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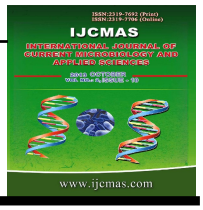

Original Research Article

PC-Model Computational Studies of 4', 6'-bis-(2, 4-dinitro-aniline)-(2'-aryl-amine)-S-triazine and Biological Activity Studies

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A B S T R A C T

Keywords

S-triazine; thiazoline;isoxazoline;Benzoxazine; Heterocyclic.

The aromatic, six membered ring containing three nitrogen atoms are known as triazines. Three triazines are theoretically possible, 1,3,5-triazine, 1,2,4-triazine and 1,2,3-triazine[1]. The 1,3,5-triazines are amongst the oldest known organic compounds. Originally they were called the symmetric triazines. Usuelly abbreviated to s- or sys triazines. The numbering follows the usual convention of beginning at the hetero atom as shown for the parent compound 1,3,5-triazine (I). The triazine rings, each contain 6 pi electrons which fill three bonding molecular orbital there are also three pairs of non bonding electrons in each molecule which are responsible for basic properties of the compounds.

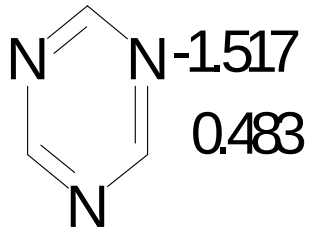
Introduction

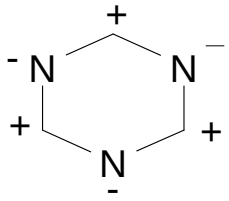
Heterocyclic compound exhibit wide range of biological activities. Quinoline derivatives are well known drugs for the treatment of malaria. Introduction of amino group in the ring of Quinoline found to be associated with a number of activities viz. antidepressant, hypoglycenic, gastric secretion inhibitory, antihaepedic, gastriculcer inhibitory, psychonnaleptic and also active against HIV-1 integrate sulindecand and indomethacin are the recent drugs used for the treatment of anti-inflammatory agents in therapy. Both are indole acitic acid derivatives acridine based antimalaraial and antibacterial compounds (Mcpacrine, azacrine, protlavine and aminocrine) are known 9-(Dimethyl amino propyl) animo-1 nitro acridine has been quite extensively used as antitumor drug in poland. Besides these heterocyclic compound posses various other activities like local anesthetic , antidiabetic diuretic Cardiovascular agents, antiviral,antiparkinsoman,african sleeping sickness, herbicides, anticonvulsant muscle relaxant, antineoplastics, antimicrobial, antihypertensive , antistamine, antispasmodic tranquillizers antiulcer etc. Retinoidse are a group of synthetic compounds designed to refine the numers biological activities of retinoic acid into pharmaceuticals for several diseases including cancer. These are

conformationally Restrocted the of the structures resulted in arotinoids, that were biologically active, but with increased toxicity. Incorporation of a heteroatom in one cyclic ring of the arotinoid structures drastically reduces the toxicity while retaining biological activity.

The reactivity of cyanuric chloride may be considered as a nitrogen analogue of an acid chloride. On account of low basicity of s- triazine nucleus as well as the ring nitrogen atoms in the alpha (Position) to the chlorine atoms in the triazine ring, cyanuric chloride is a very week base. In cyanuric chloride the ring nitrogen atoms of s-triazine nucleus greatly facilitate the substitution of chlorine atom by a basic group. For the reason, at $0^{o}C$ cyanuric chloride is readily susceptible to alcoholysis and ammonolysis as well as to hydrolysis. Here the course of substitution reaction is determined not only by the nucleophilicity of the basic reactant, but also by the electrophilic character of the s-triazine ring.

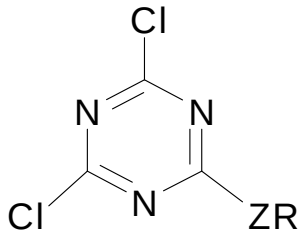
1,3,5-triazine continues the trend of decreasing aromaticity observed on going from pyridine to the diazines. The polarity of the C=N bonds increases as more pi electrons are partially located on the ring nitrogens, thereby decreasing delocalization energy. The charge distribution is shown below (v). The polar canonical form (VI) makes a major contribution to the structure These properties are reflected in the reactivity of 1, 3, 5- triazine towards nucleophiles.

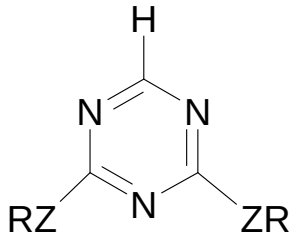




Banks (Wehner *et al.,* 2002; Tomoscikova *et al.,* 2008) brought to notice that these substitution reactions can be catalysed by acid, the more electrophilic triazonium ions (Mcculloch *et al*., 1980) infact are more reactive than the cyanuric chloride itself. An acid catalysis can also take place in aqueous medium provided that nucleophilic reactant does not prevent protonation of the triazine ring e.g. the self catalysed or the autoclaved hydrolysis of cyanuric chloride. For this reason, the reaction of cyanuric chloride, with alcohols and with aromatic amines in particular can be catalysed by acids.

The mechanism of the reaction of cyanuric chloride has been studied extensively and has been shown to vary with the reaction conditions (Aslantas Mehmet *et al*., 2008). Cyanuric chloride is insensitive to both acid catalysis and auto catalysis but the 2,4-dichloro (VII) and 2- chloro derivatives (VIII) exhibit both acid catalysis and autocatalysis on solvolysis in ethanol –acetone solutions.





Z = O, S, NH

Bitter and Zollinger (Cronstein and Kamen, 2007; Rodriguez *et al*., 2008) investigated the reaction of cynuric chloride with aniline in benzene and showed that it is catalysed by both acid and base. To prevent a possible catalysis in the substitution of chlorine atom in cynuric chloride by –OH; OCH_3- or OC_2H_5 group to give hydroxy or alkoxy dichloro-s-triazine, the reaction is best carried out in the presence of an acid binding medium preferably sodium bicarbonate.

Materials and Methods

Step I- Synthesis of 2-chloro 4',6'-bis-(2, 4 dinitro-aniline)-s-triazine

Cynuric chloride 9.3 gm was dissolved in acetone (50 ml) and cooled to 0^oC to it 2, 4-dinitro aniline (10 gms) was added at low temperature followed by sodium hydroxide (0.2 m) in water (25 ml) the temperature was raised to 45-50^oC further strirred for 2 hours poured into ice cooled water filtered and dried.

Step-II: Synthesis of 4', 6'-bis-(2, 4-dinitro-aniline)-(2'-aryl-amine)-s-triazine

2.95 gm of 2'-chloro-4',6'-bis-(2, 4-dinitro-aniline)-s-triazine was dissolved in 50 ml of dioxane to it 1.69 gm of selected amine and sodium hydroxide (0.1 mg, 25 ml of water) were added. The constants were refluxed on the water bath for 3 hours and poured into ice cooled water.

The separated compound was filtered, washed with water and dried, the amines were taken as o-toluidine, m- toluidine, p-toluidine and o-chloro aniline, m-chloro aniline, p-chloro aniline. The yields and melting points of the synthesized s-triazines are given in scheme-I. The molecular formulas of these compounds were calculated from their elemental analysis table.

The structures of s-triazines have been confirmed by elemental analysis IR and ^{1}H-NMR spectral data studies. These synthesized s-traizine compounds were screened for their antimicrobial anthelmintic and insecticidal properties and the results are presented.

Antimicrobial Studies

During the early part of this century tremendous efforts were made in the systemic treatment of certain microzoal infraction. Nevertheless these advances did not greatly effect directly the overall practice of medicine the subsequent profasion of antibacterial agents over whelmed the physician with golden tools.

The realization that certain microorganisms are successfully resisting the wonder drug "not only compounds ceaseless search for new systemic antibacterial agents but also forces a sobers return to certain ancillary art of the medical and surgical management of infectious diseases.

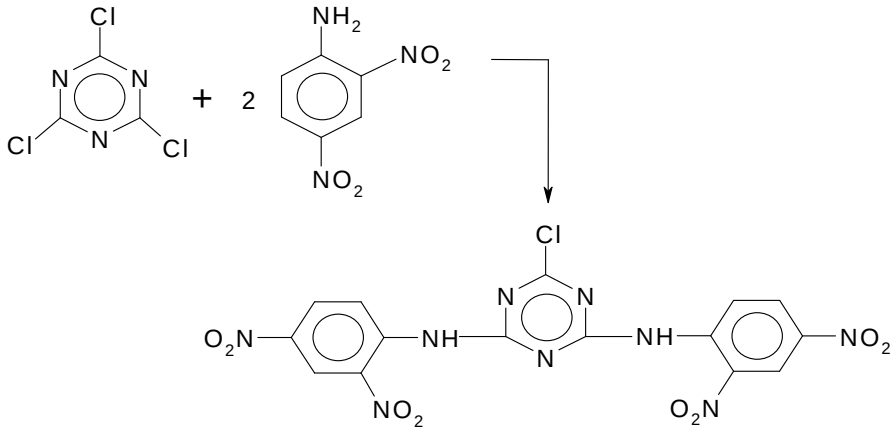
Antibacterial Activity

The sulphonamide drugs were the first effective chemotherapeutic agents to be employed systematically for prevention and cure of bacterial infection in mane sulphonamides have a wide range of antimicrobial activity agents bath gram positive and gram negative organism with after exceptions there is a direct correlation between their efficacy in vitro and vize. In general the sulphonamides extent only a bacteriostatic effect in the body cellular defense mechanisms of the infection on a weight basis sulphonamide as much less potent than clinically employed antibiotics. Antibiotics is a process in which one organisms may destroy anther to survivor itself it ideal antibacterial agent.

Antifungal Activity

Previously fungal infection was regarded as a rare disease now in recent years fungal infection have been common and know throughout the word many remedies have been used against fungal infections and research still continuous which recorded lead one to conclude that idea tropical antifungal agent has not yet been found the human disease caused by fungi are less important than bacterial or protozoal disease clinically infections are divided into two main groups.

Step I- Synthesis of 2-chloro 4',6'-bis-(2, 4 dinitro-aniline)-s-triazine



Step-II: Synthesis of 4', 6'-bis-(2, 4-dinitro-aniline)-(2'-aryl-amine)-s-triazine

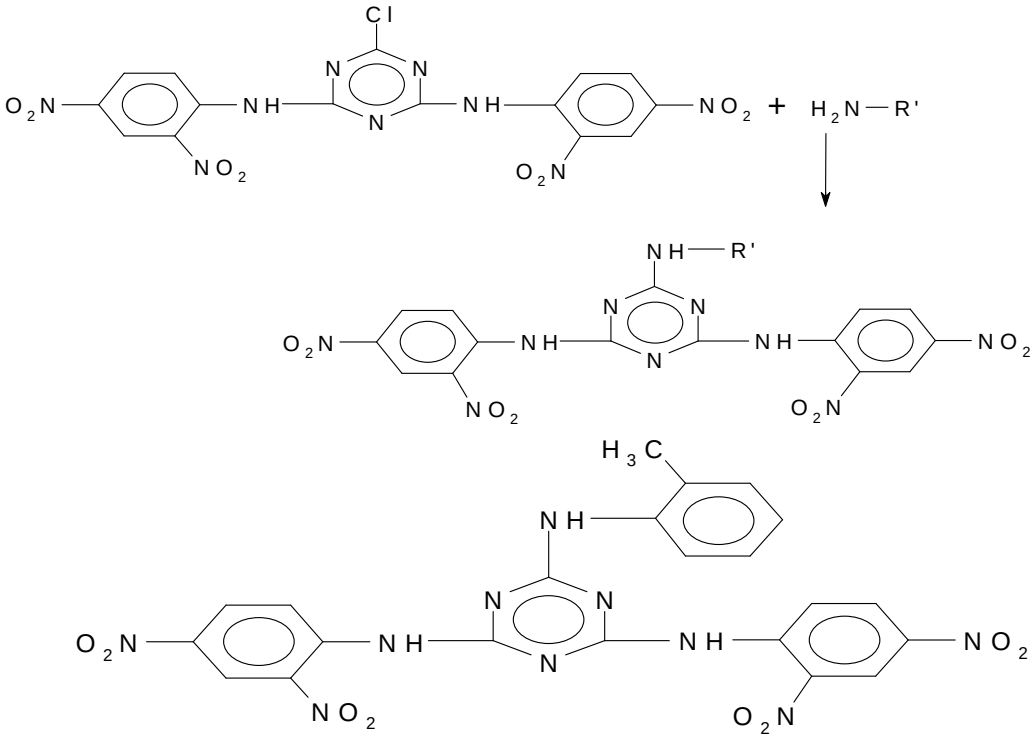


Table.1 Characterization data of compound

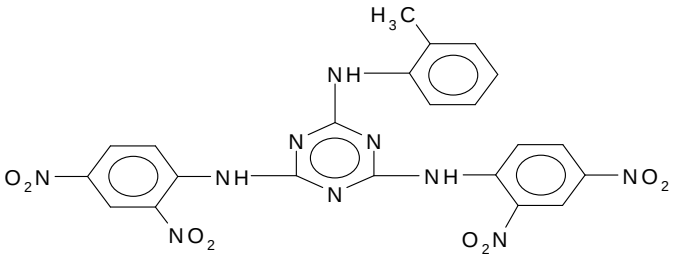
Name	4',6'-bis-(2, 4-dinitro aniline) -2'-(2-toluidine)–s-triazine					
MF	$C_{22}H_{16}N_{10}O_8$					
M.Wt	548					
MP (^oC)	245					
Yield	90 %		**H%**			
Elemental analysis	**C%**		Calculated		**N%**	
	Found	48.17	Found	Calculated	Found	Calculated
	47.88	48.17				

Table.2 IR Spectral data of compound

Type	Vibration mode	Frequency in cm^{-1}
s-triazine Ring	-C=N stretching	1560.84
	-C-N stretching	1410.41
Aromatic Ring	-C-H stretching	3014.84
	-C=C stretching	1600.49
	-C-H bending	1010.70
Secondary Amine	-N-H stretching	3363.38
	-N-H bending	1525.63
Alkyl Groups	C-H stretching	2848.96
	-C-H bending	1386.58
	-C-NO_2 stretching	1510.30

Table.3 NMR spectral data of compound

Signal No.	Signal position & ppm	Relative No of Protons	Multiplicity	Inference
1	2.58	3	S	-CH_3
2	8.08	1	S	-NH
3	8.93	2	S	-NH
4	7.12-7.81	12	M	-CH (Ar-H)

Table.4 PC-Model Computational Studies S-triazine Derivatives

III	Methyl	Molar volume	BC-343	BC 543	BL 754	BC 925	BA754	BA 975	BA 1297
Benz 1	2C-CH_3	367	1.407	1.371	1.363	1.305	125.45	122.94	120.66
Benz 2	3C-CH_3	366	1.407	1.371	1.364	1.305	125.50	122.93	120.57
Benz 3	4C-CH_3	366	1.406	1.371	1.364	1.305	126.10	122.49	120.49
Benz 4	Cl	molecule	BC 543	BC 543	BC 754	975 BA	754 BA	BA 975	BA 1297
Benz 5	2C-Cl	363	1.407	1.371	1.363	1.305	125.42	122.82	120.86
Benz 6	3C-Cl	361	1.407	1.372	1.364	1.306	125.22	122.48	120.7
Benz 7	4C-Cl	361	1.407	1.372	1.364	1.305	125.99	122.31	120.58
Benz 8	Cl	molecule	BC 543	BC 543	BC 754	975 BA	754 BA	BA 975	BA 1297

The compound have been subjected to PC model computer simulation. The details potential of PC- model (Version 3.01) have been discussed and detail in chapter two. The values for dipolmoment, vander wall forces, Molar volume and bond length and bond angle have been in corporated in there in table Chapter-III. The others of the opinion that the relatives eals or strain on the molecule is expected to appear in there PC Simulation data. the steric adjustment due to strain or is may change the values for parameters like dipolmoment Vander Wall forces and the partial molar volume where as the concomitant effect on the bond length bond angle and there dihedral angle may reflect the exhibit steric influence of different substations on the molecule A parusule of table in chapter three (both J.R NMR and PC model data) express that the methyl derivatives are more relax than there subsequent chloro derivatives where as the pera position are over all maximum following given table is a comparative account of the IR and ^{1}HNMR characterization values and the PC model data.

Results and Discussion

The possible substituents selected for the present derivative are 4',6'-bis-(chloro aniline)-2'-(2-toluidine)-s-triazine, 4',6'-bis-(chloro aniline)-2'-(3-toluidine)-s-triazine, 4',6'-bis- (chloro aniline)-2'-(4-toluidine)-s-triazine4', 6'-bis-(chloro-aniline)-2' -(2-chloro-aniline)-s-triazine, ',6'-bis-(chloro- aniline)-2'- (3-chloro-aniline) -s- triazine 4',6'-bis-(chloro-aniline)-2'-(4-chloro-aniline)-s- triazine - series two 4',6'-bis-(bromo-aniline)-2-(2-toluidine)-s-triazine, 4',6'-bis-(bromo-aniline)-2-(3-toluidine)-s-triazine, 4',6'-bis-(bromo- aniline)- 2-(4-toluidine)-s-triazine, 4',6'-bis-(bromo-aniline)-2'-(2-

chloro-aniline)-s-triazine, 4',6'-bis-(bromo-aniline)-2'-(3-chloro-aniline)-s-triazine, 4',6'-bis-(bromo-aniline)-2'-(4-chloro-aniline)-s-triazine series three 4',6'-bis-(2, 4-dinitro-aniline)-2'-(2-toluidine)-s-triazine, 4',6'-bis-(2, 4-dinitro-aniline)-2'-(3-toluidine)-s-triazine, 4',6'-bis-(2, 4-dinitro-aniline)-2'-(4-toluidine)-s-triazine, 4',6'-bis-(2, 4-dinitro-aniline)-2'-(2-chloro-aniline)-s-triazine, 4',6'-bis-(2, 4-dinitro-aniline)-2'-(3-chloro-aniline)-s-triazine, 4',6'-bis-(2, 4-dinitro-aniline)-2'-(4-chloro-aniline)-s-triazine which give rise to an all to Synthesis of eighteen s- triazines the literature survey as possible maximum as could indicate the nobelility of these compounds the synthesis processes is mainly. A substituents using electrophilic groups most of the synthesis have been carry out in three step where imphasis have been let on the final product. Through it is custmerly Advisable to very five and anlaysis the products ect. every

Table.5 Antibacterial activity of the synthesized compound (s–triazins and derivatives)

Compound Code	*E. Scherichia coli*		*Bucillus Subsniss*		*Staphyloi aures*		*Sligella*	
	2%	4%	2%	4%	2%	4%	2%	4%
Benz 1	++	+++	++	+++	++	+++	+	++
Benz 2	++	+++	++	+++	++	+++	+	++
Benz 3	+	+	+	+	-	+	-	+
Benz 4	+	++	+	++	+	++	-	+
Benz 5	++	++	-	+	+	++	-	+
Benz 6	+	++	-	+	-	+	-	+
Benz 7	++	+++	+	+++	++	+	+++	++
Benz 8	+	++	+++	++	+	++	+	+++

Std-= stremtomycin inhibition diameter in mm Highly active = +++ (inhibition zoes>15) moderatively active= ++ (inhibition zone 10-15) slightly active = + (inhibition 10) inactive inhibition zone -6)

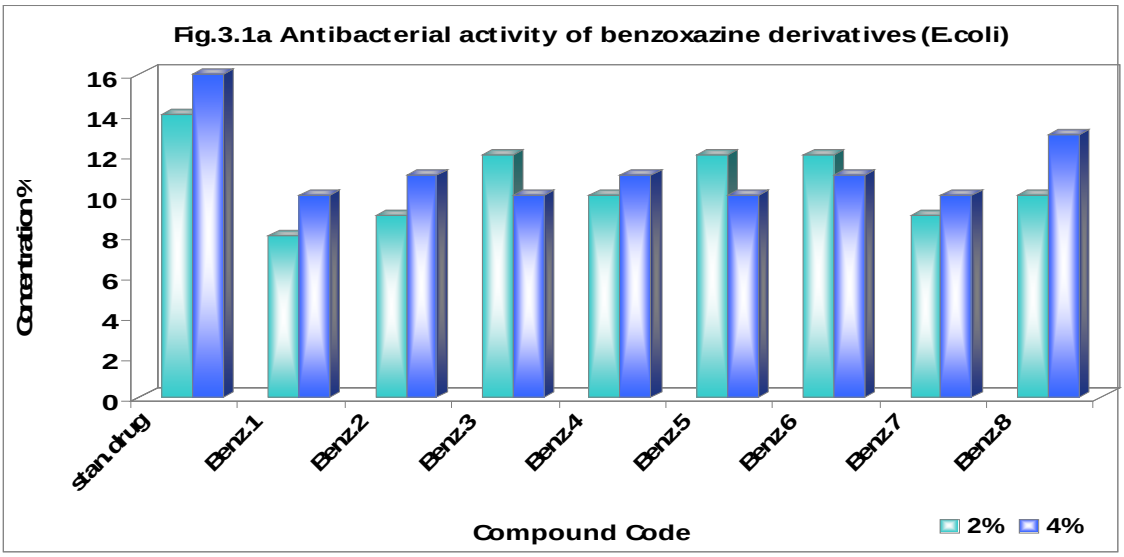


Table.6 Antifungal activity of the synthesized Heterocyclic compound (S-triazine and derivatives)

Compound code	*Aspergillus niger*		*Aspergillus Purasities*		*Tricroderm uridue*		*Chrysoporium Sps*	
	2%	4%	2%	4%	2%	4%	2%	4%
Benz 1	++	+++	++	++	++	+++	+	++
Benz 2	++	+++	+	+++	++	++	++	+++
Benz 3	-	+	-	++	-	+	+	++
Benz 4	++	+++	+	+++	++	+++	++	+++
Benz 5	++	+++	++	+++	++	+++	++	+++
Benz 6	++	+++	++	+++	++	-	++	+
Benz 7	++	+++	+	+++	++	++	++	+++
Benz 8	++	+	+++	++	++	+	+	++

Std- Exriseofulvin inhibition diameter in mm Highly active = +++ (inhibition zones>15) moderatively active= ++ (inhibition zone 10-15) slightly active = + {inhibition 10] Inactive = - (inhibition zone) Zone<-6) for bacteria

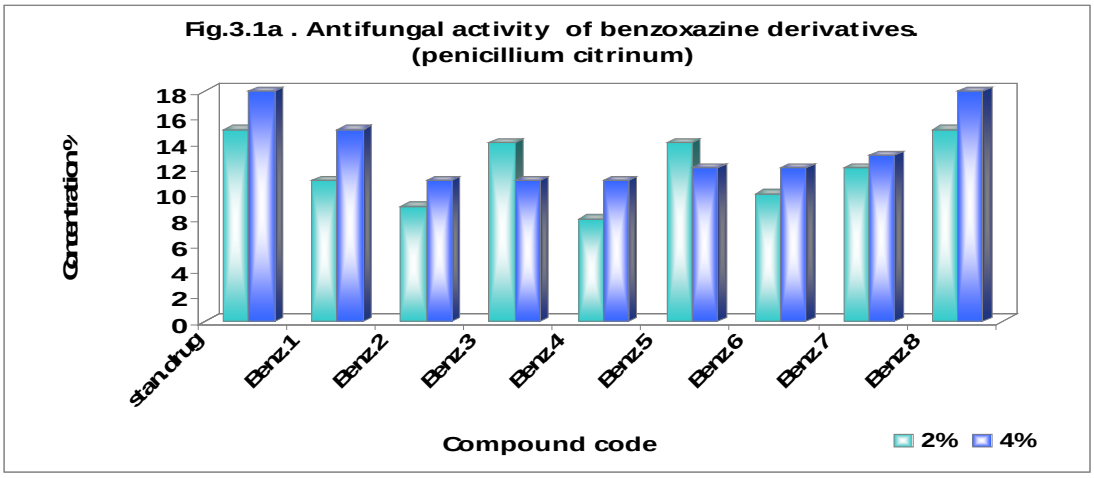


Table.7 Variation in the ^{1}H-NMR shift values for different substituted derivatives of series**.**

Compound Name	Signal Position in ppm	Relative No. of Protons	Multiplicity	Inference
Benz 1	8.08	1	S	-NH
Benz 2	8.93	2	S	-NH
Benz 3	7.12-8.10	12	M	-CH(Ar-H)
Benz 4	8.10	1	S	-NH
Benz 5	8.66	2	S	-NH
Benz 6	7.13-7.82	12	M	-CH(Ar-H)
Benz 7	8.11	1	S	-NH
Benz 8	8.69	2	S	-NH

step but the validity of final products have promenade to avoided the enter step analysis.

Acknowledgement

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References

Abd, M.E., and El- Pattah, 2006. Ind. J. Chem. 45B, 2523-2533.

Aslantas Mehmet, Kendi Engin, Ceylanunlusoy Mellem & Ertan Rahmiya, 2008. Analytical Sci. 23,113-114.

Barrows, W., 1954."Text Book of Microbiology" Sounders Worb… Co. London 16th Ed. 8 (1954).

Cronstein, B.N., and Kamen B.A. 2007. J. Pediat. Hepatol. Oncol. 29(12): 805-807,

De Cian, A., E. DeLemos, J. L. Mergny, M. P. Teulade- Fichou and D. Monchaud. 2007. "Highly Efficient G-Quadru- plex Recognition by Bisquinolinium Compounds," *J. American Chem. Soc.*129(7): 1856-1857.

Doria, F., M. Nadai, M. Folini, M. Di Antonio, L. Ger- mani, *et al.*, 2012. "Hybrid Ligand-Alkylating Agents Targeting Telomeric G-Quadruplex Structures," *Organ.Biomole. Chem.* 10(14):2798- 2806.

Halder, R., J. F. Riou, M. P. Teulade-Fichou, T. Frickey and J. Hartig. 2012. "Bisquinolinium Compounds Induce Quad- ruplex-Specific Transcriptome Changes in HeLa S3 Cell Lines," *BMC Res.Notes*, 5: 138.

Kagabu Shinzo, Aoki, E. and Ohno I., 2007. J. Pestic Sci. 32(2): 128-130.

Mcculloch, M.W., I.C. Medgett, M.J. Rand and Story D.F., Br. J. Pharmac. 69:397-407.

Müller, S., S. Kumari, R. Rodriguez and S. Balasubrama- nian, 2010. "Small-Molecule-Mediated G-Quadruplex Isolation from Human Cells," *Nature Chem.* 2(12): 1095-1098.

Prescatt, S.C., and Duna C.G. 1969. "Industrial microbiology" McGraw Hill Kogukosha, 3rd Ed. 519

Robert Bailey, W., and Scatt E.G. 1966. "Diagnostic Microbiology the C.V. Masby Co. Saint Louis 257.

Rodriguez, R., S. Müller, J. A. Yeoman, C. Trentesaux, J. F. Riou, *et al.*, 2008. "A Novel Small Molecule That Alters Shelterin Integrity and Triggers a DNA-Damage Re-sponse at Telomeres," J.American Chem. Soc. 130(47): 15758-15759..

Tomoscikova, J., J. Imrich, I. Danihel, S.K. Bohn and Klika, D. 2008. Molecules, 13:501-518.

Wehner, V.K., H.U. Stitz, W. Schimidt and Sciffge Dirk, 2002. U.S. Patent, 6:423,712,B1.