7. Ya. P. Stradyn', G. Ya. Dubur, Yu. I. Beilis, Ya. R. Uldrikis, and A. F. Korotokova, Khim. Geterotsikl. Soed., No. 1, 84 (1972).
8. V. P. Kadysh, Ya. P. Stradyn', E. L. Khanina, G. Ya. Dubur, and D. Kh. Mutsenietse, Khim. Geterotsikl. Soedin., No. 1, 117 (1985).
9. K. Folkers, H. J. Harwood, and T. B. Johnson, J. Am. Chem. Soc., 54, 3751 (1932).
10. G. Ya. Dubur and E. L. Khanina, Khim. Geterotsikl. Soedin., No. 2, 220 (1976).

SYNTHESIS AND MESOMORPHIC PROPERTIES OF ARYL 5-ALKYL-(AND ALKOXY) PYRIMIDINE-2-CARBOXYLATES

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UDC 547.562'853.9:532.783

Some aryl 5-alkyl(and alkoxy)pyrimidine-2-carboxylates (I) and 5-alkylpyrimidinoyloxybenzoates (II) have been obtained. It has been found the former do not display mesomorphism, but the latter are nematic liquid crystals with a range over which the mesophase exists of 50-90°C. The transition to the liquid crystal state in these compounds takes place at approximately the same temperatures as in their benzene analogues, but the thermal stability of the mesophase is somewhat less. Cyano-derivatives of pyrimidine effectively increase the value of the dielectric anisotropy of the matrix mixture, but they have a marked effect on its clarification temperature.

It has been shown that substituted aryl 5-arylpyrimidine-2-carboxylates and pyrimidinoyloxybenzoates possess liquid crystal properties, forming a nematic phase [1]. However, the presence of a 5-aryl group in the pyrimidine ring results in high-melting and sparingly soluble compounds, presenting obstacles to their study. It would be expected that aryl 5-alkylpyrimidine-2-carboxylates would possess liquid crystal properties with lower mesophase temperatures.

We here report the preparation and study of the aryl 5-alkyl(and alkoxy)pyrimidine-2-carboxylates (I) and (II), which are analogues of the extensively studied arylbenzoates [2-5].

The starting 5-substituted pyrimidine-2-carboxylic acids (IIIa, b) were obtained by hydrolyzing the cyanopyrimidines (IV), which are readily accessible by introducing the cyano-group into the sulfones (V). Attempts to utilize information on the oxidation of 5-alkyl-2-methylpyrimidines [6] for the preparation of 5-heptylpyrimidine-2-carboxylic acid (IIIb) from 5-heptyl-2-methylpyrimidine (VIb) were unpromising, the yields of the acid (IIIb) being very small (see scheme on following page).

A frequently employed route to 2,5-disubstituted pyrimidines (including the mercapto-derivatives (VII, VIII)) [7, 8] makes use of various acrolein derivatives [9-11] (such as (IX) and (X)), obtained by a multistage synthesis from the acetals (IX) via the vinyl ethers (XII) and tetraethoxypropanes (XIII). This laborious route can be shortened by preparing the acroleins (X) directly from the acetals (XI), as described in [12].

5-Pentyloxypyrimidine-2-carboxylic acid (IIIc) was obtained by a convenient route for the preparation of 5-alkoxypyrimidines (from the 4-hydroxypyrimidines).

Acids (IIIa-c) were converted into their aryl esters (Ia-d) and (IIa-d) as described in [1].

Liquid Crystal Properties of (I) and (II). The p-cyanophenyl esters (Ia) and (Ic) and the hexyloxyphenyl ester (Id) did not display mesomorphism, in contrast to their benzene

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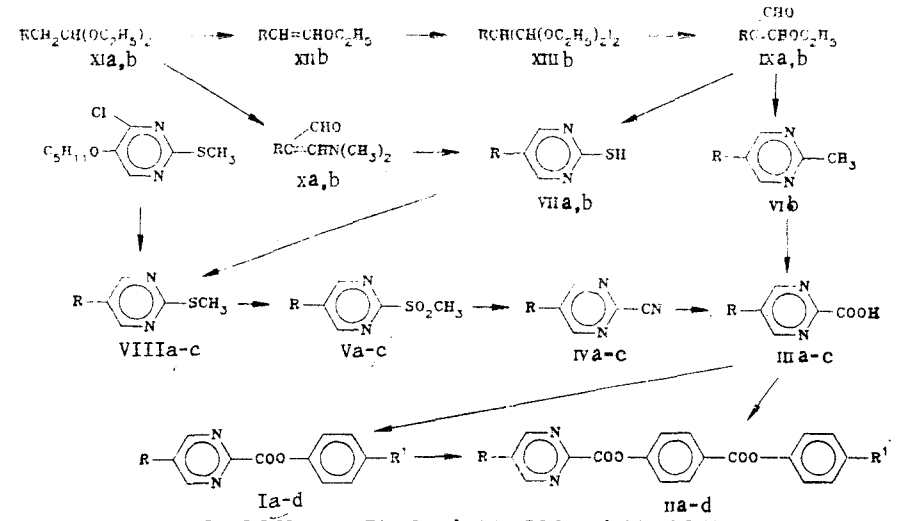


Ia,b R = C_7H_{15}, c,d R = OC_5H_{11}; a, c R' = CN, b R' = COOH, d R' = OC_6H_{13}; IIa R = C_5H_{11}, b-d R = C_7H_{15}; a,c R' = C_5H_{11}, b R' = CN, d R' = OC_5H_{11}; III—XI a R = C_5H_{11}, b R = C_7H_{15}, c R = OC_5H_{11}

analogues, which are nematic liquid crystals [2, 3]. The pyridine analogue of the ester (Ic) is monotropically nematic [13].

The diesters (IIa-d) display liquid crystal properties, the range of existence of the nematic mesophase in (IIa, c, d) being ~50°C, and in the cyano-compound (IIb), 90°C. As compared with the analogous esters of 5-phenylpyrimidine-2-carboxylic acid [1], the esters (II), as expected, have substantially lower temperatures of transition to the liquid crystal state (by 50-100°C), the range in general being maintained.

Comparison of the properties of diesters of p-alkylbenzoic acids [4, 5] with those of the diesters (II) shows that the latter have a less thermally stable mesophase, but the transition to the nematic state takes place at approximately the same temperature.

Although the Schiff's bases of 2-substituted-5-aminopyrimidines are more prone to display smectic properties than benzylideneanilines [14], esters of pyrimidine acids (see [1] and, for example, esters (IIb, c)), unlike aryl benzoates [4, 5], do not form a smectic mesophase.

Dielectric Properties of Pyrimidine Derivatives. The dielectric properties of (Ia), (IVb), and (XV) (the latter was obtained as described in [15]), which contain the pyrimidine moiety, were examined in connection with their molecular structure. For each pyrimidine derivative, an aromatic compound of analogous structure was selected in order that the effects of replacing the benzene ring by the pyrimidine ring on the dielectric properties could be found. It has previously been shown that the dipole moment of the pyrimidine ring, directed along the longer axis of the molecule, has a considerable effect on the dielectric properties, with a considerable increase in dielectric anisotropy [14].

The measurements were made, as described in [14], with a mixture of the pyrimidine and a weakly polar liquid crystal matrix (a mixture of azoxy-compounds A [16]), since the compounds (Ia), (IVb), and (XV) do not themselves possess liquid crystal properties. No calculations of the effective values of the dielectric constants from the data for the mixtures of pyrimidine and matrix A by the additivity rule were carried out for (Ia), (IVb), and (XV), since the experimental concentration dependence of the clarification temperature (T_{cl}) revealed highly nonadditive behavior, having a clearly apparent minimum or maximum, indicating strong specific interactions of the molecules of these compounds with the weakly polar matrix [17, 18]. The concentration of the cyano-compounds in the matrix was kept low (10 and 20 wt. %) in order to avoid association effects resulting from the strong intermolecular interactions of the strongly and weakly polar components of the mixture [17, 18] and the cyano-derivatives themselves [19], and in order that the clarification temperature should remain in a range convenient for measurement. Comparisons of the values of the dielectric constants were carried out at the same relative temperatures τ.

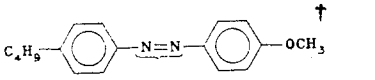
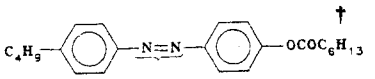
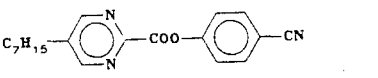
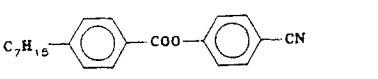
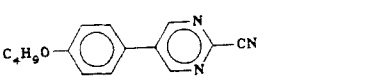
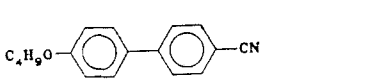
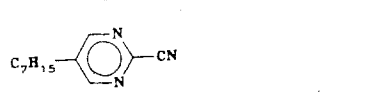
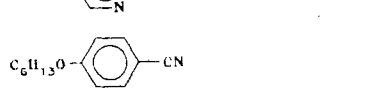
The compound selected for comparison with the pyrimidine (Ia) (p-cyanophenyl p-heptylbenzoate (XIV)) has a nematic phase range of 43-56°C [3] and high dielectric anisotropy ($\Delta\varepsilon$ = +20.7 at 35°C), and was successfully used to increase the dielectric anisotropy of the mixtures used in the indicator technique. It will be seen from Table 2 that the compound

TABLE 1. Aryl 5-Alkyl(and alkoxy)pyrimidine-2-carboxylates (Ia, c, d) and (IIa-d)

Compound	$T_{transition}$, °C* T_{nem}	T_{iso}	IR spectrum (KBr), ν, cm^{-1}	Found, % C	H	N	Empirical formula	Calculated, % C	H	N	Yield, %
Ia	—	91—92	1770, 2230	70,6	6,77	13,0	$C_{19}H_{21}N_3O_2$	70,7	6,50	13,0	42
Ic	—	113—114	—	65,4	5,40	13,6	$C_{17}H_{17}N_3O_3$	65,6	5,50	13,5	26
Id	—	95	—	68,3	7,94	7,29	$C_{22}H_{30}N_2O_4$	68,4	7,82	7,24	64
IIa	92	137—145	—	73,2	6,88	5,88	$C_{28}H_{32}N_2O_4$	73,0	6,96	6,09	40
IIb	112	201	1740, 1760, 2230	70,9	5,57	9,73	$C_{26}H_{25}N_3O_4$	70,4	5,64	9,48	68
IIa	91	148—149	1730, 1760	74,1	7,38	5,68	$C_{30}H_{36}N_2O_4$	73,8	7,37	5,74	50
IId	102	152—156	1740, 1765 ($CHCl_3$)	71,3	7,19	5,65	$C_{30}H_{36}N_2O_5$	71,4	7,14	5,55	16

*Compounds (Ia) and (IId) were crystallized from alcohol, (Ic) and (Id) from hexane, (IIa) and (IIc) from aqueous alcohol, (IIb) from a 1:1 mixture of ethyl acetate and hexane. T_{nem} is the temperature of the nematic mesophase, and T_{iso} the temperature of the isotropic mesophase.

TABLE 2. Dielectric Properties of Mixtures*

Compound	ε at 25°C	c, %	T_{cl}, °C	τ = 0.95 $\varepsilon_\parallel$	$\varepsilon_\perp$	Δε	τ = 0.90 $\varepsilon_\parallel$	$\varepsilon_\perp$	Δε
 †	—	—	72	4,66	4,86	−0.20	4,75	5,10	−0,35
 †									
Ia 	—	10	65,7	8,68	5,98	+2,70	9,88	6,15	+3,73
		20	57,5	12,51	6,51	+6,00	13,67	6,60	+7,07
XIV 	—	10	69,1	7,30	5,44	+1,86	7,91	5,56	+2,35
		20	67,5	9,82	5,91	+3,91	10,67	5,87	+4,80
XV 	—	10	78,5	9,19	5,79	+3,40	10,01	5,91	+4,10
		20	86,1	12,8	6,6	+6,2	14,42	6,33	+8,09
XVI 	—	10	75	7,29	5,43	+1,86	7,78	5,54	+2,24
		20	79	9,21	5,49	+3,72	10,11	5,40	+4,71
IVb 	35	10	49	8.48	6,33	+2,15	9,60	6,30	+3.30
		20	31	12,80	7,65	+5,15	14,00	7,50	+6,50
XVII 	18	10	50	7,86	6,12	+1,74	8,80	6,40	+2,40
		20	35	9,60	6,60	+3,00	11,2	6,6	+4,6
XVIII 	11	10	40	6,4	5,9	+0,5	6,8	6,2	+0,6

*c is the concentration of the cyano-derivative in the mixture A (wt. %): T_{cl} is the temperature of clarification of the mixture; τ is the relative temperature, $\tau = (T_{iso} + 273°C)/(T_{cl} + 273°C)$; $\Delta\varepsilon = \varepsilon_\parallel - \varepsilon_\perp$, where $\varepsilon_\parallel$ and $\varepsilon_\perp$ are the dielectric constants of the compounds, measured in directions parallel and perpendicular to the director of the liquid crystal.

†Mixture A, 2:1.

(Ia), as compared with the analogous compound (XIV), increases the dielectric anisotropy of the mixture much more effectively (by a factor of more than 1.5). A drawback of (Ia), however, is that it considerably reduces the clarification temperature of the mixture, and can only be used in low concentrations.

The benzene analogue of (XV) is 4,4'-butoxycyanobiphenyl (XVI), which has T_{mp} 78°C and T_{cl} 75.5° (monotropic liquid crystals [20]), which is used extensively in liquid crystal mixtures for electrooptical equipment. As in the previous case, the pyrimidine (XV) increases the $\Delta\varepsilon$ value of the mixture to a much greater extent than its benzene analogue (XVI) (by a factor of ~2). A characteristic feature of this pair of compounds is that they increase, rather than reduce, the T_{cl} of the mixture, this effect not being due to the high T_{cl} of the cyano-compounds themselves, but to the nature of the phase diagram for such systems, mixtures of alkoxy-cyano derivatives with weakly polar liquid crystal matrices usually having a maximum on the concentration–T_{cl} plots and an induced smectic phase being present. These features are clearly apparent in these compounds.

Studies of mixtures of matrix A with monocyclic cyano-compounds (IVb, XVII [21], and XVIII [22]) also provide reliable evidence of the effectiveness of pyrimidines as compared with their phenyl and cyclohexyl analogues as additives which increase the dielectric anisotropy of mixtures. The $\Delta\varepsilon$ values for mixtures were found to be sufficiently high, despite the fact that the degree of ordering of monocyclic compounds in a liquid crystal matrix must be low. Table 2 shows the values of the dielectric constants for the cyano-compounds themselves (IVb, XVII, and XVIII), which confirm that the pyrimidines possess high dipole moments corresponding to the dipole moment of the cyano-group, which also favors their use for increasing the $\Delta\varepsilon$ values of mixtures. However, the T_{cl} values of the mixtures were found to be unsatisfactorily low, since the monocyclic cyano-compounds themselves are not liquid crystals.

The $\Delta\varepsilon$ value for the ester (Ic), calculated as described in [14], was found to be +44 (for a 10% solution in mixture A). The analogous derivative of pyridine-2-carboxylic acid, which is a monotropic liquid crystal, had $\Delta\varepsilon$ = +25 [13].

EXPERIMENTAL

IR spectra were obtained on a UR-20 spectrometer, and PMR spectra on a Varian A56/60A, internal standard HMDS. Molecular masses were measured by mass spectrometry on a high-resolution MS 902 instrument. Phase transition temperatures were measured on a miniature Boetius hot plate with an RNMK-0.5 direct-reading apparatus. TLC was carried out on Silufol UV-254 plates in chloroform.

The characteristics of the compound prepared are given in Table 1-3.

p-Cyanophenyl 5-Heptylpyrimidine-2-carboxylate (Ia). A mixture of 1.8 g (8 mmole) of the acid (IIIb), 0.7 g (6 mmole) of triphenylphosphine, 0.8 g (8 mmole) of triethylamine, and 1.2 g of CCl_4 in 10 ml of acetonitrile was stirred for 8 h at 20°C. The mixture was then filtered, the acetonitrile distilled off on a rotary evaporator, and the residue extracted with boiling hexane (5 × 40 ml). The solid which remained after the residue cooled was dissolved in 50 ml of ether, filtered, the ether distilled off, and the residue recrystallized twice from alcohol to give 0.5 g of the ester (Ia). The hexane and ether solutions were evaporated, combined with the ether-insoluble residue, and submitted to the same sequence of operations to give a further 0.3 g of the ester, overall yield 0.8 g.

p-Cyanophenyl 5-Pentyloxypyrimidine-2-carboxylate (Ic). In an analogous way to the preparation of 5-methoxypyrimidines as described in [23], there was obtained from methyl pentyloxyacetate and thiourea 65% of 5-pentyloxy-2-mercapto-4-hydroxypyrimidine, mp 220-230°C. Methylation of this with dimethyl sulfate in NaOH gave the S-Me derivative in 81% yield, mp 103-110°C. The latter was converted without further purification into the chloro-derivative by boiling with $POCl_3$ (yield 56%, bp 147°C/1 mm), which was then reduced with zinc in methanol in the presence of NaOH to give the pyrimidine (VIIIc) (yield 75%, mp 145°C/1 mm). This (VIIIc) was oxidized with hypochlorite as described in [24] to give 5-pentyloxy-2-methylsulfonylpyrimidine (Vc) in 60% yield, mp 80-83°C. Treatment of the latter with NaCN in DMSO gave 5-pentyloxy-2-cyanopyrimidine (IVc), yield 86%, which on hydrolysis with 10% NaOH gave 82% of the carboxylic acid (IIIc), mp 132-136°C (from benzene).

A mixture of 2.1 g (10 mmole) of the acid (IIIc) and 4.8 g (0.04 mole) of thionyl chloride was boiled for 8 h. Excess thionyl chloride was distilled off under a water pump vacuum, and the residue treated with 50 ml of dry benzene, 1.19 g (10 mmole) of p-cyanophenol, and

TABLE 3. 2,5-Disubstituted Pyrimidines (III-VIII)

Compound	mp,* °C, or bp, °C (mm Hg)	M	R_f	Found, %			Empirical formula	Calculated, %			Yield, %
				C	H	N		C	H	N	
IIIb	41—43	222	0.5†	59.3	8.10	11.5	$C_{12}H_{18}N_2O_2\times\times H_2O$	60.0	8.30	11.6	65
IVb	130 (2)	203	0.60	71.4	8.60	—	$C_{12}H_{17}N_3$	70.9	8.40	—	71
Va	50—51.5	—	0.30	52.7	6.90	12.4	$C_{16}H_{16}N_2O_2S$	52.6	7.00	12.3	60
Vb	44—46	—	0.30	56.1	7.80	11.0	$C_{12}H_{20}N_2O_2S$	56.3	7.80	10.9	73
VIb	126—128 (6)	192‡	—	75.4	10.5	—	$C_{12}H_{20}N_2$	75.0	10.4	—	15
VIIb	175—180	—	0.10	62.8	8.60	13.3	$C_{11}H_{18}N_2S$	62.9	8.60	13.3	80
VIIIa	126—128 (1)	—	—	61.6	8.30	13.8	$C_{16}H_{16}N_2S$	61.2	8.20	14.3	80
VIIIb	128—131 (1)	—	0.65	64.4	8.60	13.0	$C_{12}H_{20}N_2S$	64.3	8.90	12.3	78

*Crystallization solvents: (IIIb), ethyl acetate; (Va, b), light petroleum; and (VIIb) alcohol.
†In the system chloroform—ethanol (20:1).
‡ Contains an impurity with m/z 171.

2 g (20 mmole) of triethylamine, and the mixture boiled for 4 h. After cooling, the solid was filtered off, and the organic layer evaporated under a water pump vacuum to give 0.8 g of the ester (Ic).

Similarly, from (IIIc) and p-hexylphenol there was obtained the ester (Id), which was purified by chromatography in benzene on alumina.

p-Cyanophenyl p-(5-Heptylpyrimidinoyl-2-oxy)benzoate (IIb). A mixture of 1.35 g (6.1 mmole) of the acid (IIIb), 3 ml of thionyl chloride, 5 ml of dry benzene, and 5 drops of DMF was boiled for 38 h (followed by TLC). Thionyl chloride and benzene were then removed under a water pump vacuum, the residue treated with 5 ml of dry benzene, and again evaporated to dryness at the water pump, to give a dark-colored liquid residue of the acid chloride of (IIIb). IR spectrum ($CHCl_3$): 1785 cm^{-1}. To this was added 0.84 g (6.1 mmole) of p-hydroxybenzoic acid in 6 ml of pyridine, and the mixture stirred with a magnetic stirrer for two days. The solid was filtered off, washed with water acidified to pH 2-3 (2 × 15 ml) to remove traces of pyridine, and dried in air to give 0.8 g (38%) of the carboxyester (Ib), mp 182-187°C. IR spectrum (KBr): 1695, 1770 cm^{-1}. To a suspension of 0.68 g (2 mmole) of the acid (Ib) in 20 ml of dry benzene was added 3 ml of thionyl chloride, and the mixture boiled for 5 h. The benzene was distilled off at the water pump, and the residue treated with 0.23 g (1.9 mmole) of p-cyanophenol in 10 ml of dry pyridine. The mixture was stirred at 20°C for two days, poured into a mixture of 100 g of ice and 30 ml of 3 N HCl, and the precipitated ester (IIb) filtered off. Recrystallization from a mixture of ethyl acetate and hexane, 1:1, followed by ethyl acetate with the addition of activated charcoal, gave 0.6 g of the ester (IIb).

p-Pentylphenyl p-(5-Heptylpyrimidinoyl-2-oxy)benzoate (IIc). A mixture of 0.4 g (1.8 mmole) of the acid (IIIb), 0.4 g (1.4 mmole) of p-pentylphenyl p'-hydroxybenzoate, 0.47 g (1.8 mmole) of triphenylphosphine, 0.28 g (1.8 mmole) of CCl_4, and 0.18 g (1.8 mmole) of triethylamine in 2.5 ml of acetonitrile was stirred for 8-10 h at 20°C. The actonitrile was distilled off in a rotary evaporator, and the residue extracted with boiling hexane (5 × 20 ml), cooled, and the solid filtered off to give 0.4 g of the ester (IIc).

Similarly obtained were p-pentylphenyl p-(5-pentylpyrimidinoyl-2-oxy)benzoate (IIa) and p-pentyloxyphenyl p-(5-heptylpyrimidinoyl-2-oxy)benzoate (IId).

5-Pentylpyrimidine-2-carboxylic Acid (IIIa). A mixture of 8.43 g (37 mmole) of the pyrimidine (Va) and 2.86 g (44 mmole) of KCN in 200 ml of DMFA was heated for 5 h at 100°C. The DMFA was distilled off at the water pump, the residue extracted with chloroform (3 × 100 ml), and the chloroform removed in a rotary evaporator to give the cyanopyrimidine (IVa) as a dark-colored liquid, which was purified by distillation into a flanged attachment at 120-130°C (2 mm), Rf 0.70. IR spectrum ($CHCl_3$): 2250 cm^{-1} (CN). To this cyano-derivative (IVa) was added 80 ml of 2N NaOH, and the mixture was boiled for 6 h, cooled, acidified to pH 2-3 with 20% HCl, and the acid (IIIa) filtered off. Yield 5.38 g (75%), mp 84-87°C (from ethyl acetate). According to [6], mp 86-87°C.

5-Heptylpyrimidine-2-carboxylic Acid (IIIb). A. A mixture of 13.6 g (6.7 mmole) of the cyanopyrimidine (IVb) and 130 ml of 2N NaOH was boiled for 8 h, cooled to 5-10°C, acidified with 20% HCl to pH 2-3, and the resulting suspension extracted with benzene (3 × 100 ml). The extract was dried over $MgSO_4$, and the benzene distilled off at the water pump to give 11 g of a residue which crystallized on trituration with ethyl acetate. The acid (IIIb) was filtered off and air-dried.

B. The methylpyrimidine (VIb) (4.12 g, 21.4 mmole) was dissolved in 40 ml of pyridine, the solution heated to 110°C, and 3.5 g (31 mmole) of selenium dioxide added in three portions at 2 h intervals, with stirring. Heating and stirring were continued for three days. The precipitated selenium was then filtered off, and the filtrate diluted with 100 ml of chloroform, washed with water acidified to pH 2-3 with HCl (3 × 50 ml), dried over $MgSO_4$, and evaporated at the water pump. The oily residue (mostly unreacted (VIb)) partially crystallized on standing in air for 10-12 h. The solid was filtered off, and washed with 2-5 ml of CCl_4 to give 0.75 g (15%) of product. IR spectrum (KBr): 1730 cm^{-1}. Found: M 222.136 $C_{12}H_{18}N_2O_2$. Calculated: M 222.1368.

5-Heptyl-2-cyanopyrimidine (IVb). A mixture of 20.7 g (80 mmole) of the pyrimidine (Vb) and 6.3 g (97 mmole) of KCN in 500 ml of DMFA was stirred at 100°C for 5 h. The DMFA was distilled off at the water pump, and the residue extracted with methylene chloride (3 × 100 ml). Removal of the solvent gave 13.6 g of a liquid residue, which was purified by passing it through a column of silica gel in chloroform followed by distillation into a flanged attachment. Yield 11.6 g. IR Spectrum ($CHCl_3$): 2250 cm^{-1} (CN w).

5-Heptyl-2-methylsulfonylpyrimidine (Vb). A solution of 21.6 g (96 mmole) of the pyrimidine (VIIIb) and 50 ml (480 mmole) of 30% H_2O_2 in 250 ml of glacial acetic acid was stirred at 70°C for 8 h. The mixture was cooled, poured into 800 ml of water, neutralized with solid $NaHCO_3$, extracted with chloroform (3 × 150 ml), the extract washed with water until neutral, dried over $MgSO_4$, and distilled on the rotary evaporator, yield 18.5 g. PMR spectrum (in CCl_4): 0.82-1.22 (m, C_7H_{15}); 3.17 (s, 3H, CH_3); 8.65 ppm (s, 2H, 4- and 6-H of pyrimidine ring).

5-Pentyl-2-methylsulfonylpyrimidine (Va) was obtained similarly. IR spectrum (CCl_4): 1140, 1330, 1410 cm^{-1}.

2-Methyl-5-heptylpyrimidine (VIb). A mixture of 76 g (385 mmole) of the acrolein (IXb), 36.4 g (385 mmole) of acetamidine hydrochloride, and 250 ml of alcohol was heated to the boil, and a solution of CH_3ONa, obtained from 16.7 g (730 mmole) of metallic sodium in 150 ml of absolute methanol, was added dropwise with stirring. The mixture was then boiled for 3 h, the alcohol distilled off at the water pump, and the residue treated with 450 ml of 10% NaOH. The mixture was extracted with chloroform (8 × 50 ml), and the extract washed with water until neutral, dried over $MgSO_4$, and the chloroform removed in a rotary evaporator. The residue was fractionated in an oil-pump vacuum to give 44 g of a mixture, bp 95-110°C (2 mm). Repeated fractionation separated the mixture into fractions with bp 95-115°C (7 mm) (containing, in addition to the main product (VIb), an unidentified impurity with m/z 171) and 120-135°C (6 mm). The latter was redistilled to give 10.9 g of the methylpyrimidine (VIb). PMR spectrum (in the pure state): 0.83-1.27 (m, C_6H_{13}), 2.43 and 2.50 (t and s, 5H, 2-CH_3 and CH_2), 8.55 ppm (s, 2H, 4, 6H of the pyrimidine ring).

5-Heptyl-2-mercaptopyrimidine (VIIb). A. To a boiling mixture of 34.5 g (175 mmole) of the acrolein (Xb) and 13.3 g (175 mmole) of thiourea in 150 ml of absolute alcohol was added over 1.5 h a solution of 9.4 g of sodium methoxide in 100 ml of absolute alcohol. The mixture was boiled with stirring for 8 h, cooled, and poured into 800 ml of 30% acetic acid. The yellow solid which separated was filtered off, washed with 10% $NaHCO_3$ (3 × 50 ml) and water until neutral, and air-dried. Yield 28.8 g.

B. From the acrolein (Xb) and thiourea, as described in [7], yield 51%, mp 175-180°C (from alcohol).

5-Pentyl-2-mercaptopyrimidine (VIIa) was obtained by method A, from acrolein (Xa), in 62% yield, mp 190-195°C (from alcohol). According to [8], mp 195-196°C.

5-Heptyl-2-methylmercaptopyrimidine (VIIIb). To a suspension of 34 g (162 mmole) of the pyrimidine (VIIb) in 160 ml of 1N NaOH was added dropwise with stirring at 20°C ml (320 mmole) of methyl iodide. The mixture was stirred for 5 h, extracted with chloroform (3 × 50 ml), dried over $MgSO_4$, the chloroform removed at the water pump, and the residue

distilled under an oil pump vacuum. Yield 28.5 g. PMR spectrum (CCl_4): 0.82-1.22 (m, 15H, C_7H_{15}), 2.40 (s, 3H, SCH_3), 8.17 ppm (s, 2H, 4, 6H of the pyrimidine ring).

5-Pentyl-2-methylmercaptopyrimidine (VIIIa) was obtained similarly, from (VIIa).

2-Pentyl-3-ethoxyacrolein (IXa) was obtained as described in [9], yield 82%, bp 132-135°C (15 mm). According to [9], bp 127-128°C (12 mm).

β-Heptylvinyl Ethyl Ether (XIIb). Obtained in 87% yield from pelargonaldehyde acetal (XIb) [11] as described in [25], yield 87%, bp 84-85°C (12 mm), n_D^{20} 1.4310. Found, %: C 77.4, H 13.0. $C_{11}H_{22}O$. Calculated, %: C 77.6, H 13.0.

2-Heptyl-1,1,3,3-tetraethoxypropane (XIIIb) was obtained from (XIIb) as described in [26], yield 67%, np 137-139°C (4 mm), n_D^{20} 1.4282. Found, %: C 67.7, H 12.0. $C_{18}H_{38}O_4$. Calculated, %: C 67.9, H 12.0.

2-Heptyl-3-ethoxyacrolein (IXb) was obtained from the tetraethoxypropane (XIIIb) as described in [27], yield 70%, bp 130-138°C (4 mm). IR spectrum (CCl_4): 1650, 1685, 1730 cm^{-1}. PMR spectrum (CCl_4): 1.22 (m, CH_3, CH_2—C), 2.14 (m, CH_2—C=C), 3.38 (m, CH_2), 4.24 (q. OCH_2), 7.0 (s, —CH=), 9.1 ppm (s, CHO). An analytically pure sample was not obtained.

2-Pentyl-3-dimethylaminoacrolein (Xa). Enanthaldehyde diethyl acetal (XIa) was obtained in 65% yield, bp 84-87°C (10 mm), from heptyl bromide and orthoformic ester as described in [28]. This was reacted with the $POCl_3$—DMFA complex as described in [12] to give the acrolein (Xa) in 48% yield, bp 166-171°C (5 mm). According to [10], bp 100-105°C (0.1 mm).

2-Heptyl-3-dimethylaminoacrolein (Xb) was obtained as described in [12] from pelargonaldehyde acetal (XIb) in 82% yield, bp 135-140°C (0.5 mm), n_D^{20} 1.5220. According to [11], bp 122°C (0.01 mm), n_D^{20} 1.5239.

LITERATURE CITED

1. M. A. Mikhaleva, G. A. Kolesnichenko, K. I. Rubina, Yu. Sh. Gol'dberg, V. A. Savel'ev, L. Ya. Leitis, M. V. Shimanskaya, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 3, 380 (1986).
2. M. E. Neubert and L. T. Carlino, Mol. Cryst. Liq. Cryst., 59, 253 (1980).
3. V. V. Titov, E. I. Kovshev, A. I. Pavluchenko, V. T. Lazareva, and M. G. Grebenkin, J. Phys., 36, C1, 387 (1975).
4. J. P. Van Meter and A. K. Seidel, J. Org. Chem., 40, 2998 (1975).
5. J. P. Van Meter, R. T. Klingbiel, and O. J. Genova, Solid State Commun., 16, 315 (1975).
6. H. Yamanaka, M. Mizugaki, M. Sagi, and K. Edo, Heterocycles, 12, 1323 (1979).
7. R. Kruse and E. Breitmaier, Chem. Ztg., 101, 305 (1977).
8. L. Rylski, F. Sorm, and Z. Arnold, Collect. Czech. Chem. Commun., 24, 1667 (1959).
9. E. Breitmaier and S. Gassenmann, Chem. Ber., 104, 665 (1971).
10. Z. Arnold and F. Sorm, Collect. Czech. Chem. Commun., 22, 452 (1958).
11. H. Bredereck, H. Herlinger, and J. Renner, Chem. Ber., 93, 230 (1960).
12. D. H. R. Barton, G. Dressaire, B. J. Willis, A. G. M. Barrett, and M. Pfeffer, J. Chem. Soc., Perkin 1, No. 3, 665 (1982).
13. A. I. Pavlyuchenko, N. I. Smirnova, E. I. Kovshev, V. V. Titov, and K. M. Dyumaev, Author's Cert. (USSR), No. 681,056; Byull. Izobret., No. 31, 94 (1979).
14. M. A. Mikhaleva, V. T. Lazareva, M. F. Grebenkin, V. A. Savel'ev, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 11, 1545 (1982).
15. H. Zaschke, Z. Chem., 17, 63 (1977).
16. M. I. Barnik, V. V. Belyaev, M. F. Grebenkin, V. G. Rumyantsev, V. A. Seliverstov, V. A. Tsvetkov, and N. M. Shtykov, Kristallografiya, 23, 805 (1978).
17. G. A. Beresnev and M. F. Grebenkin, Kristallografiya, 28, 998 (1983).
18. V. V. Belyaev and M. F. Grebenkin, Kristallografiya, 29, 815 (1984).
19. W. H. De Jeu, Phil. Trans. Roy. Soc., London, A309, 217 (1983).
20. G. W. Gray, J. Phys., 36, C1, 337 (1975).
21. M. W. Partridge, J. Chem. Soc., No. 11, 3043 (1949).
22. Jap., Application No. 92,789; Chem. Abs., 96, 77607 (1982).
23. Z. Budesinsky J. Prikryl, and E. Svatek, Collect. Czech. Commun., 29, 2980 (1964).
24. Z. Budesinsky, V. Bydzovsky, J. Kopecky, Svab, and J. Vavrina, Cesk. Farm., 10, 241 (1961).
25. M. G. Voronkov, Zh. Obshch. Khim., 20, 2060 (1950).

*Obtained from I. A. Nizovaya.

26. V. T. Klimko and A. P. Skoldinov, Zh. Obshch. Khim., 29, 4027 (1959).
27. R. Rüegg, H. Lindlar, M. Montavon, G. Saucy, S. Schaeren, U. Schwieter, and O. Isler, Helv. Chim. Acta, 42, 847 (1959).
28. J. N. Zaganiaris, Berichte, 71, 2002 (1938).

SYNTHESIS AND SPECTRAL EXAMINATION OF THE POSITION OF TAUTOMERIC EQUILIBRIUM IN 2-THIOXO-4-QUINAZOLONE

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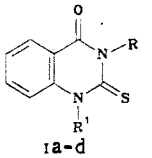
UDC 547.856.1.07:543.422.6:541.623

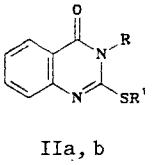
2-Thioxo-4-quinazolone and its derivatives mono- and dimethylated at ring atoms $N_{(1)}$ and $N_{(3)}$ and the exocyclic sulfur have been synthesized. Using model compounds, UV spectroscopy has been used to show that 2-thioxo-4-quinazolone exists in the thioketo-form, no appreciable amounts of the thiol or enol isomers being present.

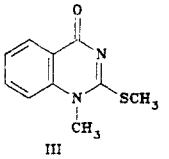
2-Thioxo-4-quinazolones display biological activity, and are therefore of practical importance [1, 2]. These compounds are also of interest from the theoretical point of view, since they could exist in a variety of tautomeric forms. No studies of the position of the prototropic equilibrium in thioxoquinoxalines have been carried out, as a result of the nonavailability of a complete set of methylated models, the electronic structures of which reduplicate the structures of the probable tautomeric forms.

We have examined the alkylation of 2-thioxo-4-quinazolone (Ia) with methyl tosylate in dimethyl formamide, which gives a mixture of compounds alkylated at $N_{(1)}$ (Ib), $N_{(3)}$ (Ic), and the exocyclic sulfur (IIa), the last product predominating in the reaction mixture [3]. The separation of the mixture of isomeric compounds (Ib), (Ic), and (IIa) was difficult, and we were able to separate preparatively only (IIa), the model compounds (Ib) and (Ic) being obtained by fusing 1-methyl- and 3-methyl-4-quinazolones with sulfur [4]. The course of alkylation was established from the PMR spectra, in which 2-methylthio-4-quinazolone (IIa) gives rise to a singlet signal for the methylene protons at 2.58 ppm, whereas (Ib) and (Ic) give signals for methyl protons at 3.70 and 3.35 ppm, respectively.

When monomethylated 2-thioxo-4-quinazolones (Ib) and (IIa) were methylated with methyl iodide in alcoholic alkali, dialkyl derivatives (IIb) and (III) were isolated. Compound (Id) was obtained by condensing N-methylanthranilic acid with methyl isothiocyanate.


Ia-d


IIa, b


III

Ia $R=R^1=H$; b $R=H$, $R^1=CH_3$; c $R=CH_3$, $R^1=H$; d $R=R^1=CH_3$; II a $R=H$, $R^1=CH_3$; b $R=R^1=CH_3$

The UV spectrum of (Ia) contained two bands at 218 and 292 nm, due to $\pi \rightarrow \pi^*$ transitions in the amide and thioamide groupings, respectively. Maxima similar in intensity and position are seen in the spectra of (Ib-d), the carbonyl and thiocarbonyl groups in which are unchanged as compared with (Ia).

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0009-3122/86/2209-1001$12.50 © 1987 Plenum Publishing Corporation