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SYNTHESIS, SPECTRAL CHARACTERISATION AND PHYSIOCHEMICAL PROPERTIES DETERMINATION OF SUBSTITUTED {4-(1H-BENZIMIDAZOL-2-YL) PHENYL} DIAZENYL DERIVATIVES

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ABSTRACT

*Conventional synthesis of substituted {4-(1H-benzimidazol-2-yl) phenyl} diazenyl derivatives had been synthesized at laboratory scale by diazotization followed by coupling with different phenols and amines. The compound structures were characterized by IR, H^1 and C^{13} NMR spectroscopic methods. The synthesis was followed by chemical calculations by using Chemicalize an online software providing chemical calculations and predictions like logP, PKa and solubility mg/mL. The results observed describes that values of intrinsic solubility are less than zero which indicates that the compounds were categorised with low aqueous solubility. The isoelectric points for the compounds **8s** (4.57), **7s** (5.70) and other compounds having values ranging from 6.03 to 8.70 representing the pH at which the molecule carries no net charge required to predict the solubility of a compound.*

KEY WORDS

Chemicalize, spectroscopy, solubility, isoelctric point.

INTRODUCTION:

Benzimidazole is an important heterocyclic fused ring system that possesses various pharmacological actions such as antimicrobials[(1)], antivirals [(2)], antiparasitic [(3)], anticancer, anti-inflammatory[(4)], antioxidants[(5)], proton pump inhibitors[(6)], antihypertensives[(7)], anticoagulants[(8)], immunomodulators[(9)], hormone modulators[(10)], CNS stimulants as well as depressants [(11-15)], lipid level modulators[(16-19)], antidiabetic, etc. has made it an indispensable anchor for development of new therapeutic agents. Varied substituents around the benzimidazole nucleus have provided a wide spectrum of biological activities [(19-26)]. However, owing to fast development of new drugs possessing benzimidazole nucleus many researchers were continuously reporting the current status of benzimidazole nucleus in medicinal chemistry research. In the present study, various azo derivatives of substituted phenyl ring in the benzimidazole ring system were synthesised by fragment-based approach of synthesis. This fragment-based approach of synthesis is a method used for synthesising lead compounds as part of the drug designing process.

MATERIALS AND METHODS:

Reagents Used:

The following chemicals and reagents were used in the synthesis:

Ortho phenylene diamine-(LOSA-S.NO-0520700250), 4-amino benzoic acid - (KEMPHASOL-S.NO-12PU05016) , Sodium Nitrite purified- (CENTRAL DRUG HOUSE PVT LTD -S.NO-14103) , Hydrochloric acid- (LOSA-S.NO-

0017100500) , Sodium Hydroxide- (LOSA-S.NO-0590000500), Salicylic Acid-(LOSA-S.NO-V249105), Sodium carbonate-(HI-PURE- FINE CHEM INDUSTRIES-S.NO-0404396), 1-Naphthol-(LOSA-S.NO-0475500100) , 2-Naphthol-(SDS FINE CHEM LIMITED-S.NO-0996-696-220S13), Resorcinol-(QUALIGENS FINE CHEMICALS-S.NO-), O-Cresol-(LOSA-S.NO-0300600500), Aniline-(LOSA-S.NO-0003200500) , Silica gel G -(LOSA-S.NO-0570001000), Ethyl Acetate-(LOSA-S.NO-0013702500), n-Hexane-(LOSA-S.NO-0016102500), Dimethyl Sulphoxide -(LOSA-S.NO-0012300500), Phenol-(LOSA-S.NO-0516900500) , Phloroglucinol-(SDS FINE CHEM LIMITED -S.NO-V03088/8068) , m-Cresol-(SD FINE CHEM LIMITED-S.NO- L00A-0500-0212-13) , 1-Naphthylamine- (SD FINE CHEM LIMITED- S.NO-1198/0598/3108/02) , N,N-Dimethyl aniline -(SD FINE CHEM LIMITED- S.NO- E04A-0304-0805-13) ,

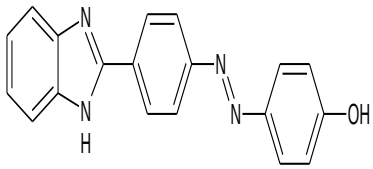
General Procedure for the Synthesis of Compounds (1s-12s):

Step1: Synthesis of 4-(1*H*-benzimidazol-2-yl) aniline 4-(1*H*-benzimidazol-2-yl) aniline was prepared by condensing equimoles of O- phenylene diamine with P-amino benzoic acid. The reaction mixture was refluxed for 2 hrs under solvent free conditions. The mixture was added to ice cold water; precipitate was filtered, dried and recrystallized from methanol. The purity and progress of reaction was confirmed by thin layer chromatography and melting point.

Step-2: Synthesis of substituted {4-(1H-benzimidazol-2-yl) phenyl} diazenyl derivatives**.** 2gms of step1 product was dissolved in a mixture of equal volumes of concentrated hydrochloric acid (6.4 ml) and water (6.4 ml) in a small beaker. The above solution was diazotized by adding the sodium nitrite solution (6.4 gms of $NaNO_2$ in 30 ml of water) and the temperature was maintained below 5^0C. Phenolic or amine solution was prepared. (1 gm of phenolic compound in 10% NaOH solution and amine in 10% HCl) , The solution was cooled to 5^0C by immersion in an ice bath,. The phenolic solution was stirred vigorously and the cold diazonium salt solution was added very slowly. A red colour was developed and red crystals of {4-(1H-benzimidazol-2-yl) phenyl} diazenyl derivatives were separated. When all the diazonium salt solution had been added, the mixture was allowed to stand in an ice bath for 30 minutes with occasional stirring. The solution was filtered through a buchner funnel with gentle suction, washed well with water and drained thoroughly. The compounds were synthesized as per the scheme shown in Fig 1.

Physical and Spectral Characterisation of Compounds:

Compound-1s:



IUPAC name: 4-{(*E*)-[4-(1*H*-benzimidazol-2-yl)phenyl]diazenyl} phenol ,**Molecular formula**: $C_{19}H_{14}N_4O$, **Molecular weight**: 314.35, **Melting Point**: Estimated-240°c, Observed-250°c **Elemental composition**:- C%-72.61, H%-4.46, O%-5.09, N%-17.83 **% yield** :69% , **R_F value:** 0.5 , ethyl acetate: n-hexane (7:3).**IR Data: FTIR** (ɣ max, cm^{-1}) 3677(-*NH* stretch), 3500-2899 (broad, OH stretch), 1591 (-C=N), 1476 (Aromatic -*C=C* stretch), 1251(*C-N* stretch), 1150(-*C-O* stretch) **,NMR data: H^1NMR: (400MHZ, DMSO)** δ 11.839 (S, 1H, imidazole NH) δ 4.497 (S, 1H, phenolic OH) , 7.192 , 7.381 , 7.416 , 7.418 , 7.452 , 7.471 , 7.510 , 7.518 , 7.589 , 7.631 ,7.650 , 7.668 , 7.786 , 7.789 , 7.805 , 7.822 , 7.966 , 7.970 , 7.987 , 8.63 , 8.640 (multiplet, Ar-H) .**C13NMR:** 167.30, 167.17,(C=N) 155.01, (phenolic OH) 138.74, 130.85, 130.48, 125.25, 120.94, 114.88, 103.13(Aromatic carbons,C=C)

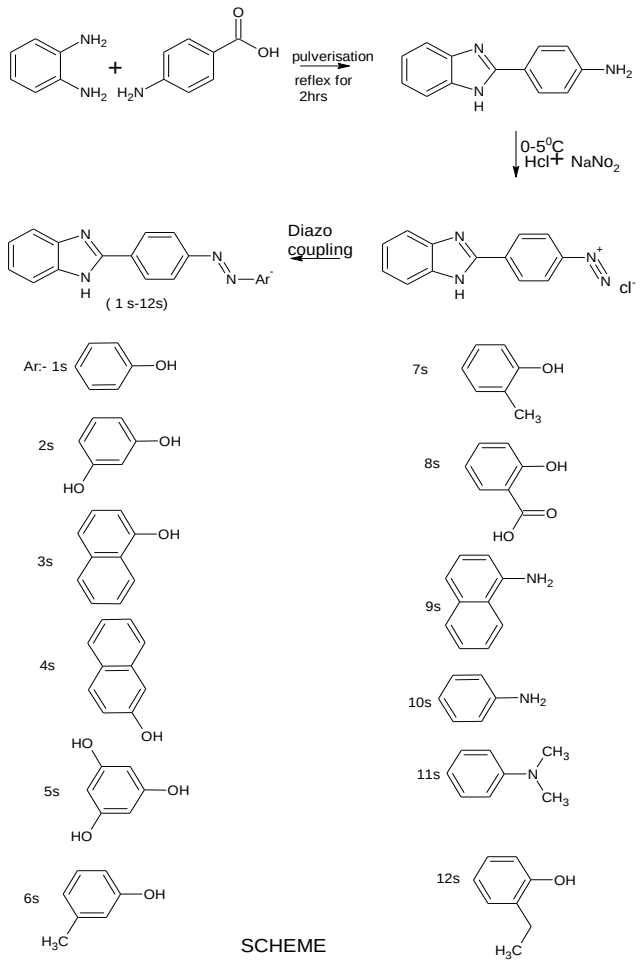
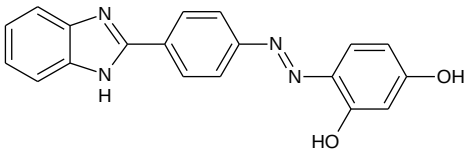


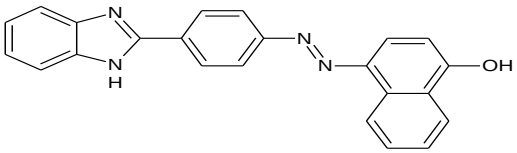
Fig 1: Synthesis of various substituted {4-(1H-senz imidazol-2-yl) phenyl} diazenyl derivatives

Compound-2s



IUPAC name: 4-{(*E*)-[4-(1*H*-benzimidazol-2-yl)phenyl] diazenyl} benzene-1,3-diol **Molecular formula:** $C_{19}H_{14}N_4O_2$, **Molecular weight:**330 , **Melting point**: Estimated-260°c,Observed-250°c , **Elemental Composition:** C%-69.09, H%-4.24,O%-9.69, N%-16.97, **%yield:** 62%, **R_F value:** 0.24 ethyl acetate: n-hexane (7:3)**IR Data:** FTIR (γ max, cm^{-1}) 3739(-*NH* stretch), 3450-2680 (broad, OH stretch), 1697 (-C=N), 1497 (Aromatic -*C=C* stretch), 1250 (*C-N* stretch), 1141(*-C-O stretch*) ,**^{1}H NMR:** (400MHZ, DMSO) 11.529(S, 1H, imidazole NH) , 8.640, 8.631, 7.987, 7.970, 7.966, 7.822, 7.805, 7.789, 7.786, 7.668, 7.650, 7.631, 7.589, 7.570, 7.555, 7.471, 7.452, 7.418, 7.416, 7.399, 7.381, 7.192(multiplet, Ar-H), 4.517. (S, 2H, phenolic OH) .**^{13}CNMR:** (400MHZ,DMSO) 166.98, ,(C=N) 155.01 (phenolic OH), 152.95(phenolic OH)142.73,131.28, 130.42,125.18, 121.63,111.55(Aromatic -***C=C***).

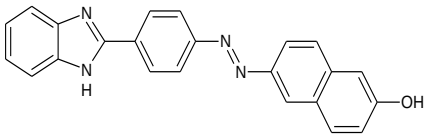
Compound-3s



IUPAC name : 4-{(*E*)-[4-(1*H*-benzimidazol-2-yl) phenyl]diazenyl}naphthalen-1-ol, **Molecular formula :** $C_{23}H_{16}N_4O$, **Molecular weight :** 364.41, **Melting point** : Estimated - 250°c Observed - 270°c , **Elemental Composition :**C%-75.74,H%-4.39,O%-4.39,N%-15.37**, %yield:**64% **,R_F value:** 0.30 , ethyl acetate**:** n-hexane (7:3).**IR Data:** FTIR (γ max, cm^{-1}) 3740(-***NH*** stretch), 3560-2841 (broad, **O-H** stretch), 2641 (**C-H** stretch), 1699 (-**C=N**),1599 (Aromatic -***C=C*** stretch), 1249(***C-N*** stretch), 1102(*-**C-O stretch***) , **^{1}H NMR:** (400MHZ, DMSO) 11.675(S, 1H, imidazole NH),9.969,9.576,8.370, 8.133, 8.123, 8.111, 7.982, 7.968, 7.958, 7.923, 7.902, 7.882, 7.723, 7.705, 7.675, 7.582, 7.572, 7.560, 7.535,

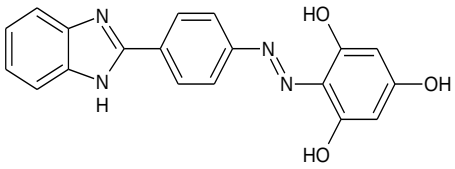
7.519, 7.499, 7.482, 7.464, 7.446, 7.362, 7.120, 7.100, 6.888 , 6.868 (multiplet, Ar-H) , 3.854(S, 1H, phenolic OH) .**^{13}CNMR:** (400MHZ,DMSO): 162.74,(C=N) ,152.17(phenolic OH),145.63 ,138.78.132.64, 130.83,126.98, 125.13,115.45, 114.89, 114.51(Aromatic -***C=C***).

Compound-4s



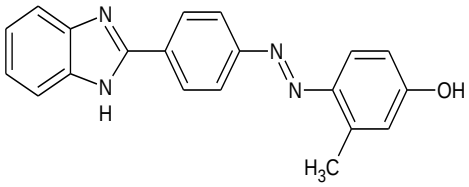
IUPAC name :6-{(*E*)-[4-(1*H*-benzimidazol-2-yl) phenyl]diazenyl}naphthalen-2-ol **, Molecular formula:** $C_{23}H_{16}N_4O$**, Molecular weight :**364.41**,Melting point**: Estimated-270°c**,**Osserved- 280°c**,Elemental Composition:-** C%-75.74,H%-4.39,O%-4.39,N%-15.37**, %yield:**53%**,R_F value:** 0.43 ,ethyl acetate**:** n-hexane (7**:**3).**IR Data:** FTIR (γ max, cm^{-1}) 3726(-***NH*** stretch), 3400-2600 (broad, **OH** stretch), 2659 (**C-H** stretch), 1580 (Aromatic -***C=C*** stretch), 1226 (***C-N*** stretch), 1137(-***C-O stretch***). **^{1}H NMR:** (400MHZ, DMSO) 11.570(S, 1H, imidazole NH),8.370, 8.133, 8.123, 8.112, 7.981, 7.968, 7.958, 7.933, 7.902, 7.882, 7.723, 7.705, 7.675, 7.582, 7.572, 7.560, 7.535, 7.519, 7.499, 7.482, 7.464, 7.446, 7.362, 7.120, 7.100, 6.888, 6.868 (multiplet, Ar-H),4.100(S, 1H, phenolic OH). **^{13}CNMR:** (400MHZ,DMSO): 159.84,(C=N), 150.9, 150.37(phenolic OH),147.00, 141.45, 141.25, 140.33, 136.86, 132.68, 132.54, 132.41, 132.29, 132.09, 131.23, 128.86, 127.96, 127.90, 127.48, 127.40, 123.45, 123.11, 122.82, 122.26, 121.99, 121.35, 119.70, 119.34, 117.01, 116.88, 115.42, 115.22, 115.09, 110.15(Aromatic -***C=C***).

Compound-5s



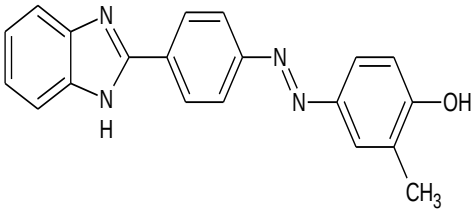
IUPAC name : 2-{(*E*)-[4-(1*H*-benzimidazol-2-yl) phenyl] diazenyl}senzene-1,3,5-triol , **Molecular formula:** $C_{19}H_{14}N_4O_3$, **Molecular weight :** 346.35, **Melting point** : Estimated -250°c, Observed - 240°c, **Elemental Composition:-** C%65.83,H%-4.04,O%-13.86,N%-16.17**, %yield:** 75%,**R_F value:** 0.27,ethyl acetate**:** n-hexane (7**:**3). **IR Data:** FTIR (γ max, cm^{-1}) 3741(-***NH*** stretch), 3333(**O-H** stretch(H-sond)), 2642(**C-H** stretch), 1627 (-**C=N**), 1479(Aromatic -***C=C*** stretch), 1305(***C-N*** stretch), 1088(-***C-O stretch***) . **^{1}H NMR:** (400MHZ, DMSO): 11.215(S, 1H, imidazole NH),7.936, 7.918, 7.819, 7.799, 7.716, 7.711, 7.596, 7.578, 7.560, 7.513, 7.494, 7.476, 7.449, 7.444, 7.428, 7.423, 7.225(multiplet, Ar-H), 5.902(S, 3H, phenolic OH). **^{13}CNMR:** (400MHZ,DMSO): 158.24, 155.68,(C=N) , 150.95(phenolic OH), 148.15, 148.06,133.59, 133.26, 132.10, 131.59, 131.27, 131.10, 128.60, 128.45, 128.16, 127.81, 126.48, 126.38, 126.04, 125.92, 125.41, 125.27, 124.40, 121.98, 115.49, 109. 14(Aromatic -***C=C***).

Compound-6s



IUPAC name:4-{(*E*)-[4-(1*H*-benzimidazol-2-yl) phenyl] diazenyl}-3-methylphenol **Molecular formula: :** $C_{20}H_{16}N_4O$ **,Molecular weight :** 328.38, **Melting point** : Estimated - 240°c, Observed-230°c, **Elemental Composition:-** C%-73.08, H%-4.87, O%-4.87, N%-17.05**, %yield:**65%**, R_F value:** 0.5,ethyl acetate**:** n-hexane (7**:**3). **IR Data:** FTIR (γ max, cm^{-1}) 3650(-N-H stretch), 3310(O-H stretch(H-sond)), 2845(**C-**H stretch), 1633 (-C=N), 1593(Aromatic -***C=C*** stretch), 1244 (***C-N*** stretch), 1099(-***C-O stretch***) , **^{1}H NMR:** (400MHZ, DMSO): 11.116(S, 1H, imidazole NH),7.936, 7.918, 7.819, 7.799, 7.716, 7.711, 7.596, 7.578, 7.560, 7.513, 7.494, 7.476, 7.449, 7.444, 7.428, 7.423, 7.225(multiplet, Ar-H), 4.226(S, 1H, phenolic OH),1.749(S, 3H, CH3).**^{13}CNMR:** (400MHZ,DMSO): 161.17,157.81(C=N) , 150.22(phenolic OH) , 134.79, 133.44, 132.26, 130.89, 130.25, 128.64, 128.30, 128.13, 127.59, 127.06, 127.02, 126.85, 125.05, 124.16, 119.30, 115.96(Aromatic -***C=C***),19.85 (CH3).

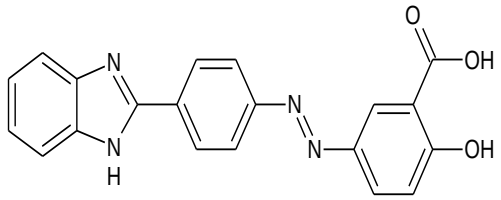
Compound-7s



IUPAC name:4-{(*E*)-[4-(1*H*-benzimidazol-2-yl)phenyl]diazenyl}-2-methylphenol , **Molecular formula: :** $C_{20}H_{16}N_4O$**,Molecular weight:**328.38**,Melting point**: Estimated-240°c, Observed-230°c,**Elemental Composition:-**C%-73.08,H%-4.87,O%-4.87,N%-17.05**, %yield:**60%**,R_F value:** 0.41 ,ethyl acetate**:** n-hexane (7**:**3). **IR Data:** FTIR (γ max, cm^{-1}) 3727(-*NH* stretch), 3400-2800(broad, O-H stretch), 2792(C-H stretch), 1591(Aromatic -*C=C* stretch), 1268 (*C-N* stretch),

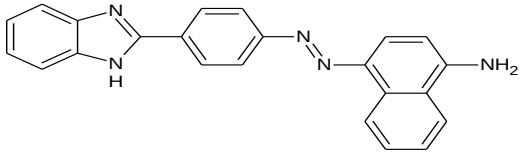
1150(-*C-O stretch*), **^{1}H NMR:** (400MHZ, DMSO): 11.529(S, 1H, imidazole NH), 8.640, 8.631, 7.987, 7.970, 7.966, 7.822, 7.805, 7.789, 7.786, 7.668, 7.650, 7.631, 7.589, 7.570, 7.555, 7.471, 7.452, 7.418, 7.416, 7.399, 7.381, 7.192(multiplet, Ar-H),4.529(S, 1H, phenolic OH),1.839(S, 3H, C**H3**).. **^{13}CNMR:** (400MHZ, DMSO): 162.26, 158.64(C=N), 150.22(phenolic OH), 134.79, 133.44, 132.26, 130.89, 130.25, 128.64, 128.30, 128.13, 127.59, 127.06,127.02, 126.85, 125.05, 124.16, 119.30, 115.96(Aromatic -***C=C***),19.85(CH3).

Compound-8s



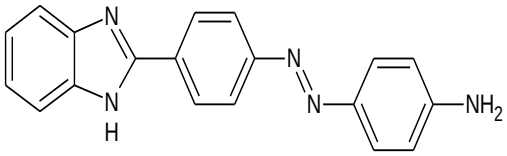
IUPAC name:5-{(*E*)-[4-(1*H*-benzimidazol-2-yl) phenyl]diazenyl}-2-hydroxybenzoic acid, **Molecular formula: :** $C_{20}H_{14}N_4O_3$, **Molecular weight :** 358.36,**Melting point**: Estimated-270°c , Observed-240°c , **Elemental Composition:-** C%-66.97,H%-3.91,O%-13.39,N%-15.63, **%yield:** 71%**, R_F value:** 0.36 ,ethyl acetate**:** n-hexane (7**:**3).**IR Data:** FTIR (γ max, cm^{-1}) 3739(-*NH* stretch), 3665(O-H stretch (carboxylic acid)), 2804(C-H stretch), 1672 (-C=N), 1581(Aromatic -*C=C* stretch), 1282(*C-N* stretch), 1212(-*C-O* stretch) **^{1}H NMR:** (400MHZ, DMSO): 11.693(S, 1H, imidazole NH),9.952(S, 1H, COOH),, 8.398, 8.135, 8.127, 8.114, 7.982, 7.969, 7.960, 7.925, 7.904, 7.890, 7.871, 7.718, 7.700, 7.665, 7.582, 7.573, 7.563, 7.535, 7.521, 7.502, 7.482, 7.462, 7.445, 7.374, 7.225, 7.205, 7.059, 7.039(multiplet, Ar-H), 4.366(S, 1H, phenolic OH), 4.354, 4.342. **^{13}CNMR:** (400MHZ, DMSO): 171.31(C=0), 165.87, 165.20, 161.17, 157.81(C=N), 150.22(phenolic OH),134.79, 133.44, 132.26,130.89, 130.25, 128.64, 128.30, 128.13, 127.59, 127.06, 127.02, 126.85, 125.05, 124.16, 119.30, 115.96(Aromatic -***C=C***)

Compound-9s



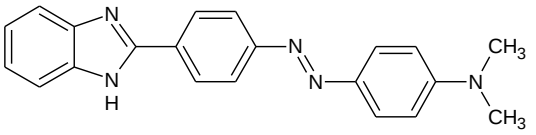
IUPAC name:4-{(*E*)-[4-(1*H*-benzimidazol-2-yl)phenyl]diazenyl}naphthalen-1-amine **Molecular formula: :** $C_{23}H_{17}N_5$, **Molecular weight:** 363.42,**Melting point**: Estimated-260°c, Observed-210°c ,Elemental Composition:- C%-75.94,H%-4.67,N%-19.26**, %yield:**68%**,R_F value:** 0.28 ,ethyl acetate**:** n-hexane (7**:**3). **IR Data:** FTIR (γ max, cm^{-1}) 3739(-*NH* stretch), 2798(C-H stretch), 1680 (-C=N), 1582(Aromatic -*C=C* stretch), 1314(*C-N* stretch). **^{1}H NMR:** (400MHZ, DMSO): 12.005(S, 1H, imidazole NH),8.370, 8.133, 8.123, 8.111, 7.982, 7.968, 7.958, 7.923, 7.902, 7.882, 7.723, 7.705, 7.675, 7.582, 7.572, 7.560, 7.535, 7.519, 7.499, 7.482, 7.464, 7.446, 7.362, 7.120, 7.100, 6.888, 6.868(multiplet, Ar-H), ,3.854 (S, 2H, NH2),.**^{13}CNMR:** (400MHZ,DMSO): 144.22(C=N),134.79(C-NH2), 133.44, 132.26, 130.89, 130.25, 128.64, 128.30, 128.13, 127.59, 127.06, 127.02, 126.85, 125.05, 124.16, 119.30, 115.96(Aromatic -***C=C***)

Compound-10s



IUPAC name : 4-{(*E*)-[4-(1*H*-benzimidazol-2-yl) phenyl] diazenyl}aniline **Molecular formula: :** $C_{19}H_{15}N_5$,**Molecular weight:**313.36,**Melting point**: Estimated-240°c, Observed-230°c ,**Elemental Composition:-** C%-72.76,H%-4.78,N%-22.34, **%yield:**98%**, R_F value:** 0.66 ,ethyl acetate**:** n-hexane (7**:**3). **IR Data:** FTIR (γ max, cm^{-1}): 3741(-*NH* stretch), 2905(C-H stretch),1679 (-C=N), 1596(Aromatic -*C=C* stretch), 1285(*C-N* stretch). **^{1}H NMR:** (400MHZ, DMSO): 12.726(S, 1H, imidazole NH),8.013, 7.992, 7.983, 7.966, 7.945, 7.913, 7.906, 7.893, 7.757, 7.738, 7.686, 7.665, 7.636, 7.631, 7.614, 7.608, 7.589, 7.576, 7.558, 7.541, 7.532, 7.522, 7.514, 7.494, 7.471, 7.460, 7.449, 7.441, 7.421, 7.402, 7.399, 7.390, 7.278, 7.260, 7.242, 6.696, 6.692, 6.674, 6.107(multiplet, Ar-H), 3.349 (S, 2H, NH2). **^{13}CNMR:** (400MHZ, DMSO): 166.98 ,152.81, 152.48, (C=N)142.86 , 131.16 (C-NH2), 130.96, 129.40, 129.32, 129.27, 129.12, 126.41, 125.10, 122.40, 122.00, 121.67, 119.34, 115.21, 113.38, 112.56 (Aromatic -***C=C***)

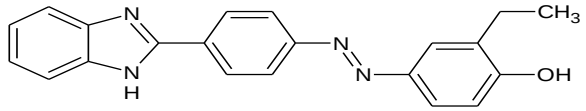
Compound-11s



IUPAC name: 4-{(*E*)-[4-(1*H*-benzimidazol-2-yl) phenyl]diazenyl } -*N*,*N*- dimethyl aniline, **Molecular formula: :** $C_{21}H_{19}N_5$, **Molecular weight :** 341.42, **Melting point**: Estimated - 240°c , Observed - 230°c ,**Elemental Composition :-** C%-73.81,H%-5.56,N%-20.5, **%yield:**69%**,R_F value:** 0.25 ,ethyl acetate**:** n-hexane

(7:3).**IR Data:** FTIR (γ max, cm^{-1}) 3733(-*NH* stretch), 2922(C-H stretch),1681 (-C=N), 1586(Aromatic -*C=C* stretch), 1208(*C-N* stretch), **^{1}H NMR:** (400MHZ,DMSO) 11.225(S, 1H, imidazole NH) ,7.936, 7.918, 7.819, 7.799, 7.716, 7.711, 7.596, 7.578, 7.560, 7.513, 7.494, 7.476, 7.449, 7.444, 7.428, 7.423, 7.211(multiplet, Ar-H), 4.210 (S, 3H ,N- CH3), 3.749(S, 3H , N-CH3). **^{13}CNMR:**(400MHZ, DMSO): 149.62, 138.71, 135.99(C-N), 133.61, 133.26, 131.91, 131.58, 131.27, 131.11, 129.04, 128.80, 128.74, 128.67, 128.63, 128.53, 128.43, 128.15, 127.82, 127.03, 126.47, 126.37, 126.03, 125.80, 125.74, 125.39, 125.43(Aromatic -***C=C***),18.51(CH3)

Compound-12s



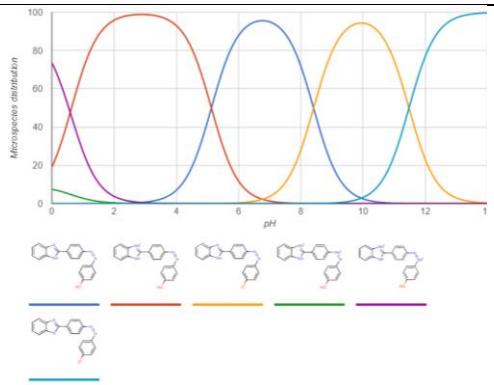
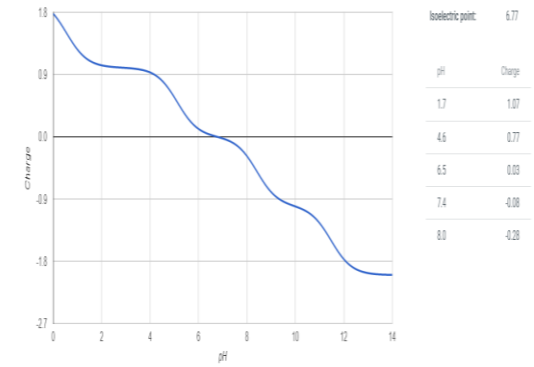
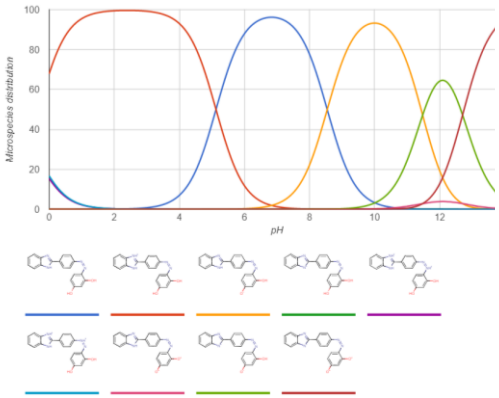
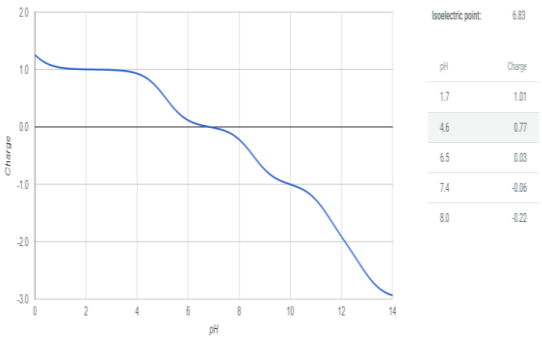
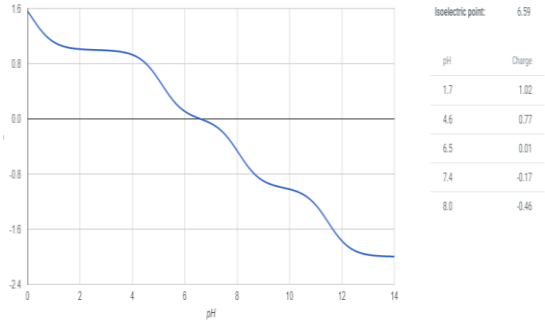
IUPAC name:1-(5-{(*E*)-[4-(1*H*-benzimidazol-2-yl) phenyl]diazenyl}-2-hydroxyphenyl) ethanone , **Molecular formula:** $C_{21}H_{16}N_4O_2$, **Molecular weight:**356.38, **Melting point**: Estimated-250°c, Observed-260°c , **Elemental Composition:-** C%-70.71,H%-4.48,O%-8.98,N%-15.71, **%yield:**42% **,, R_F value:** 0.29 ,ethyl acetate**:** n-hexane (7:3).**IR Data:** FTIR (γ max, cm^{-1}) 3739(-*NH* stretch)*;* 3400-2890(broad, O-H stretch), 2832(C-H stretch), 1678 (-C=N), 1573(Aromatic -*C=C* stretch), 1360(*C-N* stretch), 1151(-*C-OH stretch*) **^{1}H NMR:** (400MHZ,DMSO) 11.036 (S, 1H, imidazole NH), 7.936, 7.918, 7.819, 7.799, 7.716, 7.711, 7.596, 7.578, 7.560, 7.513, 7.494, 7.476, 7.449, 7.444, 7.428, 7.423, 7.225(multiplet, Ar-H), 5.902(S, 1H , phenolic-OH)., **^{13}CNMR:**(400MHZ,DMSO): 150.33(ArylC- OH), 145.63, 138.78, 132.64, 130.83, 126.98, 125.13, 115.45, 114.89, 114.51(Aromatic C=C), 25.26(CH2), 21.19(CH3)

ChemAxon's Physio-Chemical Property Predictor [27] :

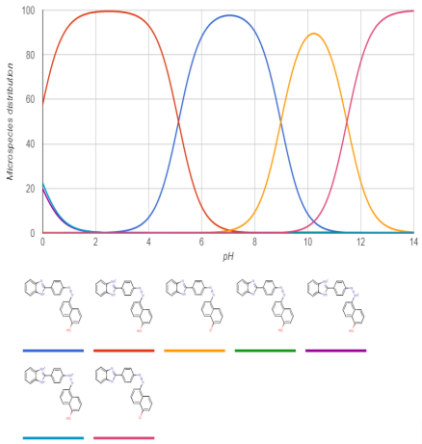
The website provides computational values of PKa, solubility mg/mL, isoelctric point and log P values that provides a detailed insight of solubility and ionisation.At various pH due to the micro species or chemical fragments that are responsible for the changes in the aqueous solubility which is one of the most important property in modern drug discovery. As solubility has impact on ADME-related properties like drug uptake, distribution and even oral bioavailability. Solubility can also be a relevant descriptor for property-based computational screening methods in the drug discovery process. Hence this method serves as a fast, reliable, structure-based method for predicting solubility in water for promising drug candidate. The results were tabulated in tables 1&2.

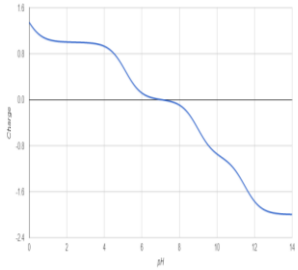
The PKa prediction program is based on the calculation of partial charge distribution of atoms in the molecule and the predictor uses a fragment-based method that identifies different structural fragments in the molecule (micro and macro species) that alter the PKa of a molecule. The below PKa graphs is assigned against pH and micro species that alter the PKa value of the compound. The table 1 presents isoelctric points of the compounds indicating 4.57 **(8s)**, 5.70**(7s)** and other compounds having values ranging from 6.03 to 8.70 these representing the pH at which the molecule carries no net charge that is necessary to predict the solubility of a compound. The micro acidic dissociation constant PKa is obtained from the equilibrium concentration of the conjugated acid-base pairs. The macro acidic dissociation constant is obtained from the global mass and charge conservation law. When a molecule has N ionisable sites, the total number of micro species in the solution is 2^N. LogP calculations are based on a pool of fragments predefined in the log*P* calculator and solubility categorised based on intrinsic solubility predictor. The tabulated results of intrinsic solubility and log p values clearly indicates ionisation constants ranging from 4.50 to 7.02 obtained from graphs drawn against log D and pH. The values of intrinsic solubility is also less than zero which indicates the compounds were categorised with low aqueous solubility.

Table 1: PKa & Isoelectric point graphs of compounds 1s-12s determined by chemaxon online software.

Compound	PKa	Isoelectric point
1s		
2s		
3s		

4s

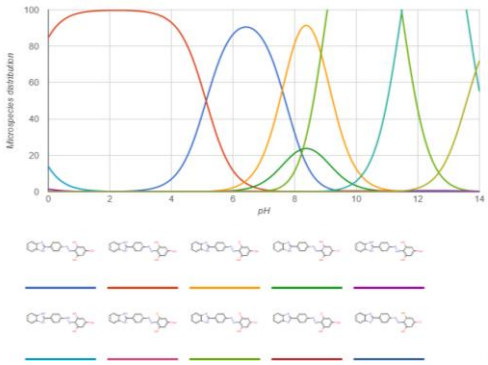


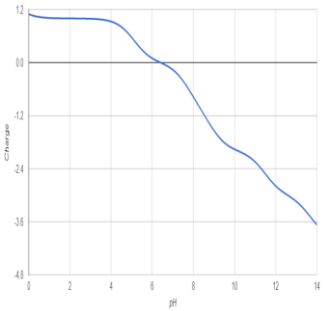


Isoelectric point: 7.05

pH	Charge
1.7	1.01
4.6	0.77
6.5	0.04
7.4	-0.02
8.0	-0.09

5s

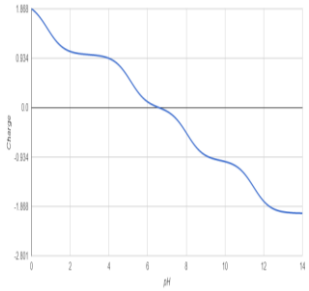




Isoelectric point: 6.40

pH	Charge
1.7	1.00
4.6	0.77
6.5	-0.02
7.4	-0.35
8.0	-0.78

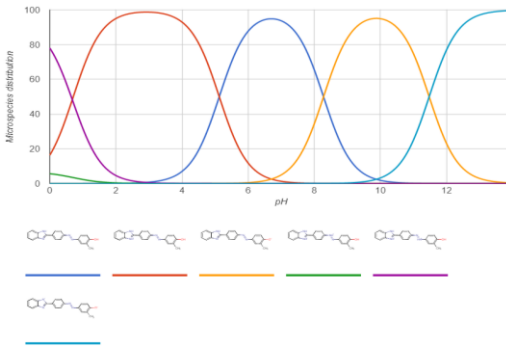
6s

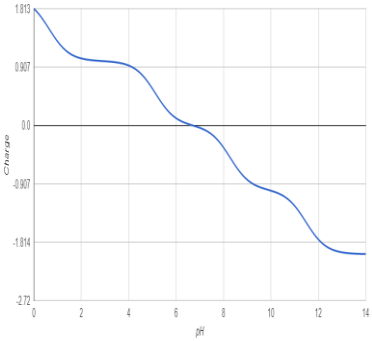


Isoelectric point: 6.58

pH	Charge
1.7	1.11
4.6	0.77
6.5	0.01
7.4	-0.10
8.0	-0.48

7s

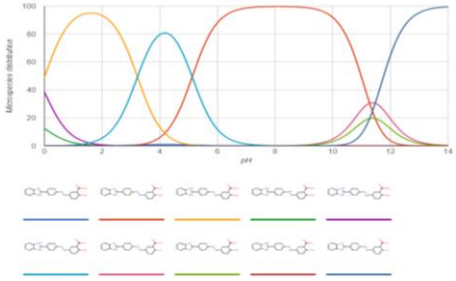


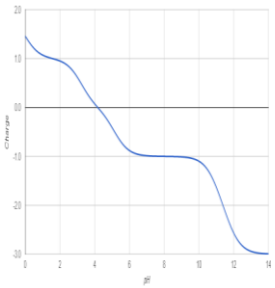


Isoelectric point: 6.70

pH	Charge
1.7	1.08
4.6	0.77
6.5	0.02
7.4	-0.11
8.0	-0.34

8s

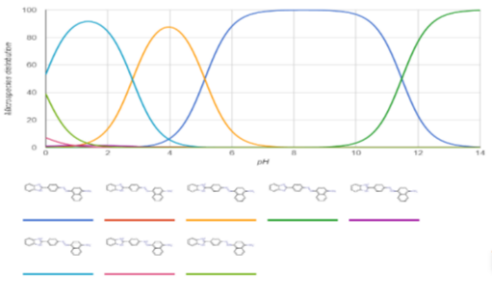


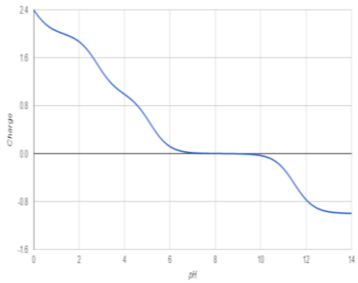


Isoelectric point: 4.17

pH	Charge
1.7	0.99
4.6	-0.19
6.5	-0.96
7.4	-0.99
8.0	-1.00

9s

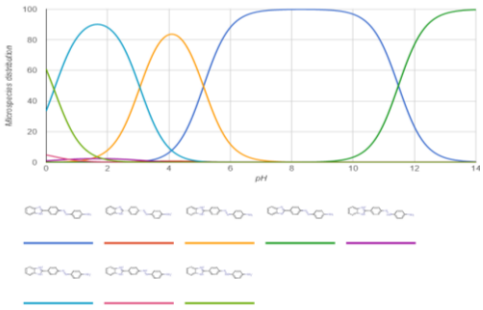


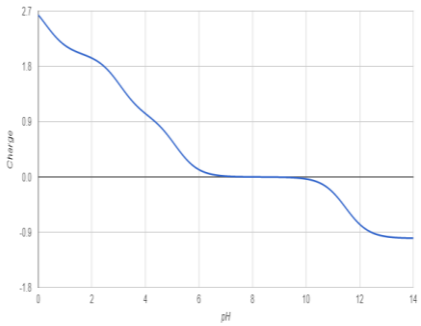


Isoelectric point: 8.30

pH	Charge
1.7	1.94
4.6	0.79
6.5	0.04
7.4	0.01
8.0	0.00

10s

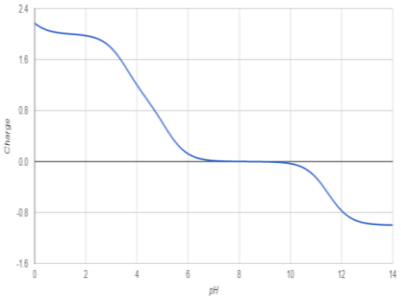




Isoelectric point: 8.30

pH	Charge
1.7	1.99
4.6	0.80
6.5	0.04
7.4	0.01
8.0	0.00

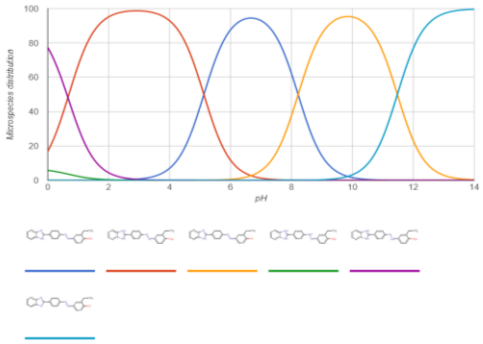
11s

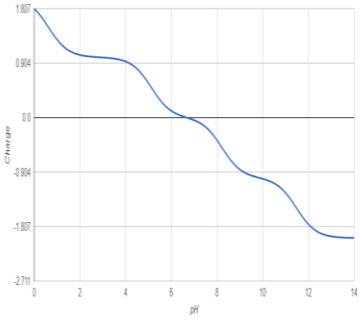


Isoelectric point: 8.31

pH	Charge
1.7	1.99
4.6	0.86
6.5	0.04
7.4	0.01
8.0	0.00

12s

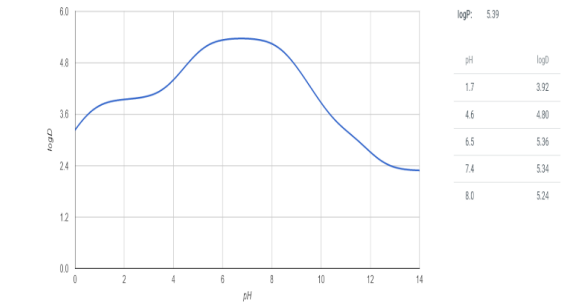
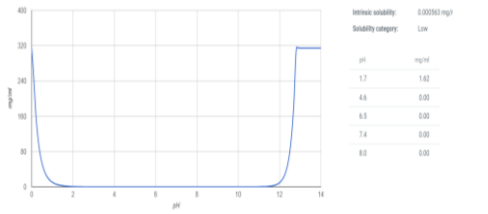
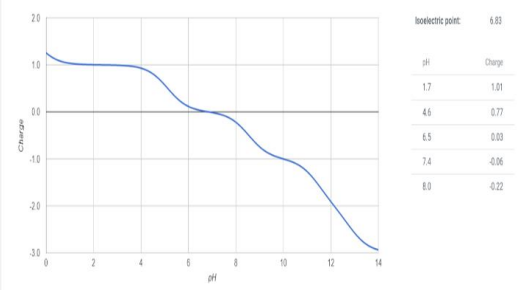
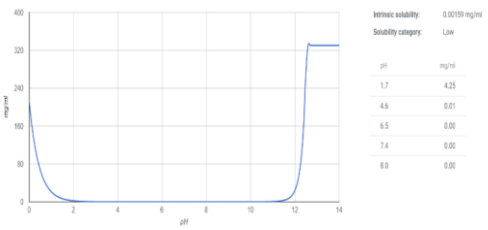
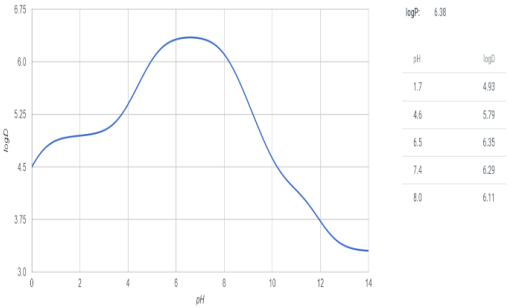
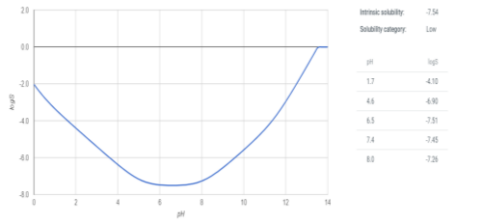
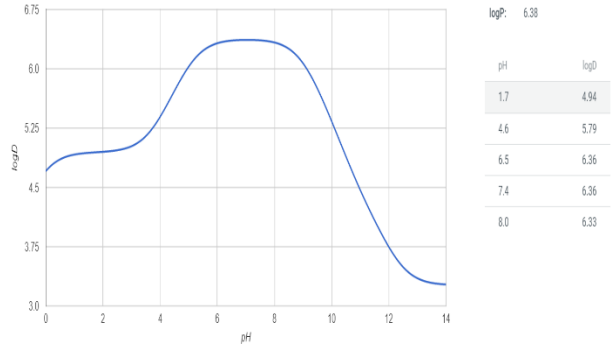
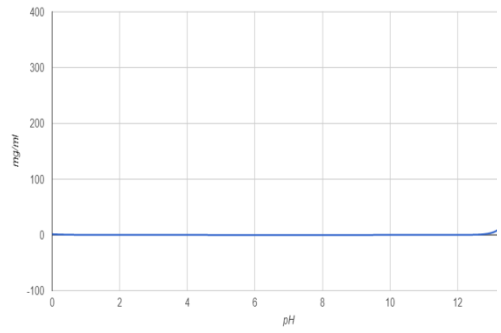
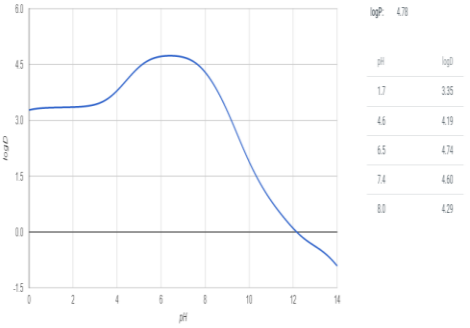
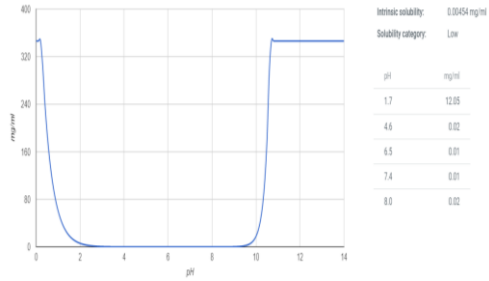




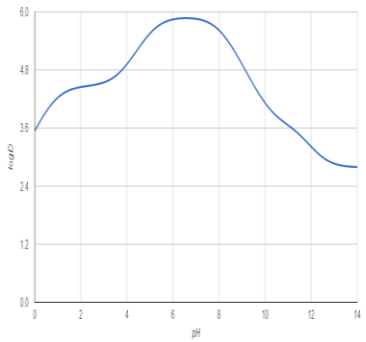
Isoelectric point: 6.67

pH	Charge
1.7	1.08
4.6	0.77
6.5	0.02
7.4	-0.13
8.0	-0.38

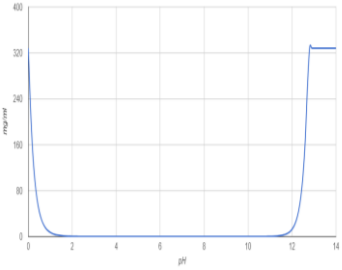
Table 2: Log p & Solubility (mg/ml) graphs of compounds 1s-12s determined by ChemAxon's online software.

Compound	Log P	Solubility (mg / mL)
1s		
2s		
3s		
4s		
5s		

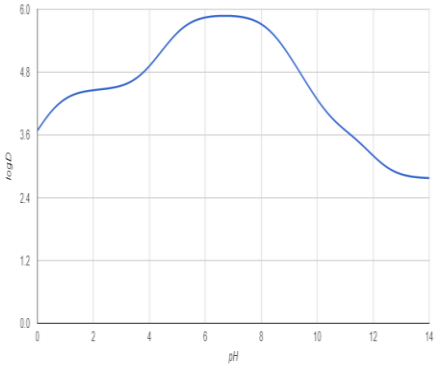
6s



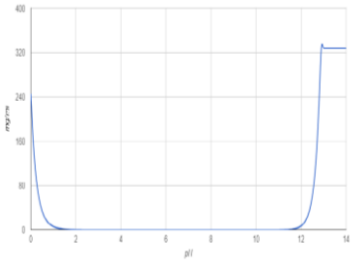
pH	logD
1.7	4.41
4.6	5.31
6.5	5.87
7.4	5.81
8.0	5.62



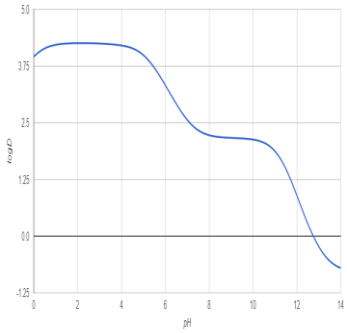
7s



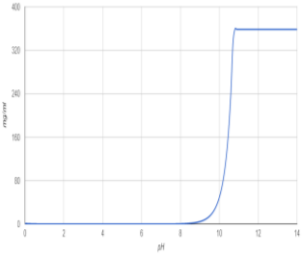
pH	logD
1.7	4.43
4.6	5.31
6.5	5.88
7.4	5.84
8.0	5.72



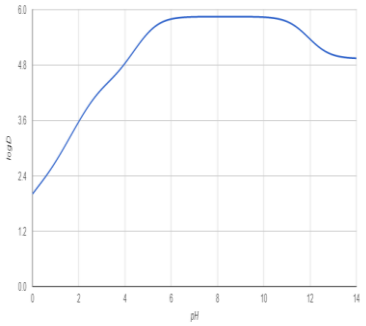
8s



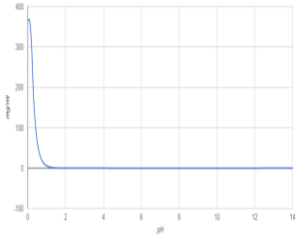
pH	logD
1.7	4.25
4.6	4.12
6.5	2.92
7.4	2.37
8.0	2.23



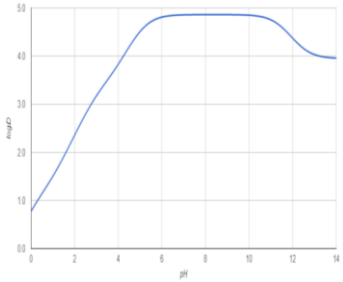
9s



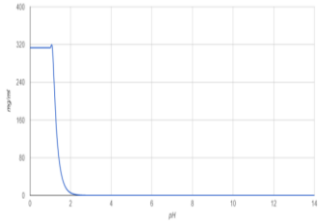
pH	logD
1.7	3.31
4.6	5.26
6.5	5.83
7.4	5.85
8.0	5.85



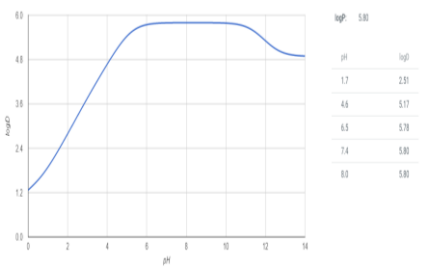
10s

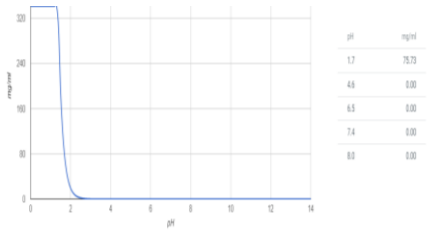


pH	logD
1.7	2.09
4.6	4.26
6.5	4.84
7.4	4.86
8.0	4.86

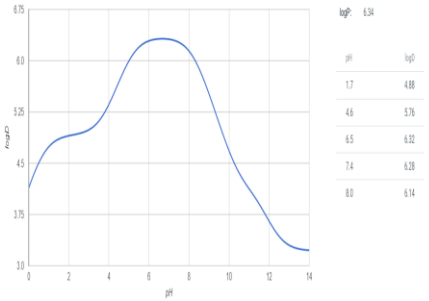


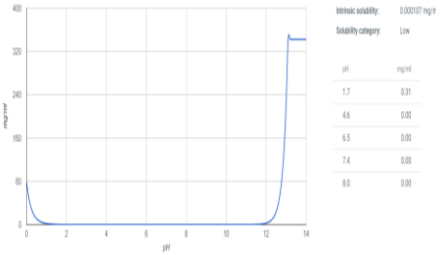
11s





12s





RESULTS AND DISCUSSION:

The above mentioned benzimidazole dyes were synthesised by conventional diazotisation reaction followed by coupling with various phenols and amines. The compounds were characterised by IR method by the presence of strong absorption band around 1400–1650 cm-1 for –C=N– stretching, 3454 cm-1 (N-H str), 2959.5 cm-1 (=C-H str) and 1637 cm-1 (C=C str), 1558 cm-1 (C=N str),1400-1450 cm-1 (N=N str) and the disappearance of NH2 absorption band present in step-1 product. Proton NMR data reveals a multiplet peak at δ 6.9-8.3 may be due to aromatic protons and peak at δ10-12 may be due to NH proton of benzimidazole ring. C13 spectral data shows the presence of aromatic carbons in the range s from δ (115-145ppm), 150-165 ppm for the presence of aromatic hydroxyl group. The online cheminformatics software ChemAxon's shows the values of intrinsic solubility is less than zero which indicates the compounds were categorised with low aqueous solubility. The Isoelectric points for the compounds **8s** (4.57), **7s** (5.70) and other compounds having values ranging from 6.03 to 8.70 were representing the pH at which the molecule carries no net charge and necessary to predict the solubility of a compound.

CONCLUSION:

A series of new substituted {4-(1H-Benzimidazol-2-yl) Phenyl} Diazenyl derivatives were prepared by conventional method and characterised by spectral methods. The physiochemical properties were determined to evaluate its solubility and PKa. It is intended that the results from these studies will assist in providing an approach for further optimization and development to get new leads.

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