ing material. The mother liquor from this crystallization was chromatographed on a column of alumina (Woelm, non-alkaline, activity grade I) using benzene as the eluting solvent. Evaporation of the initial fractions yielded a brown oil, whilst the later fractions gave a white solid (0.608 g.), m.p. 181–183°. This solid was crystallized from ethanol yielding small colorless prisms of 1,1'-dimethyl-2,2'-diphenyl-3,3'-diindolylmethane, m.p. 185–186°.

Anal. Calcd. for $C_{31}H_{26}N_2$: C, 87.29; H, 6.14; N, 6.57. Found: C, 87.58; H, 6.32; N, 6.57.

3-Hydroxymethyl-1-methyl-2-phenylindole was recovered unchanged when it was refluxed a short time (2 hr.) with 10% sodium hydroxide solution. No reaction took place when it was refluxed with ethanol in the presence of sodium hydroxide.

Reactions of 2-Hydroxymethylindole.—This alcohol was obtained by the reduction of 2-carbethoxyindole with excess lithium aluminum hydride in ether.[19] It sublimed *in vacuo* (120°, 0.001 mm.) without decomposition, in contrast to the 3-hydroxymethylindole which split out formaldehyde on heating above its melting point. It was recovered unchanged after refluxing with water or 10% sodium hydroxide for 15 hr. No reaction occurred when it was refluxed with ethanol in the presence of sodium hydroxide. It was, however, decomposed by acids, yielding polymeric materials.

MINNEAPOLIS 14, MINN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELAWARE]

Heterocyclic Studies. III. A Ring Closure Reaction of Diazoacetylpyrazolines

BY JAMES A. MOORE AND ROBERT W. MEDEIROS

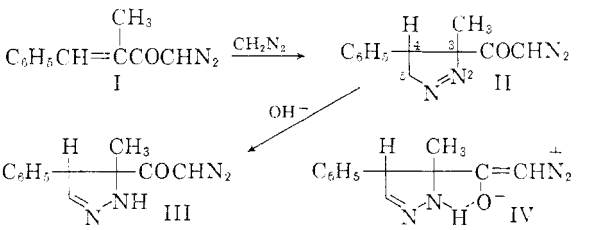
RECEIVED FEBRUARY 19, 1959

Isomerization of 3-diazoacetyl-3-methyl-4-phenyl-Δ^1-pyrazoline (II) occurs under very mild basic conditions, leading to the Δ^5-pyrazoline III. Further treatment with alkali furnishes 3-methyl-4-phenylpyrazole (V). Treatment of III with mild acid gives the diazobicyclo[3.2.0]heptenone (VII). Isomerization of VII with mild acid or alkali leads to the diazepinone XI.

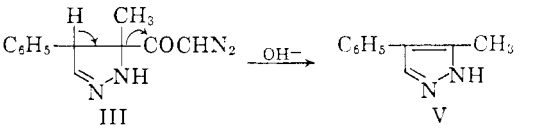
In the first communication of this series[1] it was reported that the reaction of 3-diazoacetyl-3-methyl-Δ^1-pyrazoline (II) with acetic acid furnishes a colored product having the composition $C_{12}H_{12}ON_2$ which was formulated as a diazepine derivative. In this and subsequent papers we wish to describe further studies on the formation, structure and reactions of this product.

The preparation of the pyrazoline II by addition of diazomethane to 1-diazo-3-methyl-4-phenyl-3-buten-2-one (I) was described in a previous paper.[2] The structure of II followed from the well-known method of preparation; the absence of absorption in the N–H region of the infrared spectrum confirmed the position of the double bond. In the course of a number of preparations of II a minor product isomeric with II occasionally has been isolated. This compound also was obtained readily by subjecting II to mild alkaline treatment. The infrared spectrum of the new compound showed strong bands at 2.9 (N–H), 4.68 (diazomethyl) and 6.20 μ (diazocarbonyl); the compound was thus clearly also a diazoacetylpyrazoline, and the presence of an N–H band indicated that it was the Δ^5-isomer III. It has been observed[3] previously that a Δ^1-pyrazoline such as II, in which isomerization to the conjugated Δ^2-structure is blocked by a substituent in the 3-position, can be isomerized to the Δ^5-structure. The ultraviolet spectrum of III was noteworthy in that the maximum was displaced from the usual[2] position of 270 to 254 mμ. This hypsochromic shift may be due to hydrogen bonding (IV) with consequent constraint of the diazocarbonyl chromophore.

More vigorous alkaline treatment of the Δ^5-pyrazoline furnished in 60% yield a compound having the composition $C_{10}H_{10}N_2$. This product was characterized as 3-methyl-4-phenylpyrazole (V)[4] by



oxidation to 4-phenylpyrazole-3-carboxylic acid and comparison with an authentic specimen. The formation of V by this facile base-catalyzed elimination provides a rigorous confirmation of the pyrazoline structures II and III.

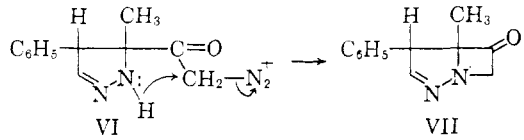


On warming in acetic acid, the Δ^5-pyrazoline III was converted to the same colored $C_{12}H_{12}ON_2$ product previously obtained by similar treatment of the Δ^1-pyrazoline.[1] In contrast to the latter reaction, however, nitrogen evolution occurred at room temperature, and the red color characteristic of the final product appeared only upon heating to 60–70°. When the solution was frozen after gas evolution had nearly stopped and the solvent evaporated at low temperature, a pale yellow oil was obtained. This material has not yet been crystallized, but analysis of a crystalline picrate indicated the composition $C_{12}H_{12}ON_2$. The infrared spectrum of the oil (Fig. 1) was very well resolved, and contained a prominent band at 5.58 μ, indicative of a small-membered-ring carbonyl group. The compound was converted in good yield by treatment with acids *or alkali*, to the above-mentioned isomeric colored product.

It is evident from these data that the reaction of the diazoacetylpyrazoline III with acetic acid involves ring closure. The most likely process is that

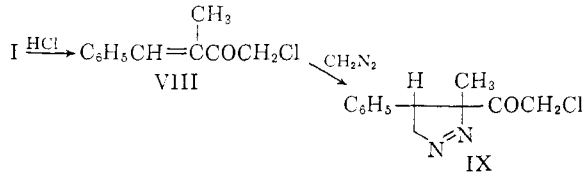
(1) J. A. Moore, THIS JOURNAL, **77**, 3417 (1955).
(2) J. A. Moore, *J. Org. Chem.*, **20**, 1607 (1955).
(3) K. von Auwers and U. König, *Ann.*, **496**, 27 (1932).
(4) W. E. Parham and J. L. Bleasdale, THIS JOURNAL, **72**, 3843 (1950).

indicated in VI, with formation of 5-methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-hepten-6-one (VII). This structure is supported by the infrared spectrum and, as discussed below, is the only one consistent with the observed isomerization. The analogous formation of a four-membered heterocyclic ketone by treatment of an α-hydroxydiazoketone with acetic acid has been described,[5] but a comparable ring closure to a nitrogen substituent has not previously been effected.[6]



VI VII

In an attempt to obtain the cyclization product VII by another path, the chloromethylpyrazoline IX was prepared by addition of diazomethane to the unsaturated chloroketone VIII. The product was assigned the Δ^1-structure on the basis of the infrared spectrum (6.40 μ band corresponding to —N=N—, rather than 6.2–6.3 μ band due to —C=N—; absence of absorption in the N—H region). The chloromethylpyrazoline was a highly unstable substance; purified crystalline material decomposed to a dark resin on storage at 0°, and no identifiable reaction products were obtained.



VIII IX

The product obtained by treating the diazoacetylpyrazolines II and III with warm acetic acid or the intermediate bicyclic ketone VII with very dilute mineral acid or alkali is an orange-colored, feebly acidic compound with absorption maxima of, respectively, decreasing intensities at 235, 312 and 403 mμ, and infrared absorptions at 3.05 and 6.05 μ. These spectra require a rather highly conjugated unsaturated carbonyl system which could not be accommodated by any bicyclic structure and, if completely implausible alternatives are dismissed, one is immediately led to consideration of structures containing a seven-membered ring. Conversion of the strained bicyclo[3.2.0] system of VII to a diazepine derivative can be formulated readily (X) as collapse of the N-1 → C-5 bond and loss of a proton at C-4, initiated in acid media by protonation of N-1, and in alkali by abstraction of the proton at C-4. A similar fission of a carbocyclic [3.2.0] structure has been described by Dryden[7] in his elegant synthesis of cycloheptatriene. A substantial body of information has been accumulated which confirms the structure X of the diazepine product which would arise by this path; these data are presented in the following article.[8] The transformation VII → XI under mild acid or basic conditions supplies the most trenchant argument presently available for the correctness of the course of the ring closure reactions of the diazoacetylpyrazolines II and III and the diazabicyclo[3.2.0]heptenone structure VII. The further characterization of this highly reactive ring system will be described in a subsequent paper.

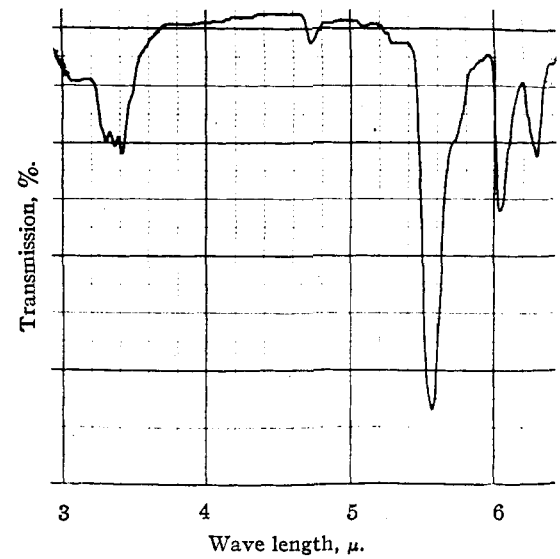
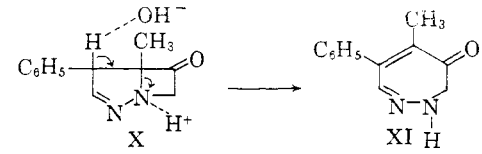


Fig. 1.—Infrared spectrum of VII.



X XI

Acknowledgments.—We thank Mr. Donald Hoffman and Dr. H. C. Beachell for the infrared spectra.

Experimental[9]

3-Diazoacetyl-3-methyl-4-phenyl-Δ^5-pyrazoline (III).—A solution of 18 g. of the Δ^1-pyrazoline II[2] in 400 ml. of methanol was treated with 3 ml. of 5% potassium hydroxide solution and allowed to stand overnight at room temperature. After evaporation *in vacuo* to about one-third volume the solution was diluted with water, chilled and scratched; a total of 13.6 g. (76%) of crystals was obtained. This material was recrystallized by dissolving in 200 ml. of benzene and diluting with 800 ml. of hexane; cream colored needles were obtained, m.p. 105–106°, λ_{max}^{EtOH} 254 mμ (ε 14,900); λ^{KBr} 3.0, 3.2, 4.68, 6.2 μ.

Anal. Calcd. for $C_{12}H_{12}N_4O$ (228.25): C, 63.14; H, 5.30; N, 24.55. Found: C, 63.10; H, 5.18; N, 24.93.

This product was also obtained directly in the preparation of II. In a typical experiment, the reaction mixture from 70 g. (0.37 mole) of I with 0.88 mole of diazomethane in 2.8 l. of ether and 0.6 l. of methanol[10] was concentrated *in vacuo* and chilled, giving 31 g. of the Δ^1-pyrazoline II, m.p. 86°. After further concentration of the mother liquor, slow crys-

(5) J. R. Marshall and J. Walker, *J. Chem. Soc*, 467 (1952).

(6) K. Miescher and H. Kägi, *Helv. Chim. Acta*, **24**, 1471 (1941), and H. Kägi, *ibid.*, **24**, 141E (1941), studied the reaction of 2-amino-3-diazoacetylpyridine with a variety of acidic reagents and obtained the substituted 3-acetyl derivative in every case. The anticipated cyclization product, 7-azaindoxyl, was not obtained as inferred by later authors[8]; the oxindole was formed under conditions of the Wolff rearrangement.

(7) H. L. Dryden, Jr., THIS JOURNAL, **76**, 2841 (1954); H. L. Dryden, Jr., and B. E. Burgert, *ibid.*, **77**, 5633 (1955).

(8) Paper IV, J. A. Moore and J. Binkert, *ibid.*, **81**, 6029 (1959).

(9) Infrared spectra of all compounds were obtained in KBr disks. Only the most significant strong bands are recorded.

(10) The presence of methanol in this reaction significantly improves the reproducibility and the yield as compared to the previously described procedure[2] in which ether alone was used as solvent in the pyrazoline step.

tallization furnished a total of 16 g. of mixed crystals. After mechanical separation of the large prisms of II, recrystallization of the remaining material gave III, m.p. and mixed m.p. with a sample obtained from alkali isomerization 105–106°.

Conversion of III to 3-Methyl-4-phenylpyrazole (V).—To a solution of 200 mg. of III in 40 ml. of methanol was added 6 ml. of 10% methanolic potassium hydroxide. After standing at room temperature for 24 hours the dark brown solution was chilled, neutralized with acid, evaporated, and diluted with water. After standing at 0° for 1 hour the white precipitate, 85 mg., was collected. Crystallization from ether gave white prisms, m.p. 142°[11], λ_{max}^{EtOH} 244 mμ (11,800); λ^{KBr} 6.23, 6.3 μ. The analytical sample was sublimed.

Anal. Calcd. for $C_{10}H_{10}N_2$ (158.2): C, 75.92; H, 6.37; N, 17.71. Found: C, 75.91; H, 6.35; N, 17.63.

The picrate was prepared and crystallized from ethanol, m.p. 156°.[11] For further characterization, a sample of V was oxidized with alkaline permanganate at 100° and the acidic material (12%) was crystallized to give **4-phenylpyrazole-3-carboxylic acid**, m.p. 253°, no depression on mixing with an authentic sample prepared by oxidation of 4-phenyl-Δ^2-pyrazolinecarboxylic acid.[12]

5-Methyl-4-phenyl-1,2-diazabicyclo[3.2.0]-2-hepten-6-one (VII).—A solution of 100 mg. of the Δ^5-pyrazoline III in 2 ml. of glacial acetic acid was allowed to stand at room temperature for 15 min., at which time gas evolution had nearly ceased. The solution was then shell-frozen and evaporated under reduced pressure; the resulting amber oil was taken up in ether and again evaporated to remove traces of acetic acid. The infrared spectrum of this product is shown in Fig. 1. Material with an identical infrared spectrum was obtained by treatment of a solution of III in methanol with one drop of hydrochloric acid; after the vigorous gas evolution had ceased the solution was poured into water, extracted with ether and the ether solution washed, dried and evaporated.

For preparation of the **picrate**, a sample of VII prepared from 100 mg. of III was treated in acetone–ether (1:1) with 75 mg. of picric acid. The dark yellow solid, 140 mg. (75%), obtained after standing overnight at 5°, was recrystallized from acetone to give bright yellow prisms, m.p. 129–130° dec.; λ^{KBr} 4.2–4.6, 5.50 μ.

Anal. Calcd. for $C_{18}H_{15}N_5O_8$ (429.3): C, 50.35; H, 3.52; N, 16.31. Found: C, 50.44; H, 3.82; N, 16.29.

2,3-Dihydro-5-methyl-6-phenyl-4H-1,2-diazepin-4-one (XI). a. **From II.**—Fifty-five grams of II, recrystallized from methanol, was dissolved in 300 ml. of glacial acetic acid and the solution was warmed at 85–90° for 2.5 hours; nitrogen evolution became almost negligible after 2 hours. The very dark red solution was concentrated to a thick sirup which was dissolved in ethanol and again evaporated to give a red crystalline mass. A total of 37 g. (77%) of orange-red prisms, m.p. 148–150°, was obtained in two crops. The compound was recrystallized from ethanol and from ether, orange prisms, m.p. 150–151°; λ_{max}^{EtOH} 220 mμ (ε 17,500), 312 mμ (5,000), 401 mμ (2,960); $\lambda_{max}^{0.1N\ NaOH}$ 241.5 mμ (22,000), 346 mμ (2,860), 415 mμ (5,420); λ^{KBr} 3.01, 6.08, 6.37, 6.62, 7.45 μ.

Anal. Calcd. for $C_{12}H_{12}ON_2$ (200.24): C, 71.97; H, 6.04; N, 13.99. Found: C, 71.82; H, 6.10; N, 13.76.

b. **From III.**—A solution of 500 mg. of III in 5 ml. of glacial acetic acid was heated at 70–80° for 1 hour. The dark red solution was evaporated and the residue was evaporated several times with methanol. A total of 324 mg. of orange-brown needles, m.p. 144–148°, was obtained in several crops. A small additional amount of product was obtained by dissolving the remaining sirup in 20% aqueous potassium hydroxide and then acidifying. The combined crystals were recrystallized from methanol as thick orange-brown needles, m.p. 150°.

c. **From VII.**—The bicyclic ketone VII prepared from 100 mg. of III was warmed in 2 ml. of acetic acid for 1 hour; evaporation and crystallization as described above furnished 53 mg. (60%) of XI, m.p. 148–150°. Comparable results were obtained by allowing the solution of VII to stand at room temperature for 24 hours. The diazepine XI also was obtained in 30% yield by treatment of the crystalline picrate of VII with warm acetic acid.

In another experiment, 175 mg. of VII was dissolved in 3 ml. of methanol containing 0.05 ml. of concd. sulfuric acid. After warming for 45 min. the solution was neutralized with bicarbonate, evaporated and extracted with ether; the ether solution furnished 71 mg. (40%) of brown needles, m.p. 148–150°. Similar results were obtained by the use of 0.2 *N* methanolic hydrochloric acid.

In the reaction of VII with alkali, a solution of 88 mg. of the oil in 2 ml. of methanol was treated with 3 ml. of 10% methanolic potassium hydroxide. After standing 4 hours at room temperature, the dark red reaction mixture was acidified and diluted with water. The yellow precipitate was collected (66 mg., 75%) and recrystallized to give orange prisms of XI, m.p. 150°.

3-Chloroacetyl-3-methyl-4-phenyl-Δ^1-pyrazoline (IX).—A solution of 2 g. of the unsaturated chloroketone[2] (VIII) in 30 cc. of ethereal diazomethane solution was allowed to stand overnight. The solution was filtered and concentrated to 15-ml. volume. Well-formed white plates separated on standing; the mother liquor rapidly developed a dark purple color. The product was recrystallized from methanol as white plates, m.p. 94–95°; no selective absorption in ultraviolet; λ^{KBr} 5.75, 6.40, 6.70 μ.

Anal. Calcd. for $C_{12}H_{13}ON_2Cl$ (236.70): C, 60.89; H, 5.53; N, 11.84. Found: C, 61.14; H, 5.72; N, 12.02.

This compound was extremely unstable. A sample of analytical purity became discolored in 12 hours, and on storing for 3 weeks in the ice-box, the crystals had become a black tar. No crystalline product could be isolated from this material.

NEWARK, DEL.

(11) Reported[4] for 3-methyl-4-phenylpyrazole: m.p. 141°; picrate, m.p. 155°.

(12) H. von Pechmann and E. Burkard, *Ber.*, **33**, 3594 (1900).