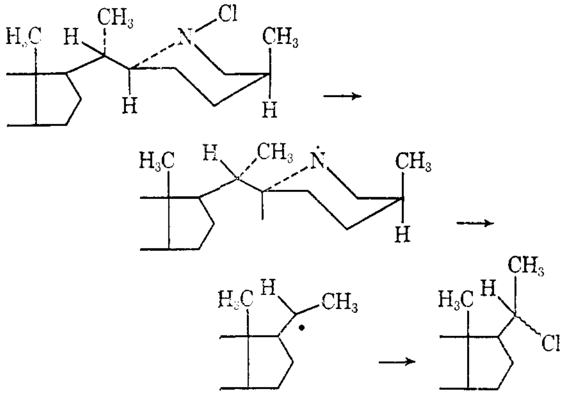
(273) G. Pannetier, *C. R. Acad. Sci.*, 233, 168 (1951); *Chem. Abstr.*, **46**, 1871 (1952).

(274) S. Wawzonek and P. J. Thelen, *J. Amer. Chem. Soc.*, **72**, 2118 (1950).

the influence of heat, light, or some other initiator to afford aminium radicals. This radical in turn intramolecularly abstracts a sterically favored hydrogen to form an alkyl radical which in a chain reaction abstracts chlorine intermolecularly. The alkyl chloride is then converted by alkali to the cyclic tertiary amine. The isolation of 4-chlorodibutylamine from N-chlorodibutylamine served to support the proposal.[275] The postulated scheme was further substantiated from examination of several features, including stereochemistry, hydrogen isotope effect, initiation, inhibition, catalysis, intermediates, and selectivity of hydrogen transfer.[276] The results pointed conclusively to a free-radical chain mechanism involving intramolecular hydrogen transfer as one of the propagation steps. An investigation of the process in relation to the mechanistic significance of side reactions and of results from alteration in experimental conditions provided additional mechanistic insight.[277] An enhanced yield of end product was observed with increase in acidity, but the overall reaction rate declined. Excess sulfuric acid reduced the rate of nonradical disproportionation of $(n\text{-Bu})_2NHCl$ to $n\text{-BuNCl}_2$ which is believed to be the primary initiator of rearrangement in the absence of external initiation. However, the dichloramine derivative apparently exerts its beneficial effect only at very low concentrations since it may also act as a chain terminator. Earlier workers[278] proposed that one role for sulfuric acid is to eliminate undesirable sid reactions of the radical type. The influence of solvent and chloramine structure was also determined.[279] The δ-chloramine from N-chloro-di-*n*-butylamine was formed in at least 71% yield in the solvents 3.9 *M* sulfuric acid in acetic acid, nitromethane, or acetonitrile, and in trifluoroacetic acid. The selectivity of hydrogen abstraction was $C_4{:}C_5 = 1.6{:}1$ for N-chloro-N-methyl-5-phenylpentylamine, lower than that from any previous example. When N-chloro-N-*t*-butylhexylamine was rearranged, attack of the aminium radical occurred almost exclusively at C_4.

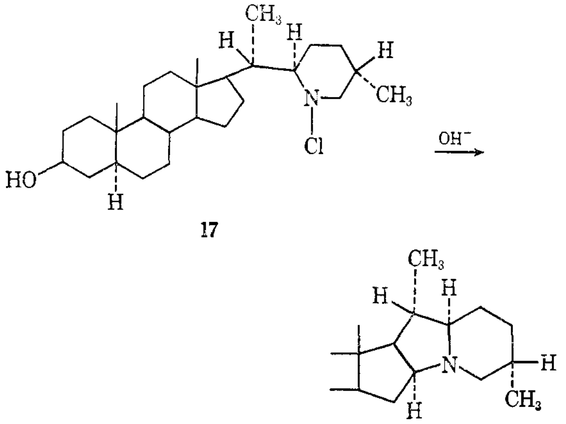
Primary amines can also be employed *via* the N-monochloro derivatives which serve as precursors for cyclization with concentrated sulfuric acid and ferrous salts.[280,281] Pyrrolidine and substituted pyrrolidines are formed in good yield.

Although it had been demonstrated that the Hofmann–Löffler reaction converts certain 20-methylamino steroids to conanines,[282] a new pathway was followed with the N-chloro derivative of (22*S*;25*S*)-22,26-imino-5α-cholestan-3β-ol.[283,284] Photochemical fragmentation took place with loss of the piperidine ring leading to a chloro-5α-pregnan-3β-ol as the end product (eq 125). Initial homolysis of the N–Cl bond leads to a nitrogen radical which cannot abstract hydrogen for stereochemical reasons. Stabilization by carbon–carbon fission results in a trigonal carbon radical which abstracts chlorine to give the stereoisomeric 20-chloropregnanes. A similar result was found with 16β-hydroxylated N-chloroiminocholestanols[285] and, in addition to the Hofmann–Löffler course, with N-chloroconiine,[286] yielding propyl chloride and Δ^1-piperideine.



(125)

The transformation of **17** to **18** was effected in the presence of base (eq 126).[225] The net result is a ring closure which bears formal resemblance to the Hofmann–Löffler cyclization.



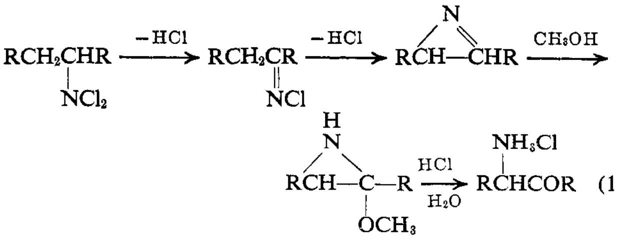
17

18

(126)

2. *Formation of α-Amino Ketones*

Another quite different type of rearrangement has received the attention of a number of investigators. The discovery of the rearrangement of N,N-dichloro-*sec*-alkylamines to α-amino ketones provides a useful synthetic scheme.[287] Further studies broadened the scope and resulted in an improved procedure,[288] namely, successive treatment of the N-halamine substrate with sodium methoxide and with dilute hydrochloric acid (Table XIX). Equation 127 was suggested,[289]



(127)

---

(275) S. Wawzonek and T. P. Culbertson, *J. Amer. Chem. Soc.*, **81**, 3367 (1959).

(276) E. J. Corey and W. R. Hertler, *ibid.*, **82**, 1657 (1960).

(277) R. S. Neale and M. R. Walsh, *ibid.*, **87**, 1255 (1965).

(278) S. Wawzonek and J. D. Nordstrom, *J. Org. Chem.*, **27**, 3726 (1962).

(279) R. S. Neale, M. R. Walsh, and N. L. Marcus, *ibid.*, **30**, 3683 (1965).

(280) E. Schmitz and D. Murawski, *Z. Naturforsch.*, **17b**, 127 (1962); *Chem. Abstr.*, **57**, 763 (1962).

(281) E. Schmitz and D. Murawski, *Chem. Ber.*, **99**, 1493 (1966).

(282) J. F. Kerwin, M. E. Wolff, F. F. Owings, B. B. Lewis, B. Blank, A. Magnani, C. Karash, and V. Georgian, *J. Org. Chem.*, **27**, 3628 (1962).

(283) G. Adam and K. Schreiber, *Tetrahedron Lett.*, 923 (1965).

(284) G. Adam and K. Schreiber, *Tetrahedron*, **22**, 3581 (1966).

(285) G. Adam and K. Schreiber, *Chem. Ind. (London)*, 989 (1965).

(286) E. Leete and A. R. Hargens, *Tetrahedron Lett.*, 4901 (1966).

(287) H. E. Baumgarten and F. A. Bower, *J. Amer. Chem. Soc.*, **76**, 4561 (1954).

(288) H. E. Baumgarten and J. H. Peterson, *ibid.*, **82**, 459 (1960).

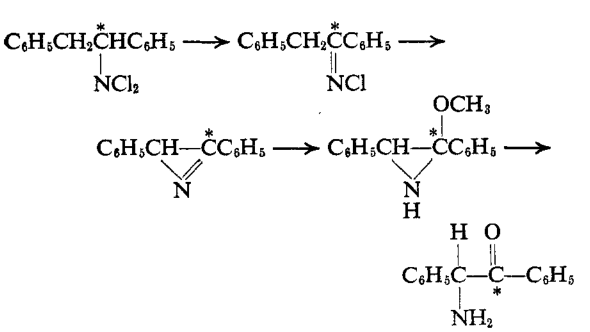
(289) M. J. Hatch and D. J. Cram, *ibid.*, **75**, 38 (1953).

Table XIX

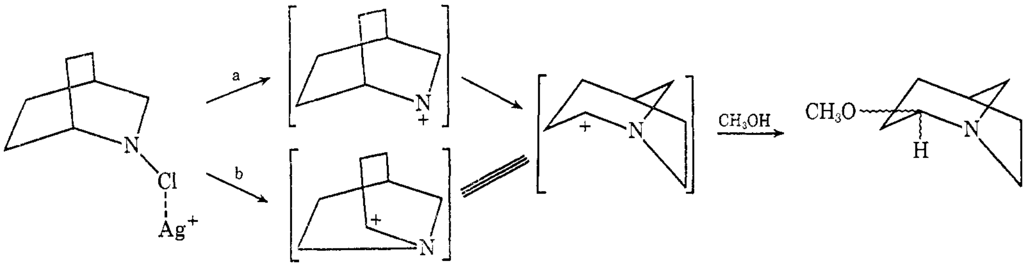
α-Amino Ketones from N,N-Dichloro-*sec*-alkylamines

Starting material	*Product*	*Yield, %*
Cyclohexylamine	2-Aminocyclohexanone	72
2-Aminoheptane	3-Amino-2-heptanone	72
α-Phenylethylamine	Phenacylamine	78
α-(*p*-Bromophenyl)ethylamine	*p*-Bromophenacylamine	72
α-(*p*-Anisyl)ethylamine	*p*-Methoxyphenacylamine	73
α-(*p*-Tolyl)ethylamine	*p*-Methylphenacylamine	72
1,2,3,4-Tetrahydro-1-naphthylamine	2-Amino-1-tetralone	69

analogous to the Neber rearrangement.[290] Support for the postulated mechanism was provided by isolation of the N-chlorimine and subsequent transformation to the α-amino ketone.[290] An excellent mechanistic study[291] of the base-promoted rearrangement of N,N-dichloro-1,2-diphenylethylamine-1-^{14}C confirmed the original proposal.[287] Exposure to the standard conditions resulted in the formation of desylamine. Application of two degradation procedures to the product provided unequivocal evidence that the labeled carbon atom was incorporated almost exclusively in the carbonyl group (eq 128).



(128)

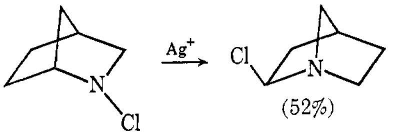


(129)

3. Via Nitrenium Ion and Miscellaneous Types

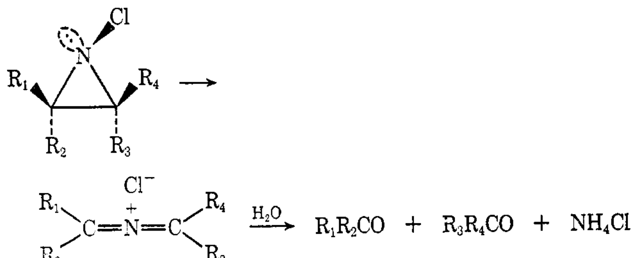
Mechanistically, there are a number of other categories of rearrangements involving N-halamines. One of the types most thoroughly investigated apparently proceeds *via* a cationic-type nitrogen. Gassman and coworkers have recently made significant contributions toward the understanding of nitrenium ion chemistry through studies of N-chloroalkylamines.

From an investigation of the solvolysis of N-chloroisoquinuclidine with methanol in the presence of silver nitrate, alkyl migration was found to occur giving 2-methoxy-1-azabicyclo[3.2.1]octane (60%).[292,293] The rearrangement could conceivably occur by either of two routes, each requiring the alkyl group to migrate with its electron pair. Path a (eq 129) involves the formation of a nitrenium ion as a discrete intermediate, followed by alkyl migration, while path b suggests a concerted process with simultaneous loss of chloride during alkyl migration. Additional examples were provided in this general category, *e.g.*, eq 130.[294,295]



(130)

Mechanistic evidence supporting the hypothesis that the nitrenium ion exists as a discrete intermediate prior to alkyl migration was obtained by kinetic studies. Methanolysis of several 2-chloro-2-azabicyclo[2.2.1]heptane derivatives gave thermodynamic parameters in accord with those expected for a process involving separation of charged ions.[109] The kinetics of N-chloroaziridine solvolysis in polar media provided more concrete evidence for a heterolytic process (eq 131).[296] The rates and products (Table XX) were found to be consistent with a Woodward–Hoffmann disrotatory type of concerted carbon–carbon bond cleavage in the transition state. The increase in the relative rate of solvolysis of **20** and **21** over **19** can be attributed to the greater stability of secondary *vs.* primary carbonium ions. Since the development of positive charge in **20** and **21** is spread over two secondary centers, the increased rate of **21** over **20** apparently reflects relief of methyl–methyl steric interaction through disrotatory ring opening. Considering the nitrenium ion as a discrete intermediate, one can visualize its existence either with the electron spins paired (singlet) or unpaired (triplet). The distributions derived from the solvolysis of 4,7,7-trimethyl-2-chloro-2-azabicyclo[2.2.1]heptane in the presence and absence



(131)

---

[290] G. H. Alt and W. S. Knowles, *J. Org. Chem.*, **25**, 2047 (1960).

[291] S. Oae and N. Furukawa, *Bull. Chem. Soc. Jap.*, **38**, 62 (1965).

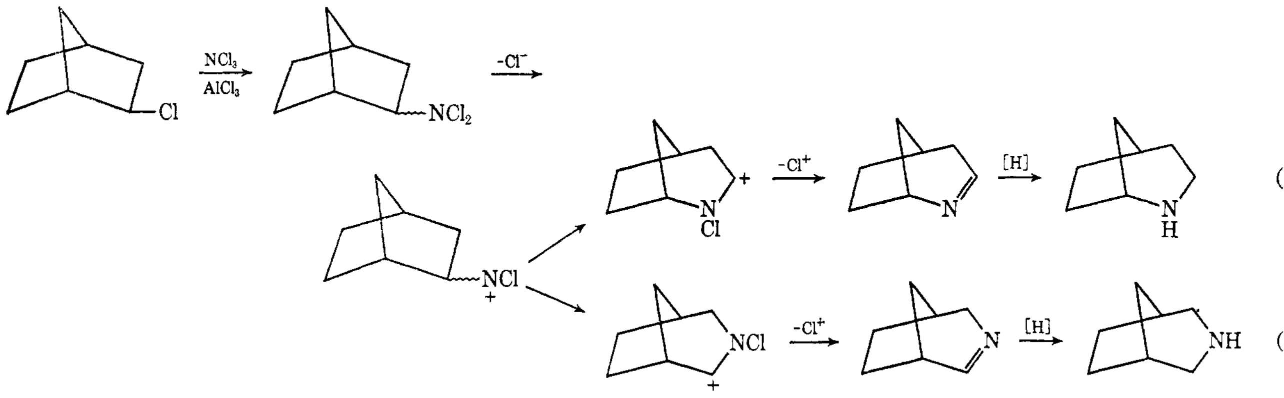
[292] P. G. Gassman and B. L. Fox, *Chem. Commun.*, 153 (1966).

[293] P. G. Gassman and B. L. Fox, *J. Amer. Chem. Soc.*, **89**, 338 (1967).

[294] P. G. Gassman and R. L. Cryberg, *ibid.*, **91**, 2047 (1969).

[295] P. G. Gassman and R. L. Cryberg, *ibid.*, **90**, 1355 (1968).

[296] P. G. Gassman and D. K. Dygos, *ibid.*, **91**, 1543 (1969).

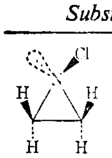
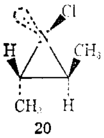
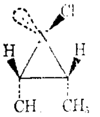


(132)

(133)

Table XX

Solvolysis of N-Chloroaziridines

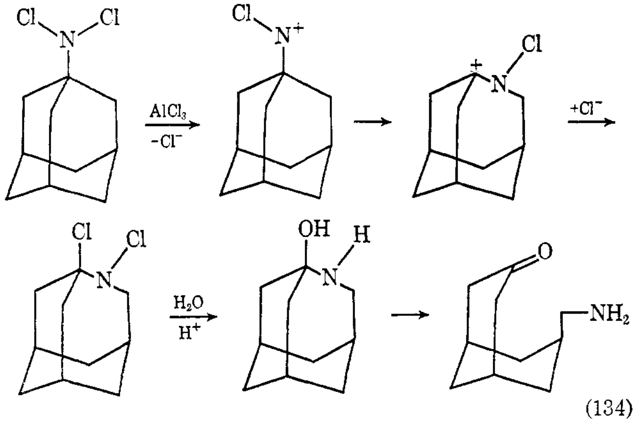
Substrate	k_{rel}	*Products*
 19	1	$2CH_2O + NH_4Cl$
 20	1,490	$2CH_3CHO + NH_4Cl$
 21	155,000	$2CH_3CHO + NH_4Cl$

of heavy atom solvents are consistent with the hypothesis that both types of nitrenium ions can be formed in these systems.[297]

The synthetic usefulness of this technique has been demonstrated by the preparation of azabicyclics in reasonable yields.[109]

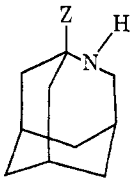
Similar rearrangements in the bicyclic and tricyclic series which apparently involve positive nitrogen generated from N-halamines have been studied. When *exo*-2-chloronorbornane reacted with nitrogen trichloride–aluminum chloride,[85] the products after reduction were 2-azabicyclo[3.2.1]-octane (88%), 3-azabicyclo[3.2.1]octane (6%), and 2-aminonorbornane (6%), with an over-all yield of 45%. A reasonable mechanistic scheme was formulated for the ring-expanded products (eq 132 and 133). The N,N-dichloro derivative serves as precursor to 2-aminonorbornane. Relief of ring strain may be an important driving force. Further investigations suggested that a stereoselective rearrangement was taking place. The synthesis of *exo*-N,N-dichloro-2-aminonorbornane and subsequent subjection to ring expansion conditions showed that the product was mainly 2-azabicyclo[3.2.1]-octane (eq 132). Similarly, with predominantly *endo*-N,N-dichloro-2-aminonorbornane, the major product was mainly 3-azabicyclo[3.2.1]octane (eq 133). The stereoselectivity is analogous to the situation involving ring expansion with the 2-norbornylcarbinyl cation.[298]

A similar rearrangement was found upon treatment of 1-N,N-dichloroaminoadamantane with aluminum chloride in methylene chloride (eq 134).[299] The product, 7-amino-



(134)

methylbicyclo[3.3.1]nonan-3-one, was isolated in 56% yield. It may be that the 1,2 shift takes place in a concerted manner. When the reaction mixture was worked up by exposure to thiophenol or methanol–hydrogen chloride, substituted 4-azahomoadamantanes of type **22** were obtained.



22, Z = OCH_3 or SC_6H_5

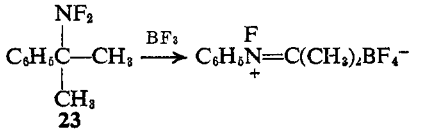
An intramolecular migration in the N-fluoramine series, in which nitrogen seemingly displayed positive character, is reported.[82] Compound **23**, prepared by the acid-catalyzed addition of difluoramine to α-methylstyrene, was converted to N-phenyl-N-fluoroisopropylidenimmonium fluoroborate on exposure to boron trifluoride (eq 135).

---

[297] P. G. Gassman and R. L. Cryberg, *J. Amer. Chem. Soc.*, **91**, 5176 (1969).

[298] W. Kraus and P. Schmutte, *Tetrahedron*, **24**, 1537 (1968), and references therein.

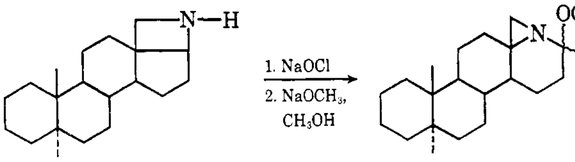
[299] P. Kovacic, J.-H. Liu, P. D. Roskos, and E. M. Levi, *Chem. Commun.*, 1034 (1970), and unpublished data.



$$C_6H_5\overset{NF_2}{\underset{CH_3}{C}}-CH_3 \xrightarrow{BF_3} C_6H_5\overset{F}{\underset{+}{N}}=C(CH_3)_2BF_4^- \qquad (135)$$

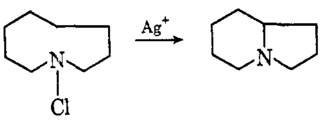
23

A base-catalyzed counterpart to these rearrangements has been described. 18(N)-Cyclo-17β-amino-5α-androstane was treated with sodium hypochlorite, followed by sodium methoxide in methanol producing 18(N)-cyclo-17ε-methoxy-17a-aza-D-homo-5α-androstane (eq 136).[300]



(136)

When N-chloroazacyclononane was exposed to silver ion, indolizidine (68% yield) (eq 137) was obtained.[301] The mechanism was postulated as a transannular hydride abstraction by nitrenium ion followed by attack of the carbonium ion on nitrogen.



(137)

The Stieglitz rearrangement has received attention from various groups during a span of more than 50 years. Initially, the reaction supposedly involved formation of nitrenes, for example, during the rearrangement of N-halo- and N,N-dihalotritylamines.[302,303] Benzophenone anil was observed from thermal rearrangement of N,N-dichlorotritylamine (eq 138) or from the treatment of the N-bromo derivative with base (eq 139). Use of *p*-chlorophenyldiphenylmethyldichloramine

$$(C_6H_5)_3CNCl_2 \xrightarrow{\Delta} (C_6H_5)_2{=}NC_6H_5 \qquad (138)$$

$$(C_6H_5)_3CNHBr \xrightarrow{\text{base}} (C_6H_5)_2C{=}NC_6H_5 \qquad (139)$$

contributed to elucidation of the nature of the intramolecular competition. The phenyl groups were found to migrate three times as fast as the *p*-chlorophenyl moiety. When Stieglitz and Morgan continued the study of migration aptitudes, an almost statistical ratio was obtained[304] (eq 140 and 141).

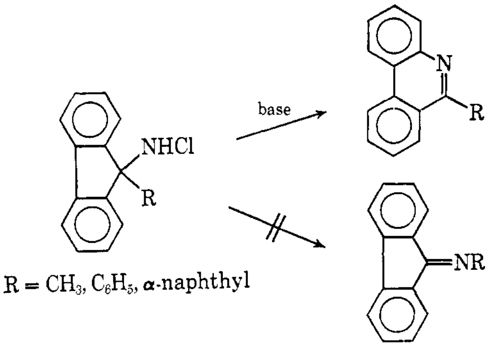
$$(p\text{-}ClC_6H_4)_2(C_6H_5)CNHCl \longrightarrow \underset{67\%}{p\text{-}ClC_6H_4NH_2} + \underset{33\%}{C_6H_5NH_2} \qquad (140)$$

$$(p\text{-}ClC_6H_4)(p\text{-}BrC_6H_4)(C_6H_5)CNHCl \longrightarrow$$
$$\underset{35\%}{p\text{-}ClC_6H_4NH_2} + \underset{32\%}{p\text{-}BrC_6H_4NH_2} + \underset{33\%}{C_6H_5NH_2} \qquad (141)$$

Migratory aptitudes and the fact that N-chloro-N-methyltritylamine did not undergo rearrangement, but N-chlorotritylamine did, influenced Stieglitz's thinking.

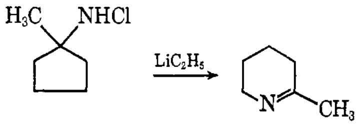
However, recent studies have forced a revision of the mechanistic picture. A reinvestigation of the migratory aptitudes of aryl groups in tritylhydroxylamines[305] furnished results similar to those obtained from the rearrangement of substituted pinacols,[306] but in sharp disagreement with prior work.[304] Furthermore, the rearrangement of *para*-substituted N-chlorotritylamines gave values (p-$CH_3OC_6H_4$ = 664; p-$NO_2C_6H_4$ = 0.05 relative to phenyl) paralleling those observed in the pinacol rearrangement,[307] and N-chloro-N-methyltritylamine does rearrange when suitable conditions are used.[109] These findings suggest that Stieglitz was actually generating a nitrenium-type species. Other examples of reactions which apparently proceed *via* nitrenium-like ions have appeared recently.[225,308,309]

9-Substituted phenanthridines have been synthesized by an application of the Stieglitz method, entailing rearrangement of various N-halo-9-aryl- and 9-alkyl-9-fluorylamines (eq 142).[310] The determining factors in the rearrangement are apparently relief of strain in the five-membered ring and the energy gained through extended conjugation. In a related, more recent investigation, interaction of N-chloro-1-methylcyclopentylamine with ethyllithium gave a cyclic imine[311] (eq 144). Formation of a nitrene by α elimination and a concerted mechanism were considered as possible rationalizations of the observed result.



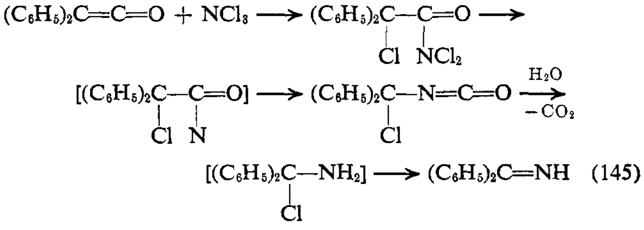
(142)

(143)



(144)

A nitrene intermediate was proposed in the formation of 1,1-diphenylmethylenimine from treatment of diphenylketene with nitrogen trichloride (eq 145).[107]



$$(C_6H_5)_2C{=}C{=}O + NCl_3 \longrightarrow (C_6H_5)_2\underset{Cl}{C}-\underset{NCl_2}{C}{=}O \longrightarrow$$
$$[(C_6H_5)_2\underset{Cl}{C}-\underset{N}{C}{=}O] \longrightarrow (C_6H_5)_2\underset{Cl}{C}-N{=}C{=}O \xrightarrow[-CO_2]{H_2O}$$
$$[(C_6H_5)_2\underset{Cl}{C}-NH_2] \longrightarrow (C_6H_5)_2C{=}NH \qquad (145)$$

Early investigators were unable to accomplish redistribution of the groups in N-chlorimines which at one time were thought

---

[300] C. Benezra and X. Lusinchi, *Can. J. Chem.*, **47**, 1547 (1969).

[301] O. E. Edwards, D. Vocelle, J. W. ApSimon, and F. Haque, *J. Amer. Chem. Soc.*, **87**, 678 (1965).

[302] J. Stieglitz and I. Vosburgh, *Chem. Ber.*, **46**, 2151 (1913).

[303] I. Vosburgh and J. Stieglitz, *J. Amer. Chem. Soc.*, **38**, 2081 (1916).

[304] J. Stieglitz and A. F. Morgan, *ibid.*, **38**, 2095 (1916).

[305] M. S. Newman and P. M. Hay, *ibid.*, **75**, 2322 (1953).

[306] H. Adkins in "Organic Chemistry," Vol. I, 2nd ed, H. Gilman, Ed., Wiley, New York, N. Y., 1937, p 1068.

[307] R. J. Bochis, *Diss. Abstr. B*, **27**, 4300 (1967).

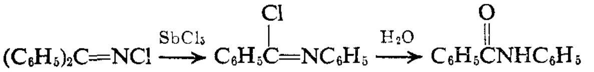
[308] P. Kovacic, R. P. Bennett, and J. L. Foote, *J. Amer. Chem. Soc.*, **84**, 759 (1962).

[309] P. Kovacic, R. L. Russell, and R. P. Bennett, *ibid.*, **86**, 1588 (1964).

[310] L. A. Pinck and G. E. Hilbert, *ibid.*, **59**, 8 (1937).

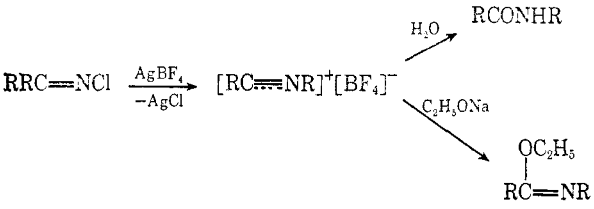
[311] R. A. Amos and L. W. Haynes, personal communication.

to be intermediates in the Beckmann rearrangement.[298,312] In contrast, a later study revealed that antimony pentachloride is an effective catalyst under appropriate conditions (eq 146).[313] Similarly, N-chloroketimines react with silver



$$(C_6H_5)_2C{=}NCl \xrightarrow{SbCl_5} C_6H_5\overset{Cl}{\overset{|}{C}}{=}NC_6H_5 \xrightarrow{H_2O} C_6H_5\overset{O}{\overset{\|}{C}}NHC_6H_5 \quad (146)$$

tetrafluoroborate in aqueous dioxane to produce amides from rearrangement.[314] The nitrilium ion, postulated as an intermediate (eq 147), was trapped with sodium ethoxide in aprotic solvent. The reaction rate was found to increase with increasing solvent polarity. With R = C_6H_5, benzanilide was formed in yields of 65–70%.



(147)

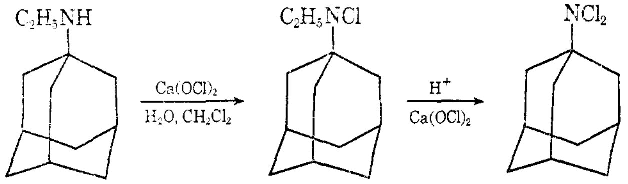
F. DEALKYLATION

A few reports reveal that dealkylation of N-haloalkylamines can take place under acidic conditions. In an investigation of the Hofmann–Löffler reaction, nonradical disproportionation of $(n\text{-Bu})_2NHCl$ to $n\text{-BuNCl}_2$ was observed in the presence of sulfuric acid.[277] The indicated outline of the reaction pathway is presented in eq 148–150. Preliminary results[315] provide evidence for the indicated transformation (eq 151). Presumably, ammonium ion formation occurs by attack of H^+ or Cl^+ on **24**, followed by dealkylation.

$$Bu_2\overset{+}{N}HCl + H_2O \longrightarrow BuNHCl + H_3O^+ + C_4 \text{ fragment} \quad (148)$$

$$BuNHCl + H^+ \rightleftarrows Bu\overset{+}{N}H_2Cl \quad (149)$$

$$BuNHCl + Bu_2\overset{+}{N}HCl \longrightarrow BuNCl_2 + Bu_2\overset{+}{N}H_2 \quad (150)$$



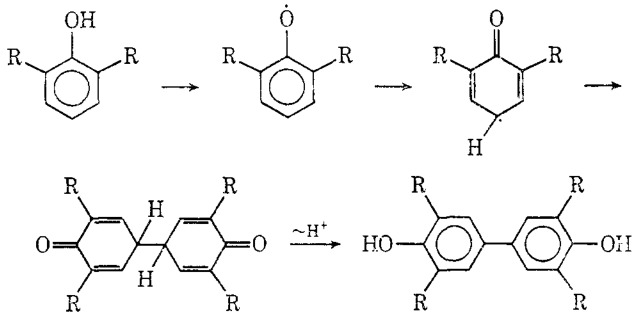
24

(151)

Isobutylene was generated (>80% yield) on treatment of N,N-dichloro-*t*-butylamine with silver fluoride.[232]

G. MISCELLANEOUS

Several 2,6- and 2,4,6-alkyl-substituted phenols were observed to undergo a chloramine-induced oxidative dimerization[316] (eq 152). The mechanism was postulated to entail an initial proton transfer from phenol to chloramine followed by a redox reaction to give phenoxy and aminium radicals, in addition to chloride ion. Mercaptans can be converted to disulfides by oxidation with chloramine or dimethylchloramine.[317]



(152)

There are a few miscellaneous reactions of N-halamines which have been cited previously in the review literature[5,7] and are included here for the sake of completeness.

$$NH_2Cl + OH^- \longrightarrow NH_3 + OCl^- \quad (153)$$

$$NH_2Cl + OR^- \longrightarrow NH_2OR + Cl^- \quad (154)$$

$$2NH_2Cl + 2KCN \longrightarrow NH(CN)_2 + NH_3 + 2KCl \quad (155)$$

$$NH_2Cl + BF_3 \longrightarrow BF_3NH_3 + NH_4Cl + N_2 + NCl_3 \quad (156)$$

$$(CH_3)_2NCl + BF_3 \longrightarrow F_3B{:}N(CH_3)_2Cl \quad (157)$$

$$(CH_3)_2NCl + H_2SO_4 \longrightarrow [HN(CH_3)_2Cl]HSO_4 \quad (158)$$

$$R_2NCl + HNO_3 \longrightarrow R_2NNO_2 + HOCl \quad (159)$$

H. GENERAL CONSIDERATIONS

The chemistry of N-halamines is very diversified, not only because both the nitrogen and halogen act as reaction sites, but also because of the different modes by which these functionalities react. Examples have been given wherein nitrogen acts as a cation (bicyclic rearrangements) anion (hydrazine formation), radical (photolysis and addition to alkenes), radical cation (Hofmann–Löffler reaction), and a base (nucleophilic substitution). The halogen has also been shown to exhibit cationic (halogenation), anionic (Grignard reactions), and radical (photolysis) character. In addition, when N–H is present, reactions typical of this structure are observed. As a result of this versatility, N-halamines serve as useful precursors for the preparation of various classes of organic compounds.

Acknowledgment. We wish to thank Dr. Roger J. Hopper for assistance with the literature work. We are grateful for support provided by the National Science Foundation and the National Institutes of Health, Public Health Service.

---

(312) P. P. Peterson, *Amer. Chem. J.*, **46,** 325 (1911).

(313) W. Theilacker and H. Mohl *Ann.*, **563,** 99 (1949); *Chem. Abstr.*, **43,** 7464 (1949).

(314) R. N. Loeppky and M. Rotman, *J. Org. Chem.*, **32,** 4010 (1967).

(315) P. Kovacic, J.-H. Liu, and E. M. Levi, unpublished data.

(316) L. A. Paquette and W. C. Farley, *J. Org. Chem.*, **32,** 2718 (1967).

(317) H. H. Sisler, N. K. Kotia, and R. E. Highsmith, *ibid.*, **35,** 1742 (1970).