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Liquid Crystalline 4,4′-diaryl-2,2′-bithiazoles†

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Several new non-symmetrically substituted 4,4′-diphenyl-2,2′-bithiazole derivatives were synthesized with the use of a novel synthetic methodology comprising modified Hantzsch synthesis and palladium-catalyzed Kharash cross-coupling reaction at the key steps. Mesogenic properties of the new compounds were studied by optical and calorimetric methods. The most promising for practical applications are easily accessible non-symmetrical 4,4′-diaryl-2,2′-bithiazoles containing alkyl and alkoxy substituents at the para*-positions of the aryl moieties that exhibit wide-range high-temperature smectic-C phases.*

Keywords Bithiazoles; Hantzsch synthesis; Kharash cross-coupling reaction; smectic C phase

1. Introduction

Readily available by cost effective synthetic methods, 4,4′-diaryl-2,2′-bithiazoles **1** consisting of symmetrical molecules were shown to possess nematic and smectic A thermotropic mesophases [1]. However, the relatively high phase transition temperatures of these symmetric compounds **1** do not enable their practical use as smectic hosts. Moreover, the synthetic approach applied restricts variability of the molecular structure of such compounds and consequently decrease possibility to tune their mesogenic properties.

Thus, the aim of this work is to improve the mesogenic properties of 4,4′-diaryl-2,2′-bithiazoles **1** (i.e., to reduce their melting points and, preferably, to increase the mesomorphic range) by varying the molecular structure of such compounds. For this purpose, non-symmetrically substituted bithiazoles **2a**—**d** and **3**, and also symmetrically substituted compound **4** were synthesized with the use of novel synthetic

†Dedicated to the memory of Professor Lidiya Kutulya (1939–2010).

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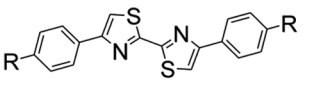
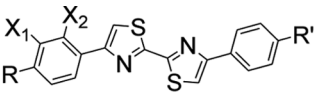
methods, and their mesogenic properties were investigated.



1b: R = OC_6H_{13}

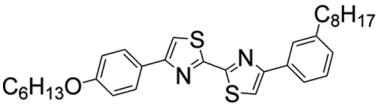


2a: $X_1 = X_2 = H$, R = C_9H_{19}, R' = C_5H_{11}

2b: $X_1 = X_2 = H$, R = OC_6H_{13}, R' = C_8H_{17}

2c: $X_1 = F$, $X_2 = H$, R = OC_6H_{13}, R' = C_8H_{17}

2d: $X_1 = X_2 = F$, R = OC_6H_{13}, R' = C_8H_{17}



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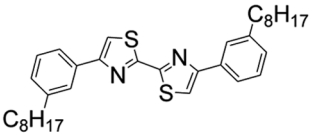

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Variations of the molecular structure of compounds **2**—**4** (with the reference to the known symmetrical compound **1b**) consist in the introduction of terminal alkyl and/or alkoxy substituents of different length, lateral fluorination and changing the molecular shape of these compounds by terminal *metha*-substitution.

2. *Experimental Methods*

^{1}H NMR spectra were recorded on a Varian Mercury VX-200 (200 MHz) and a Bruker Avance-400 (400 MHz) spectrometers in $CDCl_3$ or C_6D_6/CCl_4 using signal of residual protons as inner standard [2]. Mass spectra were recorded on a Varian 1200 L GC-MS instrument either in GC-MS mode or with the use of direct exposure probe (DEP) method with EI at 70 eV. HPLC analyses were performed on a Bischoff HPLC system equipped with 4.0 × 250 mm Prontosil 120-5-C18H reversed phase column using acetonitrile and mixtures of acetonirtile with chloroform as eluents; for preparative HPLC the 20 × 200 mm Prontosil 120-10-C18H reversed phase column was used.

Optical textures and phase transition temperatures were studied using a Kofler hot stage and LOMO polarizing microscope. DSC measurements were done by means of Mettler TA-3000 thermoanalitical instrument at 5°C/min heating/cooling rate.

Bromine, rubeanic acid, bromopentane, bromooctane, magnesium turnings and $PdCl_2$dppf (complex with DCM) are commercially available and were used without additional purification. All used solvents were distilled immediately before use. THF was distilled over potassium-benzophenone prior to use.

Synthesis of Thioamides 7 and 8 (General Procedure). A solution of the corresponding α-bromo acetophenone **5** or **6** (30 g, 0.1 mol) in DMF (80 mL) was added dropwise for 3 h to a stirred solution of rubeanic acid (26 g, 0.2 mol, 2 equiv) in DMF (180 mL). The mixture was stirred for three days. Then the precipitate of symmetrically substituted bithiazole by-product (**9** or **10** correspondingly) was filtered off and the solution obtained was treated with

stirring with the solution of KOH (9 g) in water (40 mL). The precipitate formed was filtered, washed with diluted aqueous KOH (3 × 50 mL) and water and dried in air at ambient temperature. Then the precipitate was re-crystallized from isopropyl alcohol-acetone mixture (3:2 vol.) and filtered while hot. The crystals formed at cooling of the filtrate were collected and dried. Yields: 42% (**7**), 63% (**8**).

Synthesis of Bithiazoles 12a—d and 13b (General Procedure). The corresponding acyl bromide **11a—d** (6 mmol) and thioamide **7** or **8** (6 mmol) were mixed together in DMF (20 mL) and the mixture was stirred overnight. The precipitate formed was filtered off, washed with butanol (2 × 20 mL) and recrystallized from the mixture of acetonitrile and chloroform (3:1 vol.). Yields: 44% (**12a**), 50% (**12b**), 64% (**12c**), 67% (**12d**), 54% (**13b**).

Synthesis of the Target Compounds 2 and 3 (General Procedure). The corresponding alkylmagnesium bromide (obtained from corresponding alkyl bromide, magnesium turnings (1.2 equiv) in THF (1 mL per 1 mmol of alkyl bromide) by well-known Grignard methodology) was added dropwise under atmosphere of dry argon to the stirred mixture of the corresponding aryl bromide (0.5 equiv based on alkyl bromide), $PdCl_2$dppf (0.05 equiv based on aryl bromide) in THF (1 mL per 1 mmol of aryl bromide) (*CAUTION*! The reaction mixture undergoes spontaneous heating) and then was left overnight with stirring. Methanol was added to the mixture dropwise (2 mL per 1 mmol of alkyl bromide) and the suspension obtained was evaporated to dryness. The residue was diluted with dichloromethane and filtered through the short pad of Celite, and the filtrate was evaporated to dryness. The residue was transferred onto silica and extracted with hot heptane/benzene (3:1 vol.) in the modified Soxhlet apparatus, and then further purified by appropriate methods (see below).

4-(4-Nonylphenyl)-2-(4-(4-pentylphenyl)thiazol-2-yl)thiazole 2a. Re-crystallized from isopropyl alcohol. Yield 55%. Purity 98.8% (HPLC). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm, J/Hz): 7.89 (4H, d, $J = 8.0$), 7.53 (2H, s), 7.27 (4H, d, $J = 8.2$), 2.66 (4H, t, $J = 7.6$), 1.66 (4H, m), 1,35 (8H, m), 1,28 (8H, m), 0.91 (3H, t, $J = 6.8$), 0.89 (3H, t, $J = 7.1$). MS (m/z, (I, %)): 516 (M^+, 100), 459 (21), 403 (48), 347 (22), 147 (45).

2-(4-(4-(Hexyloxy)phenyl)thiazol-2-yl)-4-(4-octylphenyl)thiazole 2b. Re-crystallized from acetonitrile/acetone/$CHCl_3$ (3:1:1 vol.). Yield 78%. Purity 98.4% (HPLC). ^{1}H NMR (C_6D_6/CCl_4 (1:3 vol.), 200 MHz, δ, ppm, J/Hz): 7,77 (2H, d), 7.76 (2H, d), 7.06 (2H, d, $J = 8.3$), 6.91 (1H, s), 6.83 (1H, s), 6.78 (2H, d, $J = 8.8$), 3.66 (2H, t, $J = 6.4$), 2.47 (2H, t, $J = 7.6$), 1.54 (4H, m), 1.19 (16H, m), 0.82 (3H, t), 0.81 (3H, t). MS (m/z, (I, %)): 532 (M^+, 100), 447 (38), 349 (77), 335 (60), 147 (15).

2-(4-(3-Fluoro-4-(hexyloxy)phenyl)thiazol-2-yl)-4-(4-octylphenyl)thiazole 2c. Re-crystallized from acetonitrile/acetone (3:1 vol.). Yield 72%. Purity 95.0% (HPLC). Analyticaly pure sample (purity 99.2% (HPLC)) was obtained by preparative HPLC. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm, J/Hz): 7.88 (2H, d, $J = 7.5$), 7.72 (1H, d, $J = 12.2$), 7.67 (1H, d, $J = 8.0$), 7.53 (1H, s), 7.46 (1H, s), 7.27 (2H, d, $J = 7.6$), 7.02 (1H, t (dd), $J = 8.5$), 4.08 (2H, t, $J = 6.5$), 2.65 (2H, t, $J = 7.6$), 1.85 (2H, m), 1.65 (2H, m), 1.50 (2H, m), 1.31 (14H, m), 0.92 (3H, t), 0.89 (3H, t). MS (m/z, (I, %)): 550 (M^+, 100), 465 (66), 366 (32), 147 (15).

2-(4-(2,3-Difluoro-4-(hexyloxy)phenyl)thiazol-2-yl)-4-(4-octylphenyl)thiazole 2d. Re-crystallized from acetonitrile/acetone (3:1 vol.). Yield 60%. Purity 93.0% (HPLC). Analytically pure sample (purity 95.8% (HPLC)) was obtained by preparative HPLC. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm, J/Hz): 7.97 (1H, dd, $J=8.5$), 7.88 (2H, d, $J=12.2$), 7.75 (1H, s), 7.53 (1H, s), 7.27 (2H, d. $J=7.6$), 6.84 (1H, t (dd), $J=7.8$), 4.09 (2H, t, $J=6.5$), 2.66 (2H, t, $J=7.5$), 1,85 (2H, m), 1.65 (2H, m), 1.50 (2H, m) 1.32 (14H, m), 0.93 (3H, t), 0.90 (3H, t). MS (m/z, I, %): 568 (M^+, 100), 483 (95), 384 (15), 147 (25).

2-(4-(4-(Hexyloxy)phenyl)thiazol-2-yl)-4-(3-octylphenyl)thiazole 3. Re-crystallized from isopropyl alcohol/$CHCl_3$ (3:1 vol.). Analyticaly pure sample (purity 96.1% (HPLC)) was obtained by preparative HPLC. Yield 24%. ^{1}H NMR (C_6D_6/CCl_4 (1:3 vol.), 200 MHz, δ, ppm, J/Hz): 7.72 (2H, d, $J=8.7$), 7.67 (1H, s), 7.61 (1H, d, $J=7.8$), 7.14 (1H, t), 7.06 (1H, s), 6.96 (1H, d), 6.94 (1H, s), 6.75 (2H, d, $J=8.7$), 3.71 (2H, t, $J=6.4$), 2.51 (2H, t, $J=7.6$), 1.56 (4H, m), 1.18 (16H, m), 0.81 (3H, t), 0.79 (3H, t). MS (m/z, (I, %)): 532 (M^+, 100), 350 (42).

Synthesis of Symmetrically Substituted Bithiazoles 1b and 4 (General Procedure). The corresponding α-bromoacetophenone **11b** or **14** (15 mmol), rubeanic acid (0.09 g, 7.5 mmol) and DMF (5 mL) were mixed together and the mixture was stirred overnight. The precipitate formed was filtered and recrystallized from isopropyl alcohol.

4-(4-(Hexyloxy)phenyl)-2-(4-(4-(hexyloxy)phenyl)thiazol-2-yl)thiazole 1b. Yield 68%. Purity 99.4% (HPLC). ^{1}H NMR (C_6D_6/CCl_4 (1:3 vol.), 200 MHz, δ, ppm, J/Hz): 7.75 (4H, d, $J=8.2$), 6.88 (2H, s), 6.76 (4H, d, $J=8.0$), 3.68 (4H, t, $J=6.0$), 1.59 (4H, quintet), 1.21 (12H, m), 0.81 (6H, t). MS (m/z, (I, %)): 520 (M^+, 100), 435 (15), 350 (65).

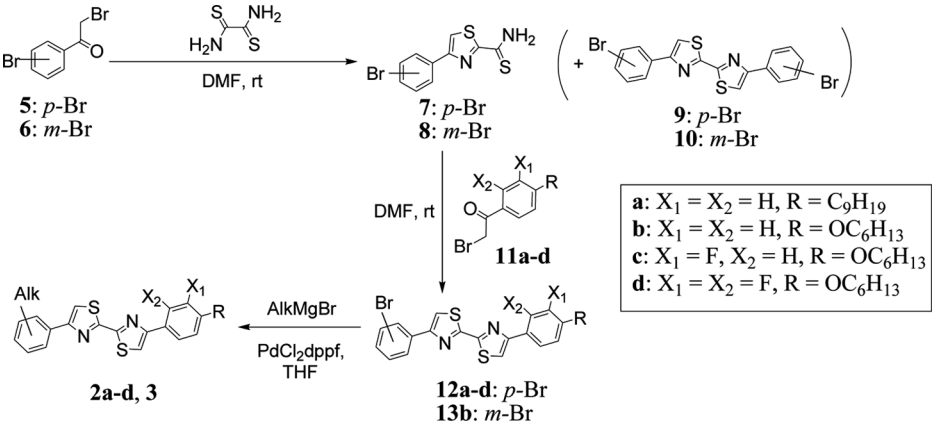
4-(3-Octylphenyl)-2-(4-(3-octylphenyl)thiazol-2-yl)thiazole 4. Yield 33%. Purity 99.7% (HPLC). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm, J/Hz): 7,80 (2H, s), 7.79 (2H, d), 7.58 (2H, s), 7.37 (2H, t, $J=8.1$), 7.20 (2H, d, $J=7.3$), 2.70 (4H, t, $J=7,4$), 1.69 (4H, quintet), 1.33 (20H, m), 0.89 (6H, t). MS (m/z, (I, %)): 544 (M^+, 100), 445 (18).

3. Results and Discussion

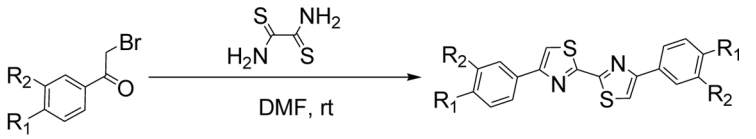
3.1. *Synthesis*

A novel synthetic procedure comprising modified Hantzsch methodology and palladium-catalyzed Kharash cross-coupling reaction at the key steps was used for the synthesis of non-symmetrically substituted bithiazoles **2a**—**d** and **3** (Scheme 1).

Our modification of Hantzsch synthesis (with respect to the known method [1,3,4]) consists of using DMF as solvent. This allows carrying out the reaction at room temperature which is found to be favorable for the enhancement of the reaction selectivity. Thus, the intermediate bromophenyl thioamides **7** and **8** are obtained under these conditions in moderate to good yields from the reaction of α-bromo acetopenones **5** and **6** correspondingly with a double excess of rubeanic acid. Moreover, low solubility of the symmetrically substituted bithiazole by-products **9** and **10** in DMF at room temperature allows them to be easily removed by simple filtration of the reaction mixture. Using similar modified protocol for the next step, bithiazoles **12a**—**d** and **13b** are synthesized in moderate to good yields. And again, the low



Scheme 1. Synthesis of non-symmetrically substituted bithiazoles **2a**—**d** and **3**.



11b: $R_1 = OC_6H_{13}$, $R_2 = H$
14: $R_1 = H$, $R_2 = C_8H_{17}$

1b, 4

Scheme 2. Synthesis of symmetrically substituted bithiazoles **1b** and **4**.

Table 1. Phase transition temperatures of bithiazoles **1b**, **2**—**4**[a]

Entry	Compound	Cr		SmC		SmA		N		I
1[b]		•	107			•	180	•	197	•
2	**1b**	•	181 (+97.9)	•	*197*	•	*206*	•	230 (+4.6)	•
									230 (−.4.3)	
3	**2a**	•	117 (+37.7)			•			190 (+16.5)	•
			115 (−34.7)						189 (−16.8)	
4	**2b**	•	131 (+39.9)	•	*165*	•	198	•	200 (+12.6)[c]	•
			121 (−36.2)				196		198 (−12.3)[c]	
5	**2c**	•	132 (+64.9)	•	*147*	•			189 (+17.7)	•
			120 (−57.9)						187 (−17.8)	
6	**2d**	•	129 (+62.9)			•			167 (+13.5)	•
			122 (−60.3)						166 (−15.0)	
7	**3**	•	112 (+91.0)							•
8	**4**	•	101 (+100.4)							•

[a]Phase transition temperatures (enthalpies) are given in °C (J/g) according to DSC (in the corresponding cells, top data set corresponds to heating, lower data set corresponds to cooling) or according to microscopic investigation at cooling (values shown *in italics*).
[b]Data from [1].
[c]Sum of coalescent peaks of SmA ↔ N and N ↔ I phase transitions.

solubility of compounds **12a**—**d** and **13b** in DMF favors their simple isolation and purification. The target non-symmetrically substituted bithiazoles **2a**—**d** and **3** were obtained by Kharash cross-coupling reaction [5] of aryl bromides **12a**—**d** and **13b** with corresponding alkyl Grignard reagents in the presence of catalytic amount of $PdCl_2$dppf.

The symmetrically substituted bithiazoles **1b** and **4** were also synthesized by modified Hantzsch procedure from the corresponding α-bromo acetopenones **11b** and **14** and 0.5 equiv of rubeanic acid in moderate to good yields (Scheme 2).

3.2. *Mesomorphic Properties*

Characteristic optical textures and phase transitions of mesophases formed by the new compounds **2**—**4** were studied by polarizing microscopy. Temperatures and enthalpies of the first order phase transitions were measured using DSC technique.

The determined phase transition temperatures for the new compounds **2**—**4** and the previously described compound **1b** are given in Table 1. Typical optical textures are shown in Figure 1.

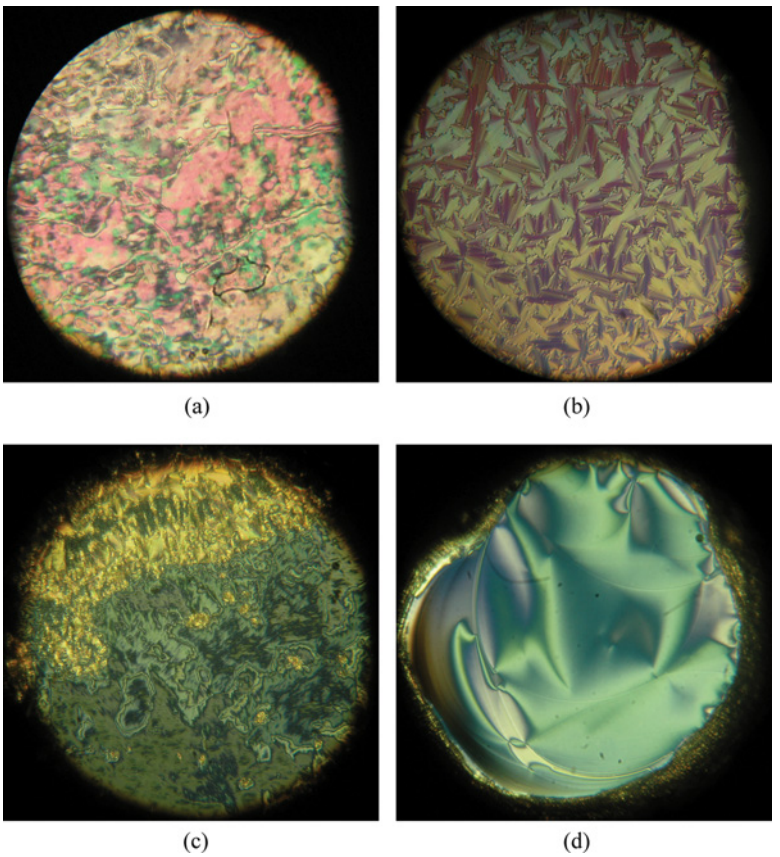


Figure 1. Typical optical textures of bithiazoles **1b**, **2**—**4**; (*a*) compound **1b**, glass plates, 216°C, nematic phase; (*b*) compound **2a**, glass plates, 143°C, SmA phase; (*c*) compound **2b**, glass plates, 158°C, SmC phase at different boundary conditions; (*d*) compound **2c**, free-suspended film, 147°C, SmC phase. (Figure appears in color online.)

Surprisingly, in our hands, known compound **1b** which was synthesized and investigated in our laboratory (Table 1, entry 2) exhibits mesomorphic behavior rather different from the one described in the literature [1] (entry 1). The differences are revealed both in the aspect of phase sequence and in the phase transition temperatures of the compound **1b**.

When two terminal alkyl substituents of different length are introduced into the 4,4′-diaryl-2,2′-bithiazole core (compound **2a**, Table 1, entry 3), a substantial reduction of the melting temperature and some increase of the mesomorphic range as well as suppression of SmC and N phases formation occur in comparison to the reference compound **1b**. In comparison with **2a**, the substitution of the terminal alkyl substituent with an alkoxy group (compound **2b**, entry 4) leads to some increase of the melting temperature and narrowing of the mesomorphic range, however the SmC phase again occurs. The substitution of the lateral hydrogen atom with fluorine (**2c**, entry 5) does not lead to the essential reduction of the melting temperature but substantially decreases mesomorphic range as well as ability of this compound to form the SmC and completely suppresses the N phase formation. The introduction of the second fluorine atom (**2d,** entry 6) furthermore decreases the mesomorphic range and completely suppresses the ability to form SmC and N phases. The change of the shape of 4,4′-diaryl-2,2′-bithiazole molecules by *metha*-substitution in the aryl moieties (compounds **3** and **4**, entries 7 and 8 respectively) leads to the complete suppression of mesomorphic properties.

It is worth mentioning that despite of rather high clearing temperature observed for compounds **2a**—**d**, they do not show any changes in the phase transition temperatures even after several heating-cooling cycles. As an exeption, the most high-thermal range compound **1b** exhibits some decrease in isotropic transition temperature after several heating-cooling cycles, however only slight changes in its composition are detectable by HPLC analyses.

4. Conclusions and Perspectives

Non-symmetrical substitution of 4,4′-diaryl-2,2′-bithiazole molecules with terminal alkyl and/or alkoxy groups of different length in comparison to symmetrical substitution lead to the substantial reduction of the melting temperature and some increase of the mesomorphic range. At least one alkoxy substituent in 4,4′-diaryl-2,2′-bithiazole molecules is required for the formation of SmC phase. Lateral fluorination of 4,4′-diaryl-2,2′-bithiazole molecules does not lead to essential reduction of the melting temperature but substantially decreases the mesomorphic range and ability to form SmC phase. Change in the molecular shape of 4,4′-diaryl-2,2′-bithiazole molecules by *metha*-substitution at the aryl moieties leads to suppression of the mesomorphic properties.

The most promising for practical applications are easy accessible non-symmetrical 4,4′-diaryl-2,2′-bithiazoles comprising alkyl and alkoxy substituents in *para*-positions of the aryl moieties.

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