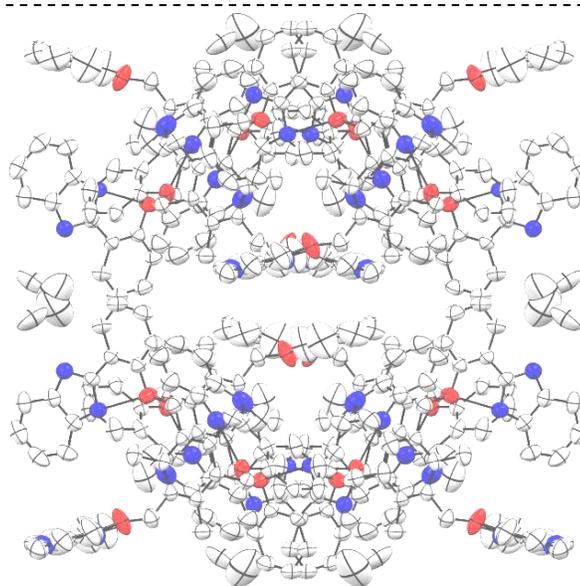## CHAPTER V

Synthesis, characterization and study of 1,3,5-tris[n-(1,3-benz-imidazol-2-yl)-phenyloxymethyl]-2,4,6-trimethylbenzenes

5.1 INTRODUCTION

In this chapter, the C_3 symmetric compounds having benzimidazoles as heterocyclic functional arms have been prepared and studied. The benzimidazole **1** is a fused heteroaromatic system in which the imidazole heterocycle is attached to a benzene ring from side d. Thus it is named as 1*H*-benzo[d]imidazole (Figure 1).
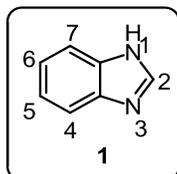

Figure 1 1*H*-benzo[d]imidazole

Interest in the study of benzimidazoles started with the discovery of benzimidazole moiety as a part of vitamin B_{12}.[1] Benzimidazoles are not commonly found in nature. The chemistry of benzimidazole developed mainly because of a spectrum of biological activities exhibited by the compounds with benzimidazole scaffold.[2] Tuning of substituents around the benzimidazole moiety has resulted in many bioactive compounds such as Albendazole **2**, an anthelmentics, Omeprazole **3** a proton pump inhibitors, Astemizole **4** an antihistaminic and many more compounds of therapeutic value[3] (Figure 2).
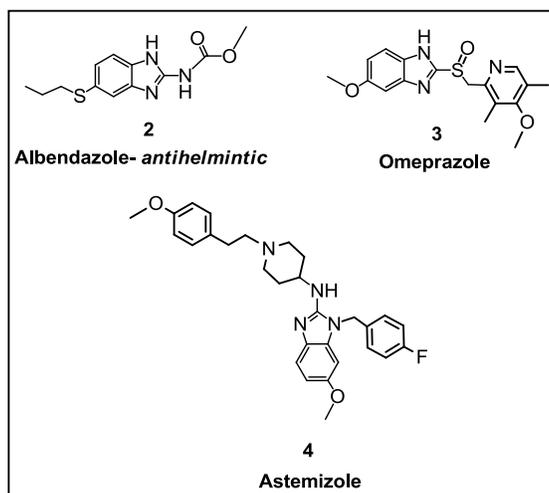

Figure 2 *Benzimidazole based commercially available drugs*[3]

Benzimidazole containing compounds are reported to have antiinflammatroy, antiulcer,[4] antiviral,[5] antitumor,[6] antimicrobial,[6] antidiabetic, anticoagulant activities and are found

to be psycho active agents. Medicinal importance of benzimidazoles has been well described in a number of recent reviews.[2–6,7]

The most common synthetic route leading to the synthesis of benzimidazole is cyclocondensation of various carbonyl compounds with 1,2-diamino arenes. The other closely related synthesis involves condensation of 2-amino aryl azide with aldehyde followed by cyclization.[8] Imines from ortho-nitro aniline on reductive cyclization also lead to benzimidazoles.[9]

Aromatic imidines can also be cyclized to benzimidazoles by oxidative cyclization. Imidines with *ortho*-halo aryl substitution undergo cyclization in the presence of a base and DMSO (oxidizing solvent)[10] or in the presence of Cu catalyst in aqueous medium.[11] 1,2-Diamino arenes on reaction with aliphatic amines in the presence of elemental sulfur as an oxidizing agent under solvent free condition can give benzimidazole derivatives.[12] 1,2-Diamino arenes can also react with 1,3-diketones in acid catalyzed condensation process to give benzimidazoles.[13]

One of the most extensively employed and studied method for the synthesis of benzimidazoles involves oxidative cyclization of 1,2-diamino benzene **5** and aromatic aldehydes **6** carried out in the presence of a variety of oxidizing agents (Figure 3) such as cerric ammonium nitrate (CAN) **7**,[14] (diacetoxy)iodobenzene (IBD) **8**,[15] molecular iodine **9**,[16] molecular oxygen **10**,[17] potassium peroxymonosulfate ($KHSO_5$) **11**,[18] sodium metabisulfite ($Na_2S_2O_5$) **12**[19] (Figure 3).

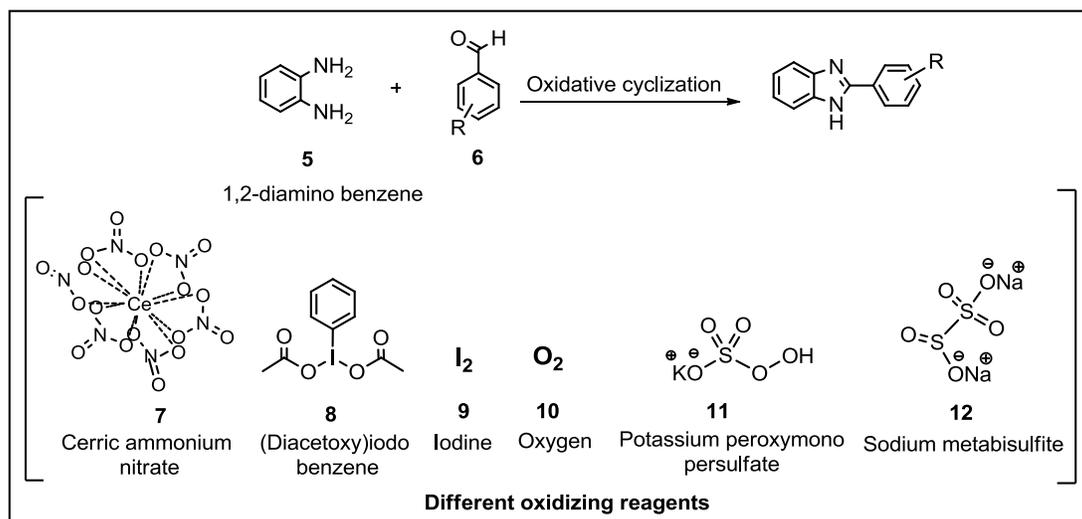**Figure 3** *Oxidants in the synthesis of benzimidazoles via oxidative cyclization*

5.1.1 Tripodal benzimidazoles as sensors

Supramolecular interactions of C_3 symmetric benzimidazole derivatives have been studied mainly for tris-benzimidazolyl derivatives or tris-benzimidazolium salts. One such benzimidazolyl derivative with free amino groups attached **13** has been found to selectively recognize iodide ion in preference to the other ions under study[20] (Figure 4).
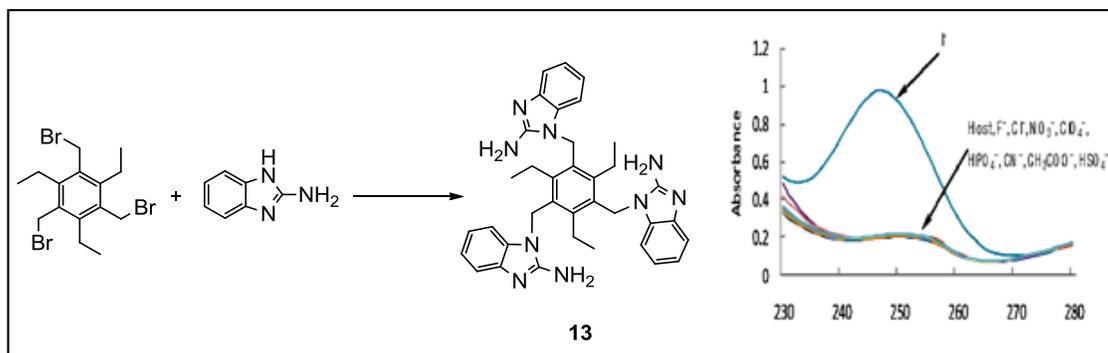

Figure 4 *Selective anion recognition by tris-benzimidazolyl host*

Two molecules of unsubstituted tris-benzimidazolyl derivatives **14** were held together in the presence of NO_3^- ions (**15**) while 1:1 host guest complexation was taking place in the presence of halides **16**[21] (Figure 5).
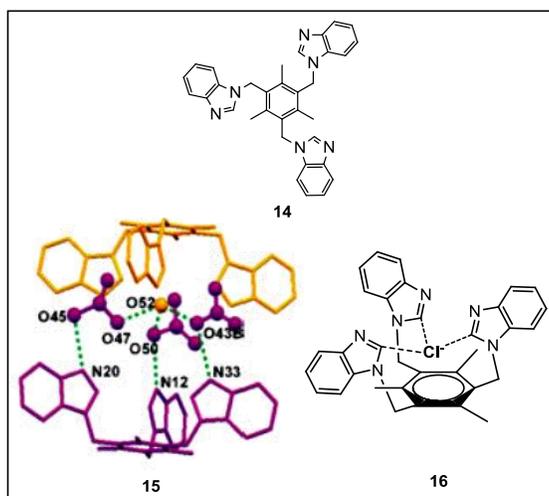

Figure 5 *Host-guest complexation of tris-benzimidazolyl derivative*

Tris-benzimidazolium salt attached to naphthyl fluorophore groups (**17**) had selectively switch–on fluorescence in the presence of Cl^- ions with conformational re-orientation as shown in figure 6.[22]
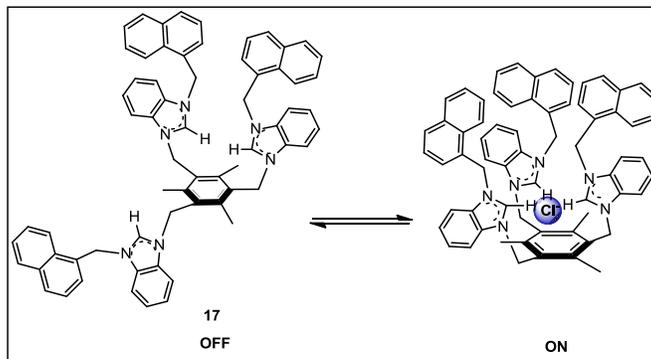
Figure 6 *Selective switch 'ON' fluorescence by tris-benzimidazolium salt in presence of Cl^- ions*

Unlike flexible armed tripodal benzimidazol derivatives as mentioned above, a rigid tripodal tris-benzimidazole **18** was studied for reversible anion exchange in porous metal organic frameworks (MOFs)[23] (Figure 7).
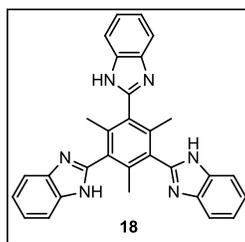

Figure 7 *Rigid tris-benzimidazole for application in MOFs*

Tripodal benzimidazoles with central 1,3,5-triazine **19** exhibited antimicrobial activity[24] (Figure 8).
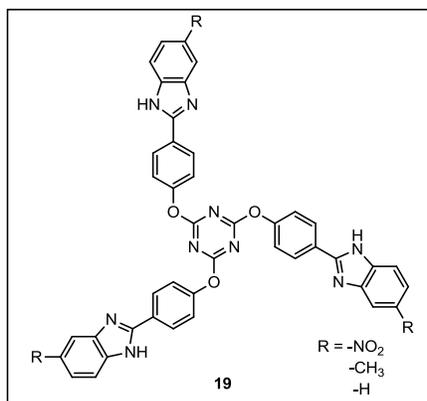

Figure 8 *Tripodal benzimidazoles with antimicrobial activity*

Looking at the importance of benzimidazole heterocycle and its derivatives, and applications of tris-benzimidazole compounds, several new tripodal benzimidazoles have been synthesized and studied in the present chapter.

5.2 RESULTS AND DISCUSSION

In an endeavor to synthesize new C_3 symmetric compounds with heterocyclic tripodal arms using the tripodal tris-aromatic aldehydes as key synthetic intermediates, synthesis of the fused 1,3-diazole, benzimidazole containing C_3 symmetric tripodal compounds was carried out.

Application of 1,2-diamino benzene (ortho-phenylene diamine, OPD) for the reaction with carbonyl compounds leading to benzimidazole moiety is most frequently used synthesis methodology. As described in the earlier section, the condensation takes place in the presence of various oxidizing reagents, many of them being expensive, sodium metabisulfite ($Na_2S_2O_5$) was found to be handy, less expensive and easy to handle among them.[19] Thus OPD was heterocyclized by condensation with the expanded tris-aldehydes, 1,3,5-tris-formylaryloxymethyl)-2,4,6-trimethylbenzene in dimethylacetamide (DMAc) as a polar solvent in the presence of $Na_2S_2O_5$ by heating at 100 °C (Scheme 5.1). The reaction was completed in comparatively short time of about 2-3 hours. The crude product obtained on pouring in water was purified in good yields by cyrstallization from alcoholic solvents. The compounds had poor solubility in less polar or moderately polar organic solvents. One of the tripodal tris-benzimidazole **22b** gave the crystals suitable for single crystal X-ray analysis. The structures of the final tris-benzimidazoles were determined based on their IR, NMR and mass spectral characteristics.
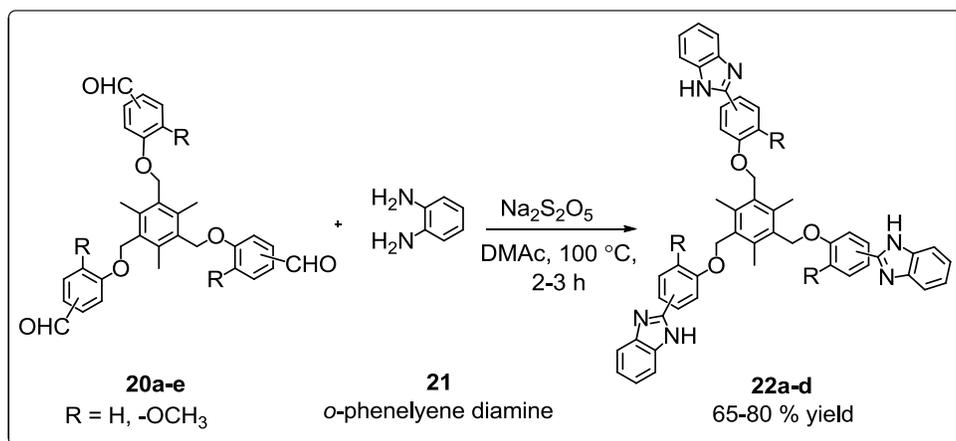
Scheme 5.1 *Threefold oxidative coupling to benzimidazoles*

The reaction with 1,3,5-tris(6-methoxy-2-formylphenyloxymethyl)-2,4,6-trimethylbenzene **20e** under same reaction condition failed to give the corresponding tris-

benzimidazole even after prolonged reaction time probably due to greater steric hindrance present in the tris-aldehyde (Scheme 5.2).
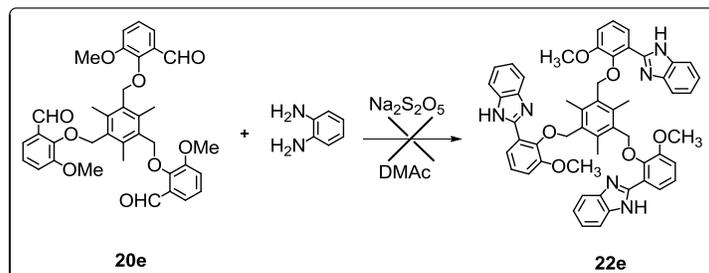
Scheme 5.2

5.2.1 Spectral characteristics of tris-benzimidazole compounds

The IR spectra of the final compounds show a strong υ_{N-H} band present in benzimidazole between 3420 to 3430 cm^{-1}. The bands from 1630 to 1430 cm^{-1} are due to $\upsilon_{C=N}$ and $\upsilon_{C=C}$ stretching and skeletal vibrations. Strong bands near 1220 to 1260 cm^{-1} and at 1171/1013 cm^{-1} are due to υ_{C-O} of the ether linkage. There are very few strong bands observed in the fingerprint region. A strong band found at 746-750 cm^{-1} is due to the heterocyclic ring breathing vibrations.

^{1}H NMR of the tris-benzimidazole compounds show a singlet near to δ 2.4 for –CH$_3$ group attached to the central ring. Another singlet is observed for the –CH$_2$ group attached to the same ring having ether linkage at δ 5.2 as expected. Aromatic ring of benzimidazole substructure having local symmetry shows two signals as a doublet of doublet with ortho and meta coupling of 6.0 and 3.0 Hz respectively. The proton attached to the heteroatom of the benzimidazole moiety (N–**H**) is observed as a broad signal with variable chemical shift ranging from δ 3 to 6. Aromatic protons for the linker aryl group are observed according to the position of the substituents they possess. 1,4 –Disubstitued phenyl ring shows two doublets at δ 7.30 and 8.18 with J = 8.8 Hz (Spectrum 2). The aromatic protons towards benzimidazole ring are observed downfield. For 1,3-disubstitued aryl ring, ^{1}H signal for each proton is observed separately (Spectrum 13). For the aromatic nucleus possessing –OCH$_3$ group shows a singlet at δ 3.89 for –OCH$_3$ protons (Spectrum 18).

In ^{13}C-NMR of the tripodal benzimidazole derivatives, the most downfield aromatic carbon signal at about δ 160 is the one which is having aryl ether linkage. The

benzimidazole carbon attached to two nitrogens is observed at δ ~ 150. The other aromatic carbons are observed between δ 140 to 110. The fused aromatic quarternary carbons in benzimidazole moiety are observed at δ 139 in all the final products. The –OCH$_2$ carbon signal is observed at δ 65 – 67 while the –CH$_3$ carbon on the central ring is observed at δ 16. The four aromatic carbons with hydrogen are distinguished by DEPT experiment (Spectral data section).

HSQC and HMBC 2D-NMR spectra were recorded for tris-benzimidazole compound **22a** which showed the correlation between respective carbons and protons. HSQC spectrum of **22a** helped in the assignment of each carbon signal due to its single bond correlation with directly attached proton/s (Spectrum 6). HMBC spectrum of **22a** was used for the assignment of various quaternary carbons on the basis of their correlation through two or three bond space with proton nuclei from the cross peaks observed (Spectrum 7).

Molecular masses of the newly synthesized tris-benzimidazole compounds were confirmed by using mass spectrometer having Q-TOF mass analyzer. The molecular ion peaks were observed as (M+H)$^+$ along with (M+Na)$^+$ for all the compounds and were in agreement with their proposed structures.

The crystals of tris-benzimidazole **22a**, suitable for single crystal X–ray diffraction analysis were developed from mixture of ethanol and *iso*-propanol by slow evaporation technique.
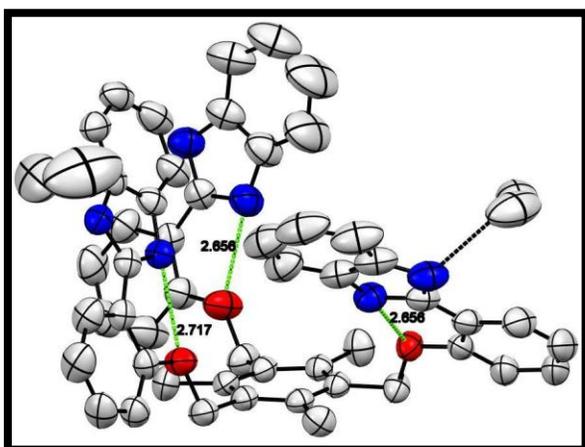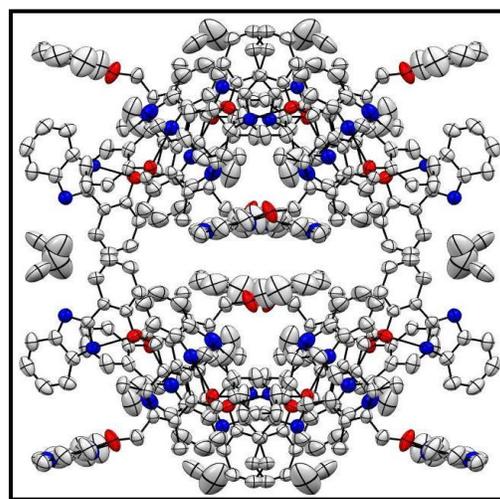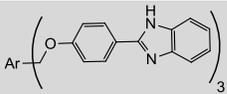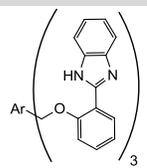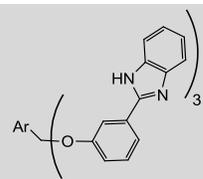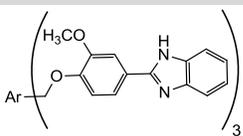

Fig. 9 *ORTEP diagram of 22b*

Fig. *10 Nut-shell shape molecular crystal packing pattern 22b*

The monoclinic crystals of the tris-benzimidazoles exhibit the orientation of all the tri-arms on same side of the plane (*syn conformation*) due to intramolecular hydrogen bonding between the –NH and –OCH_2 groups (Figure 9). The crystal packing of the compound results in to a nut-shell shape molecular pattern resulting from intramolecular hydrogen bonding (Figure 10).

Crystal data 22b: CCDC 1427888; $C_{51}H_{42}N_6O_3$ *(M =786.9176)*: monoclinic, space group C 2/c, *a* = 28.4420(7) Å, *b* = 15.7510(7) Å, *c* = 22.9010(9) Å, *α* = 90°, *β* = 123.302(1)°, *γ* = 90°, *V* = 8574.7(6) Å3, *Z* = 2, *T* = 294 K, μ(MoKα) = 0.08 mm-1, *Dcalc* = 1.272 g/mm3, 10422 reflections measured (3.2 ≤ 2Θ ≤ 56.1), 7290 unique *(R*int = 0.0226) which were used in all calculations. The final *R*₁ was 0.0474 (>2σ(I)) and *wR*₂ was 0.1421 (all data).

The yields and physical constants of the final tris-benzimidazole compounds are summarized in table **5.1.0**

Table 5.1.0 *Yields and Melting points of the newly synthesized tris-benzimidazoles*

Compound ID	1,3,5-Tris[n-(1,3-benzimidazol-2-yl)-phenyloxymethyl]-2,4,6-trimethylbenzene (Ar = 2,4,6-trimethylbenzene)	Yield [%]	M.p [°C]
22a		82	245 (decompose)
22b		69	168
22c		76	220
22d		67	265
	Standard drug Ciprofloxacin 0.5 0.5		

5.2.2 UV-Visible study of C_3 Symmetric tris-benzimidazoles as hosts with anionic guests

As benzimidzoles possess an acidic hydrogen, the C_3 symmetric compounds containing imidazole podands can well accommodate anionic guest species. With few such reports[20–22] in mind, the newly synthesized tris-benzimidazoles were subjected to binding study with various different anionic guests by using UV-Visible spectroscopy and fluorescence spectroscopy as detecting tools in solution state.

Anions used were in the form of their tetrabutylammonium salts such as of F^-, Cl^-, Br^-, I^-, HSO_4^-, PF^{6-} (TBAX, X = F, Cl, Br, I, HSO_4^-, PF^{6-}). In both the case, the tripodal hosts were dissolved in dimethylsulfoxide (DMSO) with the concentration of 6.0 x 10^{-6} M and the tetrabutylammonium salts were also dissolved in the same solvent with the concentration of 6.0 x 10^{-5} M. The solution study was carried out by mixing an equal volume of both the host and the guest solutions with the concentrations as stated above and measuring their absorption and emission spectra.

The absorption spectroscopy study started with measuring of the UV-vis spectra of hosts and tetrabutylammonium salts- the guests separately. λ_{max} of the strongest absorption band was falling in between 309 to 316 nm for all the host molecules. The guests did not show any significant absorption in the region between 250 to 500 nm as shown in the figure (Figure 11).

The solution study carried out using UV-Vis spectroscopy of host-guest interaction showed that there was considerable shift in the λ_{max} value only in the presence of F^- anions with shift towards longer wavelength (Figure 11, Graphs 1- 4). The same behavior was observed for all the host molecules except for the 1,2-disubstitued host **22b**. The host **22b** does not show any interaction because of the intramolecular hydrogen bond present in them (Figure 11, Graph 2). Thus it was concluded that the host-guest interactions take place with the F^- ions to an observable extent because of strongly negative charge present on the F^- guest anions.
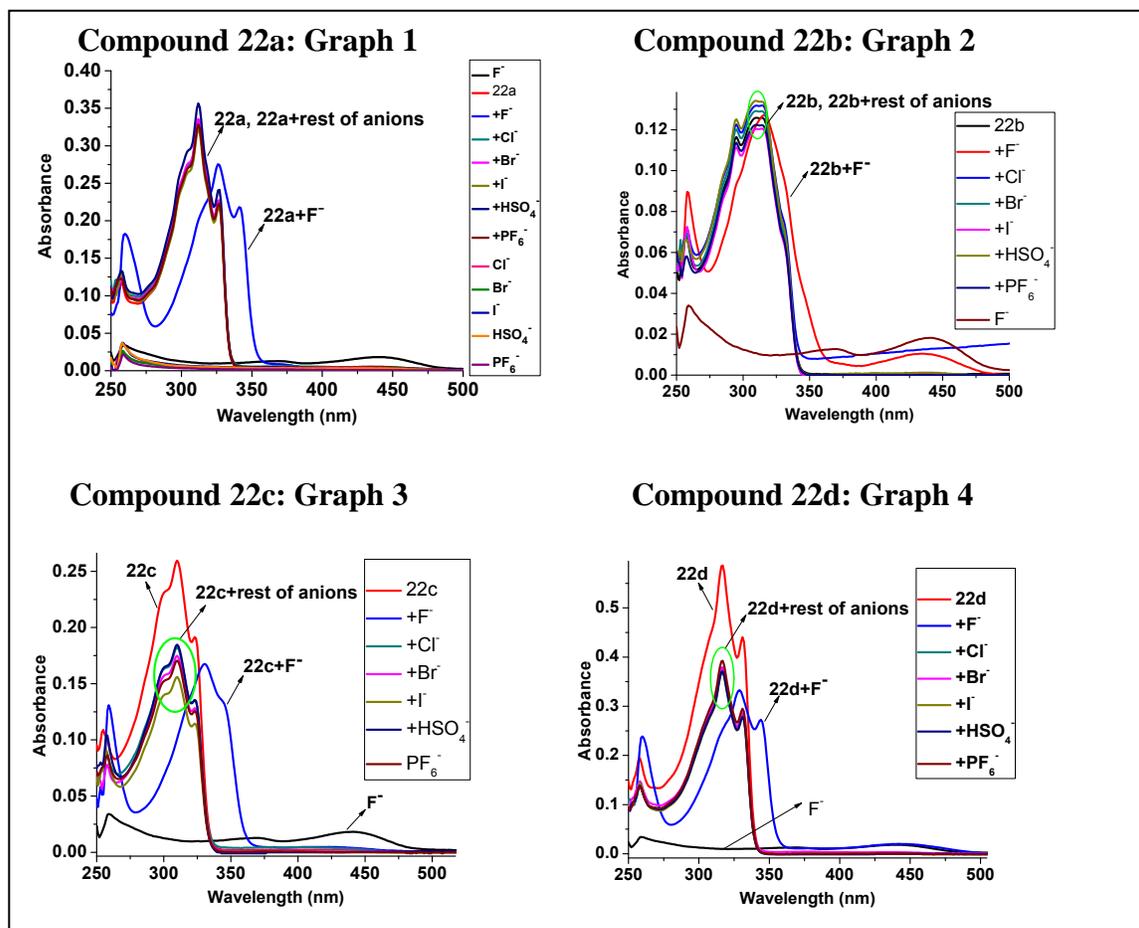
Figure 11 *UV-Visible spectra of compounds 22a-d in presence of anions*

The maximum absorption wavelength of the hosts **22a-d** and the wavelength shift of host-guest solution of $22+F^-$ has been summarized in the following table (Table 5.1.1).

Table 5.1.1 λ_{max} *of compounds 6a-d in absence and in presence of F^- anions*

Sr No.	Sample code	λ_{max} of host (nm)	λ_{max} of host + F^- (nm)
1.	**22a**	313	326, 341
2.	**22b**	311	315
3.	**22c**	309	330, 344
4.	**22d**	316	328, 344

5.2.3 Fluorescence study of C_3 Symmetric tris-benzimidazoles as hosts with anionic guests

Similar results were observed when host-guest interactions were studied with the help of fluorescence spectroscopy. The study was carried out on excitation at λ 300 nm in all the cases. A strong emission band is observed near λ 350 nm for **22a** having 1,4-disubstituted benzimidazole attached phenyl linker. In the presence of F⁻ ions the fluorescence intensity is decreased (Figure 12, Graph 5).
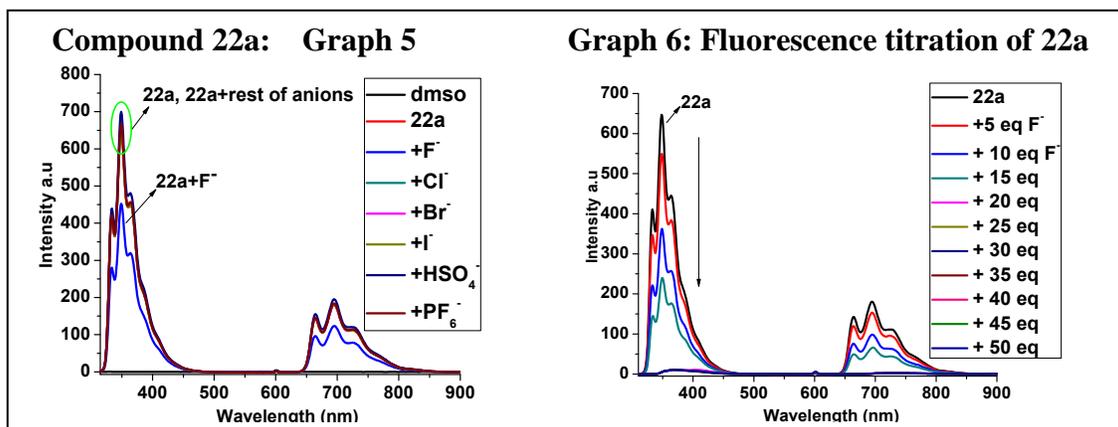

Figure 12 *Fluorescence spectra: Graph 5 = Binding study; 6 = titration study*

The effect of F⁻ ion concentration was studied and was found that fluorescence decreases with the increasing concentration while going from 5 to 15 equivalence and fluorescence gets off at 20 or higher equivalence of the guest concentration. Thus it was discovered that the tris-benzimidazole host molecules selectively recognize F⁻ ions acting as switch–off fluorescent probes (Figure 12, Graph 6).

The compound **6b** having 1,2-disubstituted benzimidazole attached phenyl linker does not bind strongly with F⁻ ions due to intramolecular hydrogen bonding as stated above (Figure 13, Graph 7).
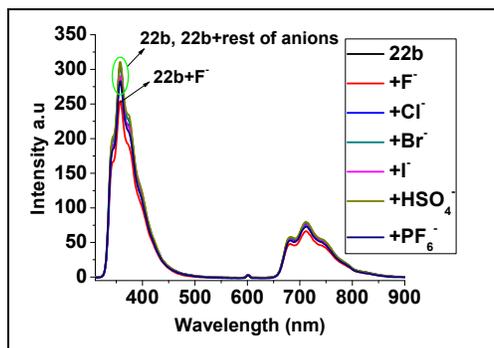

Figure 13 *Graph 7-Fluorescence spectra of compound 22b*

Similar fluorescence study spectra for host **22c** and **22d** showing binding study and titration against F⁻ are presented in the figure (Figure 14, Graphs 8- 11)
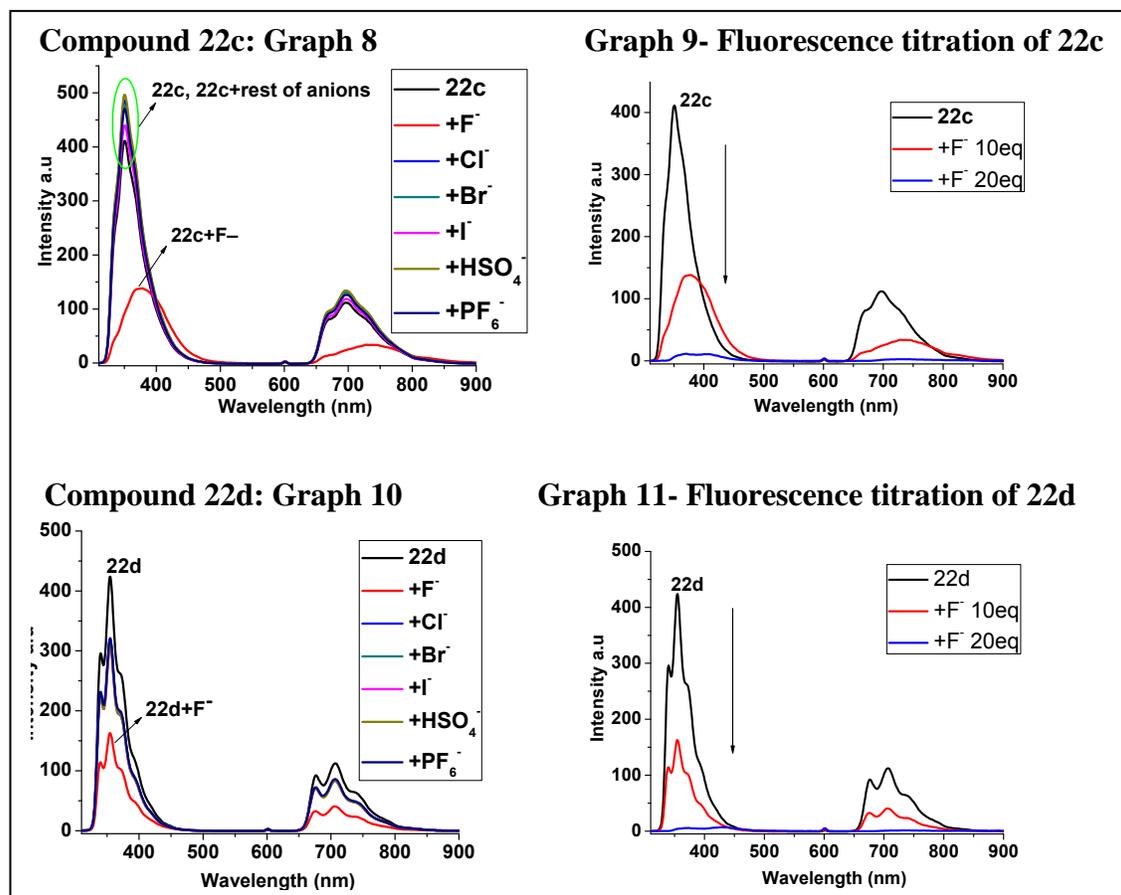

Figure 14 *Fluorescence spectra of hosts 22c and 22d presenting binding study and titration study*

The maximum emission wavelength of host-guest solution of **6+F⁻** has been summarized in the following table (Table 5.1.2).

Table 5.1.2 λ_{max} *of compounds 6a-d in presence of F⁻ anions*

Sample code	λ_{max} of host in presence of F⁻ (nm)
22a	348
22b	358
22c	351
22d	354

5.2.4 Recognition study by ^{1}H NMR titration of host molecules with F[-] anionic guest species

With the positive results from UV–vis and fluorescence study of host-guest interactions, ^{1}H NMR titrations were carried out to study the effect of F[-] anion binding on chemical shift values of proton NMR signals of the host molecules.

^{1}H NMR titrations are useful to observe host-guest interactions between H-donor host molecules and electron rich guest anions as was reported in literature.[25] Deprotonation of N–H proton on addition of guest, induces *through-bond* propagation of electronic charge onto the aromatic framework causing upfield shifts of the respective aromatic ring protons. With entering of fluoride ions, *through space effects* are also operative, it polarizes the closest C–H protons inducing a downfield shift on the affected protons.

Thus ^{1}H NMR titrations were designed by varying the concentration of guest species with respect to the tripodal host concentration. The titration study was carried out only for F[-] anion as the other anions did not show any effect during their study using UV-vis and fluorescence spectroscopy as visualizing tools.

^{1}H-NMR titrations were carried out by dissolving a weighed amount of the host **22a** in DMSO-d_6 and adding a solution of the guest TBAF in the same solvent, starting from 1.0 equivalence and step wise increasing the guest ratio as was planned keeping the earlier results in mind. A significant change was observed in the aromatic region with a change in chemical shifts of all the signals and broadening of the aromatic proton near to nitrogen of the benzimidazole moiety indicating the binding site in the host molecule (Figure 15). On increasing the quantity of guest to 2.0 equivalents, all the aromatic signals are broadened and two nearby aromatic signals around δ 7.2 (Hc and Hd) from different aromatic rings merge. On increasing the concentration of guest to 3.0 and 4.0 equivalents, the broad nature of the aromatic signals is retained with greater effect on the most downfield aromatic signal (δ 8.2, Ha) shifting further downfield to (δ 8.4). There is a distinct change when the guest concentration is increased to 5.0 equivalents with the two merged aromatic signals separating out (near δ 7.1) because of the upfield shift of only one of them (benzimidazole proton Hd) and no further downfield shift of the most downfield signal (Ha) was observed. With further increase in the concentration of guest

anions from 6.0 to 20.0 equivalents, both the benzimidazole aromatic protons (Hb and Hd) kept on moving upfield because of host and anion guest binding which increased the electron density in the interacting benzimidazole ring (Figure 15).
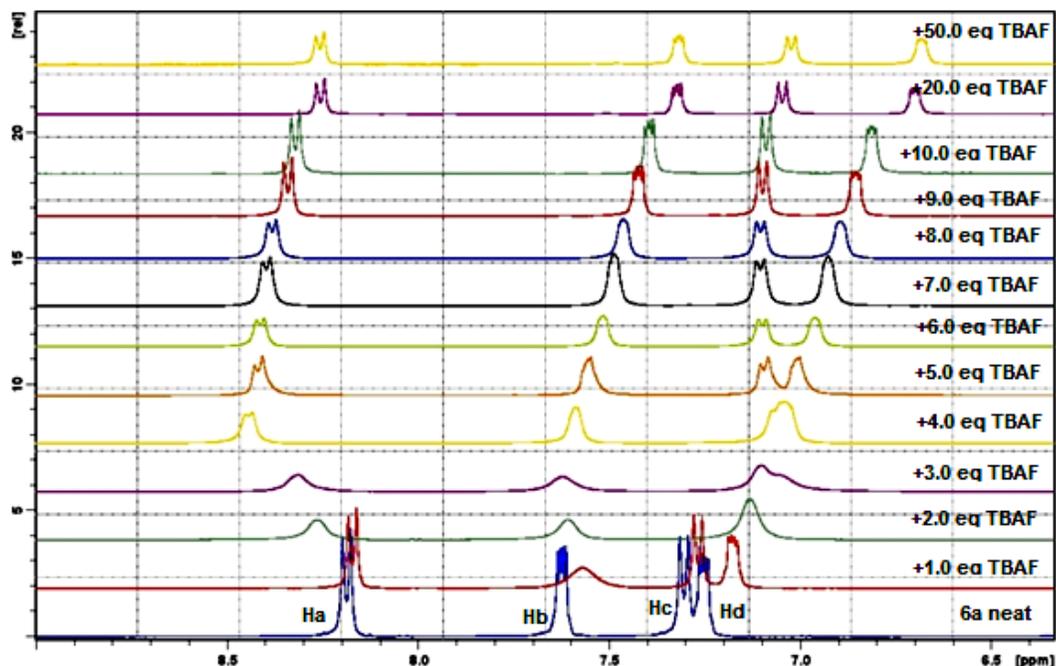

Figure 15 *Expanded ^{1}H NMR spectra of compound 22a upon titration with F$^-$*

Compared to 20.0 equivalents of the guest concentration, no further change in the chemical shifts of protons when a concentration of F$^-$ anions was increased to 50.0 equivalents as was expected based on the results from the fluorescence study (Figure 15).

The host-guest titrations for hosts **22b-d** were also conducted for the other tripodal host molecules in the presence of 10.0 and 20.0 equivalents of the F$^-$ ion concentration based on the pilot study results with the host **22a**.

Similar upfield and downfield chemical shifts were also observed in the host molecules **22b-d**. The number of magnetically non-equivalent protons was more in these compounds due to the presence of non- symmetric linker phenyl rings. The effect on these protons varied from host to host as shown in figures below (Figures 16-18).

Contrary to the UV and fluorescence study observations for **22b**, ^{1}H NMR titration of **22b** showed an observable effect on chemical shift of some of the aromatic protons (Figure 16).
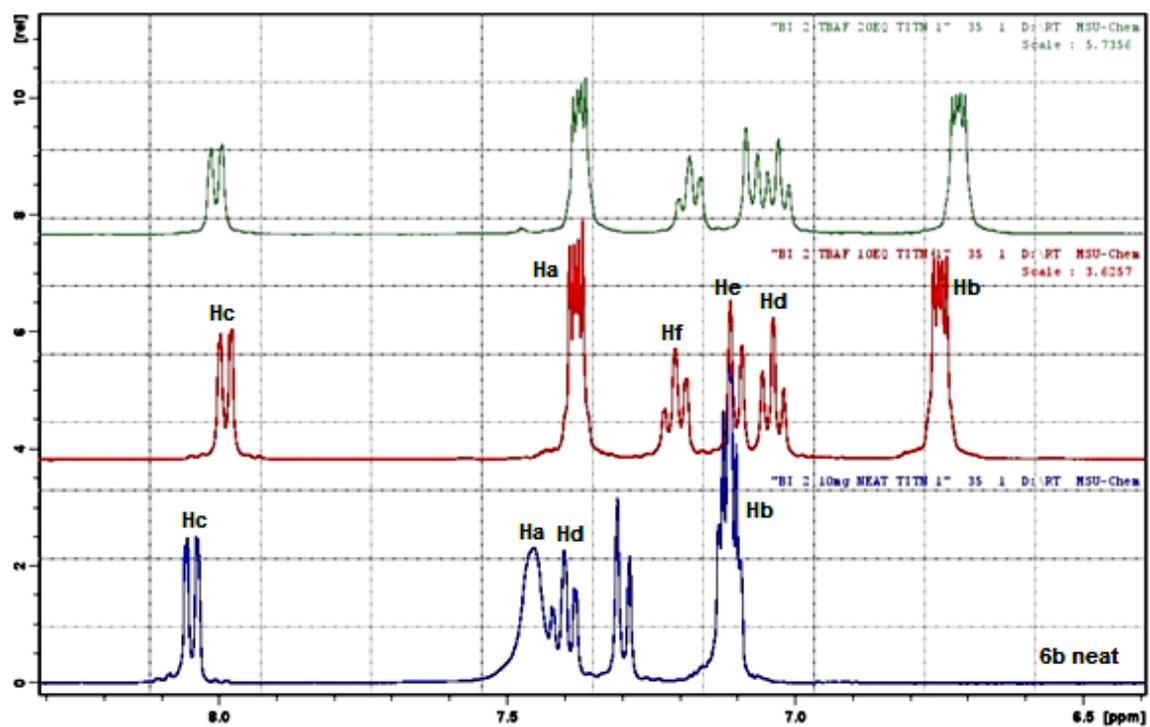
Figure 16 Partial ^{1}H NMR spectra of compound 22b upon titration with F^-

It was observed from the ^{1}H NMR titration experiments of compound **22b** that there was similar phenomenon of proton shifts as in case of **22a** upon addition of TBAF.
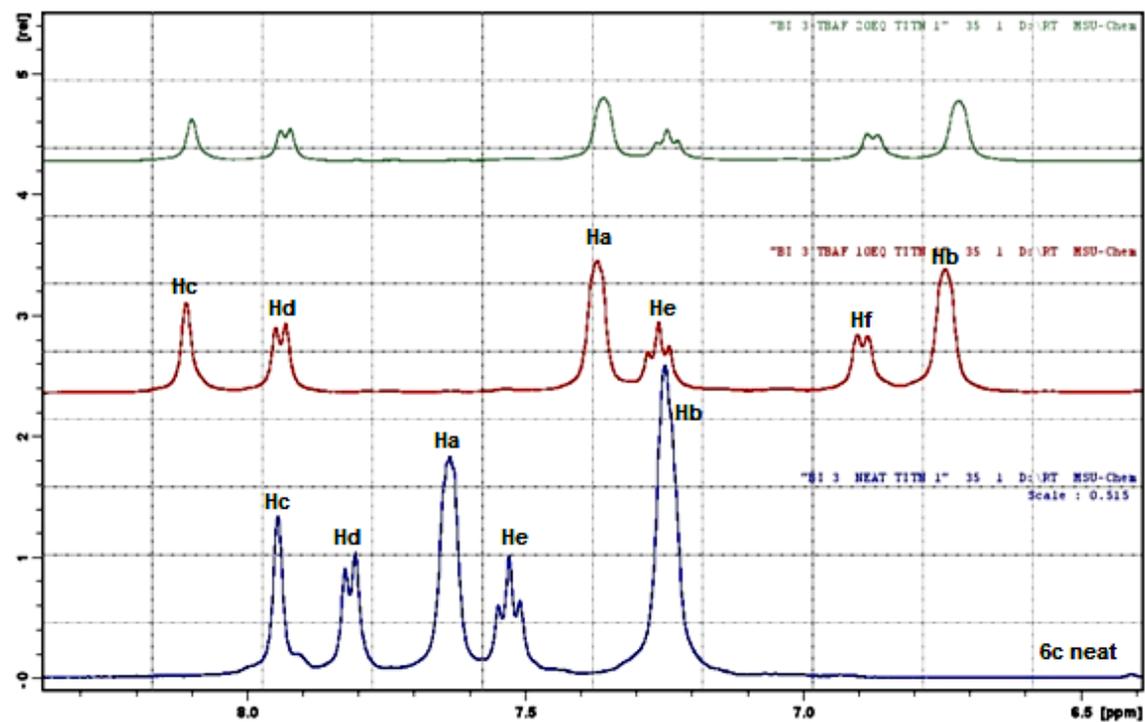

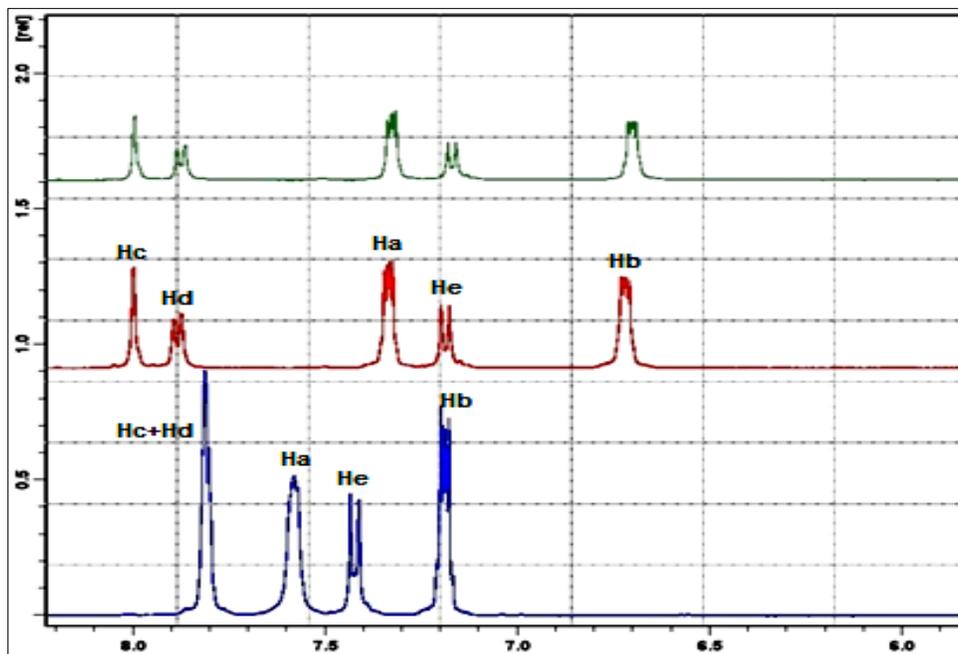**Figure 17 Partial ^{1}H NMR spectra of compound 22c upon titration with F^-**

Figure 18 *Expanded ^1H NMR spectra of compound 22d upon titration with F^-*

5.2.5 Antimicrobial Evaluation of tris-benzimidazolyl derivatives

The tris-benzimidazole tripodal supramolecules were screened for their antimicrobial acitivity against *S. aureus*, a Gram +ve bacterium and *E. coli*, a Gram –ve bacterium using Resazurin Microtitre Assay (REMA) plate method following the methodology as described in Chapter II.

The bioactivity results are summarized in the table (Table 5.1.3).

Table 5.1.3 *Antimicrobial evaluation data of newly synthesized tris-benzimidazoles*

Compound ID	MIC µg/ml	
	S. aureus	*E. coli*
22a	>125	inactive
22b	>125	inactive
22c	125	inactive
22d	125	inactive

The tested compounds showed a poor antimicrobial activity, with compound **22c** and **22d** having minimum inhibition concentration as high as 125 µg/ml against *S. aureus* while **22a** and **22b** did not show any inhibition even at the same concentration.

5.3 CONCLUSION

The new C_3 symmetric tris(1,3–benzimidazol–2–yl) derivatives were synthesized on threefold cyclocondensation of *o*-phenelyenediamine (OPD) with the tris-formyl key intermediates under oxidative reaction conditions. The tripodal compounds were characterized by various spectroscopic techniques. One of the final compounds was crystallized to get suitable crystals for single crystal X–ray analysis which gave insight on the arrangement of all the tripods coming together on one face. Host-guest binding study using fluorescence spectroscopic technique revealed the selectivity in binding of fluoride ions resulting in quenching of the fluorescence. UV-Vis spectral study also indicated the fluoride ion selectivity for the host molecules except for **22b**. ^{1}H-NMR titrations threw more light on the host-guest interactions with the effect on the chemical shift values of aromatic protons of the tripodal host compounds. Thus the tris-benzimidazoles were found to be good hosts for fluoride anions based on the various binding studies. The anti-microbial screening results showed that the tripodal benzimidazoles have a poor inhibitory activity against the bacteria studied.

5.4 EXPERIMENTAL

5.4.1 1,3,5-Tris[n-(1,3-benzimidazol-2-yl)-phenyloxymethyl]-2,4,6-trimethylbenzene 22
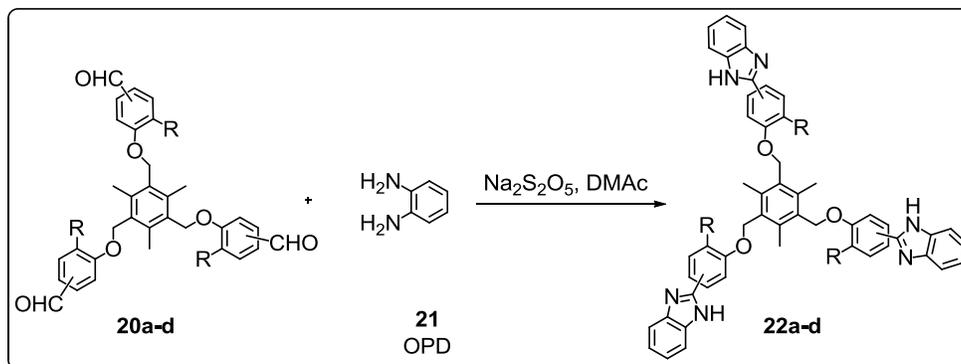
General procedure

In a 2-necked round bottom flask (100 ml) containing a mixture of *o*-phenylenediamine OPD **21** (0.61 mmol) and sodium metabisulfite (Na$_2$S$_2$O$_5$) (0.61 mmol) in DMAc (50-100 ml) was added a DMAc solution of a tris-aldehyde **20** (0.1 g, 0.19mmol) dropwise over a period of 10 min at 100 °C temperature. On the completion of the reaction (TLC), the reaction mixture was concentrated under reduced pressure, the concentrated solution was poured into cold water. Separated solid was filtered and dried to get a crude product which was purified by crystallization with ethanol/methanol technique.

1,3,5-Tris[4-(1,3-benzimidazol-2-yl)-phenyloxymethyl]-2,4,6-trimethylbenzene (22a)
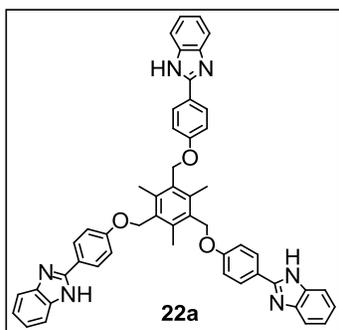
22a was prepared from **20a** (0.1 g, 0.19 mmol), **21** (0.068 g, 0.61 mmol) and Na$_2$S$_2$O$_5$ (0.12 g, 0.61 mmol) following the general procedure described above as a white solid from ethanol. Yield: 0.13 g, 82%; mp: 245 °C (decompose).

IR (KBr) : 3424, 1609, 1495, 1451, 1437, 1241, 1177 cm^{-1}; **^{1}H NMR (DMSO-*d6*) :** δ (ppm) 2.41 (9H, s, –CH$_3$), 5.23 (6H, s, –OCH$_2$–), 7.24-7.26 (6H, dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz), 7.29-7.31 (6H, d, J = 8.8 Hz), 7.61-7.63 (6H, dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz), 8.17-8.19 (6H, d, J = 8.8 Hz); **^{13}C NMR (DMSO-*d6*) :** δ (ppm) 16.1 (–CH$_3$), 65.6 (–OCH$_2$–), 115.0, 115.6, 121.9, 123.0, 128.9, 131.7, 138.4, 139.6, 151.3 (–C=N), 161.1 (Ar-O);

Mass (TOF MS ES+): calculated for $C_{51}H_{42}N_6O_3$: 786.9176 *m/z*, found 787.3478 *m/z* ((M+H)$^+$, 60%), 809.3306 *m/z* ((M+Na)$^+$, 30%), 810.3323 *m/z* ((M+Na+H)$^+$, 10%), 240.9900 (100%).

1,3,5-Tris[2-(1,3-benzimidazol-2-yl)-phenyloxymethyl]-2,4,6-trimethylbenzene (22b)
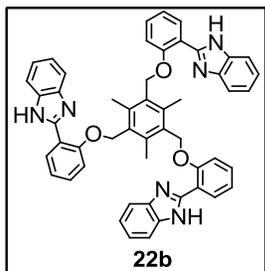

22b was prepared from **20b** (0.1 g, 0.19 mmol), **21** (0.068 g, 0.61 mmol) and $Na_2S_2O_5$ (0.12 g, 0.61 mmol) following the general procedure described earlier as a white crystalline solid from *iso*-propylalcohol+ethanol mixture. Yield 0.1 g, 69%; mp: 168 °C.

IR (KBr) : 3422, 1604, 1582, 1469, 1228, 749 cm^{-1}; **^{1}H NMR (DMSO-*d6*) :** δ (ppm) 2.26 (9H, s, –CH$_3$), 5.16 (6H, s, –OCH$_2$–), 7.10-7.13 (9H, m), 7.29-7.31 (3H, d, *J* = 8.0 Hz), 7.38-7.41 (3H, d, *J* = 8.0 Hz), 7.42-7.44 (6H, dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz); **^{13}C NMR (DMSO-*d6*) :** δ (ppm) 16.2 (–CH$_3$), 67.5 (–OCH$_2$), 115.2, 116.0, 119.2, 122.2, 123.1, 131.0, 131.4, 132.4, 137.5, 139.5, 149.1 (–C=N), 156.7 (Ar-O); **Mass (TOF MS ES+):** calculated for $C_{51}H_{42}N_6O_3$: 786.9176 *m/z*, found: (*m/z*) 787.3478 ((M+H)$^+$, 70%), 809.3306 ((M+Na)$^+$, 100%), 810.3323 ((M+Na+H)$^+$, 60%) 825.3019 ((M+2Na+3H)$^+$,40%).

### 1,3,5-Tris[3-(1,3-benzimidazol-2-yl)-phenyloxymethyl]-2,4,6-trimethylbenzene (22c)
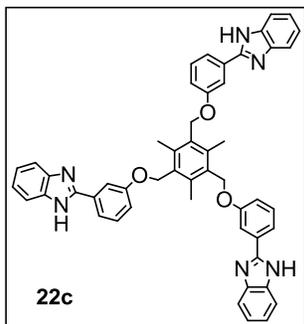
22c was prepared from **20c** (0.1 g, 0.19 mmol), **21** (0.068 g, 0.61 mmol) and $Na_2S_2O_5$ (0.12 g, 0.61 mmol) following the general procedure as described giving colorless solid. Yield 0.12 g, 76%, mp: 220 °C.

IR (KBr) : 3435, 2926, 1630, 1606, 1490, 1459, 1231, 1013, 748 cm^{-1}; **^{1}H NMR (DMSO-*d6*) :** δ (ppm) 2.47 (9H, s, –CH$_3$), 5.32 (6H, s, –OCH$_2$–), 7.36-7.38 (3H, d, *J* = 8.0 Hz), 7.41-7.43 (6H, dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz), 7.62 (3H, t, *J* = 8.0 Hz), 7.76-7.78 (6H, dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz), 7.82-7.83 (3H, d, *J* = 7.6 Hz), 7.99 (3H, s); **^{13}C NMR (DMSO-*d6*) :** δ (ppm) 16.1 (–CH$_3$), 65.7 (–OCH$_2$), 113.4, 115.0, 119.1, 120.3, 124.8, 131.2, 131.7, 135.5, 139.6, 150.2 (–C=N), 159.7 (Ar-O); **Mass (TOF MS ES+):**

calculated for $C_{51}H_{42}N_6O_3$: 786.9176 m/z, found: (m/z) 787.3420 ((M+H)$^+$, 80%), 809.3306 ((M+Na)$^+$, 60%), 701.4998 (100%).

1,3,5-Tris[2-methoxy-4-(1,3-benzimidazol-2-yl)-phenyloxymethyl]-2,4,6-trimethyl benzene (22d)
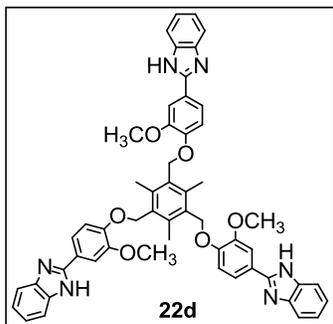
22d was prepared from **20d** (0.1 g, 0.19 mmol), OPD **21** (0.056 g, 0.61 mmol) and $Na_2S_2O_5$ (0.1 g, 0.61mmol) following the general procedure as described earlier giving white solid. Yield: 0.1 g, 67%, mp: 265 °C.

IR (KBr) : 3408, 2939, 1631, 1605, 1503, 1461, 1264, 746 cm^{-1}; **^{1}H NMR (DMSO-*d6*)** **:** δ (ppm) 2.41 (9H, s, –CH$_3$), 3.89 (9H, s, –OCH$_3$), 5.24 (6H, s, –OCH$_2$–), 7.29-7.32 (6H, dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz), 7.47-7.50 (6H, d, J = 8.8 Hz), 7.66-7.68 (6H, dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz), 7.83-7.85 (6H, d, J = 9.8 Hz); **^{13}C NMR (DMSO-*d6*)** **:** δ (ppm) 16.0 (–CH$_3$), 56.0 (–OCH$_3$), 66.0 (–OCH$_2$), 110.3, 113.8, 119.7, 122.3, 123.6, 131.8, 139.7, 149.8, 150.2 (–C=N), 151.8 (Ar-O); **Mass (TOF MS ES+):** calculated for $C_{54}H_{48}N_6O_6$: 876.3635 m/z, found: (m/z) 877.3801 ((M+H)$^+$, 100%), 899.3681 ((M+Na)$^+$, 20%).
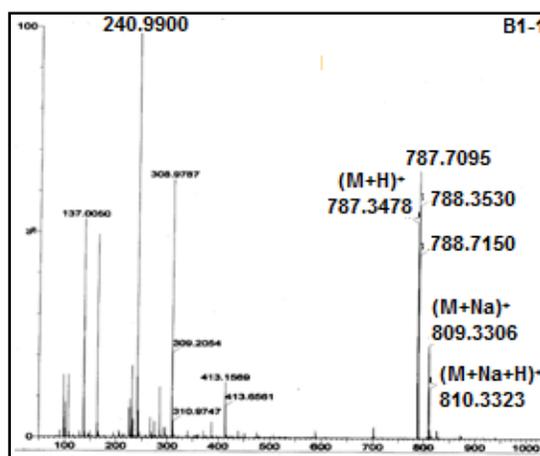
5.5 SPECTRAL DATA
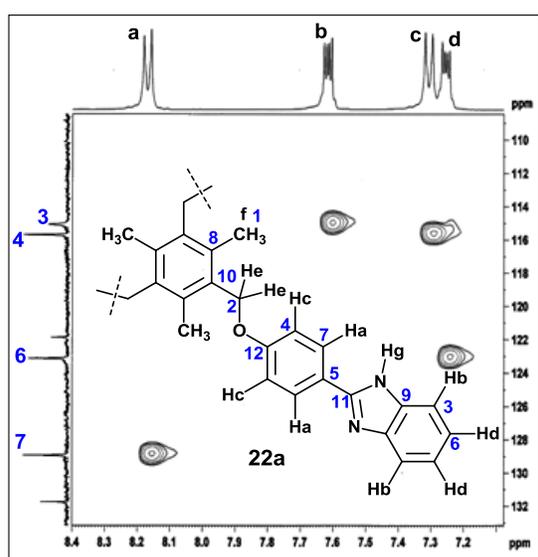
Compound 22a
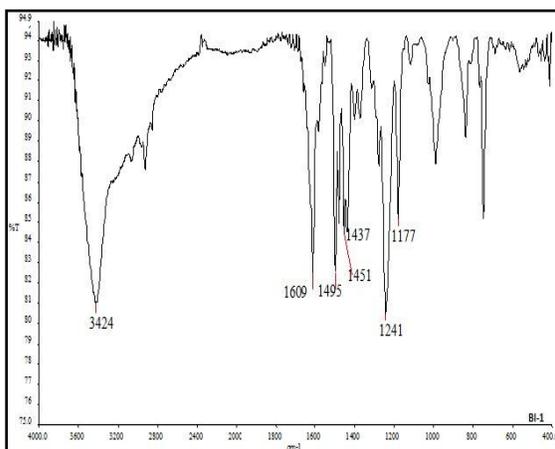
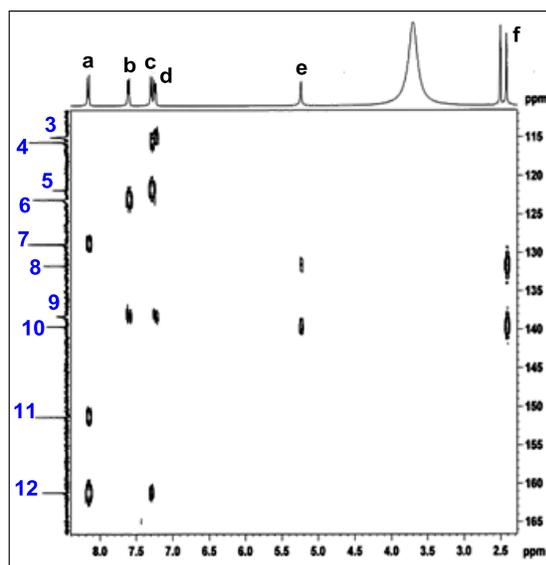Spectrum 1. IR of 22a
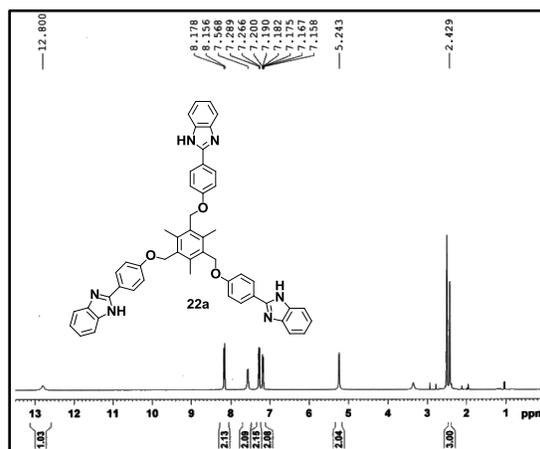
Spectrum 2. ^{1}H NMR of 22a
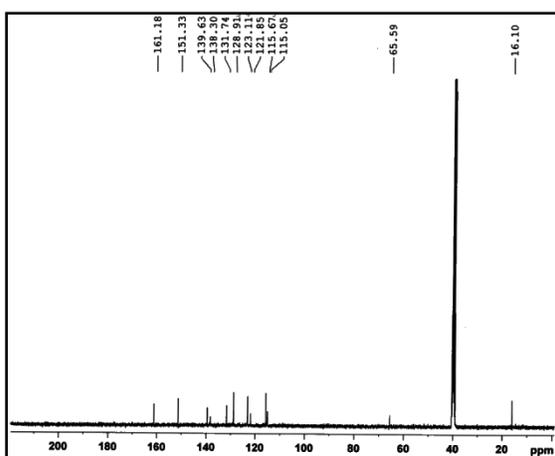
Spectrum 3. ^{13}C NMR of 22a

Spectrum 4. Mass of 22a
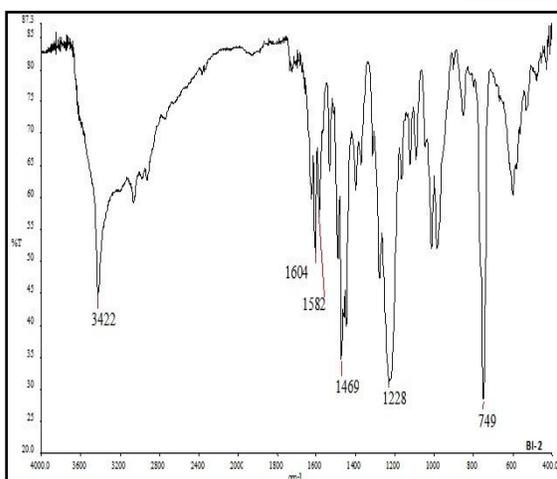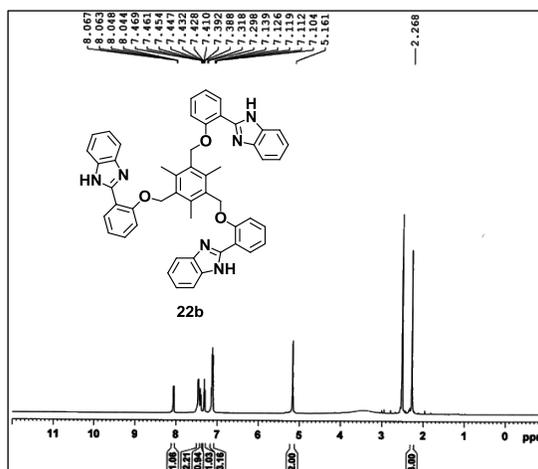

Spectrum 5. HSQC of 22a

Spectrum 6. HMBC of 22a

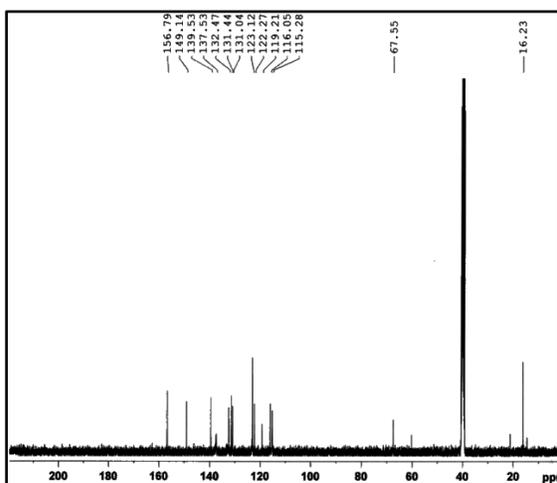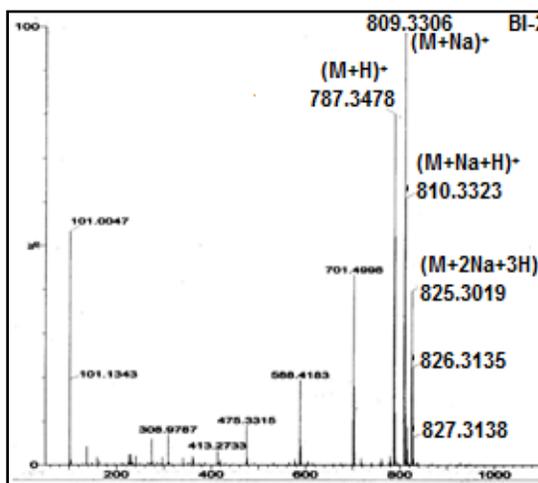## Compound 22b

Spectrum 7. IR spectrum of 22b
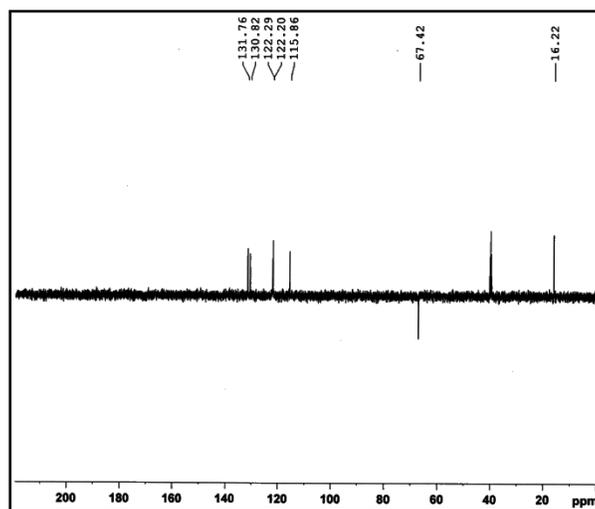

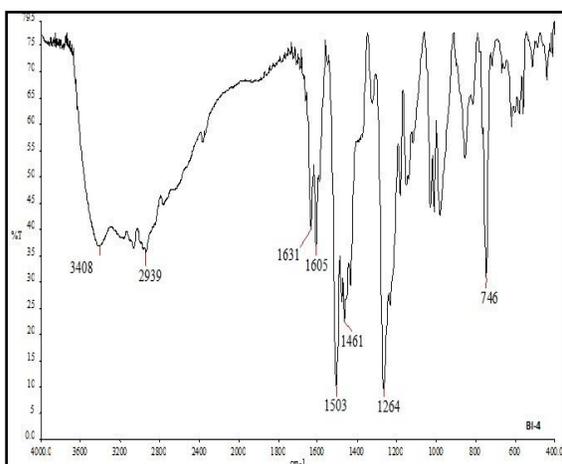Spectrum 8. ^{1}H NMR of 22b

Spectrum 9. ^{13}C NMR of 22b

Spectrum 10. Mass of 22b

Spectrum 11. DEPT135 of 22b

Compound 22c

Spectrum 12. IR of 22c

Spectrum 13. ¹H NMR of 22c

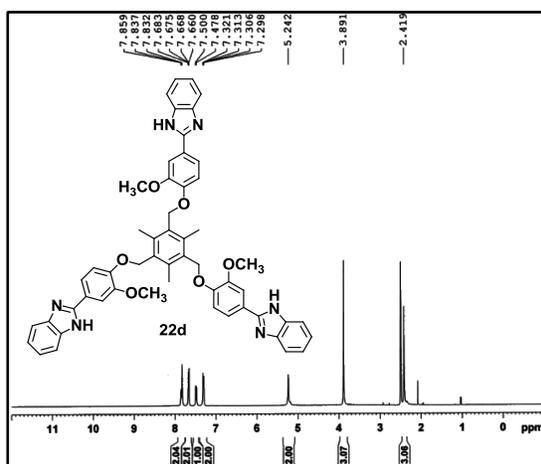**Spectrum 14. ¹³C NMR of 22c**

Spectrum 15. Mass of 22c

Spectrum 16. DEPT of 22c

Compound 22d

Spectrum 17. IR of 22d

Spectrum 18. ^{1}H NMR of 22d
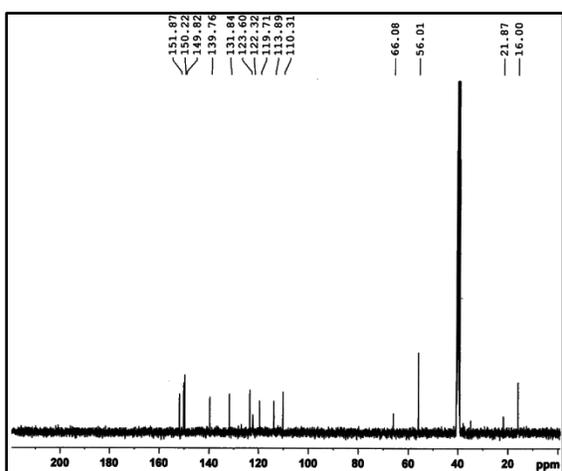
Spectrum 19. ^{13}C NMR of 22d
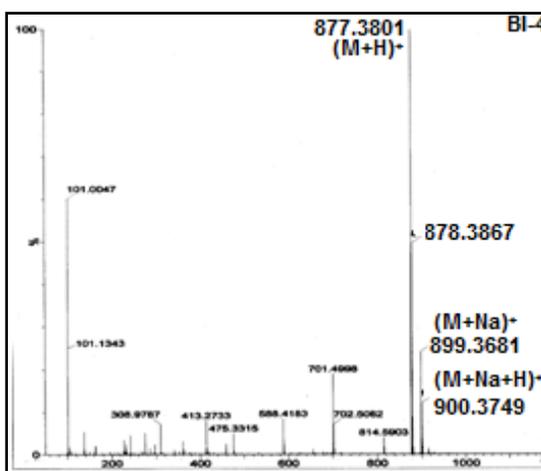
Spectrum 20. Mass of 22d
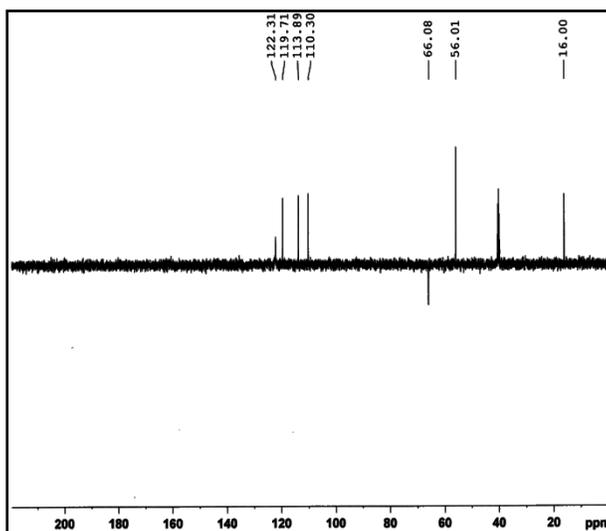
Spectrum 21. DEPT135 of 22d

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