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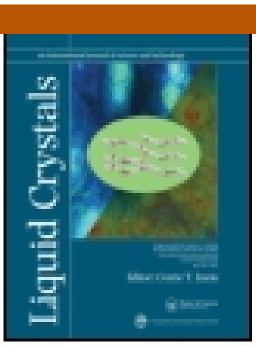

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Symmetric 3,5-pyrazole and isoxazole heterocycles comprising a bent core unit: synthesis and mesomorphic characterisation

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The synthesis and characterisation of some new liquid crystalline (LC) heteroaromatic compounds containing the five-membered pyrazole/isoxazole rings is reported. Some of the compounds exhibited enantiotropic LC properties. The transition temperatures and LC textures of the mesophases were determined using polarised optical microscopy (POM), differential scanning calorimetry (DSC) and X-ray studies. The five-membered heterocyclic compounds with the pyrazole core exhibit smectic C (SmC) phase, whereas isoxazoles show SmC and nematic (N) phases.

Keywords: liquid crystals; heterocycles; isoxazoles; pyrazoles; smectic phases; nematic phase

1. Introduction

A number of liquid crystalline (LC) compounds containing the heterocyclic rings such as pyridinyl-, pyrimidinyl-, furyl-, thiazolyl-, thiadiazolyl-, oxadiazolyl-, benzimidazolyl-, pyrazolyl-, isoxazolyl-, thiophenyl-, coumarinyl- and quinolinyl are reported.[1,2] When five- or six-membered heterocycles are involved, they form part of the core in rod-shaped, bent-shaped or disc-shaped LC molecules.[3–5] The LC compounds containing heterocyclic groups have been synthesised due to their potential wide range of multidisciplinary applications such as in optical,[6] dielectrics [7] and phamacologicals.[8,9] Thus, interest in mesomorphic heterocyclic compounds has increased significantly due to their diversified structures and distinct mesomorphic properties.[10–12]

The heterocycles as core units in thermotropic liquid crystals impart lateral and/or longitudinal dipoles combined with changes in the molecular shape.[13–16] Incorporation of heteroatoms results in considerable changes in the corresponding LC and physical properties, due to the fact that most of the heteroatoms (S, O and N) are more polarisable than carbon.[17]

Pyrazoles are normally prepared via diacetylenes– and transition metal–mediated cyclisation methods using eco-friendly, easy, environmentally green procedures.[18,19] The 3,5-disubstituted LC pyrazoles and their non-mesogenic rhodium (I), copper (II) metal complexes were also prepared and evaluated to their single crystal studies and liquid crystal properties.[20,21] Moyano et al. have reported that the amide group is essential for the aggregation leading to the mesomorphism in supramolecular arrangement in LC containing the unprecedented 4-aryl-1H-pyrazole unit with ester linkage. This moiety is able to self-assemble by H-bonding to give columnar mesophases and also display luminescent properties in the visible region. The moiety is a non-discoid molecule that displays a hexagonal columnar mesophase.[22,23]

Significant efforts have been devoted to find new synthetic methods for preparation of pyrazole derivatives.[24] Heller et al. worked out an efficient, simple and easy method for the synthesis of 3,5-disubstituted pyrazoles.[25] The reactions of 1,3-dialkynes with hydrazine hydrate proceed smoothly in dimethyl sulphoxide under mild reaction conditions to produce 3,5-disubstituted pyrazoles in satisfactory to excellent yields.[26]

Isoxazoles have also proved to be important heterocycles for the LC materials showing rich mesomorphism due to the dipole moment and polarity of the molecule. Iglesias et al. studied the structure–activity relationship of some chiral compounds having either a pyrazole or an isoxazole ring as a central bridge in the mesogenic core. The pyrazole compounds account for their lower polarity values in comparison with the isoxazole analogues. The lateral tail gives rise to the best mesomorphic and ferroelectric properties. Existence of mesomorphic property was predicted on the results of most abundant conformation of the molecules.[27]

In continuation of our research objectives which deal with the preparation, characterisation and evaluation of silyl-mediated reagents and materials, we

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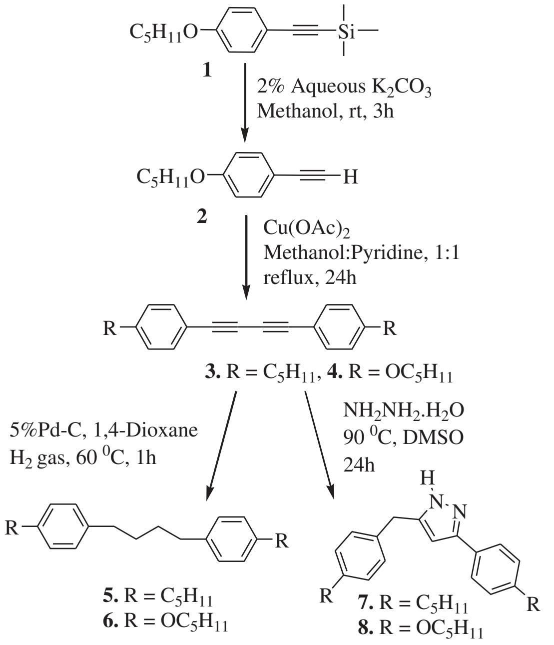
now report the synthesis, characterisation and mesomorphic evaluation of some new 3,5-substituted pyrazoles and isoxazoles from diaryldiacetylenes and 1,3-diketones.

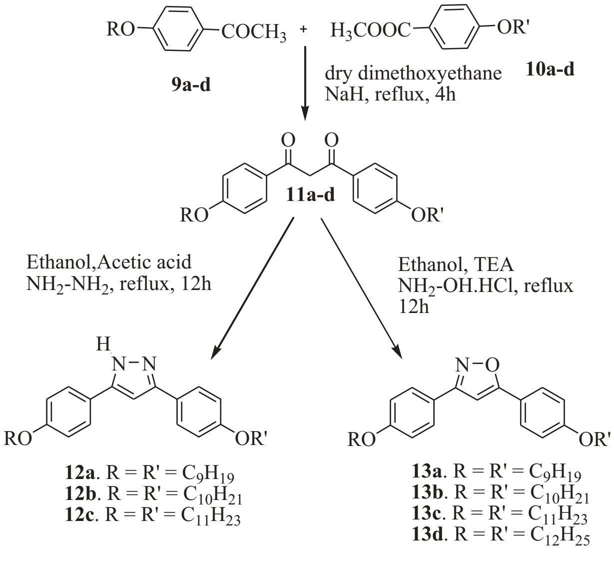
2. Results and discussions

2.1. Synthesis and structural characterisation

The methodology for the preparation of pyrazoles and isoxazoles is outlined in the Schemes 1 and 2.



Scheme 1. Synthetic route for compounds **1–8**.



Scheme 2. Synthetic route for **12a–c** and **13a–d**.

The mesogenic diaryldiacetylene compounds **3** and **4** upon palladium-catalysed hydrogenation yielded saturated flexible alkyl chain derivatives **5** and **6** which are non-mesogenic.[28,29] The diaryldiacetylenes **3** and **4** were converted into 3,5-disubstituted pyrazoles **7** and **8** in the presence of hydrazine hydrate, via the Cope-type reaction.[30] The disappearance of 2140 cm^{-1} wave number peak for acetylene group in infrared spectrum confirmed the formation of 3,5-substituted pyrazole from the diarydiacetylenes. Further, confirmation was obtained by other spectroscopic analysis. In the ^{1}H NMR spectrum of 3,5-pyrazole compounds the proton signal for the NH pyrazole was not observed. This is attributed due to quadrupole effect of nitrogen atom.

The syntheses of symmetric pyrazoles **12a–c** and isoxazoles **13a–c** are outlined in the Scheme 2. The 4-alkoxyacetophenones **9a–d** and methyl 4-alkoxybenzoates **10a–d** were prepared from 4-hydroxyacetophenone and methyl 4-hydroxybenzoat,e respectively, by the Williamson's ether reaction with the corresponding alkyl bromides. Aldol-type condensation reaction of the 4-alkoxy acetophenones and methyl 4-hydroxybenzoates with sodium hydride in dimethoxyethane afforded the symmetrical 1,3-diketones **11a–d** in yield ranging from 45% to 60%.[31] Subsequent reaction of the 1,3-diketones with hydrazine hydrate and catalytic quantity of glacial acetic acid in ethanol gave 3,5-substituted pyrazoles **12a–c**.

Reaction of the 1,3-diketones **11a–d** with hydroxylamine hydrochloride and triethylamine in ethanol gave isoxazoles **13a–d,** respectively. The compounds **12a–c** and **13a–d** were off-white crystalline materials upon recrystallisation from methanol.

2.2. Mesomorphic properties

The study of correlation between the structural relationship, molecular structure and mesomorphic behaviour of the parent diaryldiacetylenes, 1,3-diketones and their five-membered heterocyclic compounds was carried out. Pyrazoles and isoxazoles have proved high efficiency in promoting mesomorphic properties when acting as central bridges in 1,3-diphenylpyrazole and 1,3-diphenylisoxazole derivatives. These heterocyclic derivatives show a marked tendency to display smectic mesomorphism. In addition, pyrazole and isoxazole rings have shown to contribute significantly to the molecular dipole by virtue of the high dipole moment contained in the plane of the heterocycle.[32]

Gallardo et al. reported symmetrical and asymmetrical fluorescent mesogenic compounds containing the 2,1,3-benzothiadiazole chromophore as the central core substituted with 1,2,4-oxadiazole, 1,2,3-triazole and 1,2-isoxazole heterocycles. It was observed that the bending angles of the five-membered heterocyclic substituents are crucial in determining the thermal stability of the liquid crystal phases, indicating that a delicate balance of forces is involved in the phase formation. Evidently the designed compounds possess different degrees of curvatures due to different inherent bend angles of the N-heterocyclic substituents to evaluate the influence of the structure on the thermal and optical properties. All these series of compounds shows thermal stability in the order 1,2-isoxazole > 1,2,3-triazole > 1,2,4-oxadiazole.[33]

On the basis of these points, we synthesised and investigated the mesomorphic properties of some new long-chain-derived 3,5-substituted pyrazoles (**12a–c**) and isoxazole compounds (**13a–d**). Compounds **12b** and **13b** are reproduced here to serve as reference compounds as well as to plot transition temperatures with respect to number of carbon atoms at terminal alkyl chain.[25]

The transition temperatures, associated enthalpies and phase assignment of compounds **3–8, 12a–c** and **13a–d** are summarised in Tables 1 and 2. The phase transition temperatures reported in this paper were the peak values of the transition on differential scanning calorimetry (DSC) curves. Phase identification was made by comparing the observed textures with those reported in the literature. Clear-cut transition temperatures and textures could be obtained from DSC curves and polarised optical microscopy (POM) observations for all of the compounds. They were in good agreement with each other for the multiple heating/cooling cycles. Diaryldiacetylenes **3** and **4** show nematic LC phase, while compounds **5** and **6** exhibit only crystal to isotropic transitions. The terminal alkyl chain–derived diaryldiacetylene **3** has lower transition temperature than the alkoxy chain–derived diaryldiacetylene **4**, which is in good agreement with the theory. In the case of compounds **7** and **8** the mesogenic property is suppressed. This is attributed to mismatched bending angle between the two phenyl rings, polarity and shorter chain length of the molecule which also play a vital role of suppressing of LC properties.

Table 1. Phase transition temperature (*T*; °C) and associated enthalpy values (ΔH; kJ mol^{-1}) of the diaryldiacetylenes and their 3,5-pyrazoles with heating/cooling scan rates at 5°C min^{-1}.

Compound	Heating scan (°C)	Cooling scan (°C)
3	Cr 87.7 (53.9) N 110.2 (3.52) Iso	Iso 108.8 (3.49) N 82.9 (51.74) Cr
4	Cr 120.3 (89.2) N 157.3 (4.35) Iso	Iso 156.5 (4.56) N 116.9 (85.65) Cr
7	Cr 99.5 (44.3) Iso	Iso 81.7 (43.1) Cr
8	Cr 118.8 (56.7) Iso	Iso 102.2 (56.1) Cr

Note: Cr, crystal; SmA, smectic A phase; N, nematic phase; Iso, isotropic.

Table 2. Phase transition temperature (*T*; °C) and associated enthalpy values (ΔH; kJ mol^{-1}) of the synthesised pyrazoles and isoxazole mesogens.

Compound/*n*	Heating scan/cooling scan (°C)
12a/9	Cr$_1$ 99.4 (19.6) Cr$_2$ 135.71 (26.32) SmC 182.34 (0.47) SmA 189.70 (13.57) Iso Iso 187.82 (13.23) SmA 180.82 (0.38) SmC 129.61 (26.58) Cr$_2$ 90.3 (24.6) Cr$_1$
12b/10	Cr$_1$ 96.6 (17.2) Cr$_2$ 131.88 (29.75) SmC 181.05 (0.38) SmA 183.4 (12.3) Iso Iso 1182.9 (11.5) SmA 180.8 (0.31) SmC 127.06 (29.07) Cr$_2$ 93.5 (27.5) Cr$_1$
12c/11	Cr$_1$ 101.85 (106.35) Cr$_2$ 130.69 (26.79) SmC 181.80 (13.43) Iso Iso 180.05 (13.9) SmC 124.94 (25.99) Cr$_2$ 75.67 (35.6) Cr$_1$
13a/9	Cr$_1$ 83.65 (22.24) Cr$_2$ 104.67 (81.99) SmC 140.30 (4.94) N 140.76 Iso Iso 138.70 N 126.85 (4.59) SmC 98.36 (97.10) Cr$_2$ 75.83 (9.43) Cr$_1$
13b/10	Cr$_1$ 98.08 (65.89) Cr$_2$ 104.92 (50.87) SmC 153.25 (14.36) N 153.60 Iso Iso 153.0 N 152.17 (14.16) SmC 99.47 (53.63) Cr$_2$ 87.36 (64.29) Cr$_1$
13c/11	Cr$_1$ 81.4 (48.88) Cr$_2$ 92.83 (37.96) SmC 150.9 (4.59) N 151.43 Iso Iso 146.0 N 145.01 (3.66) SmC 86.95 (37.90) Cr$_2$ 52.39 (28.65) Cr$_1$
13d/12	Cr$_1$ 75.96 (41.37) Cr$_2$ 89.55 (42.06) SmC 130.0 (16.96) N 130.47 Iso Iso 130.20 N 129.96 (16.41) SmC 81.71 (54.71) Cr$_2$

Note: Cr$_1$/Cr$_2$, crystal to crystal transitions; SmA, smectic A phase; SmC, smectic C phase; N, nematic phase detected by POM.

The pyrazoles **12a–c** exhibited a wide range of enantiotropic LC property. The first homologue **12a** shows Cr$_1$–Cr$_2$–smectic C (SmC)–smectic A (SmA) phase transitions on heating and cooling cycles. The typical focal conic texture of SmA phase is shown in Figure 3a. Similar observations were found in compound **12b**. Endotherm and exotherm of (DSC thermogram) **12c** is shown in Figure 1a. Typically the compound **12c** melts from crystal to crystal at 101.85°C. It then transformed to SmC LC state at 130.69°C, and went to isotropic state at 181.80°C. Upon cooling from isotropic liquid, pseudo-focal conic texture of the SmC phase (Figure 3b) appears

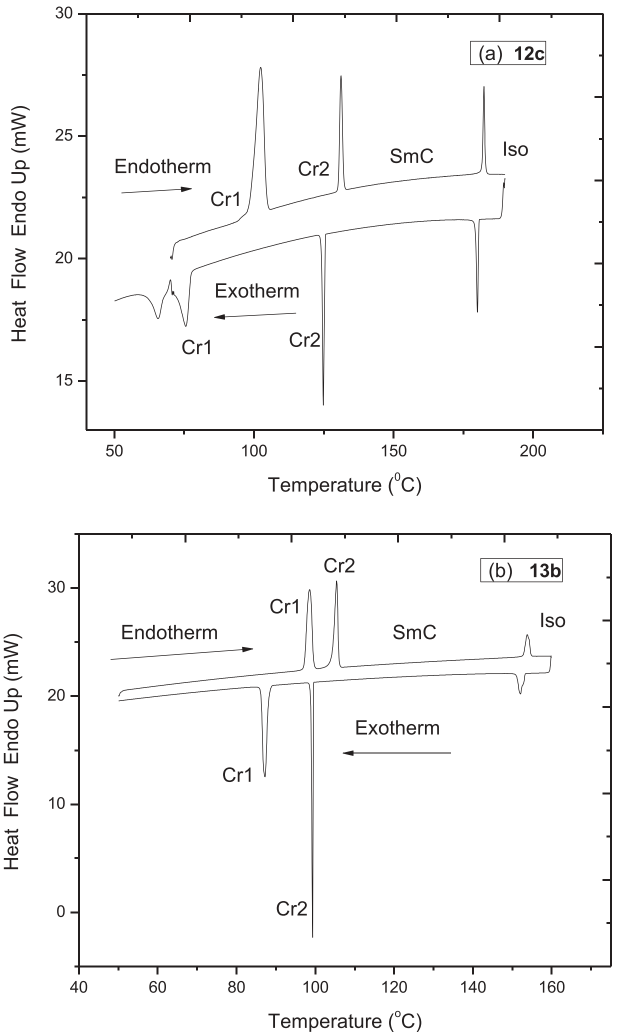


Figure 1. A DSC thermogram obtained for compound (a) **12c** and (b) for **13b** showing phase transition, heating and cooling cycles scan rate at 5°C min^{-1}.

at 180.05°C and crystallises at 124.94°C (Figure 3c). Further cooling showed it transformed to another crystalline form at 75.67°C.

In the series of isoxazoles **13a–d**, all the compounds exhibit SmC phase along with short range of nematic (N) phase. The curve associated with the SmC–N transition was not observed by the DSC as it possesses very low enthalpy value, and the N phase was confirmed by POM observations. The compound **13a** shows Cr$_1$–Cr$_2$–SmC–N phases on heating and cooling scans and SmC phase texture is shown in Figure 3d. The isoxazole **13b** transformed from crystal to crystal phase at 98.08°C, then crystal to LC SmC phase of Schlieren texture at 104.92°C. It went to short range N phase at 153.25°C, and finally it went to isotropic state at 153.60°C. Upon cooling from isotropic liquid, peculiar schlieren texture of N phase appears at 153.0°C, which went to SmC phase at 152.17°C. The material crystallises at 99.47°C, again it transforms to another crystalline form at 87.36°C (Figure 2b). The POM textures are shown in Figure 3. POM image (Figure 3e) is obtained for compound **13b** from isotropic state at 145°C and (Figure 3f) for the crystalline state the image was obtained at 80°C.

The liquid crystallinity was suppressed in compounds **7** and **8** due to saturation and flexibility of the methylene group near to pyrazole ring. This is due to the reduction in the bending angle at the centre of the bent core leading to disruption of molecular packing.

Heating scan transition temperatures as a function of number of carbon atoms in terminal alkyl chain of pyrazoles (**12a–c**) and isoxazoles (**13a–d**) are plotted in Figure 2. This trend compares to previous studies of smaller alkyl chains–derived symmetrical pyrazoles and isoxazoles. This study proves further decrease of crystal/SmC and SmC/iso transition temperatures when there is increase in number of carbon atoms at terminal alkyl chains in smaller and higher members.

The liquid crystal properties of pyrazoles and isoxazoles are due to the degree of deviation from linearity of the molecular structures clearly influencing the appearance of mesophases. In contrast, the corresponding pyrazole and isoxazole derivatives have a more linear shape with the reduction in the angle strain. From these observations, it is deduced that the more linear geometry of the heterocyclic derivatives led to the appearance of the smectic mesomorphism.

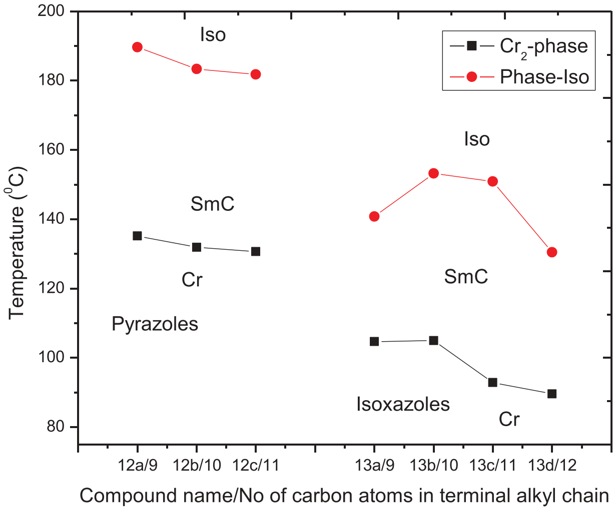


Figure 2. (colour online) A plot of heating scan transition temperatures of pyrazoles and isoxazoles as a function of number of carbon atoms in the terminal alkyl chain.

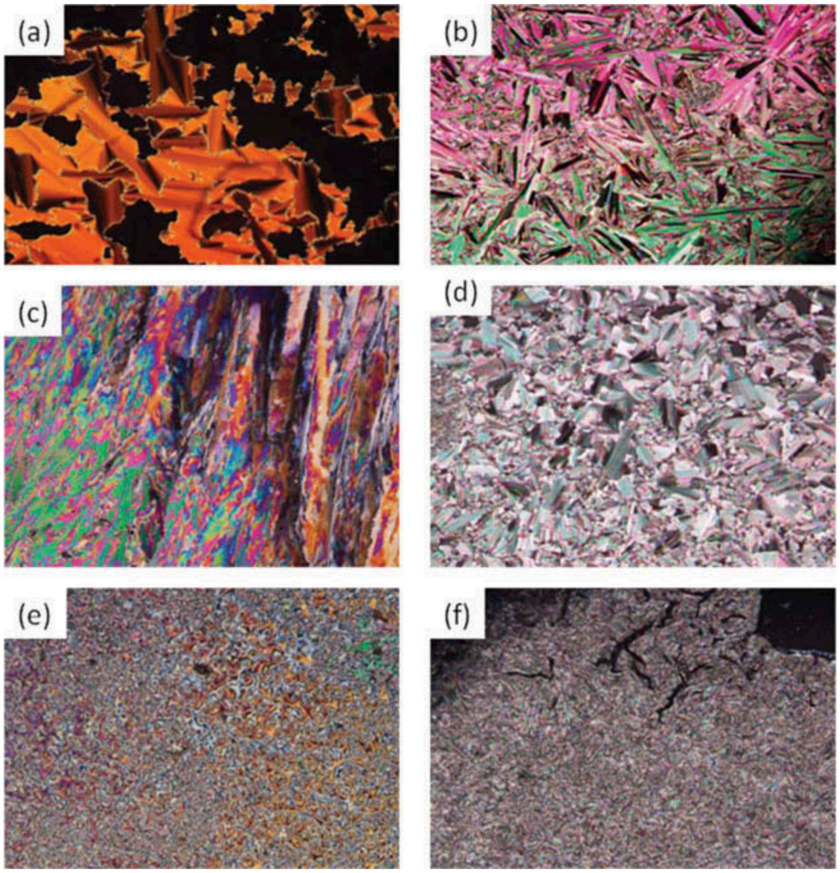


Figure 3. (colour online) Optical photomicrographs textures as seen between crossed polarisers for an unaligned samples: (a) focal-conic texture of SmA phase for **12a**; (b) pseudo-broken fan-shaped texture of SmC phase for **12c**; (c) crystallisation of **12c**; (d) pseudo-broken fan-shaped texture of SmC phase for **13a**; (e) Schlieren texture of SmC phase for **13b**; (f) crystalline state of **13b**.

2.3. *X-ray analysis*

X-ray diffraction (XRD) analysis was carried out for the compound **12c** at different temperatures to confirm the SmC phase. A plot of intensity versus theta is shown in Figure 4. XRD patterns obtained with an unaligned sample show sharp peak in the small-angle region with d_1 = 33.13 Å has clear maxima on the meridian of the diffraction pattern and diffuse scattering in the wide-angle region with d_3 = 4.49 Å which is in good agreement for smectic order. The *d*-spacing values did not change much even when the scans were taken at different temperatures. In addition the POM image of Schlieren texture of two and four brush defects also clarifies the SmC phase. The XRD scan at 100°C show clear crystallisation.

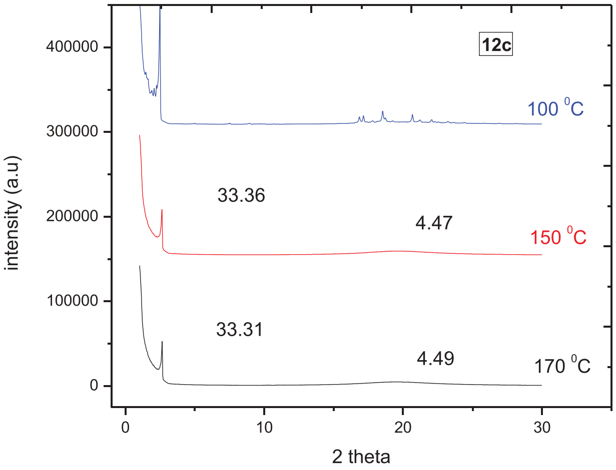


Figure 4. (colour online) XRD 2θ scan of unaligned sample of the SmC phase of compound **12c** at 170°C, 150°C and 100°C.

2.4. *Thermal stability*

The thermal stabilities of **7, 12c** and **13c** were evaluated by thermogravimetric analysis, where the samples were subjected to heating at 10°C min^{-1}. The temperature corresponding to the initial decomposition started at 200°C and the final degradation was almost completed at about 450°C as depicted in Figure 5. Since the structures of the compounds

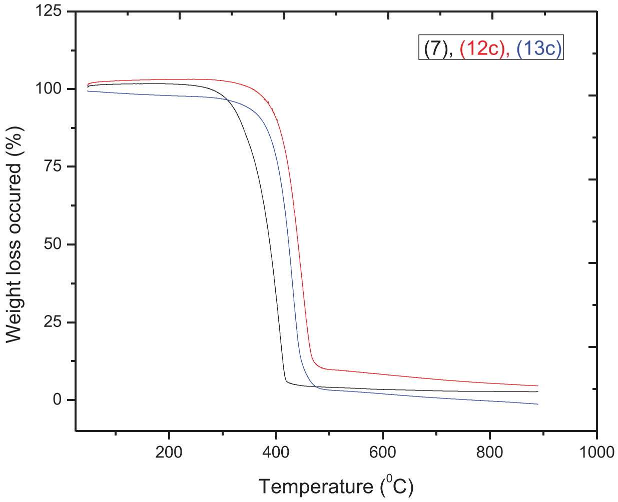


Figure 5. (colour online) TGA of **7, 12c** and **13c**.

studied here are similar in their central part and only differ along the length of the terminal carbon chain, the variation in the decomposition temperatures of the compounds is not much. We note that all the molecules lose their mass practically at once in the main process. Therefore, in general, for all the compounds the distinct decomposition stage is identified at 200–450°C.

3. Experimental

3.1. *Materials*

1-ethynyl-4-pentyl benzene, palladium on charcoal (Pd/C, 5%), bis(triphenylphosphine) palladium (II) chloride, copper iodide, copper acetate, sodium hydride, dry dimethoxyethane and hydroxylamine hydrochloride were obtained from Sigma-Aldrich (Bangalore, India) and used without further purification. N,N-dimethylformamide (DMF), dimethylsulphoxide (DMSO), tetrahydrofuran (THF), hydrazine hydrate, triphenylphosphine (TPP), 4-hydroxyacetophenone, methyl 4-hydroxybenzoate acid, acetic acid glacial, methanol and ethanol were purchased from SD Fine chemicals (Mumbai, India). Ethyl acetate, diethyl ether, ethyl methyl ketone (MEK), acetone, 1,4-dioxane, triethylamine, pyridine, potassium hydroxide (pellets), anhydrous potassium carbonate, anhydrous sodium sulphate and silica gel (100–200 mesh) were obtained from Merck (Mumbai, India) and used as received without any further purification.

3.2. *Instrument details and methods*

All the reactions were monitored by thin-layer chromatography using silica gel pre-coated on aluminium sheets with 2:8 ratio of ethyl acetate and petroleum ether (60–80°C fraction) as mobile phase. The final compounds were purified by column chromatography on ACME silica gel of 60–120 mesh size (ACME Synthetic Chemicals, Mumbai, India). FT-IR spectra of all compounds were recorded using Shimadzu FTIR-8000 spectrometer (Kyoto, Japan) using Nujol media. ^{1}H NMR and ^{13}C NMR spectra of compounds in $CDCl_3$ were run on a Bruker Biospin 500 instrument (Fallanden, Switzerland) at room temperature using tetramethylsilane as an internal standard. The resonance frequencies of ^{1}H and ^{13}C were 500 and 125 MHz, respectively. The ESI-MS spectra were recorded using a Bruker Daltonics Esquire-3000 spectrometer. Elemental analysis was recorded using an elemental analyzer for CHNS, Carlo-Erba 1106 analyzer (Rodano, Italy). The nature of the mesophase and transition temperature of the occurrence of various phases were examined using an Olympus BX51 optical polarising microscope (Tokyo, Japan) equipped with a Mettler FP82HT hot stage with a Mettler FP90 temperature controller (Greifensee, Switzerland). The mesophase-texture photographs were taken using an Olympus DP26 digital camera (Tokyo, Japan). DSC traces were recorded on a Perkin-Elmer, Model Pyris 1 (Waltham, MA, USA) instrument calibrated using indium and zinc standards with a heating rate of 5°C min^{-1} in nitrogen atmosphere. Thermogravimetry analyses of the final samples were carried out on a TGA4000 instrument (Waltham, MA, USA) in nitrogen atmosphere at a heating rate of 10°C min^{-1}, in the temperature range of 50–800°C. XRD measurements were carried out using Cu–Kα radiation (λ = 1.54 Å) generated from a 4 kW rotating anode generator (Rigaku Ultrax-18) equipped with a graphite crystal monochromator. The samples were measured using the capillary method. Samples were filled in Hampton Research capillaries (0.7 mm diameter, Hampton Research, Aliso Viejo, CA, USA) at isotropic phase, sealed and held on a heater. XRD was carried out in the mesophase obtained on cooling from the isotropic phase, and diffraction patterns were recorded on a two-dimensional image plate (Marresearch, Norderstedt, Germany). The SAXS measurements were further corrected with the silver behenate measurements.

1,4-bis[4′-(n-pentyl)phenyl]buta-1,3-diyne (3)

To a solution of dry pyridine (5 mL) and methanol (5 mL) was added 1-ethynyl-4-(pentyl)benzene (0.250 g, 1 mmol) and copper acetate (0.601 g, 2.5 mmol) under argon atmosphere. The resultant reaction mixture was refluxed at 80°C for 24 h. The reaction mixture was cooled, filtered and solvents were removed under reduced pressure; the crude brown-coloured product was purified by column chromatography on silica gel using 10% ethyl acetate in petroleum ether. The product was crystallised from chloroform as colourless crystal. IR: 2926, 2852, 2139, 1602, 1456, 1018 cm$^{-1;}$ ^{1}H-NMR: δ: 7.43 (d, 4H, J = 8.7 Hz), 7.14 (d, 4H, J = 8.7 Hz), 2.61 (t, 4H, J = 2.2 Hz), 1.58 (m, 8H), 1.34 (m, 4H), 0.93 (t, 6H, J = 4.5 Hz); ^{13}C-NMR: δ: 142.9, 141.3, 135.6, 129.3, 128.7, 128.6, 125.4, 101.7, 77.5, 77.2, 77.0, 76.7, 35.6, 35.5, 31.5, 35.4, 31.1, 31.0, 29.7, 22.5, 14.0; elemental analysis: $C_{26}H_{30}$ required C, 91.17; H, 8.83; found C, 91.21; H, 8.89.

1,4-bis[4-(pentyl)phenyl]butane (5)

To a suspension of 5% Pd/C catalyst (0.2 g, 3 mmol) in ethyl acetate (20 mL) was added a solution of compound **3** (0.2 g, 1 mmol) dissolved in ethyl acetate (5 mL). The contents were stirred in an atmosphere of hydrogen for 12 h. The resulting mixture was filtered and the solvent removed under reduced pressure. The solid material obtained was recrystallised from hexane. Yield: 0.160 g; Mp: 65–67°C; IR: 2922, 2852, 1654, 1456, 1375, 1244, 1174, 1018 cm$^{-1;}$ ^{1}H NMR: δ: 7.06 (d, 4H, J = 8.8 Hz), 6.81 (d, 4H, J = 8.7 Hz), 2.82 (t, 8H, J = 6.5 Hz), 2.68 (s, 8H), 1.79–1.25 (m, 8H), 0.94 (t, 6H, J = 4.6 Hz, 2 × $-CH_3$); elemental analysis: $C_{26}H_{38}$ required C, 89.07; H, 10.93; found C, 89.17; H, 11.05.

General procedure for the synthesis of 3,5-disubstituted pyrazoles from symmetric 1,3-dialkynes

A mixture of symmetric 1,3-dialkyne **3** or **4** (1 g, 2.9 or 2.7 mmol), aqueous hydrazine hydrate solution (50 wt.%, 3.0 equivalent, 76.9 mg) and DMSO (3.0 mL) were stirred at 60°C for 20 h in an inert atmosphere and then cooled to room temperature. Water (15 mL) was added to the resultant reaction mixture. The product was extracted with ethyl acetate (15 mL × 2), and the combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue obtained was purified using silica gel (60–120 mesh) chromatography using petroleum ether/ethyl acetate = 9:1 as an eluent to afford 3,5-disubstituted pyrazoles **7**/**8**.

5-[4-pentylbenzyl-3-(4′-pentylphenyl)]-1H-pyrazole (7): IR: 3159, 2926, 2852, 1583, 1454, 1274, 1118, 962, 665 cm$^{-1;}$ ^{1}H-NMR: NH hydrogen signal not observed in ^{1}H-NMR; δ: 7.6 (m, 2H), 7.15 (m, 6H), 6.3 (s, 1H), 4.0 (s, 2H), 2.6 (m, 4H), 1.66–1.35 (m, 12H), 0.93 (t, 6H, J = 6.5 Hz); elemental analysis: $C_{26}H_{34}N_2$ required C, 83.37; H, 9.15; N, 7.48; found C, 83.40; H, 9.21; N, 7.56; GC-MS (m/z): 375 (M^+).

5-[4-pentyloxybenzyl-3-(4′-pentyloxyphenyl)]-1H-pyrazole (8): Mp: 118–120°C; IR: 2292, 2854, 1514, 1454, 1377, 1255, 1010 cm$^{-1;}$ ^{1}H-NMR: NH hydrogen signal not observed in ^{1}H-NMR; δ: 7.51 (m, 2H), 7.10 (m, 2H), 6.83 (m, 4H), 6.19 (s, 1H), 3.91 (m, 6H), 1.73 (m, 4H), 1.64–1.35 (m, 8H), 0.93 (t, 6H, J = 6.5 Hz); elemental analysis: $C_{26}H_{34}N_2O_2$ required C, 76.81; H, 8.43; N, 6.89; found C, 76.89; H, 8.50; N, 6.93; GC-MS (m/z): 407 (M^+).

General procedure for the synthesis of pyrazoles from 1,3-diketones

3,5-bis[4-(nonyloxy)phenyl]-1H-pyrazole (12a): A mixture of 1,3-di-(4-n-alkoxyphenyl)propane-1,3-dione (0.015 mol), catalytic quantity of acetic acid and hydrazine hydrate 96% (0.030 mol) in methanol (25 mL) was refluxed at 70°C for 6 h with stirring. The reaction mixture was cooled, extracted into diethyl ether, the organic layer was washed with water, then passed through anhydrous sodium sulphate. Solvent was removed under reduced pressure. The solid obtained was filtered and recrystallised from methanol. IR (Nujol): 3244 (–N–H), 1614 (C=N), 1506 (C=C) cm$^{-1,}$ ^{1}H-NMR (500 Hz, $CDCl_3$, TMS): δ: 7.64 (d, J = 8.6 Hz, 4H, Ar–H), 6.9 (d, J = 8.6 Hz, 5H, Ar–H and –C=H of pyrazole), 4.0 (t, J = 6.6 Hz, 4H, 2 × $-OCH_2-$), 1.81–1.31 (m, 28H, 7 × $-CH_2-$), 0.92 (t, J = 6.7 Hz, 6H, 2 × $-CH_3$) ppm; elemental analysis for molecular weight 504.75: $C_{33}H_{48}N_2O_2$ required C, 78.53; H, 9.59; N, 5.55; found C, 78.71; H, 9.63; N, 5.68; GC-MS: 505.5 (M^+).

3,5-bis[4-(undecyloxy)phenyl]-1H-pyrazole (12c): IR (Nujol): 3423 (–N–H), 1614 (C=N), 1462 (C=C) cm$^{-1,}$ ^{1}H-NMR (500 Hz, $CDCl_3$, TMS): δ: 7.63 (d, J = 8.6 Hz, 4H, Ar–H), 6.87 (d, J = 8.6 Hz, 5H, Ar–H and –C=H of pyrazole), 4.0 (t, J = 6.6 Hz, 4H, 2 × $-OCH_2-$), 1.81–1.28 (m, 36H, 9 × $-CH_2-$), 0.89 (t, J = 6.7 Hz, 6H, 2 × $-CH_3$) ppm. ^{13}C-NMR ($CDCl_3$, TMS): δ ppm = 159.32, 126.84, 114.87, 98.99, 68.14, 31.92, 29.63, 29.59, 29.42, 29.35, 29.27, 26.06, 22.70, 14.12; elemental analysis for molecular weight 560.85: $C_{37}H_{56}N_2O_2$, required C, 79.24; H, 10.06; N, 4.99; found C, 79.31; H, 10.11; N, 5.07; GC-MS: 560 (M^+).

General procedure for the synthesis of isoxazole

3,5-bis[4-(nonyloxy)phenyl]isoxazole (13a): A mixture of 1,3-di-(4-n-nonyloxyphenyl)propane-1,3-dione (0.015

mole) and hydroxylamine hydrochloride (0.030 mole) and catalytic quantity of triethylamine in ethanol (25 mL) was refluxed at 85°C for 6 h with stirring. The mixture was then cooled, extracted into diethyl ether. The organic layer was washed with water and passed through anhydrous sodium sulphate. Solvent was removed under reduced pressure and the solid obtained was filtered and recrystallised from methanol. IR (Nujol): 3107 (C–H, –CH=), 1618 (–C=N–), 1599 (C=C) cm$^{-1,}$ ^{1}H-NMR (500 Hz, $CDCl_3$, TMS): δ ppm = 7.94 (d, J = 8.5 Hz, 4H, Ar–H), 6.96 (d, J = 8.5 Hz, 4H, Ar–H), 6.72 (s, 1H, –CH= of isoxazole), 4.03 (t, J = 6.5 Hz, 4H, 2 × –OCH_2–), 1.82–1.28 (m, 28H, 7 × –CH_2–), 0.89 (t, J = 6.5 Hz, 6H, 2 × –CH_3); elemental analysis for molecular weight 505.73: $C_{33}H_{47}NO_3$, required C, 78.37; H, 9.37; N, 2.77; found C, 78.40; H, 9.41; N, 2.87.

3,5-bis[4-(undecyloxy)phenyl]isoxazole (13c): IR (Nujol): 3107 (C–H, –CH=), 1618 (–C=N–), 1599 (C=C) cm$^{-1,}$ ^{1}H-NMR (500 Hz, $CDCl_3$, TMS): δ = 7.78 (d, J = 8.5 Hz, 4H, Ar–H), 6.98 (d, J = 8.5 Hz, 4H, Ar–H), 6.64 (s, 1H, –CH= of isoxazole), 4.02 (t, J = 6.5 Hz, 4H, 2 × –OCH_2–), 1.81–1.29 (m, 36H, 9 × –CH_2–), 0.89 (t, J = 6.5 Hz, 6H, 2 × –CH_3) ppm. ^{13}C-NMR ($CDCl_3$, TMS): δ = 170.19, 162.60, 160.69, 160.56, 128.14, 127.38, 121.58, 120.20, 114.89, 114.82, 95.83, 68.21, 68.15, 31.90, 29.56, 29.40, 29.39, 29.32, 29.22, 29.18, 26.03, 26.02, 22.69 ppm; elemental analysis for molecular weight 561.84: $C_{37}H_{55}NO_3$, required C, 79.10; H, 9.87; N, 2.49; found C, 79.19; H, 9.94; N, 2.51.

3,5-bis[4-(dodecyloxy)phenyl]isoxazole (13d): IR (Nujol): 3109 (C–H, –CH=), 1619 (–C=N–), 1601 (C=C) cm$^{-1,}$ ^{1}H-NMR (500 Hz, $CDCl_3$, TMS): δ ppm = 7.93 (d, J = 8.5 Hz, 4H, Ar–H), 6.95 (d, J = 8.5 Hz, 4H, Ar–H), 6.73 (s, 1H, –CH= of isoxazole), 4.02 (t, J = 6.5 Hz, 4H, 2 × –OCH_2–), 1.83–1.29 (m, 32H, 8 × 2 –CH_2–), 0.89 (t, J = 6.5 Hz, 6H, 2 × –CH_3); elemental analysis for molecular weight 589.89: $C_{39}H_{59}NO_3$,required C, 79.41; H, 10.08; N, 2.37; found C, 79.43; H, 10.13; N, 2.43.

4. Conclusions

In this study we report the synthesis, characterisation and mesomorphic properties of 3,5-pyarazoles and isoxazoles. Acetylene compounds exhibit N phase and their saturated and pyrazole derivatives were non-LC. The 3,5-pyrazoles with an extra methylene group which induces angle strain in the molecules resulted in suppression of mesomorphic property. Mesophase disappeared in saturated compounds because flexible butyl spacer mismatched bending angle between the two phenyl rings. Since the most favourable geometry for a molecule to show calamitic mesomorphism is linear, the molecules isoxazole and pyrazoles are in non-linear shape. The bending angle plays an important role in the formation of type of mesophase. In the case of isoxazole, linearity retained to some extent to show only SmC phase. We must remember that hydrogen-bonded calamitic molecules lead to formation of smectic mesomorphism preferably. In the case of pyrazoles, bent angle does not play any role on type of mesophase but here intermolecular hydrogen bonding may impart in the formation of type of mesophase. As a result, pyrazoles without methylene group show SmA and SmC phases.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] Yeap GY, Mohammad AKT, Osman H. Synthesis, spectroscopic and mesomorphic studies on heterocyclic liquid crystals with 1,3-oxazepine-4,7-dione, 1,3-oxazepane-4,7-dione and 1,3-oxazepine-1,5-dione cores. J Mol Str. 2010;982:33–44. doi:10.1016/j.molstruc.2010.07.043

[2] Titov VV, Pavlyuchenko AI. Thermotropic liquid crystals in the heterocyclic series (review). Chem Heterocyclic Compounds. 1980;16:1–13. doi:10.1007/BF00475380

[3] Barberá J, Iglesias R, Serrano JL, et al. Switchable columnar metallomesogens. New helical self-assembling systems. J Am Chem Soc. 1998;120:2908–2918. doi:10.1021/ja9735012

[4] Shanker G, Prehm M, Tschierske C. Liquid-crystalline heterodimesogens and ABA-heterotrimesogens

comprising a bent 3,5-diphenyl-1,2,4-oxadiazole central unit. Beilstein J Org Chem. 2012;8:472–485. doi:10.3762/bjoc.8.54

[5] Balamurugan S, Yeap G-Y, Mahmood WAK. Calamitic liquid crystals of 1,2,3-triazole connected to azobenzene: synthesis, characterization and anisotropic properties. Liq Cryst. 2014;41:776–783. doi:10.1080/02678292.2014.889231

[6] Seed AJ, Toyne KJ, Goodby JW. Synthesis of some 2,4- and 2,5-disubstituted thiophene systems and the effect of the pattern of substitution on the refractive indices, optical anisotropies, polarisabilities and order parameters in comparison with those of the parent biphenyl and dithienyl systems. J Mater Chem. 1995;5:653–661. doi:10.1039/JM9950500653

[7] Lai -L-L, Wang C-H, Hsien W-P, et al. Synthesis and characterization of liquid crystalline molecules containing the quinoline unit. Mol Cryst Liq Cryst. 1996;287:177–181. doi:10.1080/10587259608038754

[8] Musad EA, Mohamed R, Saeed BA, et al. Synthesis and evaluation of antioxidant and antibacterial activities of new substituted bis(1,3,4-oxadiazoles), 3,5-bis(substituted) pyrazoles and isoxazoles. Bioorg Med Chem Lett. 2011;21:3536–3540. doi:10.1016/j.bmcl.2011.04.142

[9] Kazimierczuk Z, Kaustova J, Andrzejewska M, et al. Synthesis and antimycobacterial activity of 2-substituted halogenobenzimidazoles. Eur J Med Chem. 2005;40:203–208. doi:10.1016/j.ejmech.2004.10.004

[10] Gallardo H, Zucco C, Dasilva L. Synthesis and characterization of a new series of liquid crystal compounds derived from isoxazoles. Mol Cryst Liq Cryst. 2002;373:181–190. doi:10.1080/10587250210533

[11] Jager V, Colinas PA. Synthetic applications of 1,3-dipolar cycloaddition chemistry toward heterocycles and natural products. Padwa A, Wh P, editors. New York (NY): John Wiley and Sons; 2002. p. 361.

[12] Westphal E, Silva DH, Molin F, et al. Pyridinium and imidazolium 1,3,4-oxadiazole ionic liquid crystals: a thermal and photophysical systematic investigation. RSC Adv. 2013;3:6442–6454. doi:10.1039/c3ra23456h

[13] Dr DS, Ags DO, Rl C, et al. Synthesis of liquid crystals materials derived from oxadiazole, isoxazole and tetrazole heterocycles. Arkivoc. 2008;xvii:157–166. doi:10.3998/ark.5550190.0009.h14

[14] Thaker BT, Solanki DB, Patel BS, et al. Synthesis and characterization of novel liquid crystalline compounds containing a pyrazole ring. Mol Cryst Liq Cryst. 2012;552:134–146. doi:10.1080/15421406.2011.609043

[15] Prajapati AK, Modi V. Mesogenic quinazolone derivatives: synthesis and characterisation. Liq Cryst. 2010;37:1281–1288. doi:10.1080/02678292.2010.504861

[16] Imrie CT, Taylor L. The preparation and properties of low molar mass liquid-crystals possessing lateral alkyl chains. Liq Cryst. 1989;6(1):1–10. doi:10.1080/02678298908027317

[17] Lai CK, Ke Y, Chien-Shen JS, et al. Heterocyclic 1,3,4-oxadiazole as columnar core. Liq Cryst. 2002;29:915–920. doi:10.1080/02678290210129957

[18] Harigae R, Moriyama K, Togo H. Preparation of 3,5-disubstituted pyrazoles and isoxazoles from terminal alkynes, aldehydes, hydrazines, and hydroxylamine. J Org Chem. 2014;79:2049–2058. doi:10.1021/jo4027116

[19] Safaei S, Baltork IM, Khosropour AR, et al. Copper (II) ionic liquid catalyzed cyclization-aromatization of hydrazones with dimethyl acetylenedicarboxylate: a green synthesis of fully substituted pyrazoles. New J Chem. 2013;37:2037–2042. doi:10.1039/c3nj40756j

[20] Torralba MC, Cano M, Campo JA, et al. Chemistry of Rh(I) complexes based on mesogenic 3,5-disubstituted pyrazole ligands. X-ray crystal structures of 3,5-di(4-n-butoxyphenyl)pyrazole (Hpzbp2) and [Rh(μ-pzR2)(CO)2]2 (R=C6H4OCnH2n+1, n=10, 12) compounds. Part II. J Organomet Chem. 2002;654:150–161. doi:10.1016/S0022-328X(02)01400-6

[21] Thaker BT, Solanki DB, Patel BS, et al. Synthesis, characterisation and liquid crystalline properties of some Schiff base and cinnamate central linkages involving 1,3,5-trisubstituted pyrazolone ring system and their Cu(II) complexes. Liq Cryst. 2013;40(9):1296–1309. doi:10.1080/02678292.2013.804606

[22] Moyano S, Barberá J, Diosdado BE, et al. Self-assembly of 4-aryl-1H-pyrazoles as a novel platform for luminescent supramolecular columnar liquid crystals. J Mater Chem C. 2013;1:3119–3128. doi:10.1039/c3tc30174e

[23] Krowczynski A, Zep A, Kuc K, et al. Liquid crystalline analogues of curcumin. Liq Cryst. 2014;41(5):685–693. doi:10.1080/02678292.2013.875227

[24] Benbayer C, Saïdi-Besbes S, Grelet E, et al. Structure–property study of new [1,2,3]-triazole liquid crystalline derivatives. Liq Cryst. 2013;40(11):1520–1528. doi:10.1080/02678292.2013.822111

[25] Heller ST, Natarajan SR. 1,3-diketones from acid chlorides and ketones: a rapid and general one-pot synthesis of pyrazoles. Org Lett. 2006;8:2675–2678. doi:10.1021/ol060570p

[26] Bartulin J, Martinez R, Gallardo H, et al. Synthesis and mesomorphic properties of 3, 5-bis(4-n-phenylalkoxy)isoxazole and 3, 5-bis(4-n-phenylalkoxy)pyrazole. Mol Cryst Liq Cryst. 1992;225:175–182. doi:10.1080/10587259308036227

[27] Iglesias R, Serrano JL, Sierra T. FLCs with a five-membered ring in the mesogenic core. Liq Cryst. 1997;22:37–46. doi:10.1080/026782997209658

[28] Srinivasa HT, Hariprasad S. Synthesis of some novel aromatic alkynyl silanes: mesomorphic characterization of ethynyl-substituted rod-shaped molecules. Mol Cryst Liq Cryst. 2014;588:17–27. doi:10.1080/15421406.2013.822299

[29] Arakawa Y, Nakajima S, Ishige R, et al. Synthesis of diphenyl-diacetylene-based nematic liquid crystals and their high birefringence properties. J Mater Chem. 2012;22:8394–8398. doi:10.1039/c2jm16002a

[30] Wang L, Yu X, Feng X, et al. Synthesis of 3,5-disubstituted pyrazoles via cope-type hydroamination of 1,3-dialkynes. J Org Chem. 2013;78:1693–1698. doi:10.1021/jo302732v

[31] Barbera J, Cativiela C, Serrano JL, et al. Mesogenic behaviour in some pyrazole and isoxazole derivatives. Liq Cryst. 1992;11:887–897. doi:10.1080/02678299208030692

[32] Brown DH, Synthesis SP. regioisomerism and characterization of unsymmetrical alkenyl-terminated isoxazole liquid crystals. Liq Cryst. 2003;30:23–30. doi:10.1080/0267829021000047525

[33] Gallardo H, Conte G, Tuzimoto PA, et al. New luminescent liquid crystals based on 2,1,3-benzothiadiazole and bent five-membered N-heterocyclic cores. Liq Cryst. 2012;39:1099–1111. doi:10.1080/02678292.2012.698313