dien-3β-ol acetate (**9**) (200 mg) (6%): mp 89–90° (from MeOH); [α]D −122°; nmr ($CDCl_3$) δ 0.80 (C-18 CH_3), 1.16 (C-19 CH_3), 5.58 (C-6 H), and 5.81 (m, C-17 and C-16 vinyl protons). *Anal.* ($C_{21}H_{30}O_2$) C, H.

***N*-Methyl-*N*-(3-dimethylamino)propyl-17α-aminoandrost-5-en-3β-ol (5).**—To a soln of **3** (0.3 g) in dry C_6H_6 (7 ml) and $N(Et)_3$ (1.5 ml) a soln of EtOCOCl (0.5 ml) in dry C_6H_6 (2 ml) was added dropwise and the mixture was refluxed for 4 hr. The reaction mixture was then allowed to cool and washed with H_2O. The organic phase was sepd, dried (Na_2SO_4), and evapd. The residue was characterized as **4**, and was used without further purification. To a slurry of LAH (0.3 g) in dioxane a soln of **4** (0.2 g) in dry dioxane (10 ml) was added, and the mixture was refluxed under N_2 for 24 hr. The excess hydride was decompd by successive dropwise addn of aq dioxane (1:3, 4 ml), 20% NaOH soln, and H_2O. The insol salts were removed by filtration and washed with hot dioxane. The filtrate was then evapd and the oily residue was extd with Et_2O. The Et_2O ext was washed with H_2O, dried (Na_2SO_4), and evapd. The oily residue solidified upon addn of H_2O. Recrystn from Me_2CO gave **5** (0.1 g, 33.3%): mp 85–87°; [α]D −93.3°; nmr ($CDCl_3$) δ 0.71, nmr (pyridine) δ 0.72 (C-18 CH_3). *Anal.* ($C_{25}H_{44}N_2O$) C, H.

17α-(3-Dimethylaminopropyl)amino-5α-androstan-3β-ol (11a).—A soln of 5α-androstan-3β,17β-diol 3-acetate 17-tosylate[14] (2.0 g) in freshly distd 3-dimethylaminopropylamine (30 ml) was refluxed for 48 hr and worked up as described above. The basic fraction afforded (250 mg, 16.6%): mp 147–149°; nmr ($CDCl_3$) δ 0.73 (C-18 CH_3); nmr (pyridine) δ 0.74 (C-18 CH_3). *Anal.* ($C_{24}H_{44}N_2O$) C, H. The neutral fraction was not examined in this case.

***N*-Methyl-*N*-(3-dimethylamino)propyl-17α-amino-5α-androstan-3β-ol (11b).**—Methylation of **11a** as described above afforded **11b** (34%) which was isolated as the dihydrochloride salt. Recrystn from *i*-PrOH gave a white solid; mp 278–280° dec; nmr (of free base) ($CDCl_3$) δ 0.72 (C-18 CH_3); nmr (pyridine) δ 0.72 (C-18 CH_3). *Anal.* ($C_{25}H_{48}Cl_2N_2O \cdot H_2O$) C, H.

(14) O. S. Madaeva, *Zh. Obshch. Khim.*, **27**, 2573 (1957); *Chem. Abstr.*, **52**, 7342a (1958).

Hypoglycemic Cyclic Amidines

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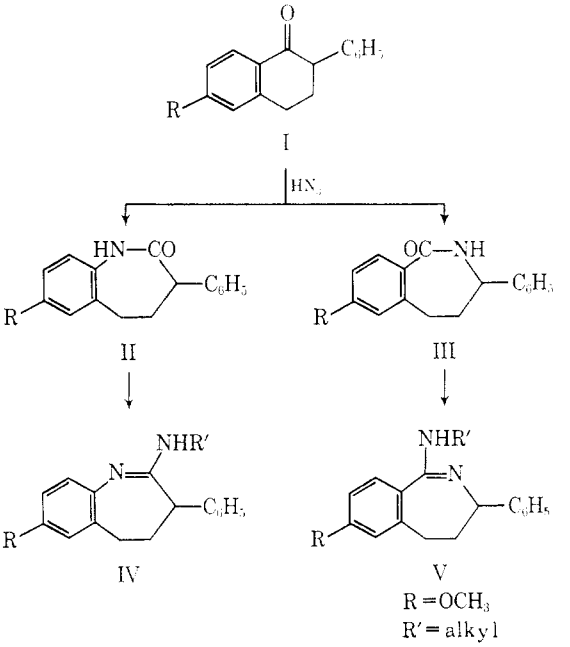
Received June 12, 1970

Substituted tetralones were converted into cyclic lactams and amidines. Nine out of sixteen cyclic amidines exhibited weak to moderate hypoglycemic activity in the rat.

Substituted tetralones[1] and dihydro- or tetrahydronaphthalenes derived from them[2,3] have been studied repeatedly in our laboratories in the past 10 years. The present report describes the preparation of a number of cyclic amidines derived from a variety of substituted tetralones and the hypoglycemic activity exhibited by some of them.

Scheme I illustrates the types of compounds which have been prepared. In general, tetralone[4] and a few 2-aryl substituted tetralones (I) yield only one of the two possible lactams when subjected to the Schmidt reaction. These lactams are 1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-ones (II). However, 6-methoxy-2-phenyltetralone (I, R = OCH_3) gave both the acylanilide (II) and the benzamide (III) type lactams. Werner and coworkers found that both lactams were produced when 3- or 4-phenyltetralones were subjected to the Schmidt reaction.[5] Evans and Lockhart studied the effects of various substituents of tetralones which guided the course of the Schmidt reaction either to afford the acylanilide or the benzamide type lactams.[6] Identification of the isomeric benzazepinones II and III was facilitated by the ease of hydrolytic fission of the acylanilide type lactams (II) by hydrochloric acid, in contrast to the stability of the benzamide type lactams (III), which under the same conditions were unaffected by acid treatment.[6]

SCHEME I



In addition, the uv, ir, and nmr spectra were found to be useful tools in the assignment of the correct structure to the isomeric benzazepinones.[6,7] We have made use of both the spectral and chemical tools in the identification of the lactams obtained from the tetralones by the Schmidt reaction. Table I shows the acylanilide type lactums, while Table II depicts the benzamide type lactums. The amidines derived from these lactums are compiled in Tables III and IV, re-

* To whom correspondence should be addressed.

(1) W. L. Bencze and L. I. Barsky, *J. Med. Chem.*, **5**, 1298 (1962).

(2) W. L. Bencze, L. I. Barsky, W. P. Sopchak, A. A. Renzi, N. Howie, and J. J. Chart, *ibid.*, **8**, 213 (1965).

(3) W. L. Bencze, L. I. Barksy, R. W. J. Carney, A. A. Renzi, and George deStevens, *ibid.*, **10**, 138 (1967).

(4) P. A. S. Smith, *J. Amer. Chem. Soc.*, **70**, 320 (1948).

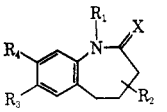
(5) L. H. Werner, S. Ricca, A. Rossi, and George deStevens, *J. Med. Chem.*, **10**, 575 (1967).

(6) D. Evans and I. M. Lockhart, *J. Chem. Soc.*, 4806 (1965).

(7) S. Minami, M. Tomita, H. Takamatsu, and S. Uyeo, *Chem. Pharm. Bull.*, **13**, 1084 (1965).

TABLE I

1,3,4,5-TETRAHYDRO-2*H*-1-BENZAZEPIN-2-ONES AND THIO ANALOGS

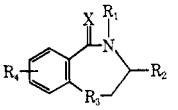


No.	R_1	R_2	R_3	R_4	X	Mp, °C	% yield	Formula[c]
1	H	3-(3-Pyridyl)	H	H	O	183–187	66	$C_{15}H_{14}N_2O$
2	H	3-Methyl-3-(3-pyridyl)	H	H	O	226–228	66	$C_{16}H_{16}N_2O$
3	H	3-C_6H_5	Cl	H	O	248–250	33	$C_{16}H_{14}ClNO$
4	H	3-C_6H_5	OCH_3	H	O	191–193	36	$C_{17}H_{17}NO_2$
5	$(CH_2)_9CH_3$	3-C_6H_5	OCH_3	H	O	50–52	75	$C_{27}H_{37}NO_2$
6	H	3-C_6H_5	OCH_3	OCH_3	O	200–202	44	$C_{18}H_{19}NO_3$
7	H	5-C_6H_5	H	H	O	179–180	84	$C_{16}H_{15}NO$
8	CH_3	5-C_6H_5	H	H	O	102–104	76	$C_{17}H_{17}NO$
9	H	H	H	C_6H_{11}[a]	O	173–175	45	$C_{16}H_{21}NO$
10	H	H	H	H	S	132–133	77	$C_{10}H_{11}NS$
11[b]	H	3-C_6H_5	H	H	S	224–225	99	$C_{16}H_{15}NS$
12[b]	H	3-(*p*-ClC_6H_4)	H	H	S	267–270	98	$C_{16}H_{14}ClNS$
13	H	3-C_6H_5	OCH_3	H	S	208–209	97	$C_{17}H_{17}NOS$
14	H	3-C_6H_5	OCH_3	OCH_3	S	208–211	59	$C_{18}H_{19}NO_2S$
15	H	5-C_6H_5	H	H	S	192–193	65	$C_{16}H_{15}NS$
16	H	H	H	C_6H_{11}[a]	S	181–183	85	$C_{16}H_{21}NS$

[a] C_6H_{11} = cyclohexyl. [b] Prepared from the corresponding lactam, ref 5. [c] All compds were analyzed for C, H, N.

TABLE II

2,3,4,5-TETRAHYDRO-1*H*-2-BENZAZEPIN-1-ONES, 3,4-DIHYDRO-1,4-BENZOXAZEPIN-5(2*H*)-ONES, AND THIO ANALOGS



No.	R_1	R_2	R_3	R_4	X	Mp or bp, °C (mm)	% yield	Formula[b]
17	H	H	CH_2	8-C_6H_{11}	O	170–172	38	$C_{16}H_{21}NO$
18	H	C_6H_5	CH_2	7-OCH_3	O	146–149	25	$C_{17}H_{17}NO_2$
19	H	H	CHC_6H_5	H	O	226–228	26	$C_{16}H_{15}NO$
20	H	H	O	H	O	116–117[a]	67	$C_9H_9NO_2$
21	$(CH_2)_2N(C_2H_5)_2$	H	O	H	O	160–165 (0.25)	79	$C_{15}H_{22}N_2O_2$
22	$CH_2C_6H_4Cl(p)$	H	O	H	O	80–81	85	$C_{16}H_{14}ClNO_2$
23	H	H	CH_2	8-C_6H_{11}	S	164–166	88	$C_{16}H_{21}NS$
24	H	C_6H_5	CH_2	7-OCH_3	S	140–141	70	$C_{17}H_{17}NOS$
25	H	H	CHC_6H_5	H	S	167–169	71	$C_{16}H_{15}NS$
26	CH_3	H	CHC_6H_5	H	S	196–197	18	$C_{17}H_{17}NS$
27	H	H	O	H	S	106–107	71	C_9H_9NOS
28	CH_3	H	O	H	S	141–144	15	$C_{10}H_{11}NOS$
29	$CH_2C_6H_4Cl(p)$	H	O	H	S	123–125	35	$C_{16}H_{14}ClNOS$

[a] D. Huckle, I. M. Lockhart, and M. Wright, *J. Chem. Soc.*, 1137 (1965), report mp 114–116°. [b] See footnote *c*, Table I.

spectively. The acids which resulted from the hydrolysis of five substituted 1-benzazepin-2-ones are listed in Table V.

Tomita, *et al.*, arrived at the conclusion that in the Schmidt reaction the direction of the rearrangement was markedly influenced by the substitutents in the aromatic ring and also, to a lesser degree, by the acid medium used in the reaction.[8] These authors also reported that certain substituents in position 7 of the tetralone moiety did not influence the direction of the rearrangement. We have found that 7-cyclohexyl-1-tetralone furnished about equimolar amounts of the two lactams **9** and **17**. Similarly, a derivative of 6-methoxy-1-tetralone was reported to afford approximately equal amounts of the aryl and the alkyl migration products.[7] This was also the case with 6-methoxy-2-phenyl-1-tetralone, which gave the two lactams **4** and **18**. While 1-tetralone yields only the acylanilide type lactam (II), 4-chromanone furnishes only the benzamide type lactam **20**.[9] A few of the lactams were alkylated on the amide N to give **5**, **8**, **21**, and **22**.

Conversion of the lactams into cyclic amidines was achieved by known methods as pictured in Scheme II.

Brown has reported that *S*-alkylthiopyrimidines react with amines more readily than do the corresponding thiopyrimidines.[10] Archer and Sternbach confirmed Brown's observation in their studies of the conversion of the thioamide and the thioimidate groups in a series of substituted 1,4-benzodiazepines.[11] Therefore, we made no attempt to convert thiolactams VII directly into amidines IX, but we prepared the in-

(8) M. Tomita, S. Minami, and S. Uyeo, *J. Chem. Soc. C*, 183 (1969).

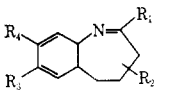
(9) D. Huckle, I. M. Lockhart, and M. Wright, *ibid.*, 1137 (1965).

(10) D. J. Brown, "The Chemistry of Heterocyclic Compounds," Vol. XVI, A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1962, p 283.

(11) G. A. Archer and L. H. Sternbach, *J. Org. Chem.*, **29**, 231 (1964).

TABLE III

4,5-DIHYDRO-3*H*-1-BENZAZEPINES

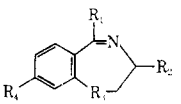


No.	R_1	R_2	R_3	R_4	Mp or bp, °C (mm)	% Yield	Formula[c]
30	SCH_3	H	H	H	121–122 (0.15)	70	$C_{11}H_{13}NS$[d]
31	SCH_3	H	H	C_6H_{11}	190–195 (0.25)	64	$C_{17}H_{23}NS$
32	SCH_3	3-C_6H_5	H	H	170–175 (0.20)	68	$C_{17}H_{17}NS$
33	SCH_3	3-(*p*-ClC_6H_4)	H	H	172–182 (0.20)	65	$C_{17}H_{16}ClNS$
34	SCH_3	5-C_6H_5	H	H	137–139	40	$C_{17}H_{17}NS$
35	SCH_3	3-C_6H_5	OCH_3	H	200–208 (0.15)	78	$C_{18}H_{19}NOS$
36	SCH_3	3-C_6H_5	OCH_3	OCH_3	162–164	62	$C_{19}H_{21}NO_2S$
37	$S(CH_2)_2NC_5H_{10}$	3-C_6H_5	H	H	*a*	36	$C_{23}H_{28}N_2S$
38	$NHCH_3 \cdot HCl$	3-C_6H_5	H	H	268–271	63	$C_{17}H_{18}N_2 \cdot HCl$
39	$NHC_2H_5 \cdot HCl$	3-C_6H_5	H	H	264–267	21	$C_{18}H_{20}N_2 \cdot HCl$
40	$NHCH_2C_6H_5 \cdot HCl$	3-(*p*-Cl-C_6H_4)	H	H	220–221	55	$C_{23}H_{21}ClN_2 \cdot HCl$
41	$NHC_3H_7 \cdot HCl$[b]	3-(*p*-ClC_6H_4)	H	H	196–197	80	$C_{19}H_{21}ClN_2 \cdot HCl \cdot 0.5H_2O$
42	$NH(CH_2)_3OCH_3 \cdot HCl$	3-(*p*-ClC_6H_4)	H	H	159–162	54	$C_{20}H_{23}ClN_2O \cdot HCl_2$
43	$NHC_3H_7 \cdot HCl$[b]	3-C_6H_5	H	H	196–197	69	$C_{19}H_{22}N_2 \cdot HCl$
44	$NHC_3H_7 \cdot HCl$[b]	5-C_6H_5	H	H	210–212	7	$C_{21}H_{28}N_2O \cdot HCl$
45	$NHCH_2C_6H_5 \cdot HCl$	5-C_6H_5	H	H	122–125	42	$C_{23}H_{22}N_2 \cdot HCl$
46	$NHCH_2C_6H_5 \cdot HCl$	H	H	H	248–250	37	$C_{17}H_{18}N_2 \cdot HCl$
47	NH–◁ ·HCl	3-C_6H_5	OCH_3	H	260–261	21	$C_{20}H_{22}N_2O \cdot HCl$
48	$NHC_3H_7 \cdot HCl$[b]	3-C_6H_5	OCH_3	H	197–198	49	$C_{20}H_{24}N_2O \cdot HCl$
49	$NHC_3H_7 \cdot HCl$[b]	H	H	C_6H_{11}	209–211	56	$C_{19}H_{28}N_2O \cdot HCl$
50	$NHCH(CH_3)_2 \cdot HCl$	H	H	C_6H_{11}	223–225	42	$C_{19}H_{28}N_2O \cdot HCl$

[a] Oil purified by chromatography. [b] $NHC_3H_7 = NHCH_2CH_2CH_3$. [c] See Table I, footnote *c*. [d] N anal. only.

TABLE IV

4,5-DIHYDRO-3*H*-2-BENZAZEPINES AND 2,3-DIHYDRO-1,4-BENZOXAZEPINES

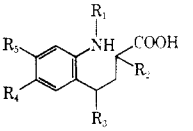


No.	R_1	R_2	R_3	R_4	Mp or bp, °C (mm)	% yield	Formula	Analyses
51	SCH_3	C_6H_5	CH_2	OCH_3	108–110	94	$C_{18}H_{19}NOS$	C, H, N
52	SCH_3	H	CHC_6H_5	H	180–185 (0.25)	39	$C_{17}H_{17}NS$	N
53	SCH_3	H	O	H	125–130 (0.15)	45	$C_{10}H_{11}NOS$	C, H, N
54	$HNCH_2C_6H_5 \cdot HCl$	H	O	H	181–183	42	$C_{16}H_{16}N_2O \cdot HCl$	C, H, N
55	$NHC_3H_7 \cdot HCl$[a]	C_6H_5	CH_2	OCH_3	211–213	24	$C_{20}H_{24}N_2O \cdot HCl$	C, H, N
56	$NHC_3H_7 \cdot HCl$[a]	H	CHC_6H_5	H	182–185	32	$C_{19}H_{22}N_2 \cdot HCl$	C, H

[a] NHC_3H_7 = NH-*n*-Pr.

TABLE V

4-(*o*-ANILINO)BUTYRIC ACIDS



No.	R_1	R_2	R_3	R_4	R_5	Mp, °C	% yield	Formula[a]
57	H	C_6H_5	H	H	H	146–147	93	$C_{16}H_{17}NO_2$
58	CH_3	C_6H_5	H	H	H	129–130	80	$C_{17}H_{19}NO_2$
59	H	H	C_6H_5	H	H	166–167	60	$C_{16}H_{17}NO_2$
60	H	C_6H_5	H	OCH_3	H	112–113	45	$C_{17}H_{19}NO_3$
61	H	C_6H_5	H	OCH_3	OCH_3	92–93	40	$C_{18}H_{21}NO_4$

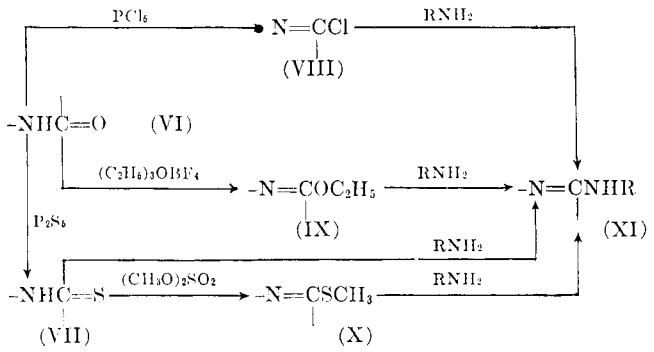
[a] See footnote *c*, Table I.

termediate thioimidates X, which were subjected to a nucleophilic replacement reaction in the presence of an excess of a primary amine to afford the desired amidines XI. We were especially interested in exploring the reactivity of the various thioimidates with primary amines (X→XI). It has been reported that the basicity of the primary amines is not a decisive factor in the aminolysis of the imidates since amino acids[12] and sulfonamides[13] also reacted with ease.

(12) S. Peterson and E. Tietze, *Justus Liebigs Ann. Chem.*, **623**, 166 (1959).

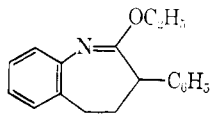
(13) S. Peterson, *Angew. Chem.*, **64**, 602 (1952).

SCHEME II

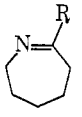


When thioimidate **32** was submitted to aminolysis with *n*-$PrNH_2$, amidine **43** was obtained. Under the same conditions, the 7-MeO analog of **32**, thioimidate **35**, also furnished the corresponding amidine **48**, but in a lower yield. However, thioimidate **36** with two MeO groups, failed to give an amidine. Thus, in this series the presence of the (inductively) electron-withdrawing MeO groups appeared to diminish the reactivity of the 2-methylthio-3,4-dihydro-1-benzazepines.

Imidate **62** failed to react with glycine in boiling MeOH and also in refluxing *o*-$PhCl_2$. However, caprolactim methyl ether **63** readily reacted with glycine in refluxing MeOH to yield *N*-(3,4,5,6-tetrahydro-2*H*-azepin-7-yl)glycine **65**, or with glycylglycine to give **66**. Hence, in this instance, the bicyclic benzazepinyl imidate **62** failed to undergo aminolysis, while the monocyclic nonaromatic azepinyl imidate **63** reacted with ease.



62



63, R = OCH_3 (see ref 14)
64, R = SC_2H_5 (see ref 12)
65, R = $NHCH_2COOH$ (see ref 12)
66, R = $NHCH_2CONHCH_2COOH$
67, R = $NHCH_2CH_2CH_2OCH_3 \cdot HCl$

Biological Activity.—Male and female rats were fasted for 18 hr. The animals were given a glucose load of 800 mg/kg sc. Each dose of the test compound was administered by stomach tube to 4 rats. Two hours later the animals were sacrificed and the blood sugar measured in the Technicon AutoAnalyzer. The results were recorded in Table VI.

Ten of 16 cyclic amidine derivatives showed weak to moderate hypoglycemic activity in the rat when compared to the standard tolbutamide. The most active compound was amidine **47**.

Fastier has reviewed the hypoglycemic activity of amidines and noted that hypoglycemic activity was evident often only when lethal or near-lethal doses were given.[15] The LD_{50} values of most of our amidines were in the range of 150–200 mg/kg ip to the mouse. The most toxic compound in this series was the monocyclic amidine **67**. The least toxic was **66**, which showed no signs of toxicity up to 450 mg/kg ip. It is noteworthy that **66**, a glycylglycine derivative, exhibited hypoglycemic activity, while the glycyl analog **65** was devoid of hypoglycemic activity.

(14) R. E. Benson and T. I. Cairns, *J. Amer. Chem. Soc.*, **70**, 2115 (1948).
(15) F. N. Fastier, *Pharmacol. Rev.*, **14**, 37 (1962).

TABLE VI

HYPOGLYCEMIC EFFECT (% REDUCTION OF BLOOD GLUCOSE)

	Dosage (mg/kg)		
No.	25	50	100
38		<5	
40		6.3	
41		15.2	
42		19.2	16.7
43		14.1	
46		12.6	
47	17.3	17.2	30.6
48	11.9	19.0	
49		<5	
50		12.4	
54		<5	
55		<5	
56		15.2	
65		<5	
66		15.9	
67		<5	
Tolbutamide	30.5	47.5	45.0

The intermediate lactams, especially **5**, **8**, and **21**, were screened for CNS activity. However, no significant activity was found.

Experimental Section

Melting points are uncorrected and were determined in a Hoover melting point apparatus. The ir spectra were taken as Nujol mulls with Perkin-Elmer infrared spectrophotometers, Models 21 and 521. Uv spectra were recorded on a Cary 14 spectrophotometer. Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements are within 0.4% of the theoretical values.

1,3,4,5-Tetrahydro-7-methoxy-3-phenyl-2*H*-1-benzazepin-2-one (4) and 2,3,4,5-Tetrahydro-7-methoxy-3-phenyl-1*H*-2-benzazepin-1-one (18). General Procedure.—To a soln of 25.2 g (0.1 mole) of 3,4-dihydro-6-methoxy-2-phenyl-1(2*H*)-naphthalenone in 125 ml of AcOH, 8.2 g (0.13 mole) of NaN_3 was added with stirring and the temp of the suspension was raised to 50°. Addition of 23.7 ml of concd H_2SO_4 was started dropwise and the internal temp of the reaction mixture was kept in the range of 50–55°. The reaction flask was provided with an outlet for N_2. The N_2 was collected in an inverted graduated cylinder filled with H_2O. This way the rate of the addn of the concd H_2SO_4 could be adjusted to obtain a steady flow of N_2 and by reading the vol of the displaced H_2O the completion of the reaction was determined. It took usually 90–120 min to obtain 2.5 l. (approx 0.1 mole) of N_2. The reaction mixture was poured slowly with stirring into a beaker contg 1 l. of 10% aq Na_2CO_3. The product was extd 4 times with EtOAc. The combined exts were washed with aq $NaHCO_3$ until free of AcOH, dried (Na_2SO_4), filtd, and evapd to dryness. The crude product weighed 17.0 g and represented a mixture of the two isomeric lactams **4** and **18**, mp 131–185°. It was recrystd from 95% EtOH, 9.5 g (**4**), mp 191–193°. A second recrystn from EtOH did not raise the melting point: ir 1660 cm^{-1} (CONH); uv max (MeOH) 245 mμ (ε 13,900).

Concn of the EtOH filtrate yielded another crop of cryst material: 7.2 g; mp 127–130°; ir 1660 and 1646 cm^{-1}. The two ir peaks indicated the presence of both the acylanilide and benzamide type lactams. Fractional crystn from aq EtOH did not result in satisfactory sepn of the isomeric lactams. Boiling 5.4 g of this binary mixt of lactams in 130 ml of concd HCl for 2 hr hydrolyzed the acylanilide lactam **4**. The hydrolysate was evapd to dryness. The residue was dild with 130 ml of H_2O contg 10 g of NaAc and extd with EtOAc. The exts were washed with 2 *N* Na_2CO_3 soln, dried (Na_2SO_4), and evapd to dryness. The residue recrystd from aq EtOH gave 3.1 g of the benzamide type lactam **18**: mp 146–149°; ir 1646 cm^{-1} (CONH); uv max (MeOH), 245 mμ (ε 12,900).

1,3,4,5-Tetrahydro-3-(3-pyridyl)-2*H*-1-benzazepin-2-one (1).—A suspension of 5.6 g (0.025 mole) of 3,4-dihydro-2-(3-pyridyl)-1(2*H*)-naphthalenone and 1.7 g (0.025 mole) or NaN_3 in 40 g of polyphosphoric acid was stirred and heated until N_2 evoln commenced (65–70°). The calcd amount of N_2 (80 ml) evolved during the course of 2 hr. After addn of ice to the reaction mixture the phosphoric acid was neutralized with concd NH_4OH with external cooling. The cryst ppt was collected and washed with H_2O. Recrystn from $CHCl_3$–Et_2O afforded 3.9 g of the product; mp 183–187°; ir 1660 cm^{-1} (CONH).

N-Alkylation of Lactams. General Procedure. 1,3,4,5-Tetrahydro-1-*n*-decyl-7-methoxy-3-phenyl-2*H*-1-benzazepin-2-one (5).—To a soln of 5.3 g (0.02 mole) of lactam **4** in 50 ml of DMF and 25 ml of PhMe was added in portions 0.95 g of NaH (56% in mineral oil suspension) with stirring at room temp. When H_2 evoln ceased (approx 20 min), 5.4 g (0.02 mole) of 1-iododecane in 25 ml of PhMe was added dropwise. The reaction mixture was stirred for 5 hr. The pptd NaI–DMF complex was filtd off and washed with C_6H_6. The filtrate was evapd to dryness. The oily residue was taken up in 5 ml of C_6H_6 and applied to a column prepd from 200 g of Al_2O_3 (Woelm, neutral, activity grade 3). Elution with a mixture of C_6H_6–hexane, 1:1, furnished an oil which crystd on standing. Recrystn from pentane gave 6.1 g of **5**: mp 50–52°; ir 1655 cm^{-1} (CONRR′).

No chromatography was necessary for the purification of the N-alkylated lactams **8**, **21**, and **22**.

Conversion of Lactams into Thiolactams. General Procedure. 1,3,4,5-Tetrahydro-7-methoxy-3-phenyl-2*H*-1-benzazepine-2-thione (13).—A mixture of 19.8 g (0.075 mole) of lactam **4** and 16.3 g of P_2S_5 in 1 l. of pyridine was heated under reflux for 2 hr. Then half of the pyridine was distd off and the remainder heated under reflux for another hr. The reaction mixture was poured, in portions, into 1 l. of boiling H_2O. Upon cooling the product pptd. It was collected, washed with H_2O, and dried in air; mp 203–206°; 20.2 g. Recrystn from EtOH raised the mp to 208–209°; uv max (MeOH) 211 mμ (ε 20,860).

For the isomer, thiolactam **24**, uv max (MeOH) were 257 mμ (ε 1790), 274 (2240), and 282 (2070).

S-Methylation of the Thiolactams. General Procedure. 4,5-Dihydro-7-methoxy-2-methylmercapto-3-phenyl-3*H*-1-benzazepine (35).—To a soln of 17.5 g (0.618 mole) of thiolactam **13** in 340 ml of DMSO and 370 ml of MeOH was added dropwise 80 ml of 1 *N* NaOH with stirring at room temp. The resulting yellow soln was cooled in an ice bath and a mixture of 9.3 g of Me_2SO_4 and 35 ml of MeOH was added to it dropwise with stirring. After completed addition, stirring was continued for 4 hr. Most of the MeOH was removed *in vacuo* on a water bath and after diln with H_2O the oily product was extd with EtOAc. The ext was washed with satd aq NaCl, dried (Na_2SO_4), concd and distd giving 14.5 g of an orange glass: bp 200–208° (air bath) (0.15 mm); uv max (MeOH) 243 mμ (ε 13,490), 300 (10,060).

For the isomer, 4,5-dihydro-7-methoxy-1-methylmarcapto-3-phenyl-3*H*-2-benzazepine (**51**), uv max (MeOH) was 254 mμ (ε 18,440).

Amidines by Aminolysis of the Imino Thioethers. General Procedure. 4,5-Dihydro-7-methoxy-3-phenyl-2-*n*-propylamino-3*H*-1-benzazepine Hydrochloride (48).—A mixture of 7.2 g (0.024 mole) of thio imidate **35**, 7.2 g (0.12 mole) of *n*-$PrNH_2$ and 50 ml of abs EtOH was heated in a sealed tube for 48 hr at 135°. The reaction mixture was evapd to dryness and the residue taken up in Et_2O. Addition of ethereal HCl afforded the HCl salt of the product, that was allowed to crystallize by storage at 5° for 2 days. Recrystn from anhyd EtOH and Et_2O gave 4.1 g of **48**: mp 197–198°; ir 1645 cm^{-1} (aryl-C=N); uv (MeOH) 262 mμ (ε 15,100).

For the isomer, 3,4-dihydro-7-methoxy-3-phenyl-1-*n*-propylamino-5*H*-2-benzazepine·HCl (**55**), ir was 1625 cm^{-1} (C=N); uv (MeOH) 262 mμ (ε 15,100).

4,5-Dihydro-2-ethoxy-3-phenyl-3*H*-1-benzazepine (62).—A soln of 4.7 g (0.02 mole) of 1,3,4,5-tetrahydro-3-phenyl-2*H*-1-benzazepin-2-one[5] and 6.1 g (0.042 mole) of triethyloxonium fluoroborate[16] in 150 ml of CH_2Cl_2 was refluxed with stirring for 2 hr and then allowed to stand at room temp for 18 hr. The reaction mixture was concd *in vacuo* to approx 20 ml and dild with Et_2O. The fluoroborate salt of the product pptd. It was collected, twice recrystd from Me_2CO and once from CH_2Cl_2 and Et_2O: 3.8 g; mp 192° dec.

The salt was converted into the free base by shaking it in a mixture of CH_2Cl_2 and aq K_2CO_3. The organic layer furnished the product which was recrystd from hexane to yield 2.0 g of **62**: mp 88–90°; ir 1630 cm^{-1} (aryl-N=C). *Anal.* ($C_{18}H_{19}NO$) C, H, N.

Attempted Preparation of *N*-(4,5-Dihydro-3-phenyl-3*H*-1-benzazepin-2-yl)glycine.—A mixture of 2.0 g of **62**, 0.6 g of glycine, 10 ml of MeOH, and 10 ml of Me_2CO was refluxed with stirring for 1 hr. The reaction mixture was allowed to stand for 18 hr, evapd to dryness, and dild with H_2O. The pptd solid was collected and dried. It was found to be unreacted **62**. In another attempt, 1.75 g of **62** and 0.5 g of glycine were heated with stirring in 50 ml of *o*-$PhCl_2$ at 210° for 3 hr. Again only unchanged **62** was isolated.

[*N*-(3,4,5,6-Tetrahydro-2*H*-azepin-7-yl)glycyl]glycine (66).—A soln of 26.4 g (0.2 mole) of glycylglycine in 90 ml of MeOH was stirred at room temp while 28.0 g (0.22 mole) of **63**[14] was added dropwise during a 30-min period. The reaction mixture was heated at 50° and for 1 hr and then dild with 60 ml of Et_2O. The crude product pptd: 48.7 g; mp 82–98°. It was recrystd several times from EtOH, MeOH, and finally from H_2O to afford the trihydrated form of **66**: 8.3 g; mp 95–135°; ir 1678, 1665, and 1594 cm^{-1}. *Anal.* ($C_{10}H_{17}N_3O_3 \cdot 3H_2O$) C, H, N.

***N*-(3,4,5,6-Tetrahydro-2*H*-azepin-7-yl)-3-methoxypropylamine·HCl (67).**—A soln of 1.8 g (0.02 mole) of 3-methoxypropylamine in 5 ml of MeOH was added dropwise to a mixture of 2.9 g (0.018 mole) of **63**[14] and 10 ml of MeOH. The reaction mixture was refluxed for 1 hr and then evapd to dryness *in vacuo*. The oily residue was taken up in Et_2O and treated with ethereal HCl. The pptd salt was collected and recrystd from EtOH and Et_2O to give 1.8 g of **67**: mp 114–116°; ir 1690 cm^{-1} (C=N). *Anal.* ($C_{10}H_{20}N_2O \cdot HCl$) C, H, N.

Acknowledgments.—The authors express their appreciation to Dr. J. J. Chart and Miss N. Howie for the hypoglycemic test report and to Mr. L. Dorfman and associates for the analytical and spectral data.

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