a retention time of 7 min compared with 4.2 min for 2-methyl-4-phenoxyquinazoline.

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.42; H, 5.24; N, 11.73.

4-Phenoxyquinazoline (15).—This compound was prepared in the same manner as **2a** from 8.00 g of 4-chloroquinazoline.[38] Recrystallizations from cyclohexane–*n*-hexane and aqueous ethanol gave 7.74 g (71%) of 4-phenoxyquinazoline: mp 72.5–74° (lit.[44] mp 78–79°); λ_{max} 310, 299, 263, and 219 mμ (ε 4160, 4000, 5850, and 48,700); $\nu_{max}^{CCl_4}$ 1625 (s), 1385 (s), and 1220 cm^{-1} (broad, m) not found in **17**. The nmr signal at $\delta_{TMS}^{CDCl_3}$ 8.82 (2 H) was absent in the spectrum of the rearranged product.

Anal. Calcd for $C_{14}H_{10}N_2O$: C, 76.65; H, 4.53; N, 12.61. Found: C, 75.82; H, 4.62; N, 12.73.

3-Phenyl-4(3*H*)-quinazolinone (17).—A solution of 2.00 g of 4-phenoxyquinazoline in 4 ml of heavy mineral oil was heated under nitrogen at 321 ± 3° for 5 hr. A combination of recrystallizations and chromatography (Florisil) yielded 1.18 g (59%) of **17** as white needles, mp 137–137.5° (lit.[45] mp 136–136.5°), undepressed on mixture with, and comparable in spectral and physical properties to, purchased quinazolinone (Aldrich Chemical Co.), and 0.21 g of recovered starting material. The ultraviolet spectrum of **17** has λ_{max} 303, 277, 267, and 225 mμ (ε 3740, 7820, 8500, and 35,200); the infrared spectrum has $\nu_{max}^{CCl_4}$ 1698 (s), 1615 (s) and 1300 cm^{-1} (m) not found in 4-phenoxyquinazoline. In glpc on a 6-ft SE-30 column at 250°, **17** had a retention time of 6 min compared with 4.1 min for 4-phenoxyquinazoline.

Anal. Calcd for $C_{14}H_{10}N_2O$: C, 75.65; H, 4.53; N, 12.61. Found: C, 75.76; H, 4.52; N, 12.74.

Relative Rearrangement Rates of 2a, 14, and 15.—In order to avoid differences in reaction temperature owing to the volatility of **14** and **15**, the rearrangements were run in sealed evacuated ampoules. Three 100-mg portions of each aryl ether were sealed in 6-mm tubing at 10–15-mm nitrogen pressure. The tubes were bundled in groups of three and immersed in a silicone oil bath maintained at 308 ± 3°.

(44) J. S. Morley and J. C. E. Simpson, *J. Chem. Soc.*, 1354 (1949).
(45) R. H. Clark and E. C. Wagner, *J. Org. Chem.*, **9**, 55 (1944).

A. Compound 2a and 3a.—At 257 mμ, **2a** has an E_1^1 of 1155 and **3a** an E_1^1 of 298. The following calculated values (E_1^1 minus 298) at 257 mμ for various times were obtained: 0 time, 857; 55 min, 699; 130 min, 508; and 255 min, 324. From these values the half-time at 308° was determined to be 175 min. A duplicate determination at 309 ± 2° gave a half-time of 185 min.

B. Compound 14 to 16.—A rate study at 308 ± 3° gave the following values for the percentage of **14** as determined by glpc: 55 min, 68.5%; 130 min, 50.4%; and 255 min, 36%. In a duplicate determination at 309 ± 2° the following values were obtained: 5 min, 94%; 50 min, 71%; 110 min, 56%; 175 min, 44%; and 225 min, 40%. If a first-order reaction is assumed, the values for the first 50 min correspond to a half-time of 105 min, and the values at 175 min and 225 min to a half-time of 360 min. The apparent deviation from first-order kinetics may be due to loss of **16** to a nonvolatile by-product.

C. Compound 15 to 17.—Gas–liquid phase chromatography gave the following values for the percentage of **15**: 55 min, 88%; 130 min, 77%; 255 min, 58%. These values correspond to a reaction with a half-time of 325 min or about 0.5 times the rate for the conversion of **2a** to **3a**.

Registry No.—**2a,** 18600-27-6; **2b,** 34281-52-2; **2c,** 34281-53-3; **2d,** 18600-28-7; **3b,** 34280-97-2; **3c,** 34280-98-3; **3d,** 34280-99-4; **6,** 1022-46-4; **8c,** 34297-91-1; **14,** 34297-92-2; **15,** 16347-97-0; **16,** 2385-23-1; **17,** 16347-60-7; 2,4-dichloroaniline HCl, 29084-76-2; 2,3,6-trimethylaniline HCl, 34297-93-3; 2,3,6-trimethylaniline *p*-toluenesulfonamide, 34297-94-4.

Acknowledgment.—The authors wish to thank Mr. C. E. Childs and his staff of our Microanalytical Department for elemental analyses and glpc work, Dr. J. M. Vandenbelt and his staff of our Physical Chemistry Department for the spectral data, and Messrs. H. D. Troutman and N. Jenesel for the synthesis of intermediates.

α-Azocarbinols. The Synthesis and Some Reactions of 3-Hydroxypyrazolines[1]

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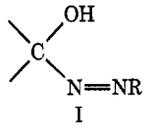
Received December 1, 1971

3-Hydroxy-1-pyrazolines, cyclic examples of α-azocarbinols, have been synthesized by hydrolysis or hydrogenolysis of 3-acetoxy-1-pyrazolines. These carbinols undergo both acid- and base-catalyzed ring opening to give ketones. The acid reactions produce both saturated and unsaturated ketones while the base reactions yield only saturated ketones but principally those of rearranged carbon skeleton. The carbinols may be esterified and etherified under closely controlled conditions.

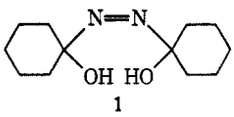
The geminal juxtaposition of an azo linkage and a hydroxyl group (I) produces a chemical structure whose



I

properties will depend upon the interplay of competing factors. Thus α-azocarbinols might resemble cyanohydrins in that they are adducts of carbonyl compounds and diazenes. From this point of view they would be expected to be unstable in basic solution and to avoid carbonium ion intermediate reactions. On the other hand, they might be viewed as diaza allylic alcohols and thus to show unusual reactivity toward electrophilic reagents.

Little is known about these compounds because it is only recently that some have been reported. The first example, 1,1′-dihydroxyazocyclohexane (**1**), was reported in 1963.[2] This compound was relatively un-



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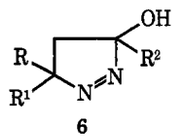
stable, reverting to cyclohexanone with loss of diimide.

Recently, Hünig has generated α-azocarbinols by two methods: the action of base on alkoxydiazenium

(1) This research was supported by grants from the Petroleum Research Fund and the National Science Foundation.

(2) E. Schmitz, R. Ohme, and E. Schramm, *Justus Liebigs Ann. Chem.*, **702**, 131 (1967).

TABLE I
3-HYDROXY-1-PYRAZOLINES



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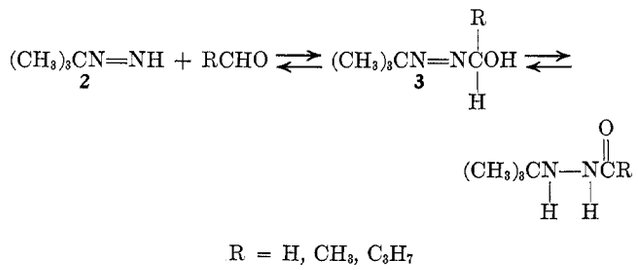
Compd[d]	R	R¹	R²	Bp (mp), °C (mm)	Yield, % Hyd	Yield, % $NaBH_4$	3,5-DNB[c] mp, °C
6a	CH_3	CH_3	CH_3	62–63 (0.5)	80.6	85.8	162–163
6b	CH_3	C_2H_5	C_2H_5	71–73 (0.25)	56.6	71.7	176–177
6c	$-CH_2(CH_2)_3CH_2-$		CH_3	*a*	55.0		206–208
6d	CH_3	CH_3	$CH{=}C(CH_3)_2$	*a*	4.6		
6e	CH_3	CH_3	C_6H_5	(95–98)[b]	84.0		
6f	CH_3	CH_3	H	*a*	64.3	56.3	

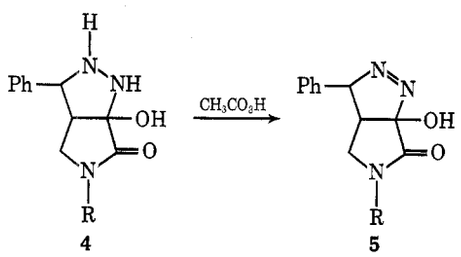
[a] Purified by column chromatography rather than distillation. [b] Recrystallized from hexane. [c] 3,5-Dinitrobenzoate ester. [d] Satisfactory analyses (±0.4% in C, H, and N) for 6a–f were reported with the following exceptions: 6a, calcd for N, 21.86, found for N, 20.94; 6b, calcd for C, 61.51, found for C, 60.54, and calcd for N, 17.93, found for N, 16.60; nitrobenzoates of 6a, calcd for C, 48.45, found for C, 49.79; 6b, calcd for C, 51.43, found for C, 52.11, and calcd for N, 15.99, found for N, 14.94; 6c, calcd for N, 15.46; found for N, 14.64.

salts,[3] and, more generally, the addition of diazenes to carbonyl compounds.[4] For example, addition of *tert*-butyldiazene (2)[4] to aliphatic aldehydes in aqueous solution reversibly yielded the corresponding α-hydroxyazo compounds **3**. These compounds could be distilled, but they slowly rearranged to the isomeric hydrazides.



R = H, CH_3, C_3H_7

A somewhat more complicated example was reported[5] recently wherein the oxidation of the α-hydroxyhydrazines **4** yielded the azocarbinols **5**.

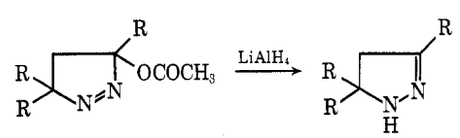


4 5

Because of the isolated structures which have so far been generated, it is not surprising that no consistent pattern of reactivity for these compounds is yet apparent. The Schmitz compound **1** was very unstable even undergoing attack by air. Hünig's compounds (**3**) behaved to some extent as unstable carbonyl adducts while the Southwick compound **5** gave typical pyrazoline reactions: thermal decomposition to cyclopropanols and acid-catalyzed dehydration to pyrazoles.

The oxidation of 2-pyrazolines with lead tetraacetate made available a wide variety of 3-acetoxy-1-pyrazolines.[6] Early attempts to convert these esters to the corresponding 3-hydroxypyrazolines were complicated by the competing acid- or base-catalyzed decomposition of these compounds to ketones.[7] Recently, we reported that this hydrolysis could be controlled to yield 3-hydroxypyrazolines,[8] compounds which contain functional group I. It is the purpose of this paper to detail the synthesis of these compounds, their acid- and base-catalyzed reactions, and their utility in organic synthesis.

Preparation (Table I).—Two methods of converting 3-acetoxypyrazolines to 3-hydroxypyrazolines were employed: hydrolysis with aqueous methanolic alkali at room temperature, and hydrogenolysis with sodium borohydride in methanol. Interestingly, lithium aluminum hydride, the more conventional hydrogenolysis reagent, could not be used because it reduced the acetoxypyrazolines to the original 2-pyrazoline.



Acetoxypyrazolines with a hydrogen atom at position 5 could not be converted to the corresponding hydroxypyrazolines because they aromatized to pyrazoles upon treatment with bases or sodium borohydride and underwent ring opening to ketones with acids. The hydroxypyrazolines were characterized by infrared spectra containing bands attributable to the hydroxyl group and the azo function (1555–1563 cm^{-1}). They could be stored for long periods of time in the refrigerator in the dark, but gradually decomposed upon storage under ordinary laboratory conditions. Apparently glass surfaces can catalyze some of the decomposition reactions discussed below since satisfactory analyses were difficult to obtain in a few cases.

Reactions. Acid Catalysis.—Attempts to dehydrate 3,5,5-trimethyl-3-hydroxypyrazoline (**6a**) using a variety of acidic catalysts failed to yield any of the known 3,5,5-trimethylpyrazolenine.[9] The carbinol also failed

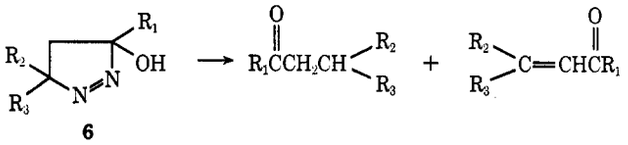
(3) S. Hünig and G. Büttner, *Chem. Ber.*, **104**, 1088 (1971).
(4) S. Hünig and G. Büttner, *ibid.*, **104**, 1104 (1971).
(5) P. L. Southwick, N. Latif, J. Klijanowicz, and J. G. O'Connor, *Tetrahedron Lett.*, 1767 (1970).
(6) J. P. Freeman, *J. Org. Chem.*, **29**, 1379 (1964).
(7) J. P. Freeman and J. L. Plonka, *J. Amer. Chem. Soc.*, **88**, 366 (1966).
(8) J. P. Freeman and C. P. Rathjen, *J. Chem. Soc. D*, 538 (1969).
(9) G. L. Closs, L. E. Closs, and W. Böll, *J. Amer. Chem. Soc.*, **85**, 3796 (1963).

to give a typical reaction with the Lucas reagent or with hydrobromic acid. On the basis of the products isolated under acidic conditions it is clear that carbonium ion formation from the tertiary carbinol does not compete effectively with ring-opening reactions.

The principal acid-catalyzed reaction was ring opening to produce ketones. In general, mixtures of saturated and unsaturated ketones were obtained with the former predominating. For example, pyrazoline **6a** yielded a mixture consisting of 93% methyl isobutyl ketone and 7% mesityl oxide (Table II).

TABLE II

ACID-CATALYZED RING OPENING



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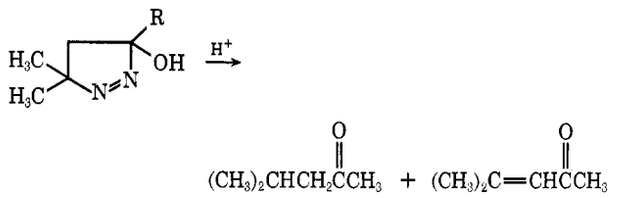
			Rel yield, %[a]	
			Satd	Unsatd
R_1	R_2	R_3	ketone	ketone
CH_3	CH_3	CH_3	93	7
C_2H_5	C_2H_5	CH_3	100	
CH_3	$-CH_2(CH_2)_2$	CH_2-	100	
$CH{=}C(CH_3)_2$	CH_3	CH_3	98	2
C_6H_5	CH_3	CH_3	95	5
H	CH_3	CH_3	100	

[a] Calculated on the basis of reacted starting material.



A scheme to account for these products is shown in Scheme I. It is not necessary that different products arise from protonation of alternative nitrogens, since it is possible that carbonium ions **7** and **8** could equilibrate, with ion **7**, the precursor of the major products, predominating because of its greater stability.

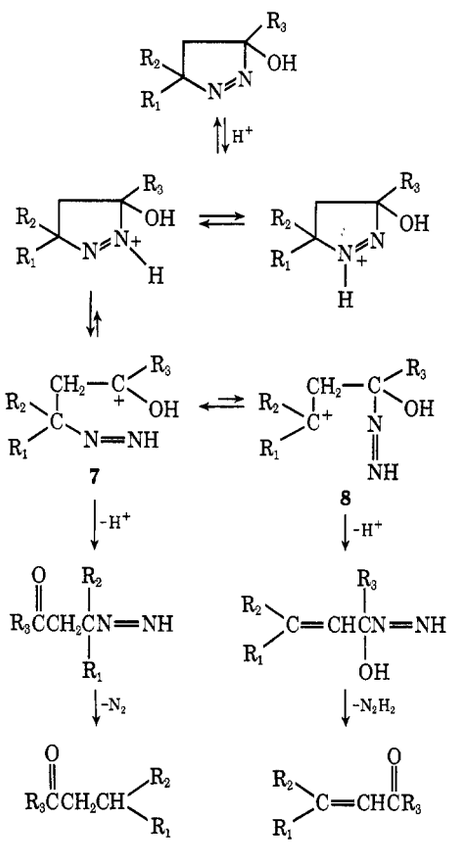
That diimide was in fact produced during these reactions was inferred from the detection of hydrazine, its disproportionation product, through azine formation with *p*-dimethylaminobenzaldehyde.[10]

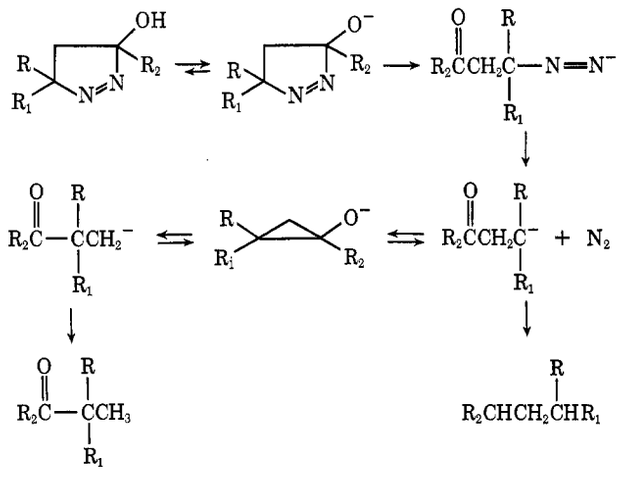
A remarkable feature of these reactions is that even under treatment with rather concentrated acids the pyrazolines survived for long periods. For example, up to 80% of **6a** could be recovered after a mixture of this carbinol and 50% methanolic HCl were heated under reflux for 1 hr. This is an extreme example, as the pyrazolines substituted at position 3 with groups other than methyl decomposed more rapidly, but it still indicates that this compound has a stability much greater than that exhibited by any other α-azocarbinol.

Base Catalysis. Cleavage.—Some years ago when the alkaline hydrolysis of 3-acetoxypyrazolines was first reported,[7] it was observed that ester hydrolysis was followed by ring opening to give a ketone of rearranged carbon skeleton. With the several carbinols now in hand this ring opening has been more closely examined. While the earlier results have been confirmed, it is clear that the intermediate alkoxide ions are far more stable to ring opening than had been realized. For example, compound **6a**, after it had been heated under reflux in methanol containing an equimolar amount of sodium hydroxide for 1 hr, was recovered to the extent of 94%. However, pyrazoline **6f** was much less stable and only 10% could be recovered under these conditions. In all cases rearranged ketones predominated in the mixtures obtained although the ratio varied with structure (Table III).

Although no new information on this point has been gathered, it still is believed that the structural rearrangement occurs after loss of nitrogen to produce cyclopropanoxide ions, which may open by alternative paths with the one giving the more stable carbanion favored.[7]

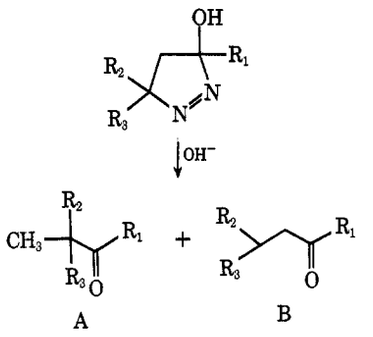
SCHEME I





(10) M. Pesez and A. Petit, *Bull. Soc. Chim. Fr.*, 122 (1947).

TABLE III
PRODUCTS OF ALKALINE DECOMPOSITION OF 3-HYDROXY-1-PYRAZOLINES[a]



Substituents	Yield, % Unreacted starting material	Carbonyl products A	Carbonyl products B
$R_1 = R_2 = R_3 = CH_3$	94.1	5.1	0.8
$R_1 = R_2 = CH_2CH_3$, $R_3 = CH_3$	71.4	12.6	6.0
$R_2, R_3 = c\text{-}C_5H_{10}$, $R_1 = CH_3$	17.6	34.2	27.1
$R_1 = CH{=}C(CH_3)_2$, $R_2 = R_3 = CH_3$	20.5	60.0	7.3
$R_1 = C_6H_5$, $R_2 = R_3 = CH_3$	59.5	20.3	16.7
$R_1 = H$, $R_2 = R_3 = CH_3$	10.2	60.0	19.6

[a] Conditions: approximately 0.05 mol of pyrazoline was heated under reflux for about 1–2 hr with an equimolar amount of methanolic NaOH.

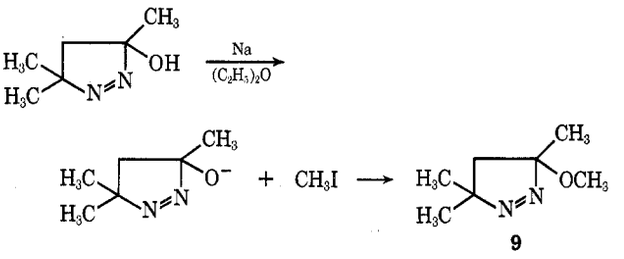
Ester and Ether Formation.—It proved to be possible to esterify the 3-hydroxypyrazolines using the Brewster technique[11] which employs the acid, benzenesulfonyl chloride, and pyridine. A wide variety of esterifications was not attempted but, merely to establish that the reaction was characteristic of these compounds, conversion to the corresponding 3,5-dinitrobenzoates was carried out. These solid esters were easy to isolate and purify. Pyrazoline **6a** could be reconverted in low yield to the parent acetate by treatment with acetic anhydride but this reaction failed with most of the other hydroxypyrazolines. Presumably steric hindrance to esterification allows other acid- or base-catalyzed reactions to compete.

Consistent with the previously described resistance of the hydroxypyrazolines to undergo acid-catalyzed reactions characteristic of tertiary alcohols, these 3,5-dinitrobenzoates failed to undergo solvolysis reactions. For example, they could all be recovered unchanged after heating under reflux in methanol. From the few experiments reported herein, we tentatively conclude that the azo linkage is deactivating with respect to carbonium ion formation, but this suggestion needs much experimental verification.

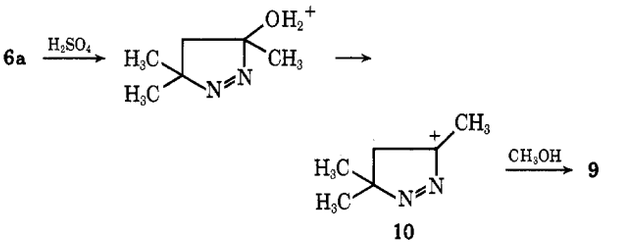
Ether formation was studied extensively with pyrazoline **6a**. While dimethyl sulfate and base could be used, the best procedure was to preform the sodium salt of the hydroxypyrazoline and treat it with methyl iodide.

It was also possible to prepare this ether by the classic acid-catalyzed method often used with tertiary

(11) J. H. Brewster and C. J. Ciotti, *J. Amer. Chem. Soc.*, **77**, 6214 (1955).



alcohols, that is, dissolution of the hydroxypyrazoline **6a** in concentrated sulfuric acid followed by mixing with methanol. Such a reaction may be interpreted as involving carbonium ion **10** and represents the only reaction where such an intermediate suggests itself. [A referee has suggested that this reaction may occur by interception of ion **7** (Scheme I) by methanol followed by loss of water and ring closure.]



As previously reported,[8] ether **9** could be converted to 1,2,2-trimethylcyclopropyl methyl ether by pyrolysis.[12]

Thermal Reactions.—While most of these hydroxypyrazolines could be stored at room temperature or below for relatively long periods with little decomposition and even distilled at low pressures in some cases, extended heating at high temperatures led to decomposition to ketonic products. Whether cyclopropanols were intermediates in these reactions was not determined, but it is known that these compounds are also converted to ketones thermally.[14]

Experimental Section

Preparation of 3-Acetoxy-Δ¹-pyrazolines.—The procedures previously described[8] were followed. Two previously unreported acetoxypyrazolines are described here. Both were rather unstable and could not be purified sufficiently for elemental analysis.

3-Acetoxy-3-methyl-5,5-pentamethylene-1-pyrazoline.—3-Methyl-5,5-pentamethylene-2-pyrazoline was prepared by the formic acid catalyzed cyclization of cyclohexanone acetone azine according to the method of Kost and Grandberg.[15] Acetoxylation according to the described procedure[6] yielded 3-acetoxy-3-methyl-5,5-pentamethylene-1-pyrazoline (51%): bp 32° (0.44 mm); ir (neat) 1745 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.78 (s, 3, $OCOCH_3$).

3-Acetoxy-3-isobutenyl-5,5-dimethyl-1-pyrazoline.—The 2-pyrazoline was synthesized from the reaction of hydrazine with phorone. Treatment of it with lead tetraacetate yielded the title compound: bp 89° (0.50 mm); ir (neat) 1737 (C=O), 1557 cm^{-1} (N=N); uv max (C_2H_5OH) 330 nm (ε 275); nmr ($CDCl_3$) δ 2.06 (s, 3, $OCOCH_3$).

(12) A recent report[13] of the conversion of hydrazones to α-azo ethers with iodine, methanol, and sodium acetate suggests a direct route from pyrazolines to ethers like **9**. A preliminary experiment to check the utility of this route may be found in the Experimental Section. Combined with the thermolysis reaction this reaction might provide a convenient route to cyclopropyl ethers.

(13) J. Schantl, *Tetrahedron Lett.*, 3785 (1970).

(14) C. H. Depuy, W. C. Arney, and D. H. Gibson, *J. Amer. Chem. Soc.*, **90**, 1830 (1968).

(15) A. N. Kost and I. I. Grandberg, *J. Gen. Chem. USSR*, **26**, 1925 (1956).

Preparation of 3-Hydroxypyrazolines (Table I). Hydrolysis Procedure.—A mixture of 10.0 g (0.059 mol) of 3-acetoxy-3,5,5-trimethylpyrazoline-1[6] and 30 ml of 5% methanolic sodium hydroxide was stirred at room temperature for 10 hr. It was diluted with water and carefully neutralized with 5% HCl. After extraction with ether, drying ($MgSO_4$), and concentration, distillation yielded 6.1 g (81%) of **3-hydroxy-3,5,5-trimethyl-1-pyrazoline**: ir (neat) 3378 (OH), 1560 cm^{-1} (N=N); nmr (neat) δ 1.32, 1.42, 1.58 (s, 3, CCH_3), 1.53 (m, 2, CH_2), 5.88 (s, 1, OH).

Hydrogenolysis Procedure.—A solution of 17.0 g (0.1 mol) of 3-acetoxy-3,5,5-trimethyl-1-pyrazoline in 100 ml of CH_3OH was added, dropwise and with stirring, to a solution of 37.85 g (1 mol) of sodium borohydride in 450 ml of CH_3OH. This mixture was heated under reflux for 1 hr, cooled, diluted with water, concentrated to half its volume, and extracted with five 50-ml portions of $CHCl_3$. The $CHCl_3$ extract was dried ($MgSO_4$), concentrated, and distilled to yield 11.0 g (86%) of 3-hydroxy-3,5,5-trimethyl-1-pyrazoline.

3-(3,5-Dinitrobenzoyloxy)-3,5,5-trimethyl-1-pyrazoline.—To a cold mixture of 1.65 g (0.0078 mol) of 3,5-dinitrobenzoic acid and 2.8 g (0.016 mol) of benzenesulfonyl chloride in 15 ml of pyridine was added 1.0 g (0.0078 mol) of 3-hydroxy-3,5,5-trimethylpyrazoline (**6a**). The mixture was stirred for 4 hr, poured into water, and filtered, and the residue was recrystallized from C_2H_5OH–C_6H_6 to give 0.7 g (28%) of the title compound, mp 162–163°.

3-Methoxy-3,5,5-trimethyl-1-pyrazoline. Procedure A.—An ether suspension of the sodium salt of **6a** was prepared by adding 12.3 g (0.096 mol) of **6a** to a suspension of 2.2 g of sodium in ether. This mixture was stirred at room temperature for several days to ensure complete reaction. Methyl iodide (28.4 g, 0.2 mol) was added dropwise and the mixture was heated under reflux for 24 hr. It was filtered, dried, and distilled to give 9.9 g (73%) of 3-methoxy-3,5,5-trimethylpyrazoline-1: bp 22° (0.25 mm); ir (neat) 1655 (N=N), 1201 cm^{-1} (COC); nmr ($CDCl_3$) δ 3.75 (s, 3, OCH_3), 1.40 (m, 2, CH_2), 1.46, 1.35, 1.27 (s, 3, CCH_3 groups).

Anal. Calcd for $C_7H_{14}N_2O$: C, 59.13; H, 9.92; N, 19.70. Found: C, 59.14; H, 9.95; N, 18.31.

Procedure B.—A 1.7-g (0.013 mol) sample of **6a** was slowly added to 1.1 ml of cold, concentrated H_2SO_4. This solution in turn was added immediately to 5 ml of cold methanol. This solution was stirred for 15 min, diluted with water, and extracted with ether. The ether extracts were dried and distilled to yield 0.98 g (54%) of the methyl ether.

Procedure C.—A solution of 11.2 g (0.1 mol) of 3,3,5-trimethylpyrazoline in 100 ml of CH_3OH was added over a 2-hr period to a solution of 25.4 g (0.1 mol) of iodine and 27.2 g (0.2 mol) of sodium acetate in 600 ml of CH_3OH. The mixture was stirred at 25° for 2 hr, concentrated *in vacuo*, diluted with ether, and washed with water, $NaHSO_3$ solution, and saturated NaCl solution. The dried ether extracts were distilled to yield 4 g (28%) of the methyl ether. Mesityl oxide and pinacolone were also present in the product mixture.

1,1,2-Trimethylcyclopropyl Methyl Ether.—3-Methoxy-3,5,5-trimethyl-1-pyrazoline (1.75 g, 0.012 mol) was heated under reflux (~200°) until N_2 evolution ceased (6 hr). The residue was distilled to yield 0.58 g (42.5%) of the title compound, identical in all respects with an authentic sample:[16] bp 48–50° (150 mm); nmr (neat) δ 3.16 (s, 3, OCH_3), 1.30, 1.13, 1.05 (s, 3, CCH_3), 0.23 (m, 2, CH_2).

Ring-Opening Reaction of Hydroxypyrazolines. Acid Catalyzed.—The general procedure was to mix methanol solutions of the hydroxypyrazoline and methanolic HCl at room temperature and then to stir the mixture for various times at various temperatures. After the reaction period the mixtures were diluted with water, washed with base, and extracted with ether. The ether extracts were dried and distilled to remove the solvent; the residue was then subjected to gas chromatographic analysis. Silicone columns operating between 50 and 100° proved to be adequate for resolving the ketones and starting material. In all cases the columns were calibrated using authentic samples (Table II).

Base Catalyzed.—The general procedure was the same except that methanolic NaOH was employed (Table III).

Registry No.—**6a**, 22883-54-1; **6a** 3,5-DNB, 34277-62-8; **6b**, 34277-63-9; **6b** 3,5-DNB, 34277-64-0; **6c**, 34277-81-1; **6c** 3,5-DNB, 34281-09-9; **6d**, 34281-10-2; **6e**, 34281-11-3; **6f**, 34281-12-4; 3-acetoxy-3-methyl-5,5-pentamethylene-1-pyrazoline, 34281-13-5; 3-acetoxy-3-isobutenyl-5,5-dimethyl-1-pyrazoline, 34281-14-6; 3-methoxy-3,5,5-trimethyl-1-pyrazoline, 23019-13-8.

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The Direct Alkylation of Pyridine 1-Oxides

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n-Butyllithium in inert nonprotic solvents abstracts a ring proton from the α position of pyridine 1-oxides to give a carbanion which can be trapped with aldehydes and ketones to give 2-(α-hydroxyalkyl)- and 2,6-di(α-hydroxyalkyl)pyridine 1-oxides. A chloro, ethoxyl, or methyl group at the 4 position is unaffected under these conditions, but a 2-methyl substituent undergoes proton abstraction morer eadily than does the C_6H. When a 3-methyl group is present it directs the entering hydroxyalkyl group to the 6 position, but 2,6-disubstituted derivatives are also formed. This orientation is discussed. The use of some bases other than butyllithium is described.

There are few methods available for the direct alkylation of pyridines and related systems, particularly since Friedel–Crafts alkylation is not possible with such π-deficient molecules. Other than high-temperature reactions, the most common modes of nuclear alkylation involve nucleophilic addition–eliminations with organometallic, and in particular organolithium, compounds and by the use of aldehydes and ketones in the Emmert reaction.[2a] More recently, the novel enamine-type alkylation of *N*-lithio-1,2-dihydropyridines has resulted in a useful route to 3-alkylpyridine derivatives.[2b] We now report a convenient method of effecting alkylations of pyridine 1-oxides which promises to have wide utility and to lead to compounds which would be otherwise tedious to prepare.[3]

Nuclear proton abstraction from substituted pyridines has only found sporadic application, this usually involving the formation of pyridyne intermediates.[4]

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