Formation of boron-based Metal Complex via Sonochemistry approach and Its Insilco study

Arun Tomar[1*], Dr. Rajeev Rathore[2]

[1*] Research scholar, Department of Chemistry, Meerut college, Western Kutchery Rd, Lalkurti Bazaar, Begambagh, Meerut, Uttar Pradesh, India 250003
[2]Guide, Department of Chemistry, Meerut college, Western Kutchery Rd, Lalkurti Bazaar, Begambagh, Meerut, Uttar Pradesh, India 250003

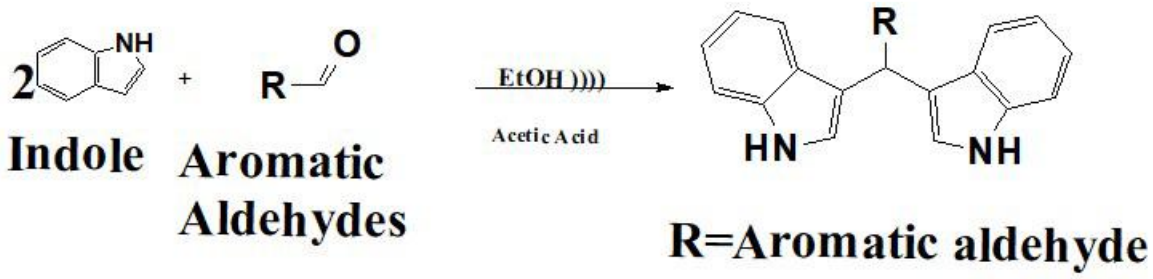
Abstract
A series of novel BODIPY–boron complexes were efficiently synthesized via a sonochemistry-assisted multicomponent reaction of indole and substituted aromatic aldehydes under green conditions. The ultrasonic irradiation protocol enabled rapid complex formation in short reaction times, minimizing solvent usage and energy input, while aligning with the principles of sustainable chemistry. This sono-assisted strategy offers an environmentally benign and time-efficient alternative to conventional synthetic methods for BODIPY-type boron complexes.
The structures of the synthesized complexes were unequivocally confirmed using a comprehensive set of spectroscopic techniques, including FTIR, 1H NMR, 13C NMR, 11B NMR, 19F NMR, and mass spectrometry, which collectively established the successful coordination of boron and the integrity of the BODIPY core structure. Furthermore, the drug-likeness and pharmacokinetic profiles of the newly synthesized derivatives were evaluated through in silico studies using Swiss ADME, including the prediction of physicochemical properties, pre-ADME parameters, and BOILED-Egg analysis for gastrointestinal absorption and blood–brain barrier penetration. The computational results indicated that the selected BODIPY–boron complexes possess favorable oral bioavailability and acceptable ADME profiles, highlighting their potential as promising candidates for further exploration in medicinal and imaging applications.

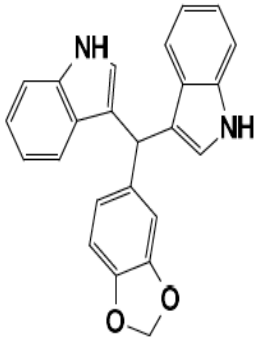
Keywords: Sonochemistry, Green Route, Pre-ADME,In-silico

Introduction: Heterocyclic compounds have been integral to organic chemistry for nearly a century, playing a pivotal role in contemporary industrial processes, medicinal agents, and elucidating biological mechanisms that enhance the quality of life. Boron-containing organic frameworks have garnered increasing interest owing to their distinctive Lewis acidity, tunable electronic properties, and extensive utility in materials science and medicinal chemistry. Within this field, boron-based 2-[di(2,3-dihydro-1H-indol-3-yl)] ligands represent a promising class of molecules with potential applications in catalysis, sensing, and biological systems, attributed to the versatile coordination behavior and bio-relevant nature of the indoline/indole scaffold. Although the synthetic routes and structural characterizations of such boron–indole derivatives have been documented, their detailed thermal behaviors and biological activity profiles remain insufficiently explored in the literature. Sonochemistry is emerging as a rapid, selective, and energy-efficient green methodology that can significantly accelerate organic transformations and improve yields under mild conditions, rendering it particularly attractive for the synthesis of advanced heterocyclic and organoboron architectures. Concurrently, in silico pharmacokinetic evaluation using tools such as SwissADME facilitates the early assessment of drug likeness, including parameters such as gastrointestinal absorption, blood–brain barrier permeation (BOILED-Egg model), and oral bioavailability radar plots, thereby guiding the rational design of biologically active boron–indole ligands. Consequently, the present study focuses on the sonochemical synthesis, thermal characterization, and biological evaluation of a series of novel boron 2-[di(2,3-dihydro-1H-indol-3-yl)]-based derivatives, complemented by pre-ADME and BOILED-Egg analyses to elucidate the structure–property relationships and identify candidates with promising pharmacokinetic profiles. Our previously reported synthesis via conventional heating methods is complemented by the application of sonochemistry**.**

Experimental Section:
Material and Methods: All chemicals and raw material purchased from local vendor and some special chemical from TCI, Analytical supported from GSS scientific service and NMR from Sathi,BHU,India.

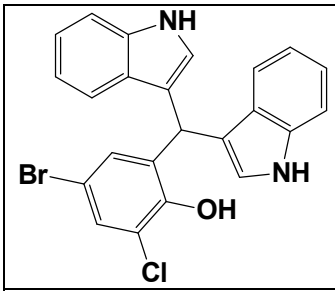
Method:
Step:01 Preparation of Ligand
Take 50 ml RBF in refluxed mode, charge 0.50 mmole Indole and 0.25 mmole 1,3-benzodioxole-5-carbaldehyde in 5 volume ethanol as a solvent with few drops of acetic acid as a catalyst refluxed for 30 mins under the solicitation and Check TLC, Reaction compiles than recrystallize by ethanol. Than structure confirmation by FT-IR, Mass Spectra and NMR.





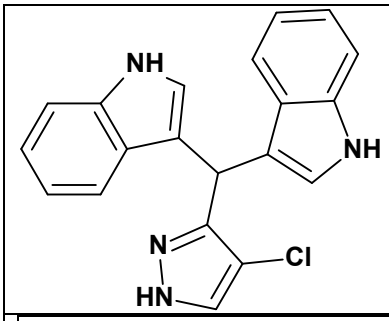
Yield:75%	Color: Green Powder	m.p.: 239-245°C
Mol.For.: $C_{24}H_{18}N_2O2$	Mol.Wt.:366.41 gm/mole	
Mass (M/Z) :366.41	UV (λmax) =278 nm,	

C,H,N,S Calc	C:78.67; H:4.95; N:7.65; O:8.73
C,H,N,S observed	C:79.10; H:5.25; N:7.85; O:8.96
FT-IR	3473.80,3658.78,3163.16,3153..56,2996.16,1818.87,1782.23,1665.51,1655.69,1567.27,1531.48,1498.59,1438.90,1377.74,1188.15,1143.79,1093.64,1058.92
1HNMR(400 MHz)	5.27 (1H), 5.93 (2H), 6.92 (1H), 6.92-7.72 (6H),7.34-7.77(8H)
13CNMR(100MHz)	101.2 (1C), 106.7 (1C), 108.3 (1C), 111.5-111.6 (3C), 117.3 (2C), 119.7 (2C), 120.1 (2C), 122.3 (2C), 124.2 (2C), 127.8-129.0 (3C), 135.94 (1C), 138.4 (2C), 148.0(2C).



Yield:62%	Color: White powder	m.p.: 310-315°C
Mol.For.: C23H16BrClN2O	Mol.Wt.:451.74 gm/mole	
Mass (M/Z) :453.19	UV (λmax) =280nm,	

C,H,N,S Calc	C, 61.15; H, 3.57; Br, 17.69; Cl, 7.85; N, 6.20; O, 3.54
C,H,N,S observed	C, 61.11; H, 4.01; Br, 17.81; Cl, 8.10 N, 6.29; O, 3.70
FT-IR	3410.20,3389.19,3105.99,2931.18,1650.15,1450.11,1310.10,1070.25,951.18
1HNMR(400MHz)	4.47 (1H), 4.98 (1H), 6.57 (1H), 6.99-7.25 (3H), 7.23-7.53 (8H), 7.74 (1H), 8.50 (1H).
13CNMR(100MHz)	71.1 (1C), 111.7 (2C), 114.9 (1C), 117.2 (1C), 118.3 (1C), 119.7 (1C), 120.1 (1C), 122.0 122.1 (2C),124.8 (1C), 126.3 (1C), 126.5 (1C), 127.0 (1C), 127.7 (1C), 128.7 (1C), 130. (1C), 131.3 (1C), 137.1 (1C), 142.0 (1C), 143.6 (1C), 151.3-151.5 (2C).



Yield:61%	Color: Light Yellow	m.p.: 210-212°C
Mol.For.: C20H15N4Cl	Mol.Wt.:346.81gm/mole	
Mass (M/Z) :347.1	UV (λmax) =310nm,	

C,H,N,S Calc	C, 69.26; H, 4.36; Cl, 10.22; N, 16.15
C,H,N,S observed	C, 69.56; H, 4.46; Cl, 10.50; N, 16.41
FT-IR	3460.53,3159.63,3093.63,2918.15,2553.84,2422.67,1623.60,1589.40,1489.10, 1373..6,1257.63,1171.33,1083.89,1057.03 887.28,825.56,756.12
1HNMR	4.97(3H),5.74(1H),6.82-7.28(5H),7.35-7.66(6H).
13CNMR	19.9(1C),112.5-116.3(3C),117.5-120.2(2C),122.2-134.3(2C),138.2(3C),150.23(1C),155.6(1C)

Step:02 Preparation of BODIPY:

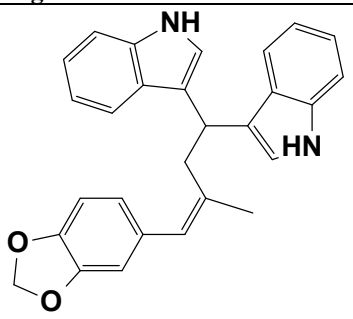
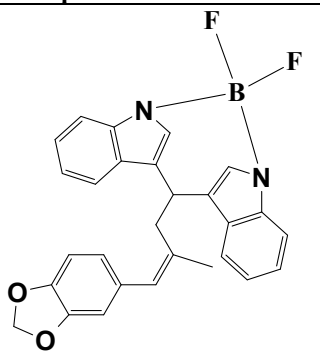
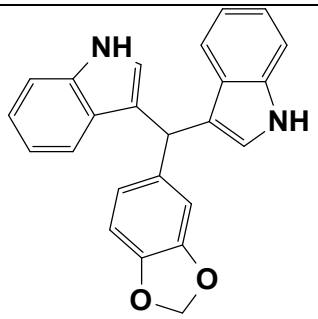
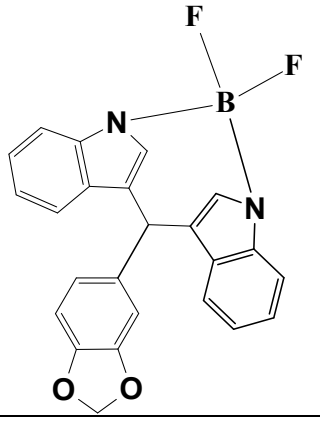
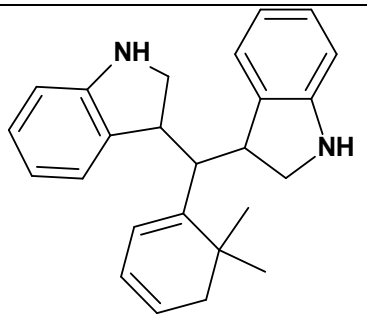
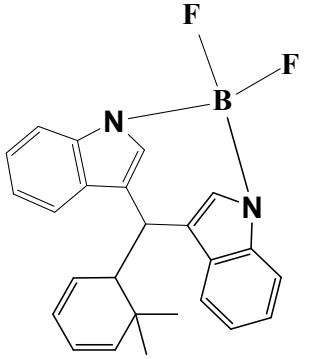
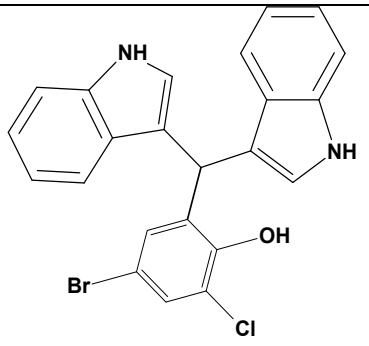
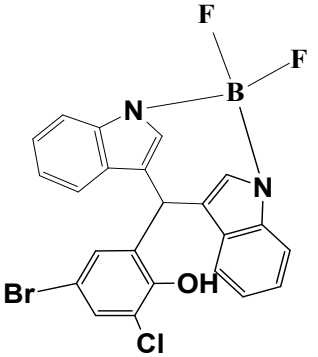
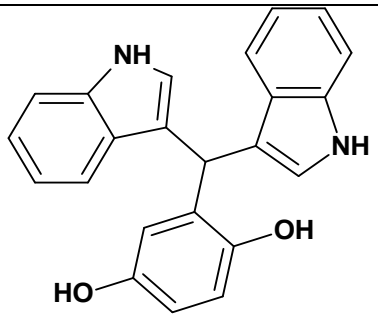
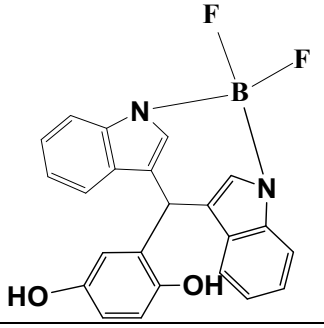
BODIPY Derivatives was prepared from condensation of Schiff's base in CH2Cl2 and then reacted with BF_3OEt sonication for 1.5 hours at 85°C and 40HZ formed the precipitation filter it and washed by ethanol and dry it.this reaction must be in Amber colour flask due to the this compound easy to reaction in sunlight and compound turn to blackish colour.

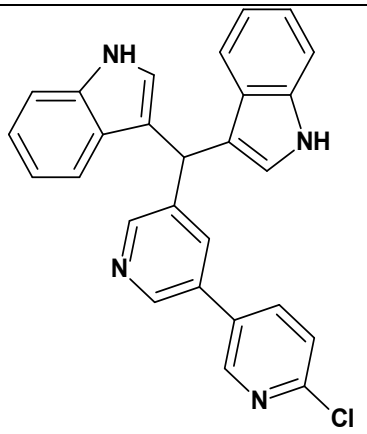
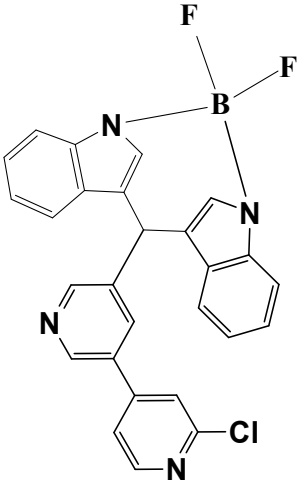
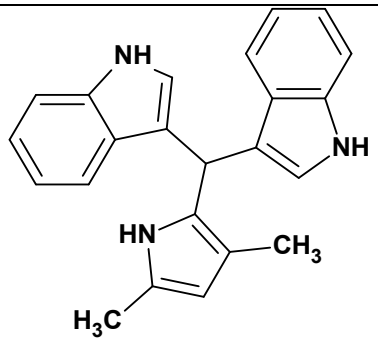
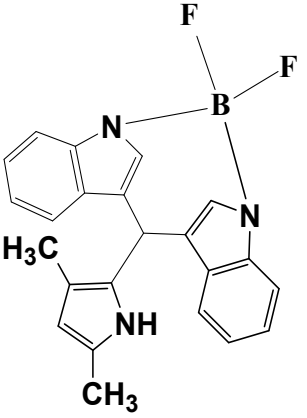
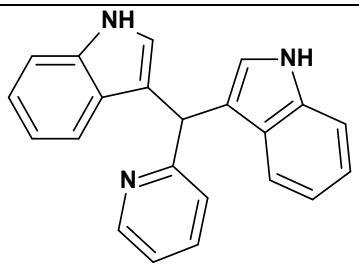
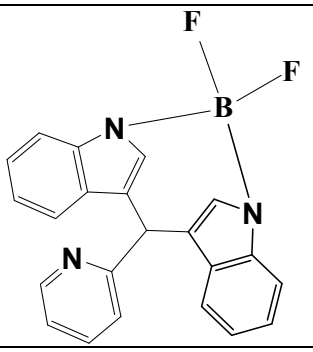
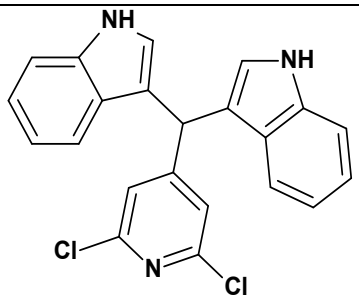
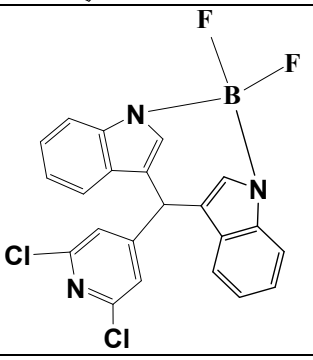
Synthesis of 2-[3-(2,3-dihydro-1,4-benzodioxin-6-yl)allyl]-6,11-dihydro-5H-indolo[3,2-c]carbazole AL1 L(BF2)2:
2.65 g, 0.63 mmol was dissolved in CH2Cl2 (50 mL) in a 100 mL round-bottomed flask. Subsequently, TEA (1.10 mL, 7.1 mmol) was added to the solution, followed by stirring for 2 min at 50°C under sonication. BF3·Et2O (1.5 mL, 12.6 mmol, corresponding to 2 equivalents relative to the ligand), 1.92 mL (15.6 mmol), and 2.2 mL (17.6 mmol) were then gradually introduced to the resulting mixture. The reaction was maintained for 1 h at 85°C under an argon atmosphere with sonication at 40 Hz. The progress of the reaction was monitored using TLC with a CHCl3/EtOH (10:1) solution. The resulting mixture was then diluted with CHCl3 (40 mL) and subsequently washed with a NaHCO3 solution. The extraction with CHCl3 (3 × 15 mL) was conducted. The organic layer was then collected, dried with Na2SO4, filtered, and evaporated. The raw product was finally purified by column chromatography on silica gel with CHCl3/methanol (100:1) as the mobile phase.The same protocol was followed, but ligand amount was the only factor that was changed and it should be tailored according to the specifications. All other substances remained the same. The solvents, namely CH2Cl2, ethanol, and methanol, should be chosen according to the specific requirements of the experiment.

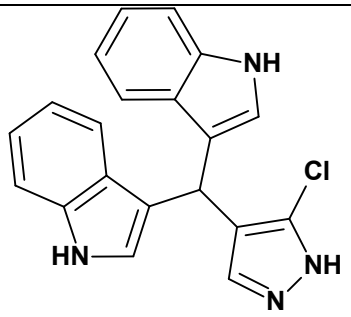
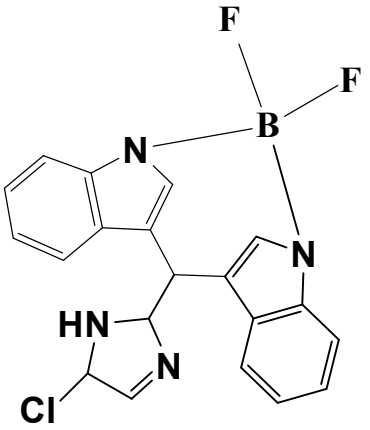
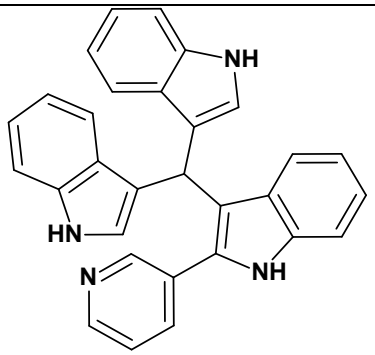
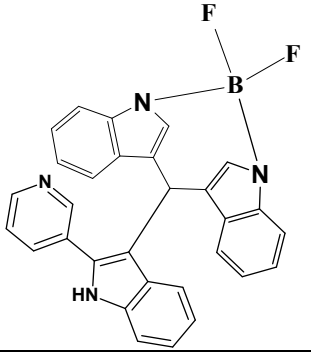
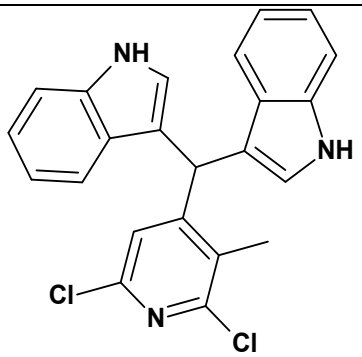
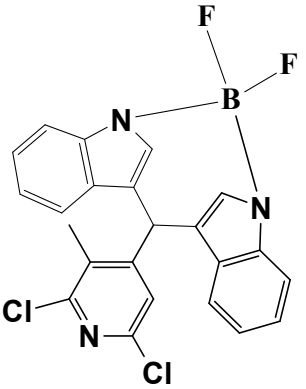
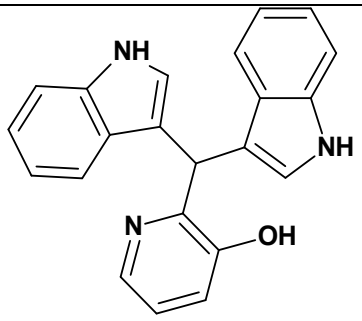
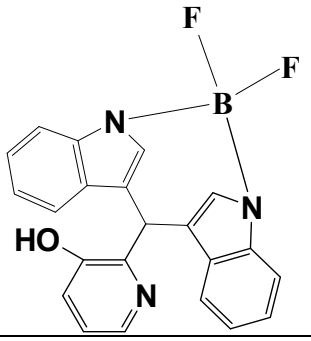
Table :3 Ligand quantity as below:

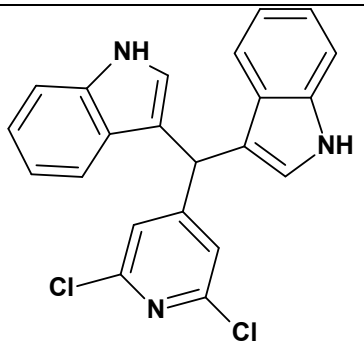
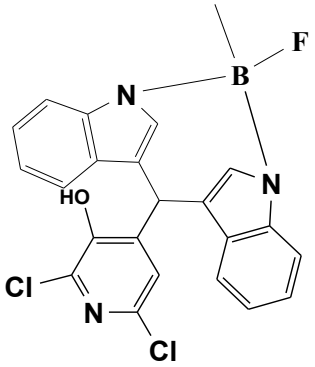
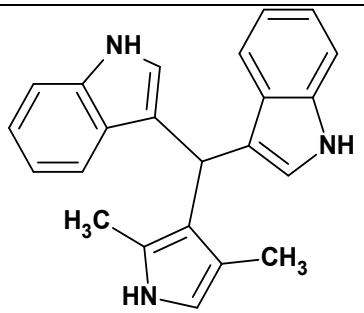
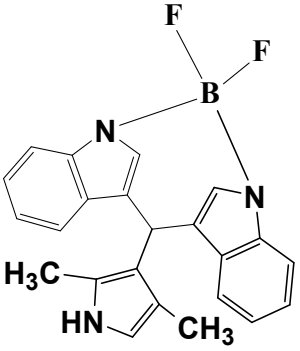
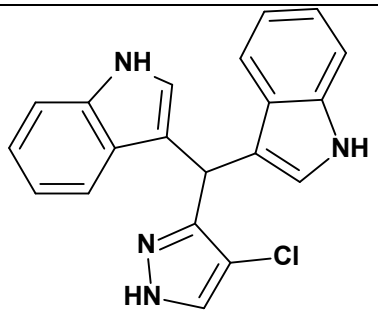
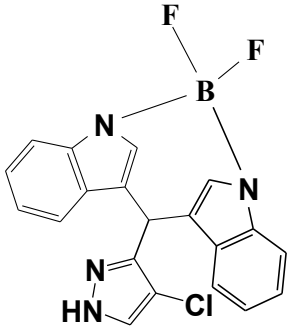
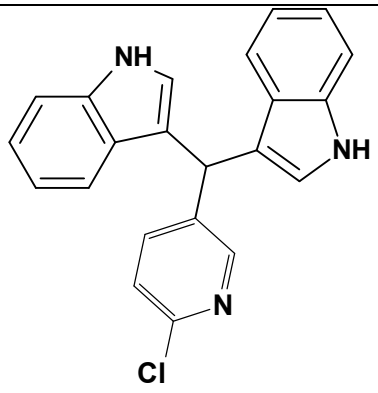
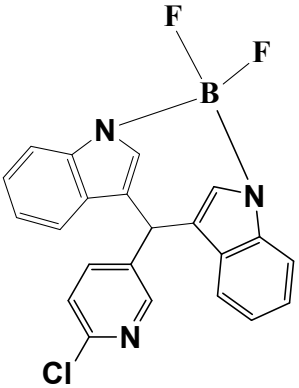
Ligand	Qty in grams	MW	Complex Code
L1	**2.65**	**420.5**	**AL1**
L2	**2.31**	**366.41**	**AL2**
L3	**2.22**	**352.47**	**AL3**
L4	**2.85**	**451.74**	**AL4**
L5	**2.23**	**354.4**	**AL5**
L6	**2.74**	**434.92**	**AL6**
L7	**2.14**	**339.43**	**AL7**
L8	**2.04**	**323.14**	**AL8**
L9	**2.46**	**391.06**	**AL9**
L10	**2.19**	**346.81**	**AL10**
L11	**2.76**	**438.52**	**AL11**
L12	**2.55**	**405.08**	**AL12**
L13	**2.14**	**339.39**	**AL13**
L14	**2.46**	**391.06**	**AL14**
L15	**2.14**	**339.43**	**AL15**
L16	**2.19**	**346.81**	**AL16**
L17	**2.26**	**357.84**	**AL17**
L18	**2.34**	**371.86**	**AL18**

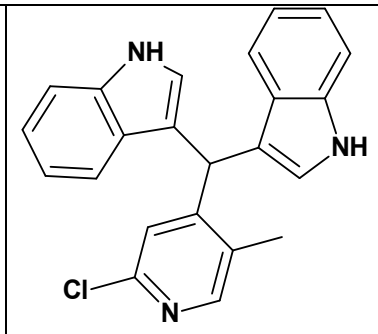
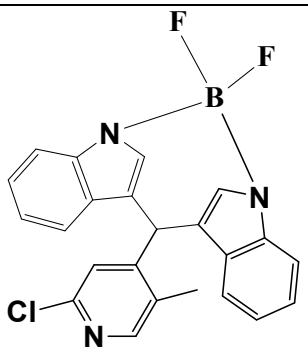
Table3.2.1 Ligand and Metal Complex:

Code	Ligand structure	Complex
AT-01		
AT-02		
AT-03		
AT-04		
AT-05		

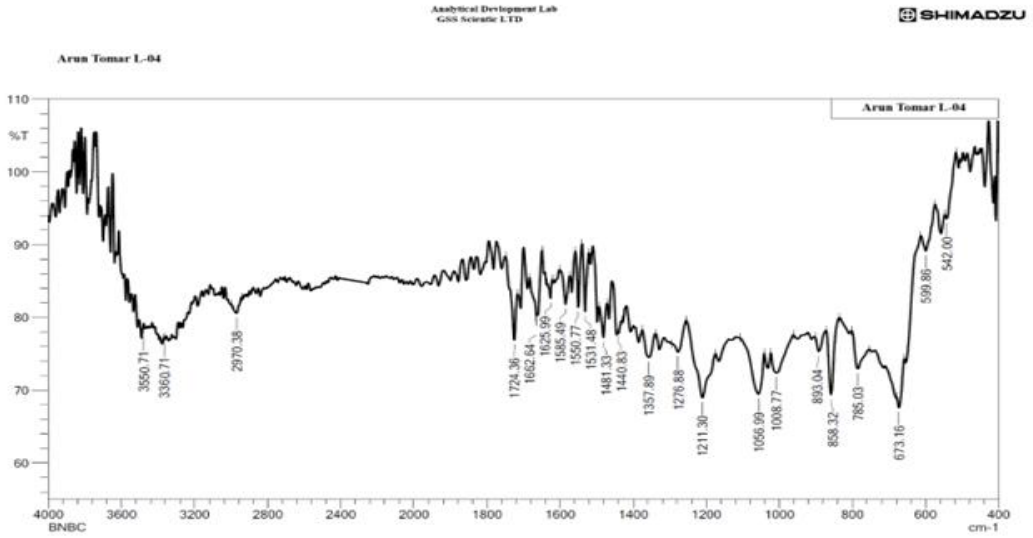
AT-06		
AT-07		
AT-08		
AT-09		

AT-10		
AT-11		
AT-12		
AT-13		

AT-14		
AT-15		
AT-16		
AT-17		

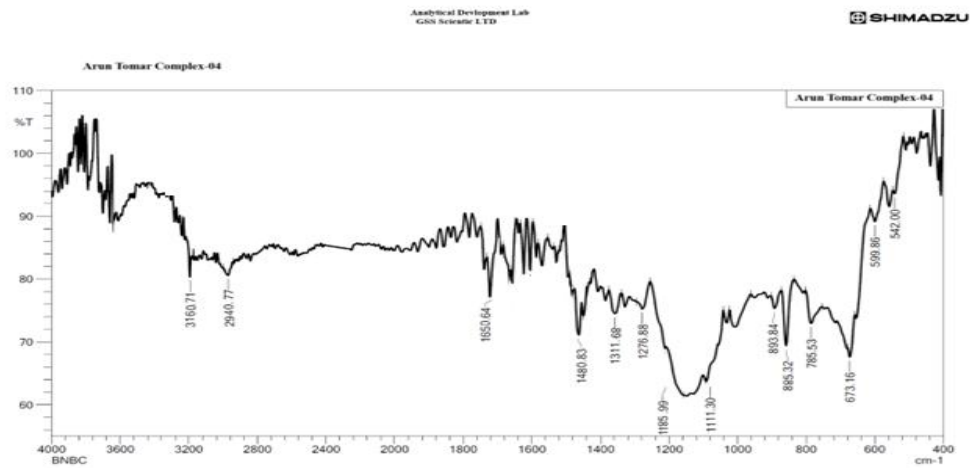
AT-18		

FT-IR SCTUCTURE CONFIRMATION
AT-04



Range in cm^{-1}	Probable functional group,
3350.71,3360.71	O–H stretch (phenolic hydroxyl group), N–H stretch (indole, azine NH group)
2970.38	Aromatic C–H stretch (phenyl, indole),
1724.36	C=O stretch
1662.64,1625.99, 1585.49	C=N stretch (azomethine from Schiff base)
1481.13,1440.83 1357.89	Aromatic C=C stretch
1211.30,1056.99 1008.77	C–O stretch (phenol or ether linkage)
858.32	Aromatic C–H out-of-plane bending

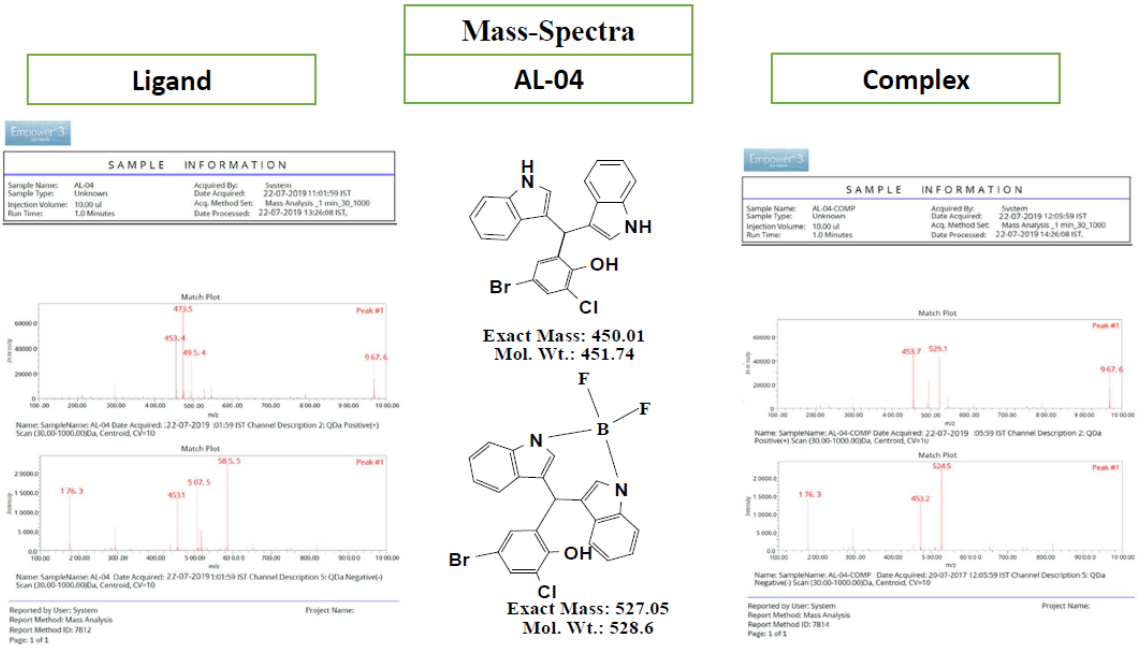
Results and Discussion:



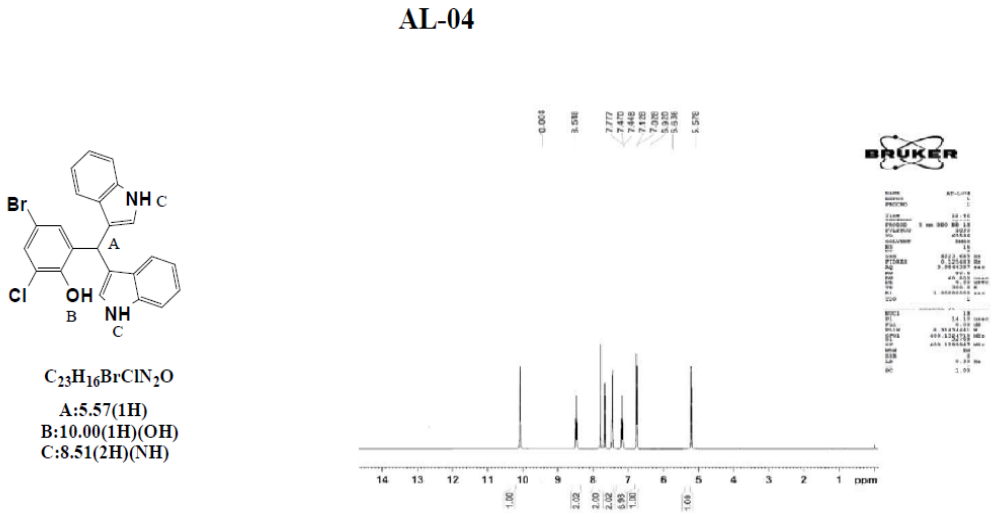
Range in cm^{-1}	Probable functional group,
3160.71,2940.77	O–H stretch (phenolic hydroxyl group), N–H stretch (indole, azine NH group)
1650.64	Aromatic C–H stretch (phenyl, indole),
1480.83	C=O stretch
1311.68	B–N bond formation
1276.88	Aromatic C=C stretch
1185.99,1111.30	B–F stretch (for boron–fluorine units if present)
885.32	Aromatic C–H out-of-plane bending
758.53, 673.16	C–Cl stretch (aromatic chlorine); C–Br stretch (aromatic bromine)

The FT-IR spectra of Ligand-04 exhibit peaks at 1662, 1625, and 1585 cm^{-1}, indicative of C=O and C=N bond formation in the Schiff base. In contrast, the FT-IR spectra of Complex AL-04 reveal a new peak at 1185 and 1111 cm^{-1}, which corresponds to the B-F stretching, signifying the formation of a metal bond.

Mass-Spectra

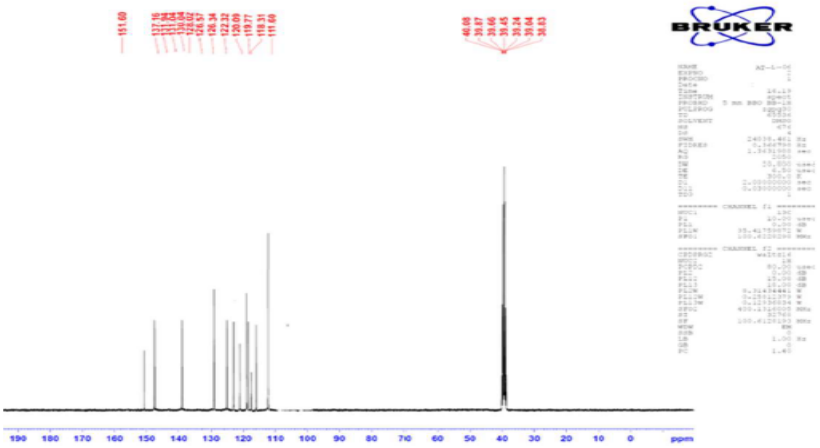


^{1}HNMR



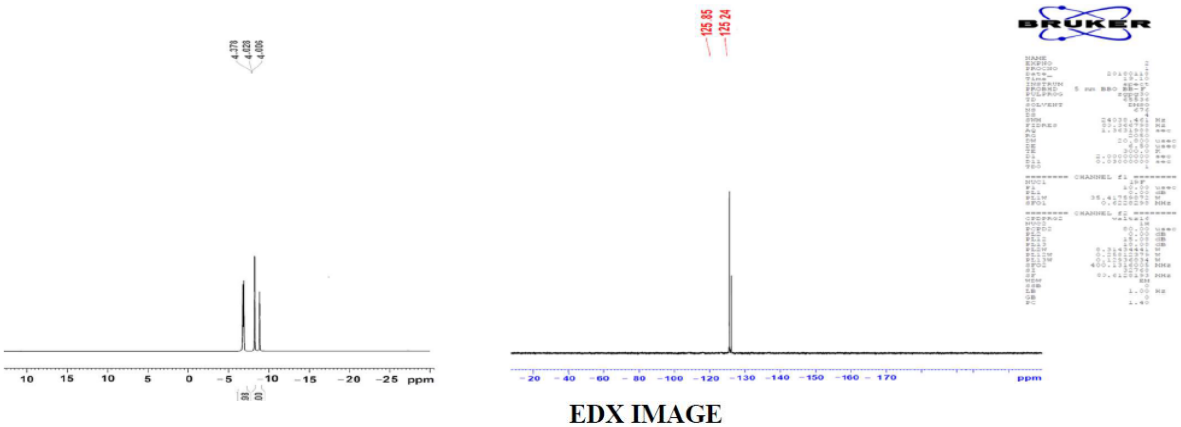
^{13}CNMR

AL-04

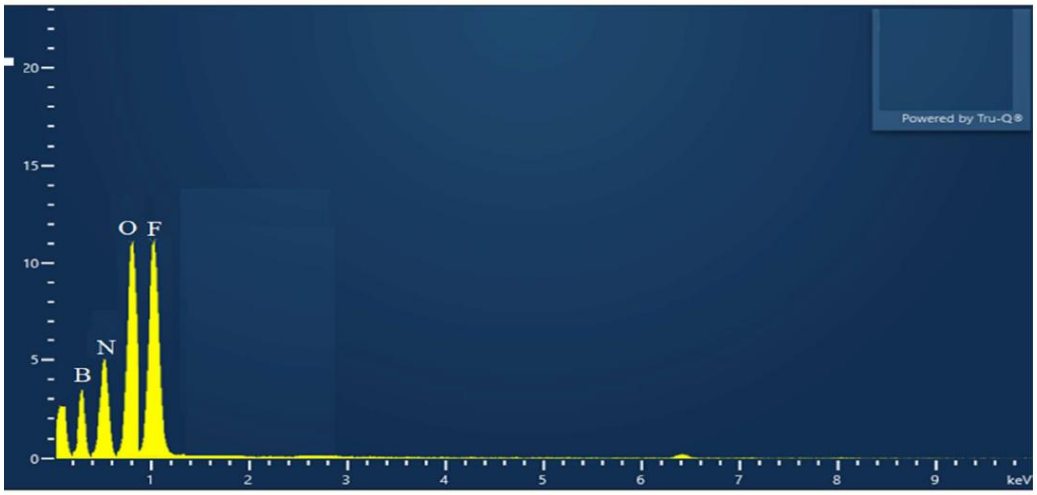


19^F NMR: COMP-01

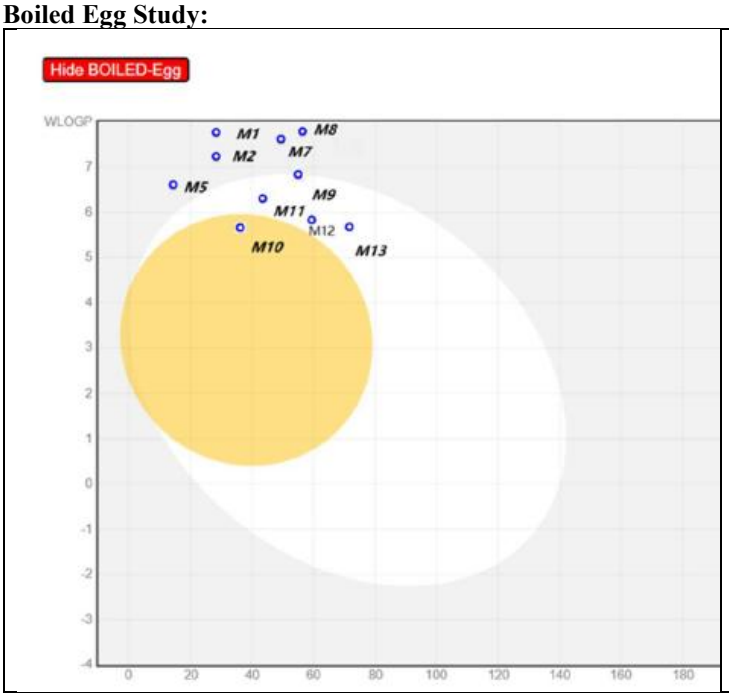
11^B NMR: COMP-01



EDX IMAGE



Boiled Egg Study:



The BOILED-Egg model (Brain Or Intestinal Estimated permeation method) is a computational method developed for the quick, intuitive, and robust prediction of two essential pharmacokinetic properties of small molecules.
Gastrointestinal (GI) Absorption (HIA: Human Intestinal Absorption)
Blood-Brain Barrier (BBB) Permeation (brain access)
This approach helps researchers in the early drug discovery stages to filter or optimize compounds for desirable absorption and/or central nervous system penetration, using only two fundamental physicochemical traits: lipophilicity (WLOGP) and polarity (TPSA).

Conclusion:

Sonochemistry applicable for green and environment friendly method for the formation of indole-based Schiff bases, for boron based BODIPY synthesis, with boron and fluoride metal complexation. Ths method is quick and rapid synthesis within 15-30 minutes for Schiff base and BODIPY compounds with high selectivity,purity. The sono-chemical noel aroch for metal complex formation for green chemistry approach reaction time compared to traditional methods, its same fundamental applicable for BODIPY derivatives. The sonochemical method is a novel, fast, and selective method for the synthesis of schf base and bodify compound and complex formation, which is more suitable for BODIPY compounds and boron metal complexes. The synthesized compounds confirmed by FT-IR,NMR and MASS SPECTORSCOPY discussed in results and decussation. .

The FT-IR spectra of Ligand-04 exhibit peaks at 1662, 1625, and 1585 cm^{-1}, indicative of C=O and C=N bond formation in the Schiff base. In contrast, the FT-IR spectra of Complex AL-04 reveal a new peak at 1185 and 1111 cm^{-1}, which corresponds to the B-F stretching, signifying the formation of a metal bond.

The FT-IR spectra of Ligand-16 exhibit peaks at3460., and 1623 cm^{-1}, indicative of C=O and C=N bond formation in the Schiff base. In contrast, the FT-IR spectra of Complex AL-16 reveal a new peak at 1589 and 1489 cm^{-1},1257,1157 which corresponds to the B-F stretching and B-N stretching, signifying the formation of a metal bond.

Due to all observation, we conclude that B-F and B-N peak observed In FT-IR

After this we observed the H^NMR,C^NMR the no f hydrogen and Num of carbon is matched with molecular formula,

Than we checked this Complex via BORON and Fluoride NMR we observed the Boron and Fluorine peak due to present f boron and fluorine bond coordination.

Due all of above analysis, we conclude the al ligand turn to metal complex formation and its biological potent some molecules Most molecules M1, M2, M5, etc near the GI (white) or BBB (yellow) favorable zones. So its biological potent.

Reference:

1. Mahida, J., & Patel, R. B. (2019). Application of Silica Supported Aluminium Hydroxide as a Low Cost Green Catalyst for the One Pot MCR Sythesis via Thermal Method. *Journal of Drug Delivery & Therapeutics*, *9*.
2. **Comprehensive Investigation of Thermal and Biological Properties of novel boron based Metal Complex"**, International Journal of Emerging Technologies and Innovative Research (www.jetir.org), ISSN:2349-5162, Vol.6, Issue 6, page no.222-228, June-2019
3. C.K. Modi, D.H. Jani, *J. Therm Anal Calorim.,* 102(3), **2014,** 1001.
4. C.K. Modi, D.H.Jani, H.S. Patel and H.M. Pandya, *spectrochimica Acta.*, 75A, **2010**, 1321.
5. (a) M.F Ikander, L.Saved, A.F.M Hefny, S.E Zayan, *J.Inorg. Nucl.Chem*, 38, **1976,** 2209.
6. H. Adams, D.E. Fenton, C. Minardi, E. Mura, M. Angelo, *Inorg. Chem. Commun.,*3, **2000,** 24.
7. Z.Y. Yang, R.D. Yang, F.S. Li, K.B. Yu, *Polyhedron*, 19, **2000,** 2599.
8. S.Sathiyaraj, K. Sampath, C. Jayabalakrishnan., *Chem*., 44, **2014,** 161.
9. K. M. Vyas, R. N. Jadeja, D. Patel, R. V. Devkar, V. K. Gupta, *Polyhedron*, 80, **2014,** 20.
10. J. Hu, L. Liu, D. Jia, J. Guo, X. Xie, D. Wu, R. Sheng, *Chem*., 217, **2011,** 117.
11. B. Pang, G. Liu, L. Liu and D. Jia, *Tetrahedrone*, 61, **2005,** 5926
12. 8. K.C Gupta, A.K. Sutar, Coord. *Chem. Rev*., 252, **2008,** 1420.
13. 9. R. Kumar, G. Mani, *Dalton Trans*. 44**, 2015,** 6896.

14. 10. K. Nejati, Z. Rezvani, B. Massoumi. *Dyes Pigments*, 75, **2007,** 653.
15. M.F Ikander, L. Saved, A.F.M Hefny, S.E Zayan, *J.Inorg. Nucl.Chem*, 38, **1976,** 2209. **2000,** 24