REACTION OF DIMETHYLFORMAMIDE DIMETHYLACETAL WITH METHYLPYRIMIDINES

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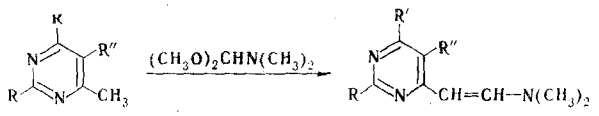
The reaction of dimethylformamide dimethylacetal with methylpyrimidines and methyltriazines was studied, and β-dimethylaminovinylpyrimidines and β-dimethylaminovinyltriazines were obtained. It is shown that electron-acceptor substituents facilitate the reaction.

Continuing our study of active methyl groups in methylpyrimidine [1], we investigated the reaction of methylpyrimidines with dimethylformamide dimethylacetal (I). The reactivity of acetal I is probably explained by the existence of the $[(CH_3)_2N{=}CH{-}OCH_3]^+OCH_3^-$ ionic structure [2, 3].

4,6-Dimethylpyrimidine (IIa) reacts with acetal I during prolonged heating at 100°C to give 4-methyl-6-(β-dimethylaminovinyl)pyrimidine (IIIa) in low yield.



IIa-c IIIa-c

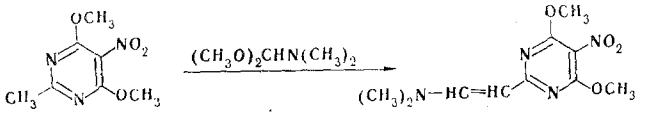
II–IIIa R=R″=H, R′=CH$_3$; b R=R′=OCH$_3$, R″=NO$_2$; c R=Cl, R′=CN, R″=H

The introduction of acceptor substituents in the pyrimidine ring increases protonization of the hydrogens of the methyl group. Thus 5-nitro-2,4-dimethoxy-6-methylpyrimidine (IIb) reacts vigorously with acetal I at 20°C to give dimethylaminovinylpyrimidine IIIb.

A strong electron-acceptor substituent such as the nitro group suppresses the slight donor effect of the methoxy groups, which is apparent in the case of 4,6-dimethoxypyrimidine, the pK_a of which is 1.49, as compared with 1.31 for pyrimidine [4].

The reaction with 2-chloro-6-methyl-4-cyanopyrimidine (IIc) also proceeds readily.

The methyl group attached to the C_4 atom in IIb is more active than the methyl group attached to the C_2 atom in IV as a consequence of the considerably stronger negative inductive effect of the NO_2 group, as compared with the mesomeric effect. A similar effect of the NO_2 group is observed in benzoic acids (the pK_a values for o- and p-nitrobenzoic acids are 2.17 and 3.43 [4]). In contrast to 5-nitro-2,4-dimethoxy-4-methylpyrimidine (IIb), 5-nitro-4,6-dimethoxy-2-methylpyrimidine (IV) reacts with I only with heating.



IV V

The reaction of methylpyrimidines with acetal I probably commences with detachment of a proton of the methyl group by the methoxide anion and subsequent electrophilic attack of the resulting methylpyrimidine carbanion by the $[(CH_3)2N{=}CH{-}OCH_3]^+$ cation. The methyl groups of pyrimidine do not react with acetal I when donor substituents are present (for example, 4-

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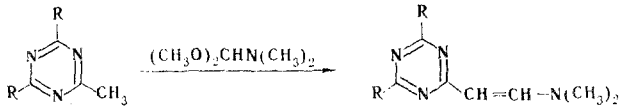
methoxy- and 4-dimethylamino-6-methylpyrimidines). Substituents in the methyltriazines have the same effect on the activity of methyl groups in reactions with acetal I.

2,4-Bis(trichloromethyl)-6-methyltriazine (VIa) reacts readily with acetal I at 20°C, whereas 2,4-diphenyl-6-methyltriazine reacts only after prolonged heating.



VIa,b VIIa,b

VI–VII a R=CCl_3; b R=C_6H_5

All of the compounds obtained are colored (from pale-yellow to bright-orange). Absorption bands at 340-418 nm are observed in the electronic spectra of these compounds; this is associated with an increase in the length of the conjugation chain due to the vinyl group and the presence of a dimethylamino group. The structure of the compounds was confirmed by the PMR spectra. The compounds obtained are of interest for further study, since they are enamines that contain pyrimidine and triazine residues.

EXPERIMENTAL

The PMR spectra of the compounds were recorded with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane as the external standard; the chemical shifts are given on the δ scale. The electronic spectra of ~10^{-4} mole/liter solutions of the compounds in alcohol were recorded with a Specord UV-vis spectrophotometer. The individuality of the compounds was monitored by thin-layer chromatography (TLC) on activity II Al_2O_3 in a benzene–methanol system (10:1) with development in UV light.

4-Methyl-6-(β-dimethylaminovinyl)pyrimidine (IIIa). A solution of 2.2 g (20 mmole) of 4,6-dimethylpyrimidine and 5.2 g (44 mmole) of acetal I in 20 ml of dimethylformamide (DMF) was heated on a boiling-water bath for 20 h, after which it was poured into water, and the aqueous mixture was extracted with chloroform. The chloroform layer was washed with water and dried over magnesium sulfate. The chloroform was evaporated, and the DMF was removed by vacuum distillation to give 0.2 g (6%) of IIIa with mp 92-95°C (from hexane). UV spectrum, λ_{max} (log ε): 355 nm, (4.40). PMR spectrum (CCl_4): 2.55 (s, 3H, C_4–CH_3), 3.2 [s, 6H, N–$(CH_3)_2$], 5.06 (4, 1H, =CHN–), 6.7 (s, 1H, 5-H), 7.95 (d, 1H, C=CH), and 8.66 ppm (s, 1H, 2-H). Found: C 66.4; H 7.9; N 25.6%. $C_9H_{13}N_3$. Calculated: C 66.2; H 8.0; N 25.7%.

5-Nitro-2,4-dimethoxy-6-(β-dimethylaminovinyl)pyrimidine (IIIb). A 2.8-g (11 mmole) sample of acetal I was added to a solution of 2 g (10 mmole) of 5-nitro-2,4-dimethoxy-6-methylpyrimidine in 20 ml of DMF, during which the solution immediately became bright-red. The mixture was stirred at 20°C for 3 h, after which it was poured into ice water. The bright-orange precipitate of IIIb was removed by filtration to give 2.5 g (98%) of a product with mp 157-159°C (from CCl_4). UV spectrum, λ_{max} (log ε) 341 nm (4.67). PMR spectrum ($CDCl_3$): 3.33 [s, 6H, $N(CH_3)_2$], 4.33 (d, 6H, 2-OCH_3 and 4-OCH_3), 5.67 (d, 1H, =CHN–), and 8.34 ppm (d, 1H, C=CH). Found: C 47.1; H 5.5; N 22.0%. $C_{10}H_{14}N_4O_4$. Calculated: C 47.2; H 5.5; N 22.0%.

2-Chloro-4-cyano-6-(β-dimethylaminovinyl)pyrimidine (IIIc). This compound was obtained by the method described above for IIIb. Bright-orange IIIc, with mp 161-163°C (from petroleum ether), was obtained in 29% yield. UV spectrum, λ_{max} (log ε): 331 (3.93) and 418 nm (4.04). PMR spectrum ($CDCl_3$): 3.5 [s, 6H, $N(CH_3)_2$], 5.36 (d, 1H, =CH–N), 7.23 (s, 1H, 5-H), and 8.36 ppm (d, 1H, C=CH). Found: C 52.4; H 4.2; N 27.3%. C_9H_9ClN. Calculated: C 51.8; H 4.3; N 26.8%.

5-Nitro-4,6-dimethoxy-2-(β-dimethylaminovinyl)pyrimidine (V). This compound was obtained by the method described above for IIIb. The mixture was stirred at 75°C for 5 h. The product, with mp 132-136°C (from hexane), was obtained in quantitative yield. UV spectrum, λ_{max} (log ε): 340 (4.25) and 406 nm (4.34). PMR spectrum ($CDCl_3$): 3.40 [s, 6H, $N(CH_3)_2$], 4.40 (s, 6H, 4-OCH_3, 6-OCH_3), 5.51 (d, 1H, =CHN–), and 8.21 ppm (d, 1H, C=CH). Found: C 47.6; H 5.6; N 22.2%. $C_{10}H_{14}N_4O_4$. Calculated: C 47.2; H 5.5; N 22.0%.

2,4-Bis(trichloromethyl)-6-(β-dimethylaminovinyl)triazine (VIIa). This compound was obtained by the method described above for IIIb. The bright-yellow product, with mp 163-167°C (dec., from alcohol), was obtained in 52% yield. UV spectrum, λ_{max}(log ε): 358 nm (4.62). PMR spectrum ($CDCl_3$): 3.50 [d, 6H, $N(CH_3)_2$], 5.69 (d, 1H, =CHN–), and 8.58 ppm (d, 1H, C=CH). Found: C 28.3; H 2.0; Cl 55.0%. $C_9H_8Cl_6N_4$. Calculated: C 28.1; H 2.1; Cl 55.3%.

2,4-Diphenyl-6-(β-dimethylaminovinyl)triazine (VIIb). A 0.65-g (5.5 mmole) sample of acetal I was added to a solution of 1.2 g (5 mmole) of 2,4-diphenyl-6-methyltriazine in 30 ml of DMF, and the mixture was heated on a boiling-water bath for 20 h. It was then poured into 150 ml of ice water, and 1.9 g of the bright-orange precipitate was removed by filtration. The mixture of reaction product and starting substance was separated by crystallization from petroleum ether. The reaction product precipitated when the petroleum ether was cooled, while the starting triazine was isolated by evaporation of the ether. The reaction yielded 0.48 g (32.6%) of VIIb with mp 178-180°C (from petroleum ether). UV spectrum, λ_{max} (log ε): 262 (4.57) and 350 nm (4.56). PMR spectrum ($CDCl_3$): 2.95 [d, 6H, $N(CH_3)_2$], 5.73 (d, 1H, =CHN), 8.61 (d, 1H, C=CH), and 8.41 ppm (m, 10H, C_6H_5). Found: C 75.5; H 6.1; N 18.5%. $C_{19}H_{18}N_4$. Calculated: C 75.5; H 6.0; N 18.5%.

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