

Synthesis and Mesomorphic Properties of New 3-Aryl-5-cyano-4,5-dihydroisoxazoles

V. S. Bezborodov, N. N. Kovganko, and V. I. Lapanik

Sevchenko Research Institute of Applied Physical Problems, Belarussian State University,
ul. Kurchatova 7, Minsk, 220064 Belarus
e-mail: bezborodov@bsu.by

Received December 29, 2002

Abstract—New 3-aryl-5-cyano-4,5-dihydroisoxazoles possessing liquid crystalline properties were synthesized in two ways. The key stage in both procedures is 1,3-dipolar cycloaddition of nitrile oxides to acrylonitrile.

Mesomorphic heterocyclic compounds attract strong interest from the viewpoint of creation of materials for electrooptical display devices (LCD) [1, 2]. These substances give rise to smectic or nematic phase at low temperature and over a wide temperature range [3]; they are characterized by high positive or negative dielectric anisotropy and are efficient components of liquid crystalline compositions with a low threshold and saturation voltage.

We previously described the synthesis and liquid crystalline properties of 3-alkyl-5-aryl-4,5-dihydroisoxazoles [4] and 5-alkyl-3-aryl-4,5-dihydroisoxazoles [5]. The key stage in the synthesis of these compounds was 1,3-dipolar cycloaddition of nitrile oxide generated from the corresponding hydroxamoyl chloride to 1-heptene (1-hexene) or methyl 4-vinylbenzoate, respectively.

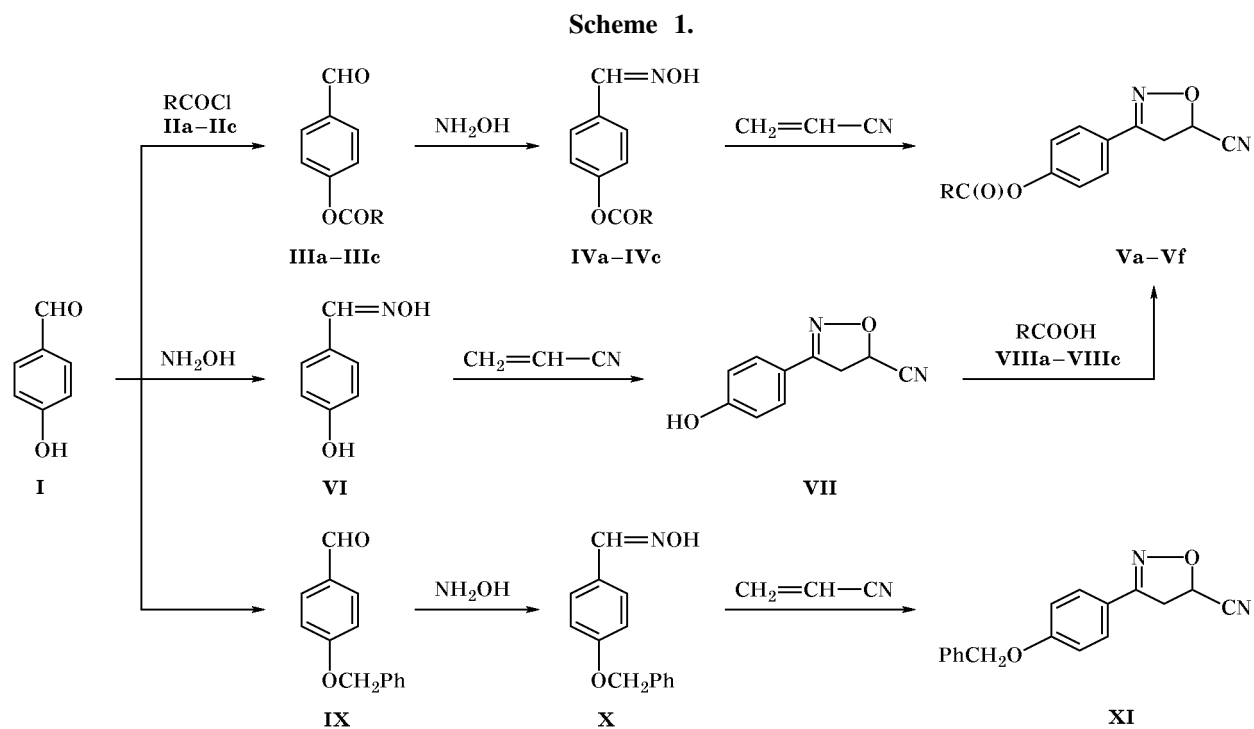
The goal of the present study was to synthesize new 3-aryl-5-cyano-4,5-dihydroisoxazoles **V** and examine their liquid crystalline properties. Unlike ferroelectric mesomorphic derivatives of pyrazole and isoxazole [6], compounds **V** could be utilized in liquid crystalline devices based on nematic materials.

We tried to obtain 3-aryl-5-cyano-4,5-dihydroisoxazoles **V** in two ways. The first of these includes building up of dihydroisoxazole ring at the last stage via 1,3-dipolar cycloaddition of nitrile oxide generated from oxime **IV** to acrylonitrile. It is known that such reactions occur in a regioselective fashion, yielding the corresponding 5-cyano derivatives [7]. Following this approach, 4-hydroxybenzaldehyde **I** was treated with 4-(octyloxy)benzoyl chloride (**IIa**) in the presence of pyridine to obtain 90% of ester **IIIa**. The latter was converted into the corresponding oxime **IVa**

in 68% yield by reaction with hydroxylamine hydrochloride in the presence of sodium acetate. Generation of nitrile oxide from **IVa** was effected by chlorination with *N*-chlorosuccinimide and subsequent dehydrochlorination with triethylamine in the presence of acrylonitrile. As a result, the target 5-cyano-4,5-dihydroisoxazole **Va** was synthesized in 66% yield. Ester **Vb** was obtained using an analogous reaction sequence.

The second approach is based on esterification of 5-cyano-4-(4-hydroxyphenyl)-4,5-dihydroisoxazole **VII** with acids **VIIIa–VIIIc**. As above, phenol **VII** was prepared from 4-hydroxybenzaldehyde oxime (**VI**). It should be noted that the chlorination of **VI** in the presence of pyridine led to formation of a complex mixture of products, from which we failed to isolate dihydroisoxazole **VII**. When hydrogen chloride was used as catalyst [8], compound **VII** was synthesized in 56% yield. We also made an attempt to obtain phenol **VII** from acetoxy derivative **Vc**. However, hydrolysis of **Vc** with potassium hydroxide in aqueous methanol gave a mixture of poorly soluble products. Analogous results were obtained in the debenylation of compound **XI** with hydrogen over Pd/C. According to the TLC data, a mixture of products was also formed in the synthesis of **VII** from benzyloxy derivative **XI**. Presumably, strong electron-acceptor character of the cyano group favors decomposition of the isoxazole ring in the above reactions. Esters **Vd–Vf** were synthesized by esterification of phenol **VII** with acids **VIIIa–VIIIc** in the presence of *N,N'*-dicyclohexylcarbodiimide (Scheme 1).

The structure of the products was confirmed by the IR and ¹H NMR spectra. The IR spectra of oximes



II–V, R = 4-C₈H₁₇OC₆H₄ (a), 4-C₉H₁₉OC₆H₄ (b), Me (c); Vd, VIIIa, R = 4-C₇H₁₅C₆H₄; Ve, VIIIb, R = 4-C₈H₁₇C₆H₄;
Vf, VIIIc, R = C₅H₁₁

IV, VI, and X lack aldehyde absorption bands but contain bands in the region 3120–3580 cm⁻¹, which correspond to stretching vibrations of the oxime hydroxy group. In the ¹H NMR spectra of dihydroisoxazole derivatives V, VII, and XI we observed two doublets at δ 3.64–3.83 ppm from the methylene protons on C⁴ and a doublet of doublets at δ 5.29–5.74 ppm from the 5-H proton.

Esters Va, Vb, and Vd–Vf were found to exhibit properties of liquid crystals. 4-Alkoxybenzoic acid derivatives Va and Vb give rise to monotropic smectic phase A. Compound Ve, which is a derivative of 4-alkylbenzoic acid, gives hard smectic phase E whose structure is similar to crystalline phase. *trans*-4-Pentylcyclohexanecarboxylate Vf forms thermotropic smectic phase A in the temperature range from

Table 1. Yields, phase transition temperatures, and IR spectra of oximes IVa–IVc, VI, and X

Compound no.	Yield, %	mp or phase transition temperature, °C	IR spectrum, ν, cm ⁻¹
IVa	68	Cr 88 N 122 I	3580, 3480–3200 (O–H), 3010 (C–H _{arom}), 2930, 2860 (C–H _{aliph}), 1725, 1255, 1070 (COOAr), 1600, 1500 (C=C _{arom}), 1165 (C–O)
IVb	96	Cr 93 N 130 I	3575, 3490–3140 (O–H), 3005 (C–H _{arom}), 2930, 2855 (C–H _{aliph}), 1725, 1250, 1065 (COOAr), 1600, 1500 (C=C _{arom}), 1160 (C–O)
IVc	56	96–97 (toluene)	3575, 3500–3120 (O–H), 3025 (C–H _{arom}), 1750 (C=O), 1600, 1500 (C=C _{arom})
VI	71	107–108 (toluene–ethyl acetate)	3595–3040 (O–H), 1675 (C=N), 1600, 1500 (C=C _{arom})
X	98	109–110 (toluene)	3570, 3465–3120 (O–H), 3000 (C–H _{arom}), 1600, 1500 (C=C _{arom}), 1170 (C–O)

Table 2. Yields, phase transition temperatures, and IR and ¹H NMR spectra of dihydroisoxazoles **Va–Vf**, **VII**, and **XI**

Comp. no.	Yield, %	mp or phase transition temperature, °C	IR spectrum, ν , cm^{-1}	¹ H NMR spectrum, δ , ppm (J , Hz)
Va	66	Heating: Cr 132 I Cooling: Cr 86 SmA 132 I	3005 (C–H _{arom}), 2920, 2850 (C–H _{aliph}), 1730, 1255, 1065 (COOAr), 1600, 1500 (C=C _{arom}), 1165 (C–O)	0.87 t (3H, CH ₃ , J = 4.5), 1.15–1.90 m (12H, CH ₂), 3.67 d (2H, 4-H, J = 8.3), 3.98 t (2H, OCH ₂ , J = 6.3), 5.31 t (1H, 5-H, J = 8.3), 6.91 d (2H, H _{arom} , J = 9.0), 7.24 d (2H, H _{arom} , J = 9.0), 7.66 d (2H, H _{arom} , J = 9.0), 8.07 d (2H, H _{arom} , J = 9.0)
Vb	55	Heating: Cr 136.5 I. Cooling: Cr 87 SmA 136.5 I	3005 (C–H _{arom}), 2925, 2850 (C–H _{aliph}), 1720, 1245, 1065 (COOAr), 1600, 1500 (C=C _{arom}), 1165 (C–O)	0.83 t (3H, CH ₃ , J = 4.5), 1.15–1.90 m (14H, CH ₂), 3.68 d (2H, 4-H, J = 8.3), 3.98 t (2H, OCH ₂ , J = 6.3), 5.32 t (1H, 5-H, J = 8.3), 6.91 d (2H, H _{arom} , J = 9.0), 7.24 d (2H, H _{arom} , J = 9.0), 7.66 d (2H, H _{arom} , J = 9.0), 8.07 d (2H, H _{arom} , J = 9.0)
Vc	46	137–138 (2-propanol)	3025 (C–H _{arom}), 1755 (OAc), 1600, 1500 (C=C _{arom})	2.25 s (3H, AcO), 3.64 d (1H, 4-H, J = 8.2), 3.65 d (1H, 4-H, J = 9.0), 5.29 d.d (1H, 5-H, J_1 = 8.2, J_2 = 9.0), 7.11 d (2H, H _{arom} , J = 9.0), 7.61 d (2H, H _{arom} , J = 9.0)
Vd	77	121 (2-propanol)	3025 (C–H _{arom}), 2955, 2930, 2855 (C–H _{aliph}), 1730, 1265, 1065 (COOAr), 1600, 1505 (C=C _{arom}), 1165 (C–O)	0.83 t (3H, CH ₃ , J = 7.2), 1.20–1.33 m (8H, CH ₂), 1.60 quint (2H, CH ₂ , J = 7.2), 2.64 t (2H, CH ₂ , J = 7.2), 3.66 d.d (1H, 4-H, J_1 = 6.8, J_2 = 16.4), 3.71 d.d (1H, 4-H, J_1 = 10.4, J_2 = 16.4), 5.32 d.d (1H, 5-H, J_1 = 6.8, J_2 = 10.4), 7.25 d (2H, H _{arom} , J = 2.0), 7.27 d (2H, H _{arom} , J = 2.0), 7.67 d (2H, H _{arom} , J = 8.8), 8.04 d (2H, H _{arom} , J = 8.8)
Ve	83	Cr 92–98 SmE 110 I	3015 (C–H _{arom}), 2920, 2865 (C–H _{aliph}), 1725, 1250, 1050 (COOAr), 1600, 1500 (C=C _{arom})	0.82 t (3H, CH ₃ , J = 7.2), 1.15–1.33 m (10H, CH ₂), 1.59 quint (2H, CH ₂ , J = 7.2), 2.64 t (2H, CH ₂ , J = 7.2), 3.66 d.d (1H, 4-H, J_1 = 6.8, J_2 = 16.4), 3.71 d.d (1H, 4-H, J_1 = 10.4, J_2 = 16.4), 5.32 d.d (1H, 5-H, J_1 = 6.8, J_2 = 10.4), 7.24 d (2H, H _{arom} , J = 2.0), 7.27 d (2H, H _{arom} , J = 2.0), 7.67 d (2H, H _{arom} , J = 8.8), 8.04 d (2H, H _{arom} , J = 8.8)
Vf	81	Cr 107 SmA 121 I	3020, (C–H _{arom}), 2960, 2930, 2855 (C–H _{aliph}), 1740, 1160, 1115 (COOAr), 1600, 1505 (C=C _{arom})	0.88 t (3H, CH ₃ , J = 5.8), 1.14–1.38 m (10H, CH ₂), 1.43–2.35 m (7H, CH and CH ₂), 2.48 t.t (1H, CHCOO, J_1 = 3.4, J_2 = 11.9), 3.70 d (1H, 4-H, J = 7.0), 3.71 d (1H, 4-H, J = 8.9), 5.35 d.d (1H, 5-H, J_1 = 7.0, J_2 = 8.9), 7.14 d (2H, H _{arom} , J = 8.8), 7.66 d (2H, H _{arom} , J = 8.8)
VII	56	150.5–151.5 (toluene–ethyl acetate)	3530–3050 (O–H), 1600, 1505 (C=C _{arom})	3.82 d (1H, 4-H, J = 8.9), 3.83 d (1H, 4-H, J = 7.0), 5.74 d.d (1H, 5-H, J_1 = 7.0, J_2 = 8.9), 6.85 d (2H, H _{arom} , J = 8.8), 7.55 d (2H, H _{arom} , J = 8.8), 10.10 br.s (1H, ArOH)
XI	43	147 (2-propanol–methyl ethyl ketone)	3010 (C–H _{arom}), 1695 (C=N), 1600, 1500 (C=C _{arom}), 1165 (C–O)	3.64 d (1H, 4-H, J = 7.2), 3.65 d (1H, 4-H, J = 9.5), 5.07 s (2H, PhCH ₂ O), 5.28 d.d (1H, 5-H, J_1 = 7.2, J_2 = 9.5), 6.97 d (2H, H _{arom} , J = 9.0), 7.28–7.41 m (5H, H _{arom}), 7.55 d (2H, H _{arom} , J = 9.0)

107 to 121°C. It should be noted that the obtained compounds are characterized by a high positive dielectric anisotropy ($\Delta\epsilon > 10$); therefore, they can be used in the preparation of nematic liquid crystalline compositions with a low threshold voltage.

EXPERIMENTAL

The melting points and phase transition temperatures were determined on a heating device coupled with a polarization microscope. The IR spectra were recorded on a Specord 75IR spectrometer. The ^1H NMR spectra were measured on Tesla BS-567A (80 MHz) and Tesla BS-567 (100 MHz) instruments using HMDS as internal reference.

Esters **IIIa–IIIc** were synthesized by reaction of 4-hydroxybenzaldehyde (**I**) with carboxylic acid chlorides **IIa–IIc** according to the procedure described in [9]. Chlorides **IIa** and **IIb** were prepared by treatment of the corresponding acids with thionyl chloride. The properties of esters **IIIa** and **IIIb** were in agreement with published data [9].

4-(Hydroxyiminomethyl)phenyl 4-octyloxybenzoate (IVa). A solution of 12.8 g of aldehyde **IIIa** in 100 ml of 2-propanol was heated to the boiling point, and a solution of 3.0 g of hydroxylamine hydrochloride and 3.6 g of sodium acetate in a mixture of 20 ml of 2-propanol and 40 ml of water was added dropwise. The mixture was stirred for 1.5 h on heating under reflux, 50 ml of water was added to the hot mixture, and the mixture was cooled to -20°C . The precipitate was filtered off, and an additional amount of the product was isolated from the mother liquor. Yield 9.0 g (68%).

Oximes **IVb**, **IVc**, **VI**, and **X** were synthesized in a similar way (Table 1).

4-(5-Cyano-4,5-dihydroisoxazol-3-yl)phenyl 4-octyloxybenzoate (Va). To a solution of 1.8 g of oxime **IIIa** in 15 ml of chloroform and 5 ml of dimethylformamide we added 0.8 g of *N*-chlorosuccinimide and one drop of pyridine. The mixture was cooled with ice to 0°C , and 5 ml of acrylonitrile was added. A solution of 0.85 ml of triethylamine in 10 ml of chloroform was then added dropwise over a period of 1.5 h. The mixture was stirred for an additional 1 h and filtered, and the filtrate was treated with dilute (1:9) hydrochloric acid, washed with three

portions of water, and dried over sodium sulfate. The solvent was removed under reduced pressure, and the residue was subjected to column chromatography on aluminum oxide using methylene chloride as eluent. Yield of **Va** 1.36 g (66%).

Compounds **Vb**, **Vc**, **VII**, and **XI** were synthesized in a similar way (Table 2).

4-(5-Cyano-4,5-dihydroisoxazol-3-yl)phenyl 4-heptylbenzoate (Vd). A catalytic amount of 4-dimethylaminopyridine was added to a mixture of 0.393 g of 4-heptylbenzoic acid, 0.352 g of 3-(4-hydroxyphenyl)-4,5-dihydroisoxazole-5-carbonitrile (**VII**), and 0.394 g of *N,N'*-dicyclohexylcarbodiimide in 15 ml of methylene chloride. The mixture was stirred for 20 h at room temperature, and the precipitate was filtered off through a layer of aluminum oxide and washed with two portions of methylene chloride. The filtrate was evaporated under reduced pressure, and the residue was recrystallized from 2-propanol. Yield 0.537 g (77%).

Esters **Ve** and **Vf** were synthesized in a similar way (Table 2).

REFERENCES

1. Nagashima, Y., Ichihashi, T., Noguchi, K., Iwamoto, M., Aoki, Y., and Nohira, H., *Liq. Cryst.*, 1997, vol. 23, p. 537.
2. Brettle, R., Dunmur, D.A., Marson, C.M., Pinol, M., and Toriyama, K., *Liq. Cryst.*, 1993, vol. 13, p. 515.
3. Friedman, M.R., Toyne, K.J., Goodby, J.W., and Hird, M., *Liq. Cryst.*, 2001, vol. 28, p. 901.
4. Min'ko, A.A., Bezborodov, V.S., Kovganko, N.N., and Lapanik, V.I., *Vestn. Bel. Gos. Univ., Ser. 1*, 2002, p. 44.
5. Bezborodov, V.S., Kovganko, N.N., and Lapanik, V.I., *Vestsi Nats. Akad. Navuk Belarusi, Ser. Khim. Navuk*, 2003, p. 48.
6. Iglesias, R., Serrano, J.L., and Sierra, T., *Liq. Cryst.*, 1997, vol. 22, p. 37.
7. Rai, K.M.L. and Hassner, F., *Indian J. Chem., Ser. B*, 1997, vol. 36, p. 242.
8. Liu, K.-C., Shelton, B.R., and Howe, R.K., *J. Org. Chem.*, 1980, vol. 45, p. 3916.
9. Malhete, J., Canceill, J., Gabard, J., and Jacques, J., *Tetrahedron*, 1981, vol. 37, p. 2815.