ing point determination with authentic 2,4-methylene-xylitol caused no depression of this value. The yield was 2.8 g. (88%). The series of reactions constitutes a definitive proof that monomethylene-gluco-*gulo*-heptitol is 3,5-methylene-gluco-*gulo*-heptitol.

Although the expected dialdehydo oxidation product from 3,5-methylene-gluco-*gulo*-heptitol could not be crystallized, it was isolated in a separate experiment in the form of its di(phenylhydrazone). The latter compound crystallized from 30 parts of alcohol as small, light yellow plates which melted with decomposition at 188–190°.

Anal. Calcd. for $C_{18}H_{20}O_3N_4$: C, 63.51; H, 5.92; N, 16.46. Found: C, 63.23; H, 6.10; N, 16.56.

Summary

Proof is presented that the monobenzylidene-gluco-*gulo*-heptitol (m. p. 218°) which Emil Fischer discovered is the 3,5-benzylidene acetal. The condensation of gluco-*gulo*-heptitol with formaldehyde also gives a high yield of a monoacetal which proves to be 3,5-monomethylene-gluco-*gulo*-heptitol. These 3,5-monoacetals are those to be expected from generalizations relating the configuration of polyhydric alcohols and the structure of their derived benzylidene and methylene acetals.

Crystalline 2,4-benzylidene-xylitol and a number of its derivatives have been described.

BETHESDA, MARYLAND RECEIVED MAY 9, 1946

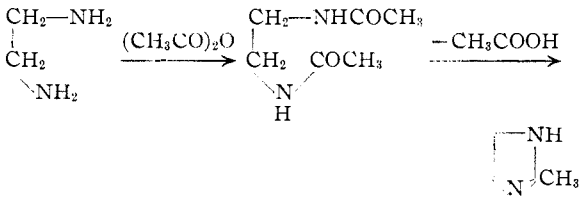
[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

The Preparation of Some Monoalkyl- and Symmetrical Dialkylethylenediamines

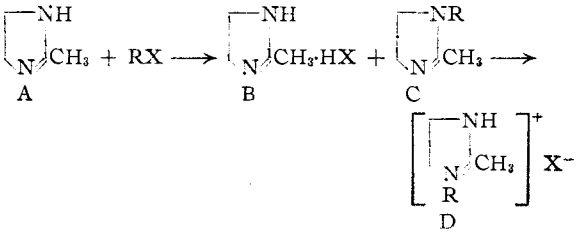
BY JOHN A. KING AND FREEMAN H. MCMILLAN

It was hoped that a convenient preparation of monoalkylethylenediamines[1,1a] could be realized by making use of the fairly readily available 2-methylimidazoline. Following the observation of Ladenburg[2] that 2-methylimidazoline methylated easily, and the finding by Aspinall[3] that 2-substituted imidazolines could be hydrolyzed to ethylenediamine without great difficulty, it seemed reasonable to assume that the preparation of 1-alkyl-2-methylimidazolines and their hydrolysis to monoalkylethylenediamines should afford a satisfactory source of such diamines. In the present work only moderate success was attained by this method.

Commercial (70%) ethylenediamine was converted in essentially quantitative yield to the symmetrical diacetyl derivative[4] with acetic anhydride. By a procedure based on Chitwood and Reid's[5] modification of Ladenburg's original preparation of the material, symmetrical diacetylethylenediamine was pyrolyzed over magnesium powder to give 2-methylimidazoline in yields ranging from 86 to 94%. This represents some improvement over previously reported yields for this reaction.[6]



The alkylation reaction proved to be much more complex than had been anticipated; in addition to the desired product (C) there was



formed the quaternary ammonium salt (D), as well as the hydrohalide salt (B) of the starting material (A).

In an effort to prevent the formation of the hydrohalide of the initial imidazoline, which removed the starting material from participation in any addition reaction, some of the reactions were run in the presence of potassium carbonate to neutralize the halogen acid as soon as it was formed. However, only quaternary products were formed.

The results obtained are summarized in Table I.

Our alkylation data are in general agreement with the very recently available results of Kyrides[6] who obtained 30 to 40% yields (based on halide used) of 1-higher alkyl-2-lower alkyl imidazolines by alkylation of 2-substituted imidazolines with only one-half mole of alkyl halide in an hydrocarbon solvent. He did not hydrolyze the imidazolines to ethylenediamines or report any investigation of higher alkylation products.

(1) A literature review of the preparation of monoalkylethylenediamines has been given by Aspinall, THIS JOURNAL, **63**, 852 (1941). Bloom, Breslow and Hauser, *ibid.*, **67**, 539 (1945), have recently reported the preparation of isoamylethylenediamine in 20% yield by sodium and alcohol reduction of isoamylaminoacetonitrile; while still more recently Linsker and Evans, *ibid.*, **67**, 1581 (1945), have reported the preparation of higher monoalkylethylenediamines in 83 to 98% yield by direct alkylation. The present work was completed before the appearance of the last paper cited.

(1a) Pearson, Jones and Cope, *ibid.*, **68**, 1225 (1946), have very recently described the preparation of cyclohexylethylenediamine and isopropylethylenediamine.

(2) Ladenburg, *Ber.*, **27**, 2957 (1894).

(3) Aspinall, *J. Org. Chem.*, **6**, 895 (1941).

(4) Hofmann, *Ber.*, **21**, 2332 (1888).

(5) Chitwood and Reid, THIS JOURNAL, **57**, 2424 (1935).

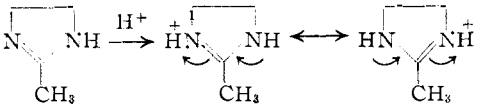
(6) Kyrides, U. S. Patent 2,392,326, prepared this and other lower alkyl 2-substituted imidazolines in substantially lower yields by calcium oxide cyclization of monoacylethylenediamines.

TABLE I[a]

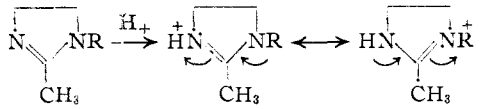
Alkyl halide used	Moles of halide	Solvent	Yield (%) of imidazoline hydrohalide	Yield (%) of monoalkylethylenediamine	Yield (%) of dialkylethylenediamine
$C_6H_5CH_2Cl$	2	C_6H_6	46	8.3[b]	6.2[b]
n-C_4H_9Br	2	C_6H_6	24	23	19
n-C_4H_9Br	2	H_2O, K_2CO_3, EtOH	0	0	34
n-C_4H_9Br	1	H_2O, K_2CO_3, EtOH	0	0	38[b]
CH_3I	2	C_6H_6			34[c]
n-C_3H_7Br	1	H_2O, EtOH		23	11.5
n-$C_5H_{11}Br$	1	H_2O, EtOH		23	12

[a] All yields are based on imidazoline used. [b] As monoacetyl derivative. [c] As alkyl halide quaternary of the dialkylimidazoline.

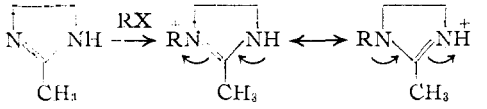
The formation of the various products in the alkylation can be readily explained by consideration of some theoretical aspects of the reaction. The relative basicities of A and C are determined by the relative stabilities of the ions produced by adding a proton to each. In the case of A this ion has two absolutely equivalent resonance forms and the resonance energy is maximal, while in



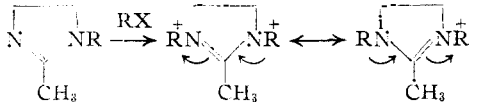
the case of C the forms are only approximately equivalent; therefore A is a stronger base than C (the ions formed from A and C in which the proton



adds to the already substituted nitrogen atom do not make major contributions to the resonance). However, the situation is somewhat different when an alkyl group is added to A and C, to form a quaternary ammonium ion. The addition of



an alkyl halide RX to A forms an ion in which the resonance structures are non-equivalent,



while the addition of the same molecule to C produces an ion which has completely equivalent resonance forms (here, as well as with proton addition, the ions formed from A and C in which RX adds to the already substituted nitrogen atom do not make major contributions to the resonance). From this reasoning it becomes clear that although the 2-alkyl imidazolines are stronger bases than the 1,2-dialkyl imidazolines, the tendency to quaternization by addition of an alkyl cation will be greater in the latter case, when the alkyl group added is identical with the group already present in the 1-position. In other words, there is no exact parallelism between basicity and quaternizability in these compounds.

We take pleasure in acknowledging the suggestions of Dr. Elmer J. Lawson regarding the alkylation mechanism herein presented.

Experimental[7,8]

2-Methylimidazoline.—In a 500-cc., round-bottomed flask was placed a mixture of *sym*-diacetylethylenediamine[4] (258 g., 1.79 moles) and magnesium powder (21.6 g., 0.90 mole). The flask was fitted with a downward condenser and was heated in a metal-bath at 310–315°. The 2-methylimidazoline distilled as a nearly colorless liquid which crystallized in the receiver. The distillate was crystallized from dry benzene (250 cc.) to give 142 g. (94% yield) of material, m. p. 85°. This melting point is considerably lower than that of a redistilled sample which melted at 100–103°. While the redistilled material compared favorably with that of Ladenburg[2] who reported a m. p. of 105°, the once recrystallized material was white, nicely crystalline and of satisfactory purity for the alkylation reactions.

Alkylation with Benzyl Chloride.—Benzyl chloride (126 g., 1.00 mole) was dropped into a solution of 2-methylimidazoline (42.0 g., 0.50 mole) in dry benzene (150 cc.). The solution was refluxed two hours then all the solvent was removed under vacuum. The residue was taken up in a small amount of dry ethanol, the solution was heated to boiling and ethyl acetate was added to incipient cloudiness. After the solution was chilled there was obtained 26.0 g. (46%) of 2-methylimidazoline hydrochloride, m. p. 155–159°. After two recrystallizations from ethanol–ethyl acetate the material melted at 171°.

Anal. Calcd. for $C_4H_8N_2$·HCl: N, 23.24. Found: N, 23.43.

The filtrate from the hydrochloride was taken to dryness under vacuum and the residue was refluxed for three hours with concentrated hydrochloric acid (400 cc.). The hydrolysis mixture was taken to dryness under vacuum and the residue was made strongly alkaline with 35% aqueous caustic soda (200 cc.). The resultant oil was separated and dried over anhydrous potassium carbonate. Fractionation gave 16 g. (8.3%) of material, b. p. 160–167° (14 mm.), and 17.5 g. (6.2%) of material, b. p. 247–257° (14 mm.).[9]

The lower boiling fraction gave a picrate melting at 155°.

Anal. Calcd. for $C_{11}H_{16}N_2O$·$C_6H_3N_3O_7$: N, 16.63. Found: N, 16.46.

The lower boiling fraction (1.0 g.) was refluxed for one hour with 10% aqueous caustic soda (20 cc.). The product was extracted with ether, the solvent was removed, and the residue was converted into a dipicrate, m. p. 216°.[10]

Anal. Calcd. for $C_9H_{14}N_2$·$2C_6H_3N_3O_7$: N, 18.41. Found: N, 18.31.

The higher boiling fraction (1.0 g.) was refluxed with concentrated hydrochloric acid (15 cc.) for two hours. A solid soon started separating from the solution. This solid was removed by filtration from the cooled reaction mixture and, after recrystallization from aqueous ethanol, did not melt up to 265°.[11]

(7) All melting points and boiling points are uncorrected.

(8) All analytical determinations were carried out under the direction of Mr. Morris E. Auerbach in the Analytical Laboratories of this Institute.

(9) These two fractions are apparently the acetyl derivatives of N-benzylethylenediamine and N,N'-dibenzylethylenediamine, respectively.

(10) Aspinall, ref. 1, reported the melting point of the dipicrate of N-benzylethylenediamine as 222°.

(11) Bleier, *Ber.*, **32**, 1829 (1899), reported that the dihydrochloride of *sym*-dibenzylethylenediamine did not melt up to 270°.

Anal. Calcd. for $C_{16}H_{20}N_2 \cdot 2HCl$: N, 8.95; Cl (ionic), 22.68. Found: N, 9.26; Cl (ionic), 22.46.

Alkylation with *n*-Butyl Bromide. A. Benzene Solution.—Quantities and procedure were the same as were used with benzyl chloride. There was obtained 19.5 g. (24%) of 2-methylimidazoline hydrobromide which melted at 159–160° after recrystallization.

Anal. Calcd. for $C_4H_8N_2 \cdot HBr$: N, 16.97. Found: N, 17.65.

The filtrate from which the hydrobromide was separated was hydrolyzed as described above and yielded on fractionation 13.5 g. (23%) of N-*n*-butylethylenediamine, b. p. 78–80° (25 mm.), and 16.3 g. (19%) of N,N'-di-*n*-butylethylenediamine, b. p. 119–125° (23 mm.).

The N-*n*-butylethylenediamine was redistilled and the fraction of b. p. 71° (13 mm.) was analyzed.

Anal. Calcd. for $C_6H_{16}N_2$: N, 24.14. Found: N, 24.10; 1.976 equivalents of hydrochloric acid consumed on direct titration.

N-*n*-Butylethylenediamine (2 cc.) was added to concentrated hydrochloric acid (25 cc.) and the resulting solution was taken to dryness under vacuum. The residue, after recrystallization from ethanol (400 cc.), melted at 231–232°; another recrystallization did not raise the m. p. of the material.

Anal. Calcd. for $C_6H_{16}N_2 \cdot 2HCl$: Cl (ionic), 37.56. Found: Cl (ionic), 37.66.

n-Butylaminoacetonitrile was prepared in 56% yield by the method of Bloom, Breslow and Hauser[1] and was reduced with sodium and alcohol to give a 14% yield of N-*n*-butylethylenediamine, b. p. 71° (13 mm.). This material gave the same dihydrochloride of m. p. 231–232°.

The N,N'-di-*n*-butylethylenediamine was redistilled and the fraction of b. p. 130° (30 mm.) was analyzed.[11a]

Anal. Calcd. for $C_{10}H_{24}N_2$: N, 16.28. Found: N, 15.7.

N,N'-Di-*n*-butylethylenediamine gave a dipicrate melting at 188–188.5°.

Anal. Calcd. for $C_{10}H_{24}N_2 \cdot 2C_6H_3N_3O_7$: diamine, 27.3; picric acid, 72.7. Found[12]: diamine, 27.2; picric acid, 74.9.

B. Aqueous Alcoholic Solution.—*n*-Butyl bromide (69 g., 0.50 mole) was added dropwise to a solution of 2-methylimidazoline (21.0 g., 0.25 mole) in a solution made up of water (200 cc.), ethanol (50 cc.) and potassium carbonate (69 g., 0.50 mole). The solution was heated on a steam-cone for four hours, cooled, saturated with potassium carbonate, and then extracted with ethanol. Concentrated hydrochloric acid (200 cc.) was added to the alcoholic extract and the resulting solution was taken to dryness under vacuum. Acid hydrolysis of the residue in the described manner gave 14.5 g. (34%) of N,N'-di-*n*-butylethylenediamine, b. p. 119–125° (23 mm.). No monoalkylated product was obtained.

The same reaction was repeated, using one-half mole (42.0 g.) of 2-methylimidazoline and keeping all other quantities the same. After the reaction was over the solution was saturated with potassium carbonate and extracted with ether.[13] The solvent was removed from the extract and the residue this time was subjected to alkaline hydrolysis for three hours with 20% aqueous caustic soda (200 cc.). The organic layer was separated, dried over potassium carbonate, and distilled to give 39.5 g. (75% based on the halide used) of monoacetyl-N,N'-di-*n*-butylethylenediamine, b. p. 184–188° (16 mm.). Acid hydrolysis of this material (21.4 g., 0.10 mole) gave 8.5 g. (50%) of N,N'-di-*n*-butylethylenediamine, b. p. 114–119° (17 mm.). There was recovered 7.0 g. (31%) of starting material.

Alkylation with Methyl Iodide.—Replacement of benzyl chloride by methyl iodide in the former procedure gave 24.2 g. (34%) of the methyl iodide quaternary of 1,2-dimethylimidazoline, m. p. 222° (dec.) after recrystallization. The filtrate was not worked up.

Anal. Calcd. for $C_5H_{10}N_2 \cdot CH_3I$: N, 11.66. Found: N, 11.37.

Alkylation with *n*-Propyl Bromide.—*n*-Propyl bromide (61.5 g., 0.50 mole) was added dropwise to a solution of 2-methylimidazoline (42.0 g., 0.50 mole) in water (150 cc.) and ethanol (50 cc.). The mixture was heated on the steam-cone for two hours, then the solvent was removed under vacuum and the residue was refluxed for six hours with concentrated hydrochloric acid (400 cc.). The hydrolysis mixture was taken to dryness under vacuum and the residue was made strongly alkaline with 35% aqueous caustic soda. The oily layer was separated, dried over solid caustic soda and fractionated to give 11.5 g. (23%) of N-*n*-propylethylenediamine, b. p. 155–156°, and 8.4 g. (11.5%) of N,N'-di-*n*-propylethylenediamine, b. p. 185–187°.

The N-*n*-propylethylenediamine was redistilled and the fraction boiling at 155° was analyzed.

Anal. Calcd. for $C_5H_{14}N_2$: N, 27.45. Found: N, 26.3.

N-*n*-Propylethylenediamine formed a dipicrate melting at 224° (dec.).

Anal. Calcd. for $C_5H_{14}N_2 \cdot 2C_6H_3N_3O_7$: N, 20.00. Found: N, 20.30.

The N,N'-di-*n*-propylethylenediamine was redistilled and the fraction boiling at 185° was analyzed.

Anal. Calcd. for $C_8H_{20}N_2$: N, 19.43. Found: N, 19.16.

Alkylation with *n*-Amyl Bromide.—The alkylation procedure used with *n*-propyl bromide was repeated exactly except that *n*-amyl bromide (75.5 g., 0.50 mole) was employed. The yield was 23% of N-*n*-amylethylenediamine, b. p. 135–140° (90 mm.) and 12% of N,N'-di-*n*-amylethylenediamine, b. p. 165–175° (90 mm.).

The N-*n*-amylethylenediamine was redistilled and the fraction boiling at 102° (30 mm.) was analyzed.

Anal. Calcd. for $C_7H_{18}N_2$: N, 21.54. Found: N, 21.00.

The dihydrochloride of N-*n*-amylethylenediamine, prepared by the same procedure as was used for the butyl compound, melted at 236–237°.

Anal. Calcd. for $C_7H_{18}N_2 \cdot 2HCl$: Cl (ionic), 34.97. Found: Cl (ionic), 35.36.

The N,N'-di-*n*-amylethylenediamine was redistilled and the fraction boiling at 149° (26 mm.) was analyzed.

Anal. Calcd. for $C_{12}H_{28}N_2$: N, 14.00. Found: N, 13.21.

The dipicrate of N,N'-di-*n*-amylethylenediamine melted at 185–185.5°.

Anal. Calcd. for $C_{12}H_{28}N_2 \cdot 2C_6H_3N_3O_7$: diamine, 30.4; picric acid, 69.6. Found: diamine, 30.7; picric acid, 70.5.

The various hydrolyses described above, as well as an even greater number of hydrolyses carried out but not described in detail, have enabled us to draw the following conclusions regarding the liberation of the free diamines: either acid or caustic hydrolysis fairly easily opens the imidazoline ring; if the acetyl diamine so produced has the acetyl group on an unalkylated nitrogen atom either vigorous acid or vigorous caustic hydrolysis will remove the acetyl group; but if the acetyl group is on an alkylated nitrogen atom only drastic acid hydrolysis will remove it.

Summary

Alkylation of 2-methylimidazoline in either benzene or aqueous alcoholic solution converts

(11a) Zienty, THIS JOURNAL, **68**, 1388 (1946), has very recently described the preparation of N,N'-dibutylethylenediamine, b. p. 110–111° (8 mm.), and some of its derivatives.

(12) The diamine was determined by acetone-perchloric acid titration and the picric acid was determined by titanous chloride titration.

(13) All of the diamines reported in this paper are relatively insoluble in water.

about half of the material to its mineral acid salt and the other half to a mixture of alkylated material and alkyl halide quaternary of the alkylated material. In the presence of potassium carbonate only the quaternary is obtained.

The following new ethylenediamines have been prepared and characterized: N-*n*-propyl, N,N'-di-*n*-propyl, N-*n*-butyl, N,N'-di-*n*-butyl, N-*n*-amyl and N,N'-di-*n*-amyl.

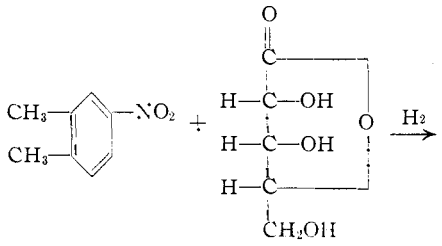
RENSSELAER, NEW YORK RECEIVED APRIL 24, 1946

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF HOFFMANN-LA ROCHE, INC.

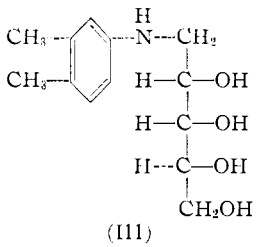
A Simplified Synthesis of N-Aryl-glycamines

BY L. M. JAMPOLSKY AND H. M. WUEST[1]

In the synthesis of riboflavin, N-(D-ribityl)-3,4-dimethylaniline (III) is an important intermediate. Some of the reported syntheses of this intermediate have been aimed chiefly at circumventing the use of D-ribose, a comparatively costly sugar. The readily available D-ribonolactone has been utilized for this purpose in procedures involving three to five steps to obtain the desired glycamine.[2] The synthesis described in this paper involves only one step, the reductive condensation of 3,4-dimethylaniline or 4-nitro-*o*-xylene (I) with D-ribonolactone (II) to yield N-(D-ribityl)-3,4-dimethylaniline (III).

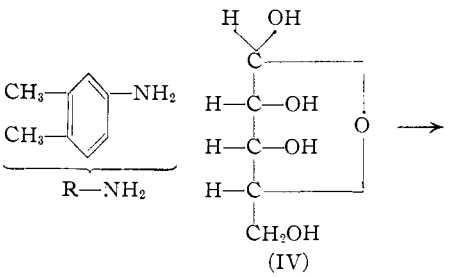


(I) (II)

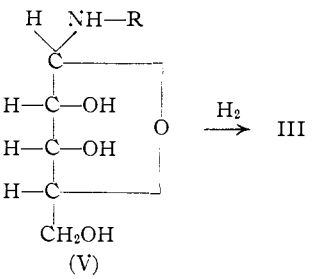


(III)

It is known that some lactones of aldonic acids (D-glucono-δ-lactone, L-rhamnono-δ-lactone, etc.) can be hydrogenated to the corresponding sugars.[3] It therefore seems probable that the 3,4-dimethylaniline used (or formed from 4-nitro-*o*-xylene by hydrogenation) immediately condenses with D-ribose (IV) (formed by hydrogenation of D-ribonolactone) to yield the easily reducible N-glycoside (V).[4]



(IV)



(V)

It is unlikely that 3,4-dimethyl-D-ribonylaniline is an intermediate because amide formation is negligible at the temperature used. Furthermore, we have confirmed the negative results of Tishler, Wendler, Ladenburg and Wellman,[2] who obtained no N-(D-ribityl)-3,4-dimethylaniline in attempting to catalytically reduce 3,4-dimethyl-D-ribonylaniline.

The reductive condensation appears to proceed favorably in ethanol in the presence of a small amount of potassium hydroxide. Although hydrogen adsorption takes place at atmospheric pressure, the reaction is very slow. Pressures of 100–200 atmospheres have been found to be convenient. Temperatures above 100° favor the irreversible formation of 3,4-dimethyl-D-ribonylaniline which, as has been stated, cannot be utilized.

Hydrogenation of D-ribonolactone alone under these conditions gives a 70% yield of adonitol. In order to test the general applicability of the method, N-(3,4-dimethylphenyl)-D-glucamine and N-(*p*-tolyl)-D-glucamine were prepared from D-glucono lactone plus 3,4-dimethylaniline and *p*-toluidine, respectively.

(1) Present address: William R. Warner & Co., New York, New York.

(2) Tishler, Wendler, Ladenburg and Wellman, THIS JOURNAL, **66**, 1328 (1944); Bergel, Cohen and Haworth, British Patent 550,169 (1942); Pasternack and Brown, U. S. Patent 2,237,263 (1941); Berger and Lee, *J. Org. Chem.*, **11**, 75 (1946).

(3) Glattfelt and Schimpff, THIS JOURNAL, **57**, 2204 (1935); Schmidt and Müller, *Ber.*, **76**, 344 (1943).

(4) Kuhn and Birkofer, *ibid.*, **71**, 621 (1938).