CHEMISTRY OF POLYENE AND POLYYNE COMPOUNDS

XXVII.* BEHAVIOR OF 5-AMINO-5-METHYL-1,3-HEXADIYNE IN ADDITION REACTIONS

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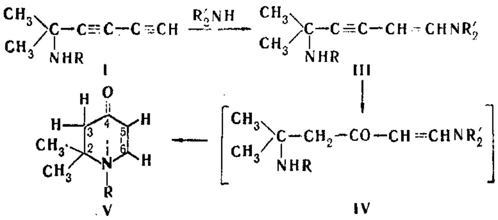
The behavior of 5-amino-5-methyl-1,3-hexadiyne (I) during hydration and during the nucleophilic addition of alcohols and secondary amines was studied. Compound I was used to synthesize 2,2-dimethyl-2,3-dihydro-4-pyridone, 2,5,5-trimethyl-$\Delta^{2,3}$-dihydro-4-pyrrolone, and 4-substituted 2,5,5-trimethyl-$\Delta^{1,2,3,4}$-pyrroles.

In a continuation of our study of reactions involving addition to a diacetylenic system of triple bonds, we have investigated the behavior of 5-amino-5-methyl-1,3-hexadiyne (I) during hydration and during the nucleophilic addition of alcohols and amines.

It was found that when I is refluxed in alcoholic alkali, one molecule of alcohol adds to the terminal acetylene bond to form 1-ethoxy-5-amino-5-methyl-1-hexen-3-yne (II), the structure of which was confirmed by the similarity between its IR and UV spectra and the spectra of the previously described 1-methoxy-5-methyl-5-hydroxy-1-hexen-3-yne [1].

Secondary amines add to 5-amino-5-methylhexadiyne to form acetylenic enamines (III, R = H); i.e., the reaction proceeds in accordance with the principles previously established for other monosubstituted diacetylenes [2].



R = H, C_6H_5

However, in contrast to the previously described reactions, in which the addition product was obtained exclusively as the cis isomer, in this case, one obtains a mixture of cis and trans isomers (~ 1 : 1), which were separated by chromatography with a column filled with aluminum oxide. The assignment of the configurations was made on the basis of the UV and PMR spectra. The cis isomer has λ_{max} 325 nm (ε 9700) and $J_{1,2}$ 10 Hz, while the trans isomer has λ_{max} 339 nm (ε 15,500) and $J_{1,2}$ 14 Hz. No cis–trans isomerization is observed when the isomeric acetylenic enamines (III, R = H) are heated. 2,2-Dimethyl-2,3-dihydro-4-pyridone (V, R = H) is formed in the reaction described above or when a mixture of the reagents is allowed to stand at room temperature for a long time. The structure of the product was confirmed by studying its PMR spectrum and also by the synthesis, via this scheme, of the previously described [3] N-phenyldihydro-

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*See Izv. Akad. Nauk SSR, Ser. Khim., 141 (1971) for communication XXVI.

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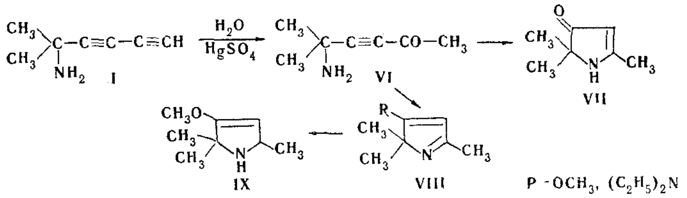
4-pyridone (V, R = C_6H_5). The formation of dihydropyridones V when 5-amino-5-methylhexadiyne is heated with secondary amines is apparently the result of intramolecular cyclization of the intermediate dialkylamino vinyl ketones (IV), which are in turn obtained by the hydration of acetylenic enamines III.

The acidic hydration of 5-amino-5-methylhexadiyne (I, R = H) leads to the aminoalkynyl ketone (VI), i.e., only the terminal triple bond is involved.



Numerous attempts to achieve the acidic hydration of the second triple bond in order to obtain five-membered nitrogen heterocycles were unsuccessful. This goal was achieved by means of the alkaline hydration of amino ketone VI in aqueous dimethylamine, as a result of which, 2,5,5-trimethyl-$\Delta^{2,3}$-dihydro-4-pyrrolone (VII) was obtained. Addition of the nucleophilic reagent accompanied by cyclization occurs during the reaction of amino ketone VI with an anhydrous diethylamine solution as well as with alcohol under alkaline conditions even at room temperature, so that the only reaction products are, respectively, 4-dimethylamino- and 4-methoxy-2,5,5-trimethyl-$\Delta^{1,2,3,4}$-pyrroles (VIII), which are extremely resistant to acid saponification. The reduction of VIII (R = OCH_3) with sodium borohydride and its catalytic hydrogenation over platinum oxide involve only the double bond at the nitrogen atom.

EXPERIMENTAL

1-Ethoxy-5-amino-5-methyl-1-hexen-3-yne (II). A solution of 1.7 g (0.015 mole) of 5-amino-5-methyl-1,3-hexadiyne in 10 ml of absolute ethanol was refluxed for 5 h in the presence of 0.1 g (0.018 mole) of potassium hydroxide. The reaction mixture was poured into water and extracted with ether. The extract was dried with potassium carbonate and distilled to give 1.4 g (57.5%) of II with bp 87-88° C (0.9 mm) and n_D^{20} 1.4974. IR spectrum: 1639, 2200 cm^{-1}. UV spectrum: λ_{max} 239 nm (ε 16,400). Found: C 71.0; H 10.0; N 9.1%. $C_9H_{15}ON$. Calculated: C 70.6; H 9.9; N 9.1%.

Reaction of 5-Amino-5-methyl-1,3-hexadiyne (I) with Dimethylamine. A) A mixture of 3.5 g (0.032 mole) of I (R = H) and 60 ml of 30% aqueous dimethylamine was heated at 100° C for 1 h and extracted with methylene chloride. The extract was dried with potassium carbonate, and the solvent was removed by distillation. The solid precipitate was recrystallized from ether–acetone (2 : 1) and additionally purified by vacuum sublimation (0.2 mm) at 90-95°C to give 3 g (75%) of 2,2-dimethyl-2,3-dihydro-4-pyridone (V, R = H) with mp 93-94° C. IR spectrum: 1580, 1620, 3300 cm^{-1}. UV spectrum: λ_{max} 315 nm (ε 13,700). PMR spectrum, δ, ppm: 1.30 (2-CH_3, singlet); 2.30 (3-CH_2, singlet); 4.83 (5-H, quartet, $J_{5,6}$ = 6.7, $J_{1,5}$ = 1 Hz); 6.93 (1-H); 7.07 (6-H, triplet, $J_{6,5}$ = 6.7 Hz). Found: C 67.2; H 8.8; N 11.4%. $C_7H_{11}NO$. Calculated: C 67.2; H 8.8; N 11.2%.

B) A mixture of 3.5 g (0.032 mole) of I and 60 ml of 30% aqueous dimethylamine was allowed to stand at room temperature for 12 h and was then extracted with chloroform. The extract was dried with potassium carbonate and distilled to give 2.1 g of a mixture with bp 70-100° C (0.7 mm), in which the presence of two products with R_f 0.57 and 0.25, as well as 0.7 g of V, was detected by thin-layer chromatography on activity II aluminum oxide in an ether–methanol system (3 : 1). Chromatography of the liquid mixture with a column (l 45 cm, d 2 cm) filled with Al_2O_3 yielded 0.85 g of cis-1-dimethylamino-5-methyl-5-amino-1-hexen-3-yne (III) with bp 70-72° C (0.6 mm) and n_D^{20} 1.5120. IR spectrum: 690, 1580, 1630, 2200, and 3400 cm^{-1}. UV spectrum: λ_{max} 325 nm (ε 9709). Found: C 71.3; H 10.7; N 18.4%. $C_9H_{16}N_2$. Calculated C 71.0; H 10.6; N 18.4%. Also obtained was 0.6 g of the trans isomer of III with bp 96-97° C (0.6 mm) and n_D^{20} 1.5425. IR spectrum: 930, 1550, 1625, 220, 3400 cm^{-1}. UV spectrum: λ_{max} 339 nm (ε 15,500). Found: C 70.8; H 10.6; N 18.2%. $C_9H_{16}N_2$. Calculated: C 71.0; H 10.6; N 18.4%.

C) A mixture of 1.5 g (0.01 mole) of I and 50 ml of a 20% dioxane solution of dimethylamine was heated in a metal ampul at 120° C for 2 h. Distillation yielded 0.6 g (40%) of the trans isomer of III, which was identical to that described above.

N-Phenyl-2,2-dimethyl-2,3-dihydro-4-pyridone (V, R = C_6H_5). A mixture of 1.6 g (0.015 mole) of I (R = C_6H_5) [obtained by the method in [4] with bp 84-85° C (0.3 mm) and n_D^{20} 1.5856] and 30 ml of 30% aqueous dimethylamine was refluxed for 1 h and extracted with chloroform. The extract was dried with potassium carbonate, the solvent was removed by distillation, and the residue was recrystallized with carbon tetrachloride and additionally purified by vacuum sublimation (0.2 mm) at 130°C to give 1.1 g (36%) of N-phenyl-2,2-dimethyl-2,3-dihydro-4-pyridone (V, $R = C_6H_5$) with mp 130-131°C (mp 132°C [3]). The oxime had mp 169-170°C (mp 167°C [3]).

Hydration of 5-Amino-5-methyl-1,3-hexadiyne (I). A solution of 2 g (0.019 mole) of I (R = H) in 10 ml of dioxane was added at 65°C to a mixture of 1 g (0.003 mole) of mercuric sulfate, 1 ml of sulfuric acid, and 20 ml of water. The mixture was stirred at 65-70°C for 1 h and extracted with ether. The ether extract was dried with potassium carbonate and distilled to give 0.8 g (34%) of 5-amino-5-methyl-3-pentyn-2-one (VI) with bp 76-77°C (10 mm) and n_D^{20} 1.4680. IR spectrum: 1720, 2200 cm^{-1}. Found: C 67.0; H 8.9; N 11.2%. $C_7H_{11}ON$. Calculated C 67.2; H 8.8; N 11.2%.

4-Methoxy-2,5,5-trimethyl-$\Delta^{1,2,3,4}$-pyrrole (VIII, $R = CH_3O$). A solution of 1.2 g (0.01 mole) of amino ketone VI in 10 ml of methanol was refluxed in the presence of 0.1 g of potassium hydroxide for 1 h. The reaction mixture was poured into water and extracted with ether. The extract was dried with potassium carbonate and distilled to give 0.8 g (55%) of VIII ($R = CH_3O$) with bp 55-56°C (8 mm) and n_D^{20} 1.4630. IR spectrum: 1550, 1660 cm^{-1}. UV spectrum: λ_{max} 255 nm (ε 4420). Found: C 68.7; H 9.5; N 10.1%. $C_8H_{13}ON$. Calculated: C 69.0; H 9.4; N 10.0%. The methiodide had mp 145-146°C (from alcohol).

Reduction of 4-Methoxy-2,5,5-trimethyl-$\Delta^{1,3}$-pyrrole (VIII, $R = CH_3O$). A solution of 1 g (0.01 mole) of VII ($R = CH_3O$) in 3 ml of ethanol was added at room temperature to a mixture of 0.8 g (0.02 mole) of $NaBH_4$, 5 ml of water, and 10 ml of a 20% solution of trimethylamine (0.03 mole) in ethanol, and the mixture was stirred for 12 h. The mixture was acidified with an acetic acid solution and extracted with ether. The aqueous solution was treated with ammonium hydroxide until it was alkaline, and it was then extracted with ether. Distillation yielded 0.5 g (39%) of 4-methoxy-2,5,5-trimethyl-$\Delta^{3,4}$-pyrroline (IX) with bp 45-46°C (15 mm) and n_D^{20} 1.4459. IR spectrum: 1630, 3300 cm^{-1}. The methiodide had mp 197-198°C (from alcohol). Found: C 38.2; H 6.5; I 44.7%. $C_9H_{18}ON$. Calculated C 38.1; H 6.5; I 44.7%. The same product was obtained by the catalytic hydrogenation of VIII ($R = CH_3O$) on platinum oxide; the amount of hydrogen required for the hydrogenation of one double bond was absorbed.

4-Diethylamino-2,5,5-trimethyl-$\Delta^{1,2,3,4}$-pyrrole [VIII, $R = (C_2H_5)_2N$]. A solution of 2.5 g (0.02 mole) of VI and 2 g (0.026 mole) of diethylamine in 20 ml of absolute ether was held at room temperature for 15 h and distilled to give 2.4 g (60%) of 4-diethylamino-2,5,5-trimethyl-$\Delta^{1,2,3,4}$-pyrrole [VIII, $R = (C_2H_5)_2N$] with bp 49-50°C (0.5 mm) and n_D^{20} 1.5064. IR spectrum: 1540, 1610 cm^{-1}. UV spectrum: λ_{max} 333 nm (ε 11,001). Found: C 73.4, H 11.0, N 15.3%. $C_{11}H_{20}N_2$. Calculated: C 73.2; H 11.2, N 15.4%.

2,5,5-Trimethyl-$\Delta^{2,3}$-dihydro-4-pyrrolone (VII). A mixture of 2 g (0.016 mole) of 5-amino-5-methyl-3-pentan-2-one (VI) and 10 ml of 30% aqueous dimethylamine was refluxed for 1 h and extracted with chloroform. The solution was dried with potassium carbonate, the solvent was removed by distillation, and the residue began to crystallize to give 0.8 g (40%) of VII with mp 104-105°C. IR spectrum: 1560, 1640, 3220 cm^{-1}. UV spectrum: λ_{max} 308 nm (ε 12,101). PMR spectrum, δ, ppm: 1.20 (gem-CH_3), 2.10 (2-CH_3); 4.63 (3-CH); 8.40 (NH). Found: C 67.1; H 8.9; N 11.6%. $C_7H_{11}ON$. Calculated: C 67.2; H 8.9; N 11.2%.

LITERATURE CITED

1. B. P. Gusev and V. F. Kucherov, Izv. Akad. Nauk SSSR, Ser. Khim., 1318 (1964).
2. B. P. Gusev, E. A. Él'perina, and V.F. Kucherov, Izv. Akad. Nauk SSSR, Ser. Khim., 2345 (1967).
3. L. Panizzi and E. Monti, Gazz. Chim. Ital., 77, 556 (1947).
4. G. F. Hennion and R. S. Hanzel, J. Am. Chem. Soc., 82, 4908 (1960).