SYNTHESIS OF ISOMERIC AMINOPHENYLBIPYRIMIDINES AND STUDY OF THE LIQUID CRYSTALLINE PROPERTIES OF ANILS STRUCTURALLY RELATED TO AMINOPHENYLPYRIMIDINES

M. A. Mikhaleva, G. A. Igonina, A. I. Shadrina, V. P. Borovik, and V. P. Mamaev*

5-Amino-2,5'bipyrimidines and bis-(5-aminopyrimidinyl-2)-p-phenylenes have been synthesized as well as isomeric bis-(p-aminophenyl)pyrimidines. From these, substituted benzylidenamino derivatives have been prepared and their liquid crystalline properties studied.

2,5-Disubstituted aminoarylpyrimidines with various relative arrangements of the structural units are of interest as precursors in new synthetic developments and have, for example, been used in the synthesis of dichroic azo dyes [1, 2], Schiff base liquid crystals [3], and polymers [4].

In the present work, we have synthesized 5-aminopyrimidines containing 2,5'-bipyrimidine (I) and bis(pyrimidine-2)-p-phenylene (II) moieties, their Schiff bases, IIIa, b, as well as Schiff bases structurally related to isomeric bis(p-aminophenyl)-pyrimidines IIIc-f, the liquid crystalline properties of which are discussed.

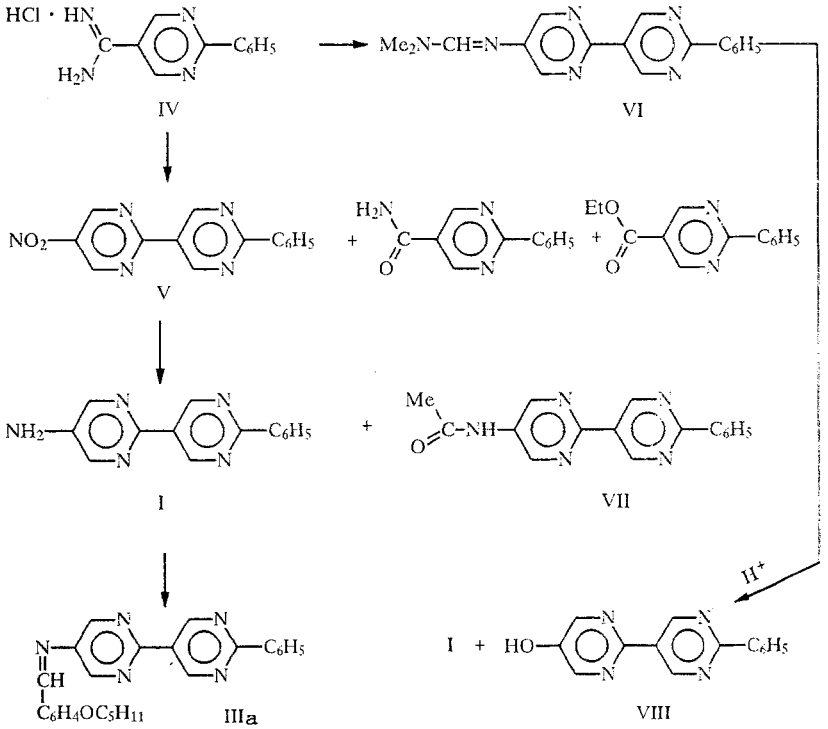

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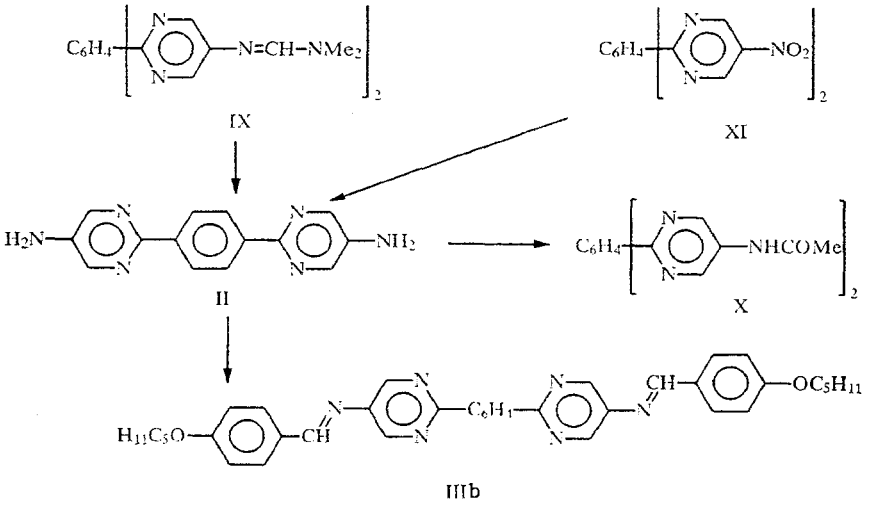
TABLE 1. Characteristics of Synthesized Compounds I-III, V-VII, X, and XI

Compound	Molecular formula	T_{mp} or $T_{mesophase}$, °C (solvent for recrystallization)	Yield, %
I	$C_{14}H_{11}N_5$	213...215 (DMF/alcohol) (2:1)	35*
II	$C_{14}H_{12}N_6 \cdot C_2H_6O_2$	348...350 (ethyl Cellosolve)	99*
IIIa	$C_{26}H_{25}N_5O$	184 S_1 320 S_2 327 N 329 I (DMF–alcohol, 1:1)	60
IIIb	$C_{38}H_{40}N_6O_2$	258 S_1 274 S_2 360 I (DMF)	15
IIIc	$C_{40}H_{42}N_4O_2$	185 S_1 235 S_2 360 I (DMF)	94
IIId	$C_{40}H_{42}N_4O_4$	185 S_1 300 S_2 320 decomp. I (DMF)	83
IIIe	$C_{40}H_{42}N_4O_2$	201...203 (DMF)	51
IIIf	$C_{40}H_{42}N_4O_2$	230...232 (DMF)	45
V	$C_{14}H_9N_5O_2$	345...345.5 (DMSO)	28
VI	$C_{17}H_{16}N_6$	232...233 (alcohol/dimethylacetamide)	50
VII	$C_{16}H_{13}N_5O$	340...345 (dimethylacetamide)	39
X	$C_{18}H_{16}N_6O_2$	>350	86
XI	$C_{14}H_8N_6O_4$	342...343 (DMF)	67

*By procedure A.

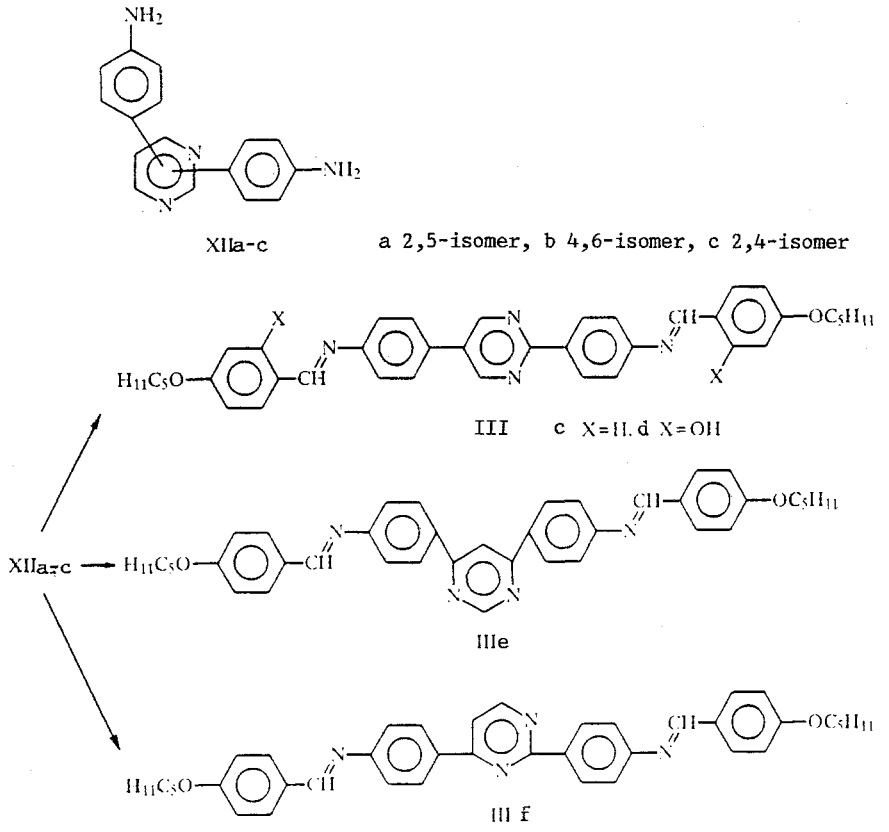
There are two methods of practical value for the synthesis of 5-aminopyrimidines, the reduction of 5-nitro derivatives [3, 5] and the hydrolysis of 5-dimethylaminomethyleneaminopyrimidine [6, 7]. As precursors of the aminobipyrimidines I we prepared nitrobipyrimidine V and methyleneamino derivative VI by condensation of amidine IV [8] with the Na salt of nitromalondialdehyde or the perchlorate of 2-dimethylaminomethyleneamino-3-dimethylaminopropene, respectively. The synthesis of nitro derivative V took place in low yield with the formation of the amide and ester of 2-phenylpyrimidine-5-carboxylic acid as by-products (see [8]). The reduction of compound V with Fe/CH_3COOH led to a mixture of amine I and its acetyl derivative, VII. In turn, the acid hydrolysis of acetyl derivative VII gave the corresponding 5-hydroxypyrimidine VIII along with aminopyrimidine I in the form of a difficultly separable mixture analogous to the previously studied conversion of 5-aminopyrimidines in acidic media [7]. Thus, according to the process discussed, the yield of compound I was low because of the occurrence of side reactions. Contrariwise, the alkaline hydrolysis of derivative VI gave pure aminobipyrimidine I in satisfactory yield. On hydrolysis in acidic media, this same derivative VI is converted into hydroxypyrimidine VIII according to [7].



To synthesize diamine II we used an analogous scheme with derivative IX as the precursor. On hydrolysis of methyleneamino derivative IX with base in Ethyl Cellosolve, amine II was isolated from the reaction mixture as a solvate with ethylene glycol, which was apparently formed from the solvent under the reaction conditions, and was further characterized as acetyl derivative X. Diamine II was also prepared by the reduction of dinitro compound XI.

From prepared amines, I and II, and the previously synthesized diamines of isomeric diphenylpyrimidines XII [9-11], we prepared Schiff bases IIIa-f, studied their liquid crystalline properties, and considered the effect of structure on mesomorphism.

Derivative IIIa and di-Schiff bases IIIb-d display high-temperature smectic polymorphism with a wide mesophase range (100-175°C), anil IIIa having a narrow nematic range, anils IIIa, c, d have the same transition temperature to the liquid crystalline state, but the mesophase of compound IIIc has a higher thermal stability, because of which it is found to have the mesophase with the greatest temperature range. The introduction of a salicylidene group, often used to stabilize Schiff bases [12], did not change the melting point in the case of anil IIId compared to anil IIIc, but did narrow somewhat the mesophase range in derivative IIId by lowering its thermal stability. It is known that the presence of VVS in salicylideneanilines leads to a decrease in the angle of rotation of the N-phenyl groups [13], and flatter molecules give denser packing in the mesophase, increasing the intermolecular interaction [14]. Probably the presence of the pyrimidine ring in molecule IIId in this case increases the repulsion forces and lowers the thermal stability of the mesophase. Schiff bases IIIe, f, isomers of IIIb, do not display liquid crystalline properties.



EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer in KBr pellets. The PMR spectra were recorded on a Varian A-56/60A spectrometer in DMSO-D_6, HMS internal standard. Phase transition temperatures were determined on a Boethiusminiature heating column with an RNMK-0.5 visual attachment; abbreviations: N) nematic, S) smectic; I) isotropic mesophases. Molecular masses were determined mass spectrometrically on a high-resolution Finnegan MAT-8200. The TLC was done on Silufol UV-254 plates with 10:1 $CHCl_3$/alcohol.

5-Amino-(I) and 5-Acetylamino-(VII)-2'-phenyl-2,5'-bipyrimidines. A. Boil a mixture of 1.6 g (5.75 mmoles) of nitrobipyrimidine V and 1 g of iron powder in 50 ml of acetic acid for 6 h. After cooling to 20°C, filter off the precipitate, wash it with acetic acid, water, alcohol, and ether, and dry it to obtain 0.65 g of derivative VII. IR spectrum: 1670 (C=O), 3290 cm^{-1} (NH). R_f 0.39. Pour the filtrate into water, filter off the precipitate that forms, wash it with water, alcohol, and ether, and dry it to obtain 0.5 g of amine I. IR spectrum: 1630, 3230, 3340, 3420 cm^{-1} (N–H). R_f 0.25.

B. To a mixture of 0.47 g (1.5 mmoles) of pyrimidine and 10 ml of Ethyl Cellosolve add 5 ml of 10% KOH solution and boil for 2 h. Pour the resultant solution into 20 ml of water, neutralize with dilute HCl, and filter off the precipitate. After recrystallization, obtain 0.3 g (76%) of amine I.

C. To a mixture of 2.5 ml of concentrated HCl and 2.5 ml of CH_3COOH add 0.4 g (1.37 mmoles) of acetylamine VII and boil for 1.5 h. Filter off the precipitate forming when the reaction mixture is cooled to 20°C and wash it with water to obtain 0.2 g of a material in which, according to TLC, there are compounds with a dark violet and a bright blue fluorescence. Mass spectrometry shows the mixture to contain the acetyl derivative VII (M^+ 291.1136), aminopyrimidine I (M^+ 249.1020), and 5-hydroxy-2′-phenyl-2,5′-bipyrimidine (VIII, M^+ 250.0864).

1,4-Bis(5-aminopyrimidinyl-2)benzene (II). A. Boil a mixture of 2 g (5.3 mmoles) of derivative IX [15] and 20 ml of 10% KOH solution in 40 ml of Methyl Cellosolve for 5 h. Cool the mixture to 20°C, filter off the precipitate that forms, wash it with water, and recrystallize it to obtain 1.73 g of diamine II containing a molecule of ethylene glycol. IR spectrum: 1630, 3200, 3320, 3460 cm^{-1} (N−H). PMR spectrum: 8.25 (8H, m, H_{arom} + 4,6-H of pyrimidine ring), 5.63 (4H, br.s, NH_2), 3.33 ppm (CH_2OH). M^+ 264.

B. Boil a mixture of 2.52 g (7.8 mmoles) of dinitropyrimidine XI, 0.26 g (16 mmoles) of reduced iron, and 2.5 ml of acetic acid in 100 ml of alcohol for 12 h with stirring. Cool the mixture to 20°C and pour it into 100 ml of water. Filter off the precipitate, wash it with water and alcohol, and dry it to obtain 1.67 g (81%) of diaminopyrimidine II. T_{mp} > 350°C (DMF). M^+ 264.

5-(p-Amyloxybenzylidineamino)-2′-phenyl-2,5′-bipyrimidine (IIIa). Heat a mixture of 0.3 g (1.2 mmoles) of aminobipyrimidine I and 0.16 g (1.2 mmoles) of p-amyloxybenzaldehyde in 12 ml of DMF for 9 h at 130-135°C. Cool the mixture to 20°C, filter off the yellow precipitate, wash it with water, and dry it to obtain 0.3 g of anil IIIa. M^+ 423.

1,4-Bis[5-(p-amyloxybenzylidineamino)pyrimidinyl-2]benzene (IIIb). Heat a mixture of 2.3 g (8.7 mmoles) of amine II, 3.35 g (17.4 mmoles) of p-amyloxybenzaldehyde, and 50 ml of DMF for 30 h at 120°C with stirring. Cool the reaction mixture to 20°C, filter off the precipitate, and wash it with ether to obtain 0.45 g of derivative IIIb. Pour the filtrate into water, filter off the precipitate, and recrystallize it twice from DMF to obtain an additional amount of anil IIIb. Total yield of anil IIIb, 0.78 g.

2,5-Bis(p-amyloxybenzylidine-p-aminophenyl)pyrimidine (IIIc). Dissolve 3 g (11.5 mmoles) of diamine XIIa [9] in 20 ml of DMF, add a solution of 4.6 g (24 mmoles) of p-amyloxybenzaldehyde in 10 ml of DMF, and heat the reaction mixture for 7 h at 120°C with stirring. Cool the mixture to 20°C, filter off the precipitate, wash it with DMF (2 × 7 ml), alcohol (2 × 15 ml), and ether (15 ml) to obtain 5.5 g of anil IIIc. Dilute the filtrate with the washings to obtain an additional amount of compound IIIc. Total yield of anil IIIc, 6.6 g.

2,5-Bis(p-amyloxybenzylidine-p-aminophenyl)pyrimidine (IIId), 4,6-bis(p-amyloxybenzylidine-p-aminophenyl)-pyrimidine (IIIe), and 2,4-bis(p-amyloxybenzylidine-p-aminophenyl)pyrimidine (IIIf) are obtained in a manner similar to IIIc from p-amyloxy-(o-hydroxy)benzaldehyde and diamines XIIa, XIIb [10], and XIIc [11], respectively.

5-Nitro-2′-phenyl-2,5′-bipyrimidine (V). To a solution of 2.34 g (10 mmoles) of amidine hydrochloride IV in a mixture of 25 ml of alcohol and 75 ml of dioxane add a solution of 1.57 g (10 mmoles) of the sodium salt of nitromalondialdehyde, and 4 drops of piperidine, and stir for 3 h at 20°C. Filter off the precipitate, wash it with water (3 × 10 ml) and alcohol (3 × 10 ml), and dry it to obtain 0.80 g of bipyrimidine V. IR spectrum: 1350, 1590 cm^{-1} (NO_2). Evaporate the filtrate under vacuum and extract the residue with 30 ml of $CHCl_3$ to obtain 0.82 g (41%) of the amide of 2-phenylpyrimidine-5-carboxylic acid [8]. Pass the chloroform solution through a layer of Al_2O_3 and then through a column of silica gel using $CHCl_3$/benzene to obtain 0.15 g (17%) of the ethyl ester of 2-phenylpyrimidine-5-carboxylic acid ($C_{13}H_{12}N_2O_2$). T_{mp} 93-95°C. IR spectrum: 1730 cm^{-1} (C=O).

5-Dimethylaminomethyleneamino-2′-phenyl-2,5′-bipyrimidine (VI). Dissolve 0.46 g (2 mmoles) of amidine hydrochloride IV, 0.75 g (3 mmoles) of the monoperchlorate of 2-dimethylaminomethyleneamino-3-dimethylaminopropene and 0.27 g (5 mmoles) of sodium methoxide in 10 ml of methanol, boil the solution for 1 h, filter off the precipitate, and wash it with water, alcohol, and ether to obtain 0.3 g of pyrimidine VI. IR spectrum: 1640 cm^{-1} (CH=N).

5-Hydroxy-2′-phenyl-2,5′-bipyrimidine (VIII). Boil a mixture of 0.5 g (1.6 mmoles) of pyrimidine VI, 8 ml of water, and 0.8 ml of concentrated H_2SO_4 for 2 h, filter off the precipitate, and wash it with water. According to TLC, this is a mixture of amino-I (R_f 0.25, bright blue fluorescence) and hydroxy derivative VIII (R_f 0.34, dark violet fluorescence). Dissolve the crude product in alcohol and freeze it in the freezing compartment of a refrigerator to obtain hydroxpyrimidine VIII (free of any amino derivative according to the mass spectrum). T_{mp} 202-205°C. Found: M^+ 250.0864. $C_{14}H_{19}N_4O$. Calculated: M 250.0854.

1,4-Bis(5-acetylaminopyrimidinyl-2)benzene (X). Boil a suspension of 0.16 g (0.6 mmole) of diamine IIc in 10 ml of acetic anhydride for 2 h. Cool the mixture to 20°C, filter off the precipitate, wash it with water and dry it to obtain 0.18 g of compound X. IR spectrum: 1680 (C=O), 3280 cm^{-1} (NH). PMR spectrum: 2.1 (6H, s, CH_3), 8.40 (4H, s, H_{arom}), 9.07 (4H, s, pyrimidine ring H), 10.40 ppm (2H, s, N–H).

1,4-Bis(5-nitropyrimidinyl-2)benzene (XI). Heat a suspension of 2 g (8.5 mmoles) of terephthalic diamide hydrochloride in 30 ml of 50% alcohol to 50°C and add a solution of 2.66 g (1.7 mmoles) of the sodium salt of nitromalondialdehyde in 40 ml of water and 2 ml of piperidine. Stir the mixture for 1 h at 20°C, filter off the precipitate, wash it with water and alcohol, and dry it to obtain 1.86 g of nitro derivative XI. IR spectrum: 1360, 1590 cm^{-1} (NO_2). R_f 0.20 (20:1 $CHCl_3$/alcohol eluent).

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