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Synthesis, Characterization, Biological Evaluation and Antibacterial Activity of some Heterocyclic Fluorene Compounds Derived from Schiff Base

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Abstract: Aseries of Schiff bases and their derivative (fluorene) have been synthesized primary amine was condensed with aromatic aldehyde (2-carbaldehyde fluorine) in DMF (dimethyl formamide) in the presence of conc. HCl acid as catalyst to yield the Schiff base (1-5). These Schiff bases on treatment with monochloroacetyl choride gave 1-substituted-4(2-fluorenyl)-3-chloro Azetidine-2-one (6-10). and with **α**-mercaptoactic acid gave 3-substituted-2(2-fluorenyl) Tiazolidine-4-one (11-15). The structure of synthesized has been established on the basis of their spectral (FT-IR, Mass, ^{1}H, ^{13}C-NMR, elemental analysis) data. The purity of the compounds was confirmed by TLC. All these compounds were evaluated for their In vitro activity against several microbes. These compounds were tested to determine their ability to inhibit bacterial in some heterocyclic fluorene compounds
Key words: Schiff bases, fluorene, antibacterial activity, Azetidine-2-one, Tiazolidine-4-one.

Introduction

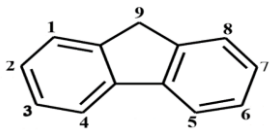


Figure1.1Chemicalstructure and atomicnumberingoffluorene.

The fluorene molecule ($C_{13}H_{10}$) is an isocyclic aromatic hydrocarbon composed of two benzene rings which are connected via a direct carbon-carbon bond and an adjacent methylene bridge (Figure1.1). It was first isolated from coal tar in 1867 and its structure was elucidated already several years later. The methylene bridge forces the two phenyl rings to be planar which increases their orbital overlap and the degree of conjugation of the aromatic system. This is why fluorene absorbs at longer wavelengths than the structurally closely related biphenyl. In bare fluorene, the protons at the sp^3 carbon in the methylene bridge (9-position) exhibit a significant CH acidity (pK_A = 22.9) since the resulting aromatic fluorenyl anion is efficiently resonance. Consequently, in the presence of base, fluorene easily reacts at the 9-position with electrophiles oxidation to 9-fluorenone is another frequently observed reaction, which is also favoured by resonance stabilization because the π-conjugated system is extended. One of the most important strategies prevent such unwanted reactions is the double alkylation or arylation of fluorene, which has the additional advantage of introducing side groups that enhance the solubility in organic solvents. The most susceptible positions for electrophilic aromatic substitutions are positions 2 and 7, although frequently also minor by products, most notably the 4-isomers, are observed[1].

Fluorene-based aromatic compounds are of increasing interest as building blocks for the production of drugs and pharmaceuticals and as fine chemicas of industrial relevance[2-6] including applications in the production of thermosetting plastics and lubricating materials. In addition, fluorene-based polymers and copolymers are of interest owing to their unusual optical and electrical properties and are for that reason commonly used in organic light-emitting diodes, flat panel displays and in solar cells[7-10].

The development of simple synthesis route to widely used organic compounds ring, using readily available reagents is one of the main objective of organic synthesis, Nitrogen, Oxegyn and Sulfur heterocycles are of a special interest because they constitute an important class of natural and non natural products, many of which exhibit useful biological activities, one–pot efficient synthesis of heterocyclic derivatives, may permit the development of novel durgs for the treatment of inflammation, pain, infaction and other acute disease[11].

Some Schiff bases bearing aryl groups[12], or heterocyclic residues possess excellent biological activities[13], which has attracted many researcher's attention in recent year. They have been reported to used as analgesic, antibacterial, antituberculer, antirheeumatoid arthritis, antiviral, anti-inflammatory, antihypertensive, antimicrobial and anticancer[14-15]. fluorene (2-carbaldehyde fluorene) derivatives introduced in 1960 for use in relief of the pain, fluorine is homologous ring. fluorene compounds have medical and biological important and they have medicinal and pharmaceutical applications. Among the wide chemical derivatives are a heteropolymer which have activity and effectiveness against cancer they also have effective against malaria and bacteria, found that some fluorene derivative is considered as medical drug against the diseases[16].

In this paper we have synthesized new Schiff bases, and heterocyclic derivatives containing fluorene moiety, from 2- carbaldehyde flourene with primary amine because these compounds have many applications in medicine and industry and have antimicrobial activity.

Material and Methods

1. General Procedures:

Melting points were determined in open glass capillaries on agallenkamp apparatus and are uncorrected. TLC was performed to assess the reactions and the purity of the products. IR spectra were recorded in KBr (pellet forms) on aNicolet-Avatar-330 FT-IR spectrophometer and note worthy absorption values (cm^{-1}) alone are listed. ^{1}H and ^{13}C-NMR Spectra were recorded at 400 MHZ Bruker AMX using $CDCl_3$ as solvent. The ESI+ve MS spectra were recorded on a Bruker Daltonics LC-MS Spectrometer. Satisfactory microanalysis was obtained on Carlo Erba 1106 CHN analyzer. Potantiostat – galvanostat from Amel instruments where used for bacterial activity.

Chemical and starting materials

2-carbaldehyde fluorene, 5-nitro 2-amino thiazol, monochloroacetyl chloride, **α**-mercaptoactic acid, P-amino phenol, anilin, P-phenylenediamine, N-phenylthiourea, dioxan and zinc chloride (all from Aldrich) were used as supplied, with out further purification.

2. General procedure for synthesis of Schiff base and its derivatives:

I. Preparation of Schiff bases (1-5)

A series of Schiff bases were prepared from the reaction of different primary amine(0,01 mole), with 2-carbaldehyde fluorine (0,01 mol), in 50 ml DMF (dimethyl formamide) and few drops of conc. HCl acid. This mixture was refluxed for 12hrs. The mixture was cooled; precepitate was obtained, then rercystallized from absolute ethanol[18-19].

II. Preparation of 1- substituted-4(2-fluorenyl)-3-chloro azetidine-2-on (6-10)

A solution of compounds (1-5) (0.002 mol) in dioxane (50 ml) was added to a well- stirred mixture of monochloroacetyl chloride (0.004 mol, 0.34 ml) and triethyl amine (0.004 mol, 0.56 ml) in dioxane (20 ml) at 0-5ºC. The mixture was refluxed for (10-12) hrs. and kept for 2 days at room temperature. The reaction mixture

was then poured into crushed ice, filtered and washed with water. The solid product was dried and recrystallized from ethanol and water[20]. Physical properties are listed in table (2).

III. Preparation of 3-substituted-2(2-fluorenyl) tiazolidine-4-on. (11-15).

To a mixture of Schiff base (0.002 mol) and α-mercaptoacetic acid (0.01 mol) dissolved in dioxan (50 ml), anhydrous zinc chloride (0.0016 mol) was added and refluxed for 12 hrs. The reaction mixture was cooled, filtered, washed with 10% w/v sodium bicarbonate solution, vacuum dried and recrystallised using absolute ethanol[21].

3. Biological Activity:

All newly synthesized compounds were test for their activity in vitro growth inhibitory against a standard strain of pathogenic microorganism including Gram–positive bacteria (Staphylococcus aureus), Gram-negative bacteria (Escherichia coli, acinetobacter, klebsiella sp,pseudomonas aeruginosa). Antibacterial activity was done by the disk diffusion methods. aureus and E. coli were subcultured in BHI medium and incubated for 18h at 37^0C, and then the bacterial cells were suspended, according to the McFarland protocol in Mueller Hinton agar solution to produce a suspended of about 10^{-5} CFU ml^{-1}:100µof this suspension was mixed with 10 ml of sterile antibiotic agar at 40^0C and poured onto an agar plate I a laminar flow cabine.Five paper disks (6.0 mm diameter) were fixed onto nutrient agar plate. 1 mg of each test compound was dissolved in 100 ml DMSO to prepare stock solution from stock solution different concentration 250,500,750, 1000 ppm of each test compound were prepared. These compounds of different concentration were poured over disk plate on to it. Streptomycin was used as standard drug (positive control) DMSO poured disk was determined by the formation of a inhibitory zone after 24h of incubation at 36^0C [22]. (Table 7)

Table 7: Antimicrobial activity for prepared compounds

Bacteria	McF	Comp. No.	250	500	750	1000
Klebseilla sp.	1.8	6	-	+	++	+++
		7	-	-	+	+++
		11	-	+	++	+++
		12	-	-	+	++
		14	-	+	+	+++
Pseudomonas sp.	2.8	6	-	+	+	++
		7	-	+	+	++
		11	-	+	+	++
		12	-	-	+	++
		14	-	+	+	++
E.coli	2.0	6	-	-	+	+
		7	-	+	-	+
		11	-	-	++	+
		12	-	+	-	+
		14	-	+	-	+
Acinetobacter	1.8	6	-	++	++	+++
		7	-	+	++	+++
		11	-	+	++	+++
		12	-	+	++	+++
		14	-	++	+	+++
Staphylococcus aureus	4.6	6	-	+	+	+++
		7	-	-	+++	+++
		11	-	+	+	++
		12	-	++	+++	+++
		14	-	+	+++	++

Key the symbols: (-) = No inhibition, (+) = 5-9 mm, (++) = 10-14 mm, (+++) = 15-.20 mm.
Gram Negative bacteria: *Escherichia coli, Pseudomonas aeruginosa, Klebsiella sp Acinetobacter.*
Gram Positive bacteria: *Staphylococcus aureus.*

Results and Discussion:

4. 1. Chemistry and characterization:

The present work involved three steps

First step:

Include preparation of new five Schiff bases (1-5) were prepared by reaction of different primary amine with 2-carbaldehyd fluorene. The synthesis of these compounds were carried out lined in Schem (1) and the physical properties for Schiff bases (1-5) including melting point range of (95-235) and % yield was range of (75-95) and these compounds were identified by FT-IR Spectroscopy, LC-MS, ^{1}H-, ^{13}C-NMR. **FT-IR** spectrum of compounds **(1-5)** showed characteristic absorption bands (1633)cm^{-1}, (3025)cm^{-1}, (3350, 3450)cm^{-1}, (3475)cm$^{-1,}$ (1580)cm^{-1}, (1236)cm^{-1} due to υ(C=N)str, υ(C-H)aromatic, υ(C=C)aromatic, υ(NH), υ(OH), υ(C=S), respectively. As shown in table (3). **^{1}H-NMR** spectrum of compound **(1)** showed multiplet signals at (7.5-7.8)ppm due to aromatic protons of fluorine and singlet signal at (8.36ppm) due to (C-H) group proton of thiazole and singlet signal at 3.51 ppm due to (CH_2) group protons of fluorene in addition to singlet signals at (8.9)due to (HC=N Azomethine) group proton. **^{13}C-NMR** of compound **(1)** show multiplet signals at (122-142)ppm due to aromatic carbons of fluorine, signals at (41.97)ppm due to (CH_2) carbon of fluorene, signals at (134.71)ppm due to (C=N) carbon of thiazole, signals at (141.59)ppm due to (CH) carbon of thiazole, in addition to signals at (163.3)ppm due to (HC=N Azomethine) group carbon[23]. The physical properties (melting points, yieldes, elemental analysis and spectral data) of compounds **(1-5)** are included in tables **(1, 2 and 5)**.

Table 1: Melting points, yield, molecular formula (M. F.) and molecular weight (M. Wt.) of compounds [1-5]

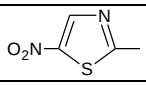
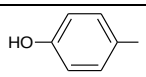
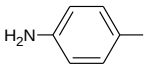
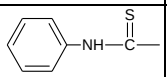
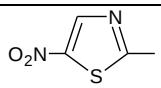
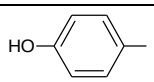
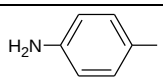
Compound	R	M.Wt.	M.F.	Yield (%)	M.P (^{0}C)
1		321	$C_{17}N_3SO_2H_{11}$	83	124 -125
2		285	$C_{20}NOH_{15}$	76	232-234
3		269	$C_{20}NH_{15}$	89	129-130
4		284	$C_{20}N_2H_{16}$	93	110
5		328	$C_{21}N_2SH_{16}$	95	95-96

Table 2: Depacited elemental analysis (C.H.N) of synthesis compounds [1-5]

Compound	R	Found				Calculated			
		C%	H%	N%	S%	C%	H%	N%	S%
1		63.72	3.37	13.53	9.76	63.55	3.43	13.08	9.97
2		88.17	5.32	4.85	0.00	88.42	5.26	4.91	0.00
3		89.23	5.80	5.41	0.00	89.22	5.58	5.20	0.00
4		84.73	5.76	9.91	0.00	84.51	5.63	9.86	0.00

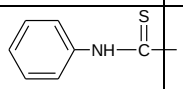
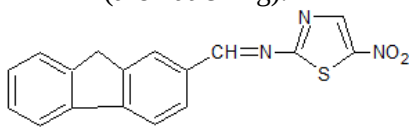
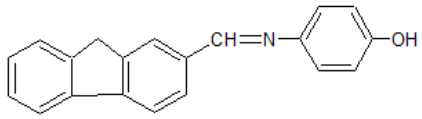
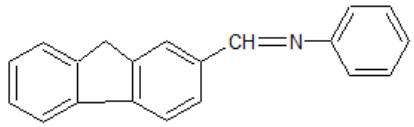
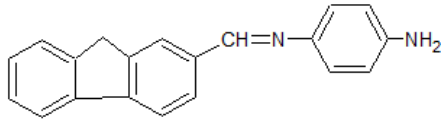
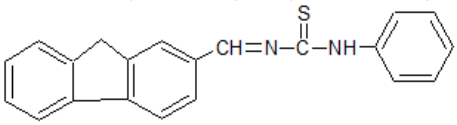
5		76.74	4.95	8.63	9.58	76.83	4.87	8.54	9.77

Table 5: Spectroscopial data of Synthesized Schiff Base of fluorene derivatives

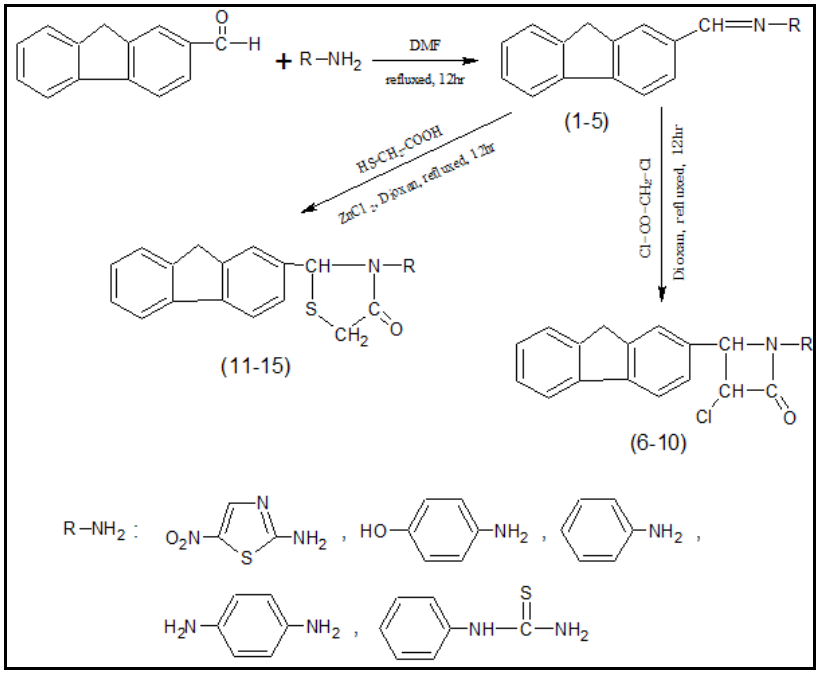
Compound NO	Spectroscopy data
1	**IR** (KBr, cm^{-1}): 3027.34 [υ(C-H)$_{Ar}$], 1627.63 [υ(C=N)], 1558.79 [υ(C=C)$_{Ar}$]. **LC-MS**: m/z = 321.06 **^{1}H-NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.51 (S, 2H, CH_2 fluorene ring), 8.36 (S, 1H, C-H thiazole), 8.9 (S, 1H, HC=N azomethine), 7.5-7.8 (m, 7H, aromatic ring). **^{13}C-NMR (400MHz, $CDCl_3$, ppm)** δC: 41.97 (CH_2 fluorene ring), 134.71 (-C=N thiazole), 139.87 (C-NO_2), 141.59 (CH thiazole), 163.3 (HC=N azomethine), 122-142 (aromatic ring). 
2	**IR** (KBr, cm^{-1}): 3475 [(OH)], 3029.68 [υ(C-H)$_{Ar}$], 1635.87 [υ(C=N)], 1550.87 [υ(C=C)$_{Ar}$]. **LC-MS**: m/z = 285.12 **^{1}H NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.49 (S, 2H, CH_2 fluorene ring), 5.08 (S, 1H, OH), 8.35 (S, 1H, HC=N azomethine), 7.03-7.77 (m, 11H, aromatic ring). **^{13}C-NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.83 (CH_2 fluorene ring), 161.9 (HC=N azomethine), 121-156 (aromatic ring). 
3	**IR** (KBr, cm^{-1}): 3031.32 [υ(C-H)$_{Ar}$], 1622.8 [υ(C=N)], 1587.13 [υ(C=C)$_{Ar}$]. **LC-MS**: m/z = 269.12 **^{1}HNMR (400 MHz, $CDCl_3$, ppm)** δH: 3.52 (S, 2H, CH_2 fluorene ring), 8.33 (S, 1H, HC=N azomethine), 7.49-7.73 (m, 12H, aromatic ring). **^{13}C-NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.98 (CH_2 fluorene ring), 161.7 (HC=N azomethine), 123-142 (aromatic ring). 
4	**IR** (KBr, cm^{-1}): (3450, 3350) [(NH_2)], 3019.98 [υ(C-H)$_{Ar}$], 1624.73[υ(C=N)], 1588 [υ(C=C)$_{Ar}$]. **LC-MS:** m/z = 284.13 **^{1}H-NMR (400MHz, $CDCl_3$, ppm)** δH: 3.55 (S, 2H, CH_2 fluorene ring), 5.18 (S, 2H, NH_2), 8.99 (S, 1H, HC=N azomethine), 6.78-7.77 (m, 11H, aromatic ring). **^{13}C-NMR (400MHz, $CDCl_3$, ppm)** δC**:** 41.84 (CH_2 fluorene ring), 162.7 (HC=N azomethine), 116-148 (aromatic ring). 

5	**IR** (KBr, cm^{-1}): (3457.74) [(NH)], 3028.21 [υ(C-H)$_{Ar}$], 1623.77 [υ(C=N)], 1584.87 [υ(C=C)$_{Ar}$], 1236.37 [υ(C=S)]. **LC-MS:** m/z = 328.1 **^{1}H-NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.48 (S, 2H, CH_2 fluorene ring), 6.08 (S, 1H, NH), 8.67 (S, 1H, HC=N azomethine), 6.82-7.78 (m, 12H, aromatic ring). **^{13}C-NMR (400MHz, $CDCl_3$, ppm)** δC**:** 41.86 (CH_2 fluorene ring), 163.6 (HC=N azomethine), 198.8 (C=S), 113-149 (aromatic ring). 

Second step:

The second step inclued preparation of new five Lactam derivatives (6-10) were prepared by reaction of Schiff bases (1-5) in (First step) with monochloroacetyl chloride in dioxan. The synthesis of these compounds which carried out are lined in scheme (1). And the physical properties for Lactam derivatives (6-10) including melting point range of (70-290)C^0 and % Yield was range (65-87) and these compounds were identified by FT-IR, LC-MS and ^{1}H, ^{13}C-NMR. **FT-IR** spectrum of compounds **(6-10)** showed clear absorption bands at (1636.55-1684.52)cm^{-1} due to the υ(C=O) Of lactam ring, (636.7-670.39)cm^{-1} due to the υ(C-Cl) Of lactam ring, (3021.52-3084.13)cm^{-1} due to the υ(C-H)aromatic, (34995)cm^{-1} due to the υ(OH), (3356.5-3510)cm^{-1} due to the υ(NH). The **^{1}H-NMR** spectrum of compound **(9)**, showed multiplet signals at (6.78-7.83)ppm due to aromatic protons and a singlet signal at (5.82)ppm due to N-CH group proton of lactam ring, a singlet signal at (4.81)ppm due to Cl-CH group proton of lactam ring. **^{13}C-NMR** spectrum of compound **(9)** showed signals at (117-148)ppm due to aromatic carbons and signals at (177.16)ppm due to (C=O) carbon of lactam, and signals at (49.09)ppm due to (HC-Cl) carbon of lactam, signals at (59.57)ppm due to (N-CH) carbon of lactam[24]. The physical properties (melting points, yieldes, elemental analysis and spectral data) of compounds **(6-10)** are included in tables **(3, 4 and 6)**.

Scheme 1: Synthesis of Schiff base and fluorene derivatives R: primary amine



Third step:

The third step inclued preparation of new five Thiazolidinone-4 derivatives (11-15) were prepared by reaction of Schiff bases (1-5) in (First step) with α-mercaptoacetic acid in dioxan. The synthesis of these compounds which carried out are lined in scheme (1). And the physical properties for Thiazolidinone-4 derivatives (11-15) including melting point range of (87-271) ^{0}C and % Yield was range of (83-95) and these compounds were identified by FT-IR, LC-MS and ^{1}H, ^{13}C-NMR. **FT-IR** spectrum of compounds **(11-15)**

showed clear absorption bands at (1638.38-1704)cm^{-1} due to the υ(C=O) Of Thiazolidinone-4 ring, (3013.22-3053.73)cm^{-1} due to the υ(C-H) aromatic, (34970.17)cm^{-1} due to the υ(OH), (3425-3525)cm^{-1} due to the υ(NH). The **^{1}H-NMR** spectrum of compound **(12)**, showed multiplet signals at (7.04-7.79) ppm due to aromatic protons and a singlet signal at (6.22)ppm due to (-CH) group proton of Thiazolidinone-4 ring, a singlet signal at (3.19) ppm due to (CH_2) group protons of Thiazolidinone-4 ring, and a singlet signal at (5.07)ppm due to (-OH) group proton. **^{13}C-NMR** spectrum of compound **(12)** showed signals at (115-155)ppm due to aromatic carbons and signals at (177.28)ppm due to (C=O) carbon of Thiazolidinone-4, and signals at (66.34)ppm due to (HC-N) carbon of Thiazolidinone-4, signals at (34.52)ppm due to (CH_2) carbon of Thiazolidinone-4 [25]. The physical properties (melting points, yieldes, elemental analysis and spectral data) of compounds **(11-15)** are included in tables **(3, 4 and 6)**.

Table 3: Melting points, yield, molecular formula (M. F.) and molecular weight (M. Wt.) of compounds [6-15]

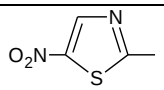
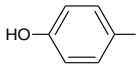
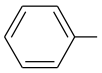
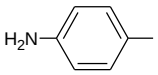
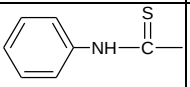
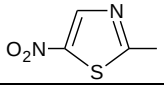
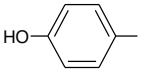
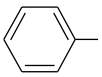
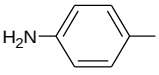
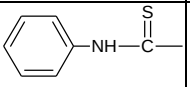
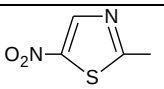
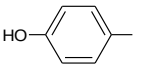
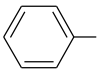
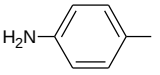
Compound	R	M.Wt.	M.F.	Yield (%)	M.P (^{0}C)
6		397.5	$C_{19}N_3SO_3ClH_{11}$	67	oil
7		361.5	$C_{22}NO_2\ ClH_{16}$	86	261
8		345.5	$C_{22}NO\ ClH_{16}$	65	74
9		360.5	$C_{22}N_2O\ ClH_{17}$	88	290
10		404	$C_{23}N_2OS$ ClH_{17}	87	oil
11		395	$C_{19}N_3S_2O_3H_{13}$	92	216
12		359	$C_{22}NSO_2H_{17}$	83	206
13		343	$C_{22}NSO\ H_{17}$	95	oil
14		358	$C_{22}N_2SO\ H_{18}$	86	271
15		402	$C_{23}N_2S_2O\ H_{18}$	94	87-89

Table 4: Depacited elemental analysis (C.H.N) of synthesis compounds [6-15]

Compound	R	Found				Calculated			
		C%	H%	N%	S%	C%	H%	N%	S%
6		57.44	3.43	10.82	4.12	57.36	3.02	10.57	4.03
7		73.31	4.22	3.93	0.00	73.03	4.43	3.87	0.00
8		76.33	4.75	5.12	0.00	76.41	4.63	5.05	0.00
9		73.24	4.83	7.65	0.00	73.23	4.72	7.77	0.00

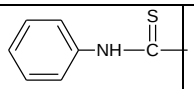
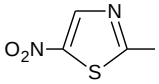
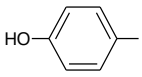
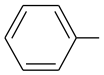
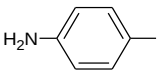
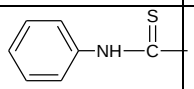
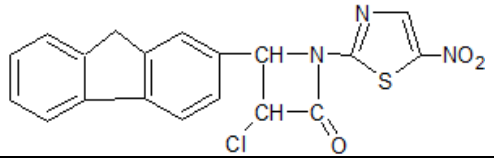
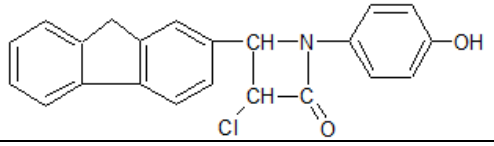
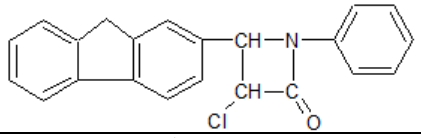
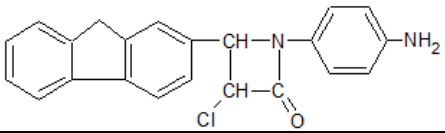
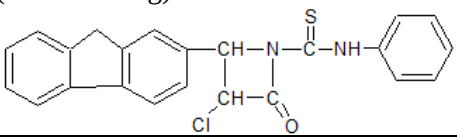
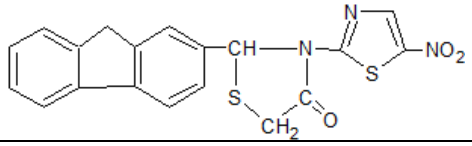
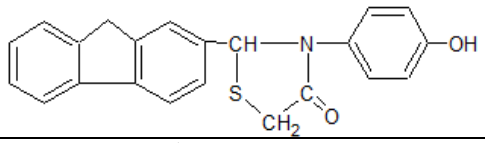
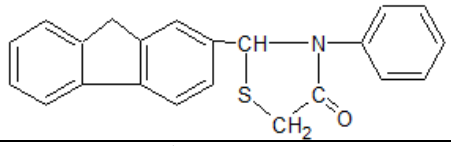
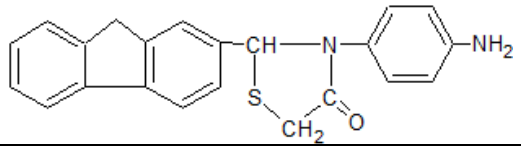
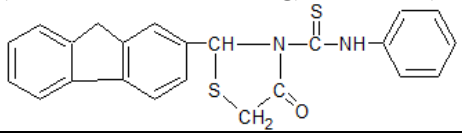
10		68.40	4.11	6.79	7.87	68.32	4.21	6.93	7.92
11		57.81	3.47	10.55	16.35	57.72	3.29	10.63	16.20
12		73.62	4.81	3.92	8.77	73.54	4.74	3.89	8.91
13		76.85	4.87	4.15	9.04	76.97	4.96	4.08	9.33
14		73.82	5.34	7.74	8.98	73.74	5.03	7.82	8.94
15		68.74	4.50	6.99	15.87	68.66	4.48	6.97	15.92

Table 6: Spectroscopial data of Synthesized Heterocyclic from Fluorene derivatives compounds

Compound NO	Spectroscopy data
6	**IR** (KBr, cm^{-1}): 3025.99 [υ(C-H)$_{Ar}$], 1652.7 [υ(C=O) lactam], 1604.01 [υ(C=N), 1541.32 [υ(C=C)$_{Ar}$], 661 [υ(C-Cl)]. **LC-MS**: m/z = 397.03 **^{1}H-NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.47 (S, 2H, CH_2 fluorene ring), 8.33 (S, 1H, C-H thiazole), 5.83 (d, 1H, HC-N lactam), 4.83 (d, 1H, HC-Cl lactam), 7.48-7.81 (m, 7H, aromatic ring). **^{13}C-NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.98 (CH_2 fluorene ring), 134.72 (-C=N thiazole), 139.71 (C-NO_2), 141.72 (CH thiazole), 59.83 (HC-N lactam), 49.18 (HC-Cl lactam), 177.34 (C=O lactam), 121-141 (aromatic ring). 
7	**IR** (KBr, cm^{-1})**:** 3495 [(OH)], 3047.02 (C-H_{Ar}), 1636.55 [υ(C=O) lactam], 1568.32 [υ(C=C)$_{Ar}$], 671 [υ(C-Cl)]. **LC-MS:** m/z = 361.09 **^{1}H NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.48 (S, 2H, CH_2 fluorene ring), 5.33 (S, 1H, OH), 5.81 (d, 1H, HC-N lactam), 4.81 (d, 1H, HC-Cl lactam), 7.05-7.75 (m, 11H, aromatic ring). **^{13}C-NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.8 (CH_2 fluorene ring), 59.64 (HC-N lactam), 49.14 (HC-Cl lactam), 178.31 (C=O lactam), 116-156 (aromatic ring). 

8	**IR** (KBr, cm^{-1}): 3021.52 [υ(C-H_{Ar})], 1649.55 [υ(C=O) lactam], 1563.14 [υ(C=C)$_{Ar}$], 670.39 [υ(C-Cl)]. **LC-MS:** m/z = 345.09 **^{1}H-NMR (400MHz, CDCl3, ppm)** δH: 3.49 (S, 2H, CH_2 fluorene ring), 5.78 (d, 1H, HC-N lactam), 4.77 (d, 1H, HC-Cl lactam), 7.46-7.79 (m, 12H, aromatic ring). **^{13}C-NMR (400MHz, CDCl3, ppm)** δC: 41.86 (CH_2 fluorene ring), 59.58 (HC-N lactam), 48.96 (HC-Cl lactam), 179.14 (C=O lactam), 121-141 (aromatic ring). 
9	**IR** (KBr, cm^{-1}): (3410, 3510) [(NH_2), 3084.13 [υ(C-H_{Ar})], 1674.27 [υ(C=O) lactam], 1589.02 [υ(C=C)$_{Ar}$], 636.7 [υ(C-Cl)]. **LC-MS**: m/z = 360.1 **^{1}H NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.53 (S, 2H, CH_2 fluorene ring), 8.33 (S, 2H, NH_2, 5.82 (d, 1H, HC-N lactam), 4.81 (d, 1H, HC-Cl lactam), 6.78-7.83 (m, 11H, aromatic ring). **^{13}C NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.87 (CH_2 fluorene ring), 59.57 (HC-N lactam), 49.09 (HC-Cl lactam), 177.16 (C=O lactam), 117-148 (aromatic ring). 
10	**IR** (KBr, cm^{-1}): 3356.5 [(NH)], 3052.76 [υ(C-H_{Ar})], 1684.52 [υ(C=O) lactam], 1606.41 [υ(C=C)$_{Ar}$], 1246.75 [υ(C=S)], 653.25 [υ(C-Cl)]. **LC-MS**: m/z = 404.07 **^{1}H NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.54 (S, 2H, CH_2 fluorene ring), 5.08 (S, 1H, NH), 5.53 (d, 1H, HC-N lactam), 4.73 (d, 1H, HC-Cl lactam), 6.86-7.78 (m, 12H, aromatic ring). **^{13}C NMR (400 MHz, $CDCl_3$, ppm)** δC: 42 (CH_2 fluorene ring), 198.3 (-C=S), 45.35 (HC-N lactam), 51.85 (HC-Cl lactam), 176 (C=O lactam), 113-149 (aromatic ring). 
11	**IR** (KBr, cm^{-1}): 3053.73 [υ(C-H_{Ar})], 1704 [υ(C=O) thiazolidinone], 1600.63 [υ(C=N)], 1557.71 [υ(C=C)$_{Ar}$]. **LC-MS**: m/z = 395.04 **^{1}H NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.56 (S, 2H, CH_2 fluorene ring), 8.37 (S, 1H, C-H thiazole ring), 6.19 (S, 1H, CH thiazolidinone ring), 3.18 (S, 2H, CH_2 thiazolidinone ring), 7.49-7.76 (m, 7H, aromatic ring). **^{13}C NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.77 (CH_2 fluorene ring), 134.66 (-C=N thiazole ring), 139.87 (C-NO_2), 141.62 (CH thiazole ring), 66.36(CH thiazolidinone ring), 34.48 (CH_2 thiazolidinone ring), 176.92(C=O thiazolidinone ring), 127-141 (aromatic ring). 

12	**IR** (KBr, cm^{-1}): 3470.17 [(OH)], 3013.22 [υ(C-H_{Ar})], 1638.38 [υ(C=O) thiazolidinone], 1563.42 [$\upsilon(C=C)_{Ar}$]. **LC-MS**: m/z = 359.1 **^{1}H- NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.49 (S, 2H, CH_2 fluorene ring), 5.07 (S, 1H, OH), 6.22 (S, 1H, CH thiazolidinone ring), 3.19 (S, 2H, CH_2 thiazolidinone ring), 7.04-7.79 (m, 11H, aromatic ring). **^{13}C- NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.92 (CH_2 fluorene ring), 66.34 (CH thiazolidinone ring), 34.52 (CH_2 thiazolidinone ring), 177.28 (C=O thiazolidinone ring), 115-155 (aromatic ring). 
13	**IR** (KBr, cm^{-1}): 3023.24 [$\upsilon(C-H)_{Ar}$], 1670.41 [υ(C=O) thiazolidinone ring], 1579.43 [$\upsilon(C=C)_{Ar}$]. **LC-MS**: m/z = 343.1 **^{1}H NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.52 (S, 2H, CH_2 fluorene ring), 6.27 (S, 1H, CH thiazolidinone ring), 3.17 (S, 2H, CH_2 thiazolidinone ring), 7.48-7.76 (m, 12H, aromatic ring). **^{13}C NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.82 (CH_2 fluorene ring), 66.24 (CH thiazolidinone ring), 34.44 (CH_2 thiazolidinone ring), 177.23 (C=O thiazolidinone ring), 121-142 (aromatic ring). 
14	**IR** (KBr, cm^{-1}): (3425, 3525) [(NH_2), 1678.38 [υ(C=O) thiazolidinone ring], 1620.53 [$\upsilon(C=C)_{Ar}$]. **LC-MS**: m/z = 358.11 **^{1}H- NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.50 (S, 2H, CH_2 fluorene ring), 5.11 (S, 1H, NH), 6.25 (S, 1H, CH thiazolidinone ring), 3.29 (S, 2H, CH_2 thiazolidinone ring), 6.74-7.81 (m, 11H, aromatic ring). **^{13}C-NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.91 (CH_2 fluorene ring), 66.35 (CH thiazolidinone ring), 34.49 (CH_2 thiazolidinone ring), 177.37 (C=O thiazolidinone ring), 116-147(aromatic ring). 
15	**IR** (KBr, cm^{-1}): 3443.02 [(NH), 1685.48 [υ(C=O) thiazolidinone ring], 1601.59 [$\upsilon(C=C)_{Ar}$]. **LC-MS**: m/z = 402.09 **^{1}H NMR (400 MHz, $CDCl_3$, ppm)** δH: 3.47 (S, 2H, CH_2 fluorene ring), 5.19 (S, 1H, NH), 5.91 (S, 1H, CH thiazolidinone ring), 3.09 (S, 2H, CH_2 thiazolidinone ring), 6.83-7.79 (m, 12H, aromatic ring). **^{13}C NMR (400 MHz, $CDCl_3$, ppm)** δC: 41.88 (CH_2 fluorene ring), 196.31 (-C=S), 52.12 (CH thiazolidinone ring), 37.42 (CH_2 thiazolidinone ring), 177.28 (C=O thiazolidinone ring), 114-149 (aromatic ring). 

4. 2 Antimicrobial activity:

The newly synthesized compounds were screened for their antibacterial activity against, *Klebsiell sp*, *Staphylococcus aureus*, *Acinetobacter* The results of such studies are given in Table 7. The data showed that

compound (6, 7, 11, 12, 14) exhibited very good activity against Klebsiell sp, Staphylococcus aureus, Acinetobacter. *There maining compounds were found to have good activity against Acinetobacter and slight or moderate activity against Escherichia coli, Pseudomonas aeruginosa.*

4. Conclusions

The main aim of the present study is to synthesize and investigate the antimicrobial of new heterocyclic derivatives containing, fluorene ring with the hope of discovering new structures serving as potential broad spectrum antimicrobial agents, the antibacterial revealed that nature of substituents on the fluorene ring viz., 5-nitro 2-amino thiazol, P-amino phenol, anilin, P-phenylenediamine, N-phenylthiourea and lactam ring and thiazolidinone-4 ring as the aryl moieties are determinant for the nature and extent of the anti-bacterial activity of the synthesized compounds, which might have influences on their inhibiting mechanism of actions.Compound (6, 7, 11, 12, 14) which contain electron donating functional moiety is most potent against bacterial it's showed good antimicrobial activity. From the results it is obvious that all five studied compounds function as effective on bacterial.

5. Acknowldgement:

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