Tareq k.ibraheem et al /J. Pharm. Sci. & Res. Vol. 11(8), 2019, 2797-2801

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Synthesis and anti-microbial screening of some substituted 1, 2, 3-triazole derivatives

Tareq k.ibraheem
Department of chemistry, College of Education, university of Diyala, Iraq ,

Suad Turky Ali Al-azawi.
Almamoon university college, Iraq ,

Mohammed A,
M Al-badri College of Education, university of Diyala, Iraq

Abstract

This research involves synthesis of some new 1,2,3-triazol derivatives then synthesis carbonyl-α,β-unsaturated derivatves as starting material. The first step includes formation of N,N'-([1,1'-biphenyl]-4,4'-diyl)bis(2-chloroacetamide [I] through reaction of benzidine with chloroacetyl chloride and triethylamine in DMF Then reaction of [I] with sodium azide in DMF to form N,N'-([1,1'-biphenyl]-4,4'-diyl)bis(2-azidoacetamide) [II] this compound reaction with 4-(prop-2-yn-1-yloxy)benzaldehyde that synthesized by reaction p-hydroxybenzadehyde with propagylbromide to give N,N'-([1,1'-biphenyl]-4,4'-diyl)bis(2-(4-((4-formylphenoxy)methyl)-1H-1,2,3-triazol-1-yl)acetamide [IV] then reaction this compound [IV] with acetophenone to give compound [V]

Keywords 1,2,3,4-tetrazole, bi-phenyl, carbonyl-α,β-unsaturated derivatves

INTRODUCTION

The preparation requires the use of 1,2,3-triazoles of 1,3-dipolar cyclo-additions of acetylenes with azides. Generally, 1,2,3,4-tetrazole and derivatives possess broad spectrum of biologicalactivates[1].1,2,3-Triazoles are N-heterocyclic compounds not present in natural products, which display different biological properties such as potential antitumor [1] anti-fungal[2] anti-hypertensive [3] anti-bacterial activity against Gram-positive bacteria in addition to Gram-negative bacteria[4], anti-inflammatory [5] cytotoxic activity against human cancer cell lines[6] and anti-viral activity against many viruses [7]. such as anti-HIV) [8], anti-epileptic activities [9], anti-diabetic [10] and cholinesterase inhibitors [11].

Moreover, members of this class in as dyes, corrosion inhibitars photostabilizers and photographic materials. However, to the best of our knowledgoe knowledge there are no report of the use of this five-membered ring in liquid crystals except for few examples containing the regioisomeric [1,2,4]-triazole [12]. Therefore, the aim of current study was the synthesis of some new 1,2,3-triazol derivatives and screening them for potential antimicrobial activities.

CHEMICALS AND SYNTHESIS METHODS

All chemical materials used in current study were supplied via Fluke Chemicals Company, BDH and Merck. Uncorrected were determined by using Stuart , SMP 10 , (UK) .. FTIR spectra were recorded on a SHIMADZU (IR Affinity-1) FTIR spectroscopy. College of Education for Pure Science(Ibn-Al-Haitham), University of Baghdad,Iraq ^{1}HNMR spectra were carried out using Ultra Shield 400 MHz and Ultra shield 500MHz, Bruker, Switzerland, at University of Kasi , Turkey.

Synthesis of N,N-([1,1-biphenyl-4,4-diyl)bis(2-chloroacetamide)][I]

Added to benzidine(0.01 mol,1.84 g) triethylamine (1 mL) in DMF, chloracetyl chloride (0.02 mol,2.24 ml) was added dropwise. The reaction mixture was stirred for (6h) in bath ice water; the solvent was evaporated. The contents were filtered and dried and recrystallized from ethanol. Yield dark brown (85 %), m.p. 156-158^{o}C

Synthesis of N,N-([1,1-biphenyl-4,4-diyl)bis(2-azidoacetamide)][II]

An amount of compound [I] (0.001mol) was dissolved in (5mL) DMF added to the mixture sodium azide (0.002mol) then added ammonium chloride (0.002mol) and refluxed for (5h) and cooled then added to ice water filtered and recrystallized from ethanol

Synthesis of 4-(prop-2-yn-1-yloxy)benzaldehyde [III]

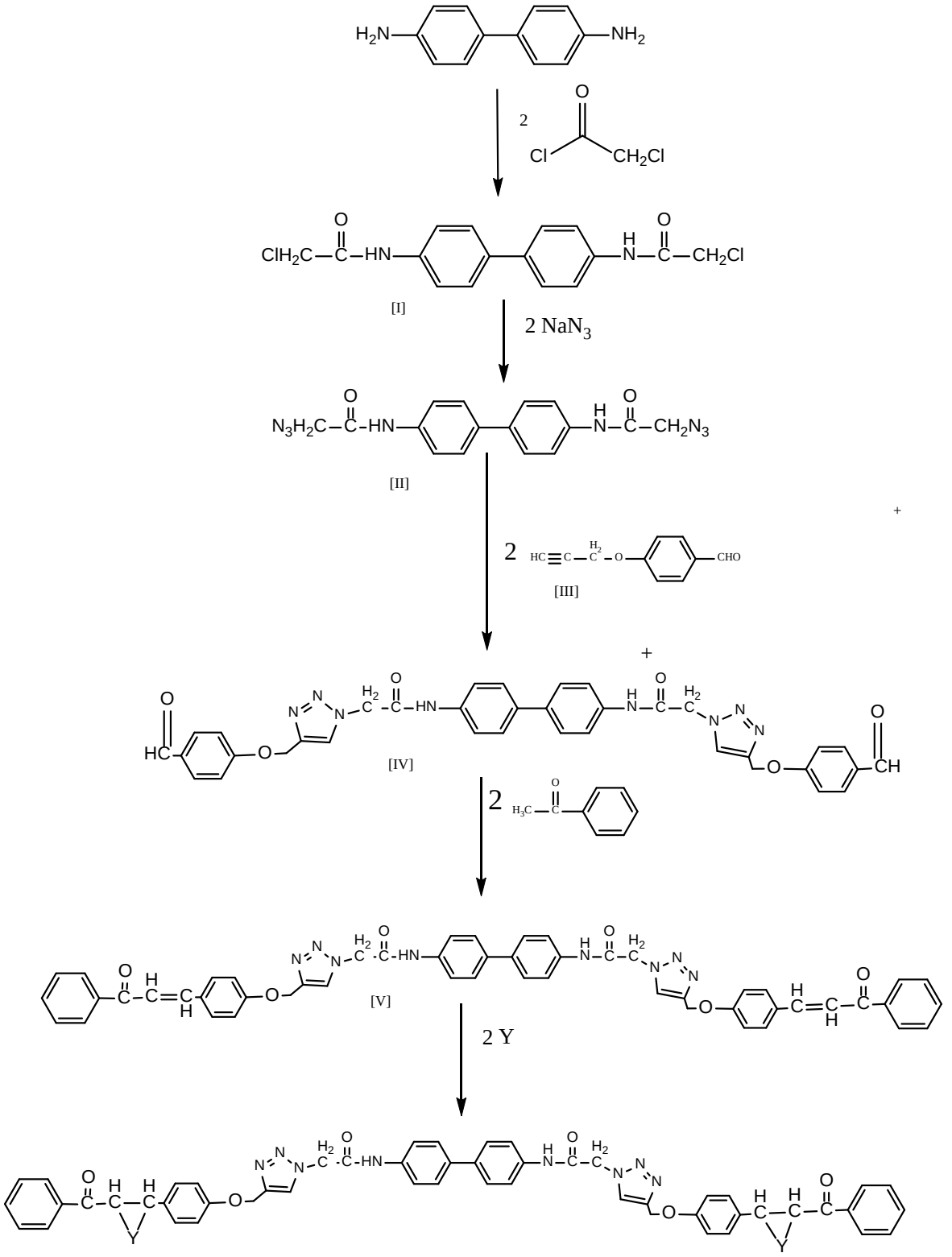
To a solution of 4-hydroxybenzaldehyde (0.0008mol) and potassium carbonate (0.0007mol) in (5mL) DMF was slowly added propargylbromide (0.0008mol) was added to the solution in bath ice if an ice water mixture was stirred for (24h) and filtered

Synthesis of N,N'-(1,4-phenylene)bis(2-(4-(4-(formylphenoxy)-1H-1,2,3-triazol-1-yl)acetamide [V]

An amount of compound [III] (0.01 mol) was dissolved in ethanol (50 mL). The proporgyl ester was added to the solution. The mixture was heated under reflux for 24 solvent then removed and under under reduced pressure was recrystallized from ethanol.

Synthesis of N,N-([1,1-biphenyl]-4,4-diyl)bis(2-(5-(4-((z)-3-oxo-3-phenylprop-1-en-1-yl)phenoxy)-1H-1,2,3-triazol-1yl)acetamide)

To a 5ml solution of potassium hydroxide 3mL of ethanol added (0.1mol) from compound [V] and (0.1mol) from acetophenone. The solution stirred for (3h) then then mixture cooled and filtered



Y= NH_2CONH_2, $NH_2NHCOCH_3$, NH_2NH_2 , $PhNHNH_2$, Br_2 , H_2O_2 , NH_2CSNH_2

[VI] [VII] [VIII] [IX] [X] [XI] [XII]

:

Scheme (1)

Table (1) the physical properties for compounds [I-XII]

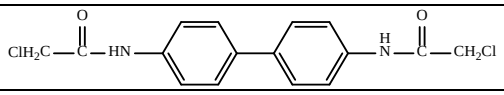
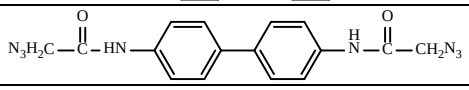
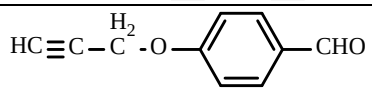
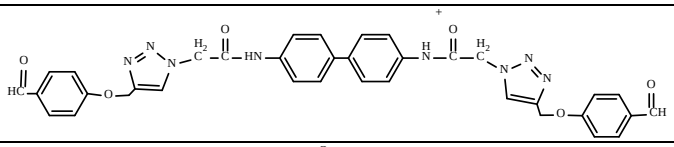
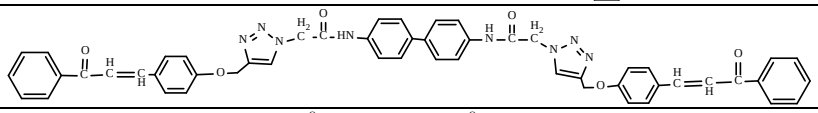
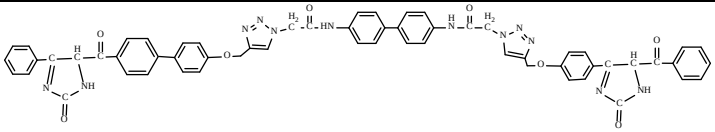
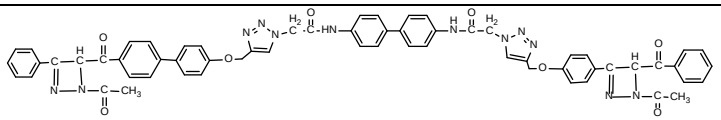
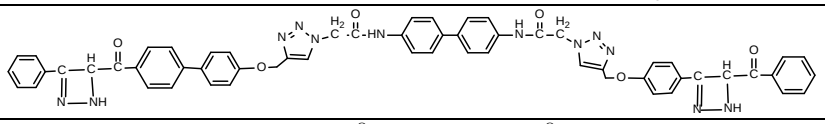
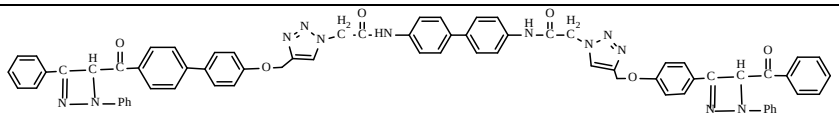
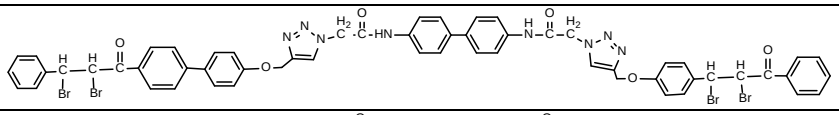
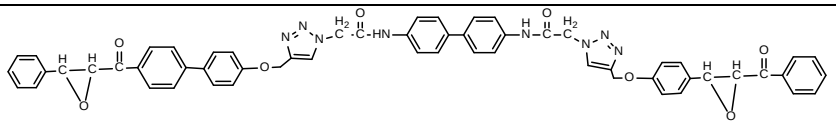
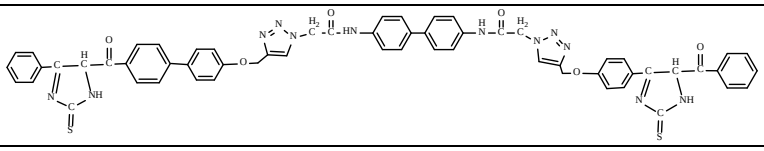
No.	structure	M.P.(°C)	% Yield
I		267	73
II		234	82
III		86	65
IV		211	70
V		195	80
VI		205	71
VII		191	70
VIII		185	68
IX		183	73
X		194	76
XI		201	64
XII		209	71

Table (2) The characterization FTIR absorption bands of compounds [1-12]

No.	ν N-H	ν C-H arom.	ν C-H aleph	ν C=O	ν N≡N	ν C=C
1	3310-3270	3091		1625		1580
2	3280-3230	3094		1633	2110	1605
3	3284-3225	3089	2931-2855	1723		1595
4	3296-3275	3109	2910-2840	1731		1603
5	3269-3215	3089	2930-2865	1628		1599
6	3309-3289	3086	2915-2855	1635		1602
7	3290-3268	3114	2925-2850	1630		1598
8	3305-3265	3099	2915-2855	1642		1578
9	3290-3145	3087	2960-2895	1633		1604
10	3311-3286	3104	2955-2895	1639		1607
11	3319-3294	3087	2930-2865	1643		1611
12	3310-3285	3079	2918-2857	1641		1599

Table (3) The diameter of inhibition zone(millimeter) of compounds

Compound No.	B.cereus	S.aureus	S.epidermidis	M.luteus	P.aeruginosa	E.coli
1	22 (1.5)	19 (2.3)	23 (1.1)	20 (2.8)	25 (3.8)	24 (2.2)
2	5 (2.3)	7 (3.8)	5 (2.1)	4 (4.1)	4 (3.2)	3 (2.7)
3	11 (0.8)	13 (0.7)	20 (0.6)	13 (1.1)	9 (2.2)	7 (1.3)
4	11 (11.3)	12 (9.2)	14 (12.3)	13 (11.7)	8 (8.4)	11 (8.9)
5	23 (11.1)	20 (9.6)	21 (11.7)	24 (12.2)	22 (9.9)	25 (11.4)
6	12 (14.2)	14 (11.2)	18 (13.1)	9 (12.9)	17 (11.6)	8 (11.1)
7	14 (9.2)	20 (6.8)	14 (8.7)	12 (7.8)	17 (105)	19 (12.4)
8	15 (11.5)	11 (12.7)	14 (10.0)	10 (8.8)	8 (4.7)	6 (12.3)
9	10 (9.2)	12 (11.3)	18 (13.8)	12 (9.2)	9 (10.2)	7 (17.5)
10	10 (18.3)	13 (10.2)	15 (11.6)	9 (10.8)	18 (5.7)	12 (7.5)
11	10 (16.3)	13 (13.2)	15 (10.9)	9 (10.6)	18 (4.4)	12 (5.6)
12	10 (19.2)	13 (12.6)	15 (12.5)	9 (11.3)	18 (4.8)	12 (6.2)
Ciprofloxacin (100 µg/disc)	28	33	32	25	30	5

Antimicrobial Screening

The antibacterial activity of the synthesized compounds was tested against four Gram-positive bacteria (, Staphylococcus epidermidis, Staphylococcus aureus Micrococcus luteus and Bacillus cereus) and two Gram-negative bacteria (Pseudomonas aeruginosa and Escherichia coli) using nutrient agar medium. The sterilized (autoclaved at 120 ^{o}C for 35 min) medium (45-55 ^{o}C) was inoculated (1 mL/100 mL of medium) with the suspension (105 mL^{-1}) of the microorganism (matched to McFarland barium sulfate standard) and poured into a Petri dish to give a depth of 3-4 mm.

The paper impregnated with the test compounds. The paper impregnated with the test compounds (µg mL^{-1}in DMF) was placed on the solidified medium. The plates were incubated at 37 ^{o}C for 24. Ciprofloxacin (100 µg/disc) was used as control. The MIC is shown in Table 3.

RESULTS AND DISCUSSION

The compound [I] was prepared from reaction of benzidine in DMF with Chloroacetylchloride and triethylamine(as catalyst). The FTIR spectrum for compound [I] showed the disappearance of absorption stretching bands of N-H and C=O groups of (amide) in starting materials together with the appearance of a new stretching band at 1634cm-1assigned to C=O group of amide. The reaction of one mole compound [I] with 2moles of sodium azide in DMF produced compound [II].The FTIR spectrum for this compound showed stretching vibration to bands of (N≡N) IN(2136)cm^{-1} as the FTIR spectrum compound[III] showed stretching vibration to(C=O) aldehyde in1723 cm^{-1} . The compound [IV] F.T-IR (KBr) cm^{-1}, 3269cm^{-1}, 3215 cm^{-1}, 1628 cm^{-1}(amide), ,^{1}H-NMR (DMSO) δ: 8.9 (s,1H), 2.4-5.2 (m, 8H), structures of these compounds were identified by FT-IR spectroscopy. FT-IR spectrum of compound [V]showed F.T-IR (KBr) cm^{-1}, 3315 cm^{-1}, 3091 cm^{-1}, 1680 cm^{-1}, 1620 cm^{-1}, ^{1}H-NMR (DMSO) δ: 9.1 (s,1H), 2.6-4.1 (m, 9H), the compound [VI] F.T-IR (KBr) cm^{-1}, 3309 cm^{-1}, 3289 cm^{-1}, 1635 cm^{-1}, ^{1}H-NMR (DMSO) δ: 9.3 (s,1H), 2.4-5.2 (m, 9H), the compound [VII] F.T-IR (KBr) cm^{-1}, 3290 cm^{-1}, 3268 cm^{-1}, 1630 cm^{-1}, ^{1}H-NMR (DMSO) δ: 9.2 (s,1H), 2.6-5.3 (m, 9H), the compound [VIII] F.T- IR (KBr) cm^{-1}, 3305 cm^{-1}, 3265cm^{-1}, 1642 cm^{-1}, ^{1}, ,^{1}H-NMR (DMSO) δ: 8.4 (s,1H), 2.3-5.0 (m, 9H), the compound [IX] F.T-IR (KBr) cm^{-1}, 3290 cm^{-1}, 3145cm^{-1}, 1633cm^{-1}, ^{1}H-NMR (DMSO) δ: 8.7 (s,1H), 2.7-4.9(m, 9H), the compound [X] F.T-IR (KBr) cm^{-1}, 3311 cm^{-1}, 3286cm^{-1}, 1639cm^{-1}, ^{1}H-NMR (DMSO) δ: 9.1 (s,1H), 2.2-5.9(m, 9H), the compound [XI] F.T-IR (KBr) cm^{-1}, 3319 cm^{-1}, 3294cm^{-1}, 1643cm^{-1}, ^{1}H-NMR (DMSO) δ: 8.6 (s,1H), 3.2-5.5(m, 9H), the compound [XII] F.T-IR (KBr) cm^{-1}, 3310 cm^{-1}, 3285cm^{-1}, 1641cm^{-1}, ^{1}H-NMR (DMSO) δ: 8.5 (s,1H), 3.4-5.6(m, 9H).

Ethical Clearance: Permissions for carrying out the study were obtained from the Scientific Research Committees at College of Education for Pure Science (Ibn-Al-Haitham)/ University of Baghdad, Iraq and University of Kasi, Turkey.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

REFERENCES

1- Kamel M.M. , Ali H.A., Anwar M.M., et al; Synthesis antitumor activity and molecular docking study of novel sulfonamides-Schiff's bases, thiazolidinones ,benzothiazinones and their C-nucleoside derivatives; European Journal of MedicinalChemistry.2010; 45 (2), 572-580.

2- Ruping T., Linhong J., Chengli M., et al , Synthesis, antifungal and antibacterial activity for novel amide derivatives containing a triazole moiety Chemistry Central Journal., 2013.7. 30.

3- Anees A. S., Ravinesh M., Mohammad S., Asif H., Mohd R. and Palash P. , Triazole incorporated pyridazinones as a new class of antihypertensive agents: Design, synthesis and in vivo screening Bioorganic & Medicinal Chemistry Letters2011; 21: 1023–1026 .

4- Dhore J. W., Pethe G. B., Wagh1 S. P., et al ; Synthesis, Characterization and Biological Studies of Some Triazolyl Isonicotinamide; Archives of Applied Science Research. 2011; 3 (1) 407-414

5- Hlasta D. J. and Ackerman J. H., Steric Effects on the Regioselectivity of an Azide-Alkyne Dipolar Cycloaddition Reaction: The Synthesis of Human Leukocyte ElastaseInhibitors J. Org. Chem. 1994; 99: 6184-6189

6- Bathula SNP and Vadla R . Bioactivity of 1, 4 disubstituted 1, 2, 3 triazoles as cytotoxic agents against the various human cell lines ,Asian J Pharm Clin Res. 2011;4, (1): 66-67.

7. Clercq E. .,Highlights the different mechanistic strategies that could be followed or envisaged towards the design and development of antiviral drugs, Nature Rev. Drug Discovery, 2002.1:13-25.

8- Hlasta DJ. and Ackerman JH. Steric Effects on the Regioselectivity of an Azide-Alkyne Dipolar Cycloaddition Reaction: The Synthesis of Human Leukocyte Elastase Inhibitors J. Org. Chem., (1994). 99, 6184-6189

9- Maqsood A M., Shaeel A and Manzoor AM. Synthesis, Structure Optimization and Antifungal Screening of Novel Tetrazole Ring Bearing Acyl-Hydrazones Int J Mol. Sci. 2012; 13, 10880-10898.

10- Bhaskar VH.,Mohite PB.,Pandhare RB., et al; Synthesis and in vitro antimicrobial activity of some novel chalcones Acta Pharmaceutica Sciencia2010;52: 505-510

11- Cristina M.M., Ovidiu O., Alina P., et al, Synthesis and antiinflammatory evaluation of some new acyl-hydrazones bearing 2-aryl-thiazole. Eur. J. Med. Chem. 2011;46:526–534.

12- Lima L.M., Frattani F.S., Dos Santos J.L., et al ,Synthesis and anti-platelet activity of novel arylsulfonate-acylhydrazone derivatives, designed as antithrombotic candidates. Eur. J Med. Chem. 2008;43:348–356.

13- Avaji PG, Kumar CHV, Patil SA, et al. Synthesis, spectral characterization, in vitro microbiological evaluation and cytotoxic activities of novel macrocyclic bis hydrazone. Eur. J Med-Chem. 2009;44:3552–3559.

14- Zang., Zang L., Liu L, et al. Anticancer activity, structure, and theoretical calculation of N-(1-phenyl-3-methyl-4- propyl-pyrazolone-5)-salicylidene hydrazone and its copper(II) complex. Inorg. Chim. Acta. 2010;363:289–29

15- Velazquez S, Alvarez R, Perez C, Gago F, De C, Balzarini J, Camaraza M, J. antiviral chemistry. Chem. Chemother. 1998; 9: 481.

16- C. Im, S.N. Maiti, R.G. Micetich, M. Daneshtalab, K. Atchson, O.A. Philips. J. Antibiot.(Tokyo), 1994;47: 1030.

17- Palhagen S, Canger R, Henriksen O, van Parys J.A, Riviere M.E, Karolchyk M.A.Epilepsy Res.2001, 43, 115. (5) Gouault.

18- Fan WQ, and Katritzky A.R, In Comprehensive Heterocyclic Chemistry II, Vol. 4, A.R. Katritzky, C.W. Rees, E.F.V. Scriven (Eds), pp. 1–126, Pergamon, New York (1996).

19- (a) O. Ferna´ndez, G. de la Torre, F. Ferna´ndez-L, J. Barbera´ , T. Torres. Chem. Mater., 9, 3017 (1997), (b) W-R. Li, J-C. Su, Y-C. Ke and C-K. Lai. J. mater. Chem.

1763 (2001); (c) C. Su, L.-X. Lee, S.-H. Yu, Y.-K. Shih, J.-C. Su, F.-J. Li and C.K. Lai. Liq. Cryst., 31, 745 (2004).