The 20*a*, 13, 9*a*, 1, 3, 18b, 10b, and 4 vibrations display variable distinctive character. For example, the 20*a*, 1, 3, and 4 vibrations are characteristic in the case of 2-monosubstitution [2] and noncharacteristic in the case of 5-substitution, while the 13, 9*a*, 18b, and 10b vibrations, which are noncharacteristic in the case of 2-substitution, become characteristic in 5-monopyrimidines. It is precisely owing to these vibrations that one can distinguish the spectra of 2- and 5-monosubstituted pyrimidines from one another. However, the most characteristic feature of the spectra of 5-monosubstituted pyrimidines is the absence in them of an intense band at ~980 cm^{-1} in the Raman spectra, which was validly pointed out in [4]. Another difference between the spectra of 5-monosubstituted pyrimidines and 2-monosubstituted pyrimidines is the appearance of an intense band at 1170 cm^{-1} in the IR spectra.

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SYNTHESIS OF 2,5'-BIPYRIMIDINES FROM SUBSTITUTED 5-CYANOPYRIMIDINES

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The Pinner method was applied to substituted 5-cyanopyrimidines to obtain 5-aminopyrimidines, which were condensed with acrolein derivatives to synthesize compounds that contain a 2,5-bipyrimidine fragment.

The study of biazines, of which 2,2'-bipyridine is of greatest interest [1], involves primarily their complexing properties [2]. Of the isomeric bipyrimidines, more study has been devoted to 2,2'-bipyrimidines (conformations [3] and complexes [4]) and substituted 4,5'-bipyrimidines as analogs of phleomycin [5] and dimers formed in the irradiation of DNA [6, 7]. The properties of all of the previously synthesized isomeric bipyrimidines, with the exception of the undescribed 2,5'-bipyrimidine system, were examined in [8, 9]. Japanese patent applications [10, 11] in which the use of 2',5-substituted 2,5'-bipyrimidines in liquid-crystal compositions was described were just published in 1986.

Continuing our research on the synthesis and study of the properties of pyrimidine derivatives [12] we have independently obtained a number of 2,5'-bipyrimidine derivatives. Their synthesis can be accomplished in conformity with the general principles of the construction of a pyrimidine ring from both 2- and 5-substituted pyrimidines. As starting compounds we used 5-cyanopyrimidines I [13], which were converted to amidines II; the latter were subsequently used to construct the pyrimidine ring.

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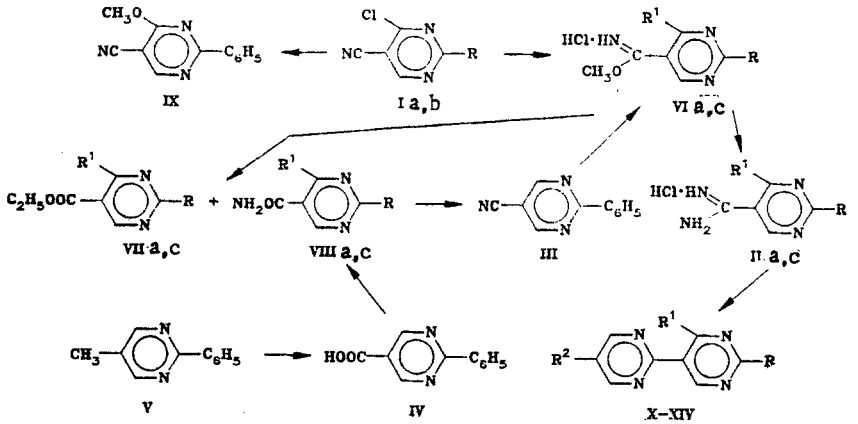
Only one example of obtaining 5-aminopyrimidine from unsubstituted 5-cyanopyrimidine by the Pinner method has been described [14]; the short time of the reaction of the cyanopyrimidine with alcohol (15 min, as compared with 24 h for benzonitriles [15]) and the incomplete conversion of the imino ester to the amidine on reaction with ammonia were unusual in this case.



I, II, VI—VIII, X—XII a,c R=C_6H_5; I, II, VI, XI b R=SCH_3; II, VI, X, XI a,b R^1=OCH_3; VII, VIII a R^1=OC_2H_5; II, VI—VIII, XI, XII c R^1=H; Xa R^2=H; XI a-c, XIII, XIV R^2=C_6H_5; XIIc R^2=C_5H_{11}; XIII R=R^1=OH; XIV R=R^1=Cl

The reductive dehalogenation of Ia under the conditions in [16, 17] led to a difficult-to-separate mixture of it with pyrimidine III, and the latter was therefore obtained from acid IV, which was synthesized by oxidation of methylpyrimidine V. It is interesting to note that the 5-alkyl group is usually not involved in the examples of the oxidation of alkylpyrimidines that are described in the literature [18, 19].

Mixtures of products due to subsequent transformations of imino esters VI, which apparently proceed readily not only when an ortho substituent is present (see [20]) but also in the absence of one, are formed in the synthesis of imino esters VI from nitriles I and III. The ester and amide (VII and VIII) of the corresponding acid, which became the preponderant reaction products when the reaction time was increased, were present in the mixture. Only 4-methoxy derivative IX was isolated in an attempt to obtain imino ester VIa from cyanopyrimidine Ia by the action of CH_3ONa/CH_3OH.

Using the Pinner method, from cyanopyrimidines I and III we obtained the corresponding imino esters VI, which were converted to amidines II by the action of NH_4Cl on their bases. By condensation of amidines II with acrolein derivatives we synthesized three- and four-ring systems with a 2,5'-bipyrimidine fragment (X-XII). In the case of XIb – by its conversion to dihydroxypyrimidine XIII and then to dichloropyrimidine XIV – we demonstrated a convenient method that opens up the possibility of obtaining various derivatives of this system.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions in $CDCl_3$ were recorded with a Varian A56/60A spectrometer with hexamethyldisiloxane as the internal standard. The molecular masses were determined with a Finnigan MAT-8200 high-resolution mass spectrometer.

5-Amidino-4-methoxy-2-methylthiopyrimidine Hydrochloride (IIb). A solution of 4.7 g (25 mmole) of nitrile Ib in 12 ml of absolute methanol and 7 ml of dry dioxane was saturated with HCl for 45 min, after which it was maintained at 20°C for 3 h. It was then cooled with ice to 0-5°C, and the precipitate was removed by filtration and washed with dry ether (five 20-ml portions) to give 4.5 g of imino ester hydrochloride VIb with mp 300-302°C. IR spectrum: 1630, 1680 cm^{-1}. The precipitated VIb was added with stirring in ~0.5-g portions to a mixture of 50 ml of chloroform and 15 ml of 10% NaOH solution. After 20 min the chloroform layer was separated, washed with water (three 20-ml portions), dried with $MgSO_4$, and evaporated. Methanol (15 ml) and 0.7 g of NH_4Cl were added to the oily residue of the base of the imino ester, and the mixture was refluxed for 2 h. It was then filtered, and the methanol was evaporated. The residue was triturated with 20 ml of dry ether to give 1.4 g (24%) of hydrochloride IIb with mp 230-240°C. IR spectrum: 1675 cm^{-1}. Found: M^+ 198.0577. $C_7 \cdot H_{10}N_4OS$. Calculated: M 198.0575.

5-Amidino-2-phenylpyrimidine Hydrochloride (IIc). A solution of 5.8 g (32 mmole) of nitrile III in 40 ml of dry dioxane and 15 ml of absolute alcohol was cooled to 0-5°C, and dry HCl was passed through it for 1 h. It was then allowed to stand at 20°C for 2-3 h, after which the solvents were removed by distillation. Dry ether (50 ml) was added to the residue, and the mixture was triturated. The precipitate was removed by filtration and washed with dry ether (three 20-ml portions) to give 7 g (83%) of imino ester hydrochloride VIc with mp 260-262°C. IR spectrum: 1650 cm^{-1} (broad). Found, %: C 59.7, H 5.0. $C_{13}H_{13}N_3O \cdot HCl$. Calculated, %: C 59.2, H 5.3. A 21.5-g sample of imino ester VIc was added in portions to a stirred mixture of 20 ml of 10% NaOH solution and 200 ml of chloroform, and the mixture was stirred for 30 min. The chloroform layer was separated, washed with water (three 20-ml portions), dried with $MgSO_4$, and evaporated. Water (5 ml), 70 ml of alcohol, and 5 g of NH_4Cl were added to the residue, and the mixture was refluxed for 1 h. The alcohol was then removed by distillation to two thirds of the original volume, and the precipitate was removed by filtration and washed with dry ether (three 30-ml portions) to give 10.6 g (53%) of amidine hydrochloride IIc with mp > 350°C. IR spectrum: 1420, 1590, 1690, 3370 cm^{-1}. Found, %: C 56.5, H 4.8, N 23.9; M^+ 198. $C_{11}H_{10}N_4 \cdot HCl$. Calculated, %: C 56.3, H 4.7, N 23.9; M_{base} 198.

5-Cyano-2-phenylpyrimidine (III). A mixture of 7.7 g (39 mmole) of amide VIIIc and 60 ml of $POCl_3$ was refluxed for 4 h, after which the excess $POCl_3$ was removed in the vacuum created by a water aspirator, and the residue was poured in small portions over 800 g of ice. The precipitate was removed by filtration and washed with water (five 30-ml portions) and alcohol (two 30-ml portions) to give 6.5 g (92%) of a product with mp 193-196°C and R_f 0.7 (Silufol UV-254, benzene). IR spectrum: 2225 cm^{-1} (CN). Found, %: C 72.9, H 3.9, N 23.2%. $C_{11}H_7N_3$. Calculated, %: C 72.9, H 3.9, N 23.2%.

2-Phenylpyrimidine-5-carboxylic Acid (IV). A 45-g sample of $KMnO_4$ was added with vigorous stirring in portions in the course of 5 h to a heated (to 100°C) solution of 15 g (88 mmole) of methylpyrimidine V [21] in 1.5 liters of water, after which the mixture was stirred at 100°C for 5 h. It was then cooled to 20°C, and the precipitated MnO_2 and unchanged pyrimidine V were removed by filtration and washed with hot water (two 50-ml portions) and 50 ml of warm chloroform. The aqueous solutions were combined and extracted with chloroform (two 75-ml portions), and the chloroform was removed from the combined chloroform solutions by distillation to give 7 g of starting pyrimidine V. The aqueous filtrates were acidified with 20% HCl to pH 3-4, and acid IV was removed by filtration to give 5 g (54%) of a product with mp 273°C (from alcohol). IR spectrum: 1690 cm^{-1}. Found: M^+ 200.0576. $C_{11}H_8N_2O_2$. Calculated: M 200.0586.

5-Ethoxycarbonyl-2-phenylpyrimidine (VIIc). A) A mixture of 0.5 g (0.25 mmole) of acid IV, 8 ml of alcohol, and 1 ml of concentrated HCl was refluxed for 4 h, after which it was cooled to 20°C, and the precipitate was removed by filtration to give a substance with mp 79-82°C. It was purified with a column packed with silica gel [elution with benzene–$CHCl_3$ (1:1)] to give 0.25 g (44%) of ester VIIc with mp 93-95°C. IR spectrum: 1720 cm^{-1}. Found, %: C 68.4, H 5.3, N 12.2; M^+ 228. $C_{13}H_{12}N_2O_2$. Calculated, %: C 68.4, H 5.3, N 12.3; M 228.

B) Hydrogen chloride gas (12 g, from the increase in weight) was passed into a suspension of 3.7 g (20 mmole) of nitrile III in 60 ml of alcohol with stirring and cooling to 5°C in the course of 4 h, after which 20 ml of absolute benzene was added, and the mixture was stirred at room temperature for 4 days. The unchanged nitrile III (1.75 g) was then removed by filtration, and the filtrate was evaporated with a rotary evaporator. The residue was triturated with 10 ml of dry ether to give 1.99 g (81% based on the nitrile used in the reaction) of ester VIIc with mp 80-83°C. The IR spectra of the samples obtained by methods A and B were identical.

Reaction of Nitrile Ia with Alcohol and HCl. Hydrogen chloride gas was passed for 4 h into an ice-cooled suspension of 4.3 g (20 mmole) of nitrile Ia in 80 ml of absolute alcohol, after which the resulting solution was allowed to stand overnight in a refrigerator. The alcohol was removed by distillation, and 70 ml of alcohol saturated with ammonia was added to the dry residue [6.3 g, IR spectrum: 1700 (broad), 1730 cm^{-1}]. The mixture was stirred for 5 h at 20°C, and the precipitate was removed by filtration and washed with alcohol (two 30-ml portions) and ether (two 30-ml portions) to give 1.93 g of 5-carbamoyl-4-ethoxy-2-phenylpyrimidine (VIIIa). The filtrates were evaporated, and the residue was washed with ether (four 25-ml portions) to give another 1 g of amide VIIIa for an overall yield of 2.93 g (60%). The product had mp 194-197°C. IR spectrum: 1690, 3300, 3350, 3475 cm^{-1}. Found, %: N 17.0;

M^+ 243. $C_{13}H_{13}N_3O_2$. Calculated, %: N 17.2; M 243. The ether solutions were evaporated, and the residue was passed through a column packed with silica gel (elution with $CHCl_3$) to give 0.74 g of 5-ethoxycarbonyl-4-ethoxy-2-phenylpyrimidine (VIIa) with mp 50-52°C. IR spectrum: 1730 cm^{-1}. M^+ 272. According to the data in [22], this compound had mp 58-59°C.

5-Carbamoyl-2-phenylpyrimidine (VIIIc). A mixture of 10 g (50 mmole) of acid IV, 50 ml of dry benzene, and 30 ml of thionyl chloride was refluxed for 3 h, after which it was cooled to 20°C, and the precipitate was removed by filtration and washed with dry ether (two 20-ml portions) to give 10 g of acid chloride IV with mp 180-182°C. The acid chloride was added in portions with stirring to 30 ml of concentrated NH_4OH, and the mixture was stirred for another 2 h. The precipitated amide VIIIc was removed by filtration and washed successively with water (until the wash water was neutral), 30 ml of alcohol, and 20 ml of ether to give 7.7 g (85%) of a product with mp 260-263°C. IR spectrum: 1690, 3160, 3340 cm^{-1}. Found, %: C 66.2, H 4.6, N 21.2. $C_{11}H_9N_3O$. Calculated, %: C 66.4, H 4.5, N 21.1.

4-Methoxy-5-cyano-2-phenylpyrimidine (IX). A mixture of 0.52 g (2.32 mmole) of pyrimidine Ia, 0.14 g (2.5 mmole) of sodium methoxide, and 10 ml of methanol was refluxed for 4 h, after which it was cooled, and the precipitate was removed by filtration and washed successively with water (two 5-ml portions) and methanol (two 5-ml portions) to give 0.31 g (63%) of methoxy derivative IX with mp 137-139°C (from methanol). IR spectrum: 2230 cm^{-1}. Found, %: C 67.6, H 4.2, N 19.8; M^+ 211. $C_{12}H_9N_3O$. Calculated, %: C 68.2, H 4.3, N 19.9; M 211.

4'-Methoxy-2'-phenyl-2,5'-bipyrimidine (Xa). A mixture of 4 g (18.5 mmole) of nitrile Ia, 20 ml of dry dioxane, and 5 ml of absolute methanol was saturated with HCl while cooling with ice in the course of 30 min, after which the mixture was maintained at 20°C for 1.5 h. The precipitated imino ester VIa was removed by filtration and washed with dry ether (two 50-ml portions) to give a product with mp 190-200°C. The action of 10% NaOH, as in the isolation of the base from salt VIb, then gave the base of imino ester VIa. The base (2.5 g) was refluxed with 0.9 g of NH_4Cl in 30 ml of alcohol for 2.5 h, after which the alcohol was removed by distillation, 20 ml of dry ether was added to the residue, and amidine IIa was removed by filtration to give 2.1 g (78%) of a product with mp 275-280°C. IR spectrum: 1680 cm^{-1}. A mixture of 1.2 g (5 mmole) of amidine IIa, 1 ml (10 mmole) of 3-ethoxyacrolein, and 0.27 g (5 mmole) of $NaOCH_3$ in 10 ml of absolute alcohol was refluxed for 2 h, after which it was cooled, and the precipitate was removed by filtration and washed with 5 ml of water and alcohol (two 2-ml portions) to give 0.1 g (7%) of bipyrimidine Xa with mp 228-231°C (from alcohol–dioxane). Found, %: C 67.4, H 4.4, N 21.1. $C_{15}H_{12}N_4O$. Calculated, %: C 68.2, H 4.6, N 21.2.

4'-Methoxy-2',5-diphenyl-2,5'-bipyrimidine (XIa). A 1.6-g (5.3 mmole) sample of 1,3-bis(dimethylamino)-2-phenylpropene perchlorate (XV) [23] was added to a mixture of 1 g (3.8 mmole) of amidine IIa and 0.54 g of $NaOCH_3$ in 25 ml of absolute methanol, and the mixture was refluxed for 2 h. It was then cooled to 20°C, and the precipitate was removed by filtration and washed successively with water (two 30-ml portions), 10 ml of alcohol, and ether (two 10-ml portions) to give 1.05 g (81%) of a product with mp 210-212°C. PMR spectrum: 4.24 (3H, s, CH_3), 7.30-7.67 (8H, m, aromatic H), 8.46-8.70 (2H, m, aromatic o-H'), 9.12 (2H, s, pyrimidine 4,6-H), and 9.35 ppm (1H, s, pyrimidine 4'-H). Found, %: C 73.7, H 4.8, N 16.1. $C_{21}H_{16}N_4O$. Calculated, %: C 74.1, H 4.7, N 16.5.

4'-Methoxy-2'-methylthio-5-phenyl-2,5'-bipyrimidine (XIb). A mixture of 3.85 g (16.4 mmole) of amidine IIb, 5.75 g (16.4 mmole) of salt XV, and 0.75 g (32.8 mmole) of CH_3ONa in 25 ml of absolute methanol was refluxed for 3 h, after which it was cooled to 20°C, and the precipitate was removed by filtration and washed with water (two 20-ml portions) and 10 ml of alcohol to give 2.75 g (50%) of a product with mp 140-141.5°C (from alcohol–dioxane). PMR spectrum: 2.62 (3H, s, SCH_3), 4.13 (3H, s, OCH_3), 7.35-7.70 (5H, m, aromatic H), and 9.10 ppm (3H, s, pyrimidine 4,4',6-H). Found, %: C 61.7, H 4.5, N 17.9. $C_{16}H_{14}N_4OS$. Calculated, %: C 61.9, H 4.5, N 18.1.

2',5-Diphenyl-2,5'-bipyrimidine (XIc). A mixture of 0.92 g (4 mmole) of amidine IIc, 1.6 g (5 mmole) of salt XV, and 0.54 g (10 mmole) of CH_3ONa in 25 ml of methanol was refluxed for 1 h, after which it was cooled, and the precipitate was removed by filtration and washed with methanol (two 30-ml portions) to give 1 g (80%) of pyrimidine XIc with mp 292-293°C (from dimethylacetamide). Found, %: C 77.2, H 4.4, N 18.2. $C_{20}H_{14}N_4$. Calculated, %: C 77.4, H 4.5, N 18.1.

5-Amyl-2'-phenyl-2,5'-bipyrimidine (XIIc). A mixture of 1.2 g (5 mmole) of amidine IIc, 1.69 g (10 mmole) of 2-amyl-3-dimethylaminoacrolein, and 0.4 g (10 mmole) of NaOH in 10 ml of methanol was refluxed for 2 h, after which it was cooled to 20°C, and the precipitate was removed by filtration and chromatographed with a column packed with silica gel [elution with $CHCl_3$–ethyl acetate (10:2)] to give 0.5 g (31%) of pyrimidine XIIc with mp 165-170°C (from alcohol). Found, %: C 75.1, H 6.8, N 18.6. $C_{19}H_{20}N_4$. Calculated, %: C 75.0, H 6.6, N 18.4.

2',4'-Dihydroxy-5-phenyl-2,5'-bipyrimidine (XIII). A mixture of 1.7 g (5.5 mmole) of pyrimidine XIb and 25 ml of concentrated HCl was refluxed for 3 h, after which it was cooled to 20°C, and the precipitate was removed by filtration and washed with water (four 20-ml portions) to give 1.4 g (95%) of pyrimidine XIII with mp > 360°C. Found: M^+ 266.0801. $C_{14}H_{20} \cdot N_4O_2$. Calculated: M 266.0804.

2',4'-Dichloro-5-phenyl-2,5'-bipyrimidine (XIV). A mixture of 1.4 g (5.3 mmole) of pyrimidine XIII, 20 ml of $POCl_3$, and 2 ml of dimethylaniline was refluxed for 5 h, after which the excess of $POCl_3$ was removed by distillation in the vacuum created by a water aspirator, and the residue was poured over ice. The precipitate was removed by filtration and purified by chromatography on silica gel by elution with chloroform to give 1.3 g (81%) of pyrimidine XIV with mp 170°C (from alcohol). Found, %: C 55.6, H 2.6, Cl 23.5, N 18.3. $C_{14}H_8Cl_2N_4$. Calculated, %: C 55.4, H 2.6, Cl 23.4, N 18.5.

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