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SYNTHESIS, ANTIMICROBIAL ACTIVITY ALONG WITH COMPUTATIONAL STUDIES OF SOME AZO MOIETIES

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ABSTRACT

Novel azo moieties were synthesized and confirmed by technical characterization. Antimicrobial screening activity was done by the moieties 1and 2 with respective strains. Theoretical calculations like HOMO – LUMO, MEP, and Mulliken populations were done by DFT using B3LYP/6-31G (d,p) basis set.

Keywords:FT-IR, NMR, Antimicrobial, HOMO-LUMO, MEP, Mulliken.

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This manuscript is focusing **SDG-3:** GOOD Health and Well Being

INTRODUCTION

Azomethine is a suitable moiety having potential application equally for inorganic and organic chemistry. The C=N connection is essential for genetic activity, numerous azomethines have been predictable to own significant antibacterial, antifungal, anticancer and antiviral, antimalarial activities.[1-4] Double bonds in the nitrogen-to-nitrogen act as a chromophore for Azo dyes.[5-7]Azo dyes are strong brilliant colors, in exacting oranges, reds, and yellows, and exhibit a range of interesting biological behavior. The medical consequences of these moieties are well-identified for their antibiotic, antifungal, and anti-HIV properties.[8-10] Schiff bases contain not just antimicrobial or antifungal activity but also chemical sensors for the discovery of metal ions.[11-13] A Schiff base was scrutinized by molecular imitation methods and molecular docking. The pharmacological conduct of bases shows potential against tested bacterial strains. DPPH free of charge and H_2O_2 scavenging assays were working to assess the antioxidant ability of synthesized Schiff bases.[14-17]Azo dyes were synthesized and identified using the analyses of Ultraviolet-Visible, IR analyses, and NMR spectroscopies. The experimental data of DFT calculations are included in supplementary data. The DFT calculations were executed to reach the inferior state geometries of the compounds by the B3LYP hybrid practical level with a 6-31^{++} G (2d,2p) set.[18-20] The estimations have proceeded with HOMO, LUMO, and Mullikan atomic charges.[21-27]

EXPERIMENTAL

Synthetic Route of Azo Moieties (1 and 2)

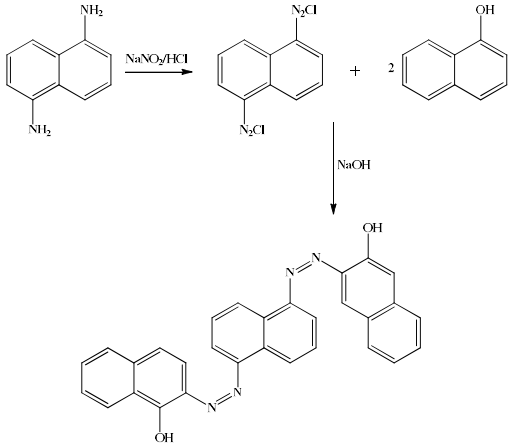
Azo ligand was ready by the precursor of *p*-cresol, β-naphthol, and sodium nitrite was reduced with 1,5-Diaminonaphthalene (2:1) molar percentage. The ligand produced was refined by chromatography technique. The TLC affirms the purity of the ligand (Scheme-1 and 2).

Measurements

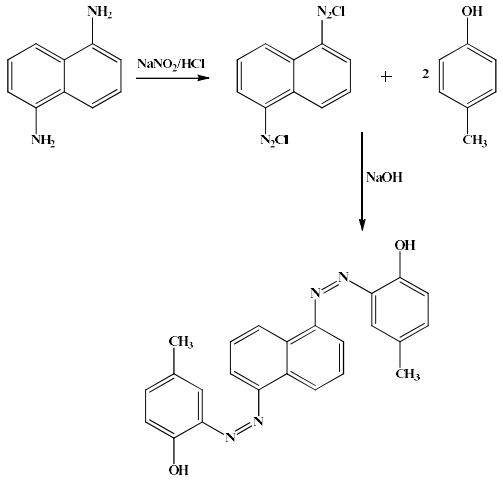
The synthesized ligand was analyzed by IR (PERKIN ELME, KBr discs) in the range of 4000-400 cm^{-1}. ^{1}H, and ^{13}C NMR spectra at 400 MHz, respectively, were existing at least temperature employed with Bruker 400 MHz NMR spectrometer (Bruker biospin, California, USA).

Computational Details

The hypothetical calculation analysis was by the Gaussian 03 package.[28] Computations of HOMO, LUMO, MEP, and Mulliken population of azo moieties were intended by the DFT method in the B3LYP/ 6-31G (d,p) level.



Scheme-1: Synthetic Route of 2-((Z)-(5-((Z)-(3-hydroxynaphthalen-2-yl)diazenyl)naphthalen-1-yl)diazenyl)naphthalen-1-ol



Scheme-2: Synthetic Route of 2,2'-((1Z,1'Z)-naphthalene-1,5-diylbis(diazene-2,1-diyl))bis(4-methylphenol)

Antimicrobial Studies[29,30]

Antibacterial

The following strains have been utilized for antibacterial screening activity like *Klebsiella pneumonia, Escherichia coli,Bacillus cereus, Pseudomonas aeruginosa,*and *Staphylococcus aureus* strains.

Antifungal

The following fungal strains are used for antifungal screening activity like *TrichodermaViride, Clodosorium, Candida albicans, Aspergillus flavus,*and *Aspergillus niger* strains.

RESULTS AND DISCUSSION

Spectral Analysis

FT-IR ranges of moiety 1the hydroxyl (-OH) stretch frequency is 3435 cm^{-1} the length of with N=N stretch frequencies were examined in the area of 1599 cm^{-1}. The C-N and C-H stretching frequency were studied at 1211 and 1900 cm^{-1}. Aromatic C=C stretching frequency at 3057 cm^{-1}.In moiety 2the -OH stretching incidence is 3433 cm^{-1} with N=N stretching incidence explored in the area of 1589 cm^{-1}. The C-N and C-H stretching frequencies were analyzed at 1271 and 1942 cm^{-1}. Aromatic C=C stretching frequency at 3062 $cm^{-1}$was observed.

2-((Z)-(5-((Z)-(3-hydroxy naphthalene-2-yl)diazenyl)naphthalen-1-yl)diazenyl) naphthalen-1-ol (1)
^{1}H NMR spectrumof 2-((Z)-(5-((Z)-(3-hydroxynaphthalen-2-yl)diazenyl) naphthalen-1-yl)diazenyl)naphthalen-1-ol the phenyl group doublets at 7.61 (t, J = 8.0 Hz, 6H), 7.94 (dd, J = 8.8 Hz, 4H) and 8.08 (dd, J = 9.0 Hz, 4H), 8.24 (d, J = 8.0 Hz, 2H), 8.46 (d, J = 9.8 Hz, 4H) protons, respectively. A sharp singlet at δ 10.93 ppm is the presence of two hydroxyls (-OH) group protons. ^{13}C NMR spectrum of ligand, the signal observed at 151.30 ppm is assigned to nitrogen substituted C-3,10 carbons. The aromatic carbon signals are observed in the area of 115.08 -151.30 ppm. The hydroxyl substituted C-27 and C-20 carbons signals are noticed at 145.76 ppm, calculated m/z 468.51.

2,2'-((1Z,1'Z)-naphthalene-1,5-diylbis(diazene-2,1-diyl))bis(4-methylphenol) (2)
^{1}HNMRspectrum of 2,2'-((1Z,1'Z)-naphthalene-1,5-diylbis(diazene-2,1-diyl))bis(4-methylphenol)the phenyl group doublets at 6.61 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 8.6 Hz, 1H), 7.26 (s, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.51 (d, 1H), 7.58 – 7.66 (m, 4H), 8.72 (d, J = 8.0 Hz, 2H). A sharp singlet at δ8.39ppm is the presence of two hydroxyls (-OH) group protons. A sharp singlet at δ2.96ppm is the presence of (-CH_3) group protons. ^{13}C NMR spectrum of ligand, the signal observed at 21.54, 100.86, 102.13, 109.44, 112.10, 120.76, 122.86, 123.09, 124.02, 124.48, 125.41, 126.21, 127.10, 128.26, 128.44, 128.63, 130.81, 135.12, 135.42, 139.91, 150.67, 151.13 ppm, calculated m/z 396.16.

Antimicrobial Activities
The preliminary antimicrobial activity of moieties 1-2is scrutinized using the disc diffusion method. DMSO is utilized as a control. Ciprofloxacin as well as Flucazonalare were employed as a standard for microbial studies.The antibacterial screening survey denotes that the compound having 1 and 2 revealed tremendous antibacterial activity against all the strains (Fig.-1). The results are tabulated in Table-1. The antifungal screening activity examines to affirm that the 1 exhibits excellent activity against *Trichoderma Viride*and, *Clodosorium.* Compound 2 shows better activity against *Aspergillus flavus, and Aspergillus niger,*and all other strains are less active against compounds 1 and 2(Fig.-2). The result is given in Table-2.

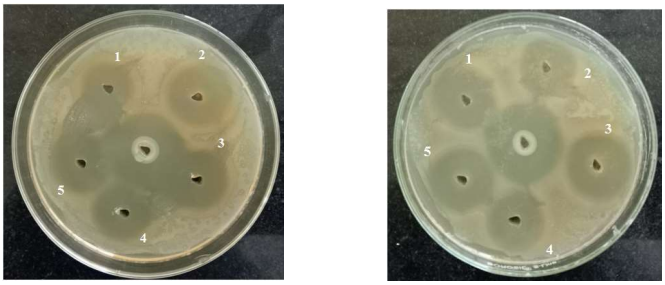


Fig.-1: Zone of Inhibition of Moieties 1 and 2Against Antibacterial Strains

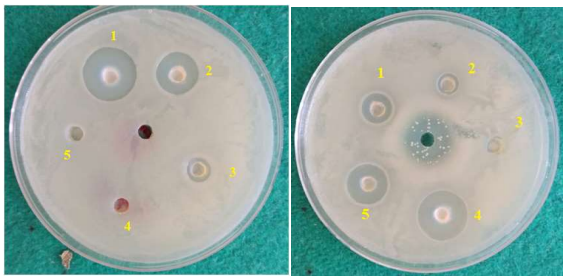


Fig.-2: Zone of Inhibition of Moieties 1, 2 Against Antifungal

Table-1: Antibacterial Activity of Compounds (1-2)

S. No.	Bacteria	Zone of inhibition mm in diameter	
		1	2
1.	*Klebsiella pneumonia*	17	19
2.	*Escherichia coli*	18	20

3.	*Bacillus cereus*	21	18
4.	*Pseudomonas aeruginosa*	19	17
5.	*Staphylococcus aureus*	20	20

**Ciprofloxacin*

Table-2:Antifungal Activities of Compounds (1-2)

S. No.	Fungi	Zone of inhibition mm in diameter	
		1	2
1.	*Trichoderma Viride*	18	10
2.	*Clodosorium*	16	05
3.	*Candida albicans*	06	01
4.	*Aspergillus flavus*	01	20
5.	*Aspergillus niger*	02	18

**Flucazonal*

Frontier Molecular Orbital

The electron thickness of FMO for (Fig.-3) composite 1 & 2 contributesto the complete particle apart from the equivalent vigor tabulated (Table-3). HOMO molecular orbital diagram of parallel molecule demonstrates that the bonding scenery is supplementary in the aryl loop while the anti-bonding nature is additional in the LUMO.

Table-3: FMO Value of Azo Moieties (1 and 2)

Compounds	HOMO (eV)	LUMO (eV)	Eg values
1	-3.9266	-2.2503	-1.6763
2	-3.5943	-2.3438	-1.2505

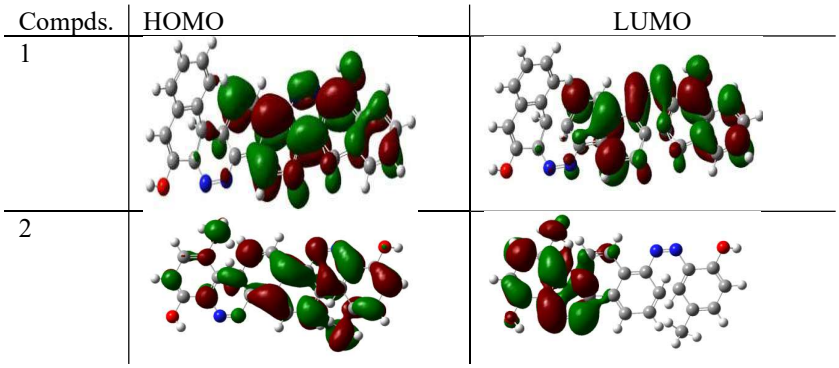


Fig.-3: HOMO-LUMO Orbital Illustration of Compounds 1 & 2

Molecular Electrostatic Potential

The MEP for compounds1 and 2is shown below. The MEP (Fig.-4) map obviously suggests that N and O atoms stand for the offset region (dark red) but the N atom suggests the use of moderately tiny negative potential in comparison with O. The H atoms stand for the greater impact of positive charge (blue region). In MEP surfaces, the green area majority indicates a potential intermediate amidst the two optimum red and dark blue. Nearby assessment of various plots, it is simple to assume how the switch of the H atom by substituent alters the photophysical nature of the ligand.

Mulliken Charge Analysis

Mulliken[31-33] populations give the simplest representation of the charge distribution. Charge mass purpose can lead to various significant characteristics of the moieties like the charges on the different atoms (Fig.-5). The Mulliken charges for the without hydrogen atoms of the ligand were determined at B3LYP/6-31G (d, P) set. The atomic charges illustrate that nitrogen and oxygen atoms contain better negative atomic charges compared to carbon. This performance can be the outcome of intramolecular N − HO hydrogen bond and double bond features (Table-4 and 5).

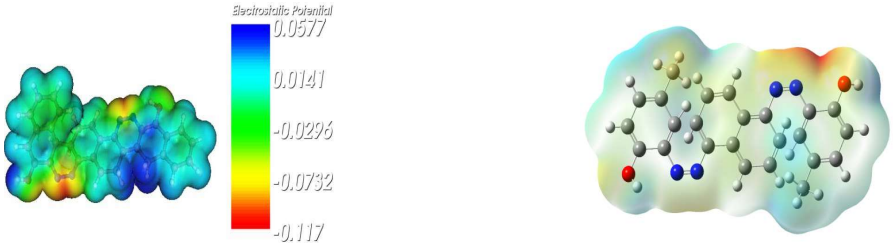


Fig.-4: MEP Picture for Compounds 1 & 2

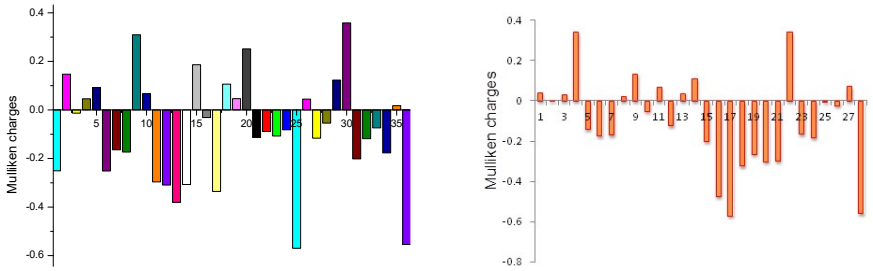


Fig.-5:MullikanCharge Allotment for Compounds1 & 2

Table-4: Mulliken Charges (q) in the Non-Hydrogen Atoms of Ligand Calculated with B3LYP/6-31G (d,P) set
Compound 1

S. No.	Atoms	DFT (q)	S. No.	Atoms	DFT (q)
1	C	-0.250541	19	C	0.046637
2	C	0.147233	20	C	0.251219
3	C	-0.013170	21	C	-0.113270
4	C	0.045891	22	C	-0.088775
5	C	0.092451	23	C	-0.107251
6	C	-0.251317	24	C	-0.081777
7	C	-0.163936	25	O	-0.569760
8	C	-0.173149	26	C	0.044689
9	C	0.309641	27	C	-0.116149
10	C	0.067113	28	C	-0.054328
11	N	-0.296158	29	C	0.123168
12	N	-0.309188	30	C	0.358482
13	N	-0.380820	31	C	-0.201604
14	N	-0.306994	32	C	-0.118190
15	C	0.186275	33	C	-0.074004
16	C	-0.031182	34	C	-0.176724
17	C	-0.335644	35	C	0.017744
18	C	0.106135	36	O	-0.554052

Table-5: Mulliken Charges (q) in the Non-Hydrogen Atoms of Ligand Calculated with B3LYP/6-31G (d,P) Set
Compound 2

S. No.	Atoms	DFT (q)	S. No.	Atoms	DFT (q)
1	C	0.039861	16	C	-0.201323
2	C	0.002616	17	C	-0.475476
3	C	0.032729	18	O	-0.570766
4	C	0.340384	19	N	-0.324131
5	C	-0.141010	20	N	-0.265322
6	C	-0.174716	21	N	-0.301965
7	C	-0.169846	22	N	-0.298933
8	C	0.021218	23	C	0.340838
9	C	0.133342	24	C	-0.165020
10	C	-0.051074	25	C	-0.182942
11	C	0.068797	26	C	-0.002353

12	C	-0.123550	27	C	-0.023031
13	C	0.036803	28	C	0.070930
14	C	0.111251	29	O	-0.560883
15	C	-0.263278	30	C	-0.454333

CONCLUSION

Antibacterial screening activity of moieties 1 and 2 showed tremendous against all the strains. The antifungal activity screening survey affirmed that the 1 showed outstanding activity against *Trichoderma Viride*and, *Clodosorium.* Compound 2 shows better activity in the case of*Aspergillus flavus and Aspergillus niger*.HOMO orbital diagram of matching particle exemplifies that the bonding scenery is extra in the aryl ring while anti-bonding scenery is supplementary in the LUMO. The MEP diagram N and O atoms stand for the downbeat region (dark red) but the N atom seems to use moderately tiny negative potential in comparison with O. The H atoms stand for the superior impact of positive charge (blue region). Mullikan populations showthe simplest representation of the charge distribution.The atomic charges illustrate that nitrogen and oxygen atoms contain better negative atomic charges compared to carbon.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript, participated in reviewing/editing, and approved the final draft for publication.The research profile of the authors can be verified from their ORCID ids, given below:

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