hydrogen chloride, and recrystallizing the precipitated salt from ethanol.

10-Acetyl-17,18-dimethoxy-15,16,17,18,19,20-hexadehydroyohimbane (XXX).—A solution of 5.2 g. of 6-acetyl-1-(3,4-dimethoxybenzyl)-1,2,3,4-tetrahydro-β-carboline hydrochloride in 75 ml. of 37% formaldehyde and 130 ml. of acetic acid was heated on a steam bath for 1 hr., treated with 100 ml. of water, and made basic in the cold with 20% sodium hydroxide solution. The precipitated product was filtered, dissolved in acetonitrile, and passed through a 25-g. Florisil column. Combined eluate and washings were evaporated *in vacuo* and the residue was recrystallized from acetonitrile, yield 50%, m.p. 216–223° dec.

Anal. Calcd. for $C_{23}H_{24}N_2O_3$: C, 73.38; H, 6.42; N, 7.44. Found: C, 73.11; H, 6.68; N, 7.20; λ_{max}, mμ (ε) 257 (46,650), 287 (14,750); ν_{max} 3300 (m), 1660 (s), 1625 (ms), 1592 (m), 1525 (m), 855 (m), and 810 (m) cm.$^{-1}$.

Acknowledgment.—We are indebted to Drs. J. Gylys and M. Osborne for their pharmacological studies. We wish to thank Mr. R. Puchalski for spectral data and Mrs. U. Zeek and Mr. T. Wildeman for analytical determinations.

Investigations in Heterocycles. XV. Methylphenidate: A Versatile Intermediate in the Synthesis of Bicyclic Heterocycles with a Bridgehead Nitrogen Atom

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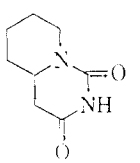
Methyl α-phenyl-2-piperidineacetate (methylphenidate[1]) has been shown to be a useful intermediate in the synthesis of a variety of compounds related to hexahydro-1H-pyrido[1,2*c*]pyrimidine-1,3-(2H)dione. In addition, this intermediate has been utilized in the synthesis of the novel bicyclo heterocycles hexahydropyrazolo-[1,5*a*]pyridin-2-(1H)one and 4,5,6,7-tetrahydropyrazolo[1,5*a*]pyridin-2-(1H)one.

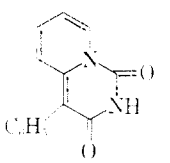
The recent treatise by Mosby[2] on compounds containing bridgehead nitrogen atoms has made evident the tremendous amount of research that has been carried out in this area of heterocyclic chemistry. It was noted particularly that an extensive amount of work has been done in 1H- and 2H-pyridoheterocycles. However, two groups of compounds in this series which have received little attention are the derivatives hexahydro-1H-pyrido[1,2*c*]pyrimidine-1,3(2H)diones and also hexahydro- and 4,5,6,7-tetrahydropyrazolo[1,5*a*]-pyridin-2(1H)ones. Each of these will now be considered separately.

Hexahydro-1H-pyrido[1,2*c*]pyrimidine-1,3-(2H)-diones.—Winterfeld and Göbel[3] reported on the synthesis of the parent substance in this series. They found that urethane readily underwent condensation with methyl 2-piperidineacetate to form I in good yields. Later, the same authors indicated that I could also be synthesized[4] by allowing methyl 2-piperidine acetate dissolved in aqueous hydrochloric acid to react with potassium cyanate. Methylation of I with

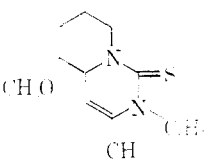


I

diazomethane afforded the corresponding 2-methyl derivative. In the meantime, Hunger and Hoffmann[5] had prepared 1H-4-phenylpyrido[1,2*c*]pyrimidine-1,3-(2H)dione (II) by condensing α-phenyl-α-(2-pyridyl)-acetamide with diethyl carbonate. Finally, Baker and McEvoy[6] produced the pyrido[1,2*c*]pyrimidine (III) through the interaction of 2-(2-oxopropyl)-3-methoxypiperidine with phenyl isothiocyanate. These reports and the availability to us of methyl α-phenyl-2-piperidineacetate (IV) suggested the synthesis of a variety of hexahydro-1H-pyrido[1,2*c*]pyrimidine-1,3-



II



III

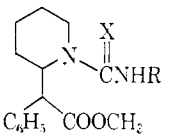
(2H)diones and 1-thioxo-3-ones. In addition, it was conceivable that chemical modifications of this biologically active substance might give rise to compounds with different biological effects. The sequence of reactions leading to the hexahydro-1H-pyrido[1,2*c*]-pyrimidine-1,3-(2H)diones and thioxo analogs is shown in Scheme I. The carbamyl and thiocarbamyl intermediates and the bridged nitrogen atom heterocycles prepared in these series are listed in Tables I and II, respectively.

It was found that compound IV readily underwent condensation with alkyl and aryl isocyanates and isothiocyanates to yield the N-substituted carbamoyl and thiocarbamoyl derivatives. These in turn were readily converted to the 2-substituted hexahydro-4-phenyl-1H-pyrido[1,2*c*]pyrimidine-1,3-(2H)diones and 1-thioxo-3-ones in refluxing ethyl alcohol containing hydrogen chloride. It was also possible to obtain the 2-substituted hexahydro-4-phenyl-1-thioxo-1H-pyrido-[1,2*c*]pyrimidine-3-ones merely by heating under reflux an ethyl alcohol solution of the substituted isothio-

(1) Ritalin®.
(2) W. J. Mosby, "Heterocyclic Systems with Bridgehead Nitrogen Atoms," Vol. I and II, Interscience Publishers, Inc., New York, N. Y., 1961.
(3) K. Winterfeld and W. Göbel, *Chem. Ber.*, **89**, 1642 (1956).
(4) K. Winterfeld and W. Göbel, *ibid.*, **92**, 637 (1959).
(5) A. Hunger and K. Hoffmann, *Helv. Chim. Acta*, **40**, 1319 (1957).
(6) B. R. Baker and F. McEvoy, *J. Org. Chem.*, **20**, 136 (1955).

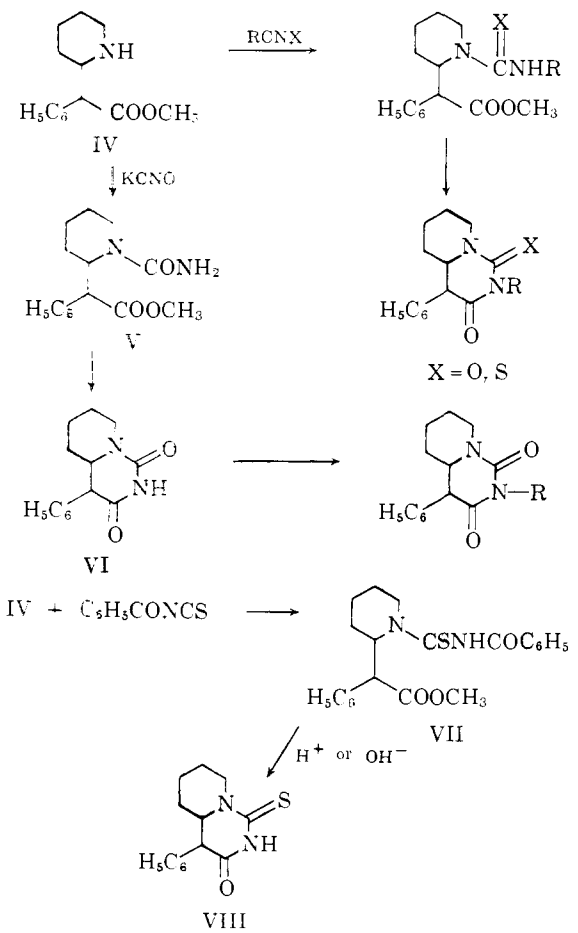
TABLE I

N-CARBAMOYL AND THIOCARBAMOYL DERIVATIVES



R	X	Yield, %	M.p., °C.	Empirical formula	% calcd. C	% calcd. H	% calcd. N	% found C	% found H	% found N
H	O	45	230	$C_{15}H_{20}N_2O_3$	65.45	6.96	10.18	65.42	6.83	10.05
2-$CH_3C_6H_4$	O	77	134–135	$C_{22}H_{26}N_2O_3$	72.09	7.35	7.64	72.02	7.04	7.12
3,4-$Cl_2C_4H_3$	O	73	147	$C_{21}H_{22}Cl_2N_2O_3$	59.72	5.26	6.65	60.13	5.38	6.85
C_6H_5	S	81	138	$C_{21}H_{24}N_2O_2S$	68.45	5.57		68.29	6.30	
3-NC-C_6H_4	S	82	136–137	$C_{22}H_{23}N_3O_2S$	67.12	5.89	10.68	67.12	5.91	10.43
4-[$(CH_3)_2N$]C_6H_4	S	76	129	$C_{23}H_{29}N_3O_2S$	67.13	7.10	10.21	67.42	7.09	9.95
4-$CH_3C_6H_4$	S	68	163–164	$C_{22}H_{26}N_2O_2S$	72.09	7.35		71.80	7.05	
4-*n*-$C_4H_9OC_6H_4$	S	88	148–149	$C_{25}H_{32}N_2O_3S$	68.15	7.32	6.36	68.25	7.24	6.03
4-*i*-$C_4H_9OC_6H_4$	S	85	161–162	$C_{25}H_{32}N_2O_3S$	68.15	7.32	6.36	68.21	7.51	6.26
C_6H_5CO	S	38	168–170	$C_{22}H_{24}N_2O_3S$	66.65	6.10	7.07	66.77	6.21	7.11
4-BrC_4H_4CO	S	35	164–165	$C_{22}H_{23}BrN_2O_3S$	55.58	4.88	5.90	55.56	4.79	5.83

SCHEME I



cyanate and of the hydrochloride of IV containing sodium ethoxide. Finally, hexahydro-4-phenyl-1H-pyrido[1,2*c*]pyrimidine-1,3-(2H)dione (VI) was allowed to react under alkaline conditions with various alkyl halides to form the corresponding 2-substituted derivatives. The possibility that the enol, rather than the lactam, tautomer of the heterocycle had undergone reaction with the alkyl halides was rendered invalid on the basis of spectral and chemical evidence. In general, the alkylated products showed carbonyl absorption bands in the infrared similar to those compounds prepared from the isocyanates. The hexahydro-4-phenyl-1H-pyrido[1,2*c*]pyrimidine-1,3-(2H)diones all absorb strongly at 1715 and 1660–1680 cm.$^{-1}$ If the 1-alkoxy derivative (enolization toward position 3 seems unlikely) had been formed, the carbonyl absorption at 1715 cm.$^{-1}$ surely would have been altered. In one case correlation of the products obtained by both methods furnished firm chemical support to the spectral data. The alkylation product using *n*-butyl bromide was found to be identical with the substance obtained by treating IV with *n*-butyl isocyanate under conditions conducive for ring closure.

The condensation of IV with benzoyl isothiocyanate in cyclohexane gave VII in quantitative yields. However, only compound VIII could be obtained after refluxing an ethanolic solution of VII to which had been added an acid or base catalyst. The lability of the benzoyl grouping of the benzoyl thiocarbamoyl derivative (VII) under hydrolytic conditions has recently been reported also by Lempert and Doleschall.[7]

Hexahydro- and 4,5,6,7-Tetrahydropyrazolo[1,5*a*]-pyridin-2-(1H)ones.—At the time this work was begun in our laboratories, the only report in the literature on of pyrazolo[1,5*a*]pyridines was that of Bower and Ramage,[8] who synthesized the parent member of this heterocyclic series by means of alkaline ferricyanide oxidation of 2-(β-aminoethyl)pyridine. Since pyrazolidones and pyrazolones have been found to have significant analgetic and antipyretic effects,[9] it became of interest to prepare the structurally related but unknown hexahydro- and 4,5,6,7-tetrahydropyrazolo[1,5*a*]pyridin-2-(1H)ones. Again, methyl α-phenyl-2-piperidineacetate proved to be a useful intermediate in the preparation of these substances (see Scheme II). This β-amino ester (IV) was treated with nitrous acid to yield the N-nitroso derivative (IX) in excellent yields. Compound IX was then reduced with zinc and acetic acid, yielding the hydrazino derivative which reacts intramolecularly *in situ* to afford in 76% yield hexahydro-3-phenylpyrazolo[1,5*a*]pyridin-2-(1H)one (X). Several attempts were made to methylate X with methyl iodide in a toluene solution containing sodium

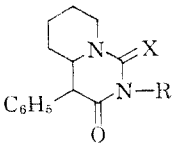
(7) K. Lempert and G. Doleschall, *Chem. Ber.*, **96**, 1272 (1963).

(8) J. D. Bower and G. R. Ramage, *J. Chem. Soc.*, 4506 (1957).

(9) A. Burger, "Medicinal Chemistry," A. Burger, Ed., Interscience Publishers, Inc., New York, N. Y., 1960, pp. 341–356.

TABLE II

OCTAHYDROPYRIDO[1,2*c*]PYRIMIDINES



R	X	Yield, %	M.p., °C.	Empirical formula	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
H[a]	O	52	255	$C_{14}H_{16}N_2O_2$	68.71	6.60	11.47	68.50	6.62	11.37
H	S	37	194	$C_{14}H_{16}N_2OS$	64.58	6.10	10.76	64.50	6.20	10.62
CH_3[b]	O	21	142	$C_{15}H_{18}N_2O_2$	69.75	7.02	10.85	69.62	7.17	10.99
2-$CH_3C_6H_5$	O	61	218	$C_{21}H_{22}N_2O_2$	75.42	6.63	8.38	75.13	6.61	8.25
$C_6H_5CH_2$[b]	O	14	152	$C_{21}H_{22}N_2O_2$	75.42	6.63	8.38	75.18	6.80	8.70
2-ClC_4H_4[a]	O	38	132	$C_{20}H_{19}ClN_2O$	67.70	5.39	7.89	67.95	5.54	7.76
n-C_4H_9[a,b]	O	40	81–82	$C_{18}H_{24}N_2O_2$	71.80	8.03	9.30	71.53	8.12	9.53
3-NC-C_6H_4[c]	S	61	178–179	$C_{21}H_{19}N_3OS$	70.45	5.27	11.66	70.09	5.22	11.71
4-NC-C_6H_4[c]	S	62	232–233	$C_{21}H_{19}N_3OS$	70.45	5.27	11.66	69.98	5.27	11.26
C_6H_5[c]	S	73	176–177	$C_{20}H_{20}N_2OS$	71.39	5.99	8.33	71.60	6.08	8.37
$(CH_3)_2N(CH_3)_2$[a]	O	45	252	$C_{18}H_{25}N_3O_2 \cdot HCl$	61.43	7.45	11.94	61.27	7.57	11.93
$(C_2H_5)_2N(CH_2)_2$[a]	O	40	183	$C_{20}H_{29}N_3O_2 \cdot HCl$	63.23	7.96	11.06	63.16	7.96	10.92
$C_4H_8N(CH_2)_2$[a,d]	O	48	233	$C_{20}H_{27}N_3O_2 \cdot HCl$	63.56	7.47	11.12	63.38	7.76	11.16
$C_5H_{10}N(CH_2)_2$[a,d]	O	35	222–224	$C_{21}H_{29}N_3O_2 \cdot HCl$	64.36	7.71	10.73	63.76	7.84	10.61
$(CH_3)_2N(CH_2)_3$[a]	O	31	278	$C_{19}H_{27}N_3O_2 \cdot HCl$	62.37	7.71	11.48	62.51	8.00	11.30

[a] Synthesized by the isocyanate or isothiocyanate procedure. [b] Synthesized by the alkylation procedure. [c] Prepared in solution containing sodium ethoxide. [d] C_4H_8N = pyrrolidino; $C_5H_{10}N$ = piperidino.

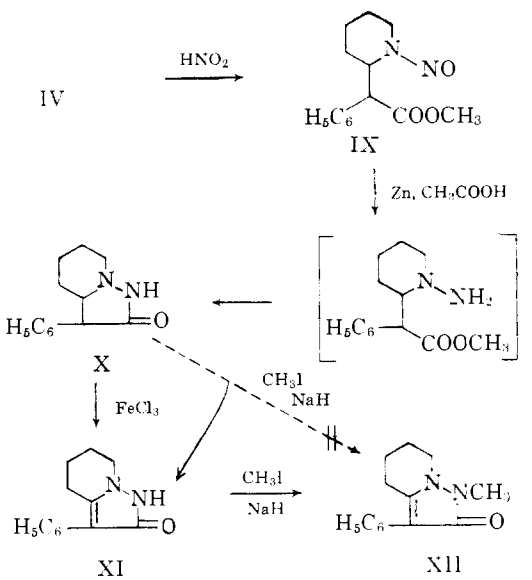
hydride. However, in each case there was isolated only a small amount (5–10%) of a highly crystalline substance, m.p. 238°, whose elemental analysis corresponds to an empirical formula of $C_{13}H_{14}N_2O$. The infrared absorption spectrum, with strong NH bonding effects at 3100 cm.$^{-1}$, zwitterionic absorption bands at 2500–2700 cm.$^{-1}$, and strong, broad absorption at 1610 and 1580 cm.$^{-1}$, suggested a pyrazolone type compound.[10]

The n.m.r. spectrum of this compound also supported a pyrazolone structure, such as XI. The protons of the methylene at C-7 absorb at 4.0 δ. This downfield signal is in a deshielded position for methylene because it is adjacent to nitrogen followed by a —C=C—. The protons on C-4 fall at 2.85 δ, characteristic of a methylene adjacent to a —C=C—. The splitting pattern for these protons is normal for a ring methylene which has only another methylene next to it.

Ferric chloride oxidation of X to 4,5,6,7-hexahydro-3-phenylpyrazolo[1,5a]pyridin-2(1H)one (XI) confirmed the spectral evidence. Thus, either air oxidation or the formation of the anion at C-3 followed by hydride elimination at C-4 with some participation by the basic nitrogen may be responsible for this transformation. In any event, XI could then be readily methylated to XII.

Biological Evaluation.—The compounds described above were evaluated in a number of different biological test systems. They were found to be devoid of cardiovascular and central nervous system (CNS) effects. The carbamoyl and thiocarbamoyl derivatives of IV show some effect against *Trypanosoma cruzi*. In this test CF_1 mice (wt. approximately 18 g.) are infected by subcutaneous inoculation of 50,000 *T. cruzi* organisms/mouse. Medication was given by the intraperitoneal route beginning on the day after infection and continuing daily for 15 days. Untreated controls died in

SCHEME II



18 to 35 days. Active compounds effected delays in deaths and survival of some animals to 60 days at which time tests were terminated. Ten animals were used for each compound at each dose level. Methyl N-(N-3,4-dichlorophenyl carbamyl)-α-phenyl-2-piperidineacetate at a dose of 10 mg./kg. extended the survival time of the animals 13 days and gave 40–50% protection *in vivo*. A comparable degree of protection was obtained by methyl N-(N-*p*-bromobenzyl thiocarbamoyl)-α-phenyl-2-piperidineacetate and methyl N-(*p*-tolyl thiocarbamoyl)-α-phenyl-2-piperidineacetate at 50 mg./kg. However, in each of these cases the LD_{50} was observed at twice the effective dose, thus affording only a narrow margin of safety.[11]

(10) C. deStevens, A. Halamandaris, P. Wenk, and L. Dorfman, *J. Am. Chem. Soc.*, **81**, 6292 (1959).

(11) We are indebted to Dr. Franz Goble and Mr. E. Konopka of our Microbiological Laboratories for these data.

Experimental[12]

Preparation of N-Carbamoyl and Thiocarbamoyl Derivatives.—With the exception of the first compound (V) listed in Table I, all other compounds outlined therein were prepared by the same general method.

Methyl N-Carbamoyl-α-phenylpiperidineacetate (V).—To a solution of 5.2 g. (0.02 mole) of methyl α-phenylpiperidineacetate hydrochloride in 50 ml. of water was added 2.0 g. (0.02 mole + 10% excess) of potassium isocyanate dissolved in 5 ml. of water. The resulting solution was allowed to stand at room temperature for 30 min. after which time it was heated on the steam bath for 4 hr. After cooling at 0° for several hours the resulting white precipitate was collected, washed with water, and recrystallized from ethyl alcohol–water (1:1) to afford a crystalline product, m.p. 230°.

The general preparation of the N-substituted carbamoyl and thiocarbamoyl derivatives is exemplified by the following procedure for the synthesis of **methyl N-(N-phenylcarbamoyl)-α-phenylpiperidineacetate.** Methyl α-phenyl-piperidineacetate (10.4 g.) was dissolved in 50 ml. of cyclohexane, and this solution was then treated with 7.8 g. of 3,4-dichlorophenyl isocyanate. This solution was allowed to stand at room temperature overnight, whereupon the white crystalline precipitate was collected and recrystallized from ethyl alcohol to yield the product, m.p. 147°.

Hexahydro-3-phenyl-1H-pyrido[1,2c]pyrimidinediones and the 1-thio analogs were prepared by two different methods. First, the N-substituted carbamoyl or thiocarbamoyl compounds after isolation and purification could be readily converted to the ring-closed substance in an ethyl alcohol solution containing hydrogen chloride (method A). Similarly, the condensation of the isocyanate or isothiocyanate with IV followed by ring closure all in one operation also proved useful (method B).

A. 2-n-Butylhexahydro-3-phenyl-1H-pyrido[1,2c]pyrimidine-1,3(2H)dione.—Methyl α-phenylpiperidineacetate (5.3 g.) was dissolved in 25 ml. of cyclohexane and then was treated with 2.0 g. of n-butyl isocyanate. An immediate reaction occurred resulting in the formation of a thick oily material. The cyclohexane was decanted and the oily substance was dissolved in ethyl alcohol containing hydrogen chloride. The resulting solution was refluxed for 4 hr. The solvent was removed *in vacuo* and the residue was crystallized on chilling. White cubic crystals, melting at 82–84°, were obtained after one recrystallization from ethyl alcohol.

The preparation of 2-N-substituted compounds involved alkylation of the parent substance VI which was obtained by method **A.**

2-(β-Dimethylaminoethyl)hexahydro-3-phenyl-1H-pyrido-[1,2c]pyrimidine-1.3(2H)dione.—Compound VI (4.8 g., 0.02 mole) was dissolved 100 ml. of toluene. To this solution was added 1.0 g. (0.02 mole) of 53% sodium hydride, and the mixture was refluxed for 4 hr. The solution was cooled to room temperature, and 10.0 g. of N,N-dimethylaminoethyl chloride dissolved in 50 ml. of toluene was added slowly over a 10-min. period. This reaction mixture was refluxed for 20 hr. After filtering the salt, the solvent was removed *in vacuo*, and the resulting residual oil was allowed to stand in the refrigerator overnight. Colorless crystals were formed which were collected and washed with ether. This crude material melted at 74–80°. The hydrochloride salt was prepared by dissolving this solid substance in 5 ml. of ethyl alcohol and then adding 5 ml. of ethyl alcohol saturated with hydrogen chloride. The white powder formed was collected, washed well with ether, and then crystallized from ethyl alcohol.

B. Hexahydro-2,4-diphenyl-1H-pyrido[1,2c]pyrimidine-1-thioxo-3-one.—To a sodium ethoxide solution prepared by dissolving 2.3 g. of sodium in 200 ml. of ethyl alcohol, there was added 26.3 g. (0.1 mole) of methyl α-phenyl piperidineacetate hydrochloride. Phenyl isothiocyanate (13.5 g., 0.1 mole) was added and the resulting solution was heated under reflux for 20 min. The mixture was filtered, and the filtrate was allowed to stand at room temperature for 4 hr. The resulting precipitate was collected and crystallized twice from excess ethyl alcohol.

C. Methyl N-Nitroso-α-phenylpiperidineacetate (IX).—A solution of 14.0 g. of $NaNO_2$ in 50 ml. of water was added dropwise over a 20-min. period to 200 ml. of water containing 4 ml. of 2 *N* HCl and 52.74 g. (0.2 mole) of methyl α-phenylpiperidineacetate. The temperature of the reaction medium was maintained at 75° during the addition, and then the resulting solution was heated at 75–80° for an additional 2 hr. The light yellow copious precipitate which formed was collected and crystallized from ethyl alcohol affording 40.0 g. (90%) of light yellow needles, m.p. 104°.

Anal. Calcd. for $C_{14}H_{18}N_2O_3$: C, 64.12; H, 6.85; N, 10.70. Found: C, 64.22; N, 6.95; N, 10.50.

Hexahydro-3-phenylpyrazolo[1,5a]pyridin-2(1H)one (X).—To a suspension of 30.4 g. (0.12 mole) of IX and 2.94 g. of 97% zinc dust in 450 ml. of water, there was added over a 2-hr. period with efficient stirring 450 ml. of 85% acetic acid. The temperature of the reaction mixture was maintained at 25–30° during this addition. The mixture was then heated on a steam bath for 2 hr. The zinc salts were removed by filtration and the filtrate (pH 5.0) was neutralized with dilute sodium hydroxide solution. A white precipitate formed which was collected and washed well with water. This substance was crystallized twice from ethyl alcohol to yield 18.5 g. (76%) of product, m.p. 144°, λ^{Nujol} (cm.$^{-1}$) 3050, 3150 (−NH), and 1738 (5-membered cyclic lactam).

Anal. Calcd. for $C_{13}H_{16}N_2O$: C, 72.18; H, 7.46; N, 12.95. Found: C, 72.79; H, 7.63; N, 13.22.

The hydrochloride of this substance melted at 217–218°.

Anal. Calcd. for $C_{13}H_{16}N_2O \cdot HCl$: C, 61.78; H, 6.78. Found: C, 61.88; H, 6.99.

4,5,6,7-Tetrahydro-3-phenylpyrazolo[1,5a]pyridin-2(1H)one (XI).—Compound X (6.48 g., 0.03 mole), dissolved in 100 ml. of toluene, was allowed to react under reflux for 4 hr. with 1.31 g. (0.03 mole) of 53% sodium hydride. Methyl iodide (5.0 g.) was added to this mixture, and the refluxing was continued for an additional 4 hr. After filtering the solid material, the filtrate was evaporated to dryness *in vacuo*, and the residual oil was treated with a few milliliters of acetone. White needles separated from solution. These were collected and recrystallized from acetone to afford 200 mg. of product, m.p. 238°, λ^{Nujol} (cm.$^{-1}$) 3000–3100 broad (bonded −NH), 2500–2700 ($-N^+-H$), and 1610, 1590 (pyrazolone amide absorption).

Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.86; H, 6.58; N, 13.07. Found: C, 72.66; H, 6.77; N, 13.32.

A similar result was obtained when the reaction was run in an ethyl alcohol solution containing sodium ethoxide.

Compound XI was obtained also by means of the following oxidation procedure. Five grams of X, dissolved in 80 ml. of ethyl alcohol, was treated at room temperature for 15 min. with 3.4 g. of ferric chloride dissolved in 20 ml. of ethyl alcohol. The mixture was stirred for an additional hour at room temperature and then was filtered. The solvent of the filtrate was removed *in vacuo*, and the residue was triturated with a small amount of acetone. The resulting solid was recrystallized from ethyl alcohol to give 1.2 g. of white needles, m.p. 239°. A mixture melting point with the substance described above gave no depression, and the infrared absorption curves were superimposable.

Anal. Calcd. for $C_{13}N_{14}N_2O$: C, 72.86; H, 6.58, N, 13.07. Found: C, 73.05; H, 6.48, N, 13.09.

4,5,6,7-Tetrahydro-1-methyl-3-phenylpyrazolo[1,5a]pyridin-2(1H)one (XII).—Four grams (0.019 mole) of XI was dissolved in 200 ml. of dry xylene and then was treated with 1.3 g. of 53% sodium hydride. This mixture was refluxed 6 hr., cooled to room temperature, and 2.65 g. (0.019 mole) of methyl iodide was added. The mixture was heated under reflux for 18 hr. and was filtered. The filtrate was concentrated *in vacuo*. The residue was triturated with ethyl acetate, and the resulting tan powder was crystallized three times from ethyl alcohol affording 1.4 g. of yellow prisms, m.p. 83–84°, λ^{Nujol} (cm.$^{-1}$) (no −NH absorption), 1610, 1580 (pyrazolone amide absorption).

Anal. Calcd. for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.06; N, 12.27. Found: C, 74.00; H, 7.11; N, 11.85.

(12) All melting points are uncorrected. These constants were determined 2 years before the journals of the American Chemical Society announced the requirement of melting point corrections.