8(9)-*p*-Menthene (IX) Isomerization.—A sample of IX obtained from The Glidden Co.[15] was treated with silica gel at 150° as described, for 20 min. The gas chromatographic and infrared analysis showed complete isomerization to 3-*p*-menthene (VII).

3-*p*-Menthene (VII) Isomerization.—3-*p*-Menthene, obtained by a preparative scale gas chromatographic separation of *d*-limonene disproportionation products, was treated for 1 hr. at 150° on silica gel. Analysis by gas chromatography and infrared spectroscopy showed no isomerization.

2-*p*-Menthene (VI) Isomerization.—2-*p*-Menthene, obtained by chromatography as described, when treated for 1 hr. at 150° on silica gel, showed no isomerization.

(16) Contributed by The Glidden Co., Jacksonville, Fla.

Acknowledgment.—The authors wish to thank Dr. Herman Pines, Department of Chemistry, Northwestern University, Evanston, Illinois, for infrared curves of 8(9)-*p*-menthene and *t*-2-*p*-menthene; Gordon S. Fisher, USDA, Olustee, Florida, for infrared curves of 1-*p*-menthene, 3-*p*-menthene, α-terpinene, and γ-terpinene; and Dr. John M. Derfer, The Glidden Company, Jacksonville, Florida, for samples of 8(9)-*p*-menthene.

Pyrazines. III. The Action of Phosphoroyl Chloride on Pyrazine N-Oxides[1,2]

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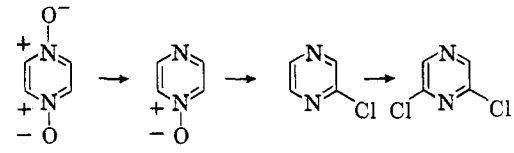
The action of phosphoroyl chloride on pyrazine N-oxides is described. Thus, pyrazine 1-oxide is converted to 2-chloropyrazine, while pyrazine 1,4-dioxide yields 2,6-dichloropyrazine. By contrast, 2-methylpyrazine 1,4-dioxide gives a mixture of dichloromethylpyrazine and a monochloromethylpyrazine N-oxide which is isomeric with the N-oxide produced by direct oxidation of 2-chloro-3-methylpyrazine or 2-chloro-6-methylpyrazine. The mechanisms of halogenation of these pyrazine N-oxides are discussed and the role of possible intermediates is examined.

Since its demonstration by Meisenheimer[3] and later by Bobranski and associates,[4a] the conversion of heterocyclic N-oxides by chlorinating agents to nuclear substituted chlorine derivatives has served as a useful syntheses.[4b,c] Among pyrazines, this procedure was used by Newbold and Spring[5] and Klein and Spoerri[6] to prepare 2-chloro-3,6-dimethylpyrazine from 2,5-dimethylpyrazine 1-oxide. When the di-N-oxide was used, the 2,5-dichloro-3,6-dimethylpyrazine was obtained. In this report, additional experiments are presented, describing the action of phosphoryl chloride on pyrazine mono- and di-N-oxide and by contrast, on 2-methylpyrazine 1,4-dioxide.

After the work presented here was completed and this manuscript was in preparation, the present authors learned of a paper by Bernardi and associates[7] also describing the action of phosphoroyl chloride on pyrazine 1,4-dioxide, 3-chloropyrazine 1-oxide, and 3-carboxamidopyrazine 1-oxide. Their observations were in essential agreement with portions of the work reported in this paper.

Pyrazine 1-oxide on treatment with phosphoryl chloride gave 2-chloropyrazine, which on further treatment with hydrogen peroxide in acetic acid formed 3-chloropyrazine 1-oxide. This agreed with an earlier observation that N-oxidation of a pyrazine bearing a halogen or an electron-donating substituent in the nucleus will take place on the nitrogen furthest from that substituent.[8] Oxidation of either 2-chloro- or 2-ethoxy-3,6-dimethylpyrazine produced the 4-oxide only. These compounds resisted further oxidation. The present investigators have prepared 2-ethoxypyrazine 1,4-dioxide by direct oxidation of 2-ethoxypyrazine.[9]

When pyrazine 1,4-dioxide was heated with excess phosphoryl chloride, 2,6-dichloropyrazine was obtained. Initially, the course of the reaction was thought to be: pyrazine 1,4-dioxide → pyrazine 1-oxide → 2-chloropyrazine → 2,6-dichloropyrazine:



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Support for this reaction sequence was derived from: (a) phosphorus halides are recognized deoxygenating agents[10]; (b) the formation of 2,6-dichloropyrazine from 2-chloropyrazine and chlorine[11]; (c) treatment of 2-hydroxypyrazine with phosphoryl bromide produced a mixture of 2-bromopyrazine and 2,6-dibromopyrazine.[12,13]

This assumption was quickly shown to be incorrect, since treatment of 2-chloropyrazine with excess phosphoryl chloride failed to produce 2,6-dichloropyrazine. Further, the smaller yield of 2-chloropyrazine from pyrazine 1-oxide obtained under similar conditions (without the formation of the 2,6-dichloro compound) would indicate that they could not arise in sequence from the same precursor. A simultaneous or sequential ionic chlorination of both N-oxide functions would

(1) Portions of this work were reported at the 140th National Meeting of the American Chemical Society, Chicago, Ill., September, 1961.

(2) The work reported here was supported in part by a grant (CY-5343) from the National Institutes of Health.

(3) J. Meisenheimer, *Ber.*, **59**, 1848 (1926).

(4) (a) B. Bobranski, L. Kochanska, and A. Kowaleska, *ibid.*, **71B**, 2385 (1938); (b) G. B. Bachman and D. E. Cooper, *J. Org. Chem.*, **9**, 302 (1944); (c) R. W. Goulay, G. W. Moersch, and H. S. Mosher, *J. Am. Chem. Soc.*, **69**, 303 (1947).

(5) G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 1183 (1947).

(6) B. Klein and P. E. Spoerri, *J. Am. Chem. Soc.*, **73**, 2951 (1951).

(7) L. Bernardi, G. Palamidessi, A. Leone, and G. Larini, *Gazz. chim. ital.*, **91**, 1431 (1961); *Chem. Abstr.*, **57**, 2223e (1962).

(8) R. A. Baxter, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, 1859 (1948).

(9) Unpublished observations.

(10) E. Ochiai, *J. Org. Chem.*, **17**, 534 (1953).

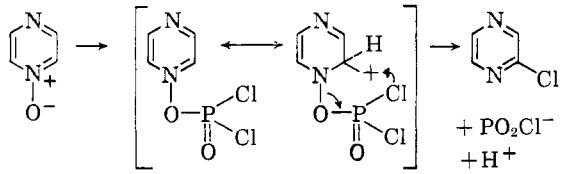
(11) W. E. Taft, U. S. Patent 2,797,219 (June 25, 1957).

(12) A. E. Erickson and P. E. Spoerri, *J. Am. Chem. Soc.*, **68**, 400 (1946).

(13) K. Schaaf and P. E. Spoerri, *ibid.*, **71**, 2043 (1949).

favor formation of 2,5-dichloropyrazine or to a lesser extent the 2,3-isomer. This was demonstrated by treating 3-chloropyrazine 1-oxide, an intermediate in such a sequence, with phosphoroyl chloride. The dichloropyrazine thus obtained closely resembled the physical characteristics of 2,5-dichloropyrazine.[14]

A mechanism of chlorination of heterocyclic N-oxides was suggested by Eisch and Gilman.[15] As applied to pyrazine N-oxides and phosphoryl chloride, this would involve initial formation of the N-O-dichlorophosphite salt, followed by attack by chloride on the electron-deficient α-carbon and removal of the oxygen.



This mechanism would provide a plausible explanation for the formation of 2-chloropyrazine and other simple ring-substituted chloropyrazines. It would appear that the formation of 2,6-dichloropyrazine is more complex.

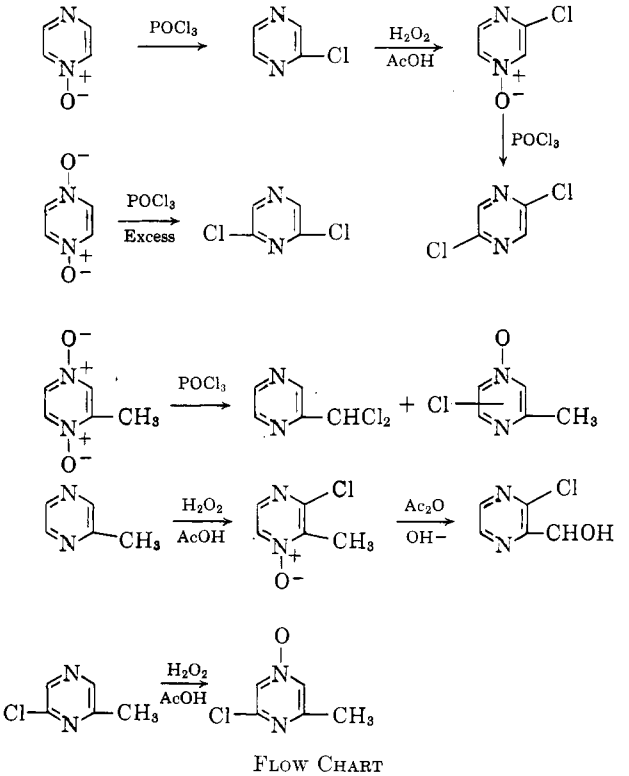
Two other possible reaction pathways, well documented in pyridine chemistry,[16-19] are being considered. Both involve halogenation of an intermediate quaternary pyrazinium salt. This is now under study.

In the reaction of 2-methylpyrazine 1,4-dioxide with phosphoryl chloride,[20a] an even more complex mechanism is suggested. A mixture of halogenated products was obtained containing mostly an intense lachrymator and vesicant and a smaller amount of a chloromethylpyrazine N-oxide. The former compound appeared similar to the dichloromethylpyrazine reported by Behun and Levine[20b] who prepared it by hypohalite oxidation of pyrazyl methyl ketone. Attempts to convert the compound to the dimethyl acetal reported by Behun and Levine[20b] were unsuccessful. In every attempt, a product still containing halogen was obtained, whose elemental analysis and infrared spectrum indicated a mixture of the desired dimethoxy derivative and a chloropyrazyl ether. Difficulty in the preparation of substituted pyrazyl diethers by conventional methods has also been reported by Karmas and Spoerri.[21]

Baxter and associates[22] describes an example of side-chain halogenation of 2-ethoxy-3,6-dimethylpyrazine 1,4-dioxide with phosphoryl chloride in which a mixture of the expected 2-chloro-5-ethoxy-3,6-dimethylpyrazine and 2-ethoxy-6-methyl-3-chloromethylpyrazine were formed.

Of further interest in this regard are the recent observations of Hirschberg and Spoerri[23] and Gainer and associates[24] that gaseous chlorine, at atmospheric pressure and with only moderate warming produced only ring halogenation of methylpyrazine and 2,5-dimethylpyrazine. Yet the same reaction conditions caused side-chain halogenation of 2,6-dimethylpyrazine.

The minor product of the reaction between 2-methylpyrazine di-N-oxide and phosphoryl chloride was isomeric with the 2-chloro-3-methylpyrazine 4-oxide obtained by direct oxidation of 2-chloro-3-methylpyrazine and the N-oxide produced by direct oxidation of 2-chloro-6-methylpyrazine. The position of the N-oxide in 2-chloro-3-methylpyrazine 4-oxide was established by rearrangement with acetic anhydride and hydrolysis to 2-chloro-3-pyrazylmethanol. As demonstrated earlier,[25] this rearrangement among pyrazine N-oxides occurs only when the N-oxide is adjacent to a methyl-bearing carbon. Attempts similarly to rearrange the N-oxide of the compound under examination with



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acetic anhydride were unsuccessful, indicating that the N-oxide was not adjacent to the C-methyl. Possible structures for this compound include 2-chloro-5-methylpyrazine 1-oxide or even the 2-chloromethyl derivative. Some evidence is available that N-oxida-

(14) A. A. Miller, U. S. Patent 2,573,268 (October 30, 1951).

(15) J. Eisch and H. Gilman, *Chem. Rev.*, **57**, 561 (1957). See also, R. C. Elderfield, "Chemistry of Quinoline," in "Heterocyclic Compounds," R. C. Elderfield, Ed., Vol. 4, John Wiley and Sons, Inc., New York, ref. 11, p. 241.

(16) E. Shaw, "Pyridine N-Oxides," in "Heterocyclic Compounds, Pyridine and Derivatives," Erwin Klingsberg, Ed., Interscience Publishers, New York, N. Y., part II, pp. 34, 124.

(17) F. Ramirez and P. von Ostwalden, *Chem. Ind.* (London), 46 (1957); *J. Am. Chem. Soc.*, **81**, 156 (1959).

(18) B. M. Bain and J. E. Saxton, *J. Chem. Soc.*, 5216 (1961).

(19) E. E. Garcia, C. V. Greco, and I. M. Hunsberger, *J. Am. Chem. Soc.*, **82**, 4430 (1960).

(20)(a) NOTE ADDED IN PROOF.—Since this manuscript was submitted, the n.m.r. spectrum of the product resulting from the phosphoryl chlorination of 2-methylpyrazine 1,4-dioxide was determined. Three resonances were noted, the first, unsplit at 7.4 τ, the second, barely split at 5.1 τ, and a third group at 1.6 τ (all relative to tetramethylsilane), in area ratios 5:1:3. This would indicate that the product is a mixture of a dichloromethylpyrazine and a monochloromethylpyrazine. The authors are grateful to Dr. David I. Schuster, Department of Chemistry, New York University, for this determination. (b) J. D. Behun and R. Levine, *J. Org. Chem.*, **23**, 406 (1958).

(21) G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **79**, 680 (1957).

(22) R. A. Baxter, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, 1859 (1948).

(23) A. Hirschberg and P. E. Spoerri, *J. Org. Chem.*, **26**, 2356 (1961).

(24) H. Gainer, M. Kokorudz, and W. K. Langdon, *ibid.*, **26**, 2360 (1961).

(25) B. Klein, J. Berkowitz, and N. E. Hetman, *ibid.*, **26**, 126 (1961).

tion of chloromethylpyrazines stabilizes the compound.[26] The identification of this compound is under further study.

The reactions described in this paper are summarized in the accompanying flow chart.

Experimental[27,28]

2-Chloropyrazine.—In an oven-dried two-neck flask containing a Teflon magnetic stirring bar, fitted with an efficient condenser whose upper end was closed with an oven-dried cotton plug, was placed 15.7 ml. (0.173 mole) of phosphoryl chloride. This was warmed with stirring to about 55° and 8.3 g. (0.086 mole) of pyrazine 1-oxide[29] was added in small portions over a 30-min. period,[30] at a rate to maintain gentle boiling. When the addition was complete, the mixture was heated under reflux for an additional 15 min. A dark solid formed during this time. The dark mixture was chilled and poured cautiously onto 200 g. of chopped ice with good stirring.

The filtered mixture was neutralized with 50% sodium hydroxide and brought to pH 9 with 10% sodium hydroxide. The solution was extracted with seven 125-ml. portions of ether with careful mixing to avoid emulsification. The combined extracts were washed with water and dried over calcium chloride.

The solvent was removed at atmospheric pressure and the residue distilled, collecting 2.44 g. (25%) product, b.p. 60.5° (26 mm.), n^{25}°D 1.5343 [lit.[6] b.p. 62.5° (29 mm.), n^{28}°D 1.5340].

The dark solid was insoluble in most organic solvents and was not further characterized.

3-Chloropyrazine 1-Oxide.—To a solution of 13.8 g. (0.12 mole) of 2-chloropyrazine[31] in 36 ml. of glacial acetic acid 23.3 ml. of 30% hydrogen peroxide was added and the solution was heated for 17 hr. at 65–75°. The solution was concentrated to one-third volume, diluted with an equal quantity of water, and reconcentrated. The residue was extracted with chloroform and the combined organic extracts were cross washed with water and dried over calcium chloride. The solvent was stripped leaving a residue of 6.8 g., m.p. 85–91°.

The aqueous portion was brought to pH 8.5–9 and re-extracted with chloroform. From this extract, on removal of solvent, an additional 0.9 g. was obtained. Total yield: 7.7 g. (49%). Recrystallization from 95% ethanol brought the m.p. to 95–96°.[32]

Anal. Calcd. for $C_4H_3N_2OCl$: C, 36.80; H, 2.31; N, 21.47%. Found: C, 36.94; H, 2.51; N, 20.98.

2,6-Dichloropyrazine.—To 73 ml. (0.8 mole) of phosphoryl chloride about 1 g. of pyrazine 1,4-dioxide[29] was added and the suspension was gradually heated with stirring until the exothermic reaction, which occurs at about 80°, subsided. The remainder of a total of 22.4 g. (0.2 mole) was added gradually in small portions. After the addition was complete (50 min.), a probe sample showed an absorption at 218 and 296 mμ with a shoulder at 275 mμ. Heating under reflux was continued for an additional 45 min.[33]

The dark mixture was cooled and poured cautiously on chopped ice with good stirring. After the decomposition was complete, the precipitated solid was collected and washed with ice–water. This weighed 11.0 g., m.p. 49–52°.

From the filtrate, on extraction with chloroform, another 1.0 g. of product, m.p. 50–54°, was obtained. Total yield: 12.0 g. (40.4%). A portion was sublimed for analysis, m.p. 51–53°. Mixture melting point with authentic material[34] produced no depression. Comparison of ultraviolet and infrared absorption spectra also established their identity.

Anal. Calcd. for $C_4H_2N_2Cl_2$: C, 32.24; H, 1.36; N, 18.81. Found: C, 32.49; H, 1.40; N, 18.33.

2,5-Dichloropyrazine.—To 12.4 ml. (0.13 mole) of warm phosphoryl chloride (60°) 6.0 g. (0.046 mole) of 3-chloropyrazine 1-oxide was added in small amounts with good stirring, keeping the reaction under good control until all was added. The solution darkened while being heated under reflux for an hour. The solution was chilled and poured cautiously onto 150 g. of chopped ice with good stirring. The product was isolated by extraction into a total of 150 ml. of chloroform. The extract was washed with water, 25 ml. of 5% sodium bicarbonate, again with water, and dried over calcium chloride.

After removal of the solvent at atmospheric pressure the residue was distilled collecting 4.4 g. (64.2%) of product, b.p. 90–91° (44 mm.), n^{27}°D 1.5592, which solidified completely on storage in a freezer (lit.[14] m.p. 0°).[35]

Anal. Calcd. for $C_4H_2N_2Cl_2$: C, 32.24; H, 1.36; N, 18.81. Found: C, 32.60; H, 1.46; N, 18.90.

2-Methylpyrazine 1,4-Dioxide.—The preparation of this compound has been simplified and improved.

One mole (94.0 g.) of 2-methylpyrazine in 570 ml. of glacial acetic acid was treated with 400 ml. of 35% hydrogen peroxide and the solution was heated 16 hr. on a steam bath under a reflux condenser.

Two-thirds of the liquid was removed under reduced pressure, the volume was restored with water, and the solution was reconcentrated. This was repeated twice more to remove most of the acetic acid and the solution was finally taken to dryness under reduced pressure (water aspirator and rotary flash evaporator). The crude product was recrystallized from 90% methanol. Yield: 99.0 g. (76.3%), m.p. 230–231°.[36]

Dichloromethylpyrazine.—To 91 ml. (1.0 mole) of warm (70°) phosphoryl chloride, 31.5 g. (0.25 mole) of 2-methylpyrazine 1,4-dioxide was added in small portions over 50 min. An exothermic reaction ensued following each addition and heat was applied only when required to maintain reflux. After the addition was complete, the dark solution was heated under reflux for an additional 30 min. A probe sample showed an absorption at 221 and 298 mμ, with a shoulder at 278 mμ.

The dark mixture was chilled and poured carefully over 300 g. of chopped ice. After all the excess reagent was decomposed, the oily layer was taken up in ether and the aqueous layer was extracted with more ether, the combined extracts were dried over anhydrous magnesium sulfate, and the solvent was stripped at atmospheric pressure. The residue was intensely lachrymatory and contained a small amount of colorless crystals.

The residue was re-dissolved in ether and extracted with 50 ml. of 20% sodium hydroxide. The ether layer was washed with water and dried ($MgSO_4$). Removal of the solvent left a residue which was distilled collecting a total of 17.9 g. (44%) of product in four fractions, b.p. 109–115° (27–31 mm.), n^{23}°D 1.5542–1.5554; and another liquid fraction, 0.4 g., b.p. 121–123° (28 mm.), n^{23}°D 1.5603–1.5610, in which a colorless solid deposited, m.p. 120–134°.

For analysis the first liquid was redistilled collecting the fraction, b.p. 105–108° (18 mm.), n^{26}°D 1.5495.

On standing this liquid underwent a series of color changes, first to pale blue, then green, and finally darkened to a dull brown with specks of polymeric material that adhered to the walls of the container.

Behun and Levine[20] give the b.p. of their compound as 87–90° (10 mm.)

Anal. Calcd. for $C_5H_4N_2Cl_2$: C, 36.84; H, 2.47; N, 17.19. Found: C, 37.03; H, 2.73; N, 17.34.

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(26) B. Klein and N. E. Hetman, unpublished observations.

(27) Melting points were taken on a heated metal block and are uncorrected.

(28) Microanalyses by Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.

(29) B. Klein and J. Berkowitz, *J. Am. Chem. Soc.*, **81**, 5160 (1959).

(30) Pyrazine mono- and di-N-oxides react with almost explosive violence, when mixed with phosphoryl chloride and heated above 60°.

(31) The authors are grateful to Mr. Fred Dorf, American Cyanamid Co., Calco Division, Bound Brook, N. J., for a generous supply of 2-chloropyrazine and 2,6-dichloropyrazine.

(32) The melting points of this compound was reported, without experimental details, as 96° by H. Shindo, *Chem. Pharm. Bull.* (Japan), **8**, 33 (1960). Bernardi, *et al.*,[7] give the m.p. as 97–98°.

(33) Among many attempts to moderate the vigor of the reaction, one experiment was conducted in the presence of dimethylaniline. A purple colored solid soon formed. This is doubtless similar to the observation by N. A. Coats and A. R. Katritzky, *J. Org. Chem.*, **24**, 1836 (1959).

(34) The authors acknowledge with thanks the gift of an authentic specimen of 2,6-dichloropyrazine by Dr. W. E. Taft, Lederle Laboratories, Pearl River, N. Y.

(35) Bernardi and associates[7] reported that both 2,3-dichloro- and 2,6-dichloropyrazine in about equal amounts were obtained following a reaction similar to the one described. It is difficult to account for the appearance of the 2,6-dichloro isomer under these circumstances. The present authors looked diligently for the 2,3-isomer, by slowly cooling the product to complete solidification and slowly allowing the temperature to rise. All the product reliquefied between 0–4°. The melting point of the 2,3-dichloropyrazine is given as 23–24°.[14]

(36) This is in closer agreement with the melting point reported by Koelsch and Gumprecht than by the present authors.[35] C. F. Koelsch and W. H. Gumprecht, *J. Org. Chem.*, **23**, 1603 (1958).

The solid obtained in the last fraction was shown to be the hydrochloride of a chloromethylpyrazine N-oxide, since it gave an immediate precipitate with aqueous silver nitrate. A solution of the material in methanol was passed through a small column containing 4.0 g. Amberlite IRA-400 (OH^-) and eluted with methanol to give needles which on recrystallization from 95% ethanol melted 114–115°.

Anal. Calcd. for $C_5H_5N_2OCl$: C, 41.53; H, 3.49; N, 19.38. Found: C, 41.46; H, 3.81; N, 19.48.

2-Chloro-3-methylpyrazine 4-Oxide.—2-Chloro-3-methylpyrazine, b.p. 74–75° (23.5 mm.), $n^{25}D$ 1.5290–1.5299, was prepared in 81% yield from 2-hydroxy-3-methylpyrazine by the method of Karmas and Spoerri.[37]

To a solution of 12.9 g. (0.1 mole) of 2-chloro-3-methylpyrazine in 30 ml. of glacial acetic acid, 9.7 ml. of 35% hydrogen peroxide was added and the solution was heated on a water bath at 70° for 3.5 hr. A similar quantity of hydrogen peroxide was added and the heating was continued for another 3.5 hr., diluted with 30 ml. of water, and refrigerated overnight.

The solution was concentrated under reduced pressure in a rotary flash evaporator to about one-quarter the original volume, diluted with water, and reconcentrated. This was repeated twice more to remove most of the acetic acid. The residue was brought to pH 8.5 with 20% sodium hydroxide and the product extracted with chloroform. The extract was washed with water, dried over calcium chloride, and concentrated at atmospheric pressure. The residue weighed 6.2 g. (43%) and melted 69–71.5°.[38]

For analysis a portion was sublimed *in vacuo* (120°, 14 mm.) and melted 71–72.5°.

Anal. Calcd. for $C_5H_5N_2OCl$: C, 41.53; H, 3.49; N, 19.38. Found: C, 41.42; H, 3.43; N, 19.45.

2-Chloro-6-methylpyrazine 4-Oxide.—2-Chloro-6-methylpyrazine, m.p. 47–49°, was prepared in 63% yield from 2-hydroxy-6-methylpyrazine (Karmas and Spoerri[36]).

One gram (0.008 mole) in 2.4 ml. of glacial acetic acid was treated with a total of 1.6 ml. of 35% hydrogen peroxide in two portions, the second added midway in the 8-hr. heating period (65–70°). The solution was worked up as described previously to give 0.3 g. (26%) of yellowish needles, m.p. 97–110°. This was recrystallized from absolute ethanol, m.p. 108–110°.

For analysis a sample was sublimed *in vacuo*, m.p. 109–110°.

Anal. Calcd. for $C_5H_5N_2OCl$: C, 41.53; H, 3.49; N, 19.38. Found: C, 41.38; H, 3.39; N, 19.48.

2-Chloro-3-pyrazylmethanol.—To a solution of 3.8 g. (0.026 mole) of 2-chloro-3-methylpyrazine 4-oxide in 7.4 ml. of glacial acetic acid, 5.3 g. (0.052 mole) of acetic anhydride was added and the solution heated under reflux for 45 min. A probe sample at this time showed a single peak at 273 mμ, indicating that the N-oxide peak had disappeared.[29] The solution was poured into ice water, neutralized with 50% sodium hydroxide, and brought to pH 9 with 10% sodium hydroxide.

The product was extracted with ether, the extract was washed with water and dried ($MgSO_4$) and the solvent removed at atmospheric pressure. The residue which was a strong lachrymator was distilled collecting 1.4 g. (37.3%) product, b.p. 120–123° (10 mm.), $n^{31}D$ 1.5600.

Anal. Calcd. for $C_5H_5N_2OCl$[39]: C, 41.53; H, 3.49; N, 19.38. Found: C, 41.16; H, 3.53; N, 19.32.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA

Compound	Solvent	mμ, max.	log ε
Pyrazine			
2-Chloro-[a]	Ethanol	268	3.80
		274	3.80
	pH 1	273	
2-Chloro-3-methyl-	Methanol	275.5	4.13
		295 (sh)	
2-Chloro-6-methyl-	Methanol	276	3.70
		295 (sh)	
2-Hydroxy-3-methyl-[b]	Water	222	3.92
		311	3.83
2-Hydroxy-6-methyl-	Water	233	3.62
		324	3.97
2,5-Dichloro-[c]	Methanol	215	4.03
		278	3.84
2,6-Dichloro-[c]	Methanol	214.5	4.03
		278	3.84
2-Dichloromethyl-	Methanol	215	3.95
		278	3.81
		292 (sh)	
3-Chloro-, 1-oxide	Water	223	4.14
		268	4.15
2-Chloro-3-methyl-, 4-oxide	Water	219	4.14
		266	4.01
		305 (sh)	3.60
(x)Chloro-2-methyl-, N-oxide	Water	218	4.24
		259	3.91
		290 (sh)	
2-Chloro-6-methyl 4-oxide	Water	222.5	4.03
		268	4.02
		300	3.53
		309	3.46
2-Chloro-3-pyrazyl-methanol	Methanol	274	3.98
2-Chloro 3,5-dimethyl-	Methanol	279	4.24

[a] F. Halverson and R. C. Hirt [*J. Chem. Phys.*, **19**, 711 (1951)] give $\lambda_{max}^{cyclohexane}$ 270 mμ (log ε 3.8); 303 mμ (sh). [b] J. Dutcher [*J. Biol. Chem.*, **171**, 321 (1947)] gives λ_{max}^{EtOH} 225 mμ (log ε 3.8), 320 mμ (log ε 3.7). [c] Halverson and Hirt (see *a*) give $\lambda_{max}^{cyclohexane}$ 2,5-dichloropyrazine: 217 mμ (log ε 3.8), 273 mμ (log ε 3.6), 303 mμ (sh); 2,6-dichloropyrazine: 217 mμ (log ε 3.9), 273 mμ (log ε 3.9), 303 mμ (sh).

2-Chloro-3,5-dimethylpyrazine. To 31.5 ml. (0.35 mole) of warm phosphoryl chloride (60–70°), 10.9 g. (0.087 mole) of 3,5-dimethylpyrazine l-oxide was added portionwise over 40 min. and, after the addition was complete, heated under reflux for an additional 20 min. A probe sample at this time indicated a single absorption peak at 295 mμ.

Excess reagent was removed by distillation under reduced pressure and the dark residue was poured onto chopped ice with good stirring. The solution was brought to pH 8 with 20% sodium hydroxide and the product extracted with ether. The combined extracts were washed with water and dried ($MgSO_4$). The residue, after removal of solvent, was distilled collecting a

(37) G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **74**, 1583 (1952). The authors are grateful to Dr. George Karmas, Ortho Research Foundation, Raritan, N. J., for a generous quantity of 2-hydroxy-3-methylpyrazine and 2-hydroxy-6-methylpyrazine.

(38) Attempts to prepare this compound using redistilled commercial 2-chloro-3-methylpyrazine, b.p. 81–84° (42 mm.), $n^{28}D$ 1.5278, obtained from Wyandotte Chemicals Corp., Wyandotte, Mich., resulted in a mixed product, containing mostly the compound just described and a second monochloromethylpyrazine N-oxide, m.p. 51–52°, colorless needles from petroleum ether (b.p. 30–60°) after repeated chromatography on neutral alumina with much loss.

Anal. Calcd. for $C_5H_5N_2OCl$: C, 41.53; H, 3.49; N, 19.38. Found: C, 41.78; H, 3.30; N, 19.30.

$\lambda_{max}^{H_2O}$ 223 mμ (log ε 4.23), 266 mμ (log ε 4.12), 299 mμ (log ε 3.71), 308 mμ (sh) (3.63). This may be the N-oxide of 2-chloro-5-methylpyrazine which was reported formed as a by-product of the action of chlorine on 2-methylpyrazine (see Hirschberg and Spoerri[24]) or an isomer of 2-chloro-6-methylpyrazine 4-oxide (private communication from Wyandotte Chemicals Corp.). However, see preceding.

(39) It had been assumed that the reaction product was the expected 2-chloro-3-pyrazylmethanol acetate. After the results of the elemental analysis were received, indicating a compound of lower carbon content, an examination of the infrared absorption spectrum indicated the presence of hydroxyl (2.9 μ) and also the absence of any absorption in the carbonyl region.

Examples of similar ease of hydrolysis of pyrazylmethanol acetates have been reported (ref. 26). This has been shown to be a common occurrence among N-heterocyclic methanolacetates (B. Klein and N. E. Hetman, unpublished observations). See Abstracts of New York–New Jersey Section Regional Meeting, New York, N. Y., January, 1962.

total of 9.7 g. (78.3%) in three fractions, b.p. 87–91° (22 mm.), n^{27}D 1.5241–1.5259. This product was a colorless oil, with small amounts of suspended colorless solid. On refrigeration the entire product crystallized in large needles, which reliquefied on warming to room temperature. This was redistilled collecting a total of 7.3 g., b.p. 92–94° (42 mm.), n^{27}D 1.5246–1.5248. Karmas and Spoerri[37] give the boiling point of this compound as 111–112° (70 mm.), n^{24}D 1.5230.[40]

Absorption Spectra.—The ultraviolet absorption spectra were taken either on a Beckman DU spectrophotometer or a Bausch and Lomb Model 505 recording spectrophotometer. These are given in Table I. Infrared absorption spectra were taken on a Perkin-Elmer Model 21 recording specctrophotometer calibrated with a polystyrene film.

(40) After this manuscript was completed, the present authors were informed by Dr. Robert I. Meltzer, Warner Lambert Research Institute, Morris Plains. N. J., that the second product resulting from the direct chlorination of 2-methylpyrazine (ref. 23 and 24) had been identified as 2-chloro-6-methylpyrazine. On the basis of this and other work contained in a paper submitted for publication by Dr. Meltzer and his associates, it is now believed that the 51–52° monochloromethylpyrazine N-oxide (ref. 38) is probably 2-chloro-3-methylpyrazine 1-oxide. The present authors are grateful to Drs. Meltzer and Wilson B. Lutz and their co-workers for the opportunity to read their paper prior to publication.

Carbonium Ion Intermediates in the Deamination of 3-Methyl-2-butylamine and Isopentylamine[1]

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The products from the solvolysis of 3-methyl-2-butyl tosylate and the deamination of 3-methyl-2-butylamine and isopentylamine in aqueous acetic acid have been determined. Comparison of the tosylate solvolysis with the deamination of 3-methyl-2-butylamine leads to the conclusion that an open 3-methyl-2-butyl carbonium ion is an important intermediate in the latter reaction. The *t*-pentyl carbonium ion from deamination of 3-methyl-2-butylamine and the *t*-pentyl and 3-methyl-2-butyl carbonium ions from deamination of isopentylamine do not behave as normal solvolytic carbonium ions. Formation of 1,2-dimethylcyclopropane in the deamination reactions is considered in relation to the general question of cyclopropane formation, 1,3-hydride shifts, and 1,2-alkyl migrations in simple carbonium ion systems.

Our general interest in exploring the relationship between the mode of formation and the behavior of carbonium ions has led to an investigation of carbonium ions generated in halide solvolyses and amine deaminations. Figure 1 diagrams the system chosen for our initial research; an earlier report has considered[2] reactions of *t*-pentyl and neopentyl starting materials in terms of the intermediates in the upper part of Fig. 1. The present paper analyzes carbonium ion reactions of 3-methyl-2-butyl and isopentyl compounds using an approach whose merits and limitations were evaluated previously[2] (*cf.* Fig. 1).

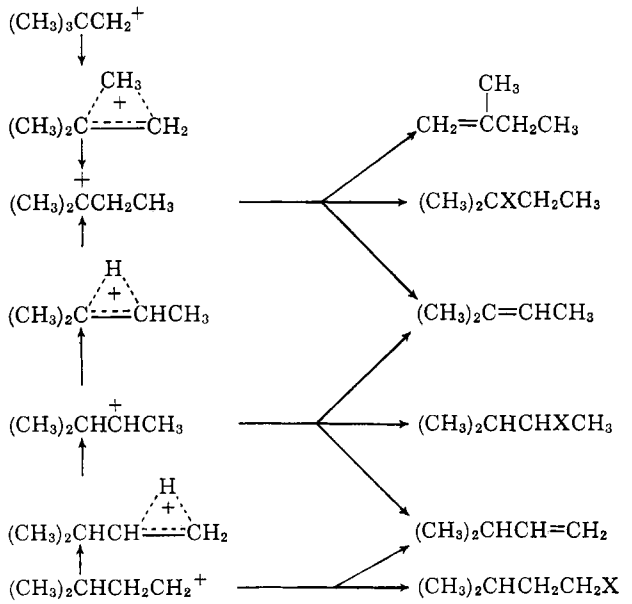

Figure 1

Results

Table I records the observed composition of the products from the deamination of 3-methyl-2-butylamine and isopentylamine, as determined by gas–liquid partition chromatography (g.l.p.c.) and infrared analysis. Reproducibility in duplicate runs is seen to be good. Control runs established the stability of the acetates and *t*-pentyl alcohol, the instability of 3-methyl-2-butanol and isopentyl alcohol and the selective destruction of 2-methyl-2-butene under the deamination conditions. The Experimental discusses determination of corrections for product instability and Table II summarizes product compositions after such corrections. Comparison of lines 7 and 11 to lines 13 and 14 (Table I) and of Table I to Table II demonstrates that corrections for the instability of the two alcohols alter the composition of the substitution product detectably but not significantly. The same comparisons reveal that corrections for olefin fractionation are more important. Since the fact that relatively little 2-methyl-2-butene is formed in the deaminations will play a prominent part in our discussion, we have applied maximum corrections for 2-methyl-2-butene destruction. The observation that the uncorrected olefin compositions for runs 9 and 12 agree with the corrected values for runs 7 and 11 (Table I), respectively, confirms the validity of these corrections. The first two reactions produced large quantities of olefin, and in such instances olefin fractionation becomes insignificant. The degree of olefin fractionation also diminishes as the water content of the solvent increases, as may be seen by comparing the data in Tables I and II for different solvent compositions.

Discussion

The 3-Methyl-2-butyl System.—Winstein and Takahashi[3] established neighboring group rate enhancement

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(2) M. S. Silver, *J. Am. Chem. Soc.*, **83**, 3482 (1961).

(3) S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958).