[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

3-Hydroxymethylindoles

BY EDWARD LEETE

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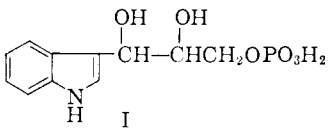
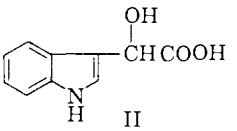
3-Hydroxymethylindoles substituted with methyl and phenyl groups on the pyrrole ring have been prepared by the reduction of the corresponding 3-indole aldehydes with sodium borohydride. These compounds, which are vinylogs of carbinolamines, were reduced to the corresponding 3-methyl derivatives with lithium aluminum hydride only when the indole nitrogen was unsubstituted. The ease with which they split out formaldehyde to yield 3,3′-diindolylmethanes varied with the substituents on the pyrrole ring; 1,2-dimethyl-3-hydroxymethylindole was the most reactive whilst 3-hydroxymethyl-2-phenylindole gave only 2-phenylindole and formaldehyde on refluxing with water. 3-Ethoxymethyl derivatives were obtained when the alcohols were refluxed with ethanol in the presence of base. The reactions of 2-hydroxymethylindole have been briefly examined.

Recently there has been considerable biological interest in compounds which are derivatives of 3-hydroxymethylindole (III, R = H). One example is 3-indoleglycerol phosphate (I), which



I



II

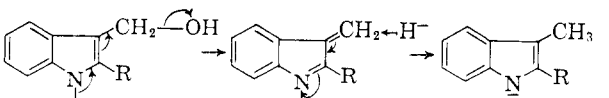
is an intermediate in the biosynthesis of indole from anthranilic acid.[1] Another example is 3-indoleglycolic acid (II) which has been suggested as a precursor of 3-indoleacetic acid.[2] It has been previously shown[3,4] that 3-hydroxymethylindole is converted by heat, acids and bases to 3,3′-diindolylmethane and is reduced by lithium aluminum hydride to 3-methylindole. In the present work we have examined the generality of these reactions by preparing derivatives of 3-hydroxymethylindole substituted with methyl and phenyl groups on the pyrrole ring.

3-Hydroxymethylindoles have been prepared by several methods. Runti[5] obtained 3-hydroxymethylindole by refluxing indole with paraformaldehyde in methanol in the presence of sodium methoxide. It was also obtained by the action of aqueous sodium hydroxide on gramine methiodide.[3] The most convenient method is by the reduction of 3-indole aldehydes with sodium or lithium borohydride.[4,6,7]

Mingoia[8] claimed to have obtained 3-hydroxymethylindole and its 2-methyl derivative by the action of trioxymethylene on indole magnesium bromide and its 2-methyl derivative. However the high melting points of his products suggest that he obtained 3,3′-diindolylmethanes or polymeric material. It now seems certain that the compound, m.p. 225°, which Plant and Tomlinson[9] obtained by treating 2,3-dimethylindole with bromine followed by water, was not 3-hydroxymethyl-2-methylindole. Their compound was stable in dilute hydrochloric acid and boiling potassium hydroxide, whereas the authentic material was decomposed under these conditions. It is also unlikely that the compound, m.p. 196°, which Sanna[10] obtained by the decarboxylation of 2-methyl-3-indoleglycolic acid was authentic 3-hydroxymethyl-2-methylindole. We were unable to repeat the work of Madinaveitia[11] who claimed to have obtained 3-hydroxymethylindole by the reaction of gramine with methyl iodide in methanol and by the catalytic reduction of 3-indole aldehyde.

The procedure of Thesing[4] has been used in the present work. All the 3-hydroxymethylindoles obtained were crystalline solids except 3-hydroxymethyl-1-methylindole which was a pale yellow oil. They were all very sensitive to acids and the attempted synthesis of acetyl derivatives or picrates led to the formation of tarry material. Crystalline derivatives were obtained with 1,3,5-trinitrobenzene.

3-Hydroxymethyl-2-methylindole and the corresponding 2-phenyl derivative were reduced by lithium aluminum hydride to 2,3-dimethylindole and 3-methyl-2-phenylindole, respectively. However the 1-methyl-3-hydroxymethylindoles were stable to hydrogenolysis and these substances could be obtained in excellent yield by the reduction of the corresponding 1-methyl-3-indole aldehydes with lithium aluminum hydride in ether. It is thus apparent that hydrogenolysis only occurs when the indole nitrogen is unsubstituted. It is suggested that the initial step in the hydrogenolysis is the elimination of water, catalyzed by the anions (AlH_4^-, H^-, etc.) which are present in the ether solution. Addition of hydride ion to the 3-methyleneindolenine (IV) so produced leads to the anion V which on protonation yields 3-methylindole.



III IV V

R = H, CH_3, C_6H_5

The 3-hydroxymethyl-1-methylindoles are vinylogs of N,N-disubstituted carbinolamines and their resistance to hydrogenolysis is consistent with previous work on N,N-disubstituted amides where

(1) C. Yanofsky, *Biochim. et Biophys. Acta*, **20**, 438 (1956); J. S. Gots and S. H. Ross, *ibid.*, **24**, 429 (1957).

(2) J. B. Greenberg, A. W. Galston, K. N. F. Shaw and M. D. Armstrong, *Science*, **125**, 992 (1957).

(3) E. Leete and L. Marion, *Can. J. Chem.*, **31**, 775 (1953).

(4) J. Thesing, *Ber.*, **87**, 692 (1954).

(5) C. S. Runti, *Gazz. chim. ital.*, **81**, 613 (1951).

(6) R. M. Silverstein, E. E. Ryskiewicz and S. Chaikin, THIS JOURNAL, **76**, 4485 (1954).

(7) D. E. Ames, R. E. Bowman, D. D. Evans and W. A. Jones, *J. Chem. Soc.*, 1984 (1956).

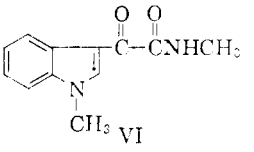
(8) Q. Mingoia, *Gazz. chim. ital.*, **62**, 844 (1932).

(9) S. G. P. Plant and M. L. Tomlinson, *J. Chem. Soc.*, 955 (1933).

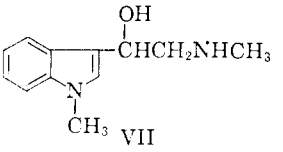
(10) G. Sanna, *Gazz. chim. ital.*, **61**, 60 (1931).

(11) J. Madinaveitia, *J. Chem. Soc.*, 1927 (1937).

the unshared electrons of the nitrogen enter into resonance with an adjacent aromatic ring. Thus 1-acylindoles are not reduced to the tertiary amines. Reduction ceases at the carbinolamines which decompose yielding indole and aldehydes which are reduced to alcohols if excess lithium aluminum hydride is present.[12] An interesting example of the resistance of N-substituted-3-hydroxymethylindoles to hydrogenolysis has recently been disclosed in a patent.[13] 1,N-Dimethyl-3-indoleglyoxamide (VI) on treatment with lithium hydride in refluxing tetrahydrofuran yielded 1-methyl - 3 - (2 - methylamino - 1 - hydroxyethyl)-indole (VII), whereas 3-indoleglyoxamide under-

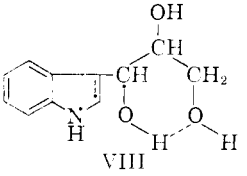


VI

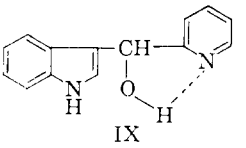


VII

went complete reduction yielding tryptamine.[14] The failure of 3-indoleglycerol[15] and 3-indolyl-2′-pyridylcarbinol[16] to undergo hydrogenolysis with lithium aluminum hydride may be due to the formation of intramolecular hydrogen bonds stabilizing the alcohol as indicated in structures VIII and IX, respectively.



VIII

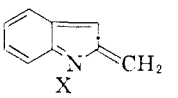


IX

All the 3-hydroxymethylindoles except the 2-phenyl derivative split out formaldehyde on refluxing in water yielding 3,3′-diindolylmethanes. 1,2-Dimethyl-3-hydroxymethylindole was especially unstable, losing formaldehyde even in the solid state. When this alcohol was dissolved in methanol, crystals of 1,1′,2,2′-tetramethyl-3,3′-diindolylmethane separated in a few minutes. On the other hand, considerable 3-hydroxymethyl-1-methyl-2-phenylindole was recovered unchanged after refluxing with water for 24 hours. When 3-hydroxymethyl-2-phenylindole was refluxed with water, formaldehyde was split out and a quantitative yield of 2-phenylindole was obtained. Dahlbom and Misiorny[17] claimed to have obtained 2,2′-diphenyl-3,3′-diindolylmethane, m.p. 184–185°, by the reaction of 2-phenylindole with formaldehyde. It seems highly probable that the material they isolated from the reaction mixture was 2-phenylindole (m.p. 187–188°); indeed, the elementary analysis which they reported for the diindolylmethane is in better agreement with 2-phenylindole. Presumably the 2-phenylindole does not react with formaldehyde in aqueous solution because of its low basicity.

3-Hydroxymethylindole and its 2-phenyl derivative reacted with ethanol in the presence of a trace of sodium hydroxide to yield 3-ethoxymethylindoles. Related reactions have been observed by Runti[5,18] who obtained 3-piperidino- and 3-morpholinomethylindole by refluxing 3-hydroxymethylindole with piperidine and morpholine in the presence of sodium ethoxide.

2-Hydroxymethylindole[19] is also formally a vinylog of a carbinolamine. However the conjugated chain joining the nitrogen with the alcohol group involves the benzene ring and this is apparently an unfavorable situation since this alcohol does not undergo hydrogenolysis with lithium aluminum hydride. Hydrogenolysis would presumably demand the formation of the intermediate X, in which the aromaticity of the benzene ring is destroyed.[20] 2-Hydroxymethylindole was also stable in boiling water and 10% sodium hydroxide solution. It was also recovered unchanged after refluxing in ethanol in ethanol in the presence of sodium hydroxide.



X

Experimental[21]

General Method for the Reduction of the 3-Indole Aldehydes.[4]—Sodium borohyride (0.76 g., 0.02 mole) was added to a solution or suspension of the aldehyde (0.01 mole) in boiling absolute ethanol (20 ml.). After refluxing the mixture for about one minute the solution was allowed to cool to room temperature for one hour and then evaporated to dryness *in vacuo*. The residue was suspended in 1% aqueous sodium hydroxide (50 ml.) and the mixture extracted with ether. The ether extract was dried over sodium sulfate and evaporated to dryness *in vacuo*. The residue was dissolved in warm benzene and crystallization was initiated by the cautious addition of petroleum ether (b.p. 30–40°). 1,3,5-Trinitrobenzene derivatives were obtained by mixing hot methanolic solutions of the indole derivative and trinitrobenzene.

3-Hydroxymethyl-1-methylindole.[7]—Reduction of 1-methyl-3-indole aldehyde[22] with sodium borohydride according to the general method yielded a pale yellow fluorescent oil (86%). Considerable decomposition occurred when this was distilled (160°, 0.001 mm.).

Anal. Calcd. for $C_{10}H_{11}NO$: C, 74.51; H, 6.88. Found: C, 74.76; H, 6.72.

The same product was obtained on reduction of the aldehyde with lithium aluminum hydride in refluxing ether. The 1,3,5-trinitro-benzene derivative was obtained as orange prismatic needles from methanol, m.p. 139–141°.

Anal. Calcd. for $C_{10}H_{11}NO \cdot C_6H_3N_3O_6$: C, 51.34; H, 3.77. Found: C, 51.41; H, 3.97.

1,1′-Dimethyl-3,3′-diindolylmethane.—3-Hydroxymethyl-1-methyl-indole (1.0 g.) was refluxed with water (50 ml.) for 18 hr. The cooled solution was filtered and the

(12) V. M. Mićović and M. Lj. Mihailović, *J. Org. Chem.*, **18**, 1190 (1953); *cf.* also N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, Inc., New York, N. Y., 1956, pp. 575–590.

(13) M. E. Speeter (to Upjohn Co.), U. S. Patent 2,825,734; *C. A.*, **52**, 12923 (1958).

(14) M. E. Speeter and W. C. Anthony, THIS JOURNAL, **76**, 6208 (1954).

(15) F. Lingens and H. Hellman, *Angew. Chem.*, **69**, 97 (1957).

(16) H. Bader and W. Oroshnik, THIS JOURNAL, **79**, 5686 (1957).

(17) R. Dahlbom and A. Misiorny, *Acta Chem. Scand.*, **9**, 1074 (1955).

(18) C. Runti and G. Orlando, *Ann. chim.* (*Rome*), **43**, 308 (1953).

(19) W. I. Taylor, *Helv. Chim. Acta*, **33**, 164 (1950).

(20) *Cf.* H. R. Snyder and P. L. Cook, THIS JOURNAL, **78**, 969 (1956), for a comparison of the reactivities of 2- and 3-dimethylaminomethylindole.

(21) All melting points are corrected. Analyses were carried out by Miss Heather King of the University of California, Los Angeles, Mrs. Olga Hamerston and Mr. William C. Kurlya of the University of Minnesota, and Clark Microanalytical Laboratory.

(22) H. Wieland, W. Konz and H. Mittasch, *Ann.*, **513**, 1 (1934).

residue (0.76 g.) was crystallized from a mixture of benzene and petroleum ether to yield colorless needles of 1,1′-dimethyl-3,3′-diindolylmethane, m.p. 112.5-113° (lit. 105–109°,[7] 109.5–111.5°[23]).

Anal. Calcd. for $C_{19}H_{18}N_2$: C, 83.17; H, 6.61. Found: C, 83.05; H, 6.69.

The di-1,3,5-trinitrobenzene derivative was obtained as bright bluish-red prisms, m.p. 141–142°, from methanol.

Anal. Calcd. for $C_{19}H_{18}N_2 \cdot 2C_6H_3N_3O_6$: C, 53.14; H, 3.45. Found: C, 52.92; H, 3.46.

The aqueous solution obtained after removal of the diindolylmethane was treated with a solution of dimedone when crystals of the dimedone derivative of formaldehyde separated (0.49 g., 27%) m.p. 194°, not depressed on admixture with an authentic specimen.

When an ethanolic solution of 3-hydroxymethyl-1-methylindole was allowed to stand at room temperature for several days, prismatic needles of the diindolylmethane separated out and the ethanolic supernatant liquid was shown to contain formaldehyde.

3-Hydroxymethyl-2-methylindole.—2-Methyl-3-indole aldehyde was obtained from 2-methylindole by the Vilsmeier method using the procedure of Smith.[24] The aldehyde was obtained as stout colorless prisms from ethanol, m.p. 206–208° (lit.[25] 202–203°). Reduction of the 2-methyl-3-indole aldehyde by the general method yielded colorless needles (88%) of 3-hydroxymethyl-2-methylindole, m.p. 112–114°.

Anal. Calcd. for $C_{10}H_{11}NO$: C, 74.51; H, 6.88. Found: C, 74.65; H, 6.75.

The 1,3,5-trinitrobenzene derivative was obtained as fine feathery orange needles from methanol, m.p. 169–170°.

Anal. Calcd. for $C_{10}H_{11}NO \cdot C_6H_3N_3O_6$: C, 51.34; H, 3.77. Found: C, 51.64; H, 4.08.

2,2′-Dimethyl-3,3′-diindolylmethane.—When 3-hydroxymethyl-2-methylindole (0.1 g.) was refluxed with water there was an almost immediate separation of a white crystalline precipitate (80 mg., 94%), m.p. 237–238°, which was identical (infrared spectrum, mixed m.p.) with authentic 2,2′-dimethyl-3,3′-diindolylmethane prepared from 2-methylindole and formaldehyde.[26] The aqueous filtrate from the reaction yielded 74.5 mg. of formaldehyde-dimedone derivative representing a 41% yield of formaldehyde, the maximum possible being 50%. Diindolyl-methane formation also occurred on boiling the alcohol with 10% sodium hydroxide solution.

2,3-Dimethylindole.—Refluxing 3-hydroxymethyl-2-methylindole or 2-methyl-3-indole aldehyde in ether with an excess of lithium aluminum hydride for 2 hr. gave 2,3-dimethylindole in 80–94% yield, m.p. 97–98°, not depressed on admixture with authentic material prepared by the cyclization of the phenylhydrazone of methyl ethyl ketone.[27]

1,2-Dimethyl-3-indole aldehyde was obtained by the methylation of 2-methyl-3-indole aldehyde using the procedure of Wieland, *et al.*[22] Crystallization from a mixture of benzene and petroleum ether yielded fine colorless needles, m.p. 131–132° (lit.[28] 132°).

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.50; H, 6.60; N, 7.99.

1,2-Dimethyl-3-hydroxymethylindole.—Reduction of 1,2-dimethyl-3-indole aldehyde by the general method yielded 1,2-dimethyl-3-hydroxymethylindole as colorless needles, m.p. 94–95° (55%). A purer product was obtained by reduction of the aldehyde with excess lithium aluminum hydride in refluxing ether. Crystallization from benzene–petroleum ether yielded fine colorless needles, m.p. 100–101°.

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.35; H, 7.35; N, 8.20.

This alcohol was unstable and decomposed at room temperature liberating formaldehyde, which was readily detected by its odor when a bottle of the substance was opened. It was not possible to prepare a pure trinitrobenzene derivative since conversion to the diindolylmethane occurred so rapidly in methanol solution.

1,1′,2,2′-Tetramethyl-3,3′-diindolylmethane was most easily obtained by dissolving 1,2-dimethyl-3-hydroxymethylindole (0.175 g.) in cold methanol (3 ml.). In 5 min. crystals of the diindolyl derivative separated (113 mg., 75%). Crystallization from benzene–petroleum ether yielded fine colorless needles, m.p. 161.5–162.5°.

Anal. Calcd. for $C_{21}H_{22}N_2$: C, 83.40; H, 7.33; N, 9.26. Found: C, 83.29; H, 6.99; N, 9.33.

It gave a mono-1,3,5-trinitrobenzene derivative as dark purple prisms from methanol, m.p. 171–172°.

Anal. Calcd. for $C_{21}H_{22}N_2 \cdot C_6H_3N_3O_6$: C, 62.90; H, 4.89. Found: C, 62.49; H, 4.82.

The diindolylmethane was also obtained in 89% yield by refluxing the alcohol with water for 1 hr. A 43% yield of formaldehyde was isolated as the dimedone derivative.

3-Hydroxymethyl-2-phenylindole.—2-Phenyl-3-indole aldehyde[29] was reduced by the general method except that a somewhat larger volume of ethanol (75 ml.) was used in the reaction. 3-Hydroxymethyl-2-phenylindole was obtained as colorless plates, m.p. 129–130°, from benzene–pentane.

Anal. Calcd. for $C_{15}H_{13}NO$: C, 80.69; H, 5.87. Found: C, 80.72; H, 5.72; N, 6.40.

With 1,3,5-trinitrobenzene it yielded what is apparently a 2:1 complex as red needles from methanol, m.p. 140–141°.

Anal. Calcd. for $C_{15}H_{13}NO \cdot 2C_6H_3N_3O_6$: C, 49.93; H, 2.95. Found: C, 49.84; H, 2.97.

3-Hydroxymethyl-2-phenylindole (0.223 g., 0.01 mole) was refluxed with 10% sodium hydroxide (100 ml.) for 90 min. The solid material which separated out (0.190 g.) was filtered off and crystallized from ethanol to yield colorless plates of 2-phenylindole, m.p. 187–188°, identical (mixed m.p., infrared spectrum and analysis) with an authentic sample of this substance. 2-Phenylindole was also obtained when the alcohol was refluxed in water, a 62% yield of formaldehyde being recovered from the aqueous solution.

3-Ethoxymethyl-2-phenylindole.—3-Hydroxymethyl-2-phenylindole (0.56 g.) was refluxed with absolute ethanol (20 ml.) containing 0.01 ml. of 10% sodium hydroxide solution for 20 hr. The solution was then taken to dryness and the residue sublimed *in vacuo* (130°, 0.001 mm.). The sublimate (0.40 g.) was crystallized from benzene–pentane yielding fine colorless needles of 3-ethoxymethyl-2-phenylindole, m.p. 116–117°.

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.24; H, 6.82. Found: C, 81.33; H, 6.81.

3-Ethoxymethylindole, m.p. 63–64° (lit.[30] 63–64°) was obtained in a similar way from 3-hydroxymethylindole. Starting material was recovered if no sodium hydroxide was added to the reaction mixture.

3-Methyl-2-phenylindole.—Reduction of 2-phenyl-3-indole aldehyde with excess lithium aluminum hydride in refluxing ether yielded 3-methyl-2-phenylindole (85%), m.p. 88–90° (lit.[27] 90–92°), not depressed on admixture with an authentic specimen prepared by the cyclization of the phenylhydrazone of propiophenone.[27]

3-Hydroxymethyl-1-methyl-2-phenylindole.—1-Methyl-2-phenyl-3-indole aldehyde[29] was reduced by the general method to yield colorless needles of the alcohol (81%), m.p. 120–121°. Reduction of the aldehyde with lithium aluminum hydride in ether gave the same product (79%).

Anal. Calcd. for $C_{16}H_{15}NO$: C, 80.98; H, 6.37. Found: C, 81.15; H, 6.13.

The 1,3,5-trinitrobenzene derivative was obtained from methanol as small orange prisms, m.p. 104–105°.

Anal. Calcd. for $C_{16}H_{15}NO \cdot C_6H_3N_3O_6$: C, 58.66; H, 4.03; N, 12.44. Found: C, 59.03; H, 4.57; N, 12.17.

1,1′-Dimethyl-2,2′-diphenyl-3,3′-diindolylmethane.—3-Hydroxymethyl-1-methyl-2-phenylindole (1.32 g., 0.005 mole) was refluxed with water (100 ml.) for 24 hr. The mixture was then filtered and the aqueous filtrate gave a 25% yield of formaldehyde-dimedone derivative. The residue (1.08 g.), which started to melt at about 80°, was crystallized from benzene–petroleum ether yielding 0.31 g. of start-

(23) H. R. Snyder and E. L. Eliel, THIS JOURNAL, **71**, 663 (1949).

(24) G. F. Smith, *J. Chem. Soc.*, 3842 (1954).

(25) G. Barger and A. J. Ewins, *Biochem. J.*, **11**, 59 (1917).

(26) R. v. Walther and J. Clemen, *J. prakt. Chem.*, [2] **61**, 249 (1900).

(27) H. M. Kissman, D. W. Farnsworth and B. Witkop, THIS JOURNAL, **74**, 3948 (1952).

(28) P. Wolff, German Patent 614,325; *C. A.*, **29**, 5861 (1935).

(29) R. C. Blume and H. G. Lindwall, *J. Org. Chem.*, **10**, 255 (1945).

(30) T. A. Geissman and A. Armen, THIS JOURNAL, **74**, 3916 (1952).

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

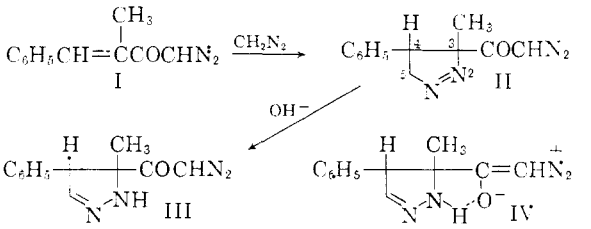
RECEIVED FEBRUARY 19, 1959

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.

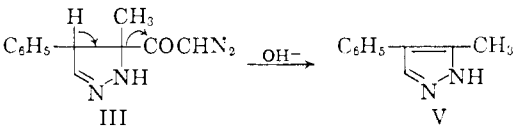
In the first communication of this series[1] it was reported that the reaction of 3-diazoacetyl-3-methyl-Δ^1-pyrazoline (II) with acetic acid furnishes a colored product having the composition $C_{12}H_{12}ON_2$ which was formulated as a diazepine derivative. In this and subsequent papers we wish to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