Chemistry of Heterocyclic Compounds, Vol.35, No. 3, 1999

SYNTHESIS AND MESOMORPHIC PROPERTIES OF *trans*-[1,4-BIS(5-R-PYRIMIDIN-2-YL]-CYCLOHEXANES AND 1,2-BIS-(5-R-PYRIMIDIN-2-YL)ETHANES

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New trans-bis(5-R-pyrimidin-2-yl)-1,4-cyclohexanes and -1,2-ethanes (R = C_7H_{15}, $C_6H_4OR^1$, *where* R^1 = *H,* $COCH_3$, C_4H_9, C_5H_{11}, C_8H_{17}*) have been synthesized. Only nematic mesophases are found from a study of their mesomorphic properties, except for bis[5-(4-octyloxyphenyl)- and -(4-acetoxyphenyl)pyrimidin-2-yl]-cyclohexanes, which also exhibit smectic properties.*

The choice of molecular fragments is very important for studying the dependence of the mesogenic properties of liquid crystals on their chemical structure. Thus, various combinations of saturated and aromatic cyclic systems, introduction of flexible bridges in the molecules, are effective in reducing the viscosity and thermal transitions and in increasing the nematogenicity [1, 2]. Among the mesomorphic derivatives of pyrimidine, 5,5'-disubstituted bis(pyrimidin-2-yl)benzenes are stable liquid crystals with a high refractive anisotropy and low viscosity. Thus, they are used as components of mesomorphic mixtures for enhancing the sharpness and contract of displayed images [3]. The influence of the nature and length of the terminal substituents on the nematogenic behavior of these compounds has also been studied [4].

In the present work we synthesized *trans*-1,4-bis(5-R-pyrimidin-2-yl)cyclohexanes (I and IIa-e) and 1,2-bis(5-R-pyrimidin-2-yl)ethanes (IIIa-d) and studied their mesomorphic behavior.

Cyclohexane derivatives I and II were prepared by condensation of the dihydrochloride of *trans*-cyclohexane-1,4-dicarboxylic acid diamidine (IVa) [5] with 2-heptyl-3-dimethylaminoacrolein (V) or 2-(*p*-hydroxyphenyl)-3-dimethylaminopropenylidenedimethylamine (VI) perchlorate with subsequent alkylation or acylation of the phenolic hydroxyl group of IIa.

The starting *trans*-1,4-dicyanocyclohexane (VIIa), which is necessary for the synthesis of the bisamidine IVa, was prepared from a commercial mixture of the *cis* and *trans* isomers of the dimethyl ester of cyclohexane-1,4-dicarboxylic acid. The *trans* isomer was isolated from this mixture using the literature method [6]. It was converted to the corresponding *trans*-diamide by reaction with concentrated ammonia. The *trans* isomer was also prepared by thermal isomerization of a mixture of *cis*- and *trans*-diamides of cyclohexane-1,4-dicarboxylic acid [7], successive conversions [5, 7] of which *via* formation of dinitrile VIIa and bisiminomethyl ester VIIIa yielded the key diamidine dihydrochloride IVa.

The synthesized *trans*-1,4-bis(5-heptylpyrimidin-2-yl)cyclohexane (I) is a structural analog of the nematic 1,4-bis(5-heptylpyrimidin-2-yl)benzene [4] and *trans*-1,4-bis(*p*-heptylphenyl)cyclohexane [8], which has a plastic mesophase. Heating in polarized light did not unambiguously resolve the question of whether it has mesomorphic properties. However, additional investigations on the heats of phase transitions in a Setaram DSC-111 scanning calorimeter indicated that I is not mesomorphic. It undergoes a crystalline transition at 40.5°C with ΔH = 4.01 kcal/mol and then changes to an isotropic state with ΔH = 3.67 kcal/mol.*

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*Research performed at NIOPIK.

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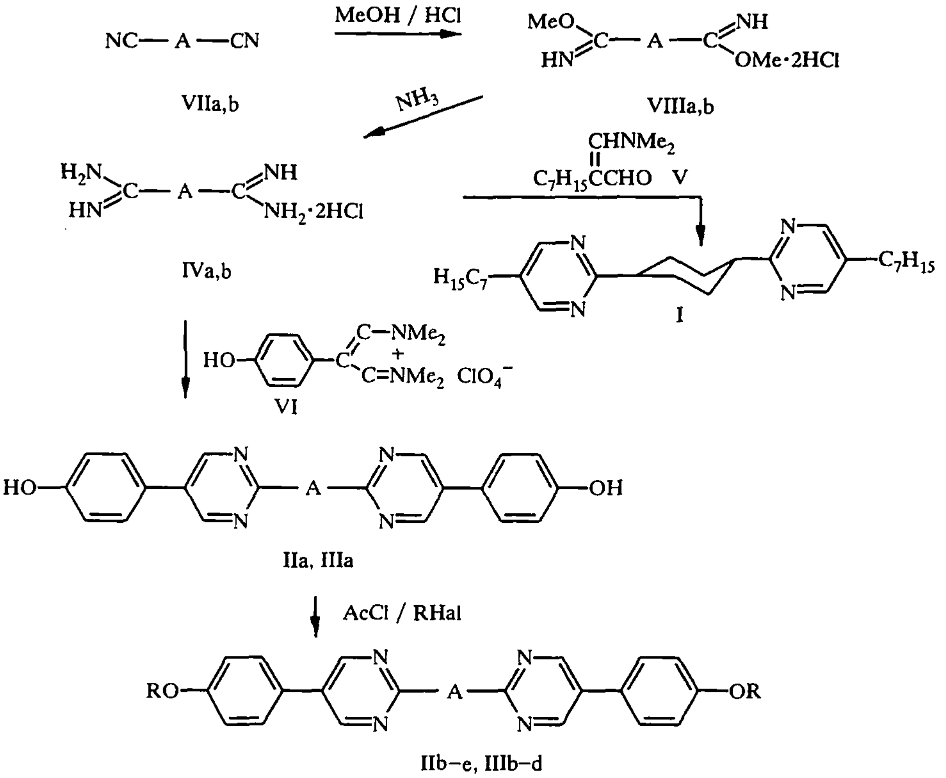
0009-3122/99/3503-0310$22.00©1999 KluwerAcademic/Plenum Publishers



IIa-e, IVa, VIIa, VIIIa A = –*trans*-1,4-C_6H_{10}–; IIIa-d, IVb, VIIb, VIIIb A = –CH_2CH_2–;
IIb R = COMe; IIc, IIIb R = C_4H_9; IId, IIIc R = C_5H_{11}; IIe, IIId R = C_8H_{17}

This result is caused by both the reduced stability of the layered mesophase on going from terphenyl derivatives (smectic) to bis(pyrimidin-2-yl)benzene derivatives (nematic) [4] and the additional unfavorable influence of introduction of *trans*-cyclohexane fragment instead of a planar phenyl one [9] between the pyrimidine rings. Similar destabilization of the mesophase is observed when comparing the mesomorphic properties of nematic 1,4-bis(5-octyloxypyrimidin-2-yl)benzene (N-I transition at 210°C [4]) and *trans*-1,4-bis(5-octyloxypyrimidin-2-yl)cyclohexane (N-I at 135°C [5]).

Going from the three-ring structure of I to the more optimal five-ring structure of II led to the occurrence of mesomorphic properties for the latter type compounds. The elongated biaryl fragments in the molecular structure of II naturally caused the increase of the temperature of the mesomorphic transitions. However, even the presence of central cyclohexane ring between these fragments did not promote the appearance of the smectic properties characteristic of cyclohexane derivatives. This bears witness of its destabilizing effect on the mesophase [10] in these systems. A less ordered nematic mesophase is characteristic of all pyrimidinylcyclohexanes II. Only compound IIb and IIe exhibit a smectic mesophase. In particular, the dibutoxy derivative IIc, in contrast with its analog 1,4-bis[5-(*p*-butyloxyphenyl)pyrimidin-2-yl]benzene [4], which is smectogenic, has only nematic mesophase with a decreased by ~50°C transition temperature to the mesophase.

Lengthening the alkyl chain of the terminal group in IIc-e causes smectic and nematic mesophases to appear (for IIe) and the melting point to be successively lowered. Compounds IIb and IIc decompose on heating to 300°C, without converting to isotropic melt; IId, with N-I transition.

Analogs of cyclohexane derivatives II described above were synthesized analogously starting with succinic dinitrile (VIIb). These four-ring derivatives of ethane IIIa-d, which belong to a class of dimesogens, i.e., compounds that contain two mesogenic fragments joined through the ends of a flexible central link, were also investigated.

The key amidine IVb was prepared from bisiminoester of succinic acid VIII [11] by treatment with ammonia. However, according to the literature [11, 12], the reaction in the stage of formation of VIIIb in both acidic and basic media is complicated by its conversion to cyclic iminoester with splitting off the alcohol molecule.

TABLE 1. Properties of Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			Mesophases, mp or T_{mph}, °C*				ΔT_{mph}, °C	Yield, %
		C	H	N	crystalline	smectic	nematic	isotropic melt		
I	$C_{28}H_{44}N_4$	76,9 77,1	10,4 10,1	12,6 12,8	•		112...113	•		8
IIa*^{2}	$C_{26}H_{24}N_4O_2$	—	—	13,0 13,2	•		>300			52
IIb	$C_{30}H_{28}N_4O_4$	70,9 70,9	5,3 5,3	10,9 11,0	• 275	• 310	• >320 dec.			55
IIc	$C_{34}H_{40}N_4O_2$	75,7 76,1	7,4 7,5	10,4 10,4	•	228	• >300 dec.			59
IId	$C_{36}H_{44}N_4O_2$	76,3 76,6	7,9 7,8	9,9 9,9	•	218	• 358 dec.	•	140	70
IIe	$C_{42}H_{56}N_4O_2$	77,7 77,8	8,6 8,6	8,6 8,6	• 185	• 253	• 335	•	150	51
IIIa*^{2}	$C_{22}H_{18}N_4O_2$	—	—	14,7 15,1	•		264...267	•		18
IIIb	$C_{30}H_{34}N_4O_2$	74,4 74,7	7,1 7,0	11,4 11,2	•	217	• 275	•	58	15
IIIc	$C_{32}H_{38}N_4O_2$	m/z	510,3001 510,2995		•	198	• 252	•	54	40
IIId	$C_{38}H_{50}N_4O_2$	76,3 76,8	8,4 8,4	9,0 9,4	•	168	• 233	•	65	19

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* T_{mph} and ΔT_{mph} are the transition temperature and mesomorphic phase range.

*^{2} Molecular mass of IIa is 424; of IIIa, 370.

The presence of side products in the starting amidine IVb leads to a low yield of IIIa and formation of second compound that on the basis of mass spectrometry data and identity of its IR spectrum to that of the authentic sample [13] identified as 5-(*p*-hydroxyphenyl)pyrimidine. Alkylation by alkyl halides of dihydroxy-substituted ethane IIIa produces the dialkoxy derivatives IIIb-d. Investigation of their mesomorphic behavior demonstrated that ethanes III by their nature are stable nematogens with a width of mesophase of 55-65°C and substantially improved nematic properties in comparison with the thermally unstable or monotropic phenylpyrimidine mesogenic unit [14]. Elongation of the terminal alkyl chain in dimesogens IIIb-d invariably lowers the melting point. However, the thermal stability of the mesophase also decreases.

Comparison of the two different structure types of mesogenic dipyrimidines II and III reveals a substantial (by ~100°C) reduction in the temperature of the N-I transition for compounds III compared with II. However, the transition temperatures to the mesophase differ insignificantly (by 10-20°C). Nevertheless, taking into account the thermal stability of the mesomorphic state of II and III analogs, the reported data indicate that introduction of flexible ethane link in the 2,2'-bipyrimidinyl system is effective in producing a stable nematic mesophase.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrometer in KBr pellets. PMR spectra were recorded on Varian A56/60A (HMDS internal standard) and Bruker WP-200 SY ($CHCl_3$ internal standard) instruments. The molecular masses were determined on a high-resolution Finnigan MAT-8200 instrument. The temperatures of the phase transitions and the types of mesophases were determined by thermal microscopy on a Boetius heating stage with a PHMK-05 viewing device. Yields and properties of the synthesized compounds are listed in Table 1.

***trans*-1,4-Di(methoxycarbonyl)cyclohexane** was isolated by filtration and subsequent washing with pentane from a mixture of the *cis* and *trans* isomers of the diester after holding for 2 h at 13°C. Yield 15%; mp 71°C. Literature mp 71°C [7].

***trans*-1,4-Di(carboxamido)cyclohexane** was prepared by holding of a mixture of the *cis* and *trans* isomers of the diamide at 245°C for 20 min. Yield 97%; mp 345°C. Literature mp 346°C [7].

***trans*-1,4-Dicyanocyclohexane (VIIa)** was prepared by refluxing of mixture of the *trans*-diamide (12.3 g, 0.08 mol) and $SOCl_2$ (120 ml) for 36 h. Yield 50%; mp 138°C. Literature mp 140°C [7].

***trans*-Cyclohexane-1,4-dicarboxylic Acid Bis(iminomethyl Ester) Dihydrochloride (VIIIa).** Mixture of absolute methanol (42 ml) and absolute benzene (82 ml) saturated with dry HCl was treated with *trans*-dinitrile VIIa (8 g, 0.06 mol). The reaction mixture was held for 3 days at room temperature. The precipitate was filtered off, washed with dry dioxane, and stored in vacuum desiccator over P_2O_5. Yield 16 g (99%) of VIIIa; mp >260°C. IR spectrum: 1110, 1480, 1640 cm^{-1}. Found, %: C 43.9; H 7.36; N 10.3; Cl 25.8. $C_{10}H_{20}Cl_2N_2O_2$. Calculated, %: C 44.3; H 7.35; N 10.3; Cl 26.2.

***trans*-Cyclohexane-1,4-dicarboxylic Acid Diamidine Dihydrochloride (IVa)** was prepared from bisiminomethyl ester VIIIa and NH_4Cl in boiling alcohol. Yield 86%; mp >340°C. IR spectrum: 1690 cm^{-1}. Found: M^+ 151.1107 (fragment ion). $C_8H_{13}N_3$. Calculated: (M - NH_3) 151.1109.

***trans*-1,4-Bis(5-heptylpyrimidin-2-yl)cyclohexane (I)** (synthesized by T. A. Kizner). Solution of sodium methoxide (1.62 g, 30 mmol) in alcohol (15 ml) was added dropwise to boiling suspension of IVa dihydrochloride (2 g, 8.3 mmol) and acrolein V [15] (3.7 g, 24 mmol) in absolute alcohol (40 ml). The reaction mixture was boiled with stirring for 9 h and cooled. The precipitate was filtered off and washed with alcohol (3x20 ml). The combined filtrates and alcohol washes were evaporated to give 3.8 g of a viscous residue. This was placed on silica gel column (5×20 cm), washed with benzene (0.4 l), and eluted with chloroform. The fraction with R_f 0.6 (Silufol UV-254, $CHCl_3$–alcohol, 10:1) was collected. The chloroform was removed. The residue (0.63 g) was purified on silica gel column (3×10 cm) as described above. Yield 0.41 g of crystalline product, which was recrystallized from alcohol to give 0.28 g of pyrimidine I. PMR spectrum ($CDCl_3$): 0.86 (6H, m, CH_3), 1.34-2.72 (32H, m, 16 CH_2), 3.00 (2H, br. s, 1- and 4-$H_{cyclohex}$), 8.57 ppm (4H, s, 4- and 6-H_{pyrim}).

***trans*-1,4-Bis[5-(*p*-hydroxyphenyl)pyrimidin-2-yl]cyclohexane (IIa).** Solution of Na (0.69 g) in absolute methanol (2 ml) was added dropwise to boiling mixture of IVa dihydrochloride (2.41 g, 10 mmol) and VI [16]

(6.36 g, 20 mmol) in absolute methanol (50 ml) with stirring. The reaction mixture was boiled with stirring for 10 h then cooled to room temperature. The precipitate was filtered off, washed with methanol and dried in air. Yield 2.2 g of IIa. The starting salt VI (1.26 g) was isolated from the filtrate after evaporating and washing the residue with ether, alcohol and water with subsequent recrystallization from alcohol with activated charcoal.

***trans*-1,4-Bis[5-(*p*-acetoxyphenyl)pyrimidin-2-yl]cyclohexane (IIb).** Mixture of IIa (0.42 g, 1 mmol) and acetic anhydride (6 ml) was boiled for 5 h and cooled to room temperature. The precipitate was filtered off and washed with water and alcohol. Yield 0.27 g of IIb. IR spectrum: 1770 cm^{-1} (COO).

***trans*-1,4-Bis[5-(*p*-alkoxyphenyl)pyrimidin-2-yl]cyclohexanes (IIc-e).** Mixture of IIa (0.85 g, 2 mmol), methylcellosolve (20 ml), of the appropriate alkyl bromide or iodide (4 mmol) and powdered KOH (0.45 g, 8 mmol) was boiled for 6 h and cooled to room temperature. The precipitate was filtered off, washed with water and alcohol and dried in air. Yield 0.33 g of IIc, 0.4 g of IId, and 0.66 g of IIe. The filtrates were diluted three times with water and held at room temperature for 2-3 days in order to coagulate the finely dispersed precipitate, which was filtered off, washed with alcohol, and dried to give additional IIc (0.3 g) and IId (0.4 g). PMR spectrum of IId ($CDCl_3$): 0.90 (6H, t, $J = 7$ Hz, $2CH_3$), 1.39 (8H, br. m, $2C\underline{H}_2C\underline{H}_2CH_3$), 1.75-2.05 (8H, m, CH_2 of the ring), 2.26 (4H, br. d, $2OCH_2C\underline{H}_2$), 3.05 (2H, br. s, 1- and 4-$H_{cyclohex}$), 3.97 (4H, t, $J = 6.5$ Hz, $2OCH_2$), 6.98 and 7.46 (8H, d, $J = 8.5$ Hz, H_{arom}), 8.83 ppm (4H, s, 4- and 6-H_{pyrim}).

1,2-Bis[5-(*p*-hydroxyphenyl)pyrimidin-2-yl]ethane (IIIa). Stream of dry HCl was passed through solution of VIIb (61 g, 0.76 mol) in mixture of dry dioxane (250 ml) and absolute methanol (100 ml) cooled with ice until saturation. The reaction mixture was held for 2 h at room temperature. The precipitate was filtered off and washed with dry ether (2×50 ml). Yield 47 g (33%) of bisdimethylimine ester of succinic acid dihydrochloride VIIIb. IR spectrum: 870, 1110, 1400 and 1650 cm^{-1}.

Compound VIIIb (27 g, 0.12 mol) was added to absolute alcohol (300 ml) saturated with ammonia. The mixture was stirred at room temperature for 50 h. The precipitate was filtered off and washed with alcohol. Yield 16 g (69%) of IVb. IR spectrum: 1170, 1390, 1410, 1500, 1690 cm^{-1}.

Solution of sodium methoxide (5.9 g, 110 mmol) in methanol (100 ml) was added dropwise to boiling suspension of IVb (7 g, 37 mmol) and VI (23.6 g, 74 mmol) in absolute methanol (150 ml). The reaction mixture was boiled for 6 h. Methanol was removed in a rotary evaporator. The residue is ground with ether (2×100 ml). Ether is decanted. The remaining mass was treated with alcohol (70 ml), the precipitate filtered off and washed with cold alcohol. Yield 9.9 g of crude product. The product was purified by dissolving in 20% NaOH, heating with activated charcoal and filtering. The filtrate was acidified to pH 5-6 with conc. HCl, the precipitate is filtered off, washed with water and dried. Yield 2.5 g of IIIa. R_f 0.59 (Silufol UV-254, $CHCl_3$–alcohol, 10:1). IR spectrum: 1440, 1670 cm^{-1}. PMR spectrum (DMSO-d_6): 3.2 (4H, m, CH_2CH_2), 7.00 (4H, m, H_{arom}), 7.73 (4H, m, H_{arom}), 9.10 ppm (4H, s, 4- and 6-H_{pyrim}).

Yellow crystals of 5-(*p*-hydroxyphenyl)pyrimidine precipitated in the filtrate in storage after separation of IIIa. Found: M^+ 172.0675. $C_{10}H_8N_2O$. Calculated: M 172.0637.

1,2-Bis[5-(*p*-butoxyphenyl)pyrimidin-2-yl]ethane (IIIb). Mixture of IIIa (2 g, 5.4 mmol), butyl iodide (1.23 ml, 10.8 mmol), powdered KOH (1.2 g, 21 mmol) and alcohol (50 ml) was boiled for 14 h. The precipitate was filtered off and washed with alcohol. Yield 0.4 g of IIIb.

1,2-Bis[5-(*p*-amyloxyphenyl)pyrimidin-2-yl]ethane (IIIc). A. Mixture of IIIa (2.7 g, 7.3 mmol), amyl iodide (2.78 g, 14.5 mmol), KOH (2.5 g, 45 mmol) and alcohol (120 ml) was boiled for 14 h and cooled to room temperature. The precipitate was filtered off, washed with alcohol, and dried. Yield 1.5 g of IIIc.

B. Mixture of IIIa (1 g, 2.7 mmol), amyl iodide (0.66 ml, 5.4 mmol), KOH (0.5 g, 9 mmol) and DMF (35 ml) was held at 80°C for 3 h and cooled. The precipitate was filtered off and washed with ether (3×20 ml). Yield 0.04 g of IIIc.

1,2-Bis[5-(*p*-octyloxyphenyl)pyrimidin-2-yl]ethane (IIId). Mixture of IIIa (2 g, 5.4 mmol), octyl bromide (1.9 ml, 10.8 mmol), KOH (1 g, 18 mmol) and alcohol (60 ml) was boiled for 7 h and cooled. The precipitate was filtered off and wahsed with ether. Yield 0.6 g of IIId.

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