Repetition of the Darco treatment and of the recrystallization afforded the product referred to in the table.

2,6-Dichloro-4-picoline.—In this reaction, as in that with the corresponding 3,4-lutidine, the reaction mixture was difficult to decompose, and warming of the aqueous mixture was necessary. Steam distillation afforded a white, crystalline solid, as indicated in the table. For analysis the substance was sublimed at 60° (8 mm.), recrystallized from low-boiling petroleum ether and sublimed again to produce shiny white blades, m.p. 65.0–66.0°.

Anal. Calcd. for $C_6H_5NCl_2$: N, 8.65. Found: N, 8.61.

When the reaction was carried out at 155° or at 205° the yields were negligible.

4-Chloropyridine-2,6-dicarboxylic Acid.—The reaction mixture was heated as indicated, decomposed with water and made basic. The dark solution was filtered through Darco and the product precipitated and dried at 135° to produce a 79% yield of crude, anhydrous product. Recrystallization from acetic acid, a repetition of the Darco treatment of a basic solution, and redrying produced the cream-colored, anhydrous material referred to in the table. It was identified by its melting point, a positive qualitative test for chlorine, and its neutral equivalent.

Anal. Calcd. for $C_7H_4NO_4Cl$: neut. equiv., 100.8. Found: neut. equiv., 102.8, 103.0.

Theobromine Reaction.—When the reaction mixture was heated as indicated in the table, then decomposed with cold water, an oily mass was formed. This produced an amorphous solid of indefinite melting range on partial neutralization. Its behavior on attempted recrystallization indicated a mixture and when it was found that the substance was completely soluble in 5% sodium bicarbonate solution it was not investigated further.

Uric Acid Reaction.—Decomposition of the dark reaction mixture with water gradually produced an amorphous, tarry solid. Since extraction with ether and evaporation produced only a small quantity of solid, whose melting point was well above that reported for 2,6,8-trichloropurine,[6] and since the ether-insoluble material, unlike 2,6-dichloro-8-hydroxypurine[6], was completely soluble in concentrated nitric acid, the reaction was not investigated further.

(6) E. Fischer, *Ber.*, **30**, 2220 (1897).

AMHERST, MASS.

[CONTRIBUTION FROM THE ORGANIC CHEMICALS DIVISION, ST. LOUIS RESEARCH DEPARTMENT, MONSANTO CHEMICAL CO.]

Adiponitrile—a Novel Self-condensation Sequence

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Adiponitrile was cyclized under heterogeneous conditions by a molecular equivalent of sodium *t*-butoxide in toluene to give the expected product 2-amino-1-cyano-1-cyclopentene (III). However, under homogeneous conditions in *t*-butyl alcohol with a catalytic amount of potassium *t*-butoxide, a dimeric substance found to have structure VII was the major product. Compound VII was converted smoothly to 4-amino-6,7-dihydro-5H-cyclopenta[d]pyrimidine-2-valeronitrile (VIb) by aqueous mineral acids. The structure of VIb was proved by synthesis. Derivatives of III and various pyrimidines related to VIb were prepared.

Thorpe and Best[1] first prepared 2-cyano-1-iminocyclopentane (II) by methods which involved as the initial step the base-catalyzed cyclization of diethyl α,α'-dicyanoadipate (I). Shortly thereafter Thorpe[2] claimed to have prepared II in 84% yield by cyclizing adiponitrile in alcohol with a catalytic amount of sodium ethoxide. Ziegler, *et al.*,[3] prepared II from adiponitrile using magnesium–diethylamide in molecular amounts to effect ring closure. The material also has been obtained as a by-product in the hydrogenation of adiponitrile,[4] from the reaction of adiponitrile with Grignard reagents,[5] in the commercial preparation of adiponitrile[6] and by high temperature catalytic methods.[7] Hammer and Hines[8] recently showed that II is more correctly represented by its enolized or enamine structure III.

All attempts in this Laboratory to repeat Thorpe's cyclization[2] of adiponitrile with catalytic amounts[9] of sodium ethoxide have failed. Essentially no cyclization occurred even when the heating time was considerably extended. On the other hand, adiponitrile was readily cyclized to III by Ziegler's procedure[3] or better by a molecular equivalent of sodium *t*-butoxide suspended in toluene.

The use of a molecular amount of sodium ethoxide with other conditions essentially the same as in the original Thorpe procedure[2] yielded two crystalline products and a recovery of adiponitrile in 35% yield. The crystalline material was found to be a mixture of III in 39% over-all yield and a new compound (dimer 1), $C_{12}H_{16}N_4$, m.p. 129.5–130.5°, λ_{max}^{alc} 263 mμ, ε 14,400, obtained in 25% yield. Extension of the reflux time to 20 hours resulted in essentially complete conversion of adiponitrile to a mixture of III and the dimeric product with the latter predominating. Preparation of the dimeric substance was effected more conveniently (76% yield) by refluxing adiponitrile in *t*-butyl alcohol with a catalytic amount of potassium *t*-butoxide.

Dimer 1 was a labile basic compound. Determination of molecular weight by cryoscopic methods gave uncertain results, but ebullioscopic determination in ethylene dibromide clearly indicated a C_{12}-compound. Acetylation or benzoylation in pyridine gave low yields of an acetate (Va) and benzoate (Vb) identical with the respective derivatives obtained directly from III. When a hot pyridine solution of the dimer was quenched in ice-water, a mixture of III (about 30%) and dimer was recovered. Conversion of III back to the di-

(1) S. R. Best and J. F. Thorpe, *J. Chem. Soc.*, 685 (1909).

(2) J. F. Thorpe, *ibid.*, 1901 (1909).

(3) K. Ziegler, H. Ahlinger and E. Eberle, German Patent 591,269; *cf. Frdl.*, **20**, 537 (1934).

(4) O. Riobe and L. Gouin, *Compt. rend.*, **234**, 1889 (1952).

(5) A. Compere, *Bull. soc. chim. Belg.*, **44**, 523 (1935).

(6) R. H. Halliwell, U. S. Patent 2,768,132; see also British Patent 728,522, and L. H. Smith, "Synthetic Fiber Development in Germany"; Textile Research Institute, New York 16, N. Y., 1946, p. 589.

(7) W. A. Lazier and B. W. Howk, U. S. Patent 2,292,949.

(8) C. F. Hammer and R. A. Hines, THIS JOURNAL, **77**, 3649 (1955).

(9) Thorpe mixed 5 g. of adiponitrile and 20 ml. of absolute ethanol and dissolved in this solution a piece of sodium the size of a grain of wheat. After one hour at reflux, 4.2 g. of III, m.p. 147°, was claimed to have crystallized from the reaction mixture on cooling.

mer was accomplished by refluxing in *t*-butyl alcohol with a small amount of potassium *t*-butoxide.

Unlike III, which is converted rapidly and quantitatively to 2-cyanocyclopentanone (IV) by aqueous mineral acids,[2] the dimer dissolved in cold acid and was converted rapidly to a second $C_{12}H_{16}N_4$ compound (dimer 2) (66% yield) and IV (29%). Dimer 2 was a stable basic substance, m.p. 140.5–141.5°. The infrared spectrum indicated the presence of $-NH_2$ and a single unconjugated nitrile. The ultraviolet spectrum showed two maxima (270 mμ, ε 5,840 and 238 mμ, ε 9,180) in neutral solution but only a single peak at 262 mμ, ε 13,300, in acid solution. The amine function could be acetylated with difficulty and appeared to be essentially unreactive with nitrous acid. This behavior and the ultraviolet spectrum in particular was suggestive of a pyrimidine.[10,11] We have now proved conclusively that dimer-2 is 4-amino-6,7-dihydro-5H-cyclopenta[d]pyrimidine-2-valeronitrile (VIb).[12] From this and other available information, it can be deduced that dimer 1 has structure VII.

Good evidence in support of the cyclopenta[d]-pyrimidine structure VIb for dimer 2 was obtained by synthesis of the model compound VIa. Acetamidine (VIIIa) condensed readily with 2-carbethoxycyclopentanone to give IXa which was converted to the corresponding 4-chloro compound Xa and thence to VIa by standard methods.[10,13] The ultraviolet spectrum of VIa was identical with that of dimer-2 both in neutral and acid solution. Expected similarities were also apparent in the infrared spectra. Final proof of dimer-2 structure was obtained by synthesis of VIb using the route outlined for VIa. Condensation of 5-cyanovaleramidine (VIIIb) with 2-carbethoxycyclopentanone gave IXb which was converted *via* Xb to VIb. Compound VIb prepared in this way was identical in all respects with dimer 2 obtained from adiponitrile. As previously noted, VIb was acetylated with some difficulty to give an acetate VIc. Solution of VIb in hot concentrated sulfuric acid followed by addition of water caused hydration of the nitrile to the amide VId without otherwise disturbing the molecule.

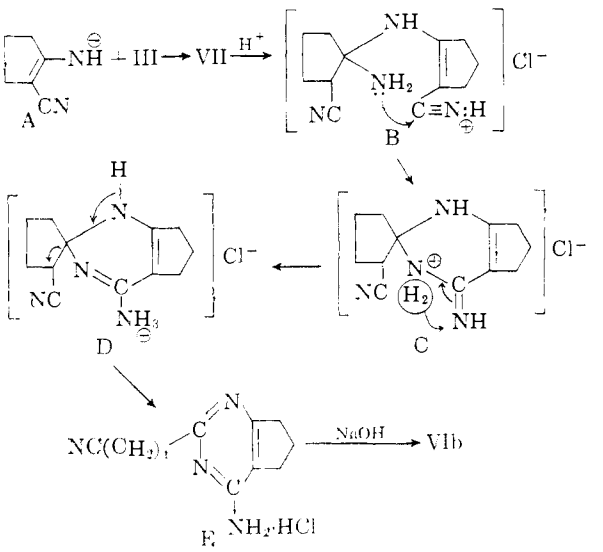
Having established the structure of VIb, it became apparent that its precursor (dimer 1) must be VII. Its infrared spectrum in dilute chloroform showed the presence of $-NH_2$ (two bands 3440 and 3520 cm.$^{-1}$) and two nitrile bands (2240 cm.$^{-1}$ unconjugated, and 2180 cm.$^{-1}$ conjugated). The dimer showed similarities in the 6.0 to 6.5 μ region to Thorpe's compound III, but three bands at 1640, 1608 and 1575 cm.$^{-1}$ were apparent instead of the two observed in III.[8] The ultraviolet spectrum, λ 263 mμ, ε 14,400, suggested that a single enamine-nitrile chromophore similar to that in III must be present.

The fact that the *cyclic* compound IV was the sole by-product in the conversion of VII to VIb eliminated alternative structures such as XI in which one of the original adiponitrile moieties remained acyclic. Acid hydrolysis of XI or a tautomer thereof would necessarily result in the formation of IV and an equal amount of either 5-cyanovaleric acid (XIIa) or amide XIIb. No evidence of XIIa or XIIb could be found in numerous experiments.[14]

In view of these facts, VII appeared to be the only acceptable structure for dimer 1. Acylation of the primary $-NH_2$ group in VII apparently decreases the stability of the ketone–ammonia system in VII causing a reversal of the dimerization process. Thus, only acyl derivatives of III were isolable.

When subjected to catalytic hydrogenation with Raney nickel in the presence of ammonia, compound VII was converted smoothly to the diaminopyrimidine VIe (72%) and a small amount of 2-aminocyclopentanemethylamine[15] (XIII) thus again illustrating the facile convertibility of VII to the stable system VI. Hydrogenation of VIb under the same conditions gave VIe in essentially quantitative yield.

The mechanism of the over-all transformation to the pyrimidine ring system may be rationalized as



Adiponitrile is cyclized under the influence of the *t*-butoxide base to give the anion A. Under heterogeneous reaction conditions, as in the case of sodium *t*-butoxide in toluene, this anion precipitates out as the sodium salt and the reaction is stopped. Under homogeneous conditions and with only catalytic amounts of base present, anion A adds to another molecule of III (or II) (*cf.* cyanoethylation)

(10) B. Lythgoe, *Quart. Revs.*, **3**, 181 (1949).

(11) J. R. Marshall and J. Walker, *J. Chem. Soc.*, 1004 (1951).

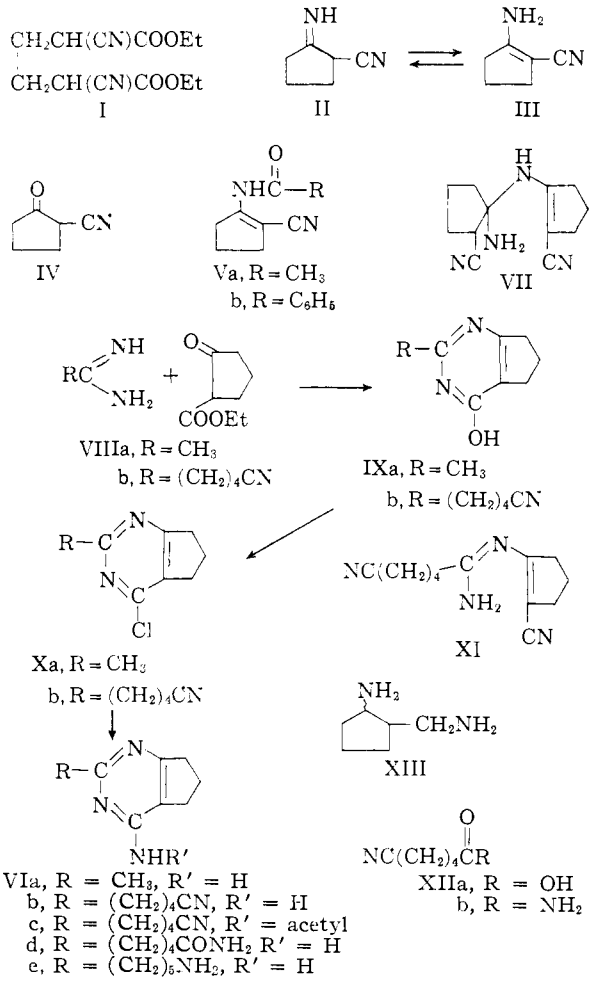
(12) This structure was first suggested by R. B. Woodward at an early stage in the work while in private conversation with the author. We are greatly indebted to Professor Woodward for this substantial contribution.

(13) H. R. Henze, W. S. Clegg and C. W. Smart, *J. Org. Chem.*, **17**, 1321 (1952).

(14) Cyanocyclopentanone was quite stable to aqueous acids but was rapidly converted to 5-cyanovaleric acid by aqueous base. Isolation of IV in these experiments to be meaningful must be done in the absence of base.

(15) Compound III has been reduced catalytically to XIII both in this Laboratory and by others (ref. 7). No evidence of pyridine formation was found. This fact coupled with the fact that III is quantitatively hydrolyzed to cyanocyclopentanone (*cf.* ref. 2) under the same conditions that dimer 1 was converted to the pyrimidine VIb indicates strongly that the latter cannot arise directly from III as has been suggested by a referee but must involve dimer 1 as its immediate precursor.

to give ultimately the dimer VII. The amine and nitrile group of VII being favorably arranged in space allow cyclization to compete advantageously with hydrolysis when subjected to treatment with aqueous acid. Enolization and transfer of the proton in C to the more basic nitrogen would afford the dihydropyrimidine system D. Aromatization and ring opening would be expected giving the stable ring system of the pyrimidine hydrochloride E. That the transformation was complete at this point was established by the fact that the hydrochloride E was identical in the infrared with the hydrochloride obtained by treating VIb with hydrochloric acid. Thus, the aqueous base added to precipitate VIb from the aqueous acid served no function other than to allow isolation of the free pyrimidine base.



The cyclization occurring during catalytic hydrogenation presumably would follow essentially the same path. In this case, the initial attack upon the nitrile in B would occur by hydrogen at the catalytic surface thus setting in motion the transformations leading to aromatization and ring opening.

Ackowledgments.—We thank Dr. Bernart Katlafsky for help with the numerous spectra required in this work. We are particularly indebted to Professor R. B. Woodward for providing the initial structural concept[12] and to Dr. W. S. Knowles for much valuable advice and discussion. The assistance of Mr. C. Dean Roth in various preparations is also gratefully acknowledged.

Experimental[16]

2-Amino-1-cyano-1-cyclopentene (III). a. Attempted Repetition of Thorpe's Procedure.[2]—Adiponitrile[17] (21.6 g.) was dissolved in 60 ml. of carefully prepared absolute alcohol.[18] To this was added 40 ml. of 0.468 molar sodium ethoxide solution prepared by addition of clean sodium to dry ethanol.[18] The golden yellow solution was refluxed under nitrogen for 1 hour, cooled and seeded with a crystal of III prepared by an alternate method. No crystallization occurred after 1.5 hr. at 5°. The reaction mixture was then heated at reflux overnight making the total heating about 20 hours. When cooled and seeded with III, again no precipitate formed. Most of the ethanol was removed *in vacuo* and 80 ml. of water added to the residue. This solution was extracted thoroughly with 200 ml. of methylene chloride in three portions. The aqueous phase was discarded and the organic phases were combined, washed with 80 ml. of water and dried with Drierite. The solvent was removed leaving 20.3 g. (94%) of essentially pure adiponitrile, $n^{25}D$ 1.4380, as compared with $n^{25}D$ 1.4364 for the starting material. The infrared spectrum of the recovered nitrile indicated that it was approximately 95% pure with the impurity being the desired cyclized product III.

b. By Magnesium—Alkyl Amide Method.—The procedure used was essentially a modification of Ziegler's procedure.[3] To a solution of 7.3 g. of anhydrous *t*-butylamine in 150 ml. of anhydrous ether under nitrogen was added dropwise 33 ml. of 3 molar methylmagnesium bromide solution at 0°. The evolution of methane was somewhat sluggish so the mixture was allowed to warm to 30° where it was maintained (1 hour) until the evolution of gas had ceased and the ether solution was essentially free of solids. Adiponitrile (10.8 g.) was added causing a copious gray precipitate to form. The thick reaction mixture was stirred vigorously and allowed to stand at 30° for 16 hours.

The mixture was decomposed by addition of 100 ml. of saturated ammonium chloride solution (exothermic). Some solid, insoluble in both the water and the organic phase, separated. This was collected by filtration and amounted to 2.1 g., m.p. 147–148°, of good quality III. Work-up of the ether phase from the filtrate by washing, drying and removing solvent gave 3.2 g., m.p. 147–148°, more of good quality III; total yield of good quality crystals 5.3 g. (49%).

c. By Sodium *t*-Butoxide Method.—A dispersion containing 23 g. of sodium in 600 ml. of toluene at 60–70° was treated dropwise with 87 g. of *t*-butyl alcohol with good stirring. When evolution of hydrogen had ceased, the thick suspension was heated at reflux for 10 minutes. Adiponitrile (108 g.) then was added dropwise with good stirring over about a 1-hour period. The reaction was quite exothermic during the early stages but slackened as more solid separated. Refluxing was continued for 1 hour after all of the adiponitrile had been added.

The heavy mixture was allowed to cool and stand overnight at room temperature. Work-up was effected by addition of about 400 ml. of water (exothermic). Considerable organic solid separating at this point was removed by filtration. The toluene phase was washed with another 200 ml. of water and more crystals separated. After these were collected, the aqueous phases were extracted once with 200 ml. of chloroform and discarded. The toluene and chloroform phases were combined, washed with a little water and taken to dryness, leaving a small crop (7.1 g.) of crude product. The various crops of crude crystals were

(16) Melting points are uncorrected. Infrared spectra were run on a Perkin-Elmer recording spectrophotometer, model 21. Ultraviolet spectra were run on a Cary recording spectrophotometer, model 11. Analyses were done by DuGood Chemical Laboratory of St. Louis.

(17) Eastman Kodak Co. white label grade fractionated to a crystallization point of 2.40°.

(18) Good commercial absolute ethanol was dried by the magnesium ethoxide method outlined by Fieser (L. Fieser "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 3rd ed., 1955, p. 286). A 10-ml. aliquot of this dry ethanol showed less than 0.2 mg. of water as indicated by titration with standard Karl Fischer reagent

allowed to air dry and then were combined and recrystallized from about 500 ml. of chloroform. In all, 92.3 g. (85%), m.p. 147–148°, of III as pale yellow needles was obtained.

2-Amino-2-(2-cyano-1-penten-1-ylamino)-cyclopentenecarbonitrile (VII).—Adiponitrile (216 g.) in 450 ml. of *t*-butyl alcohol was treated with 22 ml. of 0.9 molar potassium *t*-butoxide solution and refluxed for 8 hours under nitrogen. On cooling, a copious precipitate of light tan crystals separated. These were collected by filtration, washed with a little ether, and when dry amounted to 148.7 g., m.p. 126–130°. The filtrate containing the mother liquor and ether washing was treated with 600 ml. of water. This solution was extracted with 500 ml. of chloroform in two portions and then discarded. The chloroform layers were combined, washed once with 200 ml. of water and dried. Removal of the bulk of the chloroform gave a second crop of crystals, 16.4 g., m.p. 120–130°. A third crop (6.2 g.) of sticky crystals was obtained on complete removal of chloroform. The residual oil amounted to 35 g. which appeared to be about 70% adiponitrile and 30% compound III as evidenced by the infrared spectrum. Recrystallization of the small third crop material from methanol gave 3.5 g., m.p. 143–147°, of impure III.

The large first crop and smaller second crop were combined, decolorized and recrystallized from about 800 ml. of benzene. Approximately 145 g., m.p. 129–130°, of essentially pure VII was obtained. The analytical sample was prepared by recrystallizing a small amount of this material twice from benzene, m.p. 129.5–130.5°, λ_{max}^{alc} 263 mμ, ε 14,400.

Anal. Calcd. for $C_{12}H_{16}N_4$: C, 66.63; H, 7.46; N, 25.90; mol. wt., 216. Found: C, 66.69; H, 7.47; N, 26.14; mol. wt., 211 (ebullioscopically in ethylene dibromide).

N-(2-Cyano-1)-cyclopenten-1-yl)-acetamide (Va). a. From III.—A solution of 5.4 g. of III, 25 ml. of dry pyridine and 10.2 g. of acetic anhydride was heated at 100° for 16 hr. under a nitrogen atmosphere. The solution was cooled and poured into a mixture of ice (about 80 g.) and 100 ml. of 6 molar hydrochloric acid. On scratching, a crop of brown colored crystals separated which, when dry, amounted to 3.0 g., m.p. 115–125°. Extraction of the aqueous mother liquor with 100 ml. of chloroform in two portions followed by washing, drying and removal of solvent gave a brown oil residue from which an additional crop of impure acetate (2.5 g.), m.p. 112–120°, was obtained on trituration with ether. The crude crystalline fractions of Va were combined, dissolved in a benzene–ether mixture and chromatographed on alumina. In all, about 3.8 g. (54%) of good quality Va, m.p. 123–125°, was obtained. Recrystallization of a small portion twice from ether and benzene gave the analytical sample, m.p. 124–125°.

Anal. Calcd. for $C_8H_{10}N_2O$: C, 63.97; H, 6.71; N, 18.66. Found: C, 63.95; H, 6.75; N, 18.51.

b. From VII.—A solution of 4.32 g. of VII, 10 ml. of pyridine and 6 ml. of acetic anhydride was allowed to stand at room temperature for 64 hours. When the reaction mixture was quenched as in (a), no crystals separated. Work-up of the oily material gave 0.7 g. of light tan needles, m.p. 119–124°. Purification of this material on alumina gave 600 mg. of pure Va, m.p. 124–125°, which showed no depression on a mixed m.p. with material obtained in part (a).

Other attempts to acetylate VII by heating in pyridine as in (a) gave no better yields and the product was somewhat darker.

N-(2-Cyano-1-cyclopenten-1-yl)-benzamide (Vb). a. From III.—To a cold (10°) mixture of 5 ml. of pyridine and 1.08 g. of III was added 1.4 g. of benzoyl chloride dissolved in 3 ml. of dioxane. The reaction was allowed to stand at 5° for 0.5 hr. and then poured into about 50 ml. of cracked ice and dilute hydrochloric acid. The yellow oil which separated was taken up in chloroform, washed with water and dried. Removal of chloroform gave 1.7 g. of oil which when triturated with ether and allowed to stand overnight at −5° deposited 800 mg. of light tan crystals, m.p. 92–95°. These were dissolved in ether and the solution put through a short column of alumina. Removal of solvent gave 635 mg. of pure Vb, m.p. 96–97°. Recrystallization once from ether did not change the melting point.

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.69; H, 5.72; N, 12.85.

b. From VII.—A solution of 2.16 g. of VII, 8 ml. of pyridine and 1.5 g. of benzoyl chloride, allowed to stand overnight at 25°, gave 700 mg. of slightly yellow Vb, m.p. 94–96° when worked up as in (a). Purification gave 500 mg. of pure Vb, m.p. 96–97°, identical in the infrared with the benzoate obtained in (a). A mixed m.p. showed no depression.

6,7-Dihydro-4-hydroxy-2-methyl-5H-cyclopenta[d]pyrimidine (IXa).—2-Carbethoxycyclopentanone[19] (55.7 g.) was dissolved in 400 ml. of 1.0 molar potassium *t*-butoxide solution. Acetamidine hydrochloride (33.7 g.) was added with good stirring. The temperature rose initially to 45°, but subsided as a fine precipitate of potassium chloride separated. After stirring at room temperature for 25 hours, the bulk of the solvent was removed *in vacuo* at about 40–50°. To the thick slurry remaining was added 440 ml. of saturated sodium chloride solution, 440 ml. of chloroform and 7 ml. of glacial acetic acid. The aqueous layer was separated and extracted again with 100 ml. of chloroform. The chloroform layers were combined, washed once with 200 ml. of saturated sodium chloride solution, dried with Drierite and the solvent removed. The residue of white needles remaining was washed with 200 ml. of ether. The yield of good quality VIa obtained in this way amounted to 33.8 g., m.p. 211–212°. Recrystallization of a small portion twice from a mixture of acetone and chloroform gave pure material, m.p. 211.5–212°; λ_{max}^{alc} 232 mμ, ε 6800, 272 mμ, ε 5330. The material was soluble in both aqueous acid and alkali and slightly soluble in water.

Anal. Calcd. for $C_8H_{10}N_2O$: C, 63.97; H, 6.71; N, 18.66. Found: C, 63.74; H, 6.61; N, 18.71.

4-Chloro-6,7-dihydro-2-methyl-5H-cyclopenta[d]pyrimidine (Xa).—Twenty-five grams of IXa was refluxed for 1.5 hours with 100 ml. of phosphorus oxychloride. The excess oxychloride was removed *in vacuo* leaving a thick red oily residue from which a white solid sublimed. As soon as the sublimation became appreciable, the mixture was treated with 70 ml. of chloroform. This solution was cooled to 0° and about 50 ml. of water added dropwise (exothermic). About 70 ml. of concentrated ammonium hydroxide was next added to the well-stirred mixture keeping the temperature below 40°. Toward the end of the basification, some inorganic salts separated. These were removed by filtration and discarded. The aqueous phase was separated from the chloroform solution and extracted with 100 ml. of chloroform in two portions. The chloroform layers were combined, washed with 100 ml. of water and dried. Removal of chloroform left 28.4 g. of yellow-red oily residue, which was subjected to vacuum distillation. The bulk of the liquid 22.7 g. (81%), distilled in the range 108–112° (6.5 mm.). This material was pale yellow in color and had a powerful odor of popcorn. Redistillation of a small center cut for analytical purposes gave Xa as a clear, colorless liquid, b.p. 98° (4 mm.), λ_{max}^{alc} 262 mμ, ε 5960.

Anal. Calcd. for $C_8H_9N_2Cl$: C, 56.99; H, 5.38; N, 16.62; Cl, 21.03. Found: C, 57.19; H, 5.82; N, 16.28; Cl, 20.83.

This material evidenced considerable stability. Difficulty was encountered in obtaining good C and H values because of incomplete combustion. The compound did not give a positive Beilstein test for halogen.

4-Amino-6,7-dihydro-2-methyl-5H-cyclopenta[d]pyrimidine (VIa).—A mixture of 19.3 g. of Xa, 25 ml. of dioxane and 300 ml. of concentrated aqueous ammonia was charged to a stirred autoclave and heated at 100–105° for 16 hours. The product, 14.6 g. (86%), m.p. 250–255°, crystallized from the aqueous solution on cooling. The brown colored crude solid was dissolved in 150 ml. of 3 molar hydrochloric acid, decolorized with carbon and precipitated by addition of excess sodium hydroxide. About 13.5 g. of white powder was obtained. Recrystallization of a small amount of this material twice from ethanol gave pure VIa as colorless needles, m.p. 252–253°; λ_{max}^{alc} 270 mμ, ε 5640, and 236 mμ, ε 8670. When the alcoholic solution in the cell was acidified with a drop of hydrochloric acid and the spectrum rerun, a single maximum at 262 mμ, ε 12,700, was obtained.

Anal. Calcd. for $C_8H_{11}N_3$: C, 64.40; H, 7.43; N, 28.16. Found: C, 64.58; H, 7.64; N, 28.35.

(19) P. S. Pinkney, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 116.

5-Cyanovaleramidine (VIIIb).—Adiponitrile (108 g.) was converted to its half iminoester hydrochloride with 36.5 g. of dry hydrogen chloride and 40 ml. of methanol according to the procedure of Hoga and Sawai.[20]

The crude iminoester hydrochloride (175 g.) was treated at room temperature with a solution of 350 ml. of absolute ethanol containing 35 g. of anhydrous ammonia for 24 hours. The reaction mixture was filtered to remove a small amount of ammonium chloride. The filtrate was then concentrated *in vacuo* until all of the ethanol had been removed. A viscous red oil remained which consisted essentially of a mixture of VIIIb and its hydrochloride. This crude product was used directly in the next step without further treatment.

6,7-Dihydro-4-hydroxy-5H-cyclopenta[d]pyrimidine-2-valeronitrile (IXb).—Approximately 40 g. of the crude oily amidine mixture from above was mixed with 80 ml. of *t*-butyl alcohol and 50 g. of 2-carbethoxycyclopentanone.[18] To this was added 400 ml. of 0.95 molar potassium *t*-butoxide solution and the reaction run as previously described for the preparation of IXa.

The crude oily product was washed with ether and dried. The yield was 30.4 g. of white needles, m.p. 141–146°. One recrystallization from ethyl acetate gave 21.2 g. of long needles, m.p. 151–152°. The material was insoluble in ether but very soluble in benzene or alcohol. One additional recrystallization from ethyl acetate gave the analytical sample, m.p. 151–152°, λ_{max}^{alc} 233 mμ, ε 7,180, and 274 mμ, ε 5,990.

Anal. Calcd. for $C_{12}H_{15}N_3O$: C, 66.32; H, 6.91; N, 19.34. Found: C, 66.43; H, 7.32; N, 19.56.

4-Chloro-6,7-dihydro-5H-cyclopenta[d]pyrimidine-2-valeronitrile (Xb).—Forty grams of IXb was treated with 150 ml. of phosphorus oxychloride as described for the preparation of Xa. The crude oily Xb when subjected to vacuum distillation gave 36.5 g. (84%) of colorless oil, b.p. 211–215° (8 mm.). A center cut taken for analytical purposes was redistilled, b.p. 212–213° (8 mm.); λ_{max}^{alc} 263 mμ, ε 8,780. This compound resembled Xa in its stability and resistance to complete combustion.

Anal. Calcd. for $C_{12}H_{14}N_3Cl$: C, 61.14; H, 5.99; N, 17.83; Cl, 15.04. Found: C, 61.10; H, 6.18; N, 18.06; Cl, 15.34.

4-Amino-6,7-dihydro-5H-cyclopenta[d]pyrimidine-2-valeronitrile (VIb). (a) **From VII.**—A 250-ml. separatory funnel was charged with 17.3 g. of VII, 80 ml. of ice-water and 16 ml. of concentrated hydrochloric acid. The mixture was shaken (10 minutes) until all of the solid had dissolved. The cold aqueous solution was extracted with 150 ml. of chloroform in three portions. The chloroform extracts were combined, washed with 20 ml. of water and set aside over Drierite. The aqueous phases were combined and while stirred rapidly basified by dropwise addition of a substantial excess of 50% aqueous sodium hydroxide solution. Excellent quality VIb crystallized from the aqueous solution during the basification. The yield of VIb was 11.4 g. (66%), m.p. 137–139°. Recrystallization from water and finally from a chloroform–benzene mixture gave the analytical sample, m.p. 140.5–141.5°; λ_{max}^{alc} 238 mμ, ε 9,180, and 270 mμ, ε 5840. Acidification gave a single peak at 262 mμ, ε 13,300.

Anal. Calcd. for $C_{12}H_{26}N_4$: C, 66.63; H, 7.46; N, 25.90; mol. wt., 216. Found: C, 66.82; H, 7.60; N, 25.96; mol. wt., 255 (cryoscopically in dioxane).

The solvent was removed from the chloroform extracts from above leaving 5.16 g. of 2-cyanocyclopentanone as a colorless pleasant smelling oil. Identification was made by comparison of the infrared spectrum with that of authentic 2-cyanocyclopentanone prepared by acid hydrolysis of III[2] and by conversion of both to the same semicarbazone, m.p. 202–203°, as shining plates recrystallized from ethanol. The m.p. of this semicarbazone has been reported as 190° (crude)[1] and 194°.[4]

b. From Xb.—A mixture of 1.12 g. of Xb, 5 ml. of 95% ethanol and 10 ml. of concentrated ammonium hydroxide was heated in a sealed tube at 105–110° for 18 hours. On cooling, 725 mg. of light tan crystals, m.p. 138–140°, crystallized from the solution. When the aqueous filtrate was extracted with chloroform, an additional 160 mg. of product was obtained making the yield 86%. Recrystallization once from water and once from a chloroform–benzene mixture gave pure VIb, m.p. 140.5–141.5°. A mixed m.p. (140–141.5°) with VIb prepared by method (a) established their identity.

4-Acetamido-6,7-dihydro-5H-cyclopenta[d]pyrimidine-2-valeronitrile (VIc).—A solution of VIb in 15 ml. of pyridine and 3.0 g. of acetic anhydride was heated at reflux for 16 hours. The cooled reaction mixture was poured onto cracked ice and dilute hydrochloric acid. This brown solution was extracted with 150 ml. of chloroform in three portions. The chloroform extracts were combined, washed with water, and the solvent removed. The dark oily residue (2.5 g.) was taken up in ether and chromatographed on alumina. A total yield of 1.4 g. (39%) of excellent white needles, m.p. 120–123°, was obtained from the chromatogram. Recrystallization of this material twice from acetone and ether gave the analytical sample, m.p. 122–123°.

Anal. Calcd. for $C_{14}H_{18}N_4O$: C, 65.10; H, 7.02; N, 21.69. Found: C, 65.29; H, 7.32; N, 21.70.

4-Amino-6,7-dihydro-5H-cyclopenta[d]pyrimidine-2-valeramide (VId).—Purified VIb (3.0 g.) was dissolved in concentrated sulfuric acid. The temperature rose to 85° where it was held for 10 minutes after which the dark solution was cooled to 25° and poured onto 5 g. of cracked ice. The clear tan solution resulting was basified with 50% aqueous sodium hydroxide solution causing VId to separate as a fine white powder. The aqueous suspension was cooled at 0° for 30 min. and the solid collected by filtration. When dry the crude amide amounted to 3.0 g. (92%), m.p. 217–218°. Recrystallization twice from a methanol–water mixture gave pure VId, m.p. 217–219°.

Anal. Calcd. for $C_{12}H_{18}N_4O$: C, 61.55; H, 7.74; N, 23.91. Found: C, 61.97; H, 8.02; N, 23.54.

4-Amino-2(5-aminopentyl)-6,7-dihydro-5H-cyclopenta[d]-pyrimidine (VIe). a. **From VII.**—Compound VII (10.8 g.) in 25 ml. of methanol and 15 g. of ammonia was hydrogenated for 3 hours at 140° with 800 mg. of alcohol-washed Raney nickel and hydrogen at 1800–1100 p.s.i. A few large crystals of VIe crystallized from the reaction mixture on cooling and were collected mechanically during the filtration to remove the catalyst. Excess methanol was distilled off until the residue amounted to about 20 ml. A large crop of VIe crystallized on cooling and seeding. In all, about 8.0 g. of crystalline VIe (72%), m.p. 100–110°, was collected in several crops. This material was very soluble in water and alcohols but difficultly soluble in most non-polar organic solvents. Several recrystallizations from benzene gave essentially pure material, m.p. 108–110°; λ_{max}^{alc} 238 mμ, ε 8,500, and 270 mμ, ε 5,500, in neutral solution. In acid solution the spectrum showed a single maximum at 263 mμ, ε 12,900.

Anal. Calcd. for $C_{12}H_{20}N_4$: C, 65.42; H, 9.15; N, 25.43. Found: C, 65.24; H, 9.42; N, 25.60.

About 4 ml. of light oil remained on removal of mother liquor from the crystallization of VIe. On vacuum distillation, 1.0 g. of colorless diamine XIII, b.p. 80–85° (13 mm.) was collected. This by-product was identified by comparison of its infrared spectrum and diacetyl derivative with that of the known 2-aminocyclopentanemethylamine obtained from III by hydrogenation.[7] The diacetate was prepared by the action of excess acetic anhydride on XIII in pyridine. The m.p. of pure material was 139–140° as colorless needles from acetone.

Anal. Calcd. for $C_{10}H_{18}N_2O_2$: C, 60.56; H, 9.15; N, 14.13. Found: C, 60.51; H, 9.32; N, 14.01.

b. **From VIb.**—Catalytic hydrogenation of 5.4 g. of VIb exactly as described in VII yielded 5.5 g. (100%) of crystalline VIe, m.p. 100–104°. One recrystallization from benzene gave 4.1 g. of pure VIe, m.p. 108–110°, identical in all respects with the material originally prepared from VII. A mixed m.p. showed no depression.

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(20) T. Hoga and M. Sawai, Japanese Patent 8678 (1954); *C. A.*, **50**, 15578 (1956).