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SYNTHESIS, CHARACTERIZATION AND ANTIOXIDANT ACTIVITY OF NOVEL 26-MEMBER RING [2+2] MACROCYCLES FROM DIAMINE DERIVATIVE AND TEREPHTHALDEHYDE

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ABSTRACT

Schiff base macrocycles play a significant role in living organisms with a broad range of pharmaceutical activities. In the present study, a novel series of 26 member macrocyclic compounds were synthesized via recombination of novel diamine and terephthaldehyde. A variety of triaryl diamine derivatives react with terephthaldehyde to efficiently result in a [2+2] macrocyclic Schiff base compounds. The newly synthesized compounds were characterized by UV, IR, NMR and Mass and further confirmed by single crystal x-ray diffraction analysis. The antioxidant activity of all the synthesized compounds were tested by Reducing power activity. The compounds were screened at different concentrations from 50-250 (µg/ml) to check the absorbance of compounds. Among seven macrocycle compounds, compound 4f showed highly significant activity. The result shows that as the concentration of compound increase, the compound showed high significant activity.

Keywords: Macrocycle, Schiff base, Triarylmethanes, Terephthaldehyde, Cyclic imide, 2+2 cyclo addition, Anti-oxidant activity.

1. INTRODUCTION

Schiff-base macrocycles have been of great importance in macrocyclic and supramolecular chemistry. Numerous recent review articles have discussed the role that macrocycles can play in medicinal chemistry, in particular looking beyond the established importance of natural product macrocycles in drug discovery [1-3]. Drug-like macrocycles have received increasing interest over the past few years, since it has been demonstrated that macrocyclization can favourably alter the biological and physiochemical properties as well as selectivity [4,5].

Triarylmethanes are known to possess a wide range of biological activities such as antitumor [6], antifungal [7], antiinflammatory [7], antiviral [8], antioxidant [9], antitubercular [10] as well as anti-diabetes [11]. Macrocyclic schiff base with triarylmethane are one opportunity to expand the synthetic toolbox for medicinal chemistry to provide bioactive molecules.

Furthermore, Macrocyclic compounds have been studied extensively for their applications in molecular recognition, host-guest chemistry, supramolecular structures, material chemistry and catalysis. In this regard, structural features of the macrocycles (such as functionalities for the binding of guest molecules and tunable central cavities) are particularly significant [12-18].

Therefore we plan to design macrocycles containing triarylmethane moiety, which may solve recent burden of antioxidant and fulfill the crises. We have synthesized $1^4,1^5,3^4,3^5,9^4,9^5,11^4,11^5$-octamethoxy-2,10-bis(4-methoxyphenyl)-4,8,12,16-tetraaza-1,3,9,11(1,2),6,14(1,4)-hexabenzenacyclohexadecaphane-4,7,12,15-tetraene **(4a-4g)** derivatives and evaluated for antioxidant potential. The synthesized compounds ***4a-4g*** and their intermediates were characterized by UV, IR, NMR and Mass and further confirmed by single crystal x-ray diffraction analysis.

2. MATERIAL AND METHODS

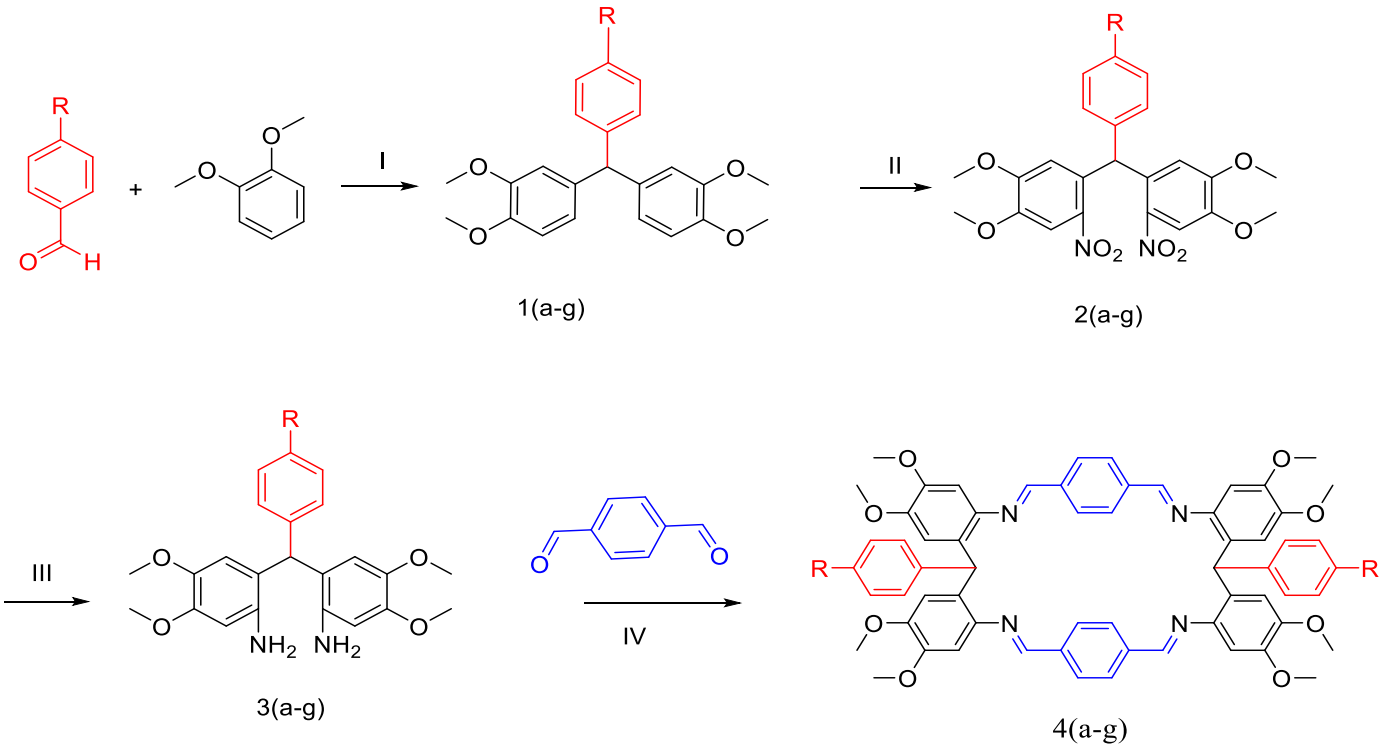
The reagents were purchased from Aldrich and used without further purification and solvents were purchased from commercial suppliers and used without further purification. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker Avance instrument in $CDCl_3$ and DMSO and using TMS as an internal standard, operating

at 300 MHz and 75 MHz, respectively. Chemical shifts (δ) are expressed in ppm and coupling constants *J* are given in Hz. For $CDCl_3$ or DMSO-*d6* solutions, the chemical shifts are reported as parts per million (ppm) to residual protium or carbon of the solvents; $CHCl_3$δH (7.26 ppm) and $CDCl_3$δC (77.03 ppm); DMSO δH (2.51ppm) and DMSO-*d6* δC (39.52ppm). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet. UV-vis spectra were recorded between 200 to 800 nm on Shimadzu (1650) UV-VIS spectrophotometer using CH_2Cl_2 as solvent. IR spectra were collected neat in the solid state on a Bruker Spectrum-1. Melting points were obtained on a Melting point instrument. LC-MS spectra were obtained on Thermoscientific LTQ Xcallibur 2.2 LCMS spectrometer equipped with an ESI source.

2.1. Synthesis of Macrocycles 4(a-g)

The first step is the Friedel Craft's acylation reaction of veratrole (1,2-dimethoxy benzene) with benzaldehyde in a ratio of 2:1 in presence of sulfuric acid at less than 5°C. During sulfuric acid addition, the reaction mass temperature was maintained below 5°C and then stirred for 16 hours at 25-30°C. Rate of the reaction was varied based on electron donating groups and electron withdrawing groups at *para*-position of benzaldehyde. This same condensation reaction did not yield triaryl compound for 4-hydroxybenzaldehyde, 4-methoxy benzaldehyde, polycyclic aromatic aldehydes, including pyrene-1-carboxaldehyde, 1- and 2-naphthaldehyde [19-21]. The same was observed when heterocyclic aldehydes (thiophene-2-carboxaldehyde, 4-pyridinecarboxaldehyde, 4,6-dichloropyrimidine- 5-carboxaldehyde) were used [22]. In the case of 4-methoxybenzaldehyde, Amberlite 15 resin was used for condensation at 120 to 130°C [23].

The second step is the nitration, using a mixture of nitric acid and acetic acid. Nitration occurred at the *para*-position of methoxy group using slow addition of nitric acid and acetic acid mixture at a temperature of 15 to 20°C. The desired conversion was achieved in all cases.



R= OCH_3, CH_3, CH_2CH_3, H, Cl, $COOCH_3$,COOH.

I) Sulfuric acid at 0-5°C, RT.
II) Nitric acid, Acetic acid at 15-20°C,
III) Raney nickel, methanol, ethyl acetate, 50°C.
IV) Methanol at 60-65°C

The third step is the reduction of nitro group using Raney nickel. This reaction was performed with a mixture of methanol and ethyl acetate as solvent at 50°C using Raney nickel catalyst under hydrogen pressure. For a majority of the cases, the reaction was completed within 3 hours.

The fourth step was Schiff base formation followed by the cyclization reaction. Diamine reacted with terephthaldehyde in methanol with a ratio of 1:1 at 60 to 65°C afforded [2+2] macrocyclic tetraimine with moderate to good yields. The cyclocon-densation does not require any anhydrous or dilute reaction conditions for the macrocycle synthesis. It required more than 10 hours for complete cyclization. Once completed, a yellow coloured solid isolated and any impurities were removed by crystallization using ethyl acetate.

The cyclized product was confirmed by UV, IR, NMR and Mass. A strong band at 1620-1624cm^{-1} in IR spectrum of the Schiff base is assigned to C=N of macrocycles. All intermediates and final compounds yield, description and melting point details are tabulated in table 1.

Macrocyclic compound (4d) was recrystallized using ethyl acetate. This crystalized solid was further confirmed by single crystal x-ray diffraction analysis. (CCDC No: Deposition Number 2089285). An ORTEP diagram of macrocycle thermal ellipsoids are shown at the 50% probability level as seen in fig.1. Packing diagram of molecule and dash lines indicates intermolecular interactions shown in fig. 2. Crystal data and refinement details are mentioned in table 2.

Table 1: Yield and Melting range of all stages

Compound Number	Substituent (R)	Yield (%)	Melting range(°C)	Description
1a	-OCH_3	70	84-86	Off white solid
1b	-CH_3	86	134-136	Off white solid
1c	-CH_2CH_3	85	114-117	Off white solid
1d	-H	87	120-122	Off white solid
1e	-Cl	92	148-150	White solid
1f	-$COOCH_3$	80	112-114	Off white solid
1g	-COOH	91	178-180	Off white solid
2a	-OCH_3	75	178-180	Yellow solid
2b	-CH_3	86	158-160	Yellow solid
2c	-CH_2CH_3	85	164-166	Pale yellow solid
2d	-H	80	192-194	Pale yellow solid
2e	-Cl	89	194-196	Pale yellow solid
2f	-$COOCH_3$	80	203-205	Pale yellow solid
2g	-COOH	76	245-247	Yellow solid
3a	-OCH_3	70	196-198	Brown colour solid
3b	-CH_3	73	216-218	Brown colour solid
3c	-CH_2CH_3	85	165-168	Brown colour solid
3d	-H	86	228-231	Brown colour solid
3e	-Cl	70	212-214	Brown colour solid
3f	-$COOCH_3$	65	195-197	Brown colour solid
3g	-COOH	76	242-245	Brown colour solid
4a	-OCH_3	72	> 300	Yellow colour solid
4b	-CH_3	80	> 300	Yellow colour solid
4c	-CH_2CH_3	65	> 300	Yellow colour solid
4d	-H	88	> 300	Yellow colour solid
4e	-Cl	89	> 300	Yellow colour solid
4f	-$COOCH_3$	89	> 300	Yellow colour solid
4g	-COOH	69	> 300	Yellow colour solid

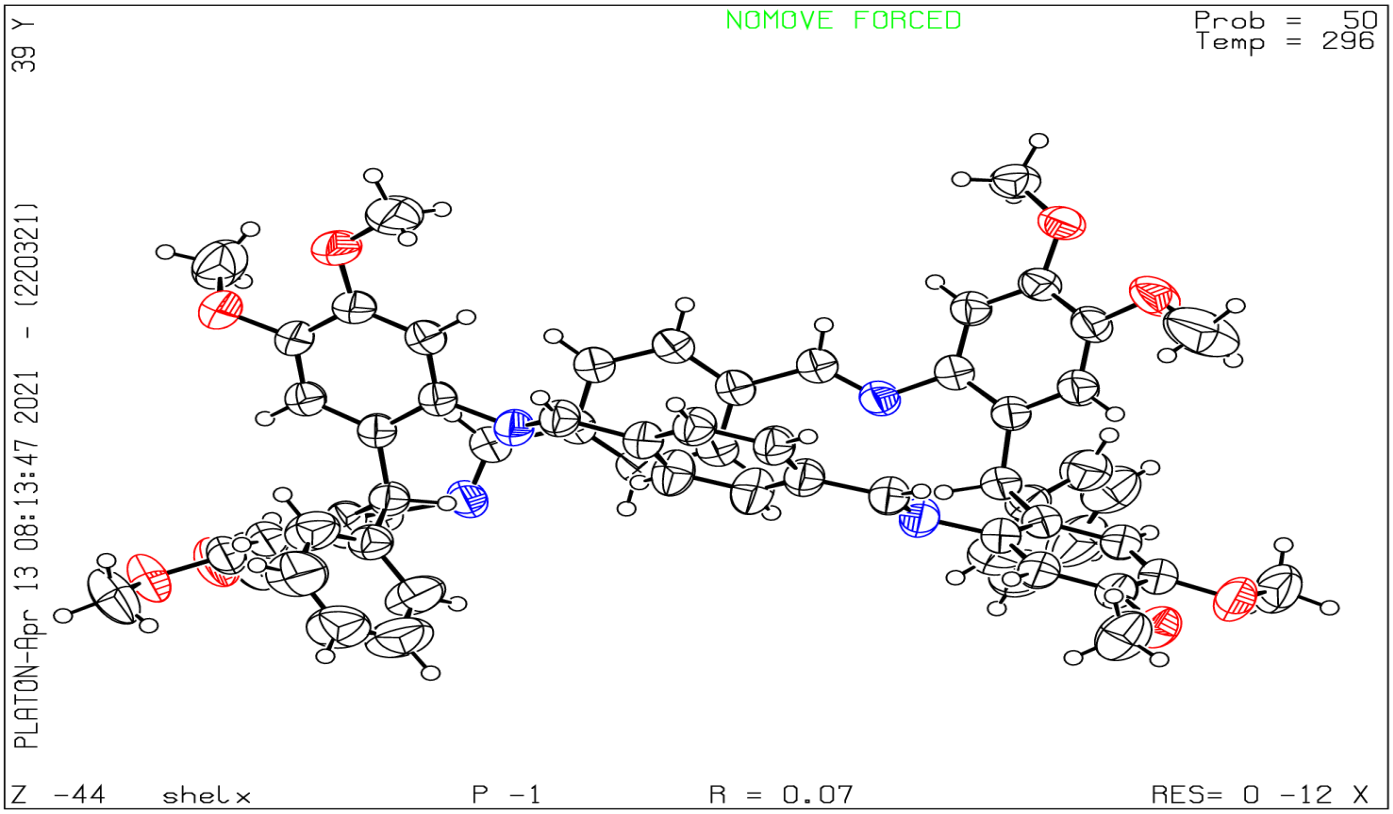


Fig. 1: An ORTEP diagram of macrocycle; thermal ellipsoids are shown at the 50% probability level

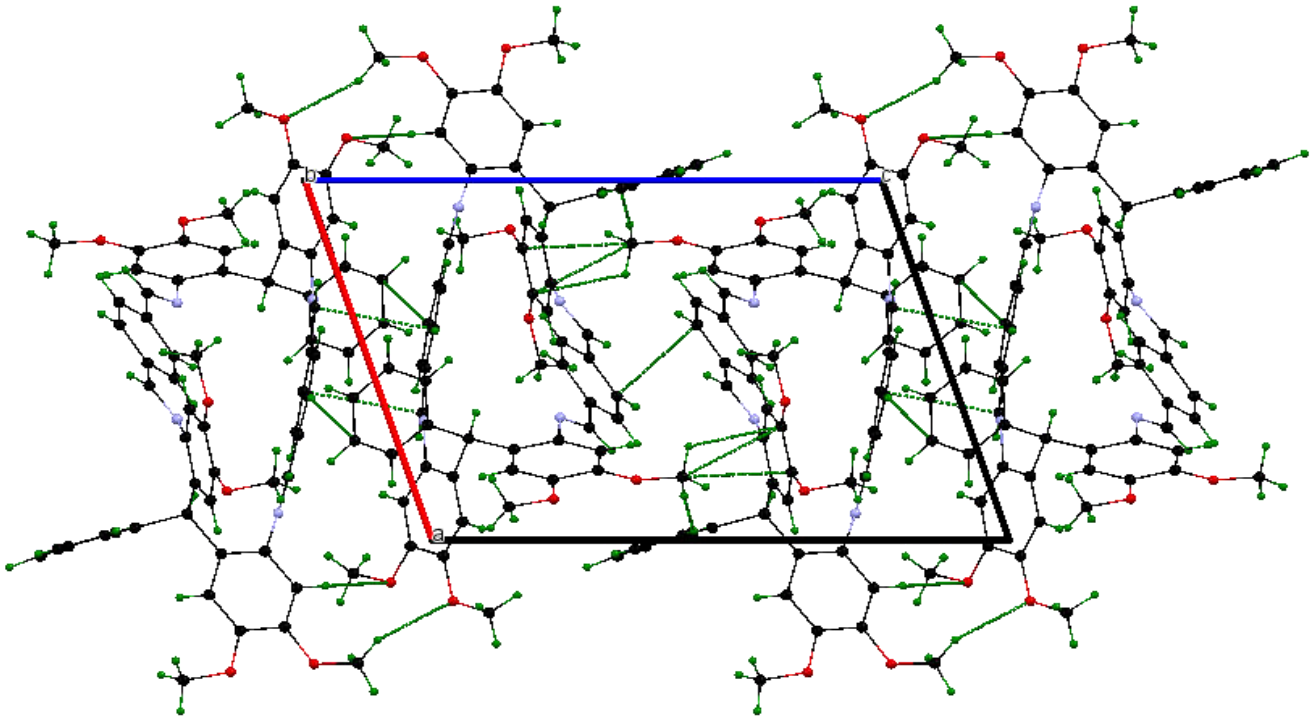


Fig. 2: Packing diagram of molecule and dash lines indicate, intermolecular interactions.

Table 2: Crystal data and structure refinement for compound 4d

Identification code	Shelx	
Empirical formula	$C_{62}\ H_{56}\ N_4\ O_8$	
Formula weight	985.10	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 11.3216(13) Å	a= 82.278(5)°.
	b = 15.6457(18) Å	b= 71.056(5)°.
	c = 16.2284(19) Å	g = 83.951(5)°.
Volume	2688.4(5) $Å^3$	
Z	2	
Density (calculated)	1.217 Mg/m^3	
Absorption coefficient	0.650 mm^{-1}	
F(000)	1040	
Crystal size	0.100 x 0.100 x 0.050 mm^3	
Theta range for data collection	2.856 to 69.721°.	
Index ranges	-13<=h<=13, -18<=k<=19, -19<=l<=18	
Reflections collected	72157	
Independent reflections	9949 [R(int) = 0.0686]	
Completeness to theta = 67.679°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7431 and 0.6036	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9949 / 0 / 676	
Goodness-of-fit on F^2	1.047	
Final R indices [I>2sigma(I)]	R1 = 0.0662, wR2 = 0.1727	
R indices (all data)	R1 = 0.0983, wR2 = 0.2206	
Extinction coefficient	0.0069(6)	
Largest diff. peak and hole	0.342 and -0.296 e.$Å^{-3}$	

2.1.1. Synthesis of 4, 4'-((4-methoxyphenyl) methylene)bis(1,2-dimethoxybenzene)(1a)

To a stirred solution of 4-methoxy benzaldehyde (10.0g, 0.073 mol) and 1,2-dimethoxy benzene (50.7g, 0.367 mol), Amberlite IRA 15 resin (10.0g) was added and stirred for 10 hours at 120-130°C. After completion of the reaction, reaction mass was dissolved in ethyl acetate (200 ml) and spent resin was removed by filtration. After evaporation crude was purified by column chromatography.

2.1.2. General procedure for preparation of 1b-1g

To a stirred solution of substituted benzaldehyde (10.0g, 0.074 mol) and 1,2-dimethoxy benzene (30.9g, 0.223 mol) in dichloromethane (150 ml), sulfuric acid (8.76g, 0.089 mol) was added drop wise at 0-5°C. After 1 hour, reaction mass was slowly warmed to room temperature and stirred for 16 hours. Then, distilled water (100 ml) was added slowly and Dichloromethane layer was separated. The dichloromethane layer was washed with 20% sodium carbonate solution (60 ml) followed by distilled water (50 ml) and dried over sodium sulfate and evaporated. The residue was purified by crystallization using hexane.

2.1.3. General procedure for preparation of 2a-2g

To a stirred solution of compoumd-1(a-g) (10.0g, 0.0225 mol) in glacial acetic acid (80.0 ml), nitric acid (70% Soln), 40 ml) was added drop wise at 15-20°C. After 1 hour, reaction mass was slowly warmed to room temperature and stirred for 16 hours. Then, reaction mass was quenched in ice water (400 ml) and the solid was filtered and washed with purified water. The residue was purified by crystallization using methanol.

2.1.4. General procedure for preparation of 3a-3g

To a stirred solution of compound-2(a-g) (8.0g, 0.016 mol) in ethyl acetate (80.0 ml), Raney nickel {4.0g (wet)} was added at 25-30°C. The reaction mass was stirred for 5 hours under 5 Kg hydrogen pressure at 45-50°C. Then, the spent catalyst was removed by filtration and the crude was isolated after evaporation. The residue was purified by crystallization using methanol.

2.1.5. General procedure for preparation of 4a-4g

To a stirred solution of compound-3(a-g) (1.0g, 2.35 mmol) in ethanol (40.0 ml) terephthaldehyde (0.316g, 2.35 mmol) was added. The reaction mass was stirred for 10 hours at 65-70°C and the crystallized solid was filtered and purified using methanol followed by ethyl acetate.

3. RESULTS AND DISCUSSION

3.1. Characterization of compounds (1a-1g)

3.1.1. 4,4'-((4-methoxyphenyl)methylene)bis(1,2-dimethoxybenzene) (1a)

Off white solid; Yield: 70%; M.P:84-86°C;UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 234 and 282nm; IR (KBr disk): 3074(Aromatic CH), 3000-2933(Aliphatic CH), 2833 (Methoxy CH), 1607-1510 (Aromatic C=C), 786, 639 (Methoxy CH) cm^{-1}; ^1H NMR ($CDCl_3$-300 MHz): δ=7.008-7.037(d, J=8.7Hz, 2H), 6.764-6.838(m, 4H), 6.659-6.665(d, J=1.8Hz, 2H), 6.573-6.606(dd, J1=8.1Hz, J2=1.8Hz, 2H), 5.389(s, 1H), 3.852(s, 6H), 3.785(s, 3H) and 3.761(s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=158.0, 148.7, 147.4, 137.1, 136.5, 130.2, 121.3, 119.0, 113.6, 112.7, 110.8, 55.9, 55.8, 55.2 and 55.1; Mass spectrum (LCMS): m/z: 412.18 (M+18) ($C_{24}H_{26}O_5$).

3.1.2. 4,4'-((4-methylphenyl)methylene)bis(1,2-dimethoxybenzene) (1b)

Off white solid; Yield: 86%; M.P: 134-136°; UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 232 and 284 nm; IR (KBr disk): 3075-3042(Aromatic CH), 3000-2907(Aliphatic CH), 2833 (Methoxy CH), 1588-1512 (Aromatic C=C), 1462-1412 (Aliphatic CH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ= 7.077-7.104(d, J=8.1Hz, 2H), 6.983-7.009(d, J=7.8Hz, 2H), 6.761-6.789(d, J=8.4Hz, 2H), 6.666-6.672(d, J=1.8Hz, 2H),6.575-6.609(dd, J1=8.4Hz, J2=1.8Hz, 2H), 5.398(S, 1H), 3.853(S, 6H), 3.761(S, 6H) and 2.323(S, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ=148.9, 147.7, 141.9, 137.2, 135.5, 129.2, 121.4, 113.5, 112.1, 55.9, 55.1 and 21.0; Mass spectrum (LCMS): m/z: 396.1(M+18) ($C_{24}H_{26}O_4$).

3.1.3. 4,4'-((4-ethylphenyl)methylene)bis(1,2-dimethoxybenzene) (1c)

Off White solid; Yield: 85%; M.P: 114-117°C; UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 231 and 284 nm; IR (KBr disk): 3077-3039(Aromatic CH), 3002-2933(Aliphatic CH), 2832 (Methoxy CH), 1588 (Aromatic C=C), 1462-1412 (Aliphatic CH), 859 (Aliphatic CH2) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ= 7.100-7.128(d, J= 8.4Hz, 2H), 7.005 - 7.032(d, J = 8.1Hz, 2H), 6.764-6.792(d, J = 8.4Hz, 2H), 6.671 - 6.678(d, J = 2.1Hz, 2H), 6.581 - 6.615(dd, J1 = 8.4Hz, J2 = 1.8Hz, 2H), 5.404(S, 1H), 3.854(S, 6H), 3.764(S, 6H), 2.589 - 2.665(q, J = 7.5Hz, 2H) and 1.225(t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=148.7, 147.4, 142.1, 141.6, 137.0, 129.2, 127.7, 121.4, 120.9, 112.8, 111.4, 110.9, 55.9, 55.8, 55.6, 28.4 and 15.5; Mass spectrum (LCMS): m/z: 393.3(M + H) ($C_{25}H_{28}O_4$).

3.1.4. 4,4'-(phenylmethylene)bis(1,2-dimethoxybenzene)(1d)

Off white solid; Yield: 87%; M.P:120-122°C; UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 236 and 284 nm; IR (KBr disk): 3073-3053(Aromatic CH), 2998-2907(Aliphatic CH), 2834 (Methoxy CH), 1590-1513 (Aromatic C=C) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) : δ=7.207-7.315(m, 3H), 7.102-7.130 (m, 2H), 6.769-6.796 (d, J=8.1 Hz , 2H), 6.665-6.671 (d, J=1.8Hz, 2H), 6.580-6.612 (dd, J1=8.1Hz, J2=1.5Hz, 2H), 5.443 (s, 1H), 3.856 (s, 6H) and 3.761 (s,6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=148.8, 147.5, 144.4, 136.7, 129.3, 128.3, 126.3, 121.4, 112.8, 110.9 and 55.9.

3.1.5. 4,4'-((4-chlorophenyl)methylene)bis(1,2-dimethoxybenzene) (1e)

White solid; Yield: 92%; M.P:148-150°C;UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 253 and 348 nm; IR (KBr disk); 2996(Aromatic CH), 2933(Aliphatic CH), 2836 (Methoxy CH), 1587 (Aromatic C=C), 1461-1412 (Aliphatic CH), 571 (Aromatic CCl) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ= 7.237 - 7.265(m, 2H), 7.026 - 7.054(d, J = 8.4Hz, 2H), 6.771 - 6.798(d, J = 8.1Hz, 2H), 6.631 - 6.637(d, J = 1.8Hz, 2H), 6.549 - 6.582 (dd, J1 = 8.1Hz, J2 = 1.5Hz, 2H), 5.404(S, 1H), 3.860(S, 6H) and 3.766(S, 6H); ^{13}C NMR (75 MHz,

$CDCl_3$): δ=148.9, 147.6, 142.9, 136.2, 132.1, 130.6, 128.4, 121.3, 112.6, 110.9, 55.9, 55.8 and 55.3; Mass spectrum (LCMS): m/z: 399.3(M + H) ($C_{23}H_{23}ClO_4$).

3.1.6. Methyl 4-(bis(3,4-dimethoxyphenyl)methyl) benzoate (1f)

Off white solid; Yield: 80%; M.P:112-114°C;UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 236 and 281 nm; IR (KBr disk): 3053(Aromatic CH), 3002-2906(Aliphatic CH), 2836 (Methoxy CH), 1723 (Ester CO), 1604 (Aromatic C=C), 1463-1410 (Aliphatic CH), 1102 (COC) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=7.944 - 7.972(dd, J1 = 6.6Hz, J2 = 1.8Hz, 2H), 7.180 - 7.207(d, J = 8.1Hz, 2H), 6.776 - 6.803(d, J = 8.1Hz, 2H), 6.634 - 6.641 (d, J = 2.1Hz, 2H), 6.558 - 6.592(dd, J1 = 8.1Hz, J2 = 1.8Hz,2H), 5.484(S, 1H), 3.904(S, 3H), 3.864(S, 6H) and 3.760(S, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ=166.9, 149.8, 148.9, 147.7, 135.8, 129.7, 129.3, 128.2, 124.6, 110.9, 55.8 and 52.0; Mass spectrum (LCMS): m/z: 440.0(M + 18) ($C_{25}H_{26}O_6$).

3.1.7. 4-(bis(3,4-dimethoxyphenyl)methyl)benzoic acid(1g)

Off white solid; Yield: 91%; M.P:178-180°C;UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 236 and 282 nm; IR (KBr disk): 3077(Aromatic CH), 3003-2908(Aliphatic CH), 2836 (Methoxy CH), 1690 (Acid CO), 1604 (Aromatic C=C), 1463-1421 (Aliphatic CH) cm^{-1}; ^1H NMR(300 MHz, $CDCl_3$)δ: 8.021 - 8.049(d, J = 8.4Hz, 2H), 7.221 - 7.249(d, J = 8.4Hz, 2H), 6.785 - 6.813(d, J = 8.4Hz, 2H), 6.645 – 6.652(d, J = 2.1Hz, 2H), 6.568 - 6.602(dd, J1 = 8.1Hz, J2 = 1.8Hz, 2H), 5.505(S, 1H), 3.867 (S, 6H and 3.768(S, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 171.9, 150.8, 148.9, 147.7, 135.7, 130.3, 129.5, 127.4, 121.4, 112.6, 110.9, 55.9 and 55.9; Mass spectrum (LCMS): m/z:409.2(M+H) ($C_{24}H_{24}O_6$).

3.2. Characterization of compounds 2a-2g

3.2.1. 5,5'-((4-methoxyphenyl)methylene)bis(1,2-dimethoxy-4-nitrobenzene)(2a)

Yellow solid; Yield: 75%; M.P:178-180°C;UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 236 and 351 nm; IR (KBr disk): 3100(Aromatic CH), 2998-2906(Aliphatic CH), 2837 (Methoxy CH), 1610-1578 (Aromatic C=C), 1519(Ar-NO_2), 1443-1391 (OCH_3), 1329 (Ar-NO_2) , 1269, 1054 (Ether C-O), cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.701(s, 2H), 7.130(S, 2H), 7.009-6.980(d, J = 8.7Hz, 2H), 6.872-6.843(m, 2H), 6.400(s, 2H), 3.949(s, 6H), 3.797(s, 3H) and 3.666(s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=158.6, 152.6, 147.5, 141.3, 132.9, 132.8, 130.6, 114.1, 112.8, 108.8, 56.4, 56.2, 55.2 and 47.5; Mass spectrum (LCMS): m/z: 502.2 (M+18)($C_{24}H_{24}N_2O_9$).

3.2.2. 5,5'-((4-methylphenyl)methylene)bis(1,2-dimethoxy-4-nitrobenzene) (2b)

Yellow solid; Yield: 86%; M.P: 158-160°C**;** UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 246 and 348 nm; IR (KBr disk): 3096(Aromatic CH), 2933(Aliphatic CH), 2844 (Methoxy CH), 1609-1576 (Aromatic C=C), 1519(Ar-NO_2), 1329 (Ar-NO_2), 1440-1389(OCH_3), 1270, 1055 (Ether C-O), cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.698(s, 2H), 7.108-7.128(d, J=9.0Hz, 3H), 6.939-6.965(d, J=7.8Hz, 2H), 6.405(s, 2H), 3.947(s, 6H), 3.660(s, 6H) and 2.329(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.6, 147.5, 141.4, 137.7, 136.9, 132.8, 129.4, 129.4, 112.9, 108.8, 56.4, 56.1, 47.9 and 21.1; Mass spectrum (LCMS): m/z: 469.3(M+H) ($C_{24}H_{24}N_2O_8$).

3.2.3. 5,5'-((4-ethylphenyl)methylene)bis(1,2-dimethoxy-4-nitrobenzene)(2c)

Pale yellow solid; Yield: 85%; M.P: 164-166°C; UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 247 and 350 nm; IR (KBr disk): 3097(Aromatic CH), 2968-2933(Aliphatic CH), 2844 (Methoxy CH), 1611-1578 (Aromatic C=C), 1519(Ar-NO_2), 1439-1390 (OCH_3), 1329 (Ar-NO_2), 1270, 1054(Ether C-O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.704(s, 2H), 7.132 - 7.159(m, 3H), 6.963-6.990 (d, J = 8.1Hz, 2H), 6.394(S, 2H), 3.948(s, 6H), 3.654 (s, 6H), 2.595 – 2.670(q, J = 7.5Hz, 2H) and 1.214(t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 152.6, 147.5, 143.2, 141.4, 137.9, 132.9, 129.4, 128.2, 112.9, 108.9, 56.3, 56.1, 47.9, 28.4 and 15.4; Mass spectrum (LCMS): m/z: 500.1(M + 18) ($C_{25}H_{26}N_2O_8$).

3.2.4. 5,5'-(phenylmethylene)bis(1,2-dimethoxy-4-nitrobenzene) (2d):

Pale yellow solid; Yield: 80%; M.P:192-194°C; UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 225 and 2350 nm; IR (KBr disk): 3080-3000(Aromatic CH), 2971-2941(Aliphatic CH), 2845 (Methoxy CH), 1613-1578 (Aromatic C=C), 1520(Ar-NO_2), 1330 (Ar-NO_2) , 1462-1391 (OCH_3), 1271, 1054 (Ether C-O) cm^{-1}; ^1H NMR ($CDCl_3$-300 MHz): δ=7.714(s, 2H), 7.266-7.353(m, 4H) 7.182(s, 1H), 6.377(s, 2H), 3.953(s, 6H) and 3.650(s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=148.8, 147.5, 144.4, 136.7, 129.3, 128.3, 126.3, 121.4, 112.8, 110.9,and

55.9; Mass spectrum (LCMS): m/z: 454.14 (M+18) ($C_{23}H_{22}N_2O_8$).

3.2.5. 5,5'-((4-chlorophenyl)methylene)bis(1,2-dimethoxy-4-nitrobenzene)(2e)

Pale yellow solid; Yield: 89%; M.P: 194-196°C; UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 233 and 350 nm; IR (KBr disk): 3077-3003(Aromatic CH), 2965-2938(Aliphatic CH), 2846 (Methoxy CH), 1613-1578 (Aromatic C=C), 1522(Ar-NO_2), 1340 (Ar-NO_2), 1460-1405 (OCH_3), 1268, 1057(Ether C-O),765 (Aromatic CCl) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.717(S, 2H), 7.292 - 7.320 (m, 2H), 7.154(s, 1H), 7.005 – 7.033(d, J = 8.4Hz, 2H), 6.358(S, 2H), 3.956(S, 6H) and 3.674(S, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 152.7, 147.7, 141.3, 139.6, 134.6, 133.1, 131.9, 130.8, 129.3, 112.7, 108.9, 56.4, 56.2 and 47.7; Mass spectrum (LCMS): m/z: 506.1(M + 18) ($C_{23}H_{21}ClN_2O_8$).

3.2.6. Methyl 4-(bis(4,5-dimethoxy-2-nitrophenyl) methyl)benzoate (2f)

Pale yellow solid; Yield: 80%; M.P: 203 - 205°C**;** UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 221 and 350 nm; IR (KBr disk): 3099-3010(Aromatic CH), 2971-2903(Aliphatic CH), 2844 (Methoxy CH), 1711 (Ester C=O), 1610-1577 (Aromatic C=C), 1519(Ar-NO_2), 1438-1390 (OCH_3), 1328 (Ar-NO_2), 1276, 1053(Ether C-O), cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.994 - 8.022(d, J = 8.4Hz, 2H),7.729(S, 2H), 7.223(S, 1H), 7.151- 7.178 (d, J= 8.1Hz, 2H), 6.345(S, 2H), 3.962(S, 6H), 3.915(S, 3H) and 3.650(S, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 166.7, 152.7, 147.8, 146.4, 141.4, 131.7, 130.0, 129.5, 129.2, 112.8, 108.9, 56.4, 56.2, 52.2 and 48.3; Mass spectrum (LCMS): m/z: 511.4(M- H) ($C_{25}H_{24}N_2O_{10}$).

3.2.7. 4-(bis(4,5-dimethoxy-2-nitrophenyl)methyl) benzoic acid (2g)

Yellow solid; Yield: 76%; M.P: 245-247°C**;** UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 245 and 346 nm; IR (KBr disk): 3074(Aromatic CH), 2963-2937(Aliphatic CH), 2846 (Methoxy CH), 1681 (Acid C=O), 1608-1578 (Aromatic C=C), 1521(Ar-NO_2), 1441-1390 (OCH_3), 1335 (Ar-NO_2), 1275, 1056 (Ether C-O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=8.068 - 8.095(d, J = 8.1Hz, 2H), 7.737(S, 2H), 7.195 - 7.267(m, 3H), 6.353 (S, 2H), 3.966(S, 6H) and 3.660(S, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=171.5, 152.8, 147.9, 147.5, 141.4, 131.5, 130.6, 129.6, 128.3, 112.8, 108.9, 56.4, 56.2 and 48.4; Mass spectrum (LCMS): m/z: 497.3(M-H) ($C_{24}H_{22}N_2O_{10}$).

3.3. Characterization of compounds 3a-3g

3.3.1. 6,6'-((4-methoxyphenyl)methylene)bis(3,4-dimethoxyaniline)(3a)

Brown colour solid; Yield: 70%; M.P: 196-198°C;UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 227 and 307 nm; IR (KBr disk): 3423-3346 (primary NH_2(s)), 2935(Aliphatic CH), 2833 (Methoxy CH), 1632-1609 (NH(b), 1609-1580 (Aromatic C=C) 1208 (Amine C-N), 762 (O-CH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.058-7.087(m, 2H), 6.845-6.874(m, 2H), 6.276-6.306(d, J=9.0Hz, 4H), 5.236(S, 1H), 3.834(S, 9H), 3.591(S, 6H) and 3.303(bs, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 158.4, 148.6, 141.9, 138.5, 133.5, 130.4, 119.4, 114.1, 114.1, 101.4, 56.7, 55.8, 55.2 and 45.8; Mass spectrum (LCMS): m/z: 849.0 (2M+H) ($C_{24}H_{28}N_2O_5$).

3.3.2. 6,6'-((4-methylphenyl)methylene)bis(3,4-dimethoxyaniline) (3b)

Brown colour solid; Yield: 73%; M.P: 216-218°C; UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 231 and 304 nm; IR (KBr disk): 3425-3356 (primary NH_2 (s)), 2997(Aromatic CH), 2933(Aliphatic CH), 2832 (Methoxy CH), 1628 (NH(b), 1578 (Aromatic C=C),1208 (Amine CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.109 - 7.135(d, J = 7.8Hz), 7.025 - 7.052(d, J = 8.1Hz, 2H), 6.285 - 6.302(d, J = 5.1Hz, 4H), 5.248(s, 1H), 3.830(s, 6H), 3.588(s, 6H), 3.302(bs, 4H) and 2.339(S, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=149.0, 140.9, 140.4, 140.0, 135.5, 129.6, 129.2, 118.8, 116.3, 101.3, 57.6, 55.7, 44.6 and 21.1; Mass spectrum (LCMS): m/z: 409.2(M + H) ($C_{24}H_{28}N_2O_4$).

3.3.3. 6,6'-((4-ethylphenyl)methylene)bis(3,4-dimethoxyaniline)(3c)

Brown colour solid; Yield: 85%; M.P: 165-168°C; UV-vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 230 and 305 nm; IR (KBr disk): 3405-3349 (primary NH_2 (s)), 2991(Aromatic CH), 2933(Aliphatic CH), 2832 (Methoxy CH), 1630 (NH (b), 1630 (Aromatic C=C), 1209 (Amine CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ= 7.132 - 7.159(d, J = 8.1Hz, 2H), 7.048 - 7.075(d, J = 8.1Hz, 2H), 6.304(s, 2H), 6.284(s, 2H), 5.258(s, 1H), 3.832(s, 6H), 3.586 (s, 6H), 3.309(bs, 4H), 2.604 - 2.680(q, J = 7.8Hz, 2H) and 1.229(t , 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 148.6, 142.7, 141.9, 138.7, 138.5, 129.4, 128.1, 119.4, 114.3, 101.4, 56.7, 55.8, 46.2, 28.4 and

15.5; Mass spectrum (LCMS): m/z: 845.1(2M + H) ($C_{25}H_{30}N_2O_4$).

3.3.4. 6,6'-(phenylmethylene)bis(3,4-dimethoxy-aniline) (3d)

Brown colour solid; Yield: 86%; M.P:228-231°C;UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 228 and 304 nm; IR (KBr disk): 3420-3347 (primary NH_2(s)), 3059(Aromatic CH), 2933(Aliphatic CH), 2831 (Methoxy CH), 1633 (NH(b), 1610-1578 (Aromatic C=C) 1208 (Amine CN) cm^{-1}; ^1H NMR (DMSO-d_6-300 MHz): δ= 7.182-7.322(m, 3H), 7.075-7.098(d, J=6.9 Hz, 2H), 6.376(s, 2H), 6.173(s, 2H), 5.263(s, 1H), 4.349(bs, 4H), 3.676(s, 6H) and 3.425(s,6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.6, 147.6, 141.4, 140.9, 132.6, 129.5, 128.7, 127.3, 112.9, 108.9, 56.4, 56.1 and 48.3; Mass spectrum (LCMS): m/z: 789.15 (2M+H) ($C_{23}H_{26}N_2O_4$).

3.3.5. 6,6'-((4-chlorophenyl)methylene)bis(3,4-dimethoxyaniline)(3e)

Brown colour solid; Yield: 70%; M.P: 212-214°C;UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 230 and 305 nm; IR (KBr disk): 3418-3353 (primary NH_2(s)), 2993(Aromatic CH), 2934(Aliphatic CH), 2832 (Methoxy CH), 1631 (NH(b)), 1577 (Aromatic C=C), 1210 (Amine CN), 761 (C-Cl) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ= 7.311-7.265(m, 2H), 7.112-7.084(d, J = 8.4Hz, 2H), 6.312(s, 2H), 6.239(s, 2H), 5.270(S, 1H), 3.836(s, 6H), 3.593(s, 6H) and 3.292(bs, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 148.9, 142.1, 140.3, 138.5, 132.6, 130.8, 128.8, 118.6, 114.1, 101.5, 56.8, 55.8 and 45.9; Mass spectrum (LCMS): m/z: 429.2(M + H) ($C_{23}H_{25}ClN_2O_4$).

3.3.6. Methyl 4-(bis(2-amino-4,5-dimethoxyphenyl)methyl)benzoate(3f)

Brown colour solid; Yield: 65%; M.P: 195-197°C;UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 236 and 304 nm; IR (KBr disk):3401-3336 (primary NH_2 (s)), 2991 (Aromatic CH), 2934(Aliphatic CH), 2831 (Methoxy CH), 1717-1710 (Ether CO), 1630 (NH(b), 1610-1577 (Aromatic C=C) 1209 (Amine CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ= 8.015-7.987 (dd, J1 = 6.6Hz, J2 = 1.8Hz, 2H), 7.264-7.236 (d, J = 8.4Hz, 2H), 6.321(s, 2H), 6.231(s, 2H), 5.355(s, 1H), 3.917(s, 3H), 3.839(s, 6H), 3.576(s, 6H) and 3.299(bs, 4H); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 166.7, 149.4, 149.2, 141.1, 140.5, 129.9, 129.5, 127.9, 117.8, 116.1, 101.3, 57.5, 55.7, 52.4 and 44.8; Mass spectrum (LCMS): m/z: 904.9(2M + H) ($C_{25}H_{28}N_2O_6$).

3.3.7. 4-(bis(2-amino-4,5-dimethoxyphenyl) methyl) benzoic acid(3g)

Brown colour solid; Yield: 76%; M.P: 242- 245°C;UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 238 and 305 nm; IR (KBr disk): 3393-3325 (primary NH_2(s)), 3076-2995(Aromatic CH), 2935(Aliphatic CH), 2831 (Methoxy CH), 1691 (Acid C=O), 1311(Acid C-O), 1207 (Amine CN),cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=8.018-7.991 (d, J = 8.1Hz, 2H), 7.250-7.223 (d, J = 8.1Hz, 2H), 6.356(s, 2H), 6.237(s, 2H), 5.354(s, 1H), 4.675(bs, 5H), 3.833(s, 6H) and 3.571(s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6): δ= 167.8, 149.2, 148.8, 141.1, 140.5, 129.8, 129.6, 129.2, 118.0, 116.2, 101.4, 57.5, 55.7 and 44.8; Mass spectrum (LCMS): m/z: 437.4(M - H) ($C_{24}H_{26}N_2O_6$).

3.4. Characterization of compounds 4a-4g

3.4.1. 14,15,34,35,94,95,114,115-octamethoxy-2,10-bis(4-methoxyphenyl)-4,8,12,16-tetraaza-1,3, 9,11(1,2),6,14(1,4)-hexabenzenacyclo-hexadecaphane-4,7,12,15-tetraene(4a)

Yellow color solid; Yield: 72%; M.P:More than 300°C; UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 224, 284 and 391 nm; IR (KBr disk): 2994(Aromatic CH), 2931(Aliphatic CH), 2832 (Methoxy CH), 1623 (C=N), 1000 (CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ= 8.299(s, 4H), 7.690(s, 8H), 6.998-7.027(d, J=8.7Hz, 4H), 6.927(s, 2H), 6.864(s, 4H), 6.766-6.795(d, J=8.7Hz, 4H), 6.635(s, 4H), 3.910(s, 12H) and 3.764-3.794(d, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 157.6, 157.1, 147.9, 147.4, 142.8, 138.6, 137.4, 130.6, 130.0, 128.8, 113.5, 113.4, 101.7, 56.2, 56.0, 55.2 and 42.2; Mass spectrum (LCMS): m/z: 1045.7(M+H) ($C_{64}H_{60}N_4O_{10}$).

3.4.2. 14,15,34,35,94,95,114,115-octamethoxy-2,10-di-p-tolyl-4,8,12,16-tetraaza-1,3,9,11 (1,2), 6, 14(1,4)-hexabenzenacyclohexadecaphane-4,7, 12,15-tetraene(4b)

Yellow color solid; Yield: 80%; M.P:More than 300°C; UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 230, 283 and 391 nm; IR (KBr disk): 2996(Aromatic CH), 2930(Aliphatic CH), 2846 (Methoxy CH), 1622 (C=N), 1004 (CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=8.296(s, 4H), 7.680(s, 8H), 6.952 – 7.059(m, 10H), 6.876(s, 4H), 6.632(s, 4H), 3.909(s, 12H), 3.793(s, 12H) and 2.292(s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 157.1, 147.9, 147.4,

142.9, 142.2, 138.6, 135.1, 130.5, 128.9, 128.8, 113.4, 101.6, 56.2, 56.0, 42.7 and 21.0; Mass spectrum (LCMS): m/z: 1013.7(M + H) ($C_{64}H_{60}N_4O_8$).

3.4.3. 2,10-bis(4-ethylphenyl)-14,15,34,35,94,95, 114,115-octamethoxy-4,8,12,16-tetraaza-1,3, 9,11(1,2),6,14(1,4)-hexabenzenacyclohexa-decaphane-4,7,12,15-tetraene(4c)

Yellow color solid; Yield: 65%; M.P:More than 300°C; UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 230, 283 and 391 nm; IR (KBr disk): 2996(Aromatic CH), 2931(Aliphatic CH), 2846 (Methoxy CH), 1621 (C=N), 1004 (CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=8.296(s, 4H), 7.678(s, 8H), 6.954 - 7.085(m, 10H), 6.885(S, 4H), 6.630(s, 4H), 3.908(s, 12H), 3.840(s, 12H), 2.562 - 2.638(q, J = 7.8Hz, 4H) and 1.204(t, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 157.2, 147.9, 147.4, 142.9, 142.4, 141.4, 138.6, 130.5, 129.0, 128.8, 127.6, 113.5, 101.7, 56.2, 56.0, 42.7, 28.4 and 15.5; Mass spectrum (LCMS): m/z: 1041.7(M + H) ($C_{66}H_{64}N_4O_8$).

3.4.4. 14,15,34,35,94,95,114,115-octamethoxy-2,10-diphenyl-4,8,12,16-tetraaza-1,3,9,11(1,2),6, 14(1,4)-hexabenzenacyclohexadecaphane-4,7,12,15-tetraene(4d)

Yellow color solid; Yield: 88%; M.P:More than 300°C; UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 222, 284 and 390 nm; IR (KBr disk): 3057-3023(Aromatic CH), 2933(Aliphatic CH), 2844 (Methoxy CH), 1623 (C=N), 1000 (CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=8.308 (s, 4H), 7.697(s, 8H), 7.089-7.240(m, 8H), 7.013 (s, 2H), 6.866(s, 4H), 6.643(s, 4H), 3.913(s, 12H) and 3.788(s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 157.1, 148.0, 147.4, 145.3, 142.9, 138.6, 130.3, 129.1, 128.8, 128.1, 125.7, 113.5, 101.7, 56.2, 56.0 and 43.0; Mass spectrum (LCMS): m/z: 985.8 (M+H) ($C_{62}H_{56}N_4O_8$).

3.4.5. 2,10-bis(4-chlorophenyl)-14,15,34,35,94,95, 114,115-octamethoxy-4,8,12,16-tetraaza-1,3,9,11(1,2),6,14(1,4)-hexabenzenacyclo-hexadecaphane-4,7,12,15-tetraene(4e)

Yellow color solid; Yield: 89%; M.P:More than 300°C; UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 230, 284 and 391 nm; IR (KBr disk): 2997(Aromatic CH), 2932(Aliphatic CH), 2845 (Methoxy CH), 1624 (C=N), 1011 (CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=8.314(s, 4H), 7.707(s, 8H), 7.180 - 7.208(d, J = 8.4Hz, 4H), 6.997 - 7.024(d, J = 8.1Hz, 6H), 6.823(s, 4H), 6.651(s, 4H), 3.918(s, 12H) and 3.795(s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 157.1, 148.2, 147.6, 143.9, 142.8, 138.6, 131.5, 130.4, 129.8, 128.9, 128.2, 113.2, 101.6, 56.2, 56.0 and 42.5; Mass spectrum (LCMS): m/z: 1053.7(M + H) ($C_{62}H_{54}Cl_2N_4O_8$).

3.4.6. Dimethyl-4,4'-(14,15,34,35,94,95,114,115-octamethoxy-4,8,12,16-tetraaza-1,3,9,11 (1,2),6,14(1,4)-hexabenzenacyclohexadeca-phane-4,7,12,15-tetraene-2,10-diyl) dibenzoate (4f)

Yellow color solid; Yield: 89%; M.P:More than 300°C; UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 223, 282 and 391 nm; IR (KBr disk): 2997(Aromatic CH), 2938(Aliphatic CH), 2843 (Methoxy CH), 1715 (C=O), 1623 (C=N), 1002 (CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=8.326(s, 4H), 7.887 - 7.914(d, J = 8.1Hz, 4H), 7.715(s, 8H), 7.102 - 7.168(m, 6H), 6.816(S, 4H), 6.664(s, 4H), 3.922(s, 12H), 3.877(s, 6H) and 3.782(s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 167.2, 157.1, 151.0, 148.2, 147.6, 142.8, 138.6, 129.6, 129.4, 129.1, 128.9, 127.7, 113.3, 101.6, 56.2, 56.0, 51.9 and 43.1; Mass spectrum (LCMS): m/z: 1101.7(M + H) ($C_{66}H_{60}N_4O_{12}$).

3.4.7. 4,4'-(14,15,34,35,94,95,114,115-octamethoxy -4,8,12,16-tetraaza-1,3,9,11(1,2),6,14(1,4)-hexabenzenacyclohexadecaphane-4,7,12,15-tetraene-2,10-diyl)dibenzoic acid(4g)

Yellow color solid; Yield: 69%; M.P: 276-280°C; UV-vis(CH_2Cl_2): $\lambda_{max}(\varepsilon)$= 250, 283 and 390 nm; IR (KBr disk): 2995(Aromatic CH), 2932(Aliphatic CH), 2845 (Methoxy CH), 1716-1689 (C=O), 1622 (C=N), 999 (CN) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ= 8.343(s, 4H), 7.947 - 7.975(d, J = 8.4Hz, 4H), 7.732(s, 8H), 7.140 - 7.195(m, 6H), 6.828(s, 4H), 6.672(s, 4H), 3.919(s, 12H) and 3.786(s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 171.8, 157.2, 152.0, 148.3, 147.6, 142.8, 138.6, 130.1, 129.4, 129.2, 128.9, 126.9, 113.2, 101.7, 56.2, 56.0 and 43.2; Mass spectrum (LCMS): m/z: 1073.6(M + H) ($C_{64}H_{56}N_4O_{12}$).

3.5. *In vitro* antioxidant activity: Reducing power assay

The reducing power of the macrocylces (4a-4g) were determined according to the method of Oyaizu [24]. A 2.5 ml of 0.2M phosphate buffer, pH 6.6 containing different concentrations of the samples were prepared. Then it was added to 2.5 ml of 1% potassium ferricyanide, and mixed. After incubation at 50°C for

20 minutes, the mixtures were mixed with 2.5 ml of 10% trichloro-acetic acid and then centrifugation at 3000 rpm for 10 min. The supernatant (2.5 ml) was mixed with 2.5 ml of distilled water and 0.5 ml of 0.1% ferric chloride. Absorbance of this resulting solution was measured at 700 nm. Increased absorbance of the reaction mixture indicated increasing reducing power (Table 3).

In the reducing power assay, the tested compounds would bring about the reduction of Fe^{+3}/ferricyanide complex to the ferrous form by giving away an electron. Increasing the absorbance at 700 nm implies an increase in its ability to reduce. The sequence for this reducing power was as follows: 4f(2.702)>4a(1.695)>4b (1.681)>4e(1.665)>4g(1.143)>4d(1.109)>4c (0.531) at the concentration of 250 µg/ml. Some degrees of electron-donating capacity were found in all examined samples. Among the examined samples, compound 4f showed the highest reducing power with the absorbance of at 700 nm, so this compound showing higher activity as electron donors and also could convert free radicals to more stable products

Table 3: Reducing power assay of compounds 4a-4g

S. No.	Concentration (µg/ml)	Reducing power activity (Abs (OD))						
		4a	4b	4c	4d	4e	4f	4g
1	50	0.876	0.655	0.151	0.07	0.684	0.003	0.388
2	100	1.274	1.421	0.212	0.081	1.175	0.971	0.679
3	150	1.467	1.449	0.22	0.106	1.371	1.019	0.871
4	200	1.564	1.477	0.291	1.107	1.513	1.456	1.089
5	250	1.695	1.681	0.531	1.109	1.665	2.702	1.143

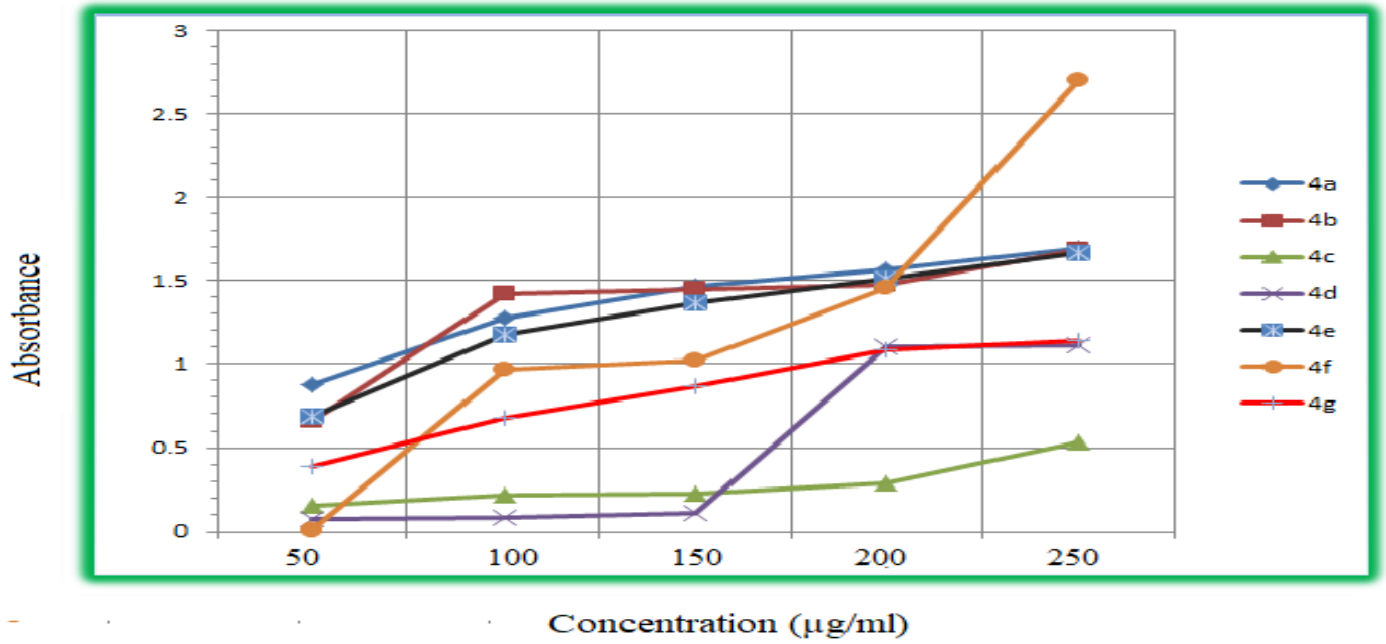


Fig. 3: Reducing power assay of compounds 4a-4g

4. CONCLUSION

In summary, we have developed a convenient protocol to make various substituted [2+2] macrocycles from diamine derivatives and terephthaldehyde. It has the efficiency to synthesize a variety of substituted macrocycles. The cyclized product was confirmed by UV, IR, NMR, Mass, and single crystal analysis. The antioxidant activity of all the synthesized compounds were tested by Reducing power activity. The compounds were screened at different concentrations from 50-250 (µg/ml) to check the absorbance of compounds. From the result presented in table 3, compound 4f showed highly significant activity. The result shows that as the concentration of compound

increase, the compound showed high significant activity. Thus, the study could be concluded as the compounds have considerable antioxidant activity. Thus, it may be concluded that the synthesized compound effectively can be further used in the treatment of above-mentioned ailment.

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Conflict of interest

The author declare no conflict of interest.

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