min. the solution was treated with water and the methylene chloride was then washed, and evaporated to an oil which was crystallized from ether. Recrystallization from ether–hexane gave 280 mg. of **19** as yellow crystals: m.p. 115°; λ_{max}^{MeOH} 215 mμ (ε 22,000), 367 (890), λ^{KBr} 5.96, 6.24 μ; δ^{CDCl_3} = 1.88 (s, 3, CH_3), 3.60 (s, 3, OCH_3), 4.83 (s, 2, CH_2), 7.0–7.8 p.p.m. (m, 10, C_6H_5).

Anal. Calcd. for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43; N, 8.38. Found: C, 72.22; H, 5.62; N, 8.28.

2-Acetyl-1-benzoyl-7-methoxy-5-methyl-6-phenyl-1,2,3,7-tetrahydro-4H-1,2-diazepin-4-one (21).—A solution of 500 mg. of the benzoyl-7-methoxydiazepinone **2** in 16 ml. of acetic anhydride was heated 4 hr. on a steam bath. The solution was evaporated and methanol was added twice and evaporated. The oil was crystallized from methanol to give 388 mg. of **21** as colorless prisms: m.p. 153–54°; λ_{max}^{EtOH} 266 mμ; λ^{KBr} 5.89, 6.00 μ; λ^{CHCl_3} 5.87, 5.95 μ; for the n.m.r. spectrum, see discussion.

Anal. Calcd. for $C_{22}H_{22}N_2O_4$: C, 69.82; H, 5.86; N, 7.40; O, 16.91. Found: C, 70.14, 69.71; H, 6.04, 5.82; N, 7.40; O, 17.25.

A solution of 50 mg. of **21** in 5 ml. of 5% methanolic KOH was allowed to stand 12 hr. at 25° and was then diluted with water and extracted with methylene chloride. Evaporation of the methylene chloride gave 26 mg. of yellow solid which was crystallized from ether to give 12 mg. (45%) of **14**, m.p. 151°, infrared spectrum identical with that of authentic sample.

Heterocyclic Studies. XXII. The Rearrangement of 2,3-Dihydro-1,2-diazepin-4-ols to Furfurylhydrazine[1]

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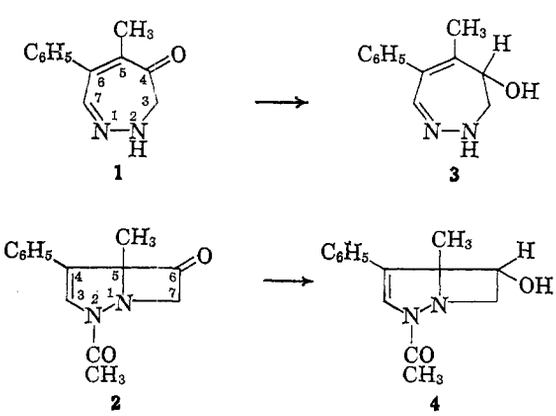
Reduction of the dihydrodiazepinone **1** and the 2-acetyl derivative with $NaBH_4$ gives the carbinols **3** and **5**, respectively. The diazepinol **3** is converted on acetylation in the presence of pyridine to the diazabicyclo[3.2.0]-heptenone system **4**, which is also obtained by reduction of the bicyclic ketone **2**. In the absence of base, acetylation of **3** leads to the transannular oxide **8**, which can also be obtained from **4**. The diazepinols **3** and **5** and the mono- and diacetyl oxides **8** and **9** undergo rearrangement in acid to 3-methyl-4-phenylfurfurylhydrazine (**10**) and the mono- and diacetyl derivatives **11–13**. A number of characterization reactions and interconversions of these hydrazines are described. Vigorous acid hydrolysis of **10** leads to hydrazine and the butenolide **20**. The oxide **8** and the furan **12** are dehydrogenated with N-bromoacetamide to the unsaturated compound **21** and the hydrazone **22**, respectively, and these compounds have been interrelated. An elimination mechanism is suggested for the formation of the furans.

Previous studies on the chemistry of the diazepinone **1** and the related bicyclic ketone **2** have revealed a variety of rearrangements and transannular reactions.[2] In a continuation of work in this diazepine series, reactions of the carbinols **3** and **4** have been explored and form the subject of this paper.



The alcohols **3** and **4** and several N-substituted derivatives of **3** were readily obtained by reduction of the corresponding ketones with sodium borohydride. The yields were quite good, and no products arising by reduction of other unsaturated centers were isolated. The carbinols could be oxidized back to the respective ketones with N-bromoacetamide or by Oppenauer conditions. The spectral properties of **3** and the 2-acetyl derivative **5**, with λ_{max} 303 and 308 mμ, respectively, were consistent with the diazepinol structures.[3]

The *endo* configuration of the hydroxyl group in the bicyclic alcohol **4** is assigned on the assumption of *exo* attack on a bicyclo[3.2.0]heptane system.

Acetylation of **3** in the presence of pyridine gave an oil whose infrared spectrum showed bands at 1750 and 1670 $cm.^{-1}$ corresponding to O- and N-acetyl groups. This product was characterized as the diazabicyclo[3.2.0] acetate **7** by mild alkaline hydrolysis to the crystalline alcohol **4**. This substitution of **3** at N-1 parallels the formation of the bicyclic ketone **2** from **1**. Acetylation of the 2-acetyldiazepinol **5**, however, occurred at the hydroxyl group; apparently the nucleophilic character of N-1 is sufficiently depressed by the adjacent acetyl group to prevent reaction at this center in **5**. The diazepinol acetate **6** could be hydrolyzed to **5** with base.

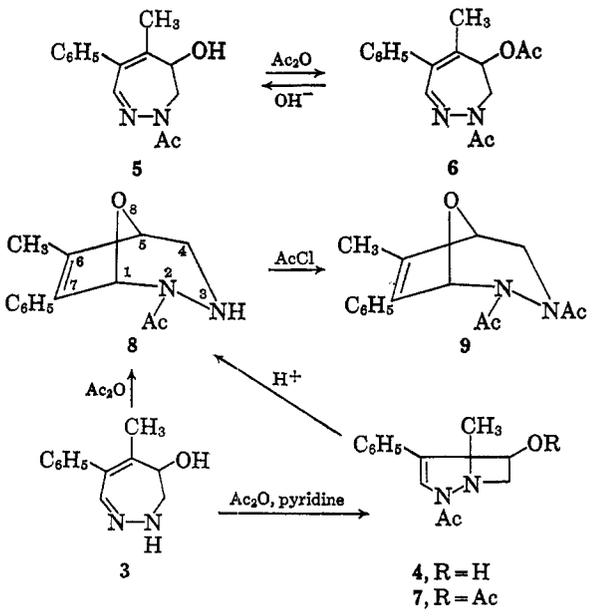
The reaction of **3** with acetic anhydride, either neat or preferably in ethanol solution, gave a third N-monoacetyl compound, different from **4** and **5**. This product was also obtained by treatment of **4** with acetic acid, indicating attachment of the acetyl group at the diazepine N-1 position and suggesting the transannular oxide structure **8**. This construction is in harmony with the ultraviolet maximum of 253 mμ and the infrared spectrum (ν^{CCl_4} 3400, 1690 $cm.^{-1}$), corresponding to NH and N-acetyl groups but no OH frequency, and thus requires an oxide function for the oxygen atom. Further reaction of **8** with acetyl chloride in pyridine or boiling acetic anhydride gave the diacetyl derivative **9**.

The 8-oxa-1,2-diazabicyclo[3.2.1]octene structures **8** and **9** are in good accord with the n.m.r. data. After exchange with D_2O, the spectrum of **8** contained an AB pattern for the C-4 methylene group, δ_A = 3.45 p.p.m., δ_B = 2.50 p.p.m., J_{AB} = 14 c.p.s. The lines

(1) This work was supported by a grant from the Geschickter Fund for Medical Research.

(2) Part XIX: J. A. Moore, *Trans. N. Y. Acad. Sci.*, **27**, 591 (1965).

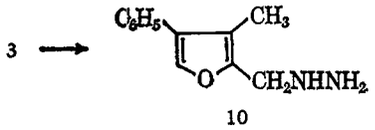
(3) L. A. Paquette [*J. Am. Chem. Soc.*, **86**, 4092 (1964)] reported λ_{max} 301 mμ for a comparable 2,3-dihydroazepine.



for H_A were further split (J = 2.3 c.p.s.) owing to coupling with H-5, which gave a broadened single peak, δ 4.52 (half-band width = 4.5 c.p.s.). The AB pattern in the 2,3-diacetyl compound **9** was shifted downfield, δ_A = 4.70 p.p.m., δ_B = 3.43 p.p.m., J_{AB} = 13 c.p.s. The lines for H_B were split (J = 2.5 c.p.s.) by H-5 (4.60 p.p.m.).

The formation of **8** on treatment of the diazepinol **3** with acetic anhydride in the absence of base probably involves initial N-2→C-5 bridging to give **4**, as observed in the reaction with pyridine which gives the acetate **7**, although a direct participation of the hydroxyl group in **3**, leading directly to **8**, cannot be excluded. Both N-2→C-5 bridging and nucleophilic attack at C-7 by external alcohol have been observed on acylation of the ketone **1**.[4] A similar collapse of the 2-acetyl-1,2-diazabicyclo[3.2.0]-3-heptene system in the ketone **2** is also initiated by acetic acid, giving either diazepinone **1** with loss of the acetyl group or the 7-methoxy-1-acyl derivative in methanol solution.

The four compounds **3**, **5**, **8**, and **9** each underwent reaction in cold 6 *N* hydrochloric acid to give an isomer in 70–80% yield. The products from **3** and **5** were isolated as hydrochlorides, but the salt from **5** was hydrolyzed in water, and only the product from **3** was basic (pK_A = 6.0). A close relationship among the four products was apparent from the similar ultraviolet spectra (λ_{max} 219–222 mμ, infl. at *ca.* 245 mμ) and the fact that the unacetylated compound from **3** and the two monoacetyl products from **5** and **8** were all convertible on acetylation to the diacetyl derivative from **9**. Information has been accumulated to define these compounds as the 3-methyl-4-phenylfurfurylhydrazines **10–13**.



10

5 ⟶ CH_2NAcNH_2

11

8 ⟶ $CH_2NHNHAc$

12

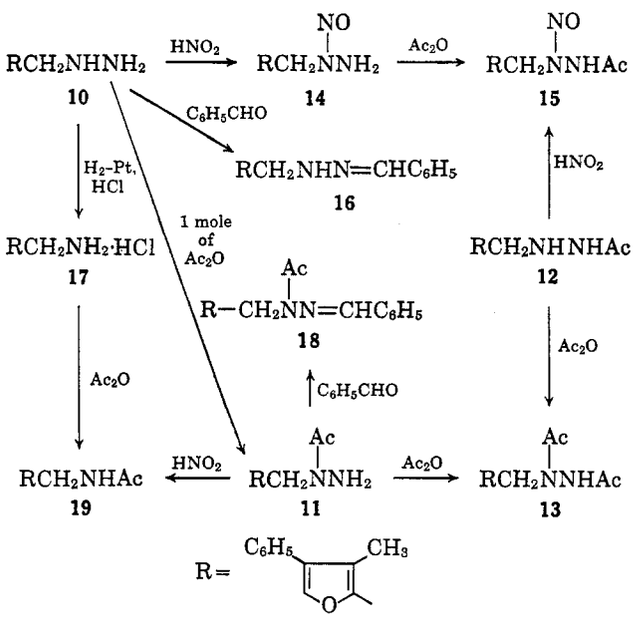
9 ⟶ $CH_2NAcNHAc$

13

An early observation showed that hydrazine was produced on vigorous acid hydrolysis of **10** (or **3**). Progress was impeded by the sensitivity of the base **10** to autoxidation and the tendency to crystallize with approximately 15 moles of water. Anhydrous material was obtained by sublimation and gave an n.m.r. spectrum with sharp single peaks at δ = 2.12 (CH_3), 3.26 (N_2H_3, lost in D_2O), 3.90 (CH_2), 7.35 (C_6H_5), and 7.43 (C.5) p.p.m.

Conclusive proof for the presence of a primary hydrazino group in **10** and the location of the acetyl groups in **11–13** was obtained by the extensive series of characteristic reactions outlined in Chart I. The

CHART I



transformation products **14–19** were all crystalline compounds and were obtained in satisfactory to excellent yields; the spectral properties in every case were consistent with the structures indicated. Nitrosation[5] and anhydride acetylation[6] of monoalkylhydrazines are known to occur at the secondary nitrogen atom, as observed with **10**. It is evident, however, that deduction of the structures of the four rearrangement products **10–13** from the interlocking pattern in Chart I does not depend upon analogies or assumptions concerning the position of substitution in **10**.

Attachment of the hydrazino group to a methylene carbon was suggested by the presence of a two-proton singlet peak at δ = 3.99 p.p.m. in the n.m.r. spectrum of **10**. This peak was broadened in the spectra of **11** and **12** and was exceedingly broad (4.0–5.2 p.p.m. at 35°) in the spectrum of the diacetyl derivative **13**. This behavior is evidently due to restricted rotation in the more bulky side chains arising from steric inter-

(4) J. A. Moore, F. J. Marascia, R. W. Medeiros, and R. L. Wineholt, *J. Org. Chem.*, **31**, 34 (1966).

(5) J. Thiele, *Ann.*, **376**, 239 (1910); T. Taguchi, T. Matsuo, and M. Kojima, *J. Org. Chem.*, **29**, 1104 (1964).

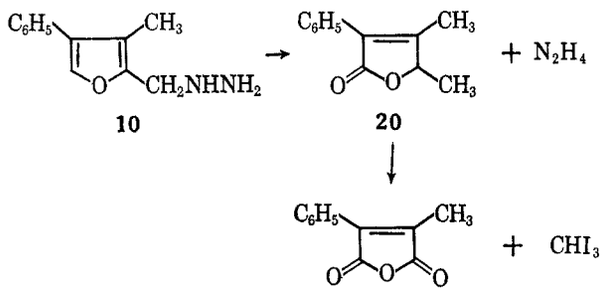
(6) R. Hinman and D. Fulton, *J. Am. Chem. Soc.*, **80**, 1895 (1958); W. J. Theuer and J. A. Moore, *J. Or. Chemg.*, **29**, 3734 (1964).

action with the *o*-methyl group. At 60° the peak height at δ = 4.70 p.p.m. was increased about fourfold; at −50° the signal became a four-line AB pattern, δ_A = 4.05 p.p.m., δ_B = 5.28 p.p.m., J_{AB} = 15 c.p.s. Conclusive evidence for the $CH_2NHNHCOCH_3$ system in **12** came from oxidation to the hydrazone, described below.

On the basis of the CH_2NHNH_2 unit, a furan ring with phenyl and methyl substituents is the only reasonable formulation for the remainder of the molecule in **10–13**. The low wave length ultraviolet absorption (219 mμ) of these products is consistent with a simple furan structure.[7] The C-5 proton of the furan ring produces a sharp signal at 7.35–7.44 p.p.m. in the n.m.r. spectra of **10–13**; values of 7.33–7.72 p.p.m. are recorded for the α-proton in ten representative furans.[8]

A direct demonstration of the furan unit was provided by the vigorous hydrolysis of **10**. Brief heating in concentrated hydrochloric acid gave a suspension of black solid from which hydrazine hydrochloride was extracted with water. The acid solution on neutralization gave a colorless solid, $C_{12}H_{12}O_2$, which was identified as 3,4-dimethyl-2-phenyl-2-butenolide (**20**).

The nitrogen-free compound had λ_{max}^{EtOH} 250 mμ; ν_{max}^{KBr} 1775 cm.$^{-1}$; δ^{CDCl_3} = 1.42 (d, 3, J = 6.5 c.p.s.), 2.10 (s, 3), 4.76 (q, 1, J = 6.5 c.p.s.), 7.33 p.p.m. (s, 5). The compound dissolved in warm aqueous alkali and was recovered unchanged on prompt reacidification. These data point to a lactone structure containing the $-\overset{|}{O}CHCH_3$ system, and this conclusion was verified by hypoiodite degradation to methylphenylmaleic anhydride and iodoform. The oxidation and n.m.r. values do not distinguish between the butenolide **20** and the 2,4-dimethyl-3-phenyl isomer, but the ultraviolet absorption is in better accord with **20**.[9]



The degradation of **10** to **20** represents a hydrolytic rearrangement of a type which is well known in the formation of levulinic acid derivatives from furfuryl alcohols,[12] although not from furfurylamines. Furfurylhydrazines have not been previously described, but it seems unlikely that this rearrangement is unique for the hydrazine leaving group. The isolation of **20** as a lactone rather than the γ-keto acid simply reflects the tendency of such systems to retain a cyclic structure. (Methylphenylmaleic acid is unknown; the anhydride can be steam distilled.)

Another reaction of **10** which may be characteristic of furfurylhydrazines is the rapid autoxidation. The reaction mixture was complex, but a product was isolated by v.p.c. which from n.m.r. data appeared to be 2,3-dimethyl-4-phenylfuran. The formation of this compound can readily be rationalized as loss of nitrogen from the intermediate RN=NH, as previously observed in the oxidation of aromatic[13] and aliphatic[14,15] primary hydrazines. Another product from the reaction of **10** with oxygen contained a single nitrogen atom; no structural suggestions can be made.

Final characterization of the furfurylhydrazine system in the products **10–13** was achieved by oxidation of the 2-acetyl compound **12** with N-bromoacetamide or ferricyanide to the hydrazone **22**. This product, which had an intense ultraviolet maximum at 306 mμ, was converted to other derivatives of the furfural by exchange reactions with substituted hydrazines and by mild alkaline hydrolysis to the azine **23**. Parallel behavior was demonstrated with the model compound **25**, prepared by acetylation of furfural hydrazone. The acetylhydrazone **22** was reduced with sodium borohydride under vigorous conditions to the hydrazine **12** in low yield; the corresponding reduction of **25** could not be effected.

This hydrazone series was entered from another direction from the bridged oxide **8**. Treatment of **8** with N-bromoacetamide gave a dehydro compound which could be reduced back to **8** with borohydride. This interconversion occurred with excellent yields, and the oxidation product is clearly the oxadiazabicycloheptadiene **21**. A connection with the furans was originally made by the rearrangement of **21** to the hydrazone **22** with methanolic aluminum chloride. Subsequent attempts to carry out this transformation with more conventional reagents were unsuccessful and the original procedure was not reproducible. The rearrangement of **21** also occurred, however, in the presence of acidic dinitrophenylhydrazone, leading to the derivative **24b**. (See Chart II.)

The five rearrangements leading to furfurylhydrazine derivatives from the diazepine and bicyclic precursors form a consistent pattern. The path of the rearrangement is clearly seen in the conversions of the oxides **8** and **9**, and it is apparent that the reactions of the diazepinols **3** and **5** to **10** and **11**, and the direct conversion of **4** to **12**, also proceed through the corresponding oxadiazabicyclo[3.2.1]octenes. The position of the acetyl group(s) in the furans is consistent with this picture in every case. The reaction leading to the furan nucleus can be viewed as a simple elimination initiated by protonation of N-1 in the bridged bicyclic system. With the diazepinols **3** and **5**, a stable bicyclic intermediate would not be formed since N-1 is unacetylated and there would presumably be little difference

(7) The ultraviolet maximum of 2,3,4-trialkylfurans is generally found in the region of 220 mμ (*cf.* A. I. Scott, "Interpretation of Ultraviolet Spectra of Natural Products," The Macmillan Co., New York, N. Y., 1964, p. 136). Data on 3-phenylfurans are not available, but in other heterocyclic systems derived from **1**, *e.g.*, pyrazoles and pyridines, phenyl substitution in a β-position produces relatively minor changes in the position of the maxima.

(8) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Vol. 1, Varian Associates, Palo Alto, Calif., 1962.

(9) The 3-phenyl isomer would be expected to have λ_{max} 270–275 mμ by comparison with 3-phenyl-2-butenolide (λ_{max}^{EtOH} 269 mμ[10]). A hypsochromic shift of *ca.* 30 mμ on going from β-phenyl to α-phenyl substitution has been observed in the corresponding 3-pyrrolin-2-ones (3-methyl-4-phenyl isomer, λ_{max} 259 mμ[10]; 4-methyl-3-phenyl isomer, 230 mμ[11]).

(10) J. A. Moore and J. Binkert, *J. Am. Chem. Soc.*, **81**, 6029 (1959).

(11) R. L. Wineholt, E. Wyss and J. A. Moore, *J. Org. Chem.*, **31**, 48 (1966).

(12) A. P. Dunlop and F. M. Peters, "The Furans," Reinhold Publishing Corp., New York, N. Y., 1953, p. 647.

(13) L. Maaskant, *Rec. trav. chim.*, **56**, 211 (1937).

(14) N. Kishner and S. Bydor, *J. Russ. Phys. Chem. Soc.*, **43**, 577 (1911).

(15) D. J. Cram and J. S. Bradshaw, *J. Am. Chem. Soc.*, **85**, 1180 (1963); L. E. Eberson and K. Persson, *J. Med. Pharm. Chem.*, **5**, 738 (1962).

CHART II

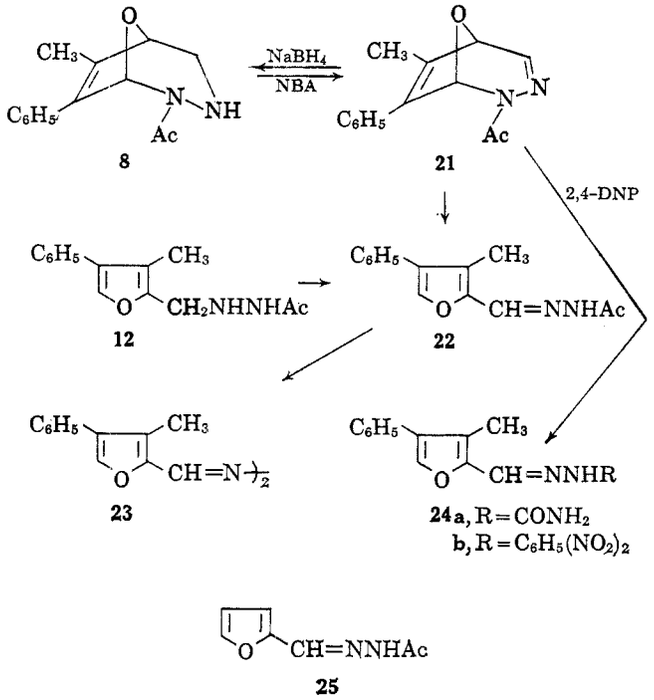
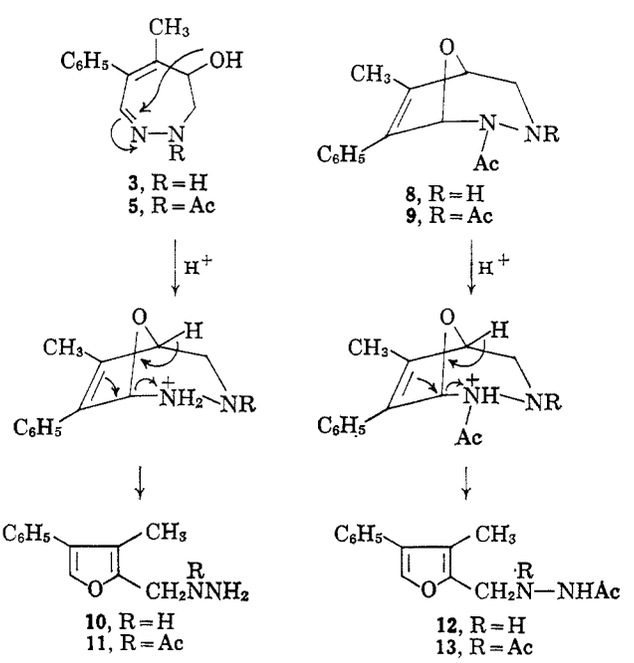
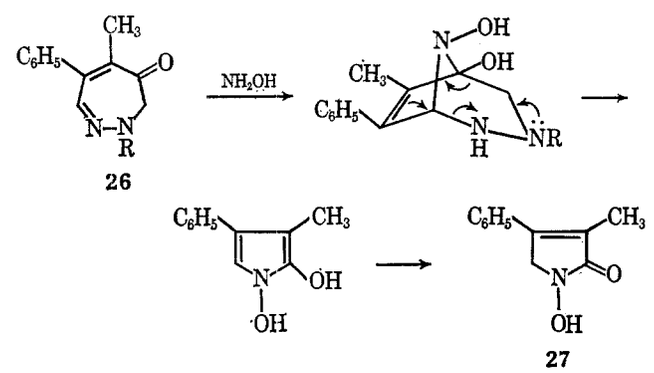


CHART III



in the basicity of this center in the diazepinol and bicyclic compounds. (See Chart III.)

The clearcut operation of this elimination in the diazepinols **3** and **5** lends support to an earlier suggestion for the path of cleavage of the diazepinones **26** to N-hydroxypyrrolones **27** which occurs on treatment with hydroxylamine.[10] In this reaction a proton is not available at C-4 as in the diazepinol, and the sequel to the 4→7 bridging is a fragmentation, with complete loss of the $-NHNRCH_2-$ bridge instead of the ring opening observed with **3**.



Experimental Section

Melting points were taken on a Fisher-Johns block with a calibrated thermometer. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrophotometer. N.m.r. spectra were recorded on a Varian Model A-60 spectrophotometer in $CDCl_3$ solution using TMS as internal standard (δ = 0 p.p.m.). Thin layer chromatography was carried out on silica gel G plates, 0.25-mm. thickness, using chloroform–methanol, usually 25:2, as developing solvent and an iodine chamber to visualize spots.

A large number of reactions was carried out in the course of this work, most of them in test tubes in a very simple manner. Reactants and reagents, generally in solution, were combined, the reaction solution was allowed to stand at an appropriate temperature for an appropriate length of time, with stirring in larger-scale reactions, and the product was then isolated. Recovery of the product usually involved either direct crystallization (often after initial evaporation) and collection of the solid or else extraction with methylene chloride or ether, washing the organic layer with acid and/or carbonate, as appropriate, drying over Na_2SO_4 or $MgSO_4$, evaporation, and crystallization, or occasionally distillation in a short-path sublimer. The identity of products obtained by different routes was established by infrared comparisons and mixture melting points. The yields quoted are based upon dry crystallized products suitable for use in further reactions but in general not having the maximum melting point and not necessarily free of trace contaminants.

To avoid extensive reiteration of the same phrases, the data for most of these reactions is compiled in Table I. Pertinent information on quantities, reaction conditions, purification, and physical constants are included. The method of isolation was in each case one of the standard operations mentioned above. A few typical procedures and exceptional or more complex experiments are described separately. Further details may be found in the Ph.D. Dissertations of R. W. Medeiros, University of Delaware, 1960, and R. L. Williams, University of Delaware, 1965.

Sodium Borohydride Reduction of Diazepinones.—In a typical procedure, a solution of 400 mg. of $NaBH_4$ in 12 ml. of ethanol–water (1:2) was added in one portion to a solution of 2.0 g. of the 2-acetyldiazepinone **5** in 100 ml. of ethanol. After standing at room temperature for 1 hr., the turbid solution was treated with acetic acid and evaporated *in vacuo* to small volume, diluted with water, and extracted with ether. The dried ether solution was concentrated to 3-ml. volume and chilled, giving 1.3 g. of colorless crystals of **5** (see Table I).

Acid Isomerization of 3, 5, 8, and 9 to 10, 11, 12, and 13.—In a typical procedure, 4 ml. of concentrated HCl was added to a suspension of 600 mg. of **5** in 5 ml. of water. The diazepinol dissolved and the hydrochloride of the furan **11** then separated as a crystalline precipitate which was collected and recrystallized from ethanol–ether to give 550 mg. of fine white needles (see Table I). The free base was an oil.

3-Methyl-4-phenylfurfurylhydrazine.—The free base **10** was prepared by addition of excess 10% KOH to an aqueous solution of the hydrochloride. The colorless plates which separated were collected and washed with water, and the moist cake was immediately placed in a sublimation cup. After drying *in vacuo* the base was sublimed (0.5 mm., 50°) and the colorless crystals, m.p. 38–40°, were removed in a nitrogen-filled drybox. The crystals became a yellow oil on exposure to air.

An ether solution of 30 mg. of the sublimed base was shaken with water. The ether phase was then dried (Na_2SO_4) and evaporated to give 77 mg. of colorless plates of the hydrated base, m.p. 52–54°. Treatment of this material with a few drops of concentrated HCl gave the hydrochloride, m.p. 194°.

Oxidation of 10.—A benzene solution of the hydrazine **10** (not sublimed) was exposed for 18 hr. to a slow stream of oxygen.

TABLE I
EXPERIMENTAL DETAILS

Product	Reaction conditions	Yield, g. (%)	Recrystn. solvent	M.p., °C.	ν_{max}^{KBr}, cm.$^{-1}$ [a]	λ_{max}^{EtOH}, mμ (ε)	N.m.r.[b] δ, p.p.m.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
2,3-Dihydro-5-methyl-6-phenyl-4H-1,2-diazepin-4-ol (3)	60 g. of 1, 15 g. of $NaBH_4$, EtOH–H_2O, 3 hr., 30°	41 (68)	EtOH–ether	101–102	3530, 3370	303 (5200)	1.83 (s, 3), ABX: 3.07, 3.48, 4.30 (J_{AB} 13.6, J_{AX} 1.5, J_{BX} 4), 6.78 (s, 1), 7.0–7.4 (m, 5)	$C_{12}H_{14}N_2O$	71.26	6.98	13.85	71.30	7.03	13.84
Ketone 1 from 3	100 mg. of 1, 93 mg. of N-bromoacetamide (NBA), pyridine, 2 min. 0°	0.058 (59)												
2-Acetyl-2,3-dihydro-5-methyl-6-phenyl-4H-1,2-diazepin-4-ol (5)	(See separate procedure)	1.3 (65)	Ether–hexane	93	3400, 1680	308 (7000)		$C_{14}H_{16}N_2O_2$	68.83	6.60	11.47	69.18	6.65	11.70
Ketone from 5	100 mg. of 5, 60 mg. of NBA, pyridine, 1 hr., 60°	0.014 (14)												
2-Benzoyl-2,3-dihydro-5-methyl-6-phenyl-4H-1,2-diazepin-4-ol	500 mg. of benzoyl ketone, 94 mg. of $NaBH_4$, EtOH, 15 min., 25°.	0.330 (66)	Ether	145–146		315 (9800)		$C_{19}H_{18}N_2O_2$	74.49	5.92		74.63	6.05	
2-Acetyl-5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-3-hepten-6-ol (4)	241 mg. of 2, 45 mg. of $NaBH_4$, EtOH, 40 min., 15°	0.147 (60)	Ether	151–152	3300, 1625	310 (22,000)	1.58 (s, 3), 2.10 (s, 3), 2.70 (OH, 1), 3.20 (m, 1), 4.0–4.5 (m, 2),[c] 7.2–7.7 (m, 6)	$C_{14}H_{16}N_2O_2$	68.83	6.60	11.47	69.36	6.79	11.37
Ketone 2 from 4	111 mg. of 4, 66 mg. of NBA, pyridine, 30 min., 25°	0.074 (67)												
4-Acetoxy-2-acetyl-2,3-dihydro-5-methyl-6-phenyl-4H-1,2-diazepine (6)	200 mg. of 5, 4 ml. of Ac_2O, 2 ml. of pyridine, 1 hr., 90°	0.209 (90)	Hexane	64	1730, 1680, 1650			$C_{16}H_{18}N_2O_3$	67.11	6.34	9.78	67.04	6.61	9.74
6-Acetoxy-2-acetyl-5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-3-heptene(7)	43 mg. of 4, 0.2 ml. of Ac_2O, pyridine, 45 min., 85°	0.045	Distilled	Oil	1750, 1670, 1230									
7 from 3	3, 200 mg. of 0.2 ml. of Ac_2O, pyridine, 25 min., 25°				1750, 1670, 1230									
Alcohol 4 from acetate 7	200 mg. of 7, 5 ml. of 10% KOH–MeOH, 30 min., 25°	0.047 (27)		155–156	3300, 1625									
2-Acetyl-6-methyl-7-phenyl-2,3-diaza-8-oxabicyclo[3.2.1]-6-octene (8)	10 g. of 3, 5.5 ml. of Ac_2O, 21 ml. of EtOH, 9 ml. of H_2O, 3 min., 25°	9 (75)	Ether, benzene, or sublime	166	3400,[d] 1690	253 (14,500)	2.18 (s, 6), ABX (see discussion), 6.87 (s, 1), 7.45 (s, 5)	$C_{14}H_{16}N_2O_2$	68.83	6.60	11.47	68.79	6.63	11.66
8 from 4	100 mg. of 4, 3 ml. of AcOH, 30 min., 50°	0.062 (62)		165										
2,3-Diacetyl-6-methyl-7-phenyl-2,3-diaza-8-oxabicyclo[3.2.0]-6-octene (9).	400 mg. of 3, 0.8 ml. of AcCl, pyridine, 30 min., 25°	0.410 (71)	Ether	122–123	1705,[d] 1680	262 (16,000)	1.67 (s, 3), 2.08 (s, 3), 2.18 (s, 3), ABX (see discussion), 6.85 (broad, 1), 7.36 (s, 5)	$C_{16}H_{18}N_2O_3$	67.11	6.34	9.78	66.83	6.43	9.74
9 from 8	26 mg. of 8, 0.5 ml. of Ac_2O, 1 hr., 100°	0.025 (82)		120										

3-Methyl-4-phenyl-furfurylhydrazine hydrochloride (10·HCl)	12 g. of 3, 225 ml. of H_2O, 56 ml. of concd. HCl, 45 min., 0°	11 (77)	EtOH–ether	193–194	3340,[d] 3250, 1600	219 (21,000)		$C_{12}H_{15}ClN_2O$	60.37	6.33	11.73	60.14	6.48	11.52
1-Acetyl-1-(3-methyl-4-phenylfurfuryl)hydrazine hydrochloride (11·HCl)	(See separate procedure)	(81)		135–140	2950, 1725, 1575	220 (15,800)							
1-Acetyl-1-(3-methyl-4-phenylfurfuryl) hydrazine (11)	70 mg. of 10, 34.6 mg. of Ac_2O, pyridine, 1 hr., 25°	0.073		Oil[e]	3400, 3300, 1670								
1-Acetyl-2-(3-methyl-4-phenylfurfuryl)hydrazine (12)	1 g. of 8, 15 ml. of H_2O, 15 ml. of concd. HCl, then basified	0.685 (68)	Ether	93	3390, 3300, 1660	221 (20,800)	1.95 (s, 3), 2.10 (s, 3), 4.01 (s, 2, half-band width = 5 c.p.s.), 4.88 (NH), 7.36 (s, 5), 7.44 (s, 1), 7.70 (NH)	$C_{14}H_{16}N_2O$	68.33	6.60	11.47	68.97	6.85	11.39
1,2-Diacetyl-1-(3-methyl-4-phenylfurfuryl)-hydrazine (13)	50 mg. of 9, 5 ml. of 3 *N* HCl, 10 min., 25°	0.026 (52)		124									
13 from hydrazine 10	90 mg. of 10, 1.5 ml. of Ac_2O, 5 min., 25°	0.061 (48)	Ether	126	3300,[d] 1680	220	1.99 (s), 2.01 (s), 2.05 (s) (total 9), 4.0–5.2 (see text) 7.31 (s, 5), 7.39 (s, 1), 8.33 (NH)	$C_{16}H_{18}N_2O_3$	67.11	6.34	9.78	67.23	6.34	9.88
13 from 11	265 mg. of 11, Ac_2O, pyridine, 2 hr., 25°	0.220 (60)		122									
13 from 12	22 mg. of 12, Ac_2O	0.018		124									
Benzaldehyde 3-methyl-4-phenylfurfuryl-hydrazone (16)	300 mg. of 10·HCl, 7 ml. of H_2O, 155 mg. of C_6H_5CHO, 1 ml. of EtOH	0.021 (63)	EtOH	93–95	3400, 1600, 1140	290 (4850), 230 (5400)	2.13 (s, 3), 4.39 (s, 2), 7.1–7.6 (m, 13)	$C_{19}H_{18}N_2O$	78.59	6.25		78.77	6.57	
1-Nitroso-1-(3-methyl-4-phenylfurfuryl)-hydrazine (14)	800 mg. of 10, 10 ml. of 20% AcOH, 260 mg. of $NaNO_2$, 0°	0.720 (93)	Ether	118–119	3400, 3300, 1285	249 (31,000)	2.22 (s, 3), 5.83 (s, 2), 5.75 (s, 2), 7.45 (s, 5), 7.57 (s, 1)	$C_{12}H_{13}N_3O_2$	62.32	5.67	18.17	62.20	5.88	18.14
1-Acetyl-2-nitroso-2-(3-methyl-4-phenylfurfuryl)hydrazine (15) from 14	50 mg. of 14, 0.1 ml. of AcCl, pyridine, 0–5°	0.041 (59)	Ether	107	3250, 1680	222 (6350)		$C_{14}H_{14}N_3O_3$	61.53	5.53	15.38	61.53	5.60	15.25
15 from 12	50 mg. of 12, 4 ml. of 20% AcOH, 20 mg. of $NaNO_2$	0.039 (70)	Ether	107									
3-Methyl-4-phenylfurfurylamine hydrochloride (17)	400 mg. of 10, 0.7 ml. of 2 *N* HCl, 100 mg. of PtO_2, 43.3 cc. of H_2, 48 hr.	0.126 (42)	EtOH	255–260	3125, 3000, 1625	240 (5200)		$C_{12}H_{14}ClNO$	64.42	6.31	6.26	64.54	6.25	5.95
3-Methyl-4-phenylfurfurylacetamide (19) from 17	12 mg. of 17, basify and extract, 0.1 ml. of Ac_2O, 30 min., 25°	0.012 (21)	Ether	96–97	3390, 1650	245 (15,000)	2.02 (s, 3), 2.12 (s, 3), 4.45 (d, 2), 7.35 (m, 7). After D_3O^+: 2.02 (s, 3), 2.12 (s, 3), 4.45 (s, 2)	$C_{14}H_{15}NO_2$	73.34	6.54	6.11	73.44	7.01	6.01
19 from 11	50 mg. of 11, 0.1 ml. of 2 *N* HCl, 30 mg. of $NaNO_2$, 20 min., 55°	0.036 (89)	Ether	96–97									
Benzaldehyde 2-acetyl-2-(3-methyl-4-phenylfurfuryl)hydrazone (18)	150 mg. of 11·HCl, 5 ml. of H_2O, 0.1 ml. of benzaldehyde, 60°	0.171 (96)	EtOH	99	1680[d]	234 (18,100), 288 (33,500)	2.13 (s, 3), 2.39 (s, 3), 5.05 (s, 2), 7.20 (m, 12)	$C_{21}H_{20}N_2O_2$	75.88	6.07	8.43	76.04	6.18	8.39

TABLE I
(*Continued*)

Product	Reaction conditions	Yield, g. (%)	Recrystn. solvent	M.p., °C.	ν_{max}^{KBr}, cm.$^{-1}$ [a]	λ_{max}^{EtOH}, mμ (ε)	N.m.r.[b] δ, p.p.m.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
3-Methyl-4-phenylfurfuralacetylhydrazone (22) from 12	967 mg. of 12, 2.4 g. of $K_3Fe(CN)_6$ in 100 ml. of 10% $NaHCO_3$, pyridine, 12 hr.	0.760 (80)	Ether	192	3225,[d] 1690, 1675	306 (27,500)	2.25 (s, 3), 2.75 (s, 3), 7.7 (s, 5), 7.98 (s, 1), 8.15 (s, 1), 8.75 (s, 1)	$C_{14}H_{14}N_2O_2$	69.40	5.83	11.56	69.48	5.99	11.50
12 from 22	150 mg. of 22, 400 mg. of $NaBH_4$, EtOH–H_2O, after 20 hr. add 50 mg. of $NaBH_4$, reflux, 48 hr.	0.012 (8)	Ether	90–92										
3-Methyl-4-phenylfurfural semicarbazone (24a)	100 mg. of 22, 5 ml. of EtOH, 100 mg. of semicarbazide·HCl, 150 mg. of sodium acetate, 60°	0.078 (78)	EtOH	224–225	3600, 3200, 1760, 1590	306 (41,000)		$C_{13}H_{13}N_3O_2$	64.18	5.39	17.28	64.12	5.48	17.51
3-Methyl-4-phenylfurfural 2,4-dinitrophenylhydrazone (24b) from 22.	50 mg. of 22, 3 ml. of EtOH, 45 mg. of 2,4-DNPH, 5 drops of H_2SO_4	0.071 (95)	Ethyl acetate	199	3325,[d] 1710	398 (54,000)		$C_{18}H_{14}N_4O_5$	59.01	3.85	15.30	59.28	3.99	15.48
24b from 24a	10 mg. of 24a, 3 ml. of EtOH, 3 ml. of 2,4-DNPH solution, 5 min., 80°	0.0034 (46)		195–196										
3-Methyl-4-phenylfurfural azine (23)	100 mg. of 22, 10 ml. of 10% KOH, 30 min. reflux	0.045 (30)	Ether	188	1625[d]	306 (30,000)		$C_{24}H_{20}N_2O_2$	78.24	5.45	7.60	78.02	5.57	7.61
Furfural acetylhydrazone (25)	2 g. of furfural hydrazone, ether, 1.85 ml. of Ac_2O, 0–5°	2.5 (90)	CH_2Cl_2–Ether	139–140	3240, 1680	301 (30,500)		$C_7H_8N_2O_2$	55.25	5.30	18.41	55.41	5.45	19.07
Furfural semicarbazone from 25	100 mg. of 25, 100 mg. of semicarbazide·HCl, 150 mg. of sodium acetate	0.044 (25)	EtOH–H_2O	197	3550, 1700, 1670, 1610									
2-Acetyl-5-methyl-6-phenyl-2,3-diaza-8-oxabicyclo[3.2.1]-3,6-octadiene (21)	500 mg. of 8, 300 mg. of NBA, pyridine, −5°, 20 min.	0.457 (92)	Ether	87–88	1680, 1540	278 (5500)	2.16 (s, 3), 2.23 (s, 3) 4.60 (d, 1, *J* 2), 7.05 (s, 1), 7.30 (m, 6)	$C_{14}H_{14}N_2O_2$	69.4	05.83	11.56	69.11	5.81	11.66
8 from 21	50 mg. of 21, 10 mg. of $NaBH_4$, EtOH–H_2O, 60–70°, 45 min.	0.041		166										
22 from 21	50 mg. of 21, 2 ml. of CH_3OH, 200 mg. of $AlCl_3$, 70°, 30 min.	0.041 (82)	Ethyl acetate	188–189										
24b from 21	50 mg. of 21, 2 ml. of EtOH, 0.5 ml. of 2,4-DNPH solution, 15 min., 80°	0.030 (40)		202										

[a] Spectra in KBr pellets unless otherwise noted. [b] In parentheses are given multiplicity of peak and number of protons from integration. [c] Multiplet at 4.0–4.5 p.p.m. probably due to C-6 H and one C-7 H. [d] Spectrum in CCl_4 solution; *J* values in cycles per second. [e] Converted to **11·HCl**, m.p. 135–140°, with concentrated HCl.

The solution became yellow, and at the end of this time no starting material could be detected by t.l.c. Evaporation of the benzene gave a yellow oil which was sublimed onto a Dry Ice cooled finger. A 50-μl. sample of the sublimate, m.p. *ca.* 0°, was injected onto a 25-in. Silicone SF-96 column at 140°. A single major peak was eluted, retention time 55 min. The spectra suggested that this material was 2,3-dimethyl-4-phenylfuran: ν 1625, 1575, 1140 cm.$^{-1}$; n.m.r. 2.03 (s, 3), 2.27 (s, 3), 7.35 p.p.m. (s, 6, slight shoulder).

The sublimation residue was triturated with ether and a pale yellow solid, m.p. 125–130°, was obtained. Recrystallization from methylene chloride–ether gave cream-colored plates: m.p. 135–136°; ν^{KBr} 3400, 1610, 1150 cm.$^{-1}$; λ_{max}^{EtOH} 305 mμ; n.m.r. 2.7 (d, 3, J = 3 c.p.s.), 4.42 (s, 1), 7.35 p.p.m. (m, 6).

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.35; H, 5.89; N, 7.99.

Hydrolysis of 10.—A suspension of 600 mg. of the hydrochloride **10**·HCl in 12 ml. of concentrated HCl was heated for 5 min. at 85°. The hot mixture was filtered to give 250 mg. of black solid. A 32-mg. sample of this cinder-like material was extracted with hot water and the clear aqueous solution was treated with 1 drop of benzaldehyde. On chilling, 6 mg. of yellow prisms of benzalazine separated, m.p. and m.m.p. 88–90°.

The aqueous acidic filtrate from the original mixture was neutralized with $NaHCO_3$ and extracted with methylene chloride. Evaporation of the methylene chloride solution gave 210 mg. of the butenolide **20**, m.p. 42–44°. Recrystallization from aqueous ethanol or sublimation gave colorless needles, m.p. 53–54°; for spectra, see discussion.

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.79; H, 6.33.

Hypoiodite Degradation of 20.—A solution of 200 mg. of **20** in 5 ml. of dioxane containing 4 ml. of 10% NaOH was treated at 60° with KI_3 solution. After a permanent brown color was present, a few more drops of NaOH solution were added, the solution was chilled, and the precipited iodoform, 173 mg. (42%), m.p. 120–121°, was collected. The aqueous filtrate was acidified and the iodine was reduced with $NaHSO_3$. The solution was again made alkaline, extracted with ether to remove impurities, and finally acidified and chilled to give 85 mg. (40%) of light yellow crystals of methylphenylmaleic anhydride, m.p. 90°. Recrystallization from acetone–hexane gave cream-colored needles, m.p. and m.m.p. (with an authentic sample[16]) 95°.

(16) J. A. Moore and F. J. Marascia, *J. Am. Chem. Soc.*, **81**, 6049 (1959).

Aziridines. XIV. 3-Oxa-6-azabicyclo[3.1.0]hexane[1]

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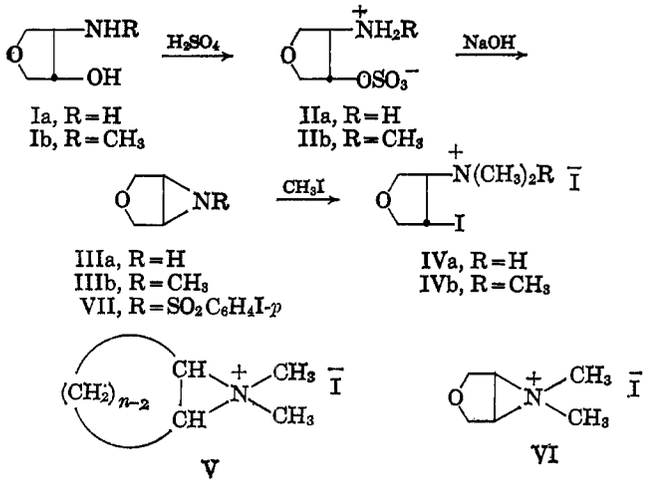
The fused, bicyclic aziridine 3-oxa-6-azabicyclo[3.1.0]hexane and its 6-methyl homolog were prepared by conventional Wenker syntheses. Both aziridines gave only ring-opened products on treatment with methyl iodide. Pyrolysis of the 6-benzoyl derivative gave the isomeric *cis*-fused bicyclic oxazoline, rather than the anticipated unsaturated amide. The same isomerization occurred on treatment of the benzoyl derivative with sodium iodide in acetone or acetonitrile.

As part of our continuing study of the chemistry of fused, bicyclic aziridines, we have now prepared 2,5-dihydrofuranimine or 3-oxa-6-azabicyclo[3.1.0]hexane, IIIa. The new aziridine was made by the conventional Wenker synthesis from the known *dl-trans*-3-amino-4-hydroxytetrahydrofuran (Ia) *via* the sulfate ester IIa. The N-methyl homolog IIIb was prepared in a similar manner from the amino alcohol Ib. The structures assigned to the aziridines IIIa and b are fully supported by the n.m.r. spectra, as shown in Figure 1.



In previous work, it had been found that the quaternary methiodides of the series of cycloalkenimines represented by V, where n = 7, 8, 10, and in *cis* and *trans* 12, are stable, crystalline compounds.[2] Three of these substances were found to be particularly suitable for the determination of the molecular structure by the three-dimensional X-ray diffraction technique.[3] On the other hand, attempts to prepare the quaternary derivative of cyclohexenimine (V, n = 6) gave only ring-opened products.[4] Similarly, the attempted preparation of the quaternary derivative VI by the treatment of IIIa or b with methyl iodide gave only the ring-opened iodides IVa and b, respectively. Therefore, the heavy element *p*-iodobenzenesulfonyl derivative VII was prepared in the conventional way, and its crystal and molecular structure is now under investigation in the laboratory of Dr. L. M. Trefonas. The n.m.r. spectrum of compound VII indicated that no isomerization of the bicyclic skeleton occurred in the course of preparation of the derivative.

In previous work, it has been found that the pyrolytic rearrangement of an N-acyl aziridine follows one of two courses.[5] At 125° N-benzoylaziridine rearranges rapidly to 2-phenyl-2-oxazoline,[6] and a similar rearrangement of other acyl derivatives of ethylenimine was observed during attempted distillation.[7] The mechanism

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(2) P. E. Fanta, R. Golden, and H.-J. Hsu, *J. Chem. Eng. Data*, **9**, 246 (1964), and preceeding papers.

(3) L. M. Trefonas and R. Towns, *J. Heterocyclic Chem.*, **1**, 19 (1964), and preceeding papers.

(4) (a) T. Taguchi and M. Eto, *J. Am. Chem. Soc.*, **80**, 4075 (1958); (b) P. E. Fanta and E. N. Walsh, *J. Org. Chem.*, **30**, 3574 (1965).

(5) H. W. Heine, *Angew. Chem. Intern. Ed. Engl.*, **1**, 528 (1962).

(6) A. A. Goldberg and W. Kelley, *J. Chem. Soc.*, 1919 (1948).

(7) C. W. Woods, A. B. Borkovec, and F. M. Hart, *J. Med. Chem.*, **7**, 371 (1964).