2. S. D. Sokolov, Usp. Khim., No. 3, 533 (1979).
3. V. P. Perevalov, L. I. Baryshnenkova, M. A. Andreeva, Yu. A. Manaev, I. A. Denisova, B. I. Stepanov, and V. I. Seraya, Khim. Geterotsikl. Soedin., No. 12, 1672 (1983).
4. V. P. Perevalov, M. A. Andreeva, L. I. Baryshnenkova, Yu. A. Manaev, G. S. Yamburg, B. I. Stepanov, and V. A. Dubrovskaya, Khim. Geterotsikl. Soedin., No. 12, 1676 (1983).
5. S. A. Giller, I. B. Mazheika, and I. I. Grandberg, Khim. Geterotsikl. Soedin., No. 1, 130 (1967).
6. I. I. Grandberg, S. V. Tabak, and A. N. Kost, Khim. Geterotsikl. Soedin., No. 1, 85 (1966).
7. V. T. Sahini and C. Rodina, Rev. Roum. Chim., 18, 1283 (1973).
8. R. A. Khmel'nitskii and P. B. Terent'ev, Usp. Khim., 48, 854 (1979).
9. P. B. Terent'ev, Mass Spectrometry in Organic Chemistry [in Russian], Vyssh. Shkola, Moscow (1979), p. 223.
10. R. Silverstein, G. Bassler, and T. Morril, Spectrometric Identification of Organic Compounds, Wiley, New York (1974).
11. H. Feuer (ed.), The Chemistry of the Nitro and Nitroso Groups, Wiley-Interscience, New York (1969).
12. R. A. Khmel'nitskii, A. P. Krasnoshchek, A. A. Polyakova, and I. I. Grandberg, Zh. Org. Khim., 3, 1540 (1967).
13. M. A. Khan and B. M. Lynch, Can. J. Chem., 49, 3566 (1971).
14. A. A. Polyakova and R. A. Khmel'nitskii, Mass Spectrometry in Organic Chemistry [in Russian], Khimiya, Leningrad (1972), p. 198.
15. Yu. A. Manaev, M. A. Andreeva, V. P. Perevalov, B. I. Stepnov, V. A. Dubrovskaya, and V. I. Seraya, Zh. Obshch. Khim., 52, 2592 (1982).

SOME TRANSFORMATIONS OF DIMETHYLAMINOVINYLPYRIMIDINES

B. M. Khutova, S. V. Klyuchko, L. P. Prikazchikova,
and V. M. Cherkasov

UDC 547.853.3'333.3'286

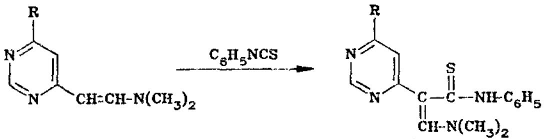
The reaction of enamines of the pyrimidine series with phenyl isothiocyanate, arenediazonium salts, and benzylamine was studied. The corresponding thioamides, pyrimidinylacetaldehydes, and benzylaminovinylpyrimidine were obtained.

The previously described [1] enamines of the pyrimidine series are reactive compounds. The reaction of dimethylaminovinylpyrimidines I with carboxylic acid chlorides, which led to the production of phenacyl- and acetonylpyrimidines, was studied in [2].

Continuing our investigation of enamines of the pyrimidine series, in the present research we studied the reaction of I with electrophilic agents and transamination.

4-(2-Dimethylaminovinyl)pyrimidines Ia,b react with phenyl isothiocyanate to give thioamides IIa,b.

The IR spectra of IIa,b contain an absorption band at 1110 cm^{-1} (NH—CS) but do not contain an absorption band at 2500-2600 cm^{-1} (SH); this confirms the thione form of thioamides

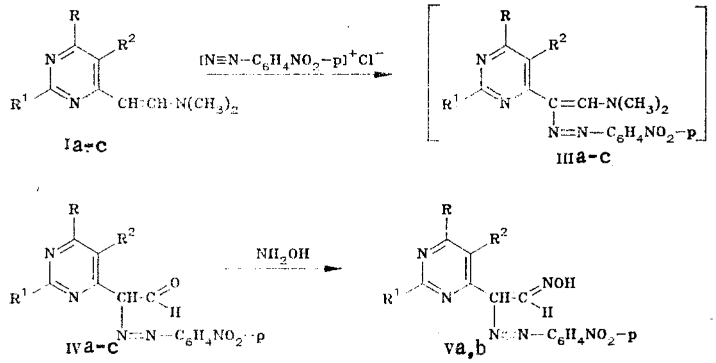


Ia,b I,II a R=H; b R=CH₃ II a,b

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev 252660.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 559-561, April, 1985. Original article submitted June 29, 1984.

0009-3122/85/2104-0468$09.50

II [3]. A singlet of two equivalent methyl groups at 3.3 ppm, signals of 2-H and 5-H protons of the pyrimidine ring at 9.7 and 7.3 ppm, and a multiplet of aromatic protons, which overlaps the signal of the proton of the =CH– group at 7.6-8.0 ppm, are observed in the PMR spectra of IIa,b.



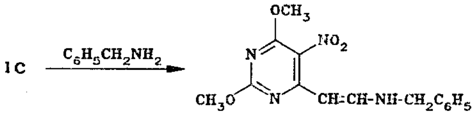
I, III—Va R=R^1=R^2=H; b R=CH$_3$, R^1=R^2=H; c R=R^1=OCH$_3$, R^2=NO$_2$

Enamines that have strong electron-acceptor substituents in the pyrmidine ring do not react with phenyl isothiocyanate. Thus 5-nitro-2,6-dimethoxy-4-(2-dimethylaminovinyl)pyrimidine (Ic) does not react with phenyl isothiocyanate as a consequence of shifting of the electron density from the double bond to the heteroring, which hinders electrophilic attack by the thioisocyanate [sic] on the α-carbon atom of the vinyl group.

4-(2-Dimethylaminovinyl)pyrimidines Ia-c react with arenediazonium salts to give pyrimidinylacetaldehydes IVa-c, probably through intermediates IIIa-c.

The reaction proceeds in the presence of electron-donor and electron-acceptor substituents in the pyrimidine ring as a consequence of the strong electrophilic character of diazonium salts. However, the yield of aldehyde IVc is considerably lower despite the presence of an electron-acceptor NO$_2$ group. The structures of IVa-c were proved by the PMR and IR spectra and the preparation of oximes Va,b by the usual method. We were unable to obtain the oxime of aldehyde IVc, since a strong electronegative substituent increases the –I effect of the α-carbon atom of the side chain; this facilitates nucleophilic attack but hinders the detachment of a hydroxide ion. Bands at 1700 cm^{-1} and bands of C=C, C=N, and N=N groups at 1500-1600 cm^{-1} and two bands of an NO$_2$ group at 1340 and 1520 cm^{-1} are observed in the IR spectra of IV. Signals of 2-H and 5-H protons of the pyrimidine ring at 9.5 and 8.9 ppm, a multiplet of aromatic protons at 7.7-8.6 ppm, and signals of protons of an aldehyde group at 10.2 ppm are present in the PMR spectra of these compounds.

The possibility of the preparation of various enamines as a result of transamination was demonstrated in the case of the reaction of enamine Ic with benzylamine.



VI

The reaction proceeds as a consequence of the fact that the resulting gaseous dimethylamine is readily removed from the reaction sphere, even though its basicity (pK_a 10.8) is greater than the basicity of the attacking benzylamine (pK_a 9.3).

Thus, new types of compounds of the pyrimidine series that are potential biologically active substances were obtained on the basis of reactive enamines.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CDCl$_3$ were recorded with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane (HMDS) as the external standard. The IR spectra of KBr pellets were recorded with a UR-20 spectrometer.

4-(2-Dimethylamino-1-phenylthiocarbamoylvinyl)pyrimidine (IIa). A mixture of 0.75 g (5 mmole) of pyrimidine Ia and 1.35 g (10 mmole) of phenyl isothiocyanate in 20 ml of absolute acetonitrile was refluxed for 3 h, after which the solution was evaporated *in vacuo*, and the residue was triturated in heptane. The solid product was removed by filtration to give 0.4 g (26%) of a product with mp 154-156°C (from methanol). IR spectrum: 1620, 1580 (C=C, C=N); 1110 cm^{-1} (NH—CS). PMR spectrum: 3.34 [6H, s, $(CH_3)_2$], 7.28 (1H, s, 5-H), 7.50-8.10 (6H, m, C_6H_5 and =CH—), 8.70 (1H, d, 4-H, J = 6 MHz), and 9.75 ppm (1H, s, 2-H). Found, %: C 63.4, H 5.7, N 19.8, S 11.3. $C_{16}H_{16}N_4S$. Calculated, %: C 63.3, H 5.7, N 19.7, S 11.3.

4-Methyl-6-(2-dimethylamino-1-phenylthiocarbamoylvinyl)pyrimidine (IIb). This compound was obtained in the same way as IIa. Workup of the reaction mixture gave 0.6 g (39%) of a product with mp 134-136°C (from methanol). IR spectrum: 1600, 1540 (C=C, C=N); 1110 cm^{-1} (NH—CS). PMR spectrum: 2.84 (3H, s, CH_3), 3.33 [6H, s, $(CH_3)_2$], 7.05 (1H, s, 5-H), 7.63-8.0 (6H, m, C_6H_5 and =CH—), and 9.23 ppm (1H, s, 2-H). Found, %: C 64.6, H 6.0, N 19.1, S 10.4. $C_{16}H_{18}N_4S$. Calculated, %: C 64.4, H 6.0, N 18.8, S 10.7.

General Method for the Preparation of Substituted Pyrimidinylacetaldehydes IVa-c. A solution of 6 mmole of sodium nitrite in 20 ml of water was added to a solution of 6 mmole of p-nitroaniline in 3 ml of concentrated HCl and 5 ml of water in such a way that the temperature of the reaction mixture did not exceed 0-5°C. A solution of 6 mmole of the enamine in 2 ml of concentrated HCl, and a saturated solution of sodium acetate (up to pH 6 of the mixture) were then added, and the resulting precipitate was removed by filtration, washed with water, dried, and crystallized from acetonitrile. Aldehydes IVa-c were yellow crystalline substances.

p-Nitrophenylazo-4-pyrimidinylacetaldehyde (IVa). This compound, with mp 197-198°C, was obtained in 77% yield. IR spectrum: 1700 (C=O); 1600, 1580 (C=C, C=N, N=N); 1510, 1330 cm^{-1} (NO_2). PMR spectrum: 7.55 (1H, s, —CH), 7.76-8.64 (4H, m, C_6H_4), 9.00 (1H, d, 5-H), 9.23 (1H, d, 4-H), 9.62 (1H, s, 2-H), and 10.00 ppm [1H, s, —C(O)H]. Found, %: C 51.3, H 3.4, N 27.0. $C_{12}H_9N_5O_3$. Calculated, %: C 51.0, H 3.5, N 27.0.

p-Nitrophenylazo-6-methyl-4-pyrimidinylacetaldehyde (IVb). This compound, with mp 195-196°C, was obtained in 82% yield. IR spectrum: 1700 (C=O); 1590 (C=C, C=N, N=N); 1520, 1340 cm^{-1} (NO_2). PMR spectrum: 3.03 (3H, s, CH_3), 7.43 (1H, s, CH), 7.73-8.66 (4H, m, C_6H_4), 8.90 (1H, s, 5-H), 9.50 (1H, s, 2-H), and 10.20 ppm [1H, s, —C(O)H]. Found, %: C 54.7, H 4.1, N 24.9. $C_{14}H_{12}N_5O_3$. Calculated, %: C 54.7, H 3.3, N 24.5.

p-Nitrophenylazo-5-nitro-2,6-dimethoxy-4-pyrimidinylacetaldehyde (IVc). This compound, with mp 209-210°C, was obtained in 33.5% yield. IR spectrum: 1640 (C=O), 1580 (C=C, C=N, N=N); 1540, 1340 cm^{-1} (NO_2). PMR spectrum: 4.02 (3H, s, 2-OCH_3), 4.07 (3H, s, 4-OCH_3), 5.51 (1H, s, CH), 7.33-8.24 (4H, m, C_6H_4), and 10.25 ppm [1H, s, —C(O)H]. Found, %: C 44.4, H 3.2, N 22.2. $C_{14}H_{12}N_6O_7$. Calculated, %: C 44.6, H 3.2, N 22.3.

p-Nitrophenylazo-4-pyrimidinylacetaldehyde Oxime (Va). A mixture of 0.1 g of aldehyde IVa, 0.1 g of hydroxylamine hydrochloride, 7 ml of alcohol, and 7 ml of pyridine was heated to the boiling point. The yellow precipitate that formed immediately was removed by filtration and washed with alcohol to give 0.1 g (100%) of a product with mp 262°C (from acetonitrile). Found, %: C 50.5, H 3.5, N 29.6. $C_{12}H_{10}N_6O_3$. Calculated, %: C 50.5, H 3.5, N 29.5.

p-Nitrophenylazo-6-methyl-4-pyrimidinylacetaldehyde Oxime (Vb). This compound, with mp 240-243°C (from DMF), was similarly obtained in 100% yield. Found, %: C 52.0, H 4.2, N 28.0. $C_{13}H_{12}N_6O_3$. Calculated, %: C 51.9, H 4.0, N 27.9.

5-Nitro-2,4-dimethoxy-6-(2-benzylaminovinyl)pyrimidine (VI). A mixture of 1.3 g (5 mmole) of enamine Ic, 1.3 g (10 mmole) of benzylamine, and a few crystals of iodine in 25 ml of absolute acetonitrile was refluxed for 4 h, after which the solution was evaporated to dryness *in vacuo*. The residue was dissolved in 2 ml of DMF, and this solution was poured into 50 ml of ice water. The resulting suspension was extracted with diethyl ether (two 50-ml portions), and the extract was dried over calcium chloride. The solvent was evaporated, and the residue was treated with 25 ml of hot ethyl acetate to give 0.5 g (31%) of enamine VI with mp 120-121°C (from CCl_4). Found, %: C 56.4, H 5.3, N 17.4. $C_{15}H_{16}N_4O_4$. Calculated, %: C 56.9, H 5.1, N 17.7.

LITERATURE CITED

1. L. P. Prikazchikova, B. M. Khutova, and V. M. Cherkasov, Khim. Geterotsikl. Soedin., No. 7, 974 (1982).
2. B. M. Khutova, L. P. Prikazchikova, and V. M. Cherkasov, Khim. Geterotsikl. Soedin., No. 4, 531 (1983).
3. A. D. Cross, Introduction to Practical Infrared Spectroscopy [Russian translation], Inostr. Lit., Moscow (1961), p. 103.