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Synthesis of New Liquid-crystalline Compounds from the 3-Aryl-5-alkylpyrazole Series

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Abstract—A method was developed for the preparation of new liquid-crystalline substances, pyrazole derivatives, through the corresponding 2-isoxazolines and isoxazoles. The hydrogenolysis of the heterocycle in 3-(4-hydroxyphenyl)-5-amylisoxazole afforded 1-amino-1-(4-hydroxyphenyl)-1-octen-3-one. The acid hydrolysis of the compound followed by treating with hydrazine hydrate resulted in 5-amyl-3-(4-hydroxyphenyl)-1*H*-pyrazole, whose benzylation and esterification with the corresponding mesogenous benzyl chlorides and benzoyl chlorides provided liquid-crystalline 5-alkyl-3-aryl-1*H*-pyrazoles.

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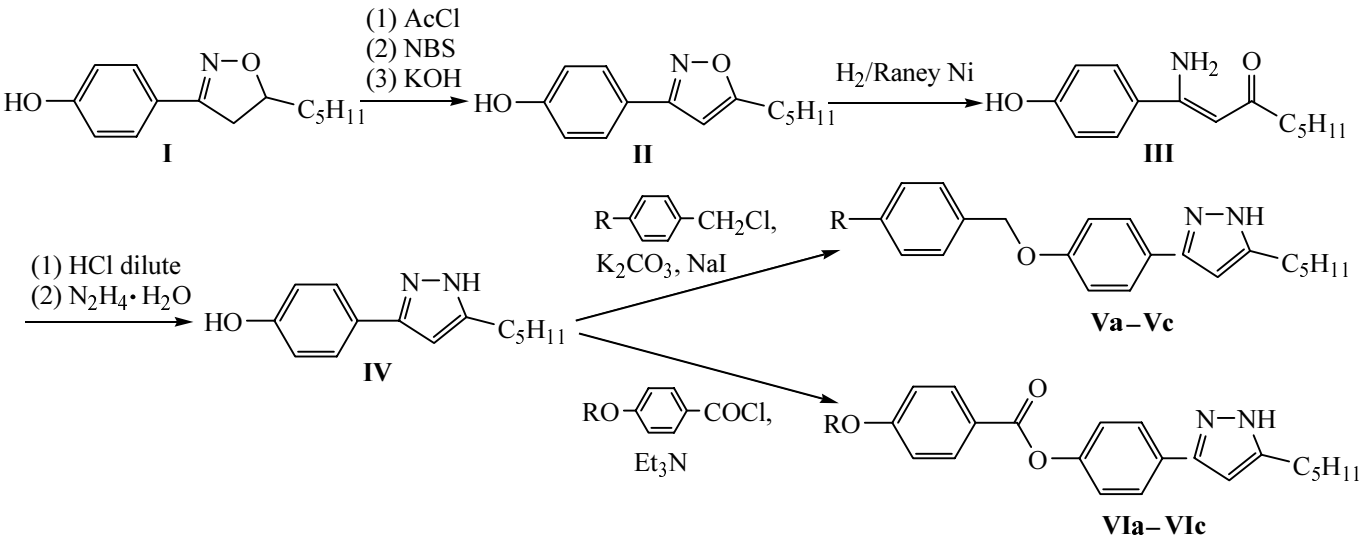
Nowadays liquid-crystalline compounds containing five-membered heterocycles are the subject of much investigation [1–3]. In particular, the pyrazole ring belongs to such structural fragments of mesomorphous compounds. Quite a number of liquid crystals based on 3,5-disubstituted pyrazoles was reported [3–10]. The majority of compounds synthesized belong to 3,5-diarylpyrazoles, whereas no published data exists on preparation of mesomorphous compounds from the group of 5-alkyl-3-arylpyrazoles. The synthesis of the compounds is the goal of the present study.

The general preparation procedure for liquid crystals based on 3,5-disubstituted pyrazoles consists in application as the key intermediate products of the corresponding β-diketones [4–10]. The substituted β-diketones are known to be produced by transformation of the corresponding isoxazoles [11]. We recently developed a method for preparation of mesomorphous 5-alkyl-3-

Scheme.



V, R = CN (**a**), 4-$C_3H_7OC_6H_4$ (**b**), 4-$C_5H_{11}C_6H_4$ (**c**); **VI**, R = C_5H_{11} (**a**), C_6H_{13} (**b**), C_9H_{19} (**c**).

arylisoxazoles proceeding from the transformation of the corresponding 2-isoxazolines [12]. In this study we planned to use these 2-isoxazolines and isoxazoles for preparation of liquid-crystalline 5-alkyl-3-arylpyrazoles.

The formerly performed [12] synthesis of liquid-crystalline 5-alkyl-3-arylisoxazoles was based on the use of compound **II** prepared by the oxidation of the corresponding 2-isoxazoline **I** [12–14]. In the further synthesis of the liquid-crystalline pyrazoles we planned to carry out the opening of the hetrocycle in isoxazole **II**.

In the first stage the hydrogenolysis of the isoxazole ring in compound **II** on Raney nickel afforded in a 92% yield enaminoketone **III** whose structure was confirmed by the data of UV, IR, and ^{1}H NMR spectra. The UV spectrum of compound **III** contained two characteristic maxima at 268 and 329 nm. In the IR spectrum of enaminoketone **III** the vibrations of the system of conjugated bonds C=O and C=C appear as strong bands in the region 1485–1600 cm^{-1}. In the ^{1}H NMR spectrum of compound **III** the vinyl proton H^2 gave rise to a singlet at δ 5.44 ppm, whereas the analogous proton in the ^{1}H NMR spectrum of the initial isoxazole **II** appeared as a singlet at δ 6.23 ppm [12]. The presence of an amino group in the enaminoketone **III** is confirmed by its stretching vibrations band at 3480 cm^{-1}. In the spectrum of the compound in question an absorption band is also observed at 3580 cm^{-1} corresponding to the stretching vibrations of the phenol hydroxy group that is also presnt in the IR spectrum of initial isoxazole **II** [12]. In the ^{1}H NMR spectrum of compound **III** the protons of OH and NH_2 groups appeared as a one-proton multiplet at 6.90–7.02 ppm and two broadened one-proton singlets at 5.25 and 10.04 ppm respectively.

In the subsequent stage of the synthesis the enaminoketone **III** was subjected to hydrolysis by boiling its tetrahydrofuran solution in the presence of diluted hydrochloric acid. The reaction of the arising β-diketone with hydrazine hydrate afforded pyrazole **IV** in a quantitative yield.

The structure of compound **IV** was also confirmed by the data of UV, IR, and ^{1}H NMR spectra. The UV spectrum of compound **IV** is characterized by the absorption maximum corresponding to the conjugation system between the phenol and pyrazole rings at 258.5 nm. In the ^{1}H NMR spectrum the proton of the heterocycle H^4 appeared as a singlet at 6.32 ppm, in a characteristic position for 3,5-disubstituted pyrazoles [4–10].

To obtain the target liquid-crystalline compounds we carried out benzylation and esterification of compound **IV** at the phenol group with mesogenous benzyl chlorides and acyl chlorides. The reaction of pyrazole **IV** with benzyl chlorides in the presence of potassium carbonate and sodium iodide furnished the corresponding benzyl ethers **Va–Vc** in 84–90% yields. The benzoylation of compound **IV** with 4-alkoxybenzoyl chlorides in tetrahydrofuran in the presence of triethyl amine afforded the corresponding esters **VIa–VIc** in 39–52% yields.

Phase transition temperature for compounds **Vb** and **Vc**, **VIa–VIc**

Compd. no.	mp, °C	Smectic phase	Nematic	T.cl., °C[a]
Vb	182	•*SmA*	–	234
Vc	153	•*SmC 207 SmA*	–	224
VIa	143.5	–	•	(139)
VIb	146	–	•	(135)
VIc	116.5	–	•	126.5

[a] T.cl. is clearing point. The temperature of monotropic transition isotropic liquid–nematic phase are given in parentheses.

Note that the preparation of compounds **Va–Vc** and **VIa–VIc** may be accompanied by benzylation and benzoylation not only of hydroxy group but also of the nitrogen of the pyrazole ring. However in the ^{1}H NMR spectra of compounds **Va–Vc** and **VIa–VIc** appears a single signal of the benzyl or benzoyl group respectively, and in their IR spectra absorption bands are observed in the region 3445–3475 cm^{-1} belonging to the vibrations of the N–H bond. Besides in the IR spectra of esters **VIa–VIc** the vibrations of the C=O bond give rise to the band at 1720–1725 cm^{-1} characteristic of substituted aryl benzoates [12, 14]. These findings support the structures of benzyl ethers **Va–Vc** and benzoates **VIa–VIc**.

The study of phase transitions in benzyl ethers **Va–Vc** and benzoates **VIa–VIc** revealed that five among them are liquid-crystalline (see the table), and compound **Va** did not form a mesophase. Compounds **VIa** and **VIb** possess monotropic nematic phases in a range of 12 and 11°C respectively. The other compounds are characterized by enantiotropic mesophases. It should be noted that the characteristic feature of 3,5-diarylpyrazoles described in the literature is in general the formation of a smectic phase *A* [4–10]. In the case of compounds we synthesized the wide range of the smectic phase *C* for benzyl ether **Vc** should be noted, and also the presence of nematic phases for benzoates **VIa–VIc**.

Hence the results of our study demonstrate that the great synthetic potential of 2-isoxazolines and isoxazoles

makes it possible to apply them as intermediate substances for preparation of liquid crystals.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Specord 75-IR in KBr cell from chloroform solutions (if not otherwise indicated). UV spectra were taken on a spectrophotometer Specord M40 from methanol solutions (if not otherwise indicated). ^{1}H NMR spectra of solutions in deuterochloroform (if not otherwise indicated) were registered on a spectrometer Bruker Avance 400 (400 MHz) using HMDS as an internal reference. The reaction progress was monitored and the purity of compounds obtained was checked by TLC on Kieselgel 60 F_{254} (Merck) plates. The melting points and phase transition temperatures were measured on a heating block coupled with a polarization microscope. The mesophase type was estimated by comparison of the observed texture with the corresponding standards given in a monograph [15].

1-Amino-1-(4-hydroxyphenyl)-1-octen-3-one (III). A dispersion of 2 g of Raney nickel in 15 ml of methanol was saturated with hydrogen at stirring for 30 min. Then a solution was added of 2.30 g (9.96 mmol) of 5-amyl-3-(4-hydroxyphenyl)isoxazole (**II**) (prepared by procedure [12]) in 40 ml of methanol. The reaction mixture thus obtained was stirred under hydrogen atmosphere for 9.5 h. The catalyst was filtered off and washed on the filter with 30 ml of methanol. The solvent from the filtrate was distilled off under a reduced pressure, and the residue was applied to a column packed with silica gel and subjected to gradient elution with a mixture of ethyl acetete with petroleum ether, from 1:3 to 2:1. On distilling off of the eluent under the reduced pressure we obtained 2.13 g (92%) of enaminoketone **III**, mp 120–121°C (from toluene–petroleum ether). UV spectrum, λ_{max}, nm: 268, 329 (CH_3OH); 256, 320 (dioxane). IR spectrum, cm^{-1}: 3580, 3480, 3425–3015 (OH, NH), 2995 (C–H_{ar}), 2950, 2925, 2855 (C–H_{alk}), 1600, 1570, 1530, 1485 (C=O, C=C, C=C_{ar}). IR spectrum (THF), cm^{-1}: 3500–3030 (OH, NH), 1600, 1575, 1530, 1485 (C=O, C=C, C=C_{ar}). ^{1}H NMR spectrum, δ, ppm: 0.87 t (3H, CH_3, *J* 7 Hz), 1.26–1.38 m (4H), 1.58–1.72 m (2H) (CH_2), 2.37 t (2H, C^4H_2, *J* 7.5 Hz), 5.44 s (1H, H^2), 6.91 d (2H, ArH, *J* 8.5 Hz), 7.45 d (2H, ArH, *J* 8.5 Hz), 5.25 br.s (1H), 6.90–7.02 m (1H), 10.04 br.s (1H) (OH, NH_2).

5-Amyl-3-(4-hydroxyphenyl)-1*H*-pyrazole (IV). To a solution of 0.726 g (3.116 mmol) of enaminoketone **III** in 20 ml of THF was added 5.5 ml of diluted hydrochloric acid, 1:10. The resulting mixture was boiled at reflux for 1 h, then 20 ml of chloroform and 30 ml of a saturated sodium chloride solution was added. The chloroform layer was separated, the water layer was additionally extracted with chloroform (2×10 ml). The combined chloroform extracts were washed with 15 ml of the saturated sodium chloride solution, then the solvent was distilled off under a reduced pressure. The residue was diluted with 10 ml of methanol, and 0.3 ml (6.18 mmol) of hydrazine hydrate was added. The solution obtained was boiled for 1 h, then diluted with 50 ml of water, and cooled to 4°C. The separated precipitate of pyrazole **IV** was filtered off, washed on the filter in succession with 100 ml of water and 5 ml of cooled petroleum ether. After drying in a vacuum we obtained 0.688 g (96%) of compound **IV**, mp 150–151°C (from toluene). UV spectrum, λ_{max}, nm: 258.5. IR spectrum (THF), cm^{-1}: 3650–3050 (OH, NH), 1610, 1525, 1500 (C=C_{ar}). ^{1}H NMR spectrum [$(CD_3)_2CO$], δ, ppm: 0.88 t (3H, CH_3, *J* 7 Hz), 1.28–1.40 m (4H), 1.67 quintet (2H, *J* 7.5 Hz), 2.64 t (2H, *J* 7.5 Hz) (CH_{2alk}), 6.32 s (1H, H^4), 6.84 d (2H, ArH, *J* 8.5 Hz), 7.63 d (2H, ArH, *J* 8.5 Hz).

5-Amyl-3-[4-(4-cyanophenyl)methoxy]phenyl-1*H*-pyrazole (Va). To a solution of 0.060 g (0.261 mmol) of phenol **IV** and 0.039 g (0.257 mmol) of cyanobenzyl chlorode in 7 ml of acetone was added 0.077 g (0.513 mmol) of sodium iodide and 0.500 g (3.623 mmol) of potassium carbonate. The reaction mixture obtained was boiled at stirring for 5 h, then 30 ml of water was added. The separated precipitate was filtered off and washed with water. Yield 0.078 g (88%). The analytically pure sample was obtained by double recrystallization from on 2-propanol. mp 136°C (from 2-propanol). UV spectrum, λ_{max}, nm: 234, 259. IR spectrum, cm^{-1}: 3445 (NH), 2950, 2920, 2850 (C–H_{alk}), 2225 (C≡N), 1605, 1570, 1550, 1515, 1495 (C=C_{ar}). ^{1}H NMR spectrum, δ, ppm: 0.89 t (3H, CH_3, *J* 7 Hz), 1.29–1.40 m (4H), 1.67 quintet (2H, CH2, *J* 7.5 Hz), 2.64 t (2H, CH_2, *J* 7.5 Hz), 5.14 s (2H, Ar'–CH_2–O–Ar), 6.29 s (1H, H^4), 6.96 d (2H, ArH, *J* 9 Hz), 7.55 d (2H, ArH, *J* 9 Hz), 7.64–7.70 m (4H, ArH).

Similarly were prepared compounds **Vb** and **Vc**.

5-Amyl-3-[4-(4'-propyloxy-4-biphenyl)methoxy]-phenyl-1*H*-pyrazole (Vb). Yield 90%. UV spectrum, λ_{max}, nm: 266. IR spectrum, cm^{-1}: 3450 (NH), 3000 (C–H_{ar}), 2955, 2925, 2855 (C–H_{alk}), 1605, 1570, 1555, 1515, 1490 (C=C_{ar}). ^{1}H NMR spectrum, δ, ppm: 0.89 t (3H, CH_3, *J* 7 Hz), 1.05 t (3H, CH_3, *J* 7 Hz), 1.30–1.40 m (4H), 1.67 quintet (2H, *J* 7.5 Hz), 1.82 sextet (2H,

J 7 Hz), 2.65 t (2H, *J* 7.5 Hz) (CH_2), 3.96 t (2H, Ar'–OCH_2, *J* 7 Hz), 5.11 s (2H, Ar'–CH_2–O-–Ar), 6.29 s (1H, C^4H), 6.96 d (2H, ArH, *J* 9 Hz), 7.01 d (2H, ArH, *J* 8.5 Hz), 7.47 d (2H, ArH, *J* 8 Hz), 7.51 d (2H, ArH, *J* 9 Hz), 7.56 d (2H, ArH, *J* 8 Hz), 7.64 d (2H, ArH, *J* 8.5 Hz).

3-[4-(4'-Amyl-4-biphenyl)methoxy]phenyl-5-amyl-1*H*-pyrazole (Vc). Yield 84%. UV spectrum, λ_{max}, nm: 263. IR spectrum, cm^{-1}: 3445 (NH), 3000 (C–H_{ar}), 2950, 2925, 2850 (C–H_{alk}), 1610, 1570, 1550, 1515, 1490 (C=C_{ar}). ^1H NMR spectrum, δ, ppm: 0.89 t (6H, CH_3, *J* 7 Hz), 1.30–1.40 m (8H), 1.60–1.72 m (4H), 2.60–2.68 m (4H) (CH_2), 5.11 s (2H, Ar'–CH_2–O–Ar), 6.29 s (1H, H^4), 7.01 d (2H, ArH, *J* 9 Hz), 7.24 d (2H, ArH, *J* 8 Hz), 7.48 d (2H, ArH, *J* 8 Hz), 7.50 d (2H, ArH, *J* 8 Hz), 7.59 d (2H, ArH, *J* 8 Hz), 7.64 d (2H, ArH, *J* 9 Hz).

4-(5-Amyl-1*H*-pyrazol-3-yl)phenyl 4-amyloxybenzoate (VIa). To a solution of 0.055 g (0.264 mmol) of 4-amyloxybenzoic acid in 5 ml of dichloromethane was added 1 drop of dimethylformamide and 0.2 ml (2.78 mmol) of thionyl chloride. The reaction mixture obtained was boiled for 1 h, the solvent and excess thionyl chloride were distilled off at the atmospheric pressure. The residue was dissolved in 5 ml of dichloromethane, and the solvent was distilled off at a reduced pressure to remove completely the thionyl chloride. The acyl chloride thus obtained was dissolved in 5 ml of THF, 0.35 ml (2.52 mmol) of triethylamine, and 0.060 g (0.261 mmol) of phenol **IV** was added. The reaction mixture was stirred for 2.5 h at 20°C, then 15 ml of water and 15 ml of chloroform was added. The organic layer was separated, the water layer was additionally extracted with chloroform (2×10 ml). The combined organic solutions were washed with 20 ml of water. After drying with sodium sulfate the solvent was distilled off under a reduced pressure, and the residue was recrystallized from 2-propanol. Yield 0.055 g (50%). UV spectrum, λ_{max}, nm: 263. IR spectrum, cm^{1}: 3475 (NH), 3005 (C–H_{ar}), 2955, 2930, 2870, 2855 (C–H_{alk}), 1725 (C=O), 1600, 1570, 1555, 1515, 1500 (C=C_{ar}), 1250, 1200, 1165, 1070 (C–O). ^1H NMR spectrum, δ, ppm: 0.90 t (3H, CH_3, *J* 7 Hz), 0.94 t (3H, CH_3, *J* 7.5 Hz), 1.30–1.50 m (8H), 1.69 quintet (2H, *J* 7.5 Hz), 1.82 quintet (2H, *J* 7 Hz), 2.67 t (2H, *J* 7.5 Hz) (CH_2), 4.04 t (2H, $ArOCH_2$, *J* 7 Hz), 6.35 s (1H, H^4), 6.96 d (2H, ArH, *J* 9 Hz), 7.23 d (2H, ArH, *J* 9 Hz), 7.77 d (2H, ArH, *J* 9 Hz), 8.14 d (2H, ArH, *J* 9 Hz).

Compounds **VIb** and **VIc** were prepared in the same way.

4-(5-Amyl-1*H*-pyrazol-3-yl)phenyl 4-hexyloxybenzoate (VIb). Yield 52%. UV spectrum, λ_{max}, nm: 267. IR spectrum, cm^{-1}: 3450 (NH), 2950, 2925, 2855 (C–H_{alk}), 1720 (C=O), 1600, 1570, 1555, 1500 (C=C_{ar}), 1245, 1200, 1160, 1070 (C–O). ^1H NMR spectrum, δ, ppm: 0.90 t (3H, CH_3, *J* 7 Hz), 0.91 t (3H, CH_3, *J* 7 Hz), 1.28–1.40 m (8H), 1.47 quintet (2H, *J* 7 Hz), 1.68 quintet (2H, *J* 7.5 Hz), 1.81 quintet (2H, *J* 7 Hz), 2.66 t (2H, *J* 7.5 Hz) (CH_2), 4.03 t (2H, $ArOCH_2$, *J* 7 Hz), 6.35 s (1H, H^4), 6.96 d (2H, ArH, *J* 9 Hz), 7.23 d (2H, ArH, *J* 9 Hz), 7.77 d (2H, ArH, *J* 9 Hz), 8.13 d (2H, ArH, *J* 9 Hz).

4-(5-Amyl-1*H*-pyrazol-3-yl)phenyl 4-nonyloxybenzoate (VIc). Yield 39%. UV spectrum, λ_{max}, nm: 268. IR spectrum, cm^{-1}: 3455 (NH), 2925, 2855 (C–H_{alk}), 1720 (C=O), 1600, 1570, 1500 (C=C_{ar}), 1250, 1200, 1165, 1070 (C–O). ^1H NMR spectrum, δ, ppm: 0.89 t (3H, CH_3, *J* 7 Hz), 0.90 t (3H, CH_3, *J* 7 Hz), 1.22–1.41 m (14H), 1.47 quintet (2H, *J* 7 Hz), 1.69 quintet (2H, *J* 7.5 Hz), 1.81 quintet (2H, *J* 7 Hz), 2.67 t (2H, *J* 7.5 Hz) (CH_2), 4.03 t (2H, $ArOCH_2$, *J* 7 Hz), 6.36 s (1H, H^4), 6.96 d (2H, ArH, *J* 9 Hz), 7.23 d (2H, ArH, *J* 9 Hz), 7.78 d (2H, ArH, *J* 9 Hz), 8.14 d (2H, ArH, *J* 9 Hz).

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