was evolved. The mixture was then diluted with 30 ml. of water and distilled. Treatment of the distillate with 2,4-dinitrophenylhydrazine reagent solution gave an orange precipitate, which was purified by chromatography on an alumina column. Elution with benzene gave 0.08 g. (8.5%) of acetone dinitrophenylhydrazone, m.p. 115–120°, undepressed by mixture with an authentic sample. Furthermore, the infrared spectrum of this product was identical with that of an authentic sample.

Benzoic acid (0.33 g., 65%) was isolated from the higher boiling part of the dioxane solution and from the undistilled part of the sulfuric acid reaction mixture.

ANN ARBOR, MICH.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

Investigation of Some Dialkylamino Isocyanides[1]

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Some 3-dialkylaminopropylamines and 2-dialkylaminoethylamines have been converted to the corresponding isocyanides by the Hofmann synthesis. Neither hydroxyalkylamines nor *N,N*-dialkylhydrazines could be converted to isocyanides. In several Hofmann syntheses formamides were formed. *N*-Dialkylaminoalkylcarbonimidyl chlorides and 1-dialkylaminoalkyltetrazoles were prepared by treating the corresponding isocyanides with chlorine or hydrogen azide.

Isocyanides have been known for 90 years due to their discovery independently by Hofmann[2] and Gautier.[3] In that time two general syntheses have been developed: the action of silver cyanide on alkyl iodides,[2–5] and the action of alkali on a mixture of chloroform and an amine.[2,5–8] Aryl isocyanides with various functional groups on the benzene nucleus have been prepared, but no aliphatic isocyanides with other functional groups have yet been reported. This paper reports the synthesis and properties of a group of dialkylaminoalkyl isocyanides, and the attempted preparation of some hydroxyalkyl isocyanides and isocyanoamines by the known general methods.

The Hofmann synthesis was used successfully to prepare 3-diethylaminopropyl isocyanide (IIa), 3-dimethylaminopropyl isocyanide (IIb), and 2-diethylaminoethyl isocyanide (IIc) from the corresponding amines (Ia, b, c). The adaptation described by Malatesta[8] was found to be the most convenient for carrying out the reaction. The yields were low, and the products were accompanied by unreacted amine and tar.

$$\underset{\text{(I)}}{\mathrm{R{-}NH_2}} \xrightarrow[\text{KOH}]{\text{CHCl}_3} \underset{\text{(II)}}{\mathrm{R{-}NC}}$$

a, R = $(C_2H_5)_2NCH_2CH_2CH_2$—;
b, R = $(CH_3)_2NCH_2CH_2CH_2$—;
c, R = $(C_2H_5)_2NCH_2CH_2$—.

A black, tarry mass remained after the isocyanides and unreacted amines were distilled from the reaction mixtures. Attempts to remove any higher boiling component from the tar by further distillation resulted, in the case of IIa, only in extensive decomposition. However, from the tar obtained in the preparation of IIb there was obtained a small amount of impure carbonyl compound. Cuprous chloride successfully freed it from an isocyanide impurity by complex formation.[9] Comparison of the boiling point and infrared spectrum with those of 3-dimethylaminopropylformamide suggests that they are the same substance. Analysis, however, indicated an impurity low in nitrogen. This is also indicated by a comparison of the relative intensities of the C—H bond N—H stretching bands in the infrared with those of an authentic sample.

The Hofmann synthesis with 3-diethylaminopropylamine (Ia) and methanolic potassium hydroxide produced no isocyanide. Besides unreacted amine, there was isolated a small amount of high-boiling material, identified as 3-diethylaminopropylformamide (III) by analysis, infrared spectrum and comparison with an authentic sample.

$$\underset{\text{(Ia)}}{\mathrm{(C_2H_5)_2N(CH_2)_3NH_2}} \xrightarrow{\text{CHCl}_3\text{, KOH}} \underset{\text{(III)}}{\mathrm{(C_2H_5)_2N(CH_2)_3NHCHO}}$$

No isocyanides were isolated when 1-amino-2-propanol or 3-aminopropanol were subjected to the Hofmann synthesis. In the latter case, however,

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[1] This work was supported by the Chemical Corps, U. S. Army, under Prime Contract No. DA18-108-CML-5271, Subcontract 7, at the University of Michigan.

[2] A. Hofmann, *Ann.*, **144**, 114 (1867); **146**, 107 (1868).

[3] A. Gautier, *Ann. chim. et Phys.*, [4] **17**, 103 (1869).

[4] W. Schneidewind, *Ber.*, 21, 1329 (1888); H. Guillemard, *Ann. chim. et phys.*, [8] **14**, 408 (1908).

[5] H. Lindemann and L. Wiegrebe, *Ber.*, **63B**, 1650 (1930).

[6] J. U. Nef, *Ann.*, **270**, 267 (1892).

[7] M. Passerini, *Gazz. chim. ital.*, **50II**, 340 (1920); M. Passerini and G. Banti, *Gazz. chim. ital.*, **58**, 636 (1928); D. Hammick, R. New, N. V. Sidgwick, and L. Sutton, *J. Chem. Soc.*, 1876 (1930); R. New and L. Sutton, *J. Chem. Soc.*, 1415 (1932); H. Dreyfus, U. S. Patent **2,347,772** (*Chem. Abstr.*, **39**, 89 (1945)).

[8] L. Malatesta, *Gazz. chim. ital.*, **77**, 238 (1947).

[9] F. Klages, K. Monkemeyer, and R. Heinle, *Ber.*, **85**, 109 (1952).

traces of an isocyanide were detected by infrared spectrum.

When methanolic potassium hydroxide was added to a chloroform solution of 3-aminopropanol, there was obtained a high-boiling compound tentatively identified as 3-hydroxypropylformamide (IV). The structural assignment is based on infrared data and the results of the analogous reaction of 3-diethylaminopropylamine. The Compound IV had only an amide carbonyl bond, at 1660 cm.$^{-1}$ (6.02 μ). An attempt to prepare an authentic sample of 3-hydroxypropylformamide (IV) by heating 3-aminopropanol with formic acid gave only 3-formamidopropyl formate. The infrared spectrum of the latter compound showed absorption due to both ester and amide carbonyl. Further investigation was precluded by the minute amount obtained and by our inability to repeat its preparation.

$$HO{-}(CH_2)_3{-}NH_2 \xrightarrow{CHCl_3,\ KOH} \underset{(IV)}{HO{-}(CH_2)_3{-}NHCHO}$$

The formation of formamides during the Hofmann isocyanide synthesis must be parallel with and not subsequent to isocyanide formation, since isocyanides, once formed, are inert to alkaline conditions. If Nef's hypothesis is correct[10] that the formation of isocyanides proceeds through initial formation of dichlorocarbene, CCl_2, from chloroform, followed by addition to the amino group and hydrogen migration to give the structure R—NH—$CHCl_2$, the formation of formamides as side products can be accounted for by hydrolysis of the intermediate competing with dehydrohalogenation.

Neither *N*-aminopiperidine nor 1,1-bis(*p*-chlorophenyl)hydrazine gave isolable isocyanides when subjected to the Hofmann synthesis. This result is contrary to the report that *N*-aminopiperidine gives "the isocyanide reaction" with chloroform and potassium hydroxide.[11]

The preparation of *N*-aminopiperidine was accomplished by reducing *N*-nitrosopiperidine with lithium aluminum hydride according to the method reported by Poirier and Benington[12] for the reduction of *N*-nitrosodiphenylamine, and found to be superior to the reduction with zinc and acetic acid customarily used. The preparation of 1,1-bis(*p*-chlorophenyl)hydrazine followed the same path. *p,p'*-Dichlorodiphenylamine, required for its synthesis, was prepared by the Chapman rearrangement.[13]

Efforts to convert 2-iodoethanol and 3-iodopropanol to isocyanides by reaction with silver cyanide resulted only in tars.

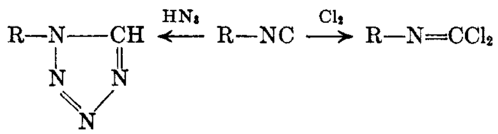
For detecting the presence of isocyanides in reaction mixtures, we found the color test of Pertusi and Gastaldi[14] useful, in which benzidine is oxidized to benzidine blue by cupric acetate when a suitable complexing agent is added. Since the test is not specific for the isocyanide function, confirmatory evidence was obtained by an examination of the infrared spectrum when possible; all of the isocyanides which we have prepared showed characteristic absorption at 2150 cm.$^{-1}$ (4.65 μ).

Samples of both 3-diethylaminopropyl and 3-dimethylaminopropyl isocyanides have been stored for weeks at room temperature in sealed ampoules without discoloring, but under identical conditions samples of 2-diethylaminoethyl isocyanide turned light yellow after one week.

Aromatic "isocyano dichlorides" (carbonimidyl chlorides) were prepared by Nef[6] by treating aromatic isocyanides with chlorine in cold chloroform solution. These compounds have been more conveniently prepared by the reaction of isothiocyanates with chlorine.[15] No aliphatic carbonimidyl chlorides have been reported before.

Passing a stream of chlorine through chloroform solutions of IIb and IIc resulted in the precipitation of rather pure *N*-(3-dimethylaminopropyl)carbonimidyl chloride and *N*-(2-diethylaminoethyl)carbonimidyl chloride. Both compounds are very hygroscopic. Treatment of 3-diethylaminopropyl isocyanide with either chlorine or bromine gave by contrast only gummy substances that could not be purified.

Isocyanides are known to give tetrazoles when treated with hydrogen azide.[16] Under such conditions, IIa, IIb, and IIc gave the corresponding 1-dialkylaminoalkyltetrazoles smoothly.



Tetrazoles are reported to have characteristic absorption in the 9 to 10 μ region of the infrared,[17] where they may have from one to three bands. The foregoing tetrazoles (as films) also absorb in this region, and each showed a band at 1100 cm.$^{-1}$ (9.08 μ), which is found in the spectra of the corresponding isocyanides. In addition, the tetrazoles showed absorption at 3100–3130 cm.$^{-1}$, which most

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(10) J. U. Nef, *Ann.*, **298**, 368 (1897).

(11) L. Knorr, *Ann.*, **221**, 299 (1883).

(12) R. Poirier and F. Benington, *J. Am. Chem. Soc.*, **74**, 3192 (1952).

(13) A. W. Chapman, *J. Chem. Soc.*, 2462 (1930).

(14) C. Pertusi and E. Gastaldi, *Chem. Ztg.*, **37**, 609 (1913); Y. Otagiri, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **70**, 263 (1949).

(15) E. Sell and G. Zierold, *Ber.*, **7**, 1228 (1874); R. Bly, G. Perkins, and W. Lewis, *J. Am. Chem. Soc.*, **44**, 2896 (1922); G. Dyson and T. Harrington, *J. Chem. Soc.*, 191 (1940), 150 (1942).

(16) (a) E. Oliveri-Mandalà, *Atti acad. Lincei*, **19I**, 228 (1910), *Chem. Abstr.*, **4**, 2455 (1910). (b) E. Oliveri-Mandalà, and B. Alagna, *Gazz. chim. ital.*, **40II**, 441 (1910). (c) F. G. Fallon and R. M. Herbst, *J. Org. Chem.*, **22**, 933 (1957). (d) F. G. Fallon, Ph.D. Thesis, Michigan State University, 1956.

(17) E. Lieber, D. Levering, and L. Patterson, *Anal. Chem.*, **23**, 1594 (1951).

likely is due to the C—H stretching frequency of the ring carbon (the usual C—H absorption was also present, at 2800–3000 cm.$^{-1}$). Somewhat similar observations have been reported by Herbst and Fallon.[16d]

Most samples of the foregoing tetrazoles also showed puzzling absorption at 2040 cm.$^{-1}$, although the samples were repeatedly distilled and gave correct analyses. These bands are undoubtedly due to impurities, however, for in one case the sample was obtained free of such absorption by careful cleaning of the distillation column immediately prior to collecting the reference cut; this technique was not successful with all samples. During the distillation of some of the crude samples of 1-(3-diethylaminopropyl)tetrazole, decomposition became evident at a bath temperature of 140° and a pressure of 0.3 mm., with concomitant distillation of a small amount of yellow, foamy, viscous liquid, prior to the actual distillation of the tetrazole fraction. The tetrazole which afterwards distilled was identical in all respects to the other samples, except for the absence of the 2040 cm.$^{-1}$ infrared absorption. This band is thus presumably due to an azide contaminant that can decompose during distillation.

EXPERIMENTAL[18]

Preparation of isocyanides. (*a*) *3-Diethylaminopropyl isocyanide* (IIa). A mixture of 40 g. of powdered potassium hydroxide and 100 ml. of benzene was placed in a 1-l. round-bottom flask equipped with a reflux condenser, drying tube, stirrer, and dropping funnel. The mixture was stirred and heated under reflux, and gradually a solution of 15.8 g. of 3-diethylaminopropylamine in 29 ml. of chloroform was added. At a point during the addition the reaction became violently exothermic. Heating was immediately discontinued, and the reaction was moderated but not quenched by cooling the mixture externally with ice water. The remainder of the chloroform solution was added at a rate to maintain vigorous refluxing, and the mixture was then allowed to stand until cool. It was then filtered, the brown, tarry precipitate was washed with benzene, and the washings were added to the filtrate. Solvent was removed, and further distillation gave a fraction of b.p. 87–107°/45 mm., and a tarry residue. Attempted further distillation of this residue at 1.0 mm. resulted only in decomposition. The distillate was redistilled to give 2.49 g. of 3-diethylaminopropylamine, 2.37 g. of mixture of b.p. 86–105°/45 mm., and 2.99 g. (20.5%) of 3-diethylaminopropyl isocyanide, b.p. 105–107°/45 mm. This product was a clear, colorless liquid having the typical isocyanide infrared absorption band at 2150 cm.$^{-1}$ (4.65 μ).

Anal. Calcd. for $C_8H_{16}N_2$: C, 68.51; H, 11.51; N, 19.98. Found: C, 68.67; H, 11.64; N, 20.06.

(*b*) *3-Dimethylaminopropyl isocyanide* (IIb). The reaction of a solution of 14.9 g. of 3-dimethylaminopropylamine in 29 ml. of chloroform with a mixture of 40 g. of powdered potassium hydroxide and 100 ml. of benzene was carried out as in (*a*) to give 2.10 of 3-dimethylaminopropylamine, 1.89 g. of mixture of b.p. 65–86°/55 mm., and 1.80 g. (11%) of 3-dimethylaminopropyl isocyanide, b.p. 86–88°/55 mm. This product was a clear, colorless liquid showing infrared absorption at 2150 cm.$^{-1}$

Anal. Calcd. for $C_6H_{12}N_2$: C, 64.23; H, 10.80; N, 24.97. Found: C, 64.19; H, 10.84; N, 25.04.

(*c*) *2-Diethylaminoethyl isocyanide* (IIc). A solution of 17.9 g. of 2-diethylaminoethylamine in 40 ml. of chloroform was treated with a mixture of 55 g. of powdered potassium hydroxide and 140 ml. of benzene as in (*a*), and gave 4.05 g. of 2-diethylaminoethylamine, 1.60 g. of fraction of b.p. 64–94°/45 mm., and 2.90 g. (14.8%) of diethylaminoethyl isocyanide, b.p. 94–95°/45 mm. The clear, colorless product gradually became yellow when stored at room temperature, even in a sealed ampoule; it showed infrared absorption at 2150 cm.$^{-1}$

Anal. Calcd. for $C_7H_{14}N_2$: C, 66.62; H, 11.18; N, 22.20. Found: C, 66.72; H, 11.20; N, 22.18.

3-Diethylaminopropylformamide. A solution of 11.2 g. of 3-diethylaminopropylamine in 20 ml. of chloroform and 20 ml. of methanol was prepared, and 40 g. of potassium hydroxide in 90 ml. of methanol was added over 0.5 hr.; the vigorous reaction which took place caused rapid refluxing. The mixture was then cooled and filtered, and the solid was washed with fresh methanol. The combined filtrates were concentrated by distillation until two layers became evident. The bottom layer was discarded, and the top layer was distilled to give 2.79 g. of recovered amine and 2.93 g. (22%) of 3-diethylaminopropylformamide, b.p. 110–114°/1.3–1.6 mm. A sample prepared for analysis had b.p. 116–118°/2 mm., and showed infrared absorption at 3250 cm.$^{-1}$ (N—H), 1540 cm.$^{-1}$ (N—H), and 1670 cm.$^{-1}$ (amide carbonyl).

Anal. Calcd. for $C_8H_{18}N_2O$: C, 60.72; H, 11.46; N, 17.71. Found: C, 60.97; H, 10.84; N, 17.87.

This substance was identical in boiling point and infrared spectrum with a sample prepared by heating and distilling a mixture of 3-diethylaminopropylamine and excess formic acid, stirring the viscous distillate with ether and solid potassium hydroxide until the initially two liquid phases had become one, filtering, and redistilling.

Anal. Found: C, 60.77; H, 11.61; N, 17.74.

3-Dimethylaminopropylformamide. A mixture of 3-dimethylaminopropylamine and excess formic acid was heated for 1.5 hr., water and formic acid were removed by distillation, and the residue was mixed with ether (two phases) and stirred with powdered potassium hydroxide. Filtration and distillation gave a colorless liquid, b.p. 92–95° at 0.7 mm., showing infrared absorption at 3275, 1540, and 1665 cm.$^{-1}$

Anal. Calcd. for $C_6H_{14}N_2O$: C, 55.35; H, 10.84; N, 21.52. Found: C, 55.40; H, 10.67; N, 21.58.

A substance of identical boiling point was obtained from distillation of the pot-residue from the preparation of 3-dimethylaminopropyl isocyanide described herein. The crude distillate from an experiment with 26.8 g. of amine weighed 1.18 g., b.p. 84–88° at 0.3 mm. It was diluted with ether, stirred with cuprous chloride to remove isocyanide contamination, dried over sodium hydroxide, and distilled at 92–94° at 0.7 mm. for comparison. Although the infrared spectrum was identical with that of 3-dimethylaminopropylformamide, except for a difference in the relative intensities of the C—H and N—H stretching bands, the analysis was not in agreement; it was not further investigated.

Anal. Found: C, 57.30, 57.39; H, 10.39, 10.35.

Hofmann synthesis with 3-aminopropanol. When 11.0 g. of 3-aminopropanol was treated with chloroform and methanolic potassium hydroxide in the usual manner, there was recovered 1.86 g. of unreacted 3-aminopropanol-1, b.p. 112–113° at 40 mm. Further distillation gave a mixture showing spectral characteristics of both amide and isocyanide, wt. 0.8 g., b.p. 70° at 0.6 mm., and 1.90 g. of an oil, b.p. 142–146° at 0.7 mm., showing infrared absorption typical of amides at 1540 and 1660 cm.$^{-1}$ and O—H absorption at 3280 cm.$^{-1}$ The last substance may be 3-hydroxypropyl-

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[18] All melting points are corrected. Infrared spectra of solids are of Nujol mulls, and of liquids are of thin films. Analyses are by Spang Microanalytical Laboratory, Ann Arbor.

formamide. Additional attempts to obtain more of these substances led only to recovered amino alcohol.

3-Formamidopropyl formate. A solution of 3-aminopropanol in excess formic acid was refluxed for 2 hr. and then distilled to remove water and formic acid. Further distillation gave a colorless, viscous distillate of b.p. 132–134°/0.7 mm. and showing infrared absorption at 3280, 1665, and 1720 cm.$^{-1}$, consistent with the presence of N—H, ester carbonyl, and amide carbonyl.

Anal. Calcd. for $C_5H_9NO_3$: C, 45.79; H, 6.92; N, 10.86. Found: C, 46.05; H, 7.15; N, 10.67.

N-Formamidopiperidine. A solution of 23.5 g. of *N*-aminopiperidine[11] in excess formic acid was refluxed for 2 hr., and formic acid and water were removed by distillation. Further distillation gave 19.9 g. (70%) of an oil, b.p. 111–114°/1 mm., which soon solidified to a white solid, m.p. 75–77.5°. An analytical sample, m.p. 77–78°, was obtained by several recrystallizations from petroleum ether.

Anal. Calcd. for $C_6H_{12}N_2O$: C, 56.22; H, 9.45; N, 21.86. Found: C, 56.28; H, 9.42; N, 21.79.

Attempts to convert *N*-formamidopiperidine to an isocyanide by dehydration *via* the imidyl chloride, using phosphoryl chloride with excess pyridine or triethylamine, were completely unsuccessful.

N-p-Chlorophenylbenzimidyl chloride.[19] This compound was prepared according to a procedure reported for *N*-phenylbenzimidyl chloride.[20] The crude product was a pale green oil which solidified when chilled in an ice bath. It was dissolved in ether and used directly for the preparation of its *p*-chlorophenyl ester.

p-Chlorophenyl N-p-Chlorophenylbenzimidate. To 20 ml. of absolute alcohol was added 1.21 g. of sodium. The solution was cooled and 6.8 g. of *p*-chlorophenol was added. An ethereal solution of the imidyl chloride prepared from 4.5 g. of benz-*p*-chloroanilide was then added. The mixture was stirred for several hours after the initial boiling had subsided, and was then filtered. Distilling the ether from the filtrate and chilling the residue gave 4.3 g. (64%) of pale yellow rods, m.p. 70–72°; Chapman[19] reports 68–69°.

N,N-Bis(p-chlorophenyl)benzamide and p,p'-Dichlorodiphenylamine. By the general method of Chapman,[21] 13.9 g. of *p*-chlorophenyl *N*-*p*-chlorophenylbenzimidate was rearranged to the diarylbenzamide, which on recrystallization from ethanol gave 10.8 g. (78%) of product, m.p. 155–156°. Claus and Schaare[22] prepared this compound by chlorination of *N,N*-diphenylbenzamide, and reported m.p. 153–154°; in our hands their method was unsuccessful.

Hydrolysis of 16.6 g. of the foregoing *N,N*-bis(*p*-chlorophenyl)benzamide by the method of Chapman[23] and recrystallization of the crude product from petroleum ether gave 10.8 g. (94%) of long, straw colored needles, m.p. 79–81°. Chapman reports 78–79°.[19]

N-Nitrosobis(p-chlorophenyl)amine. Dichlorodiphenylamine was nitrosated by the procedure reported by Fischer for nitrosating diphenylamine.[24] The initially oily product solidified when agitated and chilled; dilution of the reaction mixture with water caused a further amount to precipitate. The yellow solid was collected, washed with water, dried in air, and crystallized from petroleum ether (b.p. 60–75°) to give yellow plates, m.p. 81–82°, in yields of about 95% in several trials.

Anal. Calcd. for $C_{12}H_8N_2OCl_2$: C, 53.96; H, 3.02. Found: C, 54.19; H, 3.09.

1,1-Bis(p-chlorophenyl)hydrazine. *N*-Nitroso-*p,p'*-dichlorodiphenylamine was reduced by the procedure used by Poirier and Benington[12] with *N*-nitrosodiphenylamine. From 10 g. of nitroso compound in 50 ml. of dry ether and a slurry of 2.0 g. of lithium aluminum hydride in 75 ml. of ether, the desired hydrazine was obtained and isolated as its hydrochloride, dec. 158°. The free hydrazine was obtained by stirring a mixture of the hydrochloride, aqueous sodium hydroxide, and ether until no more undissolved hydrochloride was present, extracting the aqueous layer with ether, and evaporating the combined extracts on a steam bath. A white, crystalline mass was obtained on cooling. Recrystallization from petroleum ether (60–75°) gave white needles, m.p. 92.5–94°, in yields of about 70% in several trials. Infrared absorption occurred at 3200 and 3500 cm.$^{-1}$

Anal. Calcd. for $C_{12}H_{10}N_2Cl_2$: C, 56.94; H, 4.27; N, 11.07. Found: C, 57.21; H, 4.05; N, 11.26.

The compound formed a *benzoyl derivative*, m.p. 219–219.5° from benzene; decomposition, as evidenced by a pink discoloration, began shortly after preparation, and may have affected the analysis.

Anal. Calcd. for $C_{15}H_{14}N_2Cl_2$: C, 63.87; H, 3.95. Found C, 63.36; H, 3.82.

With acetone, the hydrazine gave *acetone bis-(p-chlorophenyl)hydrazone*, m.p. 79–79.5° from petroleum ether (b.p. 60–75°).

Anal. Calcd. for $C_{15}H_{14}N_2Cl_2$: C, 61.45; H, 4.81; N, 9.56. Found: C, 61.74; H, 4.82; N, 9.55.

2,2-Bis(p-chlorophenyl)formhydrazide. A mixture of 1,1-bis(*p*-chlorophenyl)hydrazine and excess 98% formic acid was refluxed for 2 hr. Cooling caused precipitation of the product, which was washed with water, air-dried, and recrystallized from benzene to give a fluffy matted mass of white rods, m.p. 212.5–213°. Attempts to convert this compound to an isocyanide *via* the imidyl chloride by reaction with phosphoryl chloride and pyridine or triethylamine were unsuccessful.

Anal. Calcd. for $C_{13}H_{10}N_2OCl_2$: C, 55.54; H, 3.59; N, 9.97. Found: C, 55.53; H, 3.50; N, 10.00.

N-(3-Dimethylaminopropyl)carbonimidyl dichloride. A solution of 1.44 g. of 3-dimethylaminopropyl isocyanide in 11 ml. of chloroform was well cooled in an ice bath, and a stream of chlorine was bubbled through until the solution was yellow. The resulting precipitate was filtered off, dried in air for an hour, and then *in vacuo*, to give 1.45 g. (62%) of a white, electrostatically charged powder, m.p. 130.5–132°. It was very hygroscopic.

Anal. Calcd. for $C_6H_{12}N_2Cl_2$: C, 39.36; H, 6.61; N, 15.30. Found: C, 39.48; H, 6.76; N, 15.41.

N-(2-Diethylaminoethyl)carbonimidyl dichloride. A solution of 4.10 g. of 2-diethylaminoethyl isocyanide in 30 ml. of chloroform was well cooled in an ice bath, and a stream of chlorine was passed through until saturation. The resulting precipitate was collected, washed with cold chloroform, dried in air for an hour and then *in vacuo* to give 4.06 g. (64%) of a white solid, m.p. 117–119°. After recrystallization from chloroform it had m.p. 120–122° and was very hygroscopic.

Anal. Calcd. for $C_7H_{14}N_2Cl_2$: C, 42.65; H, 7.15; N, 14.22. Found: C, 42.71; H, 7.31; N, 14.26.

1-(3-Diethylaminopropyl)tetrazole. A solution of 6.7 g. of 3-diethylaminopropyl isocyanide in 40 ml. of benzene was cooled in an ice bath, and 60 ml. of a 10% solution of hydrogen azide in benzene was added gradually. After standing overnight, the mixture had separated into two layers. The upper layer was decanted and discarded, and the lower was distilled to give 4.8 g. (55%) of a yellow liquid, b.p. 150–153° at 0.8 mm. Redistillation gave a colorless sample, b.p. 135–138° at 0.3 mm., that burned in a flame with sputtering.

Anal. Calcd. for $C_8H_{17}N_5$: C, 52.43; H, 9.35; N, 38.22. Found: C, 52.47; H, 9.22; N, 38.26.

1-(3-Dimethylaminopropyl)tetrazole. In the manner just described, 5.0 g. of 3-dimethylaminopropyl isocyanide gave 4.2 g. (61%) of tetrazole in the form of a colorless liquid, b.p. 116–120° at 0.2 mm., that burned in a flame with sputtering.

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(19) H. Ley, *Ber.*, **31**, 241 (1898).

(20) O. Wallach and M. Hoffmann, *Ann.*, **184**, 79 (1877).

(21) A. W. Chapman, *J. Chem. Soc.*, 1743 (1927).

(22) A. Claus and H. Schaare, *Ber.*, **15**, 1285 (1882).

(23) A. W. Chapman, *J. Chem. Soc.*, 569 (1929).

(24) E. Fischer, *Ann.*, **190**, 174 (1878); A. Lachman, *Ber.*, **33**, 1022 (1900).

Anal. Calcd. for $C_6H_{13}N_5$: C, 46.43; H, 8.44; N, 45.13. Found: C, 46.36; H, 8.51; N, 45.17.

1-(2-Diethylaminoethyl)tetrazole. In the manner just described, 12.2 g. of 2-diethylaminoethyl isocyanide was treated with hydrogen azide; the reaction mixture stayed as one phase. The benzene and excess hydrogen azide were distilled off, and further distillation gave 11.2 g. (69%) of a pale yellow liquid, b.p. 128–132° at 0.3 mm.

Anal. Calcd. for $C_7H_{15}N_5$: C, 49.68; H, 8.93; N, 41.39. Found: C, 49.43; H, 8.67; N, 41.53.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Some Diazine-*N*-oxides[1]

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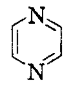
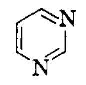
Preparations of mono- and di-*N*-oxides of pyrazine, 2-methylpyrazine, and 2,5-dimethylpyrazine, and of mono-*N*-oxides of pyrimidine and pyridazine are described. The oxides of methylated pyrazines undergo normal Boekelheide rearrangement with acetic anhydride, forming acetoxymethylpyrazines, but all of the oxides were resistant to nitration. A strong absorption at 1230–1325 cm.$^{-1}$ appears to be characteristic of the *N*-oxide function.

Heteroaromatic *N*-oxides have been studied extensively in recent years,[2] but little is known about the *N*-oxides of simple diazines.[3] Preparations and a few reactions of some of these substances are described in the present paper.


I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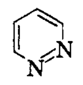
III

Pyrazine (I), 2-methylpyrazine, and 2,5-dimethylpyrazine yielded mainly mono-oxides when treated with one equivalent of hydrogen peroxide in hot acetic acid. As expected, two isomeric mono-oxides of 2-methylpyrazine were formed. In each preparation, small amounts of the corresponding dioxides were also produced, and these compounds were obtained in good yields when excess hydrogen peroxide was used.

Pyrimidine (II) was destroyed by hydrogen peroxide in hot acetic acid, but at room temperature it furnished 6.5% of its mono-oxide (m.p. 95–96°) together with 2.5% of 4(3) pyrimidone; a di-oxide could not be obtained. The yield (11%) and m.p. (85–88°) of pyrimidine mono-oxide reported recently[3j] were not duplicated, but the product obtained in the present work had the same infrared absorption as that described.

Pyridazine (III) gave only a mono-oxide, the best yield being obtained by oxidation at room temperature.

2,5-Dimethylpyrazine mono-oxide formed 1:1 addition products with hydrogen chloride, methyl iodide, or benzyl chloride. Spectral studies did not permit a definite decision as to the point of attachment of the electrophilic reagent, but basification of the benzyl chloride adduct gave no benzaldehyde, indicating that salt formation had involved the unoxidized nitrogen atom. A similar conclusion regarding salt formation was reached by Landquist[3h] in his study of quinoxaline mono-oxide.

2,5-Dimethylpyrazine mono-oxide reacted with acetic anhydride to form 2-acetoxymethyl-5-methylpyrazine, the product expected by analogy with Boekelheide's work in the pyridine series.[4] The same substance, together with 2,5-bisacetoxymethylpyrazine was obtained from 2,5-dimethylpyrazine dioxide. 2-Acetoxymethyl-5-methylpyrazine dioxide was partly deoxidized by acetic anhydride, giving 2,5-bisacetoxymethylpyrazine and its mono-oxide and 2-acetoxymethyl-5-methylpyrazine mono-oxide.

Assignment of structures to the two isomeric mono-oxides of 2-methylpyrazine was based on reactions with acetic anhydride. 2-Methylpyrazine-1-oxide (m.p. 43–45°) gave an acetate saponified to 2-hydroxymethylpyrazine, which showed strong broad —OH absorption at 3300 cm.$^{-1}$ 2-Methylpyrazine-4-oxide (m.p. 91–92°) gave an acetate saponified to 5-methyl-2(1)-pyrazinone, showing weak absorption at 1660 cm.$^{-1}$

Corresponding to observations of Adams and Miyano[5] in the pyridine series, 2,5-dimethylpyra-

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(1) From the Ph.D. thesis of W. H. Gunprecht, July 1957.

(2) C. C. J. Culvenor, *Revs. Pure and Appl. Chem.* (*Australia*), **3**, 83 (1953); E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953); A. R. Katritzky, *Quart. Revs.*, **10**, 395 (1956); M. Colonna, *Bull. sci. soc. chim. ind. Bologna*, **15**, 1 (1957).

(3) (a) E. Ochiai, M. Ishikawa, and S. Zai-Ren, *J. Pharm. Soc. Japan*, **65**, 73 (1945); (b) G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 1183 (1947); (c) R. A. Baxter, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, 1859 (1948); (d) W. Sharp and F. S. Spring, *J. Chem. Soc.*, 932 (1951); (e) G. T. Newbold, W. Sharp, and F. S. Spring, *J. Chem. Soc.*, 2679 (1951); (f) E. Ochiai and H. Yamonaka, *Pharm. Bull.* (*Tokyo*), **3**, 175 (1955); (g) W. F. Beech, *J. Chem. Soc.*, 3094 (1955); (h) J. K. Landquist, *J. Chem. Soc.*, 1885 (1956); (i) G. Karmas and P. E. Spoeri, *J. Am. Chem. Soc.*, **78**, 4071 (1956); (j) R. H. Wiley and S. C. Slaymaker, *J. Am. Chem. Soc.*, **79**, 2233 (1957).

(4) V. Boekelheide and W. J. Linn, *J. Am. Chem. Soc.*, **76**, 1286 (1954).

(5) R. Adams and S. Miyano, *J. Am. Chem. Soc.*, **76**, 3168 (1954).