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RESEARCH ARTICLE

Synthesis and Spectroscopic Characterization of Novel Hybrid Antibacterial Molecules of Fluorene and Triazole

Amol K. Patil[1]*, Bharatkumar B. Patel[2], Kokila A. Parmar[3]

[1 & 2]*Department of Chemistry, Sheth M. N. Science College, Patan-384265, Gujarat, India.*

[3]*Department of Chemistry, H N G University, Patan-384265, Gujarat, India.*

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ABSTRACT

A series of fluorene and triazole hybrids were designed and effectively synthesized through reaction of triazole at fluorene ring. These compounds were thermally and morphologically stable and it shows pharmaceuticals useful as antibacterial material. This multifunctional component to fluorene makes them potential drug candidate for the treatment of various diseases. It is intended to help medicinal chemist in designing and synthesizing novel and potent hybrid compounds for the different disorders. The structural designing of the these fluorene compounds have been made on the basis of their elemental analysis, spectral analysis and other physico chemical investigations, antibacterial activities of the synthesized compounds have been determined qualitatively against different pathogenic bacteria. The structures were confirmed by MASS, ^{1}H NMR, IR and UV spectroscopy.

KEYWORDS

Fluorene, Triazole, Drug, Spectroscopy, Pharmaceuticals, ^{1}H NMR

INTRODUCTION

Heterocyclic compounds are important in the recent years for development in science and technology taking on much more advances of both theoretical and practical relevance which shows many pharmaceutical, medicinal and biological activities. Heterocyclic compounds offer many opportunities for synthetic organic chemist. From wide variety of heterocycles that have been explored developing pharmaceutically important molecule such as fluorene and triazoles have played important role in medicinal chemistry. They are reported to possess broad spectrum of biological activities as antiulcer, anticonvulsant, antihistaminic, antiviral, anti-parasitic, cardiovascular agent as well as antihelmintic[1-15]

*Address for Correspondence:
Amol K. Patil,
Department of Chemistry, Sheth M. N. Science College, Patan, Gujarat, India.
E mail ID: akpatil21@redifmail.com

Experimental

Material and Methods

Melting points were determined by melting point apparatus and are uncorrected. These all compounds were routinely checked by for their homogeneity by Thin layer chromatography on silica gel G plates. ^{1}H NMR spectra were recorded on BRUKER spectrometer on a 400 MHz using TMS as internal standard, IR spectra were recorded by Perkin Elmer FT IR spectrophotometer and Mass spectra recorded on (FAB mass).The bacterial strains studied for activities are identified strains.

General Procedure

Preparation of 9 H-fluorene-4-carbonyl chlorides

A mixture of 9H-fluorene-4-carboxylic acid (20g, 0.12mole) in dichloromethane (100ml) and thionyl chloride (14.65g, 0.12mole) was

fitted with a condenser and nitrogen purging, The reaction mixture was refluxed with slow nitrogen flush and allowed to stir for 12 h at 35°C. After completion of reaction solvent an excess thionyl chloride distilled out at 50°C under vacuum to obtained solid recrystallize from isopropanol to get pure compound with 90% yield. Analysis observed: C-73.48%, H-4.05%.Calculated for $C_{14}H_9ClO$ is C-73.53.

1-(9H-fluorene-4-carbonyl)-3-phenyl-thiourea

To a suspension of NH_4SCN (4.05g, 0.11 mol) with acetone (100ml) added slowly 9H-fluorene-4-carbonyl chloride (17g, 0.074 mol) under dry condition in 20 min. After addition over reaction mass was stirred at refluxed for 30min. A solution of aniline (6.9g, 0.1 mol) in acetone (50ml) was added to above stirred reaction mass at reflux. After completion of addition reaction mixture was refluxed for further for 30 min. Reaction mixture cooled to RT and poured in the water and resulting solid separated by filtration. Solid was recrystallized in isopropyl alcohol giving pure compound with (20g) yield 78%. Analysis observed C73.20%, H-4.63%, N-8.10% and calculated for $C_{21}H_{16}N_2OS$ is C73.23%, H-64%, N 8.13%, S-7.41%.

Preparation of 1-(9H-Fluorene-4-carbonyl)-2-methyl-3-phenyl-isothiourea

A mixture of 1-(9H-fluorene-4-carbonyl)-3-phenyl-thiourea (18g, 0.052 mol), methyl iodide (8.1g, 0.057 mol) and anhydrous potassium carbonate (10.8g, 0.078 mol) in DMF (150 ml) with stirring. The resulting off white solid was filtered, washed with water and dried to give compound 1-(9H-Fluorene-4-carbonyl)-2-methyl-3-phenyl-isothiourea Further crystallised in ethanol to give off white solid. Yield 14.3g (81%). Analysis Observation: C-73.68%, H-5.01%, N-7.78%; Calc for $C_{22}H_{18}N_2OS$: C-73.71,H-5.06%, N-7.82%.

Preparation of [5-1-(9H-Fluoren-4-yl)-2H-[1,2,4] triazol-3-yl]-phenyl -amine

To a suspension of 1-(9H-Fluorene-4-carbonyl)-2-methyl-3-phenyl-isothiourea (12g, 0.033mol)hydrazine hydrate (2.51g, 0.050 mol) in ethanol (80ml) was refluxed for 5hr. Reaction mixture was cool to RT and dumped in water, further obtained light yellow solid separated by filtration. Solid was recrystallized in ethanol to give compound [5-1-(9H-Fluoren-4-yl)-2H-[1,2,4] triazol-3-yl]-phenyl-amine in yield 8.8g, (80%). Analysis observation: C-77.70%, H-4.95%, N-17.22%; Calc for $C_{21}H_{16}N_4$:C77.76%, H-4.97%, N-17.27%.

Preparation of 3-(9-(4-methlbenylidine)-9H-Fluoren-4-yl]-N-phenyl-1H-1,2,4 triazol-5-amine

To a suspension of [5-1-(9H-Fluoren-4-yl)-2H-[1,2,4] triazol-3-yl]-phenyl-amine (8g, 0.024 mol), potassium hydroxide (0.7g, 0.012 mol) and paratolualdehyde (4.32g, 0.036 mol) were dissolved in N,N-Dimethylformamide (75 ml) and heated to 60-70°C for 24 hr. Water (800ml) to added and reaction mass extracted with ethylacetate (3 X 200ml) and the combine extracted organic layers treated with sodium sulphate. Distilled out organic layer under vacuum to obtained residue further crystallize from ethanol to obtained pure off white compound 3-(9-(4-methlbenylidine)-9H-Fluoren-4-yl]-N-phenyl-1H-1,2,4 triazol-5-amine in 76% yield. Analysis Observed is C-81.48%, H-4.85%, N-13.53%; Calculated for $C_{28}H_{20}N_4$ is C-81.53%, H-4.89%, N-13.58%.

The progress of reaction and purity of compound checked by TLC aluminum sheet silica gel 60 F254 (E.Merck) using Hexane:acetate (60:40 V/V) and visualized in U. V (254nm).

Similarly other substituted hybrid molecules of fluorene and triazole have been prepared. The physical data are recorded in Table-1.

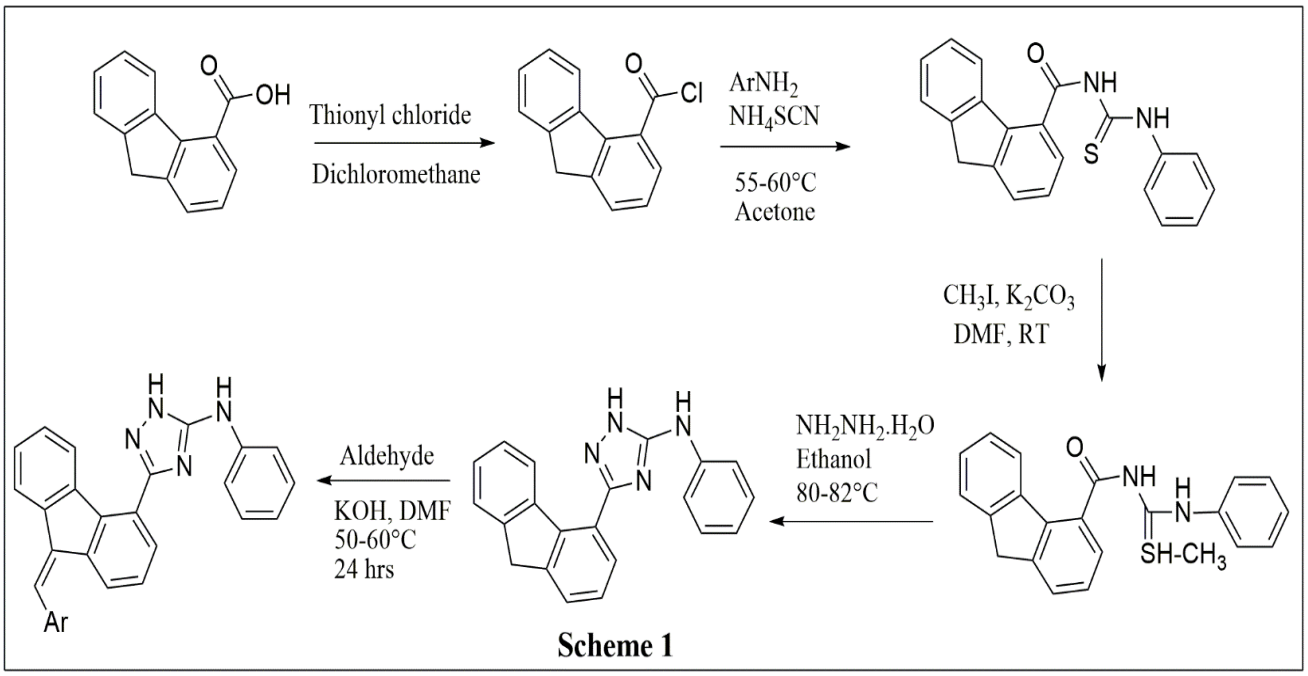
Biological Evaluation

Antibacterial activity of 3-(9-(4-methylbenzylidene)-9H-fluoren-yl)-N-Aryl-1H-1,2,4-triazole-5-amine. Novel synthesized hybrid compounds of fluorene and triazole have been tested for their antibacterial activity against gram positive and gram negative bacteria B.coccus, S aureus, E.aerogenes, P.aeruginosa by using borer medium and filled

Table 1: Physical constant of 3-(9-(4-methylbenzylidene)-9H-fluoren-yl)-N-Aryl-1H-1,2,4-triazole-5-amine

Sr. No.	Ar	Molecular formula	M P	Yield	C, H, N Elemental analysis					
					% C		% H		% N	
			°C	%	Cal.	Obs.	Cal.	Obs.	Cal.	Obs.
A-01	$-C_6H_5$	$C_{28}H_{20}N_4$	113-117	66	81.53	81.50	4.89	4.88	13.58	13.57
A-02	$-C_6H_4-CH_3$	$C_{29}H_{22}N_4$	106-111	69	81.66	81.67	5.20	5.22	13.14	13.10
A-03	$-C_6H_4-Br$	$C_{28}H_{19}BrN_4$	96-101	59	68.44	68.45	3.90	3.89	11.40	11.39
A-04	$-C_6H_4CN$	$C_{29}H_{19}N_5$	106-112	63	79.61	79.59	4.38	4.39	16.01	17.99
A-05	$-C_6H_4OH$	$C_{28}H_{20}N_4O$	95-100	59	78.49	78.48	4.70	4.69	13.08	13.06
A-06	$-CH_2-C_6H_5$	$C_{29}H_{22}N_4$	88-95	62	81.66	81.69	5.20	5.24	13.14	13.15
A-07	$-C_6H_4-C_4H_9$	$C_{31}H_{26}N_4$	113-118	57	81.91	81.88	5.77	5.78	12.33	12.29
A-08	$-C_6H_4-C_3H_7$	$C_{30}H_{24}N_4$	89-93	65	81.79	81.80	5.49	5.50	12.72	12.69
A-09	$-C_5H_4N$	$C_{27}H_{19}N_5$	98-103	55	78.43	78.45	4.63	4.59	16.94	16.95
A-10	$-C_6H_3-F_2$	$C_{28}H_{18}F_2N_4$	103-108	69	74.99	75.01	4.05	4.03	12.49	12.45

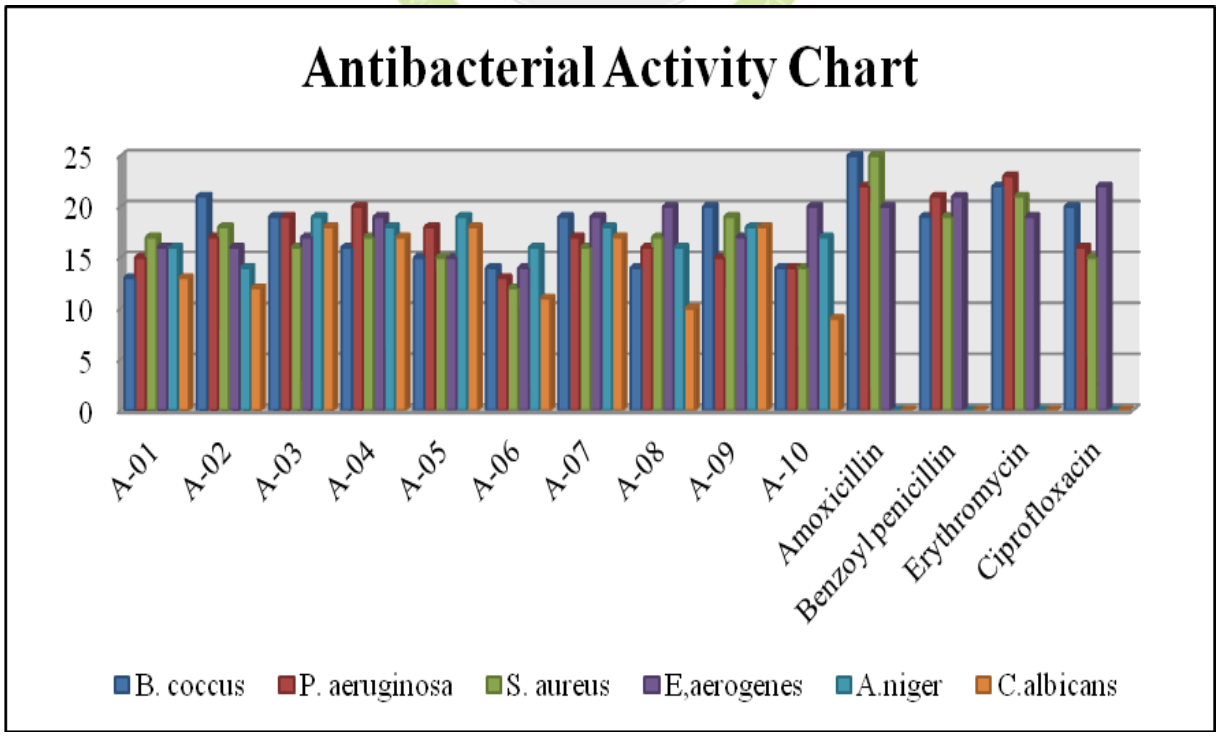
Reaction Scheme



Scheme 1

Table 2: Antibacterial activity of 3-(9-(4-methylbenzylidene)-9H-fluoren-yl)-N-Aryl-1H-1,2,4-triazole-5-amine

Compounds	Antibacterial and antimicrobial activity MIC in µg/ml					
	B. coccus	***P. aeruginosa***	***S. aureus***	***E,aerogenes***	***A.niger***	***C.albicans***
A-01	13	15	17	16	16	13
A-02	21	17	18	16	14	12
A-03	19	19	16	17	19	18
A-04	16	20	17	19	18	17
A-05	15	18	15	15	19	18
A-06	14	13	12	14	16	11
A-07	19	17	16	19	18	17
A-08	14	16	17	20	16	10
A-09	20	15	19	17	18	18
A-10	14	14	14	20	17	09
Amoxicillin	25	22	25	20	00	00
Benzoyl penicillin	19	21	19	21	00	00
Erythromycin	22	23	21	19	00	00
Ciprofloxacin	20	16	15	22	00	00



with 0.04 ml (40µg) solution of sample in DMF and Amoxicillin, Benzoylpenicillin, Ciprofloxacin and erythromycin were used as a reference compound A1, A2, A3, A4, A5, A6, A7, A8, A9 and A10 have shown moderate activity. The Zone of inhibition of the bacterial growth were measured in millimeter and are recorded in table no 2.

RESULTS AND DISCUSSION

Novel synthesized hybrid molecules of fluorene and triazole with various aryl groups having yield between 57 to 69%. The structure of novel compounds are characterized and confirmed by 1H NMR, IR and Mass spectral data which are further supported by elemental analysis data. Novel compounds A1 to A10 were shown significant activities.

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