under nitrogen for 10 hr., the molten thione became viscous with evolution of unidentified gas. Then the reaction mixture was washed with hot methanol, and 0.05 g. of white powder, m.p. 163–170° dec., was obtained. The infrared spectrum has broad absorption bands at about 1700–1620 and 1580–1540 cm.$^{-1}$.

Anal. Calcd. for C_3H_5NOS: C, 34.94; H, 4.89; N, 13.58. Found: C, 38.85; H, 6.46; N, 18.22.

Solution Polymerization of 1,3-Oxazolidine-2-thione (IV).—To a solution of 1,3-oxazolidine-2-thione (1.0 g.) was added boron trifluoride etherate (0.002 g.). After this solution was allowed to stand at room temperature for 6 days, the resulting polymer was washed with tetrahydrofuran, then dried *in vacuo* at 100° for 3 hr.: yield 0.14 g. (14%); m.p. 229° dec.; $[\eta]^{30}_{m\text{-cresol}}$ 0.06 dl. g.$^{-1}$. The analytical sample was obtained by reprecipitation from *m*-cresol–methanol.

Anal. Calcd. for C_3H_5NOS: N, 13.58. Found: N, 13.32.

Similarly, the thione was polymerized in the presence of the following catalysts (0.002 g.) (yield, melting point, and $[\eta]^{30}_{m\text{-cresol}}$): ferric chloride (53%, 229° dec., 0.06 dl. g.$^{-1}$), sulfuric acid (3%, 216°).

Poly(ethylene thiolcarbamate) thus obtained was soluble in *m*-cresol and dimethylformamide but insoluble in most organic solvents.

Reaction of 3-Phenyl-1,3-oxazolidine-2-thione (I) with Methyl Iodide.—A mixture of 3-phenyl-1,3-oxazolidine-2-thione (1.79 g., 0.01 mole) and methyl iodide (2.84 g., 0.02 mole) in 18 ml. of dry benzene was refluxed for 3 hr. After removal of benzene and excess methyl iodide, 3.1 g. (53%) of methyl N-(2-iodoethyl)-thiolcarbanilate was obtained. It was recrystallized from petroleum ether (b.p. 40–60°), m.p. 70.0–71.5°. Its infrared spectrum shows strong absorption at 1655 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{10}H_{12}INOS$: C, 37.39; H, 3.77; N, 4.36, Found: C, 37.03; H, 3.69; N, 4.36.

Reaction of 1,3-Oxazolidine-2-thione (IV) with Methyl Iodide.—A mixture of 1,3-oxazolidine-2-thione (1.03 g., 0.01 mole) and methyl iodide (2.84 g., 0.02 mole) in 10 ml. of tetrahydrofuran was refluxed for 20 hr. After removal of tetrahydrofuran and excess of methyl iodide, 2.4 g. of methyl N-(2-iodoethyl)-thiolcarbamate was obtained. It was recrystallized from petroleum ether, m.p. 77.5–78.0°. Its infrared spectrum has characteristic bands for N–H (3270 cm.$^{-1}$) and for C=O (1640 cm.$^{-1}$).

Anal. Calcd. for C_4H_8INOS: C, 19.60; H, 3.29; N, 5.72. Found: C, 19.88; H, 3.43; N, 5.96.

Attempted Polymerization of 3-Phenyl-1,3-oxazolidin-2-one.—When 3-phenyl-1,3-oxazolidin-2-one (0.5 g.) was heated in a sealed tube under nitrogen for 15 hr. at about 180°, 0.48 g. (96%) of the starting material was recovered and no polymer was obtained.

When 0.001 g. of ferric chloride was added to a solution of 3-phenyl-1,3-oxazolidin-2-one (0.5 g.) in 7 ml. of nitrobenzene and the solution was kept at 20° for 6 days, 0.49 g. (98%) of the starting material was also recovered.

Heterocyclic Studies. XVII. The Preparation and Reactions of 1,2-Diazabicyclo[3.2.0]-6-heptanone Derivatives[1,2]

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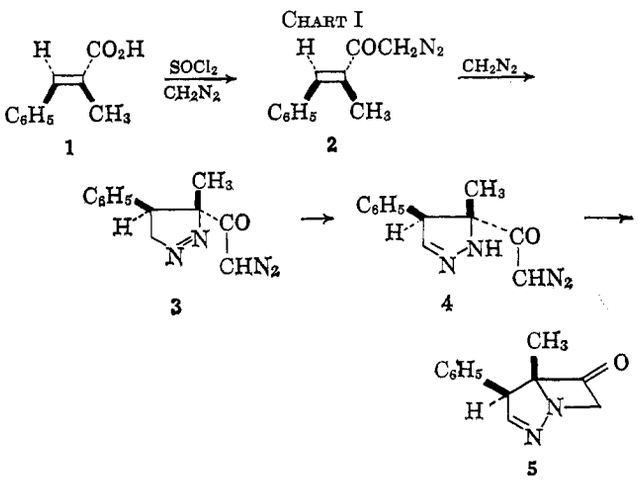
The diazoacetylpyrazoline **4** with acetic anhydride gives the acetylacetoxypyrazolidine **6** and, with acetyl chloride, pyridine, and then water, the hydroxypyrazolidine **8**. In acetic acid **6** and **8** are converted to the respective 3-*endo*-substituted 1,2-diazabicyclo[3.2.0]heptanones **9** and **10**. The Δ^2-bicyclic ketone **5** also gives **9** with acetic anhydride, and the 2-acetyl-Δ^3-ketone **12** with acetyl chloride. Acylation of the diazepinone **14** also leads to the 2-acyl Δ^3-bicyclic ketones in a transannular reaction; in the presence of methanol, benzoylation of **14** gives the 1-benzoyl-7-methoxydiazepinone **15**. All of the bicyclic ketones and benzoylmethoxydiazepinones are deacylated to give the diazepinone **14** in acetic acid; the conversion of **5**, but not the other bicyclic ketones, to **14** occurs most rapidly in base. Treatment of the 2-acyl-Δ^3 ketones **12** and **13** with acidic methanol causes ring opening to the 1-acyl-7-methoxydiazepinones **15**. In strong acid all of the acyl derivatives are converted to 1-acylamido-3-hydroxypyridines **22**. A mechanism involving an allylic diazepine cation and a bicyclo[4.1.0] intermediate is suggested.

The preparation of the bicyclic ketone **5** by the reactions shown in Chart I and the subsequent isomerization of **5** to a diazepinone were briefly described in an earlier paper.[3] We now present the results of more extensive work on these reactions and a number of additional compounds in the 1,2-diazabicyclo[3.2.0]heptane series.

The steric configuration of **5** and related compounds is defined as shown in Chart I by the *cis* addition[4] of diazomethane to the α-methylcinnamic acid, m.p. 76 or 81°, obtained by the Perkin condensation of benzaldehyde and propionic anhydride. The configuration of this acid has been established as *cis*-phenyl–methyl,[5] and the pyrazolines and bicyclic ketone thus have phenyl and methyl groups *cis*.

Acylation of the pyrazoline **4** and bicyclic ketone **5** led to the series of derivatives outlined in Chart II. Treatment of the pyrazoline **4** with acetic anhydride and pyridine gave a new diazoketone: λ^{KBr}_{max} 3.10 (NH), 4.75 ($-\overset{+}{N}\equiv N$), 5.76 (–OC=O), 6.00 (–NC=O), and 6.16 μ ($COCHN_2$); λ^{EtOH}_{max} 251 mμ. These data characterize the compound as the pyrazolidine **6**; this structure is authenticated by the reactions described below. With acetyl chloride and pyridine,

CHART I



(1) Supported in part by the Geschickter Fund for Medical Research and in part by Grant DA-CML-18-108-61-6-24 from the Army Chemical Corps.

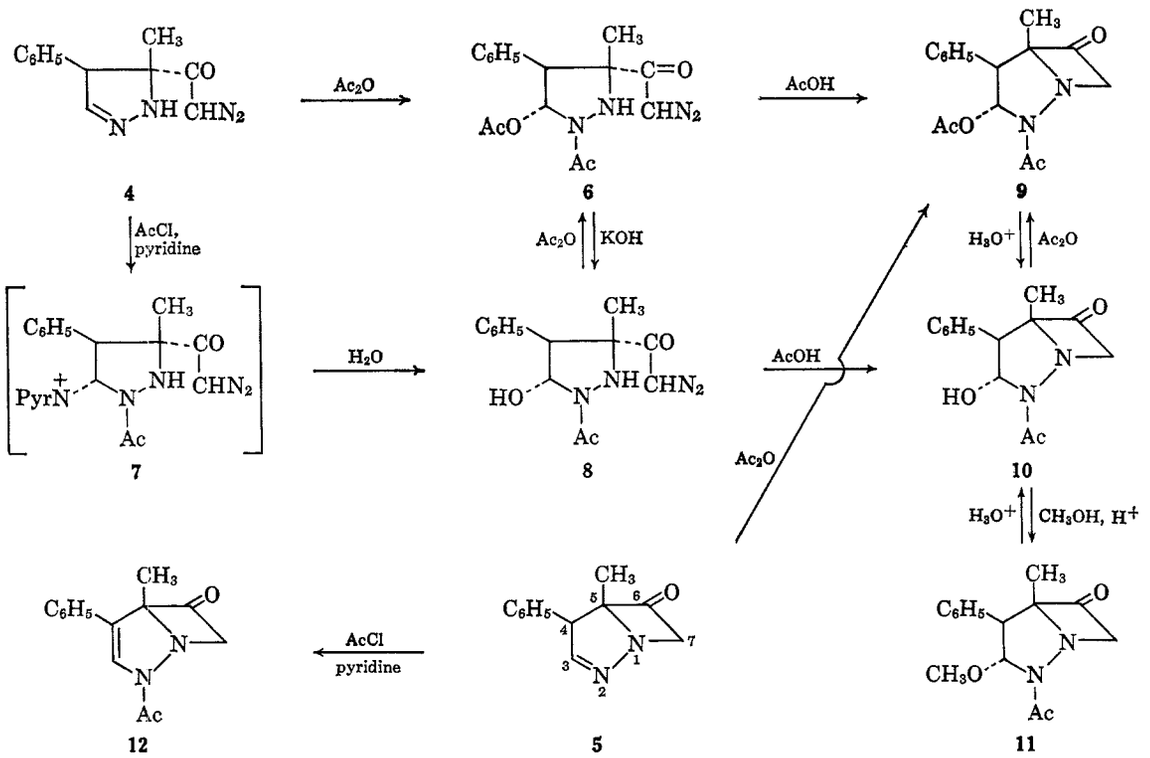
(2) Part XVI: C. L. Habraken and J. A Moore, *J. Org. Chem.*, **30**, 1892 (1965).

(3) J. A. Moore and R. W. Medeiros, *J. Am. Chem. Soc.*, **81**, 6026 (1959).

(4) R. Huisgen, *Angew. Chem. Intern. Ed. Engl.* **2**, 633 (1963), and earlier references cited there.

(5) R. Stoermer and G. Voht, *Ann.*, **408**, 47 (1915).

CHART II



a water-soluble product, presumably **7**, was formed from **4**. Hydrolysis gave the alcohol **8** (λ^{KBr} 2.83, 3.10 μ). The ultraviolet maximum at 251 mμ of **6** and **8** was previously noted also in **4**, and is characteristic of the diazocarbonyl chromophore when hydrogen bonded to NH.[3] Acetylation of **8** gave **6**, and the latter was hydrolyzed to **8** with alkali.

Both of the diazoketones **6** and **8** evolved nitrogen rapidly in cold acetic acid solution, at a rate comparable to that of **4**, giving the bicyclic ketones **9** and **10**, respectively. The infrared spectra of these products showed the characteristic carbonyl bands for a four-membered cyclic ketone at 5.53 μ, as well as a band at about 6 μ for amide carbonyl. The spectrum of **10** contained a strong band at 3.00 μ (bonded OH), and that of **9** an ester carbonyl band at 5.75 μ. The two bicyclic ketones could be interconverted by acetylation of **10** and acid hydrolysis of **9**, and both were transformed by treatment with acidic methanol to the methoxy ketone **11**. The latter was also hydrolyzed to **10** with dilute sulfuric acid. The methoxy compound **11** was conveniently obtained by treatment of the pyrazoline **4** with acetyl chloride and pyridine followed by methanol, with acylation, cyclization, and solvolysis occurring in one operation.

The reaction of the bicyclic ketone **5** with acetic anhydride and pyridine resulted in addition, as in the case of the Δ^5-pyrazoline **4**, giving the same 3-acetoxy-2-acetyl ketone obtained from **6** and from **10**. The yield in this reaction was fairly low, and other products, including the diazepinone **14** or its 2-acetyl derivative, were detected by t.l.c. It is possible that a stereoisomer of **9** was formed, but **9** was the predominant product.

With acetyl chloride and pyridine, the bicyclic ketone reacted by a different course to give in good yield a monoacetyl compound still containing the four-membered carbonyl ring (λ^{KBr} 5.58, 6.05 μ). The corresponding benzoyl derivative was obtained with benzoyl chloride. The 2-acetyl-Δ^3 ketone structure **12** can be derived from the mode of formation and reactions discussed later and is confirmed by the absence of the benzyl proton peak in the n.m.r. and the shift of the angular methyl peak from an average value of 1.1 p.p.m. in the other bicyclic ketones to 1.58 p.p.m. for **12**.

There is no precedent in the pyrazoline literature for either of the reactions observed with **4**; simple pyrazolines normally undergo acylation at a free NH group. Addition of acetic anhydride to a C=N bond is well known with acyclic azomethines,[6,7] however, and has also been observed in the indolenine series.[8] The contrasting course of the reactions of **4** and **5** with acetyl chloride was unexpected, and an adequate explanation is not available. It is clear from the reactivities of the ketones, discussed later, that **10** is not an intermediate in the formation of **12**, since any conditions leading to elimination reactions of **10** destroy **12** much more rapidly.

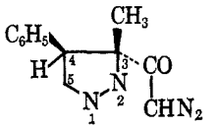
The interconversions of the two diazoketones **6** and **8** and the bicyclic ketones **9** and **10** show that the configuration at C-3 is the same in all four compounds, and that attack at C-3 (C-5 in pyrazolines) occurs from the same face of the five-membered ring in both the pyrazoline **4** and the bicyclic ketone **5**. Molecular models suggest that the phenyl group would be the most important steric factor in a cyclic addition of acetic anhydride to either **4** or **5**, leading to a tentative prediction of the *endo* configuration of the C-3 substituent in the acetates and alcohols (see eq. 1).

Support for the *endo* configuration of the 3-oxygen substituents in the bicyclic ketones **9**, **10**, and **11** is provided by the n.m.r. spectra (Table I). The con-

(6) A. W. Burgstahler, *J. Am. Chem. Soc.*, **78**, 3021 (1951).
(7) H. Breederveld, *Rec. trav. chim.*, **79**, 401 (1960).
(8) H. Leuchs, *Ann.*, **461**, 27 (1928).

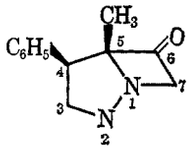
TABLE I
N.M.R. DATA ON PYRAZOLINES AND BICYCLIC KETONES[a]

Pyrazolines



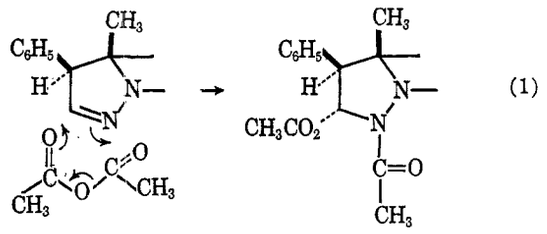
Compound	5-H	4-C_6H_5	4-H	3-CH_3	CHN_2
3	A 4.95[b] (J_{AB} −19.6) B 4.62 (J_{AX} 6.0, J_{BX} 9.2)	7.22 (m)[c]	3.79 (m)[b]	1.20	5.77
4	6.82 (d) ($J_{4,5}$ 1.5)	7.23 (m)[c]	4.38 (d) (J 1.5)	0.92	6.05
8	5.95 (d) ($J_{4,5}$ 2.7)	7.33 (m)[c]	3.98 (d) (J 2.7)	0.88	5.69

Bicyclic Ketones



Compound	3-H	4-C_6H_5	4-H	5-CH_3	7-CH_2
5	7.3[d]	7.32 (m)[c]	4.54 (d) ($J_{3,4}$ 1.7)	1.17	4.30, 4.85 (d)[e,f] (J_{gem} −17.2, $J_{3,7}$ 1.4)
9	6.9–7.03[d]	6.97, 7.27 (m)[g]	3.80	1.13	4.58, 4.95[e] (J_{gem} −17.5)
10	6.20	7.03, 7.25 (m)[g]	3.83	1.08	4.82
11	5.92	6.93, 7.27 (m)[g]	3.82	1.08	4.48, 4.85[e] (J_{gem} −17.5)
12	>7.23[d]	7.41 (m)[c]	...	1.58	4.45 (d),[f] 4.77[e] (J_{gem} −17.3, $J_{3,7}$ 0.9)

[a] Chemical shifts, δ, in parts per million in $CDCl_3$ solution, TMS = 0. A Varian A-60 instrument was used. d = doublet, m = multiplet; when not otherwise specified, the peak is a singlet. [b] Values of J_{AX}, J_{BX}, and δ_A, δ_A, and δ_X were calculated for an ABX system by the method of H. J. Bernstein, J. A. Pople, and W. G. Schneider [*Can. J. Chem.*, **35**, 65 (1957)] and checked with the theoretical spectrum computed with a Freqint III program developed by Dr. A. Bothnerby and modified for use in a Honeywell 800 computer at the National Institutes of Health. We are indebted to Dr. G. W. Milne, National Institutes of Health, for help in the calculations. [c] Position of most intense peak in multiplet. [d] Merged with aryl multiplet, multiplicity unknown. [e] The chemical shifts given are the calculated centers of gravity of the two doublets in the AB system. [f] Doublet further split into doublet. [g] Positions of most intense peaks in two separate multiplets.



(1)

stant position of the C-4 proton peak and the progressive deshielding of the C-3 proton in the series **11**–**10**–**9** attest to the similar stereochemistry in the three saturated bicyclic ketones. Although splitting of the H-4 and H-5 peaks was observed in the spectrum of the hydroxypyrazolidine **8**, there was no detectable spin coupling of the corresponding protons (H-4 and H-3) in the 3-substituted bicyclic ketones. The relative order $J_{cis} > J_{trans}$ for the coupling constants of adjacent protons in a five-membered ring is expected from the general relationship of J_{vic} and the dihedral angle.[9] The magnitude of the coupling constants also varies inversely with the electronegativity of substituent atoms.[10] In five-membered heterocyclic rings, protons adjacent to a heteroatom and a hydroxyl group therefore have relatively small coupling constants; values of J_{cis} = 4 c.p.s., $J_{trans} < 1$ c.p.s., have been reported for the 2- and 3-protons in the isomeric 3-hydroxyprolines,[11] and J_{cis} = 4.0–4.5 c.p.s., J_{trans} = 0–1.0 c.p.s., in three anomeric pairs of methyl furanosides.[12] In the bicyclic ketones **9**–**11**, a value of $J_{3,4}$ = 0 c.p.s. is thus quite reasonable for a *trans* arrangement of the C-3 and C-4 protons.

The strong geminal coupling ($|J|$ = 17–18 c.p.s.[13]) and magnetic nonequivalence (0.3–0.5 p.p.m.) of the C-7 methylene protons in **5**, **9**, **11**, and **12** is in keeping with the expected behavior for a bicyclic system. The spectrum of the hydroxy ketone **10**, in which the C-7 methylene peak is a singlet, appears to be anomalous, but, as mentioned in the following paper,[14] the equivalence of similar methylene protons is observed in the entire series of the related 3-oxygenated steroidal diazabicyclo[3.2.0]heptenones.

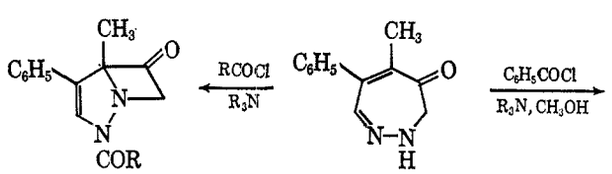
Another noteworthy effect in the series is the relatively strong long-range spin coupling between the C-7 and C-3 protons in the unsaturated bicyclic ketones **5** and **12**. In both spectra the H-3 signal was merged with the aryl multiplet, but double irradiation of **5** with a 1-w. side-band signal at 155 and 170 c.p.s. downfield caused collapse of the doublets at 4.85 and 4.53 p.p.m., respectively, confirming coupling of both

(9) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); *J. Am. Chem. Soc.*, **85**, 2870 (1963).
(10) K. L. Williamson, *ibid.*, **85**, 516 (1963).
(11) F. Irreverre, K. Morita, A.V. Robertson, and B. Witkop, *ibid.*, **85**, 2824 (1963).
(12) B. Capon and D. Thacker, *Proc. Chem. Soc.*, 369 (1964).
(13) The sign of J_{gem} is assumed to be negative: N. S. Bhacca and D. H. Williams, "Applications of N.M.R. Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, p. 54.
(14) T. Yamauchi and J. A. Moore, *J. Org. Chem.*, **31**, 42 (1966).

H-4 and H-7 with H-3, and fixing the chemical shift of H-3 at 7.3 p.p.m.[15]

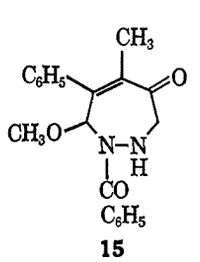
The 2-acetyl and 2-benzoyl Δ^3-bicyclic ketones **12** and **13** are of particular importance in this series because they are also produced by a transannular reaction when the diazepinone **14** is treated with the acid chloride and a tertiary amine. The compounds were first obtained in this reaction, which is by far the more practical method of preparation. The conversion of **14** to the bicyclic system comprises a tautomeric shift with valence bridging following electrophilic attack at N-1. Although valence tautomerism of multiply unsaturated seven-membered rings to bicyclo[3.2.0] derivatives is a frequent occurrence in the photoexcited state,[16] the formation of **12** and **13** on acylation is an entirely different type of reaction, resembling the acylation of 7-anilino-3H-azepine (dibenzamil) in which transannular bridging and subsequent aromatization are observed.[17] A stable bicyclo[3.2.0]heptene derivative has not previously been isolated from such a transannular displacement. A process of this kind has been considered as a possible biosynthetic pathway to the penicillins from a 1,4-thiazepine precursor[18] but has not yet been demonstrated.

When the diazepinone **14** is treated with benzoyl chloride and pyridine in *methanol* solution, the tautomeric shift and bridging are interrupted, and the 1-benzoyl-7-methoxytetrahydrodiazepinone **15** is isolated instead of **13**. The structural evidence and properties of **15** are presented in the accompanying paper.[19a] Similar attack at C-7 of an intramolecular hydroxyl group, leading to a 4→7 bridged oxide, occurs on acylation of the corresponding diazepine carbinol.[19b] The formation of **15** rules out the possibility that the bicyclo[3.2.0] acylation products **12** and **13** arise by prior tautomerization of **14** to a bicyclic system followed by substitution, as suggested in certain reactions of eucarvone that lead to bicyclo[4.1.0]products.[20]



12, R = CH_3
13, R = C_6H_5

14



15

(15) We are indebted to Mr. Robert Bradley, Laboratory of Physical Biology, National Institute for Arthritis and Metabolic Diseases, for carrying out the double irradiation; a Space Avionics spin decoupler was used with an HR-60 spectrometer.

(16) O. L. Chapman, *Advan. Photochem.*, **1**, 323 (1963).

(17) R. Huisgen and M. Appl, *Chem. Ber.*, **91**, 12 (1958).

(18) N. J. Leonard and G. E. Wilson, Jr., *J. Am. Chem. Soc.*, **86**, 5307 (1964), and earlier references cited there.

(19) (a) R. L. Wineholt, E. Wyss, and J. A. Moore, *J. Org. Chem.*, **31**, 48 (1966); (b) J. A. Moore, R. W. Medeiros, and R. L. Williams, *ibid.*, **31**, 52 (1966).

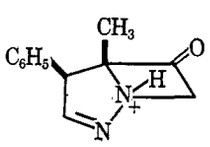
(20) E. J. Corey, W. J. Burke, and W. A. Remers, *J. Am. Chem. Soc.*, **78**, 180 (1956).

Conversion of Bicyclic Ketones to Diazepinone and 1-Aminopyridine Derivatives.—Two reactions, debridging to the diazepinone system and rearrangement to 1-aminopyridines, are general for all of the bicyclic ketones described above, but there are important differences in reactivity among the compounds.

Isomerization of the Δ^2-bicyclic ketone **5** is the preparative route to **14**; the reaction is usually carried out without isolation of intermediates **4** or **5** by heating the Δ^1-pyrazoline **3** in acetic acid. The ketone **5** has been found to be less sensitive to acid than previously reported,[3] and has been isolated by treatment of either **3** or **4** with cold mineral acid. The compound has also been crystallized, permitting study of the isomerization with pure material.

The ketone is a relatively weak base, $pK_A' = 2.6$ in 50% methanol. Crystalline samples or neutral solutions are stable for a few days at 0°, but slowly become yellow, owing to the formation of **14**, on prolonged standing The isomerization is more rapid in dilute acid and is extremely fast in dilute base. Approximate rates of isomerization in varying concentrations of 50% methanolic acid and base were determined spectrophotometrically (50% methanol = 1.0): 10^{-3} *N* KOH, 100; 1 *M* acetic acid, 10; 0.1 *M* acetic acid, 3.5; 0.01 *N* HCl, 5; 10^{-3} *N* HCl, 3.5; and 10^{-4} *N* HCl, 1.5. It is clear from these values that removal of the C-4 proton is the rate-determining step in the isomerization to **14** and that the reaction in acid solution is comparatively slow even with substantial concentrations of the conjugate acid of **5**. The data also indicate that the catalysis by acid does not depend on pH alone, since the pH of 1 *M* acetic acid and 10^{-3} *N* HCl are nearly the same. Acetic acid or acetate ion apparently assists in the deprotonation; a similar but more pronounced effect was observed in the isomerization of a related steroidal bicyclic ketone.[21]

The base-catalyzed isomerization of **5** represents a simple β elimination, presumably by an E2 mechanism. The acid-catalyzed reaction could be formulated with either of the conjugate acids **16** or **17** The n.m.r. spectrum of **5** with added trifluoroacetic acid contained all of the peaks characteristic of the base, in the same multiplicity, displaced downfield to varying extents. The largest change (from 4.85 to 6.02 p.p.m.) was in one of the C-7 methylene peaks. This shift suggests the formation of **16**, with the cationic center adjacent to C-7, but the distinction is not clearcut. The isomerization of **5** in more concentrated acid is compli-



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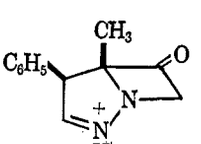
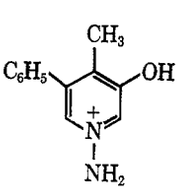


17



18

cated by the further rearrangement of the diazepinone **14** to the 1-aminopyridine **18**.[22] In 6 *N* hydrochloric acid the rearrangement of **14** is faster than the deprotonation of **5**; no diazepinone is observed, but the

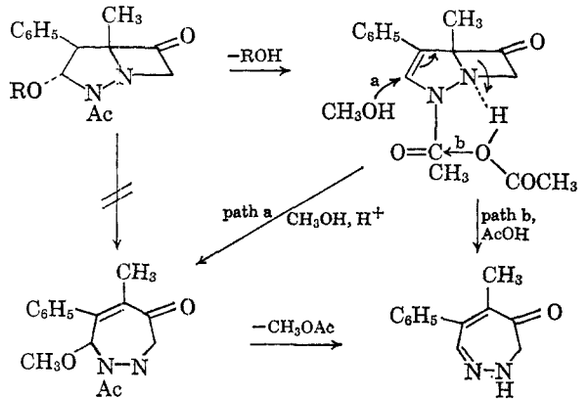
(21) J. A. Moore and L. J. Pandya, *J. Org. Chem.*, **29**, 336 (1964).

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

absorption maximum at 292 mμ characteristic for **18** appears.

The 2-acyl-Δ^3 ketones are also rapidly converted to the diazepinone **14** in acetic acid; acetyl compound **12** reacts at about one-fourth the rate of **5**. The reaction must involve displacement of the acyl group by acetic acid, possibly in a concerted fashion as indicated in Chart III. Similar acyl transfer to acetic acid has been observed with imidol acetates[23] and acetylcarbinolamine acetates.[7]

CHART III



Just as the formation of **13** can be intercepted by nucleophilic attack of methanol, this reverse reaction can also be diverted to the 1-acyl-7-methoxydiazepinones by warming **12** or **13** in methanol containing a carboxylic acid or *p*-toluenesulfonic acid. Less than a stoichiometric amount of acid is required, but the attack must be initiated by acid since a different rearrangement occurs in methanol alone.[24] Further treatment of the 7-methoxy compounds with glacial acetic acid under the same conditions used with **12** or **13** leads to **14** by elimination of the elements of methyl acetate or methyl benzoate.

In comparison to either the Δ^2- or Δ^3-bicyclic ketones **5** or **12**, the reaction of the 2-acetyl 3-substituted compounds with acetic acid is very slow; **14** was formed at a measurable rate only at elevated temperature. The separate elimination steps of debridging and loss of ester are rapid with **5** and **15**, respectively, but the driving force of formation of the stable conjugated system is absent in the initial elimination with **9**–**11**. The conversion of these derivatives to **14** probably proceeds by way of **12**, with elimination of ROH. This path is consistent with the observed relative rates for the three compounds, **10** $\cong$ **9** > **11**, and the behavior of **10** on heating, described below. The elimination–acetolysis reaction was also carried out with the semicarbazone of **11**, giving the semicarbazone of **14** in low yield.

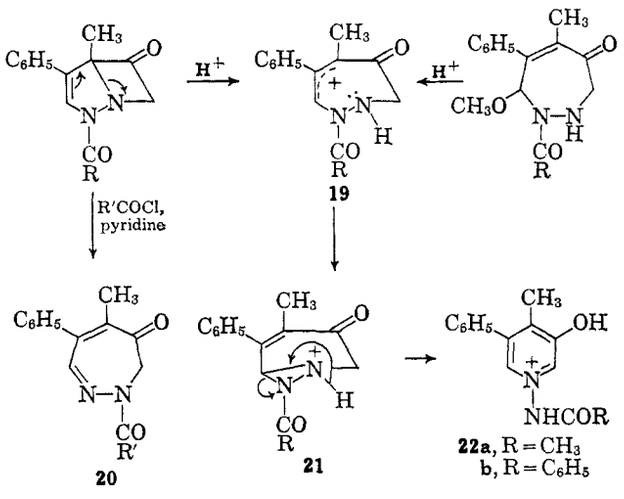
The reaction of the 3-substituted compounds with base does not lead to elimination of the bridging bond as observed with **5**. An entirely different reaction which cannot yet be specified in detail, involving attack in the four-membered ring, occurs under very mild conditions. No conditions have been found under which isomerization of the methoxyacetyl bicyclic ketone **11** to the methoxyacetyl diazepinone could be effected.

(23) W. Z. Heldt, *J. Am. Chem. Soc.*, **80**, 5880 (1958).

(24) J. A. Moore, F. J. Marascia, R. W. Medeiros, and E. Wyss, *ibid.*, **84**, 3022 (1962).

Treatment of the Δ^3-ketones **12** and **13**, the 7-methoxy-1-acyldiazepinones, or the 3-hydroxy ketone **10** with 6 *N* hydrochloric acid gives the 1-acylamidopyridinium chlorides **22**, which have also been prepared by acylation of **18** and fully characterized.[25] It is noteworthy that loss of the acyl groups does not occur; the benzamidopyridine **22b** was obtained from **13** in 87% yield. A suggested mechanism for the formation of **22** is shown in Chart IV. In strong acid either the bicyclic ketones or the 7-methoxydiazepinones can furnish the allylic cation **19** which then collapses to the pyridine *via* the bicyclo[4.1.0] intermediate **21**.

CHART IV



The formation of **22a** from the 3-hydroxy-2-acetyl ketone **10** was very slow; since the acetoxy and methoxy compounds **9** and **11** are converted to **10** in acid, only the latter need be considered. The stability of **10**, which is formally an acetylcarbinolamine, in acid is remarkable. The compound can be prepared by hydrolysis of the acetate **9** in 25% sulfuric acid, and the conversion to **22a**, determined spectrophotometrically, is only 10% complete in 6 *N* hydrochloric acid after 24 hr. In this reaction there is no driving force in the formation of the allylic cation **19** since deprotonation at C-4 must first occur. The dehydration and rearrangement of **10** to the acetamidopyridine **22a** occurs in good yield, however, on heating **10** above the melting point for a few seconds, behavior which is consistent with a *cis* elimination.

Another reaction of the Δ^3-bicyclic ketones which must also involve electrophilic attack at the bridgehead is a transacylation which leads to the 2-acyldiazepinone **20**. When the preparation of the 2-benzoyl bicyclic ketone **13** is carried out by treatment of the diazepinone **14** with benzoyl chloride in pyridine, the 2-benzoyldiazepinone is formed as a troublesome by-product. It was subsequently found that the bicyclic ketone **13** was converted to **20** with excess benzoyl chloride in pyridine, but not in dimethylaniline. Use of the latter amine permits the isolation of **13** in over 90% yield. The specific role of pyridine is not known, but the reaction occurs by loss of the original acyl group. Acyl migration was ruled out by conversion of **13** to the *p*-bromobenzoyldiazepinone (**20**, R = C_6H_4Br) with *p*-bromobenzoyl chloride.

(25) J. A. Moore and J. Binkert, *ibid.*, **81**, 6045 (1959).

Experimental Section[26]

5-Methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-2-hepten-6-one (5).[27]—To a solution of 0.86 g. of the Δ^1-pyrazoline **3** in 30 ml. of methanol was added 0.9 ml. of 6 *N* H_2SO_4. Gas was evolved very slowly; after 1 hr. an additional 1 ml. of acid was added. After 3 hr. t.l.c. showed only a trace of starting **3**, the solution was evaporated, and water was added. A small amount of diazepinone **14** which separated was collected (15 mg., m.p. 140–142°), and the yellow filtrate was cautiously neutralized with KOH and finally with $NaHCO_3$ until permanently turbid (excess KOH *must* be avoided). The solution was extracted with methylene chloride and the dried extract was evaporated to a yellow oil which crystallized on standing. This semisolid residue was then extracted thoroughly with warm hexane; a small amount of insoluble residue, m.p. 90–93°, was present. This material was not further examined; t.l.c. showed that it was not unreacted **3** (m.p. 89–91°). The pale yellow hexane solution was then passed rapidly through a column of 3 g. of coarse charcoal and the water white filtrate was evaporated. Crystallization from the oil containing a few drops of hexane gave 253 mg. (34%) of snow white prisms of **5**, m.p. 50–51.5°. An additional 60 mg of slightly yellow crystals was obtained in a second crop. Recrystallization could be effected from heptane with substantial loss to give material with m.p. 51–53°, λ^{KBr} 5.58, 6.31 μ.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 71.97; H, 6.04; N, 13.99. Found: C, 72.23; H, 5.99; N, 13.73.

5-Diazoacetyl-3-methyl-4-phenyl-5-pyrazoline (4).—The procedure originally described[3] has been found not to be reproducible, presumably because the reaction time prescribed was much too prolonged; an improved procedure is given here. A solution of 3.6 g. of the Δ^1-pyrazoline (**3**) in 80 ml. of methanol was treated with 0.5 ml. of 1 *N* KOH. After 1.5 hr. at 25°, t.l.c. showed only a faint trace of **3** and a major (slower moving) spot due to **4**. The solution was neutralized with Dry Ice and evaporated at 10–20°, replacing the methanol periodically with water. A mass of white prisms separated which was collected, washed thoroughly with water, and dried in a desiccator to give 3.3 g. of **4**, m.p. 101–103°. Recrystallization of this material is not advisable; considerable decomposition results unless solvents are scrupulously pure and heat is avoided.

5-Acetoxy-1-acetyl-3-diazoacetyl-3-methyl-4-phenylpyrazolidine (6).—A solution of 2.30 g. of the 5-pyrazoline **4** in 6 ml. of acetic anhydride containing 0.5 ml. of pyridine was allowed to stand 2.5 hr.; the solution developed a deep amber color and gas was slowly evolved. On pouring into iced KOH solution, a dark oily layer separated and quickly solidified. The solid was collected and triturated with aqueous methanol to give 1.70 g. (51%) of cream-colored prisms, m.p. 122–123° dec.

The product could also be isolated by evaporation of the reaction mixture to an oil at 40° (oil pump), followed by crystallization of the residue by the addition of a few drops of chloroform and then ether. The compound could be crystallized in large prisms from concentrated solutions in ethyl acetate. The most characteristic property was the insolubility in ether. Addition of ether to a relatively dilute solution of previously crystallized material in chloroform or methylene chloride gave a precipitate of essentially amorphous strands resembling a high polymer. The melting points of samples prepared in various ways varied from 90–125°, with decomposition. Analyses were about 2% low in carbon, evidently owing to retention of solvent. N.m.r. spectra of samples prepared in different ways invariably contained only broad structureless peaks. This appearance suggested the presence of a paramagnetic impurity, but the TMS peak was not broadened.

1-Acetyl-3-diazoacetyl-5-hydroxy-3-methyl-4-phenylpyrazolidine (8).—To a chilled solution of 1.67 g. of the Δ^5-pyrazoline **4** in 20 ml. of methylene chloride was added 1.8 ml. of pyridine and then 660 mg. (0.60 ml.) of acetyl chloride in one portion. After 20 min., 10 ml. of water and sufficient sodium bicarbonate to give a neutral reaction were added; the phases were then separated and the methylene chloride phase was extracted with water. After drying and evaporation, 90 mg. of crystalline material, m.p. 150–151° dec., was obtained from the methylene chloride layer. On standing 4 hr. the aqueous phase deposited a granular white precipitate which was collected and washed with water; 1.05 g. of dry material, m.p. 148–150° dec., was obtained (total 1.14 g. of **8**, 54%). The compound crystallized very well from water or methylene chloride–ether, but these solvents were tenaciously retained. The analytical sample was recrystallized from ethyl acetate and dried 16 hr. at 55° and 0.1 mm., m.p. 152–155° dec.

Anal. Calcd. for $C_{14}H_{16}N_4O_3$: C, 58.32; H, 5.59; N, 19.44. Found: C, 58.56; H, 5.70; N, 19.27.

Treatment of 57 mg. of **8** with 0.3 ml. of acetic anhydride and 0.1 ml. of pyridine in 0.5 ml. of methylene chloride for 3 hr. followed by evaporation, KOH hydrolysis of excess acetic anhydride, and washing with water as described above gave 49 mg. of **6**, as nearly colorless prisms, m.p. 113–115° dec. The n.m.r. spectrum contained the same broad peaks observed in samples prepared directly from **4**.

3-Acetoxy-2-acetyl-5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-heptan-6-one (9). A. From 6.—A solution of 79 mg. of the pyrazolidine **6** in 1 ml. of acetic acid was warmed at 60° until nitrogen evolution was complete (about 10 min.) and was then evaporated. The residue was diluted with ether, and the ether solution was washed with $NaHCO_3$, dried, and evaporated to give 53 mg. (73%) of **9**, m.p. 151–153°. Recrystallization from ether gave rods: m.p. 153–155°; λ^{KBr} 5.53, 5.75, 5.87 μ.

Anal. Calcd. for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.54; H, 6.19; N, 9.56.

B. From 5.—A solution of 95 mg. of the Δ^2-bicyclic ketone **5** (noncrystalline) in 1 ml. of acetic anhydride containing 0.1 ml. of pyridine was allowed to stand 15 hr. at 25° and was then concentrated *in vacuo*. After dilution of the residual syrup with a few milliliters of ether, chilling produced 54 mg. of crystalline **9**, m.p. and m.m.p. 151–152°.

2-Acetyl-3-methoxy-5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-heptan-6-one (11). A. From 6.—To a solution of 955 mg. of the pyrazolidine **6** in 15 ml. of methanol was added 8 ml. of methanol containing 0.5 ml. of concentrated H_2SO_4. After gas evolution had ceased, the solution was neutralized with $NaHCO_3$ solution and diluted with water until crystallization began. The tan crystals, 485 mg. (61%), m.p. 155–157°, were recrystallized from ether to give 269 mg. of colorless prisms: m.p. 157–158°; λ^{KBr} 5.53, 6.04 μ.

Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.67; H, 6.61; N, 10.21. Found: C, 65.40; H, 6.73; N, 10.16.

B. From 9.—A solution of 150 mg. of the acetoxybicyclic ketone **9** in 10 ml. of methanol was refluxed for 1 hr. and then concentrated; a strong smell of acetic acid was noticeable. The crystalline residue was triturated with ether to give 119 mg. (87%) of colorless crystals, m.p. 152–154°, m.m.p. (with material from A) 152–155°, m.m.p. (with starting material **9**) 136–148°.

2-Acetyl-3-hydroxy-5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-heptan-6-one (10). A. From 9.—A suspension of 119 mg. of the acetoxybicyclic ketone **9** in 2 ml. of 25% H_2SO_4 was warmed on the steam bath until a clear solution was obtained. After neutralizing the cooled solution with $NaHCO_3$, the white precipitate was collected and washed thoroughly with water to give 59 mg. (58%) of **10**, m.p. 172–173°. The compound was recrystallized from acetone–ether to give colorless needles, m.p. 174–175°.

Anal. Calcd. for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.46; H, 6.33; N, 10.68.

B. From 8.—A solution of 501 mg. of the hydroxydiazoketone **8** in 10 ml. of glacial acetic acid at 23° liberated 43 ml. of gas (collected over water) in 12 min. Evaporation of the acetic acid and addition of water gave colorless crystals, 416 mg. (91%), m.p. 160–162° dec. The infrared spectrum was identical with that of a sample from method A. The melting point of 172–175° mentioned for the analytical sample was not observed in later experiments. The melting point depends strongly on the rate of heating and is probably purely a decomposition. On scratching the dark melt at 160–170° crystallization occurs, with remelting at 180–200°. After holding a 40-mg. sample in a small test tube in a 160° bath for 30 sec., the melt was cooled and triturated with acetone to give 21 mg. of tan crystals, m.p. 206–

(26) Melting points were determined on a Fisher-Johns apparatus or a Kofler hot stage with calibrated thermometers. Infrared spectra were determined on a Baird Associates Model B spectrophotometer in KBr pellets. Ether or methylene chloride extracts were dried with sodium or magnesium sulfate prior to evaporation. Unless otherwise specified, solutions were evaporated at a water aspirator. Thin layer chromatograms were run with silica gel G plates, developed with chloroform–methanol (23:2 or 4:1), and visualized with iodine vapor.

(27) This preparation and the crystallization of **5** were first carried out by Dr. John Eby.

TABLE II

RELATIVE RATES OF ISOMERIZATION OF BICYCLIC KETONE 5 TO DIAZEPINONE 14

Solution[a]	pH	Absorbance at 400 mμ 0.6 hr.	1.5 hr.	3 hr.	10 hr.	16 hr.
H_2O	5.3	0.012	0.017	0.026	0.080	0.115
0.001 *N* KOH	10.1	1.30	1.52	1.74	>2.0	
0.1 *M* AcOH	3.5	0.036	0.052	0.082	0.25	0.38
1.0 *M* AcOH	2.9	0.102	0.155	0.26	0.72	1.04
0.0001 *N* HCl	4.3	0.020	0.025	0.032	0.105	0.16
0.001 *N* HCl	3.0	0.040	0.050	0.080	0.24	0.36
0.01 *N* HCl	2.4	0.058	0.078	0.13	0.36	0.54
1 *N* HCl	...	0.04	0.06	0.11	0.27	0.37[b]
6 *N* HCl	...			0.012[c]		0.015[d]

[a] In 50% methanol. [b] A_{290} 0.9. [c] A_{290} 0.49. [d] A_{290} 1.82 (equivalent to 30% conversion to pyridine).

208°. Recrystallization from methanol–ether gave prisms of the 1-acetamidopyridine **22a** (R = $COCH_3$), identical (mixture melting point and infrared spectrum) with material described below.

Acetylation of **10** in the usual way gave **9**, m.p. 148°, in 83% yield; warming in methanolic sulfuric acid gave **11**, m.p. 156–157°, in 56% yield.

Semicarbazone of 2-Acetyl-3-methoxy-5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]heptan-6-one.—A solution of 180 mg. of the methoxy ketone **11**, 110 mg. of semicarbazide hydrochloride, 110 mg. of NaOAc·$3H_2O$, and 0.1 ml. of pyridine in 10 ml. of methanol was refluxed for 4.5 hr. and then was evaporated until NaCl began to separate. On addition of 5 ml. of water a crystalline precipitate separated which was collected, dried, and recrystallized from methanol–ether (1:10) to give 109 mg. of feathery needles, m.p. 201–202°.

Anal. Calcd. for $C_{16}H_{21}N_5O_3$: C, 57.99; H, 6.39; N, 21.14. Found: C, 58.08; H, 6.39; N, 20.29.

The **oxime** was also prepared in the usual way, m.p. 220–222°.

Anal. Calcd. for $C_{15}H_{19}N_3O_3$: C, 62.26; H, 6.62; N, 14.52. Found: C, 62.40; H, 7.05; N, 14.63.

2-Acetyl-5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-3-hepten-6-one (**12**). **A. From 14.**—A solution of 2.0 g. (0.01 mole) of the diazepinone **14** in 30 ml. of methylene chloride containing 2.5 ml. of dimethylaniline at 25° was treated dropwise with a solution of 1.0 ml. (0.014 mole) of acetyl chloride in 8 ml. of ether. The mixture was stirred for 20 min. and then poured into a mixture of 2 ml. of concentrated HCl and 30 g. of ice. The methylene chloride layer was washed with water and $NaHCO_3$, evaporated *in vacuo*, and diluted with ether. After chilling, three crops of colorless crystals were collected; a total of 1.58 g. (65%) of **12** was obtained, m.p. 112–114°. Recrystallization from ether gave colorless prisms: m.p. 114°; λ^{KBr} 5.58, 6.05 μ; λ_{max}^{EtOH} 317 mμ.

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.40; H, 5.76; N, 11.82.

B. From 5.—To a solution of 105 mg. of the Δ^2-bicyclic ketone **5** (crystalline) in 3 ml. of methylene chloride was added 0.2 ml. of pyridine and 0.8 ml. of 1.1 *M* acetyl chloride in methylene chloride. A white precipitate separated and then redissolved. After 20 min. the solution was diluted with ether, washed with water, dried, and evaporated to a yellow oil. Crystallization gave 60 mg. of colorless prisms, m.p. 106–108°; recrystallization gave material with m.p. 109–110°. The crystalline residue from the mother liquor showed on t.l.c. a minor spot with the same R_f value as the hydroxy ketone **10**, but this was not positively identified.

2-Benzoyl-5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-3-hepten-6-one (**13**). **A. Using Pyridine.**—A solution of 10.0 g. (0.05 mole) of the diazepinone **14** in 66 ml. of pyridine at 25° was treated with 10.1 ml. of benzoyl chloride in one portion. The temperature rose to 45° and was maintained at 40–45° for 5 min. Ice was then added to the resulting slush to hydrolyze the unreacted benzoyl chloride, and, after shaking for a few minutes, the turbid solution was poured into a mixture of 300 ml. of ether, 100 ml. of methylene chloride, 70 ml. of concentrated HCl, and 100 g. of ice. The organic layer was washed several times with water until neutral, dried, concentrated to 50-ml. volume, and diluted with ether. The first crop of nearly white crystals of **13**, 8.70 g., had m.p. 116–121°; when placed on a preheated block a double melting point of 112–114°, 122–124° was observed. A second crop (3.30 g.) of mixed yellow and white crystals was recrystallized to give 1.3 g. of white **13**; total was 10.0 g. (65%). Further crops of crystals and the material from the recrystallization mother liquors were combined and recrystallized to give 1.30 g. (8%) of the yellow 2-benzoyldiazepinone,[20] m.p. 147–148°. All remaining mixed crystals were combined and treated with 0.9 ml. of benzoyl chloride in 10 ml. of pyridine at 90° for 40 min. Addition of ice gave 1.34 g. of the 2-benzoyldiazepinone **16** (R = C_6H_5), m.p. 146–147°; total yield was 2.65 g. (19%).

The bicyclic ketone **13** could be recrystallized from mixtures of methylene chloride and ether. Brief warming in alcohol solutions or benzene leads to contamination with rearrangement products. The double m.p. 110–114°, 122–124° was characteristic of the lustrous crystals obtained by relatively slow recrystallization from ether; smaller opaque crystals had a melting point as high as 126–127°. In about 60 preparations numerous intermediate melting points have been observed; λ^{KBr} 5.56, 6.13 μ; λ_{max}^{EtOH} 225 mμ (ε 14,000), 265 (8800), 305 (infl.), 331 (16,600).

Anal. Calcd. for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.21. Found: C, 75.07; H, 5.33; N, 9.15.

B. Using Dimethylaniline.—To a solution of 10 g. (0.05 mole) of **14** in 25 ml. of dimethylaniline and 200 ml. of methylene chloride at 26° was added 6.0 ml. (0.052 mole) of benzoyl chloride. There was only a slight temperature rise. The solution was allowed to stand at room temperature for 2 hr. and was then poured into a mixture of 38 ml. of 6 *N* HCl and 50 g. of ice. After thorough washing with $NaHCO_3$ and water, the amber methylene chloride solution was evaporated, diluted with ether, and chilled to give 11.6 g. of snow white needles of **13**, m.p. 122–125°; a further crop of 2.1 g., m.p. 121–125°, was obtained from the mother liquor; total yield was 13.7 g. (90%).

Conversion of Bicyclic Ketones to Diazepinone 14. A.—A solution of 42 mg. of the acetoxy ketone **9** in 2 ml. of glacial acetic acid was heated on the steam bath for 45 min. and then evaporated. Crystallization of the orange syrup from ether gave 8 mg. (24%) of orange crystals of **14**, m.p. and m.m.p. 149–150°.

B.—A solution of 150 mg. of the Δ^3-benzoyl ketone **13** in 5 ml. of glacial acetic acid was heated for 25 min. at 80° and then evaporated. The syrup was extracted with ether, and the ether solution was washed with $NaHCO_3$, dried, and evaporated to give 75 mg. (75%) of **14**, m.p. 150–151°. Acidification of the bicarbonate solution gave 25 mg. of benzoic acid.

Conversion of Semicarbazone of 11 to the Diazepinone Semicarbazone.—A solution of 38 mg. of the methoxy bicyclic semicarbazone in 0.4 ml. of glacial acetic acid was boiled for 1 min. The resulting yellow solution was evaporated to a syrup and methanol was twice added and removed by distillation. The orange syrup crystallized on seeding with an authentic sample of the diazepinone semicarbazone.[22] Two recrystallizations from methanol gave 6 mg. of yellow crystals. The melting point was indistinct, *ca.* 190–200°, not depressed on admixture with the authentic diazepinone semicarbazone (m.p. 194–196°). The infrared spectrum was not sharp but corresponded to that of the authentic sample in all peaks.

Rate of Isomerization of Δ^2-Bicyclic Ketone. A. In Glacial Acetic Acid.[28]—A solution of 2.0 mg. of the bicyclic ketone **5** in 50.0 ml. of acetic acid was kept in a 20° bath, samples were removed at intervals, and the absorbance at 400 mμ was recorded with a Zeiss spectrophotometer using quartz cells and a tungsten lamp. A value of ϵ_{400} of 2670 for pure **14** was determined and used to calculate K from the equation, $K = (2.303/t)[\log (A_\infty - A_0)/(A_\infty - A)]$. An average value of K from ten readings over a 20-hr. period was $(10.3 \pm 1.2) \times 10^{-4}$ l. mole/sec. The same

(28) We thank Dr. William Theuer for carrying out these measurements.

procedure was used for a solution of **2** in acetic acid 0.43 *M* in sodium acetate; the value of *K* was $(15 \pm 2) \times 10^{-4}$ l. mole/sec.

B. Relative Rates in Other Solutions.—Aliquots of 2 ml. of a solution of 8.7 mg. of **5** in 25 ml. of methanol were diluted with 2-ml. volumes of aqueous KOH, HCl, and acetic acid in the appropriate concentrations to give the solutions listed in Table II. The solutions were placed in a 35 ± 1° bath and absorbance at 400 mμ was measured with a Cary Model 14 spectrophotometer. In 1 *N* and 6 *N* HCl solutions, absorbance at 290 mμ owing to 1-aminopyridinium ion (**22**) was also measured. In 1 *N* HCl solution a maximum at 310 mμ owing to diazepinone also contributes to the absorbance at 290 mμ, but in 6 *N* HCl the 290-mμ peak is due entirely to **22**.

1-Benzoyl-7-methoxy-5-methyl-6-phenyl-1,2,3,7-tetrahydro-4H-1,2-diazepin-4-one (15).—A solution of 6.81 g. of the benzoyl bicyclic ketone **13** in 150 ml. of methanol containing 0.7 g. of benzoic acid was refluxed for 2.5 hr. and then concentrated. On cooling, 4.41 g. of colorless plates of **15**, m.p. 128–131°, separated. Further evaporation, extraction with methylene chloride, etc., gave an additional 1.4 g., m.p. 128–131°; total was 5.8 g. (76%). Recrystallization from ether gave plates, m.p. 133–134° (for spectra, see ref. 19a).

Anal. Calcd. for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33; OCH_3, 9.44. Found: C, 71.30; H, 5.99; N, 8.31; OCH_3, 9.23.

The preparation of **15** from the dihydrodiazepinone **14** was effected by adding 0.1 ml. of benzoyl chloride to a methanol solution of 103 mg. of **14** containing 0.2 ml. of dimethylaniline. After standing at 25° for 5 min., the solution was evaporated, the residue was dissolved in ether, and the ether solution was washed with HCl and $NaHCO_3$, dried, and evaporated finally at 0.1 mm. to remove most of the methyl benzoate. The resulting oil was crystallized from ether, giving 29 mg. of the methoxybenzoyldiazepinone **15**, m.p. 128–130°, infrared spectrum identical with material prepared from **13**.

1-Acetyl-7-methoxy-5-methyl-6-phenyl-1,2,3,7-tetrahydro-4H-1,2-diazepin-4-one.—After heating a solution of 790 mg. of **12** and 80 mg. of benzoic acid in methanol for 1 hr., 628 mg. of the acetylmethoxydiazepinone was isolated in the usual way. After crystallization from ether, it had m.p. 116–118°, λ_{max}^{EtOH} 263 mμ (ε 9500).

Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.67; H, 6.61; N, 10.21. Found: C, 65.95; H, 6.36; N, 10.23.

A solution of 72 mg. of this acetylmethoxytetrahydrodiazepinone in 2 ml. of acetic acid was heated for 15 min. on the steam bath. The orange residue remaining after evaporation of the acetic acid was crystallized from ether to give 42 mg. (68%) of the diazepinone **14**, m.p. and m.m.p. 150–151°.

1-Benzamido-3-hydroxy-4-methyl-5-phenylpyridinium Chloride (22b) from 13.—To a suspension of 455 mg. of the benzoyl bicyclic ketone **13** in 5 ml. of methanol was added 2 ml. of concentrated HCl. The mixture became warm and the solid dissolved to give a clear yellow solution. After 30 sec. water was added and a crystalline precipitate separated which was washed with water to give 446 mg. (87%) of dense white plates of the hydrochloride, m.p. 218–222°. Recrystallization from methanol gave heavy prisms: m.p. 217–224°; λ_{max}^{EtOH} 232 mμ (ε 30,000), 301 (10,200); $\lambda_{max}^{EtOH+NaOH}$ 230 mμ (ε 30,000), 333 (8600); $pK_A' = 3.4$, 6.4.[25]

Anal. Calcd. for $C_{19}H_{17}ClN_2O_2$: C, 66.95; H, 5.03; N, 8.22. Found: C, 67.21; H, 5.16; N, 8.30.

The free **1-benzamido-3-hydroxy-4-methyl-5-phenylpyridinium betaine** was obtained by crystallization of the hydrochloride from anhydrous pyridine or by treatment of a methanol solution with 1 equiv. of sodium methoxide. The betaine separated from aqueous solutions as an amorphous solid; crystallization from pyridine gave well-formed crystals, m.p. 181–182°.

Anal. Calcd. for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.21. Found: C, 75.20; H, 5.44; N, 9.04.

A comparison sample was prepared by treatment of 290 mg. of the 1-aminopyridinium chloride[22] in pyridine solution with benzoyl chloride; the base was isolated in 30% yield, m.p. and m.m.p. 181–182°.

1-Benzamido-3-methoxy-4-methyl-5-phenylpyridinium Picrate.—A solution of 100 mg. of the benzamidohydroxybetaine in methanol was treated with excess diazomethane, the solution was then evaporated, and the syrup was treated with alcoholic picric acid. The resulting picrate was recrystallized from ethanol to give 190 mg. of yellow needles, m.p. 192–194°.

Anal. Calcd. for $C_{26}H_{21}N_5O_9$: C, 57.04; H, 3.87; N, 12.79. Found: C, 57.07; H, 3.59; N, 12.90.

1-Acetamido-3-hydroxy-4-methyl-5-phenylpyridinium Betaine (22a).—A solution of 100 mg. of the acetoxy bicyclic ketone **12** in 0.5 ml. of methanol was treated with 0.5 ml. of concentrated HCl; after 10 min. the solution was neutralized with base and extracted with chloroform. Evaporation of the chloroform gave 30 mg. (30%) of the betaine as colorless plates, double m.p. 130°, 214°,[29] m.m.p. (with previously characterized sample[26]) 213–214°.

The low yield of pyridine in this experiment is not significant; the method of isolation presumably led to large losses. This pyridinium betaine was isolated directly from the reaction of the diazepinone **14** with acetyl chloride in 50% yield in one case when an insufficient amount of tertiary amine was used.

1-Benzamidopyridine 22b from 1-Benzoyl-7-methoxytetrahydrodiazepinone 15.—To a solution of 15 mg. of the diazepinone **15** in 1 ml. of methanol was added 4 drops of concentrated HCl. The solution was warmed briefly and then evaporated to an oil which crystallized from methanol to give 12 mg. of thick prisms of the hydrochloride **22b**, m.p. 215–222°. Crystallization from pyridine gave 5 mg. of the free betaine, m.p. 181–182°, no depression on mixture melting point with sample prepared from **13**.

2-*p*-Bromobenzoyl-5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-3-hepten-6-one.—A solution of 600 mg. of the diazepinone **14** in 4 ml. of pyridine was treated with 880 mg. (4 molar equiv.) of *p*-bromobenzoyl chloride (m.p. 38°). The solution became warm and a heavy crystalline precipitate separated. After warming at 40° for 5 min., ice was added and the mixture was then poured onto a mixture of iced HCl and methylene chloride. Evaporation of the methylene chloride solution gave 700 mg. of pale yellow solid, m.p. 100–110°, 128–130°. From the mother liquor a small amount of yellow material, m.p. 134–135°, was obtained. This was presumably the 2-*p*-bromobenzoyldiazepinone; it was not further characterized.

After recrystallization from methylene chloride the first-crop material was colorless but appeared to be contaminated with *p*-bromobenzoic anhydride. A sample was dissolved in pyridine, water was added until turbidity appeared, and the solution was warmed briefly, further diluted with water, and chilled to give colorless flat prisms, m.p. 133–134°.

Anal. Calcd. for $C_{19}H_{15}BrN_2O_2$: C, 59.94; H, 3.95. Found: C, 59.76; H, 3.81.

Reaction of *p*-Bromobenzoyl Bicyclic Ketone with Benzoyl Chloride.—The above bicyclic ketone (190 mg.) and 0.23 ml. of benzoyl chloride were dissolved in 2 ml. of pyridine and heated for 10 min. at 90°. The dark red solution was cooled, treated with water, and then extracted with ether. The ether solution was washed with HCl and water and then concentrated to give colorless crystals of *p*-bromobenzoic acid, m.p. >240° (subl.). Further concentration of the ether solution gave a red syrup which crystallized partially on standing. The yellow crystals, 11 mg., were recrystallized to give the 2-benzoyldiazepinone **20** (R′ = C_6H_5), m.p. and m.m.p. (with an authentic sample) 147–148°.

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(29) This double melting point was never observed in earlier preparations of this derivative by acetylation of the free aminopyridinium betaine.