tion at the mid-point of ethanol evolution, when 50 g. of phenoxazine, 65 g. of diethyl ethylmalonate, and 20 g. of clay plate chips were heated at 270–280° for 16 hr. The crude material obtained by precipitation from aqueous sodium hydroxide solution, which had m.p. 200–216°, melted at 222–226° after two recrystallizations from ethyl acetate.

Anal. Calcd. for $C_{17}H_{13}NO_3$: C, 73.15; H, 4.69. Found: C, 73.10; H, 4.22.

Acknowledgment.—Analyses were by Dr. S. Blackman and Mr. C. Marr of our laboratories, whom we thank.

The Semmler–Wolff Aromatization and Beckmann Rearrangement of 2-[β-(2- and 4-Pyridyl)ethyl]-1-tetralone Oximes[1]

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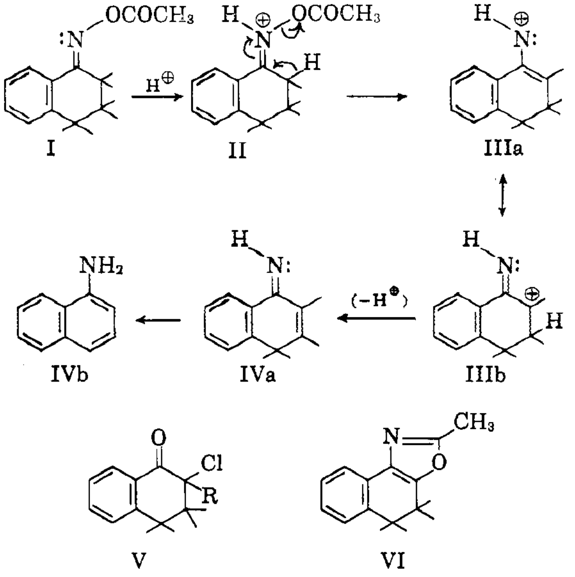
Received June 11, 1962

Treatment of the oximes mentioned in the title with acetic anhydride in acetic acid and hydrogen chloride afforded a mixture of 2-[β-(2- and 4-pyridyl)ethyl]-1-naphthylamines and 6-[β-(2- and 4-pyridyl)ethyl]-2,3-benzocaprolactams. The latter arise during a Beckmann rearrangement of these oximes which involves alkyl group migration. The isomeric 2-[β-(2- and 4-pyridyl)ethyl]-5,6-benzocaprolactams were made by the conventional Beckmann rearrangement of the oximes with polyphosphoric acid (phosphorus pentoxide in phosphoric acid), in which aryl migration occurred.

The aromatization of cyclohexenones oximes to the corresponding anilines by a variety of acidic reagents was first described by Semmler[2] and found by Wolff[3] to be a general reaction.[4,5] The most effective reagent for this reaction has been found to be "Beckmann's mixture" which consists of a mixture of acetic anhydride in acetic acid saturated with hydrogen chloride. In this acidic medium, the Beckmann rearrangement of the oxime must be considered a possible competing reaction. However, judging from the examples in the literature,[4,5] in Beckmann's mixture, cyclohexenone oximes are preferentially aromatized rather than rearranged. Ostensibly, in Beckmann's mixture, the oximes form the O-acetyl derivatives first which then lose the elements of acetic acid and water to form the corresponding anilines.

Mechanisms of this reaction have been advanced for the aromatization of 1-tetralone oximes[5–7] and the one suggested by Vorozhtsov and Koptiug[5] is presented. From the reaction of O-acetyl 1-tetralone oxime, I, with hydrogen chloride in acetic acid they isolated 1-naphthylamine, IVb (as the hydrochloride, 31%), 1-acetamidonaphthalene (3.3%), 2-chloro-1-tetralone, V(R = H), (2%) and the oxazole derivative, VI, (8.6%). They postulated the formation of all of their products *via one* common intermediate and proposed the following reaction path: Protonation of I on nitrogen leads to II which loses acetic acid to form the enamine, represented by the resonance hybrids IIIa and IIIb. From this reactive intermediate they accounted for all of their products in the following manner:



Loss of a proton from the enamine leads to IVa which tautomerizes to 1-naphthylamine, IVb; attack of a chloride ion at the carbonium ion center of IIIb would yield 2-chloro-1-tetralone imine which would hydrolyze (during the reaction or work-up) to form the ketone V (R = H); similarly, attack of acetate ion on IIIb would form 2-acetoxy-1-tetralone imine which could cyclize with the loss of water to yield VI. These workers did not isolate any lactams due to a Beckmann rearrangement of 1-tetralone oxime.

We studied the action of hydrogen chloride on 2-[β-(2- and 4-pyridyl)ethyl]-1-tetralone oximes in acetic anhydride and acetic acid solution. In

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[1] A portion of this study was taken from the thesis submitted by Richard E. Hewitson as partial fulfillment for the Master of Science degree, University of Illinois, Chicago, Illinois, June, 1962.

[2] F. W. Semmler, *Ber.*, **25**, 3352 (1892).

[3] L. Wolff, *Ann.*, **322**, 351 (1902).

[4] For examples, see the review of the Beckmann Rearrangement by L. G. Donaruma and W. Z. Heldt, "Organic Reactions," Vol. 11, J. Wiley & Sons, Inc., New York, N. Y., 1960, p. 30.

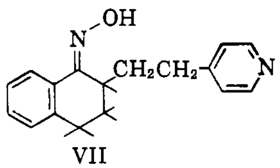
[5] N. N. Vorozhtsov and V. A. Koptiug, *J. Gen. Chem. U.S.S.R.* (Eng. Transl.), **28**, 1697 (1958), have also summarized the field.

[6] A. Hardy, E. R. Ward, and L. A. Day, *J. Chem. Soc.*, 1979 (1956).

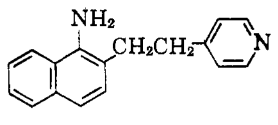
[7] M. V. Bhatt, *Experientia*, **13**, 70 (1957).

each instance, the major products were a mixture of the corresponding naphthylamine and a lactam due to a Beckmann rearrangement. Interestingly enough, for the 4-pyridyl isomer, the lactam was the predominant product and this reaction is discussed first.

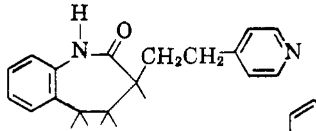
Addition of 1-tetralone to 4-vinylpyridine by the method of Levine and Wilt[8] afforded 2-[β-(4-pyridyl)ethyl]-1-tetralone which was converted to its oxime VII. The Russian workers[5] found that 1-tetralone oxime was acetylated in 97.5% yield within a minute and carried out their aromatization of the acetyl derivative. Attempts to isolate a crystalline acetyl derivative of VII only gave oils and thus the derivative was formed *in situ* prior to the introduction of hydrogen chloride gas at 100°. It was also found that a cleaner product was obtained when this procedure was followed. The mixture obtained was separated by chromatography on alumina and furnished three products: the chloro ketone [V, R = β-(4-pyridyl)ethyl] (8%); the naphthylamine, VIII (27%); and the lactam, X (56%), whose proof of structure is presented below. The structure of the chloro ketone was assigned on the basis of its elemental analysis and by analogy to the product [V, R = H] isolated previously.[5]



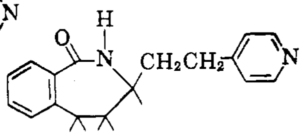
VII



VIII

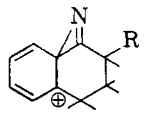


IX

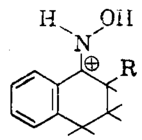


X

The Beckmann rearrangement of VII would lead to either lactam IX or X, depending on aryl or alkyl migration on the appropriate oxime. It had previously been shown that 1-tetralone oxime was rearranged by polyphosphoric acid to 5,6-benzocaprolactam,[9] and hence the oxime presumably existed in the *anti* (to arene) configuration. Rearrangement of VII with this reagent afforded a lactam whose ultraviolet and infrared absorptions corresponded to that of 5,6-benzocaprolactam (Table I) and hence its structure is represented by IX. Furthermore, on this basis the oxime VII is assigned the *anti* (to arene) configuration and aryl migration had occurred to form IX. The intermediate in this rearrangement is XI, shown as one of the resonance hybrids of the transition state.[10] However, the lactam, IX, isolated from the polyphosphoric acid rearrangement showed different physical and spectral characteristics to that from the aromatization reaction and hence the lactam from the last reaction was assigned structure X. Structures of IX and X are further substantiated by the comparison of their ultraviolet spectra with those of acetanilide and N-methylbenzamide (Table I), respectively. Since the two pure isomeric lactams were available to us, we examined all the fractions from the reaction in the Beckmann's mixture and in polyphosphoric acid for the presence of the other isomer by infrared spectroscopy. However, in each reaction medium, apparently only *one* lactam was formed. Although no attempt was made to ascertain the homogeneity of the oxime, VII, from the polyphosphoric acid rearrangement it is assumed that it exists in the *anti* (to arene) form.



XI



XII

Table I

Summary of Relevant Spectral Data

Compound	Ultraviolet spectrum (in ethanol) [high intensity (primary) bands] λ_{max} in mμ	ϵ_{max}	Infrared spectrum (in chloroform) C=O stretching frequency (in cm.$^{-1}$)
5,6-Benzocaprolactams			
Parent	239	11,100	1670
2-[β-(2-Pyridyl)ethyl]-	242	12,500	1666
2-[β-(4-Pyridyl)ethyl]-, (IX)	241	12,600	1670
2,3-Benzocaprolactams			
6-[β-(2-Pyridyl)ethyl]-	223	10,700	1650
6-[β-(4-Pyridyl)ethyl]-, (X)	226	9,670	1656
Acetanilide	242	13,700[a]	1673
N-Methylbenzamide	226	9,800	1659

[a] H. E. Ungnade, *J. Am. Chem. Soc.*, **76**, 5133 (1954), reports the primary band at 242 mμ (ε 14,400).

Several explanations can be advanced to account for the formation of lactam X during the Semmler-Wolff aromatization. The oxime or its O-acetyl derivative might have isomerized,[11] in part, *via* an intermediate such as XII, to the *syn* configuration which then rearranged with alkyl migration to

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[8] R. Levine and M. H. Wilt, *J. Am. Chem. Soc.*, **74**, 342 (1952).

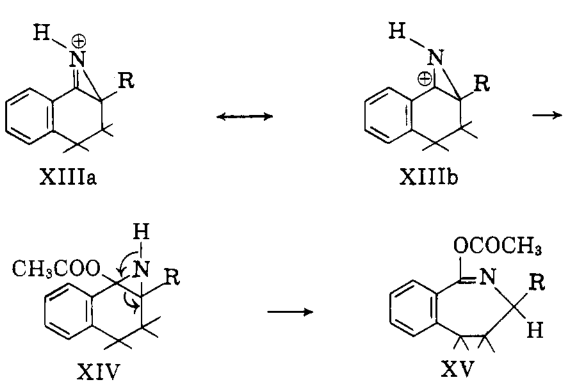
[9] E. C. Horning, V. L. Stromberg, and H. A. Lloyd, *ibid.*, **74**, 5153 (1952).

[10] Ref. 4, p. 11, discusses this transition state in detail.

[11] The acid-catalyzed isomerization of oximes is a well known phenomenon (see ref. 4, p. 53). R. S. Montgomery and G. Dougherty, [*J. Org. Chem.*, **17**, 823 (1952)] have isomerized several cyclohexenone oximes with dilute sulfuric acid. R. F. Brown, N. M. van Gulick, and G. H. Schmid [*J. Am. Chem. Soc.*, **77**, 1094 (1955)] have found that both *syn*- and *anti*-isobutyrophenone oxime rearrange alike with hydrogen chloride in acetic acid to form similar amounts of isobutyranilide. To account for this, these authors suggested that the oximes equilibrate *via* a carbonium ion of this type: $R—\overset{\oplus}{C}(C_6H_5)—NHOH$.

yield X. If a mixture of *syn*- and *anti*-oxime (or their esters) were present, either one can produce the aromatic compound. Since we did not detect any lactam due to aryl migration, one would have to assume that the *anti*-oxime would aromatize faster than it would rearrange. Alternatively, it might aromatize *via* the same intermediate proposed for the rearrangement with aryl migration, *viz.*, XI. Although such a mechanism is plausible we prefer to explain the formation of the lactam X through the enamine *intermediate* IIIa, IIIb, which was used to explain all of the products of the aromatization.

Ring closure of the counterpart of IIIa, IIIb leads to the transition state, XIIIa, XIIIb [R = β-(4-pyridyl)ethyl] which after attack by acetate yields XIV. Ring opening of the latter furnishes XV which is hydrolyzed to the lactam X.

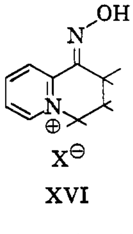


XIIIa XIIIb

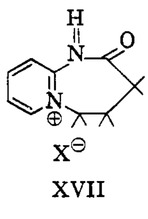
XIV XV

In a cognate experiment, the 2-pyridyl isomer (isomeric with VII) was treated with the "Beckmann's mixture" and yielded the corresponding naphthylamine (see VIII) and a small quantity of the lactam (see X). The latter was again different in its properties from that furnished by the Beckmann rearrangement of 2-[β-(2-pyridyl)-ethyl]-1-tetralone oxime, with polyphosphoric acid. Again, from the spectral characteristics, the lactam from the Beckmann rearrangement assigned structure similar to IX, that from the aromatization to X (see Table I).

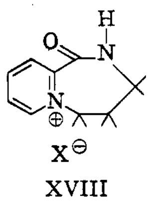
In the aromatization recently reported by Collicutt and Jones[12] the oxime, XVI, afforded a lactam which could possess either structure XVII or XVIII. On the basis of our observations and



XVI



XVII



XVIII

coupled with the mechanism advanced for aryl migration of the Beckmann rearrangement[13] we suggest that the structure of Collicutt's lactam is XVIII.

Experimental[14]

Infrared spectra were determined in chloroform solution or potassium bromide disks as indicated in each case using a Beckman IR-4, infrared recording spectrophotometer.

Starting Materials.—1-Tetralone was purchased from the Aldrich Chemical Co., Milwaukee, Wisconsin, and 2- and 4-vinylpyridine from Reilly Tar and Chemical Corp., Indianapolis, Indiana.

2-[β-(2-Pyridyl)ethyl]-1-tetralone.—To a mixture of 1-tetralone (100 g.; 0.69 mole), and 2-vinylpyridine (72 g.; 0.69 mole), was added freshly cut sodium (2.0 g.; 0.09 g.-atom) in one portion. After the initial vigorous reaction had subsided, the mixture was heated at 120° for 10 min. The reaction mixture was then poured onto a mixture of ice (250 g.) and concentrated hydrochloric acid (25 ml.) and was extracted several times with benzene. The aqueous phase was cooled, made basic with 30% sodium hydroxide, and again extracted with benzene. Distillation of this benzene extract afforded the product (112 g.; 65%), b.p. 160–164° at 0.3 mm. The C=O stretching absorption appeared as a strong band at 1687 cm.$^{-1}$ in chloroform solution.

Anal. Calcd. for $C_{17}H_{17}NO$ (251.3); C, 81.24; H, 6.82; N, 5.57. Found: C, 81.10; H, 6.77; N, 5.65.

The hydrochloride crystallized when hydrogen chloride was passed through an ether solution of the amino ketone. It was recrystallized from acetone–water, m.p. 150–155°.

Anal. Calcd. for $C_{17}H_{18}NOCl$ (287.8): C, 70.95; H, 6.30; N, 4.87. Found: C, 71.10; H, 6.33; N, 4.98.

There was a strong carbonyl stretching absorption, in a potassium bromide disk, at 1687 cm.$^{-1}$.

The oxime of the ketone was prepared by treating the ketone (25 g.; 0.1 mole) with hydroxylamine hydrochloride (25 g.; 0.35 mole) in pyridine (100 ml.) and boiling absolute ethanol (100 ml.) for 2 hr. The solvents were removed *in vacuo*, and the resulting oil was crystallized from aqueous methanol. The yield of the colorless crystals was 19.2 g. (72.5% based on the ketone), m.p. 115–118°.

Anal. Calcd. for $C_{17}H_{18}N_2O$ (266.4): N, 10.52. Found: N, 10.58.

The C=N stretching frequency of the oxime, determined in chloroform solution, appeared as a weak band at 1625 cm.$^{-1}$ and the O—H stretching occurred as a medium band at 3600 cm.$^{-1}$.

2-[β-(4-Pyridyl)ethyl]-1-tetralone.—The reaction of 1-tetralone (50 g.) and 4-vinylpyridine (36 g.) by the procedure described for the 2-isomer yielded the amino ketone (41.2 g.; 48%), b.p. 176–179° at 0.6 mm. In chloroform, the C=O stretching mode appeared at 1692 cm.$^{-1}$; ultraviolet absorption bands (in 95% ethanol) appeared at 206 (ϵ 32,700), 249 (ϵ 14,200), and 293 mμ (ϵ 1740).

Anal. Calcd. for $C_{17}H_{17}NO$ (251.3); N, 5.57. Found: N, 5.97.

The hydrochloride was prepared as above and was recrystallized from ethanol, m.p. 233–236°. Its C=O stretching vibration (in potassium bromide) showed a strong band at 1687 cm.$^{-1}$.

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[12] A. R. Collicutt and G. Jones, *J. Chem. Soc.*, 4101 (1960).

[13] Ref. 4, p. 11; the mechanism of the Beckmann rearrangement of aryl alkyl oximes involves electrophilic attack of the electron-deficient nitrogen on the arene. Attack of such an electrophilic nitrogen on the electron-deficient pyridinium ion is less likely to occur since electrophilic attack on the pyridinium ion occurs only under the most drastic conditions (see A. R. Katritzky and J. M. Lagowski, "Heterocyclic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1960, p. 48 ff).

[14] All melting points are uncorrected. Analyses were by Micro-Tech Laboratories, Skokie, Illinois, or Dr. Kurt Eder, Geneva, Switzerland.

Anal. Calcd. for $C_{17}H_{18}NOCl$ (287.8): C, 70.95; H, 6.30; N, 4.87. Found: C, 70.80; H, 6.55; N, 4.98.

The oxime was synthesized as above (in 73% yield) and was crystallized from aqueous methanol, m.p. 133–139°.

Anal. Calcd. for $C_{17}H_{18}N_2O$ (266.4): C, 76.66; H, 6.81; N, 10.52. Found: C, 76.77; H, 6.74; N, 10.61.

The C=N stretching frequency of the oxime, (in chloroform) was apparently obscured by one of the pyridine ring vibrations. The O—H stretching frequency appeared as a medium band at 3590 cm.$^{-1}$.

The Reactions of 2-[β-(2-Pyridyl)ethyl]-1-tetralone Oxime. (a) With Hydrogen Chloride and Acetic Anhydride in Acetic Acid.—A mixture of the oxime (5.0 g.; 0.019 mole), acetic anhydride (2.5 ml.; 0.024 mole), and acetic acid (20 ml.) was heated at 100° for 10 min. Then a gentle stream of hydrogen chloride gas was bubbled through the light yellow solution at 100°. After 20 min. a yellow solid separated from the now deep red solution and after 30 min. the reaction mixture was cooled to 0°, and the crystals of 2-[β-(2-pyridyl)ethyl]-1-naphthylamine dihydrochloride (2.0 g.; 37.5%) were collected. The salt recrystallized from dilute hydrochloric acid, m.p. 292–299°.

Anal. Calcd. for $C_{17}H_{18}N_2Cl_2$ (321.3): C, 63.56; H, 5.65; N, 8.72. Found: C, 63.69; H, 5.65; N, 8.78.

The broad absorption band occurring between 2500–3000 cm.$^{-1}$, indicative of amine hydrochlorides was present in the spectrum (in potassium bromide).

The colorless free base was crystallized from acetonitrile, m.p. 119–122°.

Anal. Calcd. for $C_{17}H_{16}N_2$ (248.3): C, 82.22; H, 6.49; N, 11.28. Found: C, 82.09; H, 6.15; N, 11.70.

The infrared spectrum of this amine (in chloroform) showed the NH_2 deformation frequency as a strong band at 1622 cm.$^{-1}$. The NH symmetrical and asymmetrical stretching frequencies appeared as weak to medium bands at 3375 and 3475 cm.$^{-1}$, respectively. The C—N stretching vibration seems to appear as a strong band at 1403 cm.$^{-1}$. This is higher than the range (1250–1340 cm.$^{-1}$) for primary aromatic amines as stated by Bellamy.[15]

The acetamido derivative was made from the amine and acetic anhydride and was crystallized from acetonitrile, m.p. 154–155°.

The amide C=O stretching absorption (chloroform) occurred as a strong peak at 1680 cm.$^{-1}$; the NH stretching absorptions appeared as two weak bands at 3380 and 3418 and a medium broad band at 3250 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{18}N_2O$ (290.4): C, 78.59; H, 6.24; N, 9.65. Found: C, 78.55; H, 6.26; N, 9.79.

The mother liquor from the reaction mixture (after the dihydrochloride had been filtered off) was concentrated to a sirup which was dissolved in water, made alkaline with 30% sodium hydroxide, and extracted with benzene (400 ml.). The benzene solution was concentrated (to approximately 50 ml.) and then placed on activated alumina (100 g.; Alcoa Grade F-20). The only identifiable fraction (0.5 g.) was eluted by methylene chloride–1% ethanol and consisted of 6-[β-(2-pyridyl)]-2,3-benzocaprolactam. It was recrystallized from acetone, m.p. 124–127°.

Anal. Calcd. for $C_{17}H_{18}N_2O$ (266.4): C, 76.66; H, 6.81; N, 10.52. Found: C, 76.63; H, 6.75; N, 10.53.

(b) With Phosphorus Pentoxide in Phosphoric Acid.—A mixture of phosphorus pentoxide (51 g.) in sirupy phosphoric acid (38 ml.) was heated to 120° and to it was added the oxime (6.65 g.; 0.025 mole) and the mixture heated at 120–135° for 10 min. The solution was allowed to cool just below 100° before it was diluted with ice water (350 ml.). It was extracted with methylene chloride, made alkaline, and re-extracted with methylene chloride (500 ml.). Distillation of the second extract afforded 2-[β-(2-pyridyl)ethyl]-5,6-caprolactam (3.7 g.; 56% based on the oxime), b.p. 204° at 1.5 mm. The lactam crystallized from ethanol, m.p. 130–132°.

Anal. Calcd. for $C_{17}H_{18}N_2O$ (266.4): C, 76.66; H, 6.81; N, 10.52. Found: C, 76.87; H, 6.84; N, 10.70.

The Reaction of 2-[β-(4-Pyridyl)ethyl]-1-tetralone Oxime. (a) With Hydrogen Chloride and Acetic Anhydride in Acetic Acid.—The oxime (5.0 g.) was treated with acetic anhydride in acetic acid and hydrogen chloride gas (for 1 hr.) as described above for the 2-isomer. Since no solid precipitated from the solution (even on cooling), the solvents were removed, the residue made basic, extracted with benzene, and the concentrated benzene solution chromatographed on alumina (100 g.). Elution with benzene–10% ether (500 ml.) yielded the chloro ketone, V [R = β-(4-pyridyl)ethyl], (0.44 g.; 8%) which crystallized from ethanol, m.p. 83–85°. In chloroform, the C=O stretching absorption appeared at 1692 cm.$^{-1}$. Its ultraviolet spectrum showed maxima at 205 (ϵ 27,200), 256 (ϵ 14,300), and 297 mμ (ϵ 1900).

Anal. Calcd. for $C_{17}H_{16}NOCl$ (285.8): C, 71.45; H, 5.64; N, 4.90; Cl, 12.41. Found: C, 71.34; H, 5.47; N, 4.84; Cl, 12.22.

Further elution with ether (500 ml.) and ether–10% methylene chloride (500 ml.) and methylene chloride (500 ml.) afforded the amine, VIII (total of 1.27 g.; 27%), which was crystallized from 1-propanol, m.p. 132–135°.

Anal. Calcd. for $C_{17}H_{16}N_2$ (248.3): C, 82.22; H, 6.49; N, 11.28. Found: C, 82.38; H, 6.52; N, 11.31.

Its infrared spectrum (in chloroform) showed the NH_2 deformation frequency as a strong band at 1623 and the NH asymmetrical and symmetrical stretching frequencies as medium to weak bands at 3480 and 3390 cm.$^{-1}$, respectively.

The C—N stretching frequency again appeared to occur at a higher than usual frequency[15] as a strong band at 1398 cm.$^{-1}$.

The dihydrochloride of this base was recrystallized from dilute hydrochloric acid, m.p. 278–281°.

Anal. Calcd. for $C_{17}H_{18}N_2Cl_2$ (321.3): C, 63.56; H, 5.65; N, 8.72. Found: C, 63.62; H, 5.74; N, 8.81.

The last fraction to be eluted by methylene chloride–1% ethanol (500 ml.) and ethanol (500 ml.) consisted of the lactam, X (2.81 g.; 56%). It was recrystallized from acetonitrile, m.p. 167–170°.

Anal. Calcd. for $C_{17}H_{18}N_2O$ (266.4): C, 76.66; H, 6.81; N, 10.52. Found: C, 76.32; H, 6.84; N, 10.53.

(b) With Phosphorus Pentoxide in Phosphoric Acid.—Rearrangement of the oxime (15 g.; 0.057 mole) in a cognate experiment as described for the 2-isomer afforded the lactam, IX (10.72 g.; 72%), b.p. 220–235° at 1.5 mm., which crystallized from ethanol, m.p. 131–134°.

Anal. Calcd. for $C_{17}H_{18}N_2O$ (266.4): C, 76.66; H, 6.81; N, 10.52. Found: C, 76.62; H, 6.86; N, 10.66.

Acknowledgment.—The authors thank the University of Illinois for Graduate Fellowships to one of them (R.E.H.) for the academic year, 1959–1960, and the summers of 1960 and 1961. They would also like to extend their thanks to Dr. Charles L. Bell for his help in the interpretation of the spectra and to express their appreciation to the U.S. Public Health Service for a Grant (CY-4661) which helped to defray part of the cost.

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[15] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," J. Wiley and Sons, New York, N. Y., 1958, p. 257.