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The Cyclization of Nitriles by Halogen Acids. A New Synthesis of Substituted 3H-Azepines

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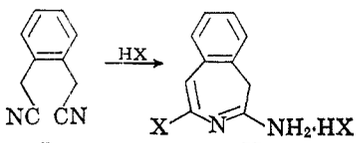
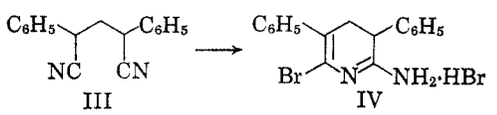
The treatment of 2-cyanomethyl-1-cyanomethylenecycloalkanes (XV) with hydrogen bromide in anhydrous media leads to 2-amino-4-bromo-1H-cycloalk[*d*]azepines (XVI). This method, which is general in nature, represents a one-step synthesis of a type of functionally substituted azepine ring which has not been available previously. A preliminary investigation of the chemistry of one of these compounds, 2-amino-4-bromo-6,7,8,9-tetrahydro-1H-3-benzazepine, has been made. Attempts to debrominate it reductively have failed so far.

In a previous paper[1] in this series, we presented a new method for the preparation of 1H-3-benzazepines and described some of their reactions. The parent member (II) was prepared by the action of a hydrogen halide HX (X = Br or I) on the dinitrile I under anhydrous conditions. Our investigation of the cyclization of I



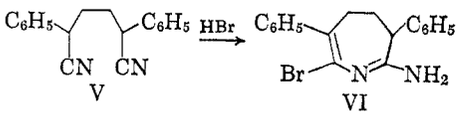
I II

was predicated on the reasoning that the nitrile groups had to be held in reasonably close proximity to one another for cyclization to II to occur. The latter conclusion was based on the facts that 1,2- and 1,3-dicyanoalkanes[2] generally gave reasonably stable cyclic products under these conditions, whereas the 1,4-dicyano compounds such as adiponitrile or *trans*-1,4-dicyanobutene-2 led to highly sensitive substances, which were extremely difficult to investigate,[1] being stable only in a hydrogen bromide atmosphere. Subsequently it was found that 2,4-diphenylglutaronitrile (III) underwent cyclization[3] to IV which contained the



III IV

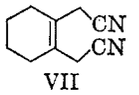
same type of chromophoric group as II. Compound IV proved to be very similar in properties to II in that on neutralization it gave rise to a stable free base spectroscopically very similar to that of II. This posed the question as to whether the presence of an aryl group, attached at the α position of one of the nitrile groups, might permit the synthesis of seven-membered rings from the appropriate 1,4-dinitriles. To this end, 2,4-diphenyladiponitrile[4] (V) was prepared and treated with hydrogen bromide gas in methylene chloride.



V VI

This gave rise to a sticky white solid whose initial infrared spectrum showed bands at 2.98 and 6.05 μ. However, 20 min later the mull showed bands characteristic only of the starting dinitrile. Attempts to trap the expected product VI by reaction of the solid with acetic anhydride were equally futile, again only starting material being obtained, after the normal isolation procedure. The over-all behavior of V was thus very similar to that of adiponitrile and we conclude that the presence of an aryl group at the α position of such dinitriles is of little or no help to the cyclization *per se*.

The most logical candidate for further study now seemed to be 1,2-bis(cyanomethyl)cyclohexene (VII). However, attempts to prepare this compound *via* normal procedures were without success. The reaction of 1,2-bis(bromomethyl)cyclohexene with sodium cyanide in a variety of solvents including dimethyl sulfoxide did not lead to the desired product and other methods that seemed logical for the preparation of VII



VII

(1) F. Johnson and W. A. Nasutavicus, *J. Heterocyclic Chem.*, **2**, 26 (1965); see also J. Gardent, *Compt. Rend.*, **259**, 4724 (1964).

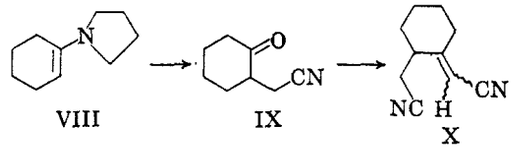
(2) E. G. Howard, Jr., U. S. Patent 2,810,726 (1957).

(3) The nature of this salt has been investigated recently. The results of this study are in the process of being published.

(4) We thank Dr. A. E. Young for information concerning the preparation of this compound.

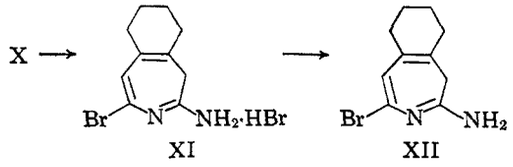
were not attempted simply because their length made them impractical. Instead we elected to investigate the cyclization of its isomer, X, even though this would introduce the difficulty of the latter's existing in two geometrical forms, only one of which we felt might yield a cyclic product.

The synthesis of X was accomplished easily by the action of the sodium salt of diethyl cyanomethylphosphonate[5] on 2-cyanomethylcyclohexanone (IX), the latter available by the reaction of chloroacetonitrile with 1-pyrrolidinocyclohexene[6,7] (VIII).



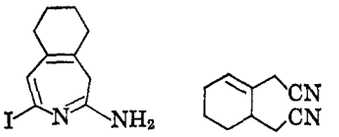
VIII IX X

The presence of two vinylic H resonances in the nmr spectrum of X at 5.18 and 5.33 ppm in ratio of 3:1, respectively, suggested both geometrical isomers to be present, but no attempt was made to separate them. Treatment of this mixture in anhydrous ethyl ether with dry hydrogen bromide gas led to a syrup which crystallized from methanol–acetone, affording the desired azepine hydrobromide XI in 72% yield. Neutralization of the latter by mild alkali gave the free base XII in 82% yield. The gross structure of the latter follows unambiguously from its nmr spectrum in trifluoroacetic acid which shows a vinylic proton absorption at 6.58 ppm and an isolated CH_2 absorption at 3.08 ppm which integrate in the ratio of 1:2. In addition, broad bands appear at 1.71 and 2.22 ppm having equal area (four protons each) which can only be assigned to the two types of CH_2 group in the cyclohexene ring. Evidence for the tautomeric distribution of the double bonds in XI follows from a comparison of its infrared spectrum with those of the free bases of II and IV. All spectra contain both a highly characteristic NH band stretching pattern in the 3-μ region and a band at 5.97 μ. Since the tautomeric forms of the free bases of II and IV have been proved[1,3] conclusively by spectroscopy and because the chemical reactions of II and XII are very similar (see below), possible tautomeric forms for the cyclization product other than that depicted in XII can be neglected.



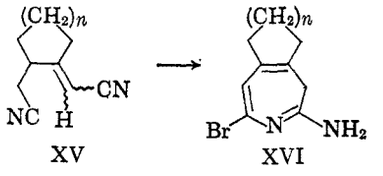
XI XII

The reactions of X with both hydrogen iodide and hydrogen chloride were studied also. As expected, the former acid led after neutralization of the initial salt to the iodo derivative XIII, although the yield (14%) in this instance was low. Treatment of X with hydrogen chloride, on the other hand, did not appear to cause cyclization even on long standing (18 days). Infrared analysis of the resulting oil after 2, 5, and 14 days indicated the gradual disappearance of the conjugated nitrile absorption at 4.48 μ and the enhancement of the saturated nitrile band at 4.43 μ. Concomitant with this change was the shrinking of a strong band at 6.14 μ owing to the C=C stretching vibrations in X and the growth of a new absorption at 5.98 μ. The final product appeared to be a mixture consisting largely of the position isomers VII and XIV together with a little X. This result suggests that the high yield of XI from X may in fact be due to the sequence of events in which there is first a proton-catalyzed equilibration of the double bond in X, which in the case of hydrogen bromide must be supposed to be very fast, followed by cyclization of either or both VII and the *syn* form of X.



XIII XIV

The extension of the synthetic procedure for XII to its homologs XVI, varying in the size of the alicyclic ring, proved highly successful. The starting materials (XV, n = 1, 3, and 4, respectively) were prepared according to the methods used above for the six-membered ring except that the 2-cyanomethylcycloheptanone, required for the synthesis of XV (n = 3), was obtained by the action of 2-cyanodiazoethane[7] on cyclohexanone.



XV XVI

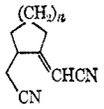
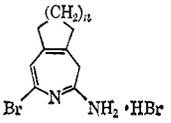
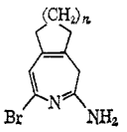
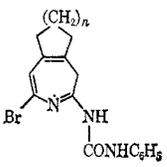
The cyclizations under the influence of dry hydrogen bromide proceeded quite well except in the case of the eight-membered ring dinitrile XV (n = 4) where the yield was only 37%. This reaction, however, was performed only once and further work would undoubtedly lead to improved results. Except for this case the azepines were characterized as their mixed ureas (XVII) by reaction with phenyl isocyanate. The physical data for these substances, the azepines themselves, their hydrobromide salts, and the starting dinitriles are given in Table I. All of the above cases of azepine synthesis could be regarded essentially as symmetrical examples of the cyclization because theoretically they could be considered as proceeding through the nonconjugated dinitriles such as VII. Lack of substitution on the alicyclic ring of VII and the apparent preference for a particular arrangement of the double bonds in the azepine itself combine to give a single entity as the product. An interesting case for further study seemed to be XVIII, where inherent dissymmetry exists and where initially a significant amount of double isomerization to the exocyclic position seems unlikely. Compound XVIII was synthesized in low yield in somewhat impure form by the dehydration of the cyanohydrin of 2-(β-cyanoethyl)cyclohexanone. Cyclization of XVIII by means of hydrogen bromide led in fair

(5) W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961).

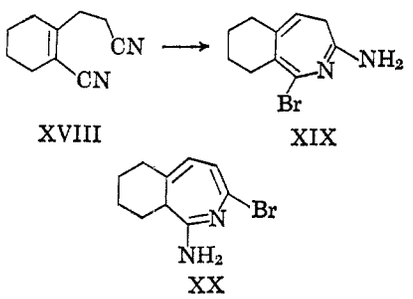
(6) (a) L. Mandell, J. U. Piper, and K. P. Singh, *J. Org. Chem.*, **28**, 3440 (1963). (b) In subsequent preparation of other 2-cyanomethylcycloalkanones, it was found that the addition of a tertiary base improved the yields; see M. E. Kuehne, *J. Am. Chem. Soc.*, **81**, 5400 (1959).

(7) D. M. Bailey, J. E. Bowers, and C. D. Gutsche, *J. Org. Chem.*, **28**, 610 (1963).

TABLE I

	n	Bp (mm) or mp, °C (uncor)	Crystd from[a]	Yield, %	Formula	Analysis, % Calcd C	H	Br	N	Found C	H	Br	N
 XV	1	104 (0.065)		74	$C_9H_{10}N_2$	73.9	6.9		19.2	74.0	7.1		19.0
	2	145 (0.12)		61	$C_{10}H_{12}N_2$	75.0	7.6		17.5	74.8	7.8		17.3
	3	87	MC-E	55	$C_{11}H_{14}N_2$	75.8	8.1		16.1	76.0	8.2		16.1
	4	133 (0.1)		50	$C_{12}H_{16}N_2$	76.6	8.7		14.9	76.5	8.6		14.9
	1	192–195	M–A–E	72	$C_9H_{12}Br_2N_2$	35.1	3.9	51.9	9.0	35.1	3.6	52.0	9.1
	2	221–222	M–A	65	$C_{10}H_{14}Br_2N_2$	37.3	4.4	49.6	8.7	37.2	4.3	49.5	8.8
	3	203–205	M–A	80	$C_{11}H_{16}Br_2N_2$	39.3	4.8	47.6	8.3	39.0	5.0	47.4	8.1
	4	228–229	M–A	37	$C_{12}H_{18}Br_2N_2$	41.2	5.2	45.6	8.0	41.3	4.8	45.7	7.9
 XVI	1	153–155	MC-E	82	$C_9H_{11}BrN_2$	47.6	4.8	35.1	12.3	47.6	5.0	35.2	12.0
	2	160–165 dec	MC	88	$C_{10}H_{13}BrN_2$	49.8	5.4	33.1	11.6	49.5	5.0	33.0	11.6
	3	170–174 dec	MC-E	49	$C_{11}H_{15}BrN_2$	51.8	5.9	31.3	11.0	51.8	6.0	31.2	11.1
	4	165–168 dec	E	87	$C_{12}H_{17}BrN_2$	53.5	6.4	29.7	10.4	53.5	6.4	29.6	10.2
 XVII	1	212–214	THF	84	$C_{16}H_{16}BrN_3O$	55.5	4.7	23.1	12.1	55.7	4.5	23.0	12.0
	2	214–215	THF	87	$C_{17}H_{18}BrN_3O$	56.7	5.0	22.2	11.7	56.8	5.0	22.2	11.6
	3	220–222	THF	68	$C_{18}H_{20}BrN_3O$	57.8	5.4	21.4	11.2	58.0	5.2	21.2	11.2

[a] A, acetone; E, ethyl ether; M, methanol; MC, methylen chloride; THF, tetrahydrofuran.



XVIII XIX XX

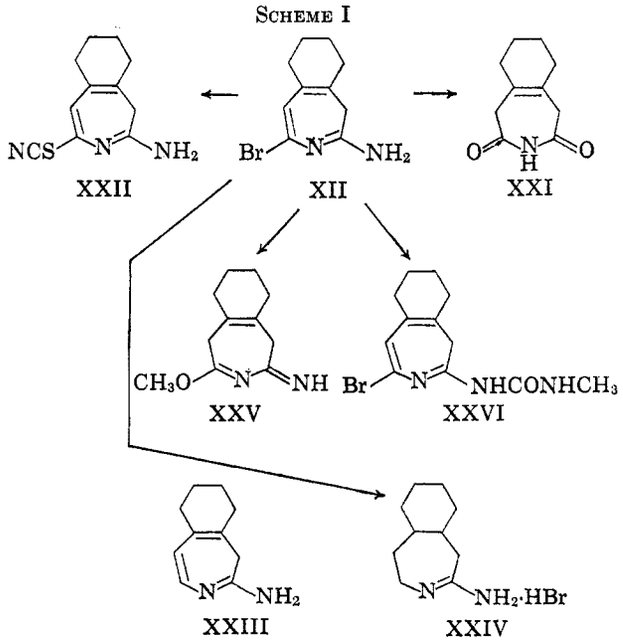
yield to a salt which when neutralized with mild base afforded a single compound that we consider to be XIX rather than XX. This structure rests largely on its nmr spectrum which shows the presence of a vinyl proton triplet absorption (J = 7 cps) at 5.49 ppm coupled with a CH_2 doublet (J = 7 cps) at 3.6 ppm. These peaks integrate in the ratio of 1:2, thus virtually excluding XX as a possibility. In addition, the infrared spectrum of this cyclization product in the 2.5–8.0-μ region again bears a marked similarity to that of II and the tautomeric arrangement of its double bonds are assigned on this basis.

The cyclization of XVIII may thus be compared with that of 2-cyanobenzyl cyanide which on treatment with hydrogen bromide also yields a single product, namely, 3-amino-1-bromoisoquinoline.[8] From this point of view of the carbon chain joining the nitrile groups, XVIII is simply a homolog of 2-cyanobenzyl cyanide and like the latter compound it obeys the rule[9] controlling these cyclizations; *i.e.*, the carbon atom of the unsaturated nitrile in the starting material is destined to bear the bromine atom in the product while the nitrogen atom of the saturated nitrile becomes the amino group.

(8) F. Johnson and W. A. Nasutavicus, *J. Org. Chem.*, **27**, 3953 (1962).
(9) F. Johnson and R. Madroñero, *Advan. Heterocyclic Chem.*, **6**, 95 (1966).

Of the above azepine compounds only the chemistry of XII has been examined, but even here the study has been more perfunctory than rigorous. In a number of ways the reactions of XII parallel those of II. Refluxing the former compound in aqueous methanol or, better, heating its hydrobromide in aqueous dimethylformamide at 90° for a few hours yielded the imide XXI. On the other hand, treatment of XII with a hot dimethylformamide solution of sodium thiocyanate led to the thiocyanate XXII. The same type of substitution, however, could not be accomplished with azide ion nor could the amino function of XII be diazotized by means of sodium nitrite in 6 N sulfuric acid, only starting material being recovered in this case. (See Scheme I.)

SCHEME I



XXII XII XXI XXV XXVI XXIII XXIV

Our major interest in this area, however, was to find a method of reductively removing the bromine atom from XII to obtain XXIII. To date we have failed, but efforts are still being made. Hydrogenation of XII in aqueous dimethylformamide in the presence of potassium bicarbonate or in dioxane containing triethylamine in the presence of a 10% palladium-on-charcoal catalyst gave none of the desired material. In each case, noncrystallizable oily mixtures were obtained. In ethanol in the absence of a base, reduction occurred rapidly with this catalyst, but only the saturated amidine hydrobromide XXIV could be isolated. Zinc dust in ethereal acetic acid was without effect on XII. The reaction of sodium borohydride in methanol with XII effected not reduction but substitution of the bromine by methoxy to give XXV. The structure of the latter compound is in little doubt. It gives a good elemental analysis and its nmr spectrum in trifluoroacetic acid shows the presence of three singlets at 3.60, 3.75, and 3.99 ppm which integrate in the ratio 2:2:3 and therefore correspond to the two methylene groups of the seven-membered ring and the methoxyl group. Two other broad peaks at 1.70 and 2.17 ppm, which each account for four protons, represent the methylene groups of the cyclohexene ring, while a broad band at 9.03 ppm accounts for N^+H_2 absorption (two protons).

The reaction of XII with fumaronitrile in ethyl acetate proved interesting. The product appears to be a 2:1 (azepine–fumaronitrile) complex of the components rather than a true Diels–Alder adduct. Surprisingly, the infrared spectrum of the material did not show an unsaturated nitrile band. On the other hand, almost all bands in the 6–10-μ region were characteristic of XII itself. Fast recrystallization of the material led to a mixture of two different types of crystals which when mechanically separated were easily recognized as fumaronitrile and XII. However, if the ethyl acetate solution was seeded with the complex, then only this substance crystallized from solution. Finally, a Diels–Alder reaction of the mixed urea XXVI (the phenyl urea was unsuitable because of its insolubility) and fumaronitrile was also attempted. However, in neither hot tetrahydrofuran nor ethyl acetate solvent could any adduct be obtained, starting materials alone being recovered.

Experimental Section

The nmr spectra were recorded using a Varian A-56/60 instrument and were recorded downfield relative to TMS at 0 ppm. Where not stated, deuteriochloroform was the solvent. Infrared spectra were obtained from a Baird spectrophotometer, Model No. 4-55. The latter were recorded in Nujol mull. Melting points were determined on a Fisher-Johns melting point block and are not corrected.

2,5-Diphenyladiponitrile (V).—To a slurry of sodium hydride (2.4 g) in dimethyl sulfoxide (100 ml) there was added with cooling a mixture of phenylacetonitrile (11.7 g) and 1,2-dibromoethane (9.3 g). The solution was allowed to come to room temperature and then left for 18 hr. Water and ice were then added and the oil which separated was dissolved in methylene chloride, washed thoroughly with water, and concentrated under reduced pressure. The solid which separated during this last step was removed by filtration and recrystallized. This afforded pure 2,5-diphenyladiponitrile (0.6 g), mp 194–195°. Its infrared spectrum showed a band at 4.43 μ corresponding to saturated nitrile.

Anal. Calcd for $C_{18}H_{16}N_2$: C, 83.0; H, 6.2; N, 10.8. Found: C, 82.8; H, 6.2; N, 10.6.

The poor yield of V in this reaction is due to the preferential formation of 1-cyano-2-phenylcyclopropane which constitutes the bulk of the product.

2-Cyanomethylcycloalkanones.—To an ice-cold solution of the pyrrolidine enamine of the cycloalkanone (0.5 mole) in 300 ml of freshly dried and distilled acetonitrile was added anhydrous triethylamine (0.5 mole) and anhydrous chloroacetonitrile (0.5 mole). The reaction was kept overnight at room temperature and then refluxed for 1 hr. The resultant triethylamine hydrochloride was removed by filtration and the filtrate concentrated to one-half the volume *in vacuo*. The reaction was acidified with 6 *N* hydrochloric acid, diluted with a large excess of water, and extracted three times with ethyl ether. The ether, after being dried over magnesium sulfate, was removed *in vacuo;* the product was distilled to give yields of 30–60%. The physical constants of the products having a five, six, or eight-membered ring were in accord with those obtained previously.[6,7,10]

2-Cyanomethyl-1-cyanomethylenecycloalkanes (XV).—Sodium hydride (0.15 mole) was placed in 100 cc of dry, freshly distilled 1,2-dimethoxyethane. The slurry was cooled in ice water and diethyl cyanomethylphosphonate (0.2 mole) was added dropwise with stirring. After the addition, stirring was continued for 1 hr while the flask was allowed to warm to room temperature. Then 2-cyanomethylcycloalkanone (0.15 mole) was added dropwise to the yellow solution which was kept cool during the addition. A gummy precipitate usually appeared during this process. The reaction was stirred for 2 hr at room temperature. Then a large excess of water was added and the product extracted with ether. The ether, after being dried over magnesium sulfate, was removed *in vacuo* and the product distilled or crystallized (see Table I).

Cyclization of the Dinitriles.—The dinitrile (XV), depending on its solubility characteristics, was dissolved in 10–20 times its volume of ether or methylene chloride and the solution cooled in an ice bath. Then anhydrous hydrogen bromide was bubbled through the liquid for approximately 30 min. The solvent was removed under reduced pressure (water pump) and the crystalline or syrupy residue crystallized from the appropriate solvent to yield the requisite azepine hydrobromide (see Table I) as a colorless material.

Preparation of the Azepine Free Bases (XVI).—The salt obtained above was dissolved in 10–20 ml of methanol and poured with stirring into excess sodium bicarbonate solution. The mixture was stirred for 15–30 min and the resultant precipitate then removed by filtration, dried, and recrystallized from methylene chloride.

Preparation of the Urea Derivatives (XVII).—The azepine was dissolved in a minimum amount of tetrahydrofuran. Then an equivalent amount of phenylisocyanate was added and the reaction allowed to stand at room temperature for 1 hr. If a precipitate did not appear at the end of this time, then the reaction was refluxed for 1 hr. Concentration of the solution yielded the urea derivatives in excellent yield. These were recrystallized from tetrahydrofuran.

2-Amino-4-iodo-6,7,8,9-tetrahydro-1H-3-benzazepine (XIII).—2-Cyanomethyl-1-cyanomethylenecyclohexane (4.0 g) in methylene chloride (100 ml) at 0° was treated with dry hydrogen iodide for 45 min and subsequently allowed to stand for 1 hr longer. Then the methylene chloride was removed under reduced pressure and the resulting solid dried in a stream of dry nitrogen. Addition of this solid to saturated sodium bicarbonate solution followed by methylene chloride extraction afforded a mixture of syrup and crystals (6 g). Crystallization of the latter from methylene chloride afforded the iodo compound, mp 156–160° dec. Its infrared spectrum showed bands at 2.87, 3.05, 6.10, 6.47, 6.61, 7.09, 7.54, 8.15, 8.84, 9.92, 10.70, 10.97, 11.49, 11.62, 11.95, and 12.43 μ.

Anal. Calcd for $C_{10}H_{13}IN_2$: C, 41.7; H, 4.5; I, 44.0; N, 9.7. Found: C, 41.4; H, 4.5; I, 44.3; N, 9.6.

1-Cyclohexene-1,2-diacetamide (XXI).—A solution of XI (1.0 g) in dimethylformamide (5 ml) and water (10 ml) was refluxed for 3 hr. When the solution was cooled, the imide (0.5 g) crystallized out in 90% yield. The analytical sample was prepared by recrystallizing a specimen from acetone: white platelets, mp 188–189°. Its infrared spectrum showed significant bands at 3.11 and 3.20 μ and a strong band at 5.88 μ, all characteristic of the imide function.

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.0; H, 7.3; N, 7.8. Found: C, 67.0; H, 7.5; N, 7.8.

(10) O. Schlichting and G. Scheuerer, U. S. Patent 2,882,292 (1959).

2-(β-Cyanoethyl)-1-cyanocyclohexene (XVIII).—2-(β-Cyanoethyl)cyclohexanone (70 g) was stirred with a solution of sodium bisulfite (75 g) in water (375 ml). After 20 min, the mixture became homogeneous and it was treated with potassium cyanide (33 g). After a further 45 min, the oil which had separated was extracted with ether and isolated in the usual way. By this procedure there was obtained 70 g of the cyanohydrin of the starting ketone. The analytical sample was prepared from ether–petroleum ether (bp 30–60°) and had mp 80–82°. The infrared had significant bands at 2.91 and 4.41 μ.

Anal. Calcd for $C_{10}H_{14}N_2O$: C, 67.4; H, 7.9; N, 15.8. Found: C, 67.3; H, 7.9; H, 15.7.

The cyanohydrin was added to phosphorus pentoxide (80 g) suspended in benzene (600 ml) and the reaction mixture was refluxed for 1 hr. Then the liquid phase was separated, added to fresh phosphorus pentoxide (80 g), and refluxed for an additional 4 hr. Quenching the reaction mixture in cold water followed by extraction with ether afforded the crude product which contained a lactonic impurity as judged by its infrared spectrum (band at 5.79 μ). A considerable amount, but not all, of this impurity was removed by extraction with 1 *N* potassium hydroxide solution. Distillation of the final material, bp 150° (~0.1 mm), afforded the required dinitrile (18 g) having absorption bands in the infrared spectrum at 4.44 and 4.49 μ. The band for lactone was also present and rather than to embark on an extensive purification procedure the compound was used as such in the cyclization reaction described below.

3-Amino-1-bromo-6,7,8,9-tetrahydro-4H-2-benzazepine (XIX).—A solution of XVIII (1.2 g) in dry ether was treated with a stream of hydrogen bromide gas for 15 min at 0°. After a further 45 min at 0°, the solvent was removed under reduced pressure and the residue crystallized from acetone–ether to give XIX·HBr (0.9 g). The analytical sample prepared by recrystallization from ether–methanol had mp 212–214°. Its infrared spectrum had absorption bands at 3.05–3.65, 6.01, 6.22, 6.32, 7.42, 8.32, 8.50, 10.25, 10.80, 11.98, 12.42, and 13.35–14.10 μ.

Anal. Calcd for $C_{10}H_{14}Br_2N_2$: C, 37.3; H, 4.4; Br, 49.6; N, 8.7. Found: C, 37.3; H, 4.0; Br, 49.7; N, 8.6.

Neutralization of the above salt with sodium bicarbonate solution led to the free base XIX which crystallized from methylene chloride as hard prisms, mp 150–155° dec. Its infrared spectrum showed significant bands at 2.90, 3.03, 3.18, 6.06, 6.40–6.50, 7.10, 7.57, 7.88, 8.11, 8.22, 8.68, 8.97, 9.52, 9.68, 10.90, 11.37, 11.58, 12.21, 12.36, and 13.05 μ.

Anal. Calcd for $C_{10}H_{13}BrN_2$: C, 49.8; H, 5.4; Br, 33.1; N, 11.6. Found: C, 49.8; H, 5.4; Br, 33.3; N, 11.7.

2-Amino-4-thiocyano-6,7,8,9-tetrahydro-1,H-3-benzazepine (XXII).—Dry sodim thiocyanate (0.45 g) and XIV (1.2 g) were dissolved in dry dimethylformamide (15 ml). The solution was refluxed for 3 hr and then poured into water. The precipitated solid was removed by filtration and dried. Recrystallization of this solid (1.1 g) afforded, after treatment with charcoal, pure XXII (0.5 g). Crystallization of a sample from methylene chloride–ether gave the analytical specimen, mp 170–174° dec. Its infrared spectrum showed a band at 4.57 μ for thiocyanate and other bands were at 2.96, 3.17, 6.02, 6.40, 6.57, 7.45, 7.80, 7.95, 8.14, 9.78, 10.78, 10.96, 11.40, 11.60, 12.18, and 12.39 μ.

Anal. Calcd for $C_{11}H_{13}N_3S$: C, 60.2; H, 6.0; N, 19.2; S, 14.6. Found: C, 60.2; H, 6.0; N, 19.0; S, 14.6.

2-Imino-4-methoxy-6,7,8,9-tetrahydro-1,5H-3-benzazepine (XXV).—A solution of XII (5.0 g) in methanol (120 ml) was treated with sodium borohydride (2 g) added in small portions during 1 hr. The mixture was then diluted with water and the precipitated solid removed by filtration and dried. Crystallization of this crude product (3.0 g) from acetone afforded pure XXV, mp 174–176°. Its infrared spectrum showed bands at 2.93, 3.17 (NH), and 6.07 (C=C) and methoxyl absorption at 8.24 and 9.13 μ.

Anal. Calcd for $C_{11}H_{16}N_2O$: C, 68.7; H, 8.4; N, 14.6. Found: C, 68.3; H, 8.3; N, 14.5.

2-Amino-4,5,5a,6,7,8,9,9a-octahydro-1H-3-benzazepine Hydrobromide (XXIV).—A solution of XII (2.4 g) in ethanol (75 ml) was stirred with hydrogen at room temperature in the presence of a 10% palladium-on-charcoal catalyst. Gas absorption (665 ml, calcd 720 ml) ceased after 3 hr. The catalyst was removed by filtration and the solvent evaporated under reduced pressure. The residual oil slowly crystallized. Recrystallization from methanol–acetone afforded pure XXIV (1.6 g), mp 204–205°. Its infrared spectrum showed bands at 2.99, 3.19, 5.99, 6.54, 7.81, 7.98, 8.06, 8.48, 9.29, 10.18, 10.50, 10.96, 12.73, 13.90, and 14.50 μ.

Anal. Calcd for $C_{10}H_{19}BrN_2$: C, 48.6; H, 7.7; Br, 32.3; N, 11.2. Found: C, 48.7; H, 7.7; Br, 32.3; N, 11.2.

1-(4-Bromo-6,7,8,9-tetrahydro-1H-3-benzazepine-2-yl)-3-methylurea (XXVI).—A sample (2.4 g) of XII in dry tetrahydrofuran (25 ml) was treated with methyl isocyanate added in one portion with swirling. After 1 hr at room temperature, benzene was added to precipitate the product which was removed by filtration. This material (2.6 g) was essentially pure XXVI. A sample crystallized for analysis from tetrahydrofuran had mp 218–220°.

Anal. Calcd for $C_{12}H_{16}BrN_3O$: C, 48.3; H, 5.4; Br, 26.8; N, 14.1. Found: C, 48.3; H, 5.2; Br, 26.6; N, 13.9.

Reaction of Fumaronitrile with XII.—An ethyl acetate solution of XII (1.2 g) and fumaronitrile (0.4 g) was allowed to stand at room temperature overnight. A small amount of an amorphous precipitate was removed by filtration and a yellow crystalline material spontaneously appeared in the filtrate. This was removed by filtration and dried. It could be recrystallized from the same solvent when seeding was employed. Otherwise the starting materials tended to crystallize out separately. The analytical sample had an indefinite melting point behavior. From 110 to 150°, the material slowly turns white. Above this temperature, decomposition sets in with melting being complete at 165–167°. Its infrared spectrum showed absorption bands at 2.91, 2.99, 3.17, 3.23, 6.09, 6.40, 6.44, 6.55, 7.52, 7.80, 8.13, 8.40, 8.47, 8.60, 9.80, 10.45, 10.80, 10.94, 11.10, 11.41, 11.60, 12.03, 12.43, 13.80–13.90, and 14.84 μ.

Anal. Calcd for $C_{24}H_{28}Br_2N_6$: C, 51.4; H, 5.0; N, 15.0; Br, 28.5. Found: C, 51.5; H, 5.3; N, 14.9; Br, 28.7.

Registry No.—V, 13100-49-7; XII, reaction product with fumaronitrile, 13095-03-9; XIII, 13095-04-0; XV, *n* = 1, 13095-05-1; XV, *n* = 2, 13095-06-2; XV, *n* = 3, 13095-07-3; XV, *n* = 4, 13095-08-4; XVI, *n* = 1, 13095-09-5; XVI·HBr, *n* = 1, 13095-10-8; XVI, *n* = 2, 13095-11-9; XVI·HBr, *n* = 2, 13095-12-0; XVI, *n* = 3, 13095-13-1; XVI·HBr, *n* = 3, 13095-14-2; XVI, *n* = 4, 13095-15-3; XVI·HBr, *n* = 4, 13095-16-4; XVII, *n* = 1, 13095-17-5; XVII, *n* = 2, 13095-18-6; XVII, *n* = 3, 13095-19-7; XVIII, 13095-20-0; XIX, 13095-21-1; XIX·HBr, 13095-22-2; XXI, 13095-23-3; XXII, 13095-24-4; XXIV, 13095-25-5; XXV, 13095-26-6; XXVI, 13095-27-7.

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