Chemistry of Heterocyclic Compounds, Vol. 31, No. 3, 1995

SYNTHESIS AND LIQUID CRYSTAL PROPERTIES OF SUBSTITUTED 5-(ARYLCARBONYLOXY)-2-(p-CYANOPHENYL)PYRIMIDINES

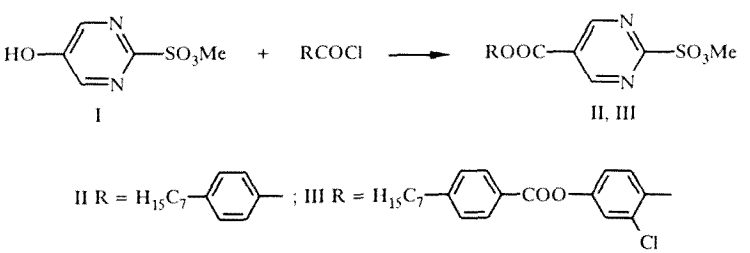
M. A. Mikhaleva, G. A. Igonina, and V. A. Savel'ev

Liquid crystal p-substituted benzoates, biphenylcarboxylates, and benzoyloxybenzoates were obtained on the basis of 5-hydroxy-2-(p-cyanophenyl)pyrimidine. The development of nematogenicity by the esters due to the p-cyanophenyl grouping was noted, and the appearance of the smectic mesophase by the variation of the ring framework of the acid fragment of the molecule was investigated.

Mesomorphic properties of liquid crystals in unsymmetrically substituted molecules are complex, and depend strongly on the electrostatic and geometrical characteristics of the bonds. On the whole, the nematic properties of molecules can be considered in the scheme of the molecular geometrical and polarizational anisotropy, and the smectic properties can be considered as the result of local lateral interactions, among which the dipole–dipole interaction has the most important role in promoting the thermal stability of the smectic mesophase [1]. Thus, for example, polar liquid crystals containing nitro or cyano groups form antiparallel dimers in the mesophase owing to the strong dipole–dipole interaction [2], and tend to manifest nematic properties [3-5]; the carbonyloxy-p-phenylene systems are characterized by smectic polymorphism, which strongly depends on the orientation of the ester group in relation to the terminal substituents [1, 6].

In the study of the influence of the molecular structure of highly polar pyrimidine liquid crystals with ester bridges on the mesomorphic properties [7-10], the attempt was made to obtain pyrimidine analogs of known nematic p-cyanophenyl esters of p-(arylcarbonyloxy)benzoic acids [11] by the sequential substitution of the benzene rings by pyrimidine rings. The esters containing the fragment of the 5-alkylpyrimidine-2-carboxylic acid exhibited nematic properties in a wide range of temperatures [8]. However, the 5-hydroxy-2-cyanopyrimidine necessary for the synthesis of other analogs could not be obtained either by the debenzylation of 5-benzyloxy-2-cyanopyrimidine, or by the substitution of the methylsulfonyl group by the cyano group in 5-hydroxy-2-methylsulfonylpyrimidine (I). The esters (II) and (III), obtained from the hydroxypyrimidine (I), did not possess liquid crystal properties.

Scheme 1



Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences (RAN), Novosibirsk 630090. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 371-376, March, 1995. Original article submitted December 19, 1994.

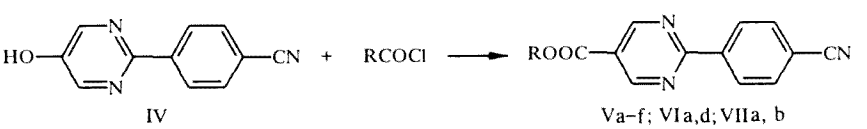
 0009-3122/95/3103-0320$12.50

TABLE 1. Characteristics of the Esters (II), (III), and (V)-(VII)

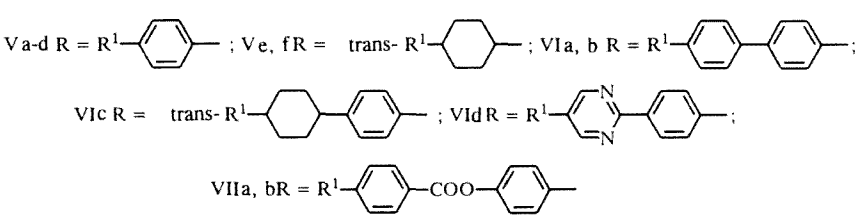
Compound	Temperatures of phase transitions, °C				IR spectra, ν, cm^{-1}	Yield, %
	K	S	N	I		
II			129...131		1750	77
III			142...145		1745, 1765	57
Va		122	247		1690, 2220	65
Vb		128	258		1680, 2230	82
Vc		162	274		1720, 2220	50
Vd	113	215	249		1720, 2210	77
Ve		108	233			40
Vf	79	132	231		1760, 2220	60
VIa		146	345 (decomp.)		1730, 2220	30
VIb		116	>300 (decomp.)		1730, 2220	24
VIc	147		>245 (decomp.)		1730, 2220	42
VId	153	349 (decomp.)			1730, 2220	10
VIIa	80	177	296		1725, 1760, 2220	20
VIIb	120	173	289		1730, 1740, 2230	15

Starting from the fact that the most favorable fragment in low-melting liquid crystal pyrimidine derivatives for the formation of the mesophase is the planar 2-arylpyrimidine fragment [12, 13], and also taking into account that the introduction of the aryl group stabilizes functional derivatives of pyrimidine [14], we utilized the bicyclic system — 5-hydroxy-2-(p-cyanophenyl)pyrimidine (IV), obtained by the acid hydrolysis of 5-(dimethylaminomethylenamino)-2-(p-cyanophenyl)pyrimidine — in the synthesis of liquid crystal ester derivatives of pyrimidine [15]. Compound (IV) was the basis for obtaining the esters (Va-f), containing three rings, as well as the monoesters (VIa-d) and diesters (VIIa, b) including four rings. By varying the framework of the molecule while preserving the terminal cyano group, favoring the development of nemetogenicity, we investigated features of the appearance of the nematogenicity in such structures including the comparison with analogous esters, not containing the terminal CN group, having the tendency to show smectic properties [10]. The characteristics of the compounds synthesized are presented in Table 1.

Scheme 2



IV Va-f; VIa,d; VIIa, b



Va, e $R^1 = C_4H_9$; Vb,f $R^1 = C_6H_{13}$; Vc $R^1 = OC_4H_9$; Vd $R^1 = OC_7H_{15}$; VIa $R^1 = C_5H_{11}$; VIb, VIIa $R^1 = C_7H_{15}$; VIc $R^1 = C_3H_7$; VId $R^1 = OC_8H_{17}$; VIIb $R^1 = OC_6H_{13}$

All the esters (V)-(VII) obtained are enantiotropic liquid crystals with wide ranges and high thermostability of the mesophase. Most of the compounds are also characterized by high temperatures for the transition into the mesophase (the mp).

The aromatic esters (Va-c) only showed nematic properties, as for the cyclohexane analog of the ester (Va), namely, the compound (Ve). A similar situation is generally observed for the properties of esters based on 4-hydroxy-4′-cyanobiphenyl: the biphenyl analogs of the esters (Va-c, e) are also purely nematic liquid crystals with ranges of the mesophase 130-160°C [16].

In contrast to the purely nematic p-cyanobiphenylyl ester of p-heptyloxybenzoic acid [17], the heptyloxy derivative (Vd) already shows smectic mesomorphism. The appearance of the smectic for the lower homologs in pyrimidine derivatives by comparison with p-phenylene systems was observed repeatedly [12, 18], and is evidently associated with the strengthening of lateral interactions [19].

Smectic mesomorphism appears in the cyclohexylcarboxylate (Vf) in contrast to the nematogens (Vb, e). In one case, this is associated with the lengthening of the terminal substituent in relation to the butyl homolog (Ve); in the other case, it is associated with substitution of the planar phenyl ring in the benzoate (Vb) by the trans-disubstituted cyclohexane ring, destabilizing the nematic mesophase [19]. It is known that the lengthening of the alkyl chain on the cyclohexane fragment stabilizes the mesophase, since the energetically advantageous transoid conformation of the alkyl group prolongs the geometry of the cyclohexane ring, which leads to the denser packing of the molecules and the appearance of smectogenicity [19]. However, the decrease of the geometrical and polarizational anisotropy in the esters (Ve, f) by comparison with the benzoates (Va, b) and the tendency of the terminal cyano derivatives for the formation of antiparallel dimers [2] leads to a decrease in the density of the packing of the molecules in the mesophase and the lowering of its thermodynamic stability. A consequence of this is the decrease in the temperatures of the N–I transition in the esters (Ve, f) by comparison with the esters (Va, b).

The appreciable difference in the properties of the two highly polar pyrimidinyl benzoates, determined by the steric and electrostatic nature of the terminal group, is observed using the example of the nematogen (Vb) and its 2-(p-nitrophenyl)pyrimidyl analog [10]. In contrast to the ester (Vb) with a wide nematic mesophase, the nitro analog forms wide smectic and narrow (4°C) nematic mesophases with the lower general extension of the mesophase (by 43°C) and the thermostability reduced by 39°C.

Therefore, the cyanophenyl derivatives (V) containing three rings tend, on the whole, to show nematogenicity with higher temperatures of the N–I transition than the p-phenylene analogs.

The monoesters (VI), having four rings, are characterized by the very high thermostability of the mesophase and decompose on heating, not reaching the transition into the isotropic state. The compounds (VIa, b) only have the nematic mesophase and thereby differ from biphenyl p-biphenylpylcarboxylates, which still also show smectic properties, and for which the N–I transition was not always successfully observed [20]. It is probable that the increase in the polarizational anisotropy in derivatives of pyrimidine with the one-sided direction of the dipole moments of the pyrimidine ring and the cyano group renders these compounds only nematogenic.

The esters (VIc, d), including correspondingly the cyclohexane ring or still one pyrimidine ring, only possess the smectic mesophase. Such a change in the properties for the cyclohexane derivative (VIc) can be explained by the geometry of the phenylcyclohexane fragment, favoring the formation of a lamellar structure; in the case of the derivative (VId), it can be explained by the appearance of an additional side interaction due to the second pyrimidine ring. These factors induce the development of smectogenicity by the compounds with the inhibition of nematic properties [19].

The introduction of an additional ester bridge in compounds of the type (VI) significantly changes their mesomorphic behavior. In contrast to the nematic monoesters (VIa, b), the diesters (VIIa, b) have a wide smectic mesophase in like manner to the geometrically folded benzoyloxybenzoates with a high-grade smectic nature (thanks to the effect of the packing of the folded molecules [1]). The presence of the terminal cyanophenyl grouping also allows the observation of the wide nematic mesophase with high thermodynamic stability.

EXPERIMENTAL

The IR spectra were recorded on the Specord M-80 instrument using KBr tablets. Temperatures of phase transitions and types of mesophases were determined by thermal microscopy using a heating stage of the Boetius type with the visual attachment of the RNMK-05 type. Designations are as follows: C for crystalline mesophase, S for smectic mesophase, N for nematic mesophase, and I for isotropic melt.

The data of the elemental analysis for the compounds obtained correspond with the calculated values.

5-Benzyloxy-2-cyanopyrimidine ($C_{12}H_9N_3O$). To the mixture of 7 g (26.5 mmole) of 5-benzyloxy-2-methylsulfonylpyrimidine [21] and 100 ml of dry DMF are added 2.6 g (0.04 mole) of KCN, and the mixture is stirred at 100°C for 3 h. The DMF is distilled off in the vacuum of a water jet pump, and the residue is treated with 50 ml of water; the product is extracted with CH_2Cl_2. The extract is dried with $MgSO_4$ and concentrated. The residue is recrystallized threefold from hexane and twice from CCl_4. The yield of 3.5 g (62%) of 5-benzyloxy-2-cyanopyrimidine is obtained. The mp is 96-98°C. The IR spectrum is characterized at 2230 cm^{-1} (C≡N).

5-(p-Heptylbenzoyloxy)-2-methylsulfonylpyrimidine (II) ($C_{19}H_{24}N_2O_4S$). To the solution of 1.65 g (6.9 mmole) of p-heptylbenzoyl chloride in 15 ml of dry pyridine is added 1 g (5.7 mmole) of the finely ground hydroxypyrimidine (I) [22]. The reaction mixture is stirred at 20°C using a magnetic stirrer for 10 h, and it is poured in a fine stream into the mixture of 30 g of ice and 20 ml of concentrated HCl. The precipitated yellow residue is filtered off, washed with acidified water, dried, and recrystallized from alcohol. The yield of 1.65 g of the ester (II) is obtained.

5-[p-(p-Heptylbenzoyloxy)-o-chlorobenzoyloxy]-2-methylsulfonylpyrimidine (III) ($C_{26}H_{27}ClN_2O_6S$). Using the method presented above, 1.73 g (4.4 mmole) of p-heptylbenzoyloxy-o-chlorobenzoyl chloride in 10 ml of dry pyridine and 0.63 g (3.6 mmole) of the pyrimidine (I) afford 1.1 g of the ester (III) after 4 h.

5-[p-Alkyl(alkoxy)benzoyloxy]-2-(p-cyanophenyl)pyrimidines (Va-d). The mixture of 0.2 mmole of the p-R-benzoic acid, 5 ml of $SOCl_2$, and 3 ml of dry benzene is boiled for 10-15 h. The excess of the $SOCl_2$ and the benzene is then distilled off. The acid chloride obtained is added to the solution of 0.2 mmole of the pyrimidine (IV) in 10 ml of pyridine, cooled to 0°C, and the mixture is stirred on a magnetic stirrer at 20°C for 48 h. The mixture is poured into 50 ml of 10% HCl, and the precipitated residue is filtered off, washed with water, and dried. The esters (Va) ($C_{22}H_{19}N_3O_2$) and (Vd) ($C_{25}H_{25}N_3O_3$) are recrystallized twice from methanol. The esters (Vb) ($C_{24}H_{23}N_3O_2$) and (Vc) ($C_{22}H_{19}N_3O_3$) are dissolved in $CHCl_3$, passed through a layer of Al_2O_3, and recrystallized as follows: the ester (Vb) sequentially from the 1:1 mixture of petroleum ether (40-70°C)–acetone and alcohol, and the ester (Vc) twice from methanol.

5-(Trans-4-butylcyclohexylcarbonyloxy)-2-(p-cyanophenyl)pyrimidine (Ve) ($C_{22}H_{25}N_3O_2$). To the mixture of 0.98 g (5 mmole) of the hydroxypyrimidine (IV) and 1 g (5 mmole) of trans-4-butylcyclohexanoyl chloride are added 20 ml of dry pyridine, and the mixture is stirred at 20°C for 40 h. The reaction mixture is filtered, and the filtrate is diluted with 100 ml of water. The residue is separated and extracted with 2 × 30 ml of boiling hexane. The hexane solution is concentrated to the volume of 15 ml and cooled. The precipitated residue is recrystallized sequentially from alcohol, hexane, and the mixture of hexane–petroleum ether (70-100°C). The yield of 0.83 g of the ester (Ve) is obtained. It has the M^+ 363, 1938.

5-(Trans-4-hexylcyclohexylcarbonyloxy)-2-(p-cyanophenyl)pyrimidine (Vf) ($C_{24}H_{29}N_3O_2$). To the mixture of 0.46 g (2 mmole) of trans-4-hexylcyclohexanoyl chloride and 10 ml of dry pyridine is added 0.39 g (2 mmole) of the hydroxypyrimidine (IV), and the mixture is stirred at 20°C for 3 days. The reaction mass is poured onto the mixture of 100 g of ice and 100 ml of 10% HCl; the mixture is stirred until the solution of the ice is effected. The residue is filtered off, washed with water, and recrystallized from alcohol. The yield of 0.46 g of the ester (Vf) is obtained. It has the M^+ 391, 2260.

5-(4-Amylbiphenylyl-4′-carbonyloxy)-2-(p-cyanophenyl)pyrimidine (VIa) ($C_{29}H_{25}N_3O_2$). The mixture of 0.3 g (1.12 mmole) of 4-amyl-4′-carboxybiphenyl and 10 ml of $SOCl_2$ is boiled for 5.5 h. The $SOCl_2$ is distilled off prior to the addition of 10 ml of benzene; the mixture is again concentrated to dryness. The resulting acid chloride is added with stirring to a solution of 0.22 g (1.12 mmole) of the hydroxypyrimidine (IV) in 10 ml of dry pyridine, cooled to 0-5°C, and the mixture is maintained at 20°C for 12 h. The reaction mixture is then poured into 50 ml of 10% HCl; the precipitated residue is filtered off, recrystallized from methanol, and purified on a column with Al_2O_3 using $CHCl_3$ as the eluent. The fraction with the R_f 0.38 (Silufol UV-254, $CHCl_3$) is evaporated, and the residue is recrystallized from ethyl acetate. The yield of the ester (VIa) is 0.15 g.

5-(4-Heptylbiphenylyl-4′-carbonyloxy)-2-(p-cyanophenyl)pyrimidine (VIb) ($C_{31}H_{29}N_3O_2$). The mixture of 0.5 g (1.7 mmole) of 4-heptyl-4′-carboxybiphenyl, 5 ml of dry benzene, and 5 ml of $SOCl_2$ is boiled for 4 h. The benzene and the $SOCl_2$ are distilled off to dryness, and 5 ml of benzene are added to the residue prior to renewed distillation. The resulting acid chloride is added to the solution of 0.34 g (1.7 mmole) of the hydroxypyrimidine (IV) in 6 ml of dry pyridine, cooled to 0-5°C, and the mixture is maintained at 60-70°C for 9 h. The cooled mixture is poured into 50 ml of 10% HCl, and the product is extracted with $CHCL_3$. The extract is washed with water, dried, and concentrated. The residue is recrystallized from the 1:1 mixture of petroleum ether (40-70°C)–acetone, and twice from methanol. The yield of the ester (VIb) is 0.19 g.

5-[p-(Trans-propylcyclohexyl)benzoyloxy]-2-(p-cyanophenyl)pyrimidine (VIc) ($C_{27}H_{27}N_3O_2$). The mixture of 0.18 g (0.59 mmole) of trans-4-propylcyclohexylcarboxylic acid, 5 ml of dry benzene, and 5 ml of $SOCl_2$ is boiled for 6 h. The excess of the $SOCl_2$ and the benzene is distilled off to dryness, and the resulting acid chloride is added to the solution of 0.12 g (0.59 mmole) of the pyrimidine (IV) in 5 ml of dry pyridine, cooled to 0-5°C. The mixture is maintained at 70°C for 16 h, cooled, and poured into 50 ml of 10% HCl. The residue is filtered off, washed with water, and dried prior to the isolation of 0.15 g of the ester (VIc), which is recrystallized twice from methanol.

5-[p-(5-Octyloxypyrimidin-2-yl)benzoyloxy]-2-(p-cyanophenyl)pyrimidine (VId) ($C_{30}H_{29}N_5O_3$). The mixture of 0.15 g (0.46 mmole) of 4-(5-octyloxypyrimidin-2-yl)benzoic acid, 7 ml of dry benzene, and 7 ml of $SOCl_2$ is boiled for 5 h.

The excess of the $SOCl_2$ and the benzene is distilled off. The resulting acid chloride is added with stirring to the solution of 0.09 g (0.46 mmole) of the pyrimidine (IV) in 10 ml of pyridine, cooled to 0-5°C, and the mixture is maintained at 20°C for 50 h. The mixture is poured into 50 ml of 10% HCl. The residue is filtered off, washed with water, dried, and chromatographed on a column with Al_2O_3 using $CHCl_3$ as the eluent, collecting the fraction with the R_f 0.8 (Silufol UV-254, the 20:1 mixture of $CHCl_3$ – alcohol). The residue remaining after the evaporation of the eluent is recrystallized from the 1:1 mixture of alcohol – benzene, and from alcohol. The yield of the ester (VId) is 0.03 g.

2-(p-Cyanophenyl)pyrimidinyl Esters of p-(p-R-Benzoyloxy)benzoic Acids (VIIa) ($C_{32}H_{29}N_3O_4$) and (VIIb) ($C_{31}H_{27}N_3O_5$). The mixture of 28 mmole of the p-R-benzoic acid and 25 ml of $SOCl_2$ is boiled for 7 h. The excess of the $SOCl_2$ is distilled off to dryness, and the resulting acid chloride is added to the solution of 3.86 g (28 mmole) of p-hydroxybenzoic acid in 30 ml of pyridine, cooled to 0-5°C. The mixture obtained is stirred at 20°C for 15 h. Subsequently, the reaction mass is poured onto ice with HCl; the residue is filtered off, dried, and recrystallized from acetic acid. The yields of the products are ~70%. The method described is utilized to obtain p-(p-heptylbenzoyloxy)benzoic acid (VIII) with the mp 123-124°C, and p-(p-hexyloxybenzoyloxy)benzoic acid (IX) with the mp 137-138°C. The IR spectrum is as follows: 1690 cm^{-1} and 1735 cm^{-1}.

The mixture of 2.8 mmole of the acid (VIII) or (IX), 10 ml of $SOCl_2$, 10 ml of CCl_4, and 2 drops of DMF is boiled for 16 h prior to the evaporation to dryness. The resulting acid chloride is added to the solution of 0.55 g (2.8 mmole) of the hydroxypyrimidine (IV) in the mixture of 5 ml of N-methylpyrrolidone and 1 ml of pyridine, cooled to 0°C. The reaction mass is stirred on a magnetic stirrer at 0°C for 12 h, and then at 20°C for 12 h. The mixture is poured into 100 ml of 10% sulfuric acid. The residue is filtered off, washed with water, dried, recrystallized from alcohol, and purified on a column with Al_2O_3 using $CHCl_3$ as the eluent, and then on a plate with silica gel using $CHCl_3$ as the eluent. The separated compounds (VIIa) and (VIIb) are recrystallized from ethyl acetate, and the diester (VIIa) is recrystallized additionally from alcohol.

REFERENCES

1. S. Takenaka, Y. Sakurai, H. Takeda, T. Ikemoto, H. Miyake, S. Kusabayashi, and T. Takagi, Mol. Cryst. Liq. Cryst., **178**, 103 (1990).
2. G. Heppke and S. Pfeiffer, Mol. Cryst. Liq. Cryst., **170**, 89 (1989).
3. M. A. Osman, Mol. Cryst. Liq. Cryst., **128**, 45 (1985).
4. R. Eidenschink, M. Rolmer, and F. V. Allan, Liq. Cryst. Ord. Fluids, Vol. 4, Plenum Press, New York (1984), p. 737.
5. V. S. Bezborodov, V. I. Lapanik, P. V. Adomenas, and R. Sirutkaitis, Liq. Cryst., **11**, 373 (1992).
6. H. Takeda, Y. Sakurai, S. Takenaka, H. Miyake, T. Doi, S. Kusabayashi, and T. Takagi, J. Chem. Soc. Faraday Trans., **86**, 3429 (1990).
7. 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).
8. M. A. Mikhaleva, V. A. Savel'ev, A. I. Pavlyuchenko, M. F. Grebenkin, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 9, 1228 (1986).
9. M. A. Mikhaleva, G. A. Kolesnichenko, T. A. Kizner, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 12, 1636 (1988).
10. T. A. Kizner, M. A. Mikhaleva, and E. S. Serebryakova, Khim. Geterotsikl. Soedin., No. 3, 386 (1991).
11. S. I. Zhdanov, Liquid Crystals [in Russian], Khimiya, Moscow (1979), p. 294.
12. A. Villiger, A. Boller, and M. Schadt, Z. Naturforsh., **34b**, 1535 (1979).
13. I. Rapthel, H. Hartung, R. Richter, and M. Jaskolski, J. Prakt. Chem., **325**, 489 (1983).
14. D. J. Brown, The Pyrimidines. The Pyrimidines, Suppl. I, II, Intersci. Publ., New York (1985).
15. M. A. Mikhaleva, G. A. Igonina, and T. A. Kizner, Khim. Geterotsikl. Soedin., No. 2, 206 (1993).
16. D. Demus and H. Zaschke, Flüssige Kristalle in Tabellen. II, VEB Deutscher Verlag für Grundstoffindustrie, Leipzig (1984), pp. 68, 287.
17. Pat. 3,951,846 USA. D. M. Gavrilovic, Ref. Zh. Khim., 2N164 (1977).
18. M. A. Mikhaleva, V. T. Lazareva, M. F. Grebenkin, V. A. Savel'ev, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 11, 1545 (1982).

19. M. A. Osman, Z. Naturforsch., **38A**, 693 (1983).
20. R. Dabrowski, K. Pyc, J. Przedmojski, and B. Pura, Mol. Cryst. Liq., **129**, 169 (1985).
21. D. T. Hurst, J. F. W. McOmie, and J. B. Searle, J. Chem. Soc., No. 12, 7116 (1965).
22. Z. Budesinsky, J. Prikryl, and E. Svatek, Coll. Czech. Chem. Commun., **32**, 1637 (1967).