SYNTHESIS OF DIENIC N,S-KETENE ACETALS OF THE PYRIMIDINE SERIES

E. A. Sokolova, A. E. Tsil'ko, and I. A. Maretina

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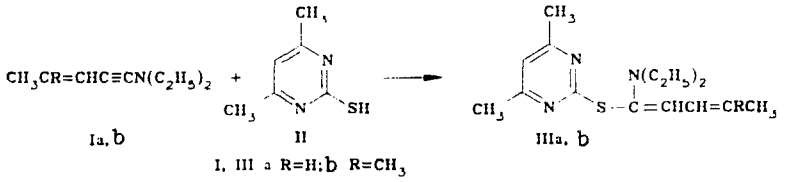
The reaction of alkenynylamines with thiols of the pyrimidine series proceeds regiospecifically at the acetylene bond with he formation of N,S-ketene acetals of the pyrimidine series.

We have previously shown the possibility of the synthesis of N,S-ketene acetals by the reaction of 1-dialkylamino-3-penten-1-ynes with alkyl- and aryl(phenyl)mercaptans [1]. The reaction proceeded selectively at the acetylene bond; stereospecificity was not observed. No data are available on the reaction of ynamines with thiols of the pyrimidine series.

The reaction of alkenynylamines with mercaptopyrimidines also proceeded at the acetylene bond with the formation of dienic N,S-acetals of the pyrimidine series.

Thus, 2-(1-diethylamino-1,3-pentadienyl)thio-4,6-dimethylpyrimidines (IIIa, b) were synthesized by the reaction of 1-diethyl-amino-3-penten-1-ynes (Ia, b) with 2-mercapto-4,6-dimethylpyrimidine (II).



The structure of compounds IIIa, b was confirmed by the IR and PMR spectral data. In the IR spectrum of compounds IIIa, b there were intense bands in the 1640-1685 cm^{-1} region, corresponding to the stretching vibrations of the dienic system of bonds. The absorption in the 1960 cm^{-1} region, characteristic for the diethylamino group signals (0.93 ppm, t, $2CH_3$); 3.20 ppm, q, $2CH_2$) signals are observed of the methyl protons of the methyl group of the unsaturated fragment in 0.58 and 1.68 ppm region (two singlets, $2CH_3$). The protons of the methyl group at the 4- and 6-positions of the pyrimidine ring give a singlet signal in the 2.18 ppm region ($2CH_3$) of the spectrum. The signals in the 5.60-6.11 ppm region correspond to olefinic protons in the side chain. The pyrimidine ring proton gives a resonance signal in the 6.43 ppm region.

EXPERIMENTAL

The elemental analysis data correspond to the calculated values.

2-(1-Diethylamino-1,3-pentadienyl)-thio-4,6-dimethylpyrimidine (III, $C_{15}H_{23}N_3S$). A 0.55-g portion (4 mmoles) of 1-diethylamino-3-penten-1-yne (Ia) was added with stirring to a suspension of 0.6 g (4 mmoles) of compound II in 30 ml of absolute benzene. At the end of the addition, the mixture was stirred at room temperature for 2 h to complete dissolution of the precipitate. After removal of the solvent, the residue was distilled at reduced pressure, bp 102°C (5 mm Hg); n_D^{20} 1.5700. Yield 0.91 g (82%).

2-(1-Diethylamino-4-methyl-1,3-pentadienyl)-thio-4,6-dimethylpyrimidine (IIIb, $C_{16}H_{25}N_3S$) was obtained under the conditions of the preceding experiment from 0.6 g (4 mmoles) of 1-diethylamino-4-methyl-3-penten-1-yne (Ib) and 0.6 g (4 mmoles) of compound II. bp 120°C (0.5 mm Hg); n_D^{20} 1.5610. Yield 1.01 g (97%).

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Thus, we obtained for the first time the dienic N,S-acetals of the pyrimidine series by direct reaction of thiols of the pyrimidine series with alkenynylamines.

LITERATURE CITED

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REACTION OF 8-BROMOTHEOPHYLLINE WITH PYRIDINE AND ALKYLPYRIDINES. 8-PYRIDINIOTHEOPHYLLINATES

V. N. Bobkov, T. V. Zvolinskaya, and I. I. Kuz'menko

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The reaction of 8-bromotheophylline with pyridine or alkylpyridines in the presence of electrophilic reagents proceeds with the formation of 8-pyridiniotheophyllinates. The possible mechanism of the reaction is discussed.

We have previously [1] shown that in the reaction of 8-bromotheophylline (I) with o-phenylenephosphoryl isocyanate in the presence of pyridine, substitution of the bromine atom by pyridine takes place with the formation of 8-pyridiniotheophyllinate (IIa) instead of the expected carbamoylation of theophylline.

The aim of the present work was to study the mechanism of this reaction. It is known that on prolonged boiling in pyridine, 8-chlorotheophylline forms a pyridinium ylide IIa in a yield of 53% [2].

We found that under similar conditions bromotheophylline I converts in the course of 4 h into ylide IIa to the extent of 11%. In the presence of acidic additives, taken in equimolar amounts [HCl, HBr, $BF_3 \cdot CH_3OH$, $(CH_3)_3SiCl$, P_2O_5), the yield of the desired end product during the same reaction time increases to 20-40%. Contrary to this, alkaline agents of sodium methylate type completely inhibit this reaction. Better results are obtained on using acid chlorides of phosphorus acids – PCl_3 and $POCl_3$. In this case, the yield of compound IIa is 60-70%, but the reaction is accompanied by strong resinification. Diphenylphosphoryl chloride and acetic anhydride were found to be the most effective. In the presence of these reagents the yield of ylide IIa after 30 min is 80-90%.

Considering the properties of these reagents, it can be assumed that phosphorylation or acetylation of 8-bromotheophylline at the $N_{(7)}$ first takes place, and the corresponding theophyllines III and IV react directly with pyridine (see scheme on page 1287.

To confirm this supposition, we synthesized and isolated substituted theophyllines III and IV in the pure state. Compounds III, IV were obtained from 8-bromotheophylline I and the corresponding acid chlorides of diphenylphosphoric or acetic acid in dry dioxane in the presence of triethylamine. The thus synthesized compounds III and IV are colorless crystalline substances, which are readily soluble in many aprotic solvents. In water and alcohols they are gradually hydrolyzed to the starting 8-bromotheophylline, and the 7-phosphorylated 8-bromotheophylline III is in particular readily hydrolyzed. Theophyllines III and IV react with pyridine even in the cold, while on boiling, according to the TLC data, the reaction is completed in 30 min with the formation of ylide IIa. Thus, the formation of 7-substituted intermediates of 8-bromotheophylline promotes their more rapid conversion with pyridine into ylides IIa. It is assumed that isocyanates [1] also react in the same way.

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