

Synthesis of some cationic chromoenoasymmetric cyanines: A study of their absorptiophotospectroscopic potentiality & antimicrobial susceptibility.

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Abstract

In recent past, the research strategies in modern perspective has resulted many. Polyenic cyanine dyes which envisaged excellent optical properties and antimicrobial properties such as they are key materials for optical information, display media, solar energy conversion systems, energy transfer and storage media, optical memory devices, laser technology and overall in photodynamic therapy for destroying the malignant tissues, where the effect is caused by generation of singlet oxygen by laser irradiation to photo sensitizer.

For the present purpose to report certain specific auxochromic chalcone derivatives and the quaternised salt of thioazoheteroaromatics were taken. Each pair was condensed catalytically under suitable condition furnishing quite a number of chromoenoasymmetric cyanines (CAC). These dyes were synthesized with a view to evaluate their absorptiophotospectroscopic potentialities & bacteriolytic susceptibilities caused by diversification in the nucleoaddivitive and the chain elongative functionalities in the dye molecules.

Conclusive findings in most of the cases were encouraging, supporting hyperbathochromism towards IR in absorptivity & photosensitivity. Their antimicrobial susceptibilities were also proven in different local as well as systemic infections.

Key words:- [CAC : chromoenoasymmetric cyanines, CABSS: chromoeno- β - styryl substituted styryl dyes, CABPS: chromoeno- β - phenyl substituted butadienyl dyes, absorptiophotospectroscopic potentiality, antimicrobial susceptibilities]

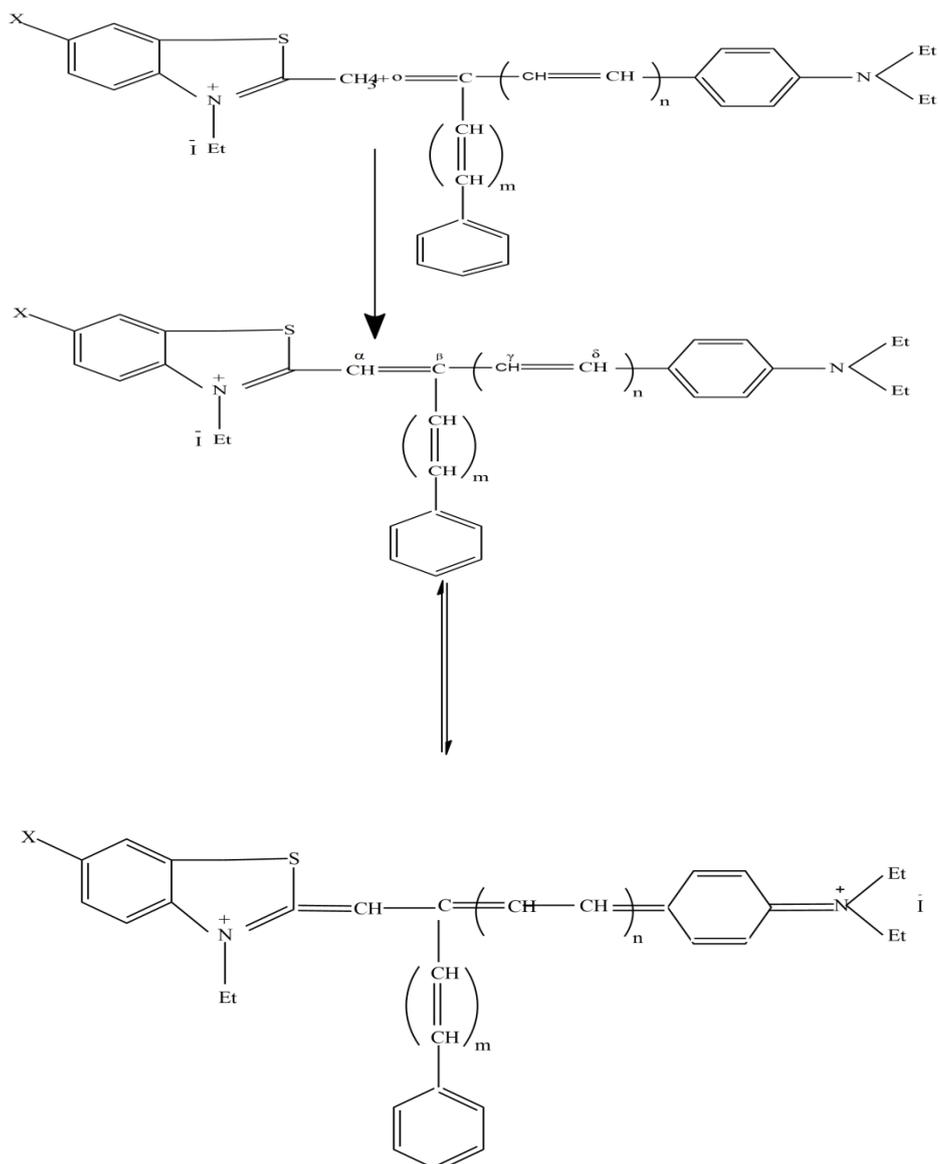
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I. Introduction:-

A number of chromophoric Chain Substituted hemicyanines utilising the quinolinic heteroaromatic system appears in the current literature¹⁻⁴. The synthesis of styryl cyanine dyes by the condensation of quaternised heterocyclic bases and various carbonyl compounds has been extensively reported and the dyes have also been studied with respect to their absorption spectra and photosensitization properties.³⁻⁶ The object of the present work is to synthesise Chromoenoasymmetric β - Styryl substituted (CABSS) styryl dyes and Chromoenoasymmetric β - phenyl substituted (CABPS) butadienyl dyes and to study the effect of such substitution as well as the effect of elongation of the conjugated chain of the dye molecules on the basis of optical properties by utilising benzothiazolylum salt as heteroaromatic system. For this purpose, two new isomeric chalcones, 4- diethylaminophenyl styryl ketone and 4- dimethylaminostyryl phenyl ketone were prepared and condensed with substituted benzothiazolylum ethiodide to give CABSS styryl and CABPS butadienyl cyanine dyes respectively as shown in scheme.1.

The visible absorption maxima of the CABPS styryl dyes and CASPS butadienyl dyes have been collated and analysed and comparison has been made with the corresponding chain B- substituted and chain unsubstituted analogue. The dyes were found to absorb at longer wavelength than the chain unsubstituted analogue and observed a uniform bathochromic shift which corroborates previous observations. Irrespective of the nature of β - substituents, the dyes carrying increasingly higher molecular weight substituent in the heterocyclic unit shows enhanced bathochromic shift in λ_{max} .



(Scheme- 1)

Dye	X	n	m	Dye	X	n	m
Cy ₁	H	0	1	Cy ₉	H	1	0
Cy ₂	Cl	0	1	Cy ₁₀	Cl	1	0
Cy ₃	Br	0	1	Cy ₁₁	Br	1	0
Cy ₄	I	0	1	Cy ₁₂	I	1	0
Cy ₅	Me	0	1	Cy ₁₃	Me	1	0
Cy ₆	OMe	0	1	Cy ₁₄	OMe	1	0
Cy ₇	OEt	0	1	Cy ₁₅	OEt	1	0
Cy ₈	5, 6 benzo	0	1	Cy ₁₆	5, 6 benzo	1	0

It has been reported that benzothiazole and certain specific chalcone derivatives possess a broad range of therapeutic activities, especially, antiseptic, analgesic, antisertoin, antimitotic, and anti microbial such as antiamoebic, antimalarial, anthelmintic, and antitubercular activities.⁷⁻⁹ A study of the clinical aspects of the newly prepared chromoenoasymmetric cyanines shows to have antimicrobial activity.

II. Results And Discussion

The absorption maxima and the sensitization data of the benzothiazolylum iodide salts are listed in Table 1. A comparative survey are listed in Table 2, the analytical data in Table 3 and the antimicrobial activity in Table 4. respectively.

2.1. Visible absorption spectra ;

A study of the absorption maxima of the CABSS Styryl dyes (Series -I) and CABPS butadienyl dyes (Series- II) and of previously reported β -unsubstituted dyes quoted from the literature leads to some interesting generalizations.

The chain β -phenyl substituents uniformly results in bathochromic shift in absorption maxima relative to their corresponding β - unsubstituted analogues irrespective of whether the β - phenyl group is replaced by β - styryl group. The bathochromic shifts are more pronounced with the β - phenyl styryl dyes and CABSS styryl dyes about (20-40 m μ) that CABPS butadienyl dyes about (2-20 m μ).

The conclusion that the close proximity of bulky substituents may lead to bathochromic shifts seems untenable when the absorption data of CABSS styryl dyes (Series-I) and CABPS styryl dyes (Series -3) are considered. If the steric crowding is operative in causing the bathochromic shift, then the CABSS Styryl dyes 2a which have less strain should absorb as shorter wavelength than the more strained β - phenyl substituted dyes 2b. The results are however the reverse of this. This is presumably due to increase in conjugation chain free from steric strain. Cross conjugation effect is likely to be more effective. The CABSS Styryl dyes absorb at longer wavelength than the corresponding β - phenyl substituted styryl dyes.

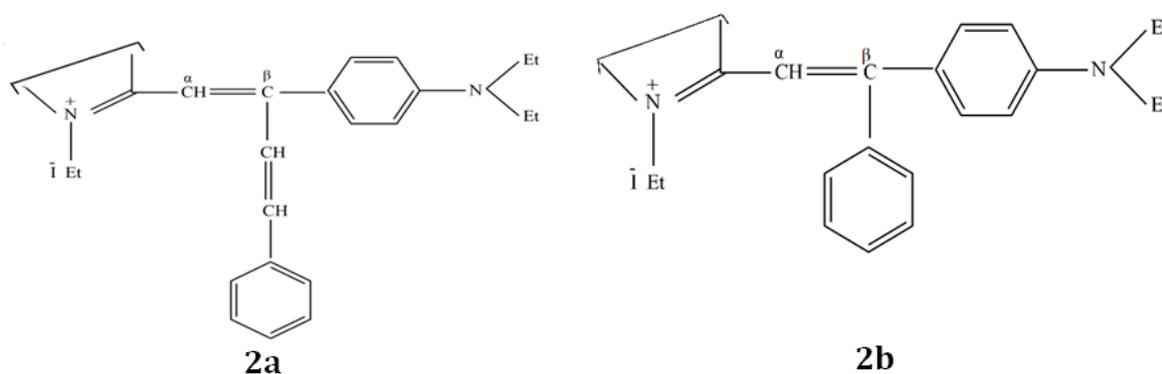
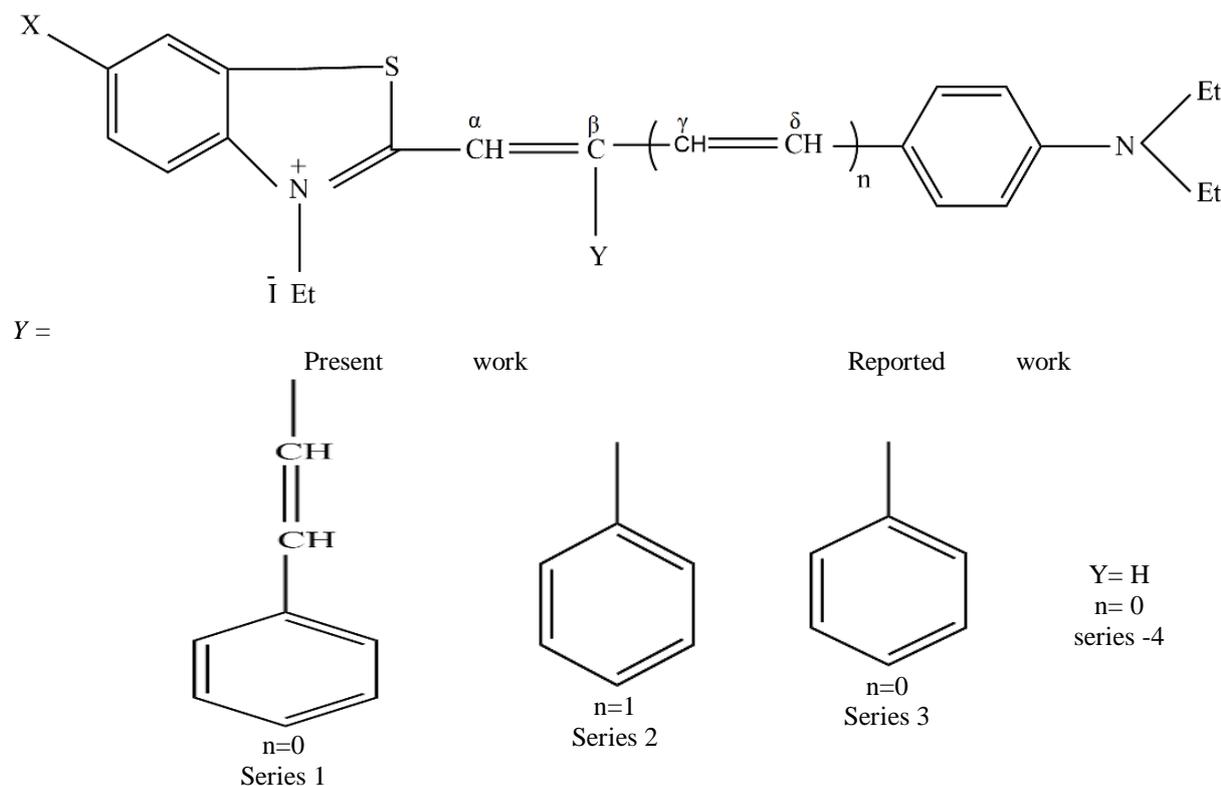


TABLE 1.

Absorption data of CABSS Styryl and CABPS Butadienyl (Etho Salt) in absolute ethanol.



X	Dye	λ_{max} m μ	Dye	λ_{max} m μ	λ_{max} m μ .	λ_{max} m μ .
H	Cy ₁	534	Cy ₉	500	530	496
Cl	Cy ₂	544	Cy ₁₀	522	538	502
Br	Cy ₃	546	Cy ₁₁	528	545	510
I	Cy ₄	552	Cy ₁₂	548	550	515
Me	Cy ₅	541	Cy ₁₃	482	515	-
OMe	Cy ₆	551	Cy ₁₄	496	531	-
OEt	Cy ₇	553	Cy ₁₅	501	535	-
5, 6 Benzo	Cy ₈	543	Cy ₁₆	533	-	-

TABLE:2.

Comparison of max. of the Butadienyl and Chain Unsubstituted styryl dyes (mu).

	H	Cl	Br	I	Ref,	
CABPS butadienyl dyes	500	522	528	548	Present work	
Chain substituted						Styryl dyes.
496	502	510	515			
Bathochromic shift		4	20	18	33	

TABLE 1.

Sensitization data of CABBS Styryl and CABPS Butadienyl dyes (Etho Salts)

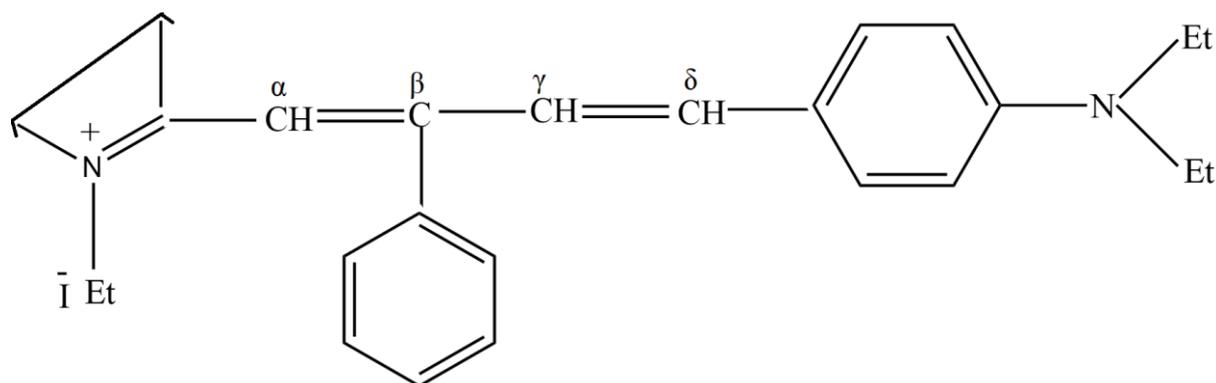
SERIES. 1			SERIES .2			
X	Dye	Range m μ	λ_{max} m μ	Dye	Range m μ	λ_{max} m μ
H	Cy ₁	590	530	Cy ₉	585	528
Cl	Cy ₂	553	553	Cy ₁₀	595	552
Br	Cy ₃	565	556	Cy ₁₁	600	558
I	Cy ₄	560	554	Cy ₁₂	620	578
Me	Cy ₅	560	550	Cy ₁₃	620	530
OMe	Cy ₆	565	549	Cy ₁₄	600	525
OEt	Cy ₇	560	551	Cy ₁₅	610	520
5,6 benzo	Cy ₈	565	555	Cy ₁₆	600	530

TABLE .2.

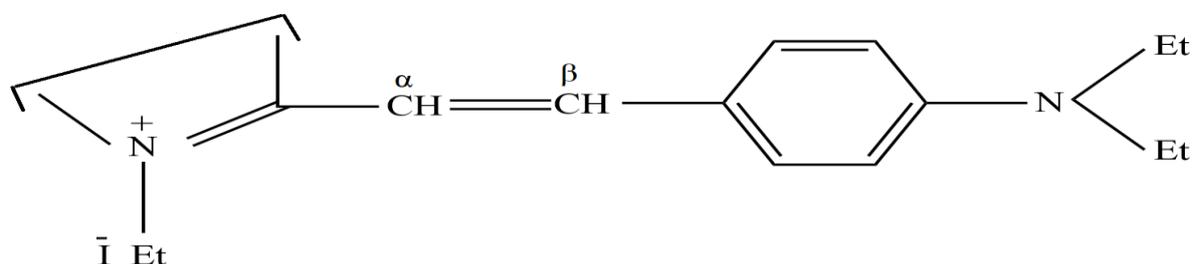
Relationship between Absorption and sensitization Maxima of CABSS styryl Dyes (mu)

Dye	Absorption λ_{max}	Sensitization λ_{max} .	Difference
Cy ₁	534	530	4
Cy ₂	544	553	-9
Cy ₃	546	556	-10
Cy ₄	552	554	-2
Cy ₅	541	500	9
Cy ₆	551	549	2

The CABPS butadienyl dyes 2c differs from the 4- diethyl aminostyryl dyes 2d in two ways, they have a longer conjugated chain and also a chromophoric chain β - phenyl substituent. However the CABPS butadienyl dyes 2c differ from the β -phenyl substituted styryl dyes 2b only in the increased length of the conjugated chain, the phenyl group being attached to the identical carbon atom of the chromophoric chain, but the steric effect of the β - substituent in the butadienyl dyes 2c is not likely to be the same as that of the same substituent in the β -phenyl substituted styryl dyes 2b. The two phenyl groups are directly linked to the sp²carbon atom in the dyes 2b, whilst in the dye 2c one of the phenyl group is 2 c atom away. The dye 2b due to bulky phenyl group adjacent to the diethylaminobenzene nucleus, may suffers an out of plane twisting such an influence is absent in the dye 2c. Further the dye 2c may also be expected to have added resonance stabilization due to additional π orbital interaction between the N atoms involved in the resonance. The data obtained confirms established results.

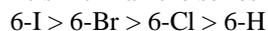


2c



2d

In the heterocyclic moiety, the influence of the 6- substituents in λ_{\max} although small, is consistent and systematic for the series. Thus progressive increase in the molecular weight of the substituent cause progressive bathochromic shift in all the series reported. The sequence being generally of the order.



And $6\text{-OEt} > 6\text{-OMe} > 6\text{-Me} > 6\text{-H}$

2.2 Photosensitization:-

A study of the sensitization data does not permit any definite generalization to be made. CABPS buthadienyl dyes (Series-2) are superior sensitizers to CABSS styryl dyes. In the series Cy_{11,12,13,15} extra high sensitization λ_{\max} having shifted toward the longer wave length by 0.160 μ . Presumably the lengthening of the conjugated chain between the two N atoms is responsible for such enhancement in spectral sensitization. There is little possibility of steric hindrance to the planarity of the resonating system and consequently the delocalization of π molecular orbital is not hindered. Cross conjugation effect in the molecule is relevant upon resonance stability and electronic transition. Data supports this.

III. Experimental

3.1. The Chalcones-

(i). 4- Diethylaminophenyl styryl ketone (Chalcone)

The general procedure for the synthesis of ketones described by Shah et al¹¹ was adopted with suitable modifications. The chalcone obtained was recrystallised from ethanol- benzene (3:1) in small fibrous yellow crystals. Yield 40% ; m.p. 170-172^oC.

Found : C 71.4% ; H= 11.6% ; N, 7.2% ; C₁₉ H₂₁ O require C, 71.5% ; H, 11.7% ; N, 7.3% IR Spectra V_{\max} (Cm⁻¹) 1165 (C-N-C); 1310 (CH=CH); 1590 (C=C); 1740(C=O).

(ii). 4- Diethylaminostyryl phenyl ketone (Chalcone)

This compound was prepared by following the procedure of Jha et al by refluxing 4-dimethylaminobenzaldehyde and acetophenone in the presence of sodium acetate afforded the chalcone, which was recrystallized from aqueous ethanol as glistening yellow leaflets; Yield 72%, m. p. 110^oc.

Found : C 71.35% ; H= 11.55% ; N, 7.25% ; C₁₉ H₂₁ O require C, 71.5% ; H, 11.7% ; N, 7.3% IR Spectra V_{\max} (Cm⁻¹) 1160 (C-N-C); 1310 (CH=CH); 1590 (C=C); 1690(C=O).

3.2. The substituted benzothiazolylium ethiodides;

The quaternised benzothiazolylium ethiodide salts were obtained by method of Jacobson.¹⁰

3.3 The styryl and butadienyl dyes-

Condensations to form the dyes were affected by reported method. A solution of the chalcone and the quaternary salt (1:1) molar in absolute ethanol, together with a few drops of piperidine, was refluxed for about 2h. The dye, which separated on cooling, was purified by crystallization from methanol. Analytical data, yield, m. p. (uncorrected) and other characteristics of the dyes are summarized in Table.3

TABLE.3.
Analytical data CABSS Styryl and CABPS Butadienyl Dyes

Dye	Yield 0%	M. P.	Molecular Formula	Found		Calc.%	
				N	Hal	N	Hal
Cy ₁	61	190	C ₂₉ H ₃₁ IN ₂	5.2	23.6	5.24	23.75
Cy ₂	67.8	215	C ₂₉ H ₃₀ ClIN ₂	4.8	28.0	4.92	28.55
Cy ₃	68.9	230	C ₂₉ H ₃₀ BrIN ₂	4.4	33.6	4.56	33.73
Cy ₄	70	255	C ₂₉ H ₃₀ I ₂ N ₂	4.1	38.2	4.24	38.45
Cy ₅	58	235	C ₂₉ H ₃₃ I ₂ N ₂	5.0	23.0	5.10	23.15
Cy ₆	68	215	C ₂₉ H ₃₃ I ₂ N ₂ O	4.8	22.3	4.96	22.49
Cy ₇	75	195	C ₃₀ H ₃₅ I ₂ N ₂ O	4.5	22.0	4.85	22.02
Cy ₈	85	192	C ₃₃ H ₃₃ I ₂ N ₂	4.4	21.6	4.79	21.72
Cy ₉	77.5	218	C ₂₉ H ₃₁ I ₂ N ₂	5.1	23.4	5.24	23.75
Cy ₁₀	62	262	C ₂₉ H ₃₀ ClI ₂ N ₂	4.5	27.8	4.92	28.55
Cy ₁₁	71	242	C ₂₉ H ₃₀ BrI ₂ N ₂	4.2	33.2	4.56	33.73
Cy ₁₂	80.4	230	C ₂₉ H ₃₀ I ₂ N ₂	3.9	38.0	4.24	38.45
Cy ₁₃	74	252	C ₂₀ H ₃₃ I ₂ N ₂	4.9	22.9	5.10	23.15
Cy ₁₄	72	256	C ₃₀ H ₃₃ I ₂ N ₂ O	4.5	22.0	4.85	22.02
Cy ₁₅	69	262	C ₃₀ H ₃₅ I ₂ N ₂ O	4.4	21.5	4.79	21.72
Cy ₁₆	73	249	C ₃₃ H ₃₃ I ₂ N ₂	4.5	21.2	4.79	21.72

3.4. Absorption and photo sensitization on spectra :

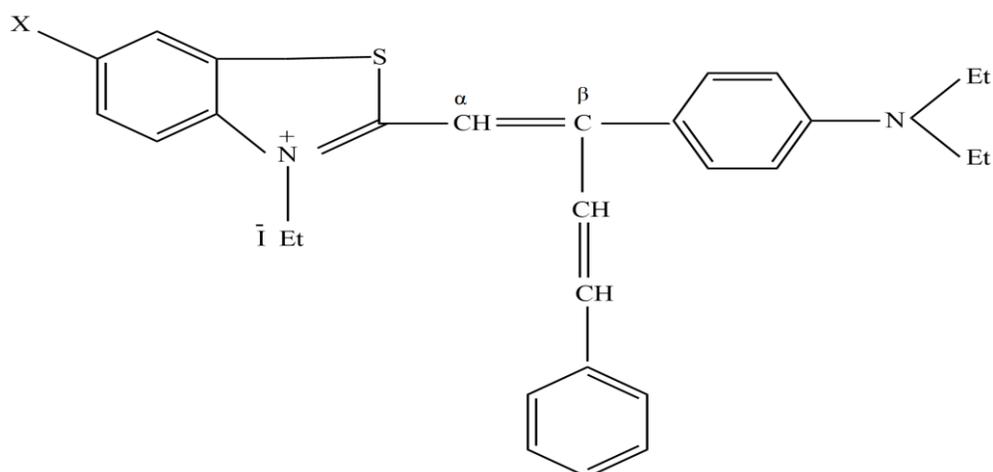
Absorption maxima were recorded on a Beckmann spectrometer, model DU, and photosensitization on an Adam Hilger wedge spectrography.

3.4. Antimicrobial activity:

The compounds were screened for their antimicrobial activities by standard method¹² at concentration level 4 mg mol⁻¹ in DMF and the results are given in Table 1. Almost all the compounds showed promising antibacterial activity, presumably the heteroaryl benzothiazole moiety is responsible for remarkable antimicrobial activity due to the presence of S atom in hetero moiety. Further the halogen derivatives Cy₂-Cy₄ and Cy₁₀-Cy₁₂ of CCBPS butadienyl CABPS styryl compounds were found to be highly active against S. aureus and E. coli, B. subtilis and C. albicans. Thus the halogen substituted compounds exhibits more pronounced antibacterial activity than the other derivatives studied. The average range of activities were found to be less as compared to antibiotics like tetracyclines, chloramphenicol, sulpha drugs glutamycin etc.

TABLE .4(a)

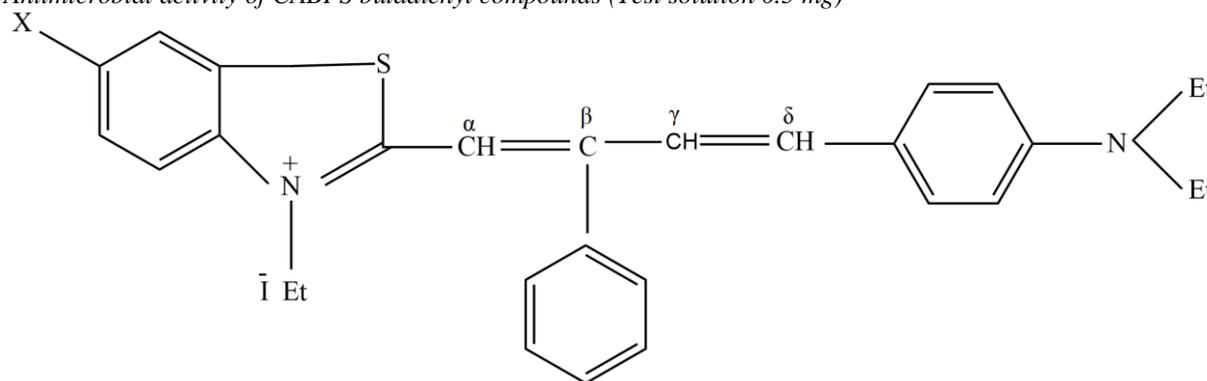
Antimicrobial activity of CABBS Styryl compounds (Test solution 0.5 mg)



X	Dye	Diameter of inhibitory zone(nm)			
		S aureus 24h	E.coli 24h	C. amblicans 24h	B. subtilis 24h
H	Cy ₁	32	26	29	27
Cl	Cy ₂	42	36	38	34
Br	Cy ₃	42	34	36	33
I	Cy ₄	38	31	35	34
Me	Cy ₅	25	20	23	22
OMe	Cy ₆	30	25	27	23
OEt	Cy ₇	28	24	26	24
5,6 benzo	Cy ₈	17	12	15	13

TABLE .4(b)

Antimicrobial activity of CABPS butadienyl compounds (Test solution 0.5 mg)



X	Dye	Diameter of inhibitory zone(nm)			
		S aureus 24h	E.coli 24h	C. amblicans 24h	B. subtilis 24h
H	Cy ₉	36	30	33	35
Cl	Cy ₁₀	47	38	43	46
Br	Cy ₁₁	47	37	42	44
I	Cy ₁₂	42	35	37	39
Me	Cy ₁₃	32	24	27	29
OMe	Cy ₁₄	35	29	31	34
OEt	Cy ₁₅	34	28	30	32
5,6 benzo	Cy ₁₆	24	18	21	23

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