ACETALS OF LACTAMS AND ACID AMIDES.

47.* INVESTIGATION OF THE BEHAVIOR OF SUBSTITUTED 6-(β-DIMETHYLAMINO)VINYL-4-PYRIMIDINONES IN ACIDIC MEDIA.

SYNTHESIS OF 3-CYANO-4-ANILINO-5-FORMYL-2-PYRIDONE AND 3-CHLORO-4-CYANOBOZINO[6]NAPHTHYRIDINE

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The hydrolysis of 1-substituted 5-cyano-6-(β-dimethylamino)vinyl-4-pyrimidinones in acidic media was studied. It was shown that the 1-benzyl derivative is converted to a mixture of α-cyano-β-benzylamino-crotonamide and 3-cyano- and 3-carbamido-4-benzyl-amino-2-pyridones. The principal product in the hydrolysis of the 1-phenyl derivative is 3-cyano-4-anilino-5-formyl-2-pyridone. Cyclization of the latter by heating in phosphorus oxychloride leads to 3-chloro-4-cyanobenzo[b][1, 6]naphthyridine.

It has been previously established that 1-substituted 5-cyano-6-(β-dimethylamino)-vinyl-4-pyrimidinones, which are formed in the reaction of secondary enamino amides with dimethylformamide diethylacetal, are readily hydrolyzed in alkaline media with opening of the pyrimidine ring and subsequent recycylation to 2-pyridone derivatives [2, 3]. In contrast to its behavior in an alkaline medium, in acids at room temperature the pyrimidine ring is quite stable, and cyclization with the participation of the enamino and cyano groups takes place under these conditions [2, 4]. Thus pyridopyrimidine derivative II was isolated when 1-benzyl-5-cyano-6-(β-dimethylamino)vinyl-4-pyrimidinone (Ia) was treated with hydrochloric acid at 20°C [4]. When we carried out this reaction with moderate heating (60-65°C) we obtained a mixture of substances, from which we were able to isolate in individual form 3-carbamido-4-benzyl-amino-2-pyridone (III), which was identical to a sample obtained by a previously described method [4]. In the mixture we also detected, by means of mass spectrometry (the mass spectrum of the mixture was compared with the spectra of pure samples obtained by the method in [3]), 3-cyano-4-benzylamino-2-pyridone (IV) [M^+ 225 (36), [PhCH_2]^+ 91 (100), and [PhCH_2 - C_2H_5]^+ 65 (9)] and α-cyano-β-benzylaminocrotonamide (V) [M^+ 215 (37), [M - OH]^+ 198 (16), [M - OH - NCN]^+ 171 (16), [PhCH_2]^+ 91 (100), and 65 (13)]. The formation of the principal product of this reaction (III) could have been due to hydrolysis of the cyano group in II. However, it was found that cyanopyridine IV remains unchanged when it is maintained under these conditions, and it may be assumed that amide III develops via cleavage of the pyrimidine ring of intermediate pyridopyrimidine II. Enamino acid V is formed as a result of opening of the pyrimidine ring and splitting out of the enamino grouping in starting pyrimidinone Ia.

One might have expected that replacement of the benzyl substituent by a phenyl substituent in the 1 position of the pyrimidine ring would not change the fundamental scheme of hydrolysis in an acidic medium. However, two substances were isolated when a solution of 1-phenyl-5-cyano-6-(β-dimethylamino)vinyl-4-pyrimidinone (Ib) was heated in 0.1 N HCl at 60-65°C. The minor component, which was obtained in ~10% yield, was 3-carbamido-4-anilino-2-pyridone (VI). An intense molecular-ion peak (M^+) at 229 (54) is observed in its mass spectrum.

*See [1] for Communication 46.
†Here and subsequently, the m/z values are given for the ions, and the relative intensities in percent are given in parentheses.

The maximally intense peak belongs to the $[M - \text{OH}]^+$ ion at 212. Subsequent elimination of a molecule of water and a molecule of CO gives peaks at 194 (25) and 184 (21), respectively. A Ph$^+$ peak at 77 (33) is also observed. To confirm the structure of VI we investigated its PMR spectrum simultaneously with the spectrum of known amide III (see Table I). The spectra of pyridones III and VI are quite similar; a characteristic feature is the presence of two doublet signals of protons in the 5 and 6 positions of the pyridone rings, which are found at 6.0 and -7.3 ppm for VI and at 5.93 and -7.3 ppm for III. A peculiarity of the PMR spectra is the presence of signals of four labile protons; by means of the method of decoupling of the signals we were able to make reliable assignments of the signals to certain NH groups. Thus we established that the strongest-field signals are the signals of the B-H protons, which do not participate in the formation of a hydrogen bond (7.07 ppm for III and -7.3 ppm for VI); in the spectra they are represented by doublets due to spin-spin coupling with the adjacent A-H protons ($^3J_{AB} = 4.5$ Hz for III and 4.3 Hz for VI). The adjacent NH protons are observed at rather weak field, viz., at 9.91 ppm (VI) and 9.84 ppm (III); this makes it possible to propose that they participate in hydrogen bonding with the pyridone carbonyl group. The signals of the protons of the ring NH groups are observed in the form of either a doublet (for III, 10.99 ppm, $^3J_{NH,6-H} = 4$ Hz) or a markedly broadened singlet (for VI, 11.21 ppm) due to spin-spin coupling with adjacent 6-H proton. Finally, the signals of the 4-RNH groups are represented in the spectra either in the form of a rather narrow singlet (for VI, 12.67 ppm) or in the form of a triplet (for III, 11.14 ppm, $^3J_{NH,CH_2} = 5.9$ Hz). This weak-field position of the signals constitutes evidence for a strong intramolecular hydrogen bond of the chelate type. All of the data presented indicate the presence in III and VI of two rather strong intramolecular hydrogen bonds.

According to the results of elementary analysis, the principal substance obtained by treatment of pyrimidinone Ib with acid could have two-ring structure VII or the structure of hydroxymethylene derivative VIII.

Structure VII can be rejected starting from the data from the IR spectrum, in which an absorption band of a cyano group at 2202 cm$^{-1}$ is observed. The PMR spectrum of IX is not in agreement with either structure VII or structure VIII. Two singlets at 9.60 ppm (1H) and 8.42 ppm (1H), two broad signals at 12.42 ppm (1H) and 10.60 ppm (1H), and a multiplet of benzene ring protons centered at 7.4 ppm (5H) are present in the spectrum. From its position, the signal at 9.6 ppm can be ascribed to an aldehyde proton, and the two broad signals can be ascribed to labile protons of NH or OH groups. It should be noted that the corresponding arylhydrazone was obtained from IX when it was heated with p-nitrophenylhydrazine; this also confirmed the presence of an aldehyde function in this compound.