TABLE II

HYDROLYSIS OF 3-CHLORO-3-METHYL-1-BUTYNE (I) AND 1-CHLORO-3-METHYL-1,2-BUTADIENE (II) WITH NaOH AT 25.0° IN 80% ALCOHOL

Compound	c_0 RCl, mole/l.	c_0 RCl/c_0 NaOH	k_2 (l./mole hr.)
I	0.0500	0.513	1.39
I	.0968	0.975	1.42
I	.2000	2.05	1.38
II	.1005	0.50	0.0083[a]
II	.1005	1.00	.0083[a]
II	.1005	2.00	.0086[a]

[a] Average. The individual k_2 values drifted in every experiment.

Reaction of I with Alcoholic Sodium Hydroxide.—Thirty-five grams (0.34 mole) of 3-chloro-3-methyl-1-butyne (I), b.p. 75.2–76.0°, was dissolved in 500 ml. of 80% ethyl alcohol containing 16 g. (0.39 mole) of sodium hydroxide. The air was flushed out in a stream of nitrogen, the flask stoppered and allowed to stand at room temperature for four days. The solution was then decanted from the crystallized sodium chloride, acidified with glacial acetic acid and dried with anhydrous potassium carbonate. The product was then distilled through a helix-packed column. The initial 100 ml. of distillate, an azeotrope boiling mostly at 72–75°, was diluted with an equal volume of cold water, causing the separation of layers. The upper layer was further washed, dried with calcium chloride and distilled. The ethyl ether (III) of 3-methyl-1-butyn-3-ol was obtained in 56.5% yield (21.5 g.); b.p. 93–94°, $n^{25}D$ 1.4010, d^{25} 0.8015. Redistillation for analysis gave a fraction b.p. 94°, $n^{25}D$ 1.4010, d^{25} 0.7995.

Anal. Calcd. for $C_7H_{12}O$: C, 74.95; H, 10.78. Found[8]: C, 75.45; H, 10.91.

Reaction of II with Alcoholic Sodium Hydroxide.—Forty-two grams (0.41 mole) of 1-chloro-3-methyl-1,2-butadiene (II), b.p. 60–64° at 175 mm., $n^{25}D$ 1.4722 (distilled from maleic anhydride) was treated with 350 ml. of 80% alcohol containing 18 g. (0.44 mole) of sodium hydroxide. After twenty days the solution was treated as described above. Distillation gave 3 ml. of 3-methyl-3-buten-1-yne, b.p. 33–40°, and 65 ml. b.p. 40–78°. The latter fraction was diluted with cold water and the ether separated (26 g.). Upon distillation it boiled from 93 to 96°, $n^{25}D$ 1.4178. The product was obviously very impure; it contained chlorine but did not react with alcoholic silver nitrate. Distillation, *in vacuo*, from 2 g. of maleic anhydride improved the physical properties; b.p. 55–56° at 190 mm., $n^{25}D$ 1.4075. The distillation residue was extracted with boiling water. The water extract deposited 4-methyl-2,3-dihydrophthalic acid (0.25 g. after two recrystallizations), m.p. 203–207°, previously described.[3] Further distillation of the original reaction mixture ultimately gave water-soluble fractions boiling above 78° which reacted readily with ammoniacal silver nitrate, indicating formation of 3-methyl-1-butyn-3-ol as well as the ether (III).

Preparation of 3-Methyl-1-butyn-3-ol Ethyl Ether.—Two gram atoms of sodium (46 g.) was converted to the acetylide in 1.5 liters of liquid ammonia and 145 g. (2.5 moles) of dry acetone added during 35 minutes. After stirring for one hour 315 g. (2.9 moles) of ethyl bromide was added dropwise. The mixture was stirred continuously until most of the ammonia had evaporated. Ice, ether and 50% sulfuric acid were then added until the mixture was faintly acidic. The ethereal layer was separated, washed and distilled, yielding 147 g., b.p. 70–106°. The distillate was washed four times with equal volumes of ice-water, dried with calcium chloride, and redistilled; yield 94 g. (41.9%), b.p. 92–93.5°, $n^{25}D$ 1.3999. When distilled again the middle fraction had b.p. 94°, $n^{25}D$ 1.4002, d^{25} 0.7972.

Semicarbazone of III.—Two ml. of the ether (III) was added to 10 ml. of 70% ethyl alcohol containing 0.5 g. of mercuric sulfate and 5 drops of sulfuric acid and the mixture heated to gentle boiling for 15 minutes. The solution was cooled, neutralized with strong sodium hydroxide solution and filtered. The filtrate was treated with 2 g. of semicarbazide hydrochloride and 3 g. of sodium acetate to prepare the semicarbazone in the usual way. After two recrystallizations from water containing a little alcohol the m.p. was 148–150°; yield 0.92 g. All samples of (III) yielded the same derivative in this manner.

Anal. Calcd. for $C_8H_{17}N_3O_2$: N, 22.44. Found[8]: N, 22.0.

Acknowledgment.—The senior author (G. F. H.) acknowledges helpful discussions during the course of this work with Profs. M. G. Evans, University of Manchester, England, and C. C. Price of this Department, D. E. M. is indebted to the University of Notre Dame and to E. I. du Pont de Nemours and Company for the grant of a Fellowship during 1950–1951.

NOTRE DAME, INDIANA RECEIVED FEBRUARY 28, 1951

(8) Analyses by Micro-Tech Laboratories, Skokie, Ill.

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Dehydrochlorination of 3,6-Bis-(β-chloroethyl)-2,5-diketopiperazine

BY HARLAN L. GOERING

It has previously been reported that 3,6-bis-(β-chloroethyl)-2,5-diketopiperazine (I) is readily dehydrohalogenated by alcoholic alkali to 3,6-divinyl-2,5-diketopiperazine (II). Anomalous reactions of the dehydrohalogenation product, particularly ease of formation and "non-Markownikoff additions" of hydrogen halides and hydrogen sulfide prompted a reinvestigation of the structure of this compound. This study showed the compound to be 3,4,5,3′,4′,5′-hexahydrodifuro[2,3-b,2′,3′-e]pyrazine (III) rather than the previously formulated isomeric divinyldiketopiperazine (II). The structure of the dehydrohalogenation product has been deduced from infrared spectra, reduction to 2,5-bis-(β-hydroxyethyl)-piperazine, and chemical reactions characteristic of iminoesters. The new structure, III, accommodates previously reported reactions as well as reactions reported in the present communication without anomalies.

During an investigation of the applicability of 3,6-bis-(β-chloroethyl)-2,5-diketopiperazine (I) as an amino acid intermediate, Snyder and Chiddix[1] observed that the dichloride (I) was unexpectedly susceptible to dehydrohalogenation. The dehydrohalogenation product was formulated as 3,6-divinyl-2,5-diketopiperazine (II).[1,2] This formulation was of considerable interest for the following reasons: (a) the dichloride (I) was considerably more readily dehydrochlorinated than would be expected for the conversion of a primary chloride to an olefin; (b) the dehydrohalogenation product added hydrogen chloride to form I; (c) the addition of hydrogen bromide and hydrogen sulfide similarly gave abnormally oriented addition products. These findings were interpreted as a demonstration of a non-Markownikoff addition to a double bond.[2]

In the present investigation the dehydrohalogenation product of I, prepared by the method of Sny-

(1) H. R. Snyder and M. E. Chiddix, THIS JOURNAL, **66**, 1000 (1944).

(2) H. R. Snyder and M. E. Chiddix, *ibid.*, **66**, 1002 (1944).

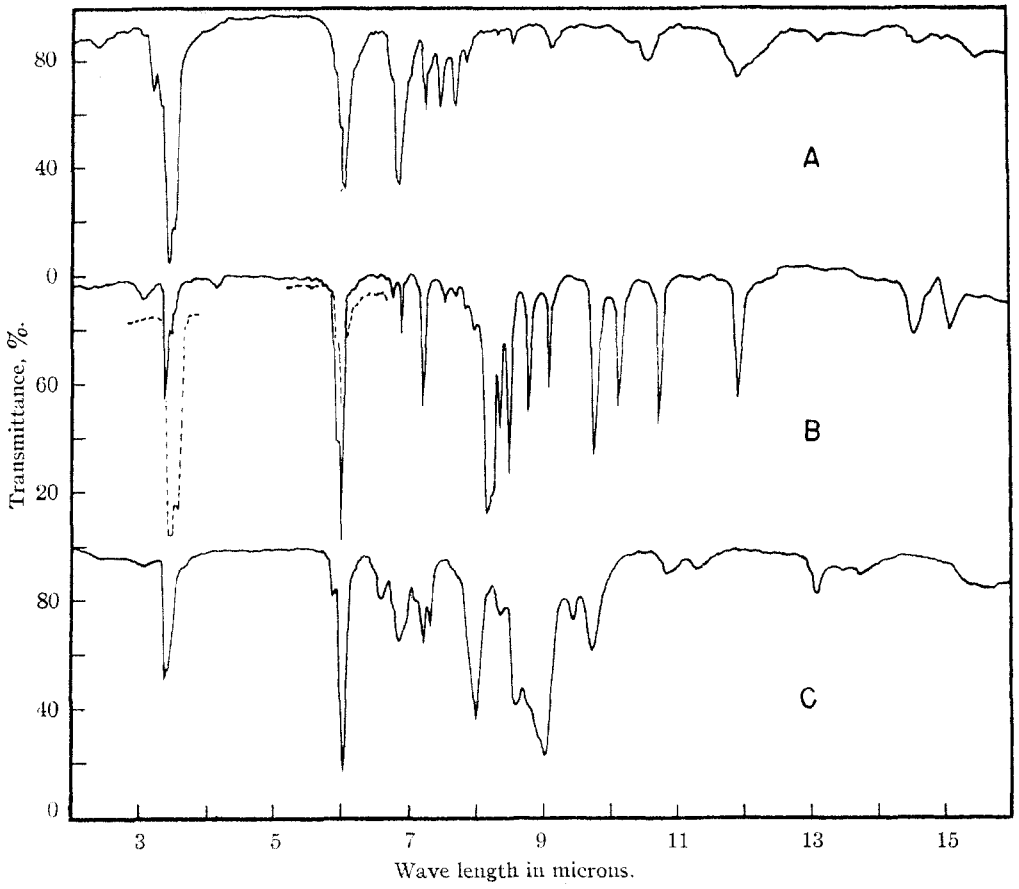
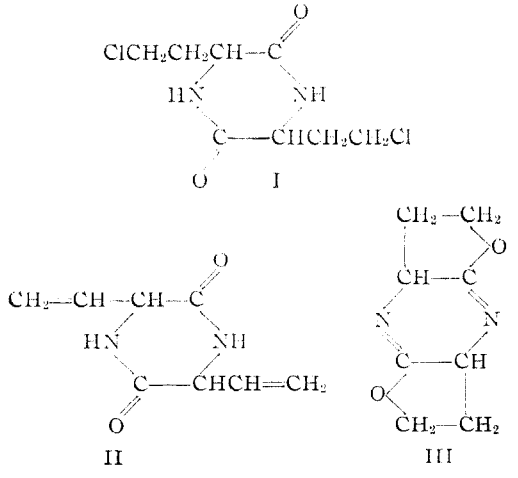


Fig. 1.—Infrared absorption spectra: A, 3,6-bis-(β-chloroethyl)-2,5-diketopiperazine (I) as nujol mull; B, 3,4,5,3′,4′,5′-hexahydrodifuro[2,3-b,2′,3′-e]pyrazine (III), solid curve in chloroform (compensated), dashed curve as nujol mull; C, ethyl α-chloro-N-methyliminoisobutyrate as capillary layer.

der and Chiddix,[1] has been found to have properties which are inconsistent with structure II, but which can be accommodated by structure III, 3,4,5,3′,4′,-5′-hexahydrodifuro[3,2-b,2′,3′-e]pyrazine.

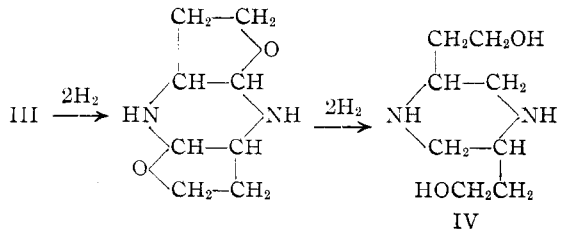


In Fig. 1 the infrared spectrum of III is shown together with the spectra of I and ethyl α-chloro-N-methyliminoisobutyrate, $(CH_3)_2CClC(OC_2H_5)=NCH_3$. The spectrum of the diketopiperazine (I) shows the N–H absorption at 3.18 μ and a strong C=O absorption at 6.0 μ. The reported spectra of several diketopiperazines[3,4,5] as well as the spectra of additional diketopiperazines investigated in the present work all show characteristic N–H and C=O absorptions. The lack of absorption in the N–H stretching region in the spectrum of III constitutes strong evidence that the compound does not contain N–H bonds and thereby casts doubt on structure II. The strong absorption shown by III at 5.95 μ is assigned to the imidoester linkage on the basis of comparison with the spectrum of ethyl α-chloro-N-methyliminoisobutyrate.

The catalytic reduction of III provided valuable evidence regarding its structure. When a methanolic solution of III was shaken at room temperature over Adams (platinum oxide) catalyst four moles of hydrogen, the last two at approximately one-half the rate of the first two, were absorbed, and 2,5-bis-(β-hydroxyethyl)-piperazine (IV) was produced. Under these conditions such amide linkages as depicted by II would not be affected, nor could this structure yield IV as a product of hydrogenation. The hydrogenation data indicate the reaction path.

The reduction product, IV, was identified by analysis and by equivalent weight determinations from potentiometric titrations. The titration

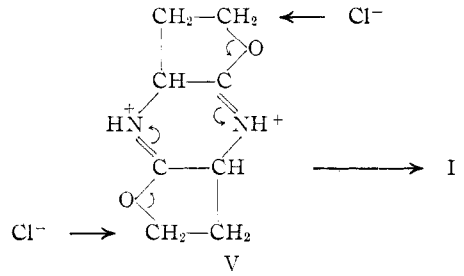
(3) H. Lenormant, *Bull. soc. chim. France*, **33** (1948).
(4) L. Kellner, *Proc. Roy. Soc. (London)*, **A117**, 447 (1941).
(5) A. M. Buswell, J. R. Downing and W. H. Rodebush, THIS JOURNAL, **62**, 2759 (1940).



IV

curve, resulting from titration of IV with 0.05 *N* hydrochloric acid, showed two inflection points confirming the presence of two basic nitrogen atoms in the molecule. The first equivalence point corresponded to a *p*H of 6.6 (pK_a 8.6)[6]; the second equivalence point occurred at *p*H 3.2 (pK_a 4.6). The titration curve of IV was found to be nearly identical with that of 2,2,5,5-tetramethylpiperazine.[7] The latter compound was found to be a somewhat stronger base with the first equivalence point at *p*H 7.0 (pK_a 9.3) and the second equivalence point at *p*H 3.25 (pK_a 4.7).

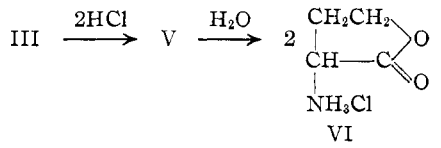
The previous observation that the dehydrohalogenation product of I interacts with hydrogen chloride in glacial acetic acid to yield I[2] is in agreement with structure III. It is well known that iminoester hydrochlorides can decompose to alkyl halides and amides[8,9]; a similar reaction involving V would yield I.



V

In the present work we have observed that III does not form a stable hydrochloride. A chilled solution of III in chloroform absorbs dry hydrogen chloride with simultaneous separation of a white crystalline compound which is only partially soluble in water and contains only small amounts of chloride ion. After recrystallization this product was shown to be primarily I by comparison of infrared spectra. The finding that III does not form a stable hydrochloride is similar to the finding of McElvain and Stevens[10] that ethyl α-chloro-N-ethyliminoisobutyrate, when treated with anhydrous hydrogen chloride in the cold yields α-chloro-N-ethylisobutyramide directly rather than the iminoester hydrochloride.

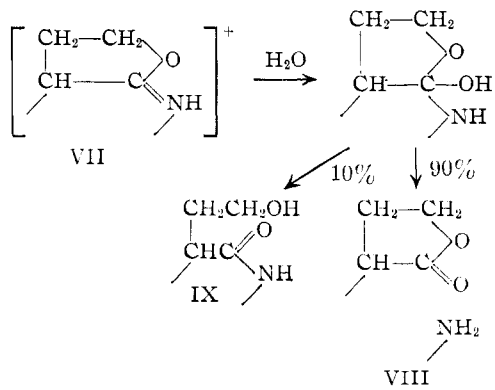
The hexahydrodifuropiperazine (III) is extremely susceptible to acid-catalyzed hydrolysis. This finding is in agreement with the known ease of hydrolysis or solvolysis of the conjugate acid of iminoesters.[8] The lability of III toward aqueous acid is readily demonstrated by potentiometric titrations of aqueous solutions of III with dilute (0.05 to 0.2 *N*) hydrochloric acid. Such titrations show that addition of small increments of acid decreases the *p*H which then rapidly drifts upward as the solution is stirred at room temperature. The acid consumption is due to rapid hydrolysis of III to α-amino-γ-butyrolactone hydrochloride (VI). Presumably the iminoester linkage is instantaneously converted to the conjugate acid which solvolyzes rapidly



VI

After the addition of two equivalents of acid the *p*H remains constant. When the resulting solution is back-titrated with base all of the originally added acid is accounted for. Additional base causes momentary increases in *p*H which rapidly drift downward until approximately two equivalents of excess base have been added after which the *p*H remains constant. The consumption of base is due to the conversion of α-amino-γ-butyrolactone to α-amino-γ-hydroxybutyric acid. When aqueous solutions of III are treated with small amounts of alkali in the cold, without previous acid titration, the alkali is not consumed as indicated by a steady *p*H value.

Quantitative titrations of III with dilute acid followed by back-titrating the resulting α-amino-γ-butyrolactone hydrochloride with dilute alkali consistently showed that *ca.* 90% of the iminoester linkages are hydrolyzed to form an amino group. The remaining iminoester linkages undergo a different type of hydrolytic cleavage which does not consume acid. The latter cleavage probably involves the conversion of the iminoester linkage to the corresponding γ-hydroxyamide (IX). The complete scheme for the acid hydrolysis of the iminoester linkages in III is summarized below.



VII IX VIII

The hydrolysis of the conjugate acid of the iminoester (VII) to IX is analogous to the hydrolysis of an oxazolinium ion (X) to the corresponding N-(β-hydroxyalkyl)-amide (XI), whereas the hydrolysis of VII to VIII is analogous to the conversion of an oxazolinium ion (X) to the *o*-acyl amino compound (XII).[9,11,12]

(6) The pK_a values were read directly from the titration curves and thus involve concentrations rather than activities. These values are not corrected for salt effects at the glass electrode.

(7) S. M. McElvain and E. H. Pryde, THIS JOURNAL, **71**, 326 (1949).

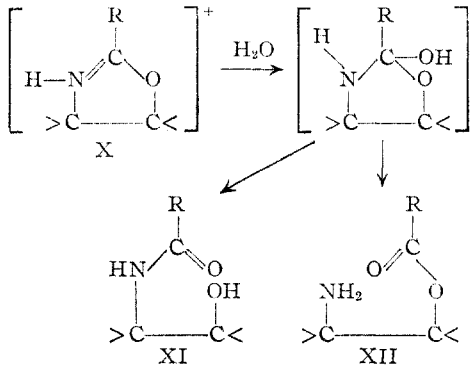
(8) S. M. McElvain and B. E. Tate, *ibid.*, **73**, 2233 (1951).

(9) S. Winstein and R. Boschan, *ibid.*, **72**, 4669 (1950).

(10) S. M. McElvain and C. L. Stevens, *ibid.*, **69**, 2667 (1947).

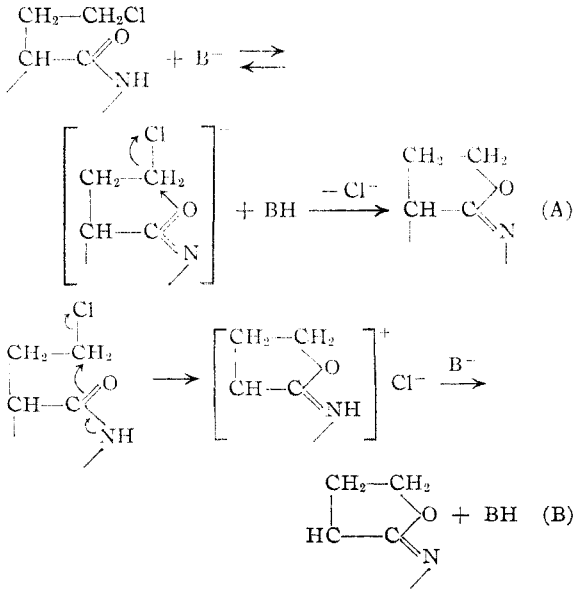
(11) W. S. Johnson and E. N. Schubert, *ibid.*, **72**, 2187 (1950).

(12) D. F. Elliott, *J. Chem. Soc.*, 62 (1950).



The rapid conversion of III to VI was confirmed by treating III with two equivalents of dilute hydrochloric acid, immediately concentrating to dryness at low temperatures and showing the residue to be α-amino-γ-butyrolactone hydrochloride (VI). Snyder and Chiddix[1] previously have reported the conversion of the dehydrohalogenation product of I to VI by refluxing with concentrated hydrochloric acid for several hours. Inasmuch as these conditions are sufficient for hydrolysis of amide linkages this conversion could be considered consistent with structure II by assuming lactonization across the β,γ-double bond. In the present work, however, the finding that III hydrolyzes very rapidly at room temperature when treated with an equivalent of dilute acid eliminates structure II as well as other diketopiperazine structures as possibilities.

The nature of the dehydrohalogenation of 3,6-bis-(β-chloroethyl)-2,5-diketopiperazine apparently involves a new type of elimination which, however, may be closely related to known reactions. The following reaction paths seem possible from the available information (B^- = base).



A concerted mechanism rather than the two-stage process depicted by (A) is also a possibility.

A striking analogy exists between the above reaction and reactions involving neighboring acylamino groups.[9,11] When a neighboring acylamino group participates the amide oxygen displaces the leaving group to form the five-membered oxazolinium ion ring or in the presence of base the free oxazoline.[9,11,13] The conversion of I to III can similarly be considered as involving a displacement by an amide oxygen to form the five-membered heterocyclic ring. The difference between the two types of reactions is that the departing group is located in different branches of the amide molecule. An investigation of N-alkyl-γ-halobutyramides and related structural analogs is under way at the present time in order to establish if participation of this type is of general importance. The fact that such a participation may be important is indicated by the behavior of 3,6-bis-(β-bromoethyl)-2,5-diketopiperazine (XIII) in polar solvents. Snyder and Chiddix[1] observed that XIII produces acid rapidly in aqueous or ethanolic solutions. When they attempted to determine the equivalent weight of XIII by titration of the acid produced, erroneous results were obtained. The facts are consistent with a rapid conversion of XIII to the dihydrobromide of III which in aqueous solution is hydrolyzed primarily to the hydrobromide of α-amino-γ-butyrolactone.[14] The presence of the lactone was probably responsible for the reported "fugitive" endpoint in the attempt to titrate the solution with alkali to the phenolphthalein end-point.[1]

In the synthesis of I from the corresponding hydroxy compound, 3,6-bis-(β-hydroxyethyl)-2,5-diketopiperazine with excess thionyl chloride at elevated temperatures[1] it is possible that V is an intermediate. Such a reaction would be analogous to that observed by Elliot in which N-benzoylthreonine ethyl ester is converted to the oxazoline by treatment with thionyl chloride.[12,15]

Although many attempted substitution reactions of I were unsuccessful due to competitive dehydrohalogenation[1,2] certain substitution reactions involving amines, thiourea, thiocyanate ion and mercaptide ion were successful.[16,17] The nature of the substitutions by amines is not clear[18]; however, the substitutions involving thiocyanate ion, mercaptide ion, and thiourea in ethanol are apparently S_N2 type[19] displacements. In these reactions the nucleophilic power of the reagent is apparently of such magnitude so that substitution can effectively compete with dehydrohalogenation.

Acknowledgment.—The author is indebted to Mr. Donald R. Johnson for the determination and interpretation of the infrared spectra.

Experimental[20]

3,6-Bis-(β-chloroethyl)-2,5-diketopiperazine (I) was prepared according to the method of Snyder and co-workers[16]

(13) R. M. Lesskin and J. J. Ritter, THIS JOURNAL, **72**, 5577 (1950).

(14) This hydrolysis is identical to that shown for VII.

(15) See also C. E. McCasland and D. A. Smith, THIS JOURNAL, **72**, 2190 (1950).

(16) H. R. Snyder, J. H. Andreen, G. W. Cannon and C. F. Peters, *ibid.*, **64**, 2082 (1942).

(17) H. R. Snyder and G. W. Cannon, *ibid.*, **66**, 511 (1944).

(18) In these reactions the solvent was excess amine and it seems possible that III might be an intermediate which could solvolyze to the substitution product.

(19) E. D. Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

(20) All melting points are corrected.

and after recrystallizations from ethanol and acetic acid[21] melted at 237–238° (lit.,[1] m.p. 233–234°).

Ethyl α-chloro-N-methyliminoisobutyrate was prepared from α-chloro-N-methyliminoisobutyryl chloride by the method of McElvain and Stevens.[10] The previously unanalyzed **α-chloro-N-methyliminoisobutyryl chloride** was purified by fractionation with an 18-in. lagged Vigreux column at high reflux ratio, b.p. 175° (760 mm.); $n^{25}D$ 1.4632.

Anal. Calcd. for $C_6H_9Cl_2N$: C, 38.98; H, 5.89. Found: C, 38.99; H, 5.59.

Ethanolysis of the above iminochloride yielded **ethyl α-chloro-N-methyliminoisobutyrate** which was purified by fractionation, b.p. 162° (760); $n^{25}D$ 1.4411 (lit.[10] b.p. 163–164°).

3,4,5,3′,4′,5′-Hexahydrodifuro[2,3-b,2′,3′-e]pyrazine (III).—3,6-Bis-(β-chloroethyl)-2,5-diketopiperazine (I) was dehydrochlorinated with alcoholic sodium hydroxide by the following modification of the previously described method.[1] Instead of dissolving the sodium hydroxide prior to the addition of I solid sodium hydroxide pellets were added to the alcoholic solution of I. In this manner 90–95% yields of crude dry III were obtained; recrystallization of this material gave 80–84% over-all yields of pure, colorless III.

The product decolorizes aqueous potassium permanganate and bromine in chloroform; it is very soluble in water, alcohol, chloroform and acetic acid and insoluble in non-polar solvents. It melted at 192.5° (clear melt) when placed in a bath at this temperature and showed the same melting point behavior as that reported for 3,6-divinyl-2,5-diketopiperazine.[1]

Anal. Calcd. for $C_8H_{10}N_2O_2$: C, 57.81; H, 6.06; N, 16.86. Found: C, 57.96; H, 5.88; N, 16.91.

A solution of 1.002 g. (6.02 mmoles) of III in exactly 60 ml. of 0.2013 *N* hydrochloric acid was concentrated to dryness under reduced pressure. The temperature was not allowed to exceed 20° during the entire operation which required *ca.* two hours. Recrystallization of the solid residue from absolute ethanol yielded 0.45 g. of product, m.p. 192–193°. After an additional recrystallization colorless **α-amino-γ-butyrolactone hydrochloride** was obtained, m.p. 196–197° (lit.[1] m.p. 199–200°).

Anal. Calcd. for $C_4H_8O_2NCl$: C, 34.92; H, 5.86. Found: C, 35.34; H, 5.79.

The rapid conversion of III to α-amino-γ-butyrolactone hydrochloride by treatment with dilute hydrochloric acid was demonstrated by reproducible potentiometric titrations in the following manner. A solution of 0.5055 g. (3.04 mmoles) of III in 5 ml. of conductivity water was titrated with 0.2013 *N* hydrochloric acid. The *p*H of the solution was determined with a Beckman *p*H meter. Addition of small increments of acid caused momentary decreases in *p*H, which rapidly drifted upward. After addition of a slight excess of acid (32.1 ml.) the *p*H (1.6) remained constant. The resulting solution was back titrated with 0.3440 *N* sodium hydroxide. The resulting titration curve showed a sharp inflection point after 3.25 ml. of base had been added and a second inflection point after 18.80 ml. of base had been added. The first equivalence point (titration of excess hydrochloric acid) occurred at *p*H 3.7 and the second equivalence point (titration of aminolactone hydrochloride) occurred at *p*H 8.5 (pK_a 6.35).[6] Additional base caused momentary increases in *p*H which rapidly drifted downward due to consumption of base by the hydrolysis of the lactone. The resulting solution gave a positive ninhydrin test. The observation that 15.55 ml. of 0.344 *N* base is required to titrate the amine hydrochloride resulting from the hydrolysis of 3.04×10^{-5} mole of III demonstrates that 88% of the iminoester linkages in III undergo hydrolytic cleavage to form an amino group.

2,5-Bis-(β-hydroxyethyl)-piperazine (IV).—A solution of 6.010 g. (0.0361 mole) of III in 15 ml. of absolute methanol was shaken over 0.612 g. of Adams catalyst at room temperature and a starting pressure of 45 lb. Sixty hours was required for completion of the hydrogen absorption. The pressure drop indicated that 4.05 mole of hydrogen per mole of III was absorbed. The ratio (hydrogen absorbed/mole of III) was reproducible as was the approximate length of time required for the hydrogenations. After separation from the catalyst the solvent was removed at room temperature under reduced pressure. The resulting solid residue was taken up in dry benzene containing enough absolute ethanol for solution. Treatment with dry ether precipitated 4.80 g. (76%) of colorless product with a large melting point range, 125–150° (clear melt) with previous softening at 90°.[22] After recrystallizations from benzene–ethanol mixture IV was obtained as a white crystalline solid, m.p. 179–180° (clear melt) with previous softening at 177°. It is soluble in alcohol and water, insoluble in polar solvents. In contrast with the unsubstituted piperazine IV does not react with carbon dioxide of the atmosphere and is not hygroscopic.

Anal. Calcd. for $C_8H_{10}N_2O_2$: C, 55.14; H, 10.41; N, 16.08; equiv. wt., 87.1. Found: C, 55.13; H, 10.49; N, 15.87; equiv. wt., 88.2 (potentiometric titration with standard acid).

2,5-Bis-(β-hydroxyethyl)-piperazine dipicrate was prepared from IV in the usual manner. After repeated recrystallizations from aqueous ethanol it melted at 249–250° (dec.).

Anal. Calcd. for $C_{20}H_{24}O_{16}N_8$: C, 37.98; H, 3.83. Found: C, 37.87; H, 3.54.

The dihydrochloride of IV was prepared by acidifying an aqueous solution of IV with dilute hydrochloric acid and concentrating the resulting solution to dryness under reduced pressure. The dihydrochloride is insoluble in organic solvents and very soluble in water. After recrystallizations from ethanol containing just enough water for solution the compound decomposed at *ca.* 210°, with previous softening at 155°, when heated rapidly in a capillary.

Anal. Calcd. for $C_8H_{20}O_2N_2Cl_2$: C, 38.87; H, 8.16. Found: C, 39.06; H, 8.03.

Reaction of 3,4,5,3′,4′,5′-Hexahydrodifuro[2,3-b,2′-3′-e]pyrazine (III) with Hydrogen Chloride.—Dry hydrogen chloride was passed through a chloroform solution of 2.00 g. of III at 0°. The hydrogen chloride was completely absorbed with simultaneous separation of a white solid which became amorphous. Evaporation of the solvent, under diminished pressure, yielded 2.83 g. (98%) of colorless crystalline product, m.p. *ca.* 230° with considerable previous darkening. The product was insoluble in water and most organic solvents. After recrystallizations from acetic acid and absolute ethanol, with an over-all recovery of 65%, the product melted at 233–234° with slight previous darkening. Additional recrystallizations did not affect the melting point. When mixed with authentic I, m.p. 234–235°, the mixture melted at 233–235°. The infrared spectrum of the above product was very similar to that of I.

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(21) Contrary to the reported limited solubility of I in hot acetic acid (ref. 16) we have found the compound to be readily soluble in this solvent.

(22) The large melting point range may be due to the fact that the product is a diastereomeric mixture. It appears that IV would have the same configuration as I from which it is derived in two steps. Evidence has been presented (ref. 2) which demonstrates that I is primarily or completely of the *meso* configuration.