RESEARCH ARTICLE

Synthesis, Characterization and Estimation the Biological Activity of New Mesomorphic Heterocyclic Compounds

Hussain A. Hamza, Nasreen R. Jber

Department of Chemistry, College of Sciences, Al-Nahrain University, Baghdad-Iraq

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ABSTRACT

This study is concerned with the synthesis and characterization of new liquid crystalline compounds that contain bis and quaternary terminal substitution, which were synthesized starting from thiocarbohydrazide. The liquid crystalline properties of the prepared compounds, the effect of these ends on the mesogenic properties and their Transitional stability were verified using a hot-stage polarizing optical microscope (POM) and differential scanning calorimeter (DSC). The synthesized compounds were characterized using FTIR, CHNS analysis, and ^{1}H-NMR. The examination of antibacterials showing data results that about all the compounds $[S]_{4,5}$ are dynamic and have mild to good antibacterial factivity with concs. (10,25,50, 100)µg/mL.

Keywords: 3-mercapto-4-amino- 1,2,4- triazole, Antibacterial activity, Thiocarbohydrazide.

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INTRODUCTION

The heterocyclic compound supports the development of life on the plant. They are commonly spread in nature and important to life and have a very important function in the metabolisms of livings cells.[1] In recent years heterocyclic compounds have more importance so it can be present in a huge number of compounds that exhibit biological activities.[2] Heterocyclic ring system that contains H, N and S hetero atoms have chemotherapeutic activity and another used. Five and six-member heterocyclic rings have paid attention to pharmaceutical society over time because they have therapeutic values.[3] Heterocyclic compounds that contain more than one hetero atom called polyfunctionalized. Heterocyclic compounds containing oxygen make essential roles in medical discoveries.[4] Triazole compounds have been attracting special interest due to the presence of unusual five-membered tri-nitrogen aromatic heterocyclic structure which may exert diverse weak interactions such as hydrogen bonds, coordination, ion-dipole, cation-π, π-π stacking, hydrophobic effect, van der Waals force and so on,[5,6] and thereby 1,2,4-triazole-based compounds exhibit extensively potential applications in medicinal, agricultural, chemical, supramolecular as well as materials sciences.

EXPERIMENTAL

Materials and Techniques

All the chemicals (the reagents and the solvents) were supplied from Mercka, BDH, Flukaa, and Alfaa chemicals Co. and used as receiveds.

The infrared spectra of the prepareda compounds were recorded using Fourier Transform Infrared (FT-IR) 8300 Fouriera transformainfrareda spectrophotometers of SHIMADZU a Company, potassiumsbromide (KBr) discs , the waves number ranges 4000-400 cm^{-1}, in Al-Nahrain University, Iraq. Uncorrected meltingspoints were recorded on hot stage Gallenskamp meltingspoint device. The ^{1}H NMR spectra were recordedr on BrükerACF 300 spectrometer at 300MHz, using deutrated acetone or D M S O as solvent with TMS as an internals standard, in the university of Exeter, England.

Synthesis of Thiocarbohydrazide [S_1]

Place (1 mol, 25.03mL) of hydrazine hydrate in a round flask and then lowred the temperature of the flask to 10°C. Then add the (0.5 mol,76g) of carbon disulfide was added drop by drop wise to the flask with maintaining a temperature of up to 15°C. Then gradually raise the temperature to 85°C for 10 hours,The mixture is then cooled to a temperature of 10°C, precipitate was filtered and washed with cold water 10°C,[7] (yield 84%) , (m . p. = 170-171ºC).

Synthesis of 1,4-phenylenebis(methanylylidene)bis(4-aminobenzoic acid) [S_2]

Terephthalaldehyde (0.04 mole, 5. 36 g) was added in 15 mL of ethanol in around bottomed flask with a solution of 4-aminobenzoic acid (0.08 mol, 10.96 g) in 15 mL of ethanol

**Author for Correspondence: Nasreen301174@yahoo.com.*

with 3 drops of glacial acetic acid as a catalyst and refluxed the mixture for (8h).Then cooled the resultant solution to room temperature. The resulting light yellow solid crystal was filtered washed with water and recrystallized from appropriate solvent to to get the compound [S_2],[8] (yield 94%) , (m . p. = >300ºC)

Synthesis of 1,4-phenylenebis(methanylylidene)bis(5-phenyl-4-amino-3-thiol-1,2,4-triazole) [S_3]:

Fusion of compounds [S_2] (0.002mol, 0.74 g) with thiocarbohydrazide (0.004 mol, 0.45 g) were taken in a round bottomed flask and heated to 145°C for (2 hours) on a mantle until the content of the flask was melted. The product obtained on cooling was treated with saturated solution of sodium bicarbonate to neutralize the unreacted carboxylic acid, then collected by filtration.[9] Recrystallization from ethanol yielded 75%, (m.p.= 286–288°C).

Synthesis of of 1,4-phenylenebis(methanylylidene)bis(5-phenyl-4-amino-3-thioalkyl-1,2,4-triazole) [S_4]a-e:

A mixture of triazole [S_3] (0.001 mole, 0.51 g) and aproprate alkylbromide (0.002 mole), potassium bicarbonate (0.002) in ethanol (20 mL) was heated under reflux for 8 hours. A solid product was obtained by filtration which was purified by recrystallization from ethanol. Table 1 shows the physical properties of the compound [S_4]a-e.

Synthesis of 1,4-phenylenebis(methanylylidene) bis(5-phenyl-4-(bis -1`,4` phenylenebis (methanylylidene)-3-thioalkyl-1,2,4-triazole)] [S_5]a-e:

A mixture of [S_4]a-e (0.002 mole) and terephthalaldehyde (0.002mole, 0.26g) in 25 mL of absolute ethanol with 2 drops of glacial acetic acid as a catalyst and refluxed the mixture for (4 hours). A solid product was obtained by filtration which was purified by recrystallization from ethanol. Table 2 shows the physical properties of the compound [S_5]a-e.

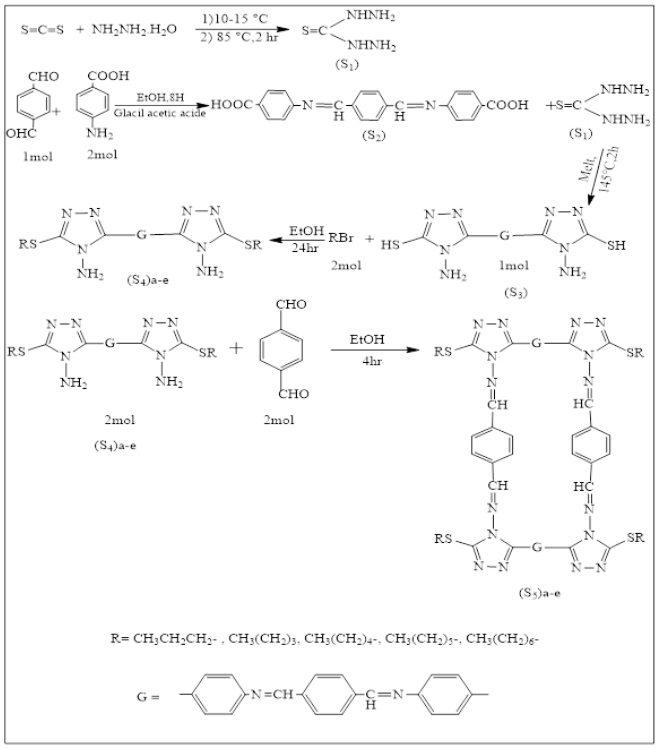
Antibacterial activities

The antibacteriall activities of several prepared compounds were studied against gram—positive bacteria (*Staphylococcush aureus***,** *Baccillus*) and gram- negative bacteria (*Pseudomonas***h,** *Enterobacter*) the microorganism was supplied as ready bacterial cultures by Biotechnology Department, College of Science, Baghdad University, at a concentration of 10, 25, 50, 100 µg/ML by Agar well Diffusion method.[10]

Synthesisiand Characterizations:

The method of the synthesisdof 1,4-phenylenebis(methanylylidene) bis(5-phenyl-4-(bis -1`,4` phenylenebis (methanylylidene)-3-thioalkyl-1,2,4-triazole)] [S_5]a-e are shown in the sequence of reactions shown in Scheme 1.

Thiocarbohydrazide [S1] was prepared by reaction of hydrazine hydrate N_2H_4 with carbon disulfide CS_2 in the presence of H_2O with subsequent heating to remove H_2S. Condensation reaction of Terephthaldehyde with *p*-aminobenzoic acid in molar ratio 1:2 afforded the corresponding Schiff base 1,4-phenylene bis (methanylylidene) bis (4-aminobenzoic acid) [S_2], Compound [S_3] was synthesized through the reaction of thiocarbohydrazide [S_1] with Schiff`s base [S_2]. Compounds



Scheme 1: Synthesis compounds (S_5)a-e

Table 1: Physical properties of the compounds (S_4)a-e

Comp. Symbol	*M.P.˚C*	*Color*	*Molecular formula*	*Yield %*
[S_4]a	201-206	Pale Yellow	$C_{30}H_{32}N_{10}S_2$	78
[S_4]b	255-258	Yellow	$C_{32}H_{36}N_{10}S_2$	75
[S_4]c	260-263	Yellow	$C_{34}H_{40}N_{10}S_2$	68
[S_4]d	250-253	Yellow	$C_{36}H_{44}N_{10}S_2$	70
[S_4]e	240-245	Yellow	$C_{38}H_{48}N_{10}S_2$	72

Table 2: Physical properties of the compounds [S_5]a-e

Comp. Symbol	*M.P.◦C*	*Color*	*Molecular formula*	*Yield %*
[S_5]a	198-202	Yellow	$C_{76}H_{68}N_{20}S_4$	76
[S_5]b	187-190	Yellow	$C_{80}H_{76}N_{20}S_4$	78
[S_5]c	174-177	Yellow	$C_{84}H_{84}N_{20}S_4$	74
[S_5]d	168-171	Dark yellow	$C_{88}H_{92}N_{20}S_4$	76
[S_5]e	111-115	Orange	$C_{92}H_{100}N_{20}S_4$	82

$[S_4]$a-e was synthesized through the reaction of compound [S3] with alkylbromide in 85% KOH. The condensation reaction of compounds $[S_4]$a-e with terephthaldehyde in acidic media afford the synthesis of $[S_5]$a-e.

The structures of synthesized compounds were identified using FT-IR and ^{1}HNMR spectroscopy.

[S1]: (FTIR); Two sharp bands at 3299 cm^{-1} and 3266 cm^{-1} that could be attributed to H–N–H stretching asymmetrical an symmetrical respectively, bands at 1641 and 1332 cm^{-1} due to N–H bending and S = C, respectively. ^{1}HNMR; (d_6-DMSO, ppm), signal observed at 8.77 ppm may be due to the NH protons (2H), while the signal at 4.47 ppm could be assigned to H–N–H protons (4H).

[S2]: (FTIR); broad band at 3100–2500 cm^{-1} and that could be attributed to O – H stretching of carboxylic group, bands at 1681, 1629, 1590 and 846 cm^{-1} due to C = O , CH = N, C = C, and out of plane bending for *p*-disubstituted benzene ring, respectively. ^{1}HNMR; (d_6-DMSO, ppm), signal observed at 12.81 ppm due to the proton of carboxylic group (2H), signal at 8.77 ppm could be assigned to the proton of imine group (2H), the aromatic protons show three signals (dd) at 7.36–8.17 (12H).

[S3]: (FTIR); sharp bands at 3455, 3417, 3355 and 3185 cm^{-1} that could be attributed to N – H stretching of NH_2 and NH (thione toutmer), bands at 1641, 1622, 1588 and 836 cm^{-1} due to CH = N, C = C, and out of plane bending for *p*-disubstituted benzene ring , respectively. ^{1}HNMR; (d_6-DMSO, ppm), signal observed at 10.1 ppm due to the proton of thiol group (2H), signal at 8.16 ppm could be assigned to the proton of imine group (2H), signal at 8.70 ppm attributed to the protons of NH_2 group (4H), the aromatic protons show three signals (dd) at 6.52–7.99 (12H).

$[S4]_{a\text{-}e}$: (FTIR); sharp bands at (3454-3360, 3412-3285) cm^{-1} that could be attributed to N – H stretching of NH_2 group, characteristic bands observed at (2966-2917 and 2885-2847) for asymmetrical and symmetrical stretching of C – H aliphatic. Bands at (1641-1630), (1601-1577) and (845-826) cm^{-1} due to CH = N, C = C, and out of plane bending for *p*-disubstituted benzene ring , respectively. ^{1}HNMR; $[S4]_a$, (d_6-DMSO, ppm), A three pairs of doublets at δ7.17-8.05 could be attributed to the twelve protons of the phenyl rings. The ^{1}HNMR also showed two proton singlet at δ 8.11 which could be assigned to the iminic proton. Four protons appeared at δ 8.74 that are attributed to NH_2, six protons appeared as triplet at δ 0.97 which could be assigned to $–CH_3$, four protons appeared as triplet at δ 2.84 which could be assigned to $–SCH_2$. The other $–CH_2$ group of propyl substituent appeared as multiplet at δ 1.90 (4H).

$[S5]_{a\text{-}e}$: (FTIR); disappearance of N–H stretching band of amino group and the appearance of bands at (3020–3060),

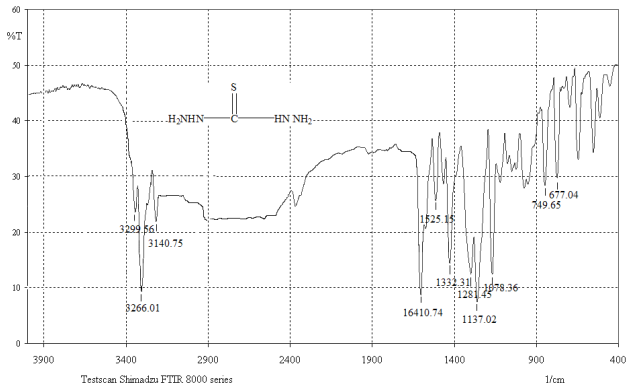


Figure 1: FT-IR spectrum of thiocarbohydrazide $[S_1]$

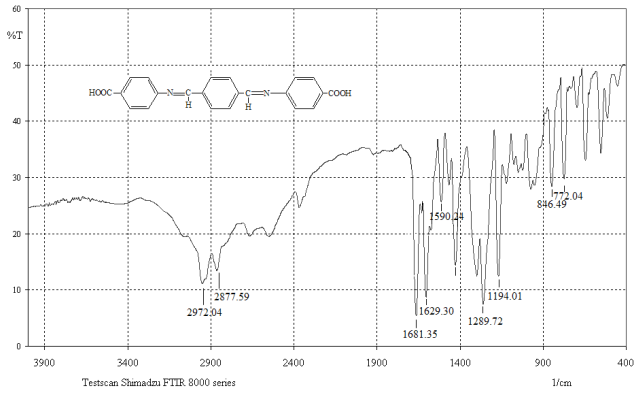


Figure 3: FT-IR spectrum of $[S_2]$

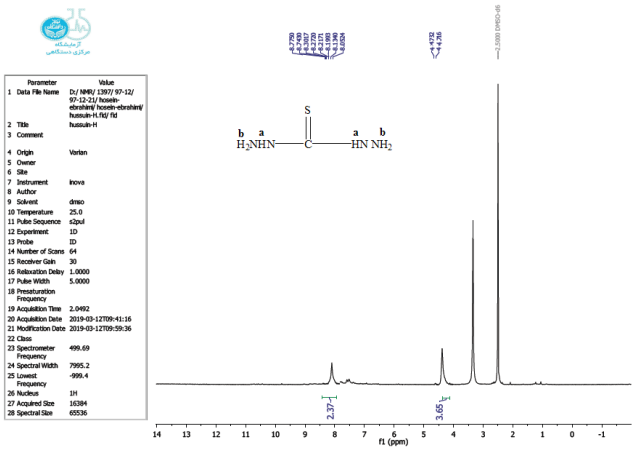


Figure 2: ^{1}HNMR spectrum of thiocarbohydrazide $[S_1]$

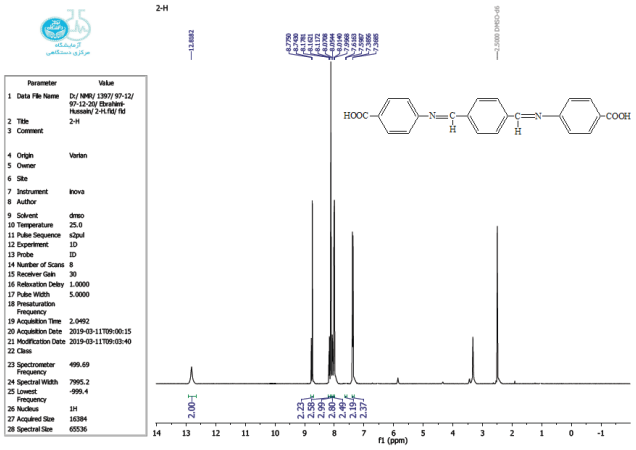


Figure 4: ^{1}HNMR spectrum of $[S_2]$

(2988-2921), (2894-2849), (1639-1624), (1588-1575), (841-821) due to Ar–H, C–H aliph., CH=N, C=C , out of plane bending for *p*-disubstituted benzene ,respectively. ^{1}HNMR; $[S5]_d$, (d_6-DMSO, ppm), A four pairs of doublets at δ 6.46-7.48 could be attributed to the thirty two protons of the phenyl rings. The ^{1}HNMR also showed eight proton singlet at δ 8.37 which could be assigned to the iminic proton. Twelve protons appeared as triplet at δ 0.86–1.21 which could be assigned to $–CH_3$, eight protons appeared as triplet at δ 3.94-4.11 which could be assigned to $–SCH_2$. The other $–CH_2$ groups of hexyl substituent appeared as multiplet at δ 1.64–1.81 (32H).

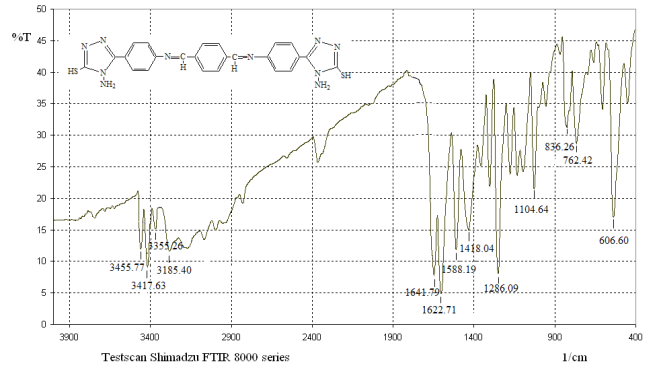


Figure 5: FT-IR spectrum of $[S_3]$

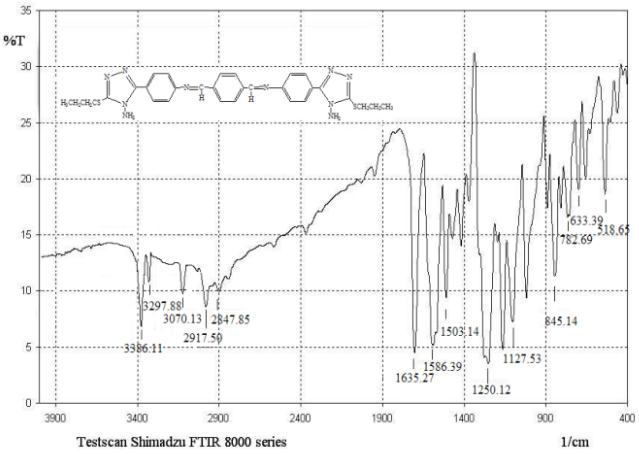


Figure 7: FT-IR spectrum of $[S_4]$a

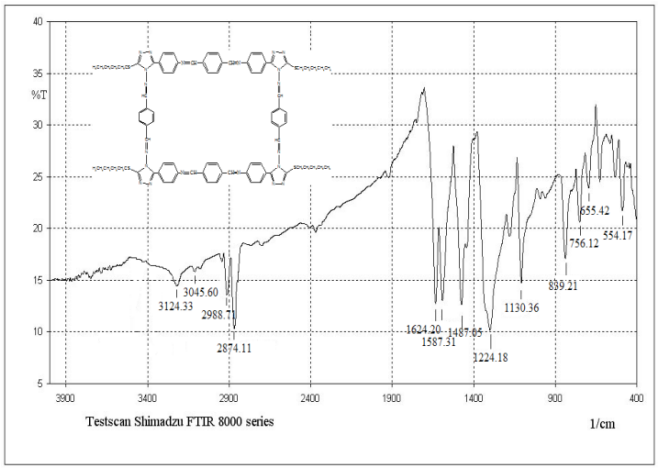


Figure 9: FT-IR spectrum of $[S_5]$c

Phase Transitions

The phase transition temperatures were determined using differential scanning calorimetry (DSC). The DSC thermogram of compounds $[S_4]$a-e show two peaks represent the crystal –crystal and crystal – isotropic transition so it did not show

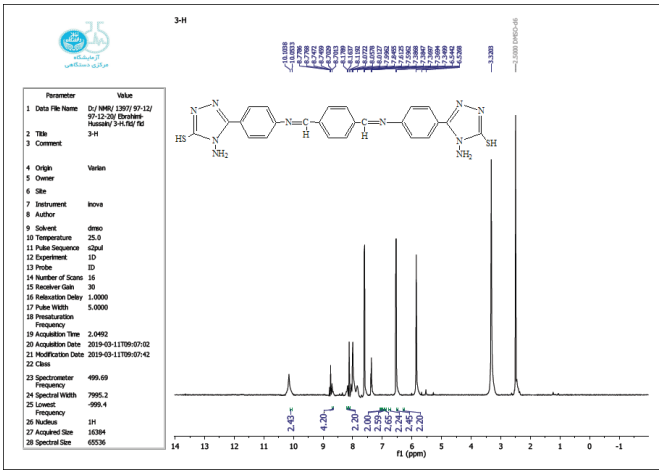


Figure 6: ^{1}HNMR spectrum of $[S_3]$

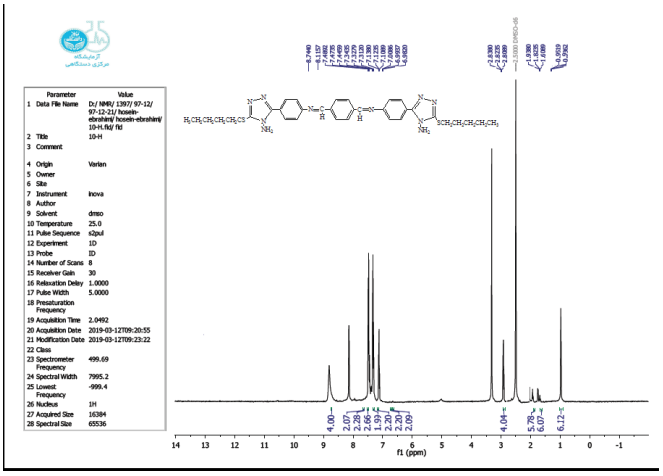


Figure 8: ^{1}HNMR spectrum of $[S_4]$c

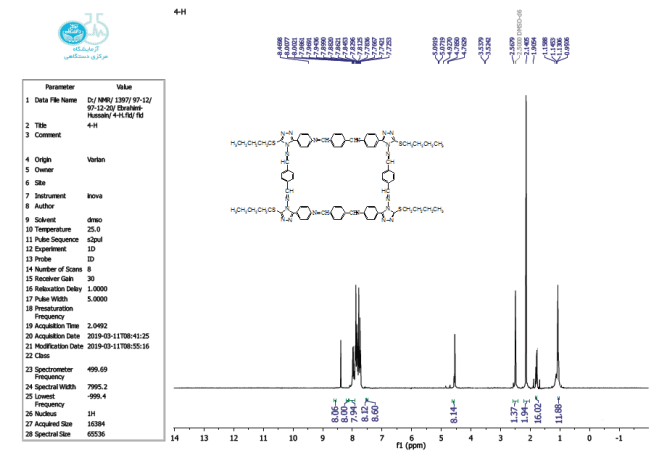


Figure 10: ^{1}HNMR spectrum of of $[S_5]$b

Table 3: Melting points and type of transition for compounds [S_5]a-e.

Comp. No.	*Melting point °C*	*Transition*	
[S_5]a	198-208	C	N
	210-217	N	I
[S_5]b	187-192	C	N
	215-221	N	I
[S_5]c	174-187	C	N
	201-211	N	I
[S_5]d	168-177	C	N
	190-198	N	I
[S_5]e	110-127	C	N
	154-172	N	I

C = Crystal; N = Nematic.

and mesomorphic properties. The absence of mesomorphicity of these compounds might be due to the absence of terminal group effect, as show in Figure 11 below.

Expected for compounds [S_5] a-e, all studied derivatives exhibit enantiotropic liquid crystalline behaviour. The DSC thermograms of compounds [S_5]a-e are shown in Figure (12), a sharp melting peak appeared was found on heating from the solid crystal to isotropic liquid, as shown in Table 3. All the synthesized compounds show discotic mesophases.

Phase structure

The phase structures were determined by polarizing optical microscope (POM), Microscopic observations of compounds [S_4]a-e revealed that these compounds did not show liquid crystal properties.

The potential mesogenic properties of [S_5]a-e have been checked with a polarizing microscope equipped with a heating stage and a single melting point has been noticed at 110 – 208 ºC. This behaviour may be explained by the flexibility of molecule,[11] that cause with the presence of alkoxy group.

Terminal substituents play a significant role in promoting liquid crystalline properties in a mesogen.[12]

Discotic LCs are mostly composed of a π-conjugated central core substituted with usually 3 to 8 flexible aliphatic

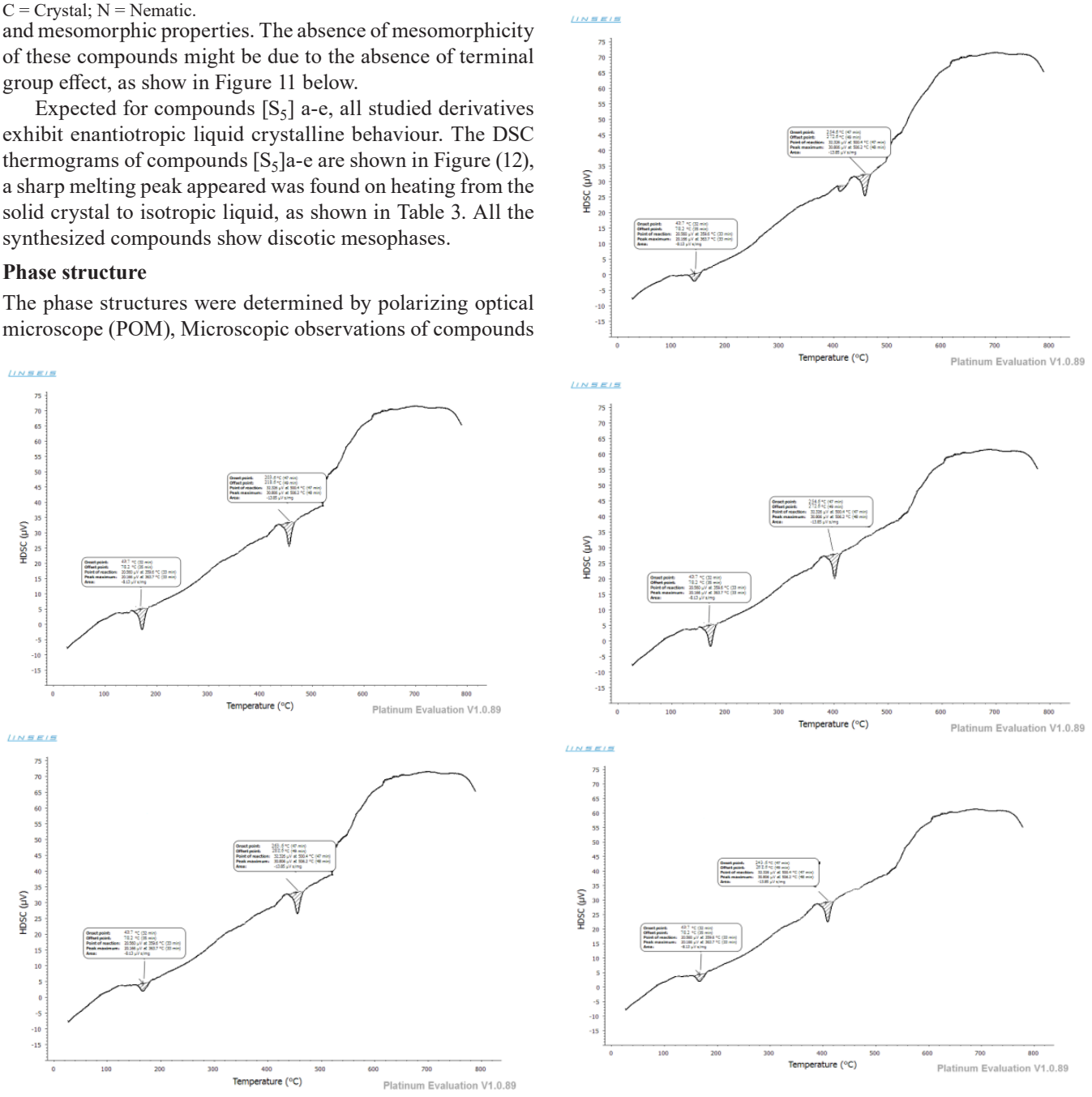


Figure 11: Differential scanning thermogram of compounds [S_4]a-e, as a function of temperature for the second heating and cooling cycles (at scan rate 10 ºC min^{-1}).

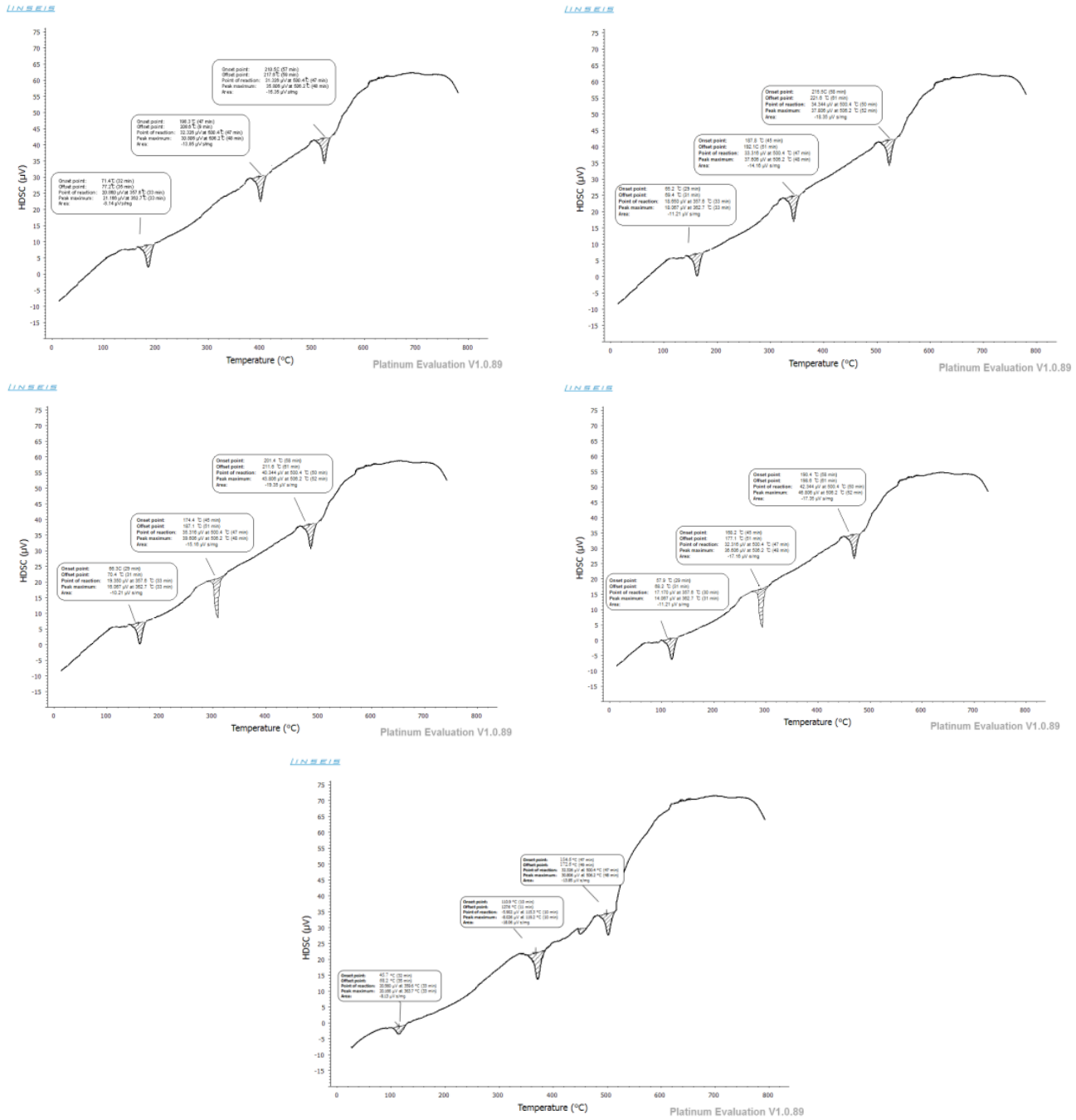


Figure 12: Differential scanning thermogram of compound [S_5]a-e as a function of temperature for the second heating and cooling cycles (at scan rate 10 $^oC\ min^{-1}$).

chains at its periphery. Probably because of intense π–π interactions, a majority of these materials (about 95%) form columnar mesophases and only a small number show a nematic phase. In the columnar phases molecules are stacked one on top of the other into columns and the columns posses two-dimensional long-range positional order. Figure 13 shows the columnar texture for compounds [S_5] a-e.

The presence of an imine ring into the principle structure of compounds [S_5] a-e could cause considerable changes of rigidity, polarity, polarizability and geometry of the molecules and influenced the type and the phase transition temperature of the mesophases.[13]

Antibacterial Studies

The study included four types of bacteria isolated and properly diagnosed.

Erythro Mycin against *Staphylococcus aureus, Bacillus, Pseudomonas and Enterobacter Enterobacter,* these types of bacteria were selected because of its vital importance in the field of medicine, which in turn affect human health causing many different diseases. Disc diffusion method,[14] was use in this study using *Erythro Mycin* as standard drug. The investigation of antibacterial screening data reveal that almost all the compounds [S_4] a,b and [S_5] b,d are active and showing

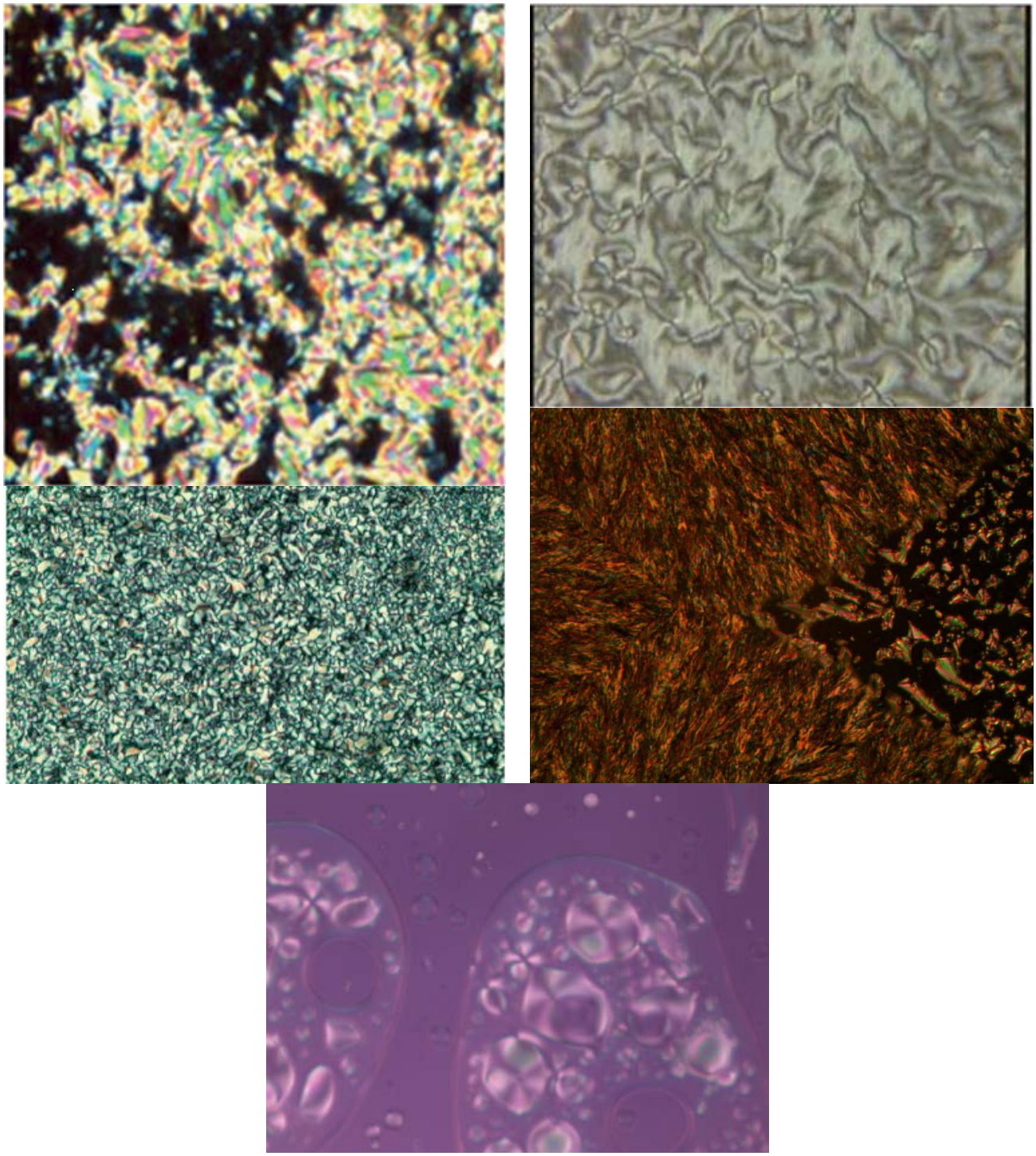


Figure 13: Columnar phase of compounds [S_5]a-e (magnification 10 × 10).

moderate to good antibacterial activity with concentrations (10, 25, 50, 100) µg/mL.

CONCLUSIONS

A new derivatives of 1,4-phenylenebis(methanylylidene)bis(5-phenyl-4-(bis-1`,4` phenylenebis(methanylylidene)-3-thioalkyl-1,2,4-triazole)] [S_5] a-e have been synthesized and evaluated for their antimicrobial activity against Gram-positive, Gram-negative bacteria. Most of the compounds showed a moderate degree of antimicrobial activity.

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