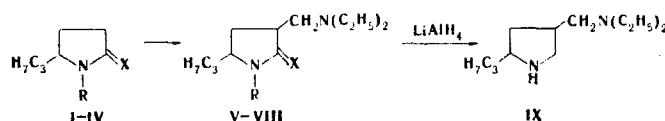


MANNICH REACTION IN A NUMBER OF 2-PYRROLIDONES AND 2-THIOPYRROLIDONES

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It is known that 2-pyrrolidones do not undergo the Mannich reaction. We have found that the replacement of the oxygen atom by a sulfur atom or the acylation of 2-pyrrolidones at the nitrogen atom results in an increase in the C-H acidity of the α -methylene group, as a result of which 2-thiopyrrolidones and 1-acetyl-2-pyrrolidones react with formaldehyde and diethylamine to form compounds V-VIII:



I, IV, V, VIII R=COCH₃; II, VI R=H; III, VII R=CH₃; I, V X=O; II-IV, VI-VIII X=S

For example, 0.01 mole of 1-acetyl-5-propyl-2-pyrrolidone (I) in an ethanolic solution was given an addition of 0.01 mole of diethylamine hydrochloride and 3 ml of 4% formaldehyde. The reaction mixture was acidified with hydrochloric acid and heated for 40 min. The salt of the Mannich base formed was treated with alkali. After extraction with ether and preparative separation by column chromatography, amine V was isolated. Compounds VI-VIII were obtained in an analogous manner. Thin-layer chromatography on Silufol following the isolation of amines V-VIII in a column demonstrated the presence of a single isomer. The following data are presented for compounds V-VIII [compound No., bp. °C (pressure in mm Hg), n_D^{20} , percentage yield]: V, 114-116 (1), 1.4540, 75; VI, 115-117 (2), 1.4905, 67; VII, 125-127 (2), 1.4955; 71; VIII, 119-121 (2), 1.4967, 67.

The IR spectra of the Mannich bases synthesized show absorption bands at 1700 (C=O), 1320 (C-N) (V) and 1542 (C=S), 1320 cm^{-1} (C-N) (VI-VIII). PMR spectrum (CCl₄): 8.05 (s, NH), 3.52 (q, 5-H), 2.50-2.65 (m, ring protons), 0.9-1.50 (m, protons of alkyl substituents in C(5) position), 2.45 ppm (t, CH₂-N). However, the data obtained from the PMR spectra do not allow us to make a rigorous assignment of the isomer to the cis or trans form.

When lithium aluminum hydride is applied to compounds V and VIII, the reduction of the C=O or C=S group is accompanied by the elimination of the acetyl group with the formation of 5-propyl-3-(diethylamino)methyl-pyrrolidine (IX).

The PMR and IR spectra and the data from the analysis for C, H, N, and S for all the compounds synthesized fit the ascribed structure.