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Synthesis and Biological Screening of Cyanopyrans

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Abstract: Substituted chalcones have been prepared by the reaction of m-(2, 5-Dichlorobenzene sulphonamido)-acetophenone with different aromatic aldehyde. Chalcones react with malononitrile in presence of piperidene to from cyanopyrans. The structures of the synthesized compounds have been assigned on the basis of elemental analysis, IR, NMR and Mass spectral studies. The compounds were evaluated for antimicrobial screening against Gram positive, Gram negative bacterial and fungal strain such as *Aspergillums Niger*.

Keywords: Cyanopyrans, Antimicrobial activity

Introduction

Oxygen containing heterocycles such as pyran derivatives represents one of the modest classes of compounds due to their wide range of biological and industrial applications**[1]**. Literature survey reveals that Cyanopyran derivatives possess various valuable biological activities, such as antifungal **[2-4]**, antibacterial **[5]**, antiviral **[6-7]** and anticonvulsant activity**[8]**. They are also used as a sweet smelling agent.

On the other hand Hanna M.A and et.al**[9]**have been reported sulphonamide derivatives as a potential hypoglycaemic agent. Antitubercular activity of sulphonamide has been reported by Gupta and et.al**[10]**.

In viewed of the above facts, we have synthesized a series of cyanopyran derivative conjugates with sulphonamide to explore their biological potency**[11]**. The targeted molecule **3a-k** has been synthesised by the condensation of chalcones**2a-k** with malononitrile**[12-14]**. The chalcone have been prepared by the claisen condensation of m-(2, 5-Dichlorobenzenesulphonamido) - acetophenone on treatment with different aromatic aldehyde in presence of basic catalyst such as 40% NaOH.

Materials and Methods

Melting points were determined in an open capillary tube and are uncorrected. IR spectra (KBr) were recorded on a SHIMADZU-IR &^{1}HNMR spectra ($CDCl_3$) δppms were recorded on a BRUKER spectrometer (400 MHz). Compounds were routinely checked for their homogeneity by TLC on silica gel plates.

Experimental

General procedure for the synthesis of 2, 5-dichloro-N-{3-[(2Z)-3-phenylprop-2-enoyl] phenyl}benzenesulphonamide (2a-k): -

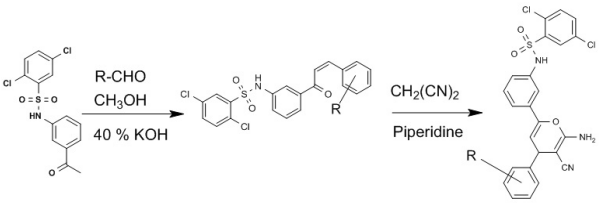
Take aEquimolar mixture of *m*-(2, 5-Dichlorobenzene sulphonamidophenyl) -acetophenone (0.01mole, 3.44g) and *p*-anisaldehyde (0.01mole, 1.36g) in a 25ml methanol, Add 40% KOH solutiondrop wise until solution becomes basic. Refluxed the reaction mixture for 8-10 hrs. Reaction maintained by TLC.After complitation of reaction, reaction mixtures poured on to ice, acidify with HCl and isolate the product,filtered it and crystallised from ethanol. TLC Solvent System Acetone: Benzene 0.5:9.5. Yield 80%, m.p. 176°C. (Found: C, 57.14 %; H, 3.24%; N, 3.0%; $C_{21}H_{15}Cl_2NO_3S$Requires: C, 57.2%; H, 4.0%; N, 3.2%). IR (KBr): 1654 cm^{-1} (C=O str.), 1600 cm^{-1} (-CH=CH str.), 1566 cm^{-1} (NHdef), 1245.9 cm^{-1} (C-O-C str. asym), 1039 cm^{-1}(C-O-C str. sym), 738.7 cm^{-1}(C-Cl str.).; ^{1}HNMR(400 MHz, DMSO-d6): δ ppm: 7.0 (doublet, 2H, Ar-H,I,I'), 7.35 (doublet, 1H, =CHX), 7.4 (multiplet, 4H, Ar-H, a',e,f,g) 7.67 (doublet, 2H, Ar-H, h,h'), 7.76 (multiplet, 2H, Ar-H, a,b), 7.86 (doublet, 1H, =CH), 8.0 (doublet, 1H, Ar-H,c).

Similarly, other chalcones were prepared.

General procedure for the synthesis of N-[3-(6-amino-5-cyano-4-phenyl-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulfonamide (3a-k):-

Take A mixture of 1, m-(2, 5-Dichlorobenzenesulphonamide phenyl)-3-(p-anisyl)-2-propene-1-one (0.01mole, 4.62g) and malononitrile (0.01mole, 0.66g) and piperidine (2-3 drops) as a catalyst, refluxed the reaction mixture on a water bath for 10 hrs. The reaction product was poured onto ice. Crude product was isolated, crystallised from isopropyl alcohol. TLC solvent system: Acetone: Benzene 1:9. Yield 75%, m.p. 152°C. (Found: C, 56.9%; H, 3.4%; N, 7.96%; $C_{24}H_{17}Cl_2N_3O_3S$requires C, 56.87%; H, 3.2%; N, 7.92%). IR (KBr): 2933.5 cm^{-1} (C-H, str. sym), 2191 cm^{-1} (C≡N str.), 1635.5 cm^{-1} (NH def), 1454.2 cm^{-1} (C-H str. asym), 790.8 cm^{-1} (C-Cl str.).;^{1}HNMR(400 MHz, DMSO-d6): δppm: 7.0 (doublet, 2H, Ar-H,i,i'), 7.3 (doublet,2H, Ar-H,h,h'), 7.4 (singlet, 2H, Ar-h,a,d), 7.6 (triplet, 2H, Ar-H,f.g), 7.7 (doublet, 1H, Ar-H,e), 7.9 (doublet, 1H,Ar-H,b), 8.0 (doublet, 1H, Ar-H,e).

Reaction scheme



Biological Evaluation

The Antimicrobial Activity**[15],[16]** was compared to with Standard DrugsvizAmpicillin, Amoxicillin, Ciprofloxacin, Erythromycin, and antifungal activity were compared with viz Greseofulvin. The zones of inhibition have been measured in mm.

(a) **Antimicrobial Activity**

It was carried out by Cup-plateMethod which has been described as under**[17-19]**.

(I) **Antibacterial activity**

The purified products were screened for their Antibacterial activity. The nutrient agar broth prepared by usual method, was inoculated aseptically with 0.5 ml of 24 hrs. Old subcultures of B.*megaterium*, *S. aureus*, *E. coli*, *P. vulgaris*

in separate conical flask at 40-50 ºC and mixed well by gently shaking. About 25ml content of the flask were poured and evenly spreader in a Petridis (13 cm in diameter) and allowed to set for 2 hrs. The cups (10 mm in diameter) were formed by the help of borer in agar medium and filled with 0.04 ml (40 µg) solution of sample in DMF.

The plates were incubated at 37 ºC for 24 hr. and the control was also maintained 0.04 mol of DMF in a similar manner and the zones of inhibition of the bacterial growth were measured in milimeter and are recorded in Graphical chart No. 1.

(II) **Antifungal activity**

A.*niger*was employed for testing antifungal activity **[20-22]** using cup-plate method. The culture was maintained on subouraud's agar slants, sterilised subouraud's agar medium was inoculated with 72 hrs. Old 0.5ml suspension of fungal spores in a separate flask. About 25 ml

Table- I: -Antimicrobial Activity of 2, 5-Dichloro-N-{3-[(2Z)-3-phenylprop-2-enoyl]phenyl} benzenesulfonamide (2a-k) and Antimicrobial Activity of N-[3-(6-amino-5-cyano-4-phenyl-4H-pyran-2-yl)phenyl]-2, 5-dichlorobenzenesulfonamide (3a-k):-

Code	S.aureus	B.mega	E.coli	P.vulgaris	A.niger
2a	14	11	9	12	16
2b	9	11	10	15	16
2c	11	10	12	16	9
2d	13	9	11	12	10
2e	12	9	11	13	10
2f	10	9	11	14	12
2g	14	9	10	14	13
2h	16	9	11	13	14
2i	11	13	15	16	14
2j	13	11	15	16	14
2k	15	11	13	9	10
Ampicillin	18	22	22	21	0
Amoxicillin	17	24	23	20	0
Ciprofloxacin	20	19	18	19	0
Erythromycin	23	27	28	25	0
Greseofulvin	0	0	0	0	25
3a	11	12	15	14	10
3b	10	12	15	11	9
3c	15	12	16	13	10
3d	15	11	13	9	14
3e	16	15	10	14	9
3f	14	16	12	9	11
3g	11	13	15	9	12
3h	12	10	9	16	11
3i	15	13	11	10	12
3j	9	11	12	16	13
3k	11	10	12	16	9
Ampicillin	18	22	22	21	0
Amoxicillin	17	24	23	20	0
Ciprofloxacin	20	19	18	19	0
Erythromycin	23	27	28	25	0
Greseofulvin	0	0	0	0	25

of the inoculated medium was evenly spreader in a Petridis and allow setting for two hrs. The cups (10 mm in diameter) were punched. The plates were incubated at 30ºC for 48 hrs. After the completation of incubation period, the zone of inhibition of growth in the form of diameter in mm was measured. Along the test solution in each Petridis one cup was filled up with solvent which act as control.

Results and discussion

Compounds were screened for their antifungal activity using cup-plate agar diffusion method at a concentration of 40 µg using Gram positive bacterial strains such as *Bacillus megaterium***(ATCC 14945)**and *staphylococcus aureus***(ATCC 55804)**and Gram negative strains such as *Escherichia coli***(ATCC 10798)** and *P.vulgaris***(ATCC 21719)**. The antifungal testing was carried out against Aspergillums Niger. Known antibiotics like ampicillin, amoxicillin, ciprofloxacin, erythromycin and Greseofulvin were used for comparison purpose. By visualizing the antimicrobial data[**23-24]**, it could be observed that most of the compounds exhibited significant activity. (Table I).

Spectral Data

2, 5-Dichloro-N-{3-[(2E)-3-biphenylprop-2-enoyl] phenyl}benzenesulphonamide (2a):

Yield:- 69%; MP: 180-182 ºC; MS: m/z = 508 ; IR (KBr): 3030cm^{-1} (aromatic) 1665 cm^{-1}(C=O str.), 1580 cm^{-1} (-CH=CH str.), 1546 cm^{-1} (NHdef), 1257 cm^{-1} (C-O-C str. asym), 1028 cm^{-1}(C-O-C str. sym), 749 cm^{-1}(C-Cl str.).;^{1}H NMR (400 MHz, DMSO-d_6) δ 7.26 – 7.58 (m, 8H), 7.60 – 7.76 (m, 8H), 7.84 – 7.93(dt, 1H), 7.94 – 8.00 (d, 1H), 8.83 – 8.88 (s, 1H); Elemental Analysis for$C_{27}H_{19}Cl_2NO_3S$:Calculated; C(63.78%)H(3.77%)N(2.75%)O(9.44%). Found:C(63.77%)H(3.78%)N(2.76%) O(9.42%).

2, 5-Dichloro-N-{3-[(2E)-3-2-chlorobiphenylprop-2-enoyl]phenyl} benzenesulphonamide(2b):

Yield:- 60%; MP: 102-104ºC; MS: m/z= 542;IR (KBr): 1654 cm^{-1} (C=O str.), 1600 cm^{-1}(-CH=CH str.), 1566 cm^{-1} (NHdef), 1245.9 cm^{-1} (C-O-C str. asym), 1039 cm^{-1}(C-O-C str. sym), 738.7 cm^{-1}(C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 7.26 – 7.51 (m, 5H), 7.51 – 7.78 (m, 10H), 7.85 – 8.00 (m, 2H), 8.83–8.88(s,1H); Elemental Analysis for $C_{27}H_{18}Cl_3NO_3S$:Calculated:C(59.74%) H(3.34%)N(2.58%)O(8.84%). Found:C(59.72%)H(3.34%)N(2.60%) O(8.82%).

2, 5-Dichloro-N-{3-[(2E)-3-4-chlorobiphenylprop-2-enoyl]phenyl} benzenesulphonamide (2c):

Yield:- 68%; MP: 120-122 ºC; MS: m/z= 542;IR (KBr): 1648 cm^{-1} (C=O str.), 1608 cm^{-1}(-CH=CH str.), 1558 cm^{-1} (NHdef), 1254 cm^{-1} (C-O-C str. asym), 1033 cm^{-1}(C-O-C str. sym), 734.2 cm^{-1}(C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 7.25 – 7.36 (m, 2H), 7.41 – 7.56 (m, 5H), 7.62 – 7.78 (m, 6H), 7.80 – 8.00 (m, 4H), 8.83 – 8.88 (s, 1H);Elemental Analysisfor $C_{27}H_{18}Cl_3NO_3S$:Calculated:C(59.74%) H(3.34%)N(2.58%)O(8.84%). Found:C(59.72%)H(3.34%)N(2.58%) O(8.83%).

2, 5-Dichloro-N-{3-[(2E)-3-biphenyl-4-ylmethyletherprop-2-enoyl] phenyl} benzenesulphonamide (2d):

Yield:- 80%; MP: 176-178 ºC; MS: m/z= 538;IR (KBr): 1735cm^{-1} (C=O-C) 1652 cm^{-1}(C=O str.), 1608 cm^{-1} (-CH=CH str.), 1568 cm^{-1} (NHdef), 1245.4 cm^{-1} (C-O-C str. asym), 1042cm^{-1}(C-O-C str. sym), 734.3 cm^{-1}(C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 3.77 – 3.82 (s, 3H), 6.93 – 7.01 (m, 2H), 7.25 – 7.36 (m, 2H), 7.41 – 7.57 (m, 5H), 7.62 – 7.75 (m, 6H), 7.85 – 7.94 (dt, 1H), 7.94 – 8.00 (d, 1H), 8.83 – 8.88 (s, 1H);Elemental Analysis for $C_{28}H_{21}Cl_2NO_4S$: Calculated: C(62.46%)H(3.93%)N(2.60%) O(11.89%).Found: C(62.42%)H(3.95%) N(2.62%) O(11.87%).

2, 5-Dichloro-N-{3-[(2E)-3-biphenyl-3-ylphenyletherprop-2-enoyl] phenyl}

benzenesulphonamide (2e):

Yield:- 64%; MP: 135-137 ºC; MS: m/z = 600 ;IR (KBr): 1649 cm^{-1} (C=O str.), 1596 cm^{-1}(-CH=CH str.), 1556 cm^{-1} (NHdef), 1242.7 cm^{-1} (C-O-C str. asym), 1049 cm^{-1}(C-O-C str. sym), 734.7 cm^{-1}(C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 6.97 – 7.05 (m, 2H), 7.10 – 7.32 (m, 5H), 7.33 – 7.56 (m, 8H), 7.62 – 7.75 (m, 5H), 7.87 – 8.00 (m, 2H), 8.51 – 8.56 (s, 1H); Elemental Analysis for $C_{33}H_{23}Cl_2NO_4S$: Calculated: C(66.00%)H(3.86%)N(2.33%) O(10.66%). Found:C(66.00%)H(3.87%) N(2.33%)O(10.64%).

2, 5-Dichloro-N-{3-[(2E)-3-biphenyl-3-olprop-2-noyl] phenyl} benzenesulphonamide (2f):

Yield:- 51%; MP: 154-156 ºC; MS: m/z = 524 ;IR (KBr):3200cm^{-1} (O-H) 1664 cm^{-1}(C=O str.), 1600 cm^{-1} (-CH=CH str.), 1570cm^{-1}(C-NO_2)1566 cm^{-1} (NHdef), 1245.9 cm^{-1}(C-O-C str. asym), 1039 cm^{-1}(C-O-C str. sym), 738.7 cm^{-1}(C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 6.78 – 6.86 (dt, 1H), 7.05 – 7.13 (dt, 1H), 7.14 – 7.38 (m, 4H), 7.43 – 7.56 (m, 3H), 7.63 – 7.75 (m, 6H), 7.85 – 8.00 (m, 2H), 8.84 – 8.89 (s, 1H), 9.09 – 9.14 (s,1H);Elemental Analysis for $C_{27}H_{19}Cl_2NO_4S$:Calculated: C(61.84%) H(3.65%)N(2.67%)O(12.20%). Found: C(61.85%)H(3.63%)N(2.67%)O(12.22%).

2, 5-Dichloro-N-{3-[(2E)-3-3-nitrobiphenylprop-2-enoyl] phenyl} benzenesulphonamide(2g):

Yield:- 72%; MP: 178-180 ºC; MS: m/z = 553 ;IR (KBr): 1668 cm^{-1} (C=O str.), 1600 cm^{-1}(-CH=CH str.), 1566 cm^{-1} (NHdef), 1245.9 cm^{-1} (C-O-C str. asym), 1039 cm^{-1}(C-O-C str. sym), 738.7 cm^{-1}(C-Cl str.).;^{1}H NMR (400 MHz, DMSO-d6) δ 7.22 – 7.36 (m, 2H), 7.55 – 7.79 (m, 10H), 7.89 – 8.00 (m, 3H), 8.04 – 8.12 (dt, 1H), 8.30 – 8.36 (t, 1H), 8.57 – 8.62 (s, 1H); Elemental Analysis for$C_{27}H_{18}Cl_2N_2O_5S$:Calculated: C(58.60%) H(3.28%)N(5.06%)O(14.46%). Found: C(58.62%)H(3.26%)N(5.07%)O(14.48%).

2, 5-Dichloro-N-{3-[(2E)-3-3methoxybiphenyl-4-olprop-2-enoyl] phenyl} benzenesulphonamide (2h):

Yield:- 64%; MP: 190-192ºC; MS: m/z = 554;IR (KBr): 1652 cm^{-1} (C=O str.), 1603 cm^{-1}(-CH=CH str.), 1562 cm^{-1} (NHdef), 1242.6 cm^{-1} (C-O-C str. asym), 1037 cm^{-1}(C-O-C str. sym), 738.2 cm^{-1}(C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 3.85 – 3.90 (s, 3H), 6.83 – 6.94 (m, 2H), 7.10 – 7.17 (dd, 1H), 7.24 – 7.32 (t, 1H), 7.34 – 7.40 (t, 1H), 7.42 – 7.57 (m, 3H), 7.61 – 7.75 (m, 6H), 7.86 – 8.00 (m, 2H), 8.85 – 8.90 (s, 1H); Elemental Analysis for $C_{28}H_{21}Cl_2NO_5S$: Calculated: C(60.66%)H(3.82%)N(2.53%) O(14.43%). Found: C(60.66%)H(3.85%) N(2.53%)O(14.45%).

2,5-Dichloro-N-{3-[(2E)-3-1, 1'-(E)-ethene-1, 2-diyldibenzeneprop-2-enoyl] phenyl} benzenesulphonamide (2i):

Yield:- 68%; MP: 90-92 ºC; MS: m/z = 534 ;IR (KBr): 1659 cm^{-1} (C=O str.), 1600 cm^{-1}(-CH=CH str.), 1566 cm^{-1} (NHdef), 1244.9 cm^{-1} (C-O-C str. asym), 1042 cm^{-1}(C-O-C str. sym), 738.7 cm^{-1}(C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 6.87 – 6.92 (s, 2H), 7.12 – 7.23 (m, 2H), 7.26 – 7.36 (m, 1H), 7.42 – 7.56 (m, 6H), 7.64 – 7.88 (m, 7H), 7.88 – 8.00 (m, 2H), 8.64 – 8.69 (s, 1H); Elemental Analysis for $C_{29}H_{21}Cl_2NO_3S$: Calculated: C(65.17%)H(3.96%) N(2.62%) O(8.98%). Found:C(65.19%)H(3.98%) N(2.62%)O(8.96%).

2, 5-Dichloro-N-{3-[(2E)-3-2-(biphenyl-4-yl) furanprop-2-enoyl] phenyl} benzenesulphonamide (2j):

Yield:- 67%; MP: 126-128 ºC; MS: m/z =574 ;IR (KBr): 1657 cm^{-1} (C=O str.), 1604 cm^{-1}(-CH=CH str.), 1566 cm^{-1} (NHdef), 1244.4 cm^{-1} (C-O-C str. asym), 1037 cm^{-1}(C-O-C str. sym), 738.4 cm^{-1}(C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 6.57 – 6.65 (t, 1H), 6.85 – 6.93(dd, 1H), 7.25 – 7.36 (m, 2H), 7.43 – 7.57 (m, 3H), 7.59 – 8.00 (m, 13H), 8.83 – 8.88 (s, 1H); Elemental Analysis for $C_{31}H_{21}Cl_2NO_4S$: Calculated: C(64.81%)H(3.68%)N(2.44%)

O(11.14%). Found:C(64.80%)H(3.66%) N(2.46%)O(11.17%).

2, 5-Dichloro-N-{3-[(2E)-3-6-bromo-2-chloro-4-phenylquinolineprop-2enoyl] phenyl} benzenesulphonamide (2k):

Yield:- 75%; MP: 140-142 ºC; MS: m/z = 672 ;IR (KBr): 1659 cm^{-1} (C=O str.), 1600 cm^{-1}(-CH=CH str.), 1568 cm^{-1} (NHdef), 1245.8 cm^{-1} (C-O-C str. asym), 1038 cm^{-1}(C-O-C str. sym), 738.2 cm^{-1}(C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 7.09 – 7.17 (d, 1H), 7.21 – 7.35 (m, 4H), 7.36 – 7.45 (dt, 1H), 7.53 – 7.75 (m, 7H), 7.80 – 7.85 (d, 1H), 7.94 – 8.00 (d, 1H), 8.02 – 8.10 (dd, 1H), 8.14 – 8.21 (d, 1H), 8.57 – 8.62 (s, 1H); Elemental Analysis for $C_{30}H_{18}BrCl_3N_2O_3S$: Calculated: C(53.56%)H(2.70%)N(4.16%) O(7.13%) .Found:C(53.54%) H(2.70%) N(4.17%)O(7.11%).

N-[3-(6-Amino-5-cyano-4-biphenyl-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulphonamide (3a):

Yield:- 70%; MP: 140-142 ºC; MS: m/z = 574 ;IR (KBr): 2938 cm^{-1} (C-H, str. sym), 2191 cm^{-1} (C≡N str.), 1638.5 cm^{-1} (NH def), 1456.2 cm^{-1} (C-H str. asym), 791.6 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 4.23 – 4.30 (dt, 1H), 5.35 – 5.41 (d, 1H), 6.97 – 7.12 (m, 2H), 7.36 – 7.54 (m, 7H), 7.59 – 7.75 (m, 6H), 7.94 – 8.00 (d, 1H), 8.84 – 8.89 (s, 2H), 8.90 – 8.95 (s,1H);Elemental Analysis for $C_{30}H_{21}Cl_2N_3O_3S$: Calculated: C(62.72%)H(3.68%)N(7.31%) O(8.36%). Found:C(62.74%)H(3.68%) N(7.33%)O(8.35%).

N-[3-(6-Amino-5-cyano-4-2-chlorobiphenyl-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulphonamide (3b):

Yield:- 72%; MP: 102-104 ºC; MS: m/z = 608 ;IR (KBr): 2942 cm^{-1} (C-H, str. sym), 2193 cm^{-1} (C≡N str.), 1635.2 cm^{-1} (NH def), 1453.2 cm^{-1} (C-H str. asym), 790.4 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 4.19 – 4.26 (dt, 1H), 5.38 – 5.44 (d, 1H), 7.00 – 7.08 (dt, 1H), 7.10 – 7.19 (t, 1H), 7.22 – 7.75 (m, 11H), 7.94 – 8.00 (d, 1H), 8.17 – 8.22 (s, 2H), 8.63 – 8.68 (s, 1H); Elemental Analysis for $C_{30}H_{20}Cl_3N_3O_3S$: Calculated: C(59.17%)H(3.31%)N(6.90%) O(7.88%). Found:C(59.18%)H(3.31%) N(6.90%)O(7.87%).

N-[3-(6-Amino-5-cyano-4-4-chlorobiphenyl-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulphonamide (3c):

Yield:- 66%; MP: 132-134 ºC; MS: m/z = 608 ;IR (KBr): 2935.5 cm^{-1} (C-H, str. sym), 2191 cm^{-1} (C≡N str.), 1635.5 cm^{-1} (NH def), 1454.2 cm^{-1} (C-H str. asym), 790.8 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 4.18 – 4.25 (dt, 1H), 5.35 – 5.42 (d, 1H), 7.02 – 7.10 (dt, 1H), 7.10 – 7.20 (m, 2H), 7.43 – 7.57 (m, 5H), 7.59 – 7.75 (m, 4H), 7.80 – 7.88 (m, 2H), 7.94 – 8.00 (d, 1H), 8.16 – 8.21 (s, 2H), 8.82 – 8.87 (s, 1H); Elemental Analysis for $C_{30}H_{20}Cl_3N_3O_3S$: Calculated: C(59.17%)H(3.31%)N(6.90%) O(7.88%). Found:C(59.19%)H(3.31%) N(6.92%) O(7.87%).

N-[3-(6-Amino-5-cyano-4-4-Methoxybiphenyl-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulphonamide (3d):

Yield:- 75%; MP: 152-154 ºC; MS: m/z = 604 ;IR (KBr): 2938 cm^{-1} (C-H, str. sym), 2194 cm^{-1} (C≡N str.), 1635.8 cm^{-1} (NH def), 1452.2 cm^{-1} (C-H str. asym), 791.6 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 3.77 – 3.82 (s, 3H), 4.23 – 4.30 (dt, 1H), 5.43 – 5.49 (d, 1H), 6.82 – 6.90 (dt, 1H), 6.93 – 7.01 (m, 2H), 7.03 – 7.13 (m, 2H), 7.43 – 7.57 (m, 5H), 7.59 – 7.75 (m, 4H), 7.94 – 8.00 (d, 1H), 8.52 – 8.57 (s, 1H), 8.67 – 8.72 (s, 2H); Elemental Analysis for $C_{31}H_{23}Cl_2N_3O_4S$: Calculated: C(61.59%)H(3.83%)N(6.95%)O(10.59%). Found:C(61.58%) H(3.84%)N(6.94%) O(10.58%).

N-[3-(6-Amino-5-cyano-4-biphenyl-3-ylphenylether-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulphonamide (3e):

Yield:- 50%; MP: 110-112 ºC; MS: m/z = 666 ;IR (KBr): 2931 cm^{-1} (C-H, str. sym), 2192

cm^{-1} (C≡N str.), 1634.5 cm^{-1} (NH def), 1454.2 cm^{-1} (C-H str. asym), 790.4 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 4.15 – 4.22 (dt, 1H), 5.25 – 5.32 (d, 1H), 6.94 – 7.05 (m, 3H), 7.09 – 7.29 (m, 5H),7.29–7.50(m, 7H),7.59 – 7.75 (m, 4H), 7.94 – 8.00 (d, 1H), 8.16 – 8.21 (s, 2H), 8.77 – 8.82 (s, 1H); Elemental Analysis for $C_{36}H_{25}Cl_2N_3O_4S$: Calculated: C(64.87%) H(3.78%)N(6.30%)O(9.60%). Found: C(64.89%)H(3.78%)N(6.31%)O(9.60%).

N-[3-(6-Amino-5-cyano-4-biphenyl-3-ol-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulphonamide (3f):

Yield:- 68%; MP: 83-85 ºC; MS: m/z = 590 ;IR (KBr): 2933 cm^{-1} (C-H, str. sym), 2191 cm^{-1} (C≡N str.), 1636.1 cm^{-1} (NH def), 1453.2 cm^{-1} (C-H str. asym), 790.2 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 4.22 – 4.29 (dt, 1H), 5.39 – 5.46 (d, 1H), 6.78 – 6.86 (dt, 1H), 7.04 – 7.25 (m, 6H), 7.43 – 7.57 (m, 3H), 7.59 – 7.75 (m, 4H), 7.94 – 8.00 (d, 1H), 8.46 – 8.51 (s, 2H), 8.97 – 9.02 (s, 1H), 9.09 – 9.14 (s, 1H); Elemental Analysis for $C_{30}H_{21}Cl_2N_3O_4S$: Calculated: C(61.02%)H(3.58%)N(7.12%) O(10.84%).Found:C(61.01%)H(3.59%) N(7.11%)O(10.82%)S(5.44%).

N-[3-(6-Amino-5-cyano-4-3-nitrobiphenyl-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulphonamide (3g):

Yield:- 62%; MP: 144-146 ºC; MS: m/z= 619 ;IR (KBr): 2937.5 cm^{-1} (C-H, str. sym), 2191 cm^{-1} (C≡N str.), 1636.2 cm^{-1} (NH def), 1454.6 cm^{-1} (C-H str. asym), 790.5 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 4.19 – 4.26 (dt, 1H), 5.34 – 5.40 (d, 1H), 7.03 – 7.18 (m, 3H), 7.44 – 7.53 (m, 2H), 7.53 – 7.77 (m, 6H), 7.90 – 8.00 (m, 2H), 8.04 – 8.12 (dt, 1H), 8.19 – 8.24 (s, 2H), 8.30 – 8.36 (t, 1H), 8.99 – 9.04 (s, 1H); Elemental Analysis for$C_{30}H_{20}Cl_2N_4O_5S$: Calculated: C(58.17%)H(3.25%)N(9.04%) O(12.91%). Found: C(58.16%)H(3.25%) N(9.03%)O(12.92%).

N-[3-(6-Amino-5-cyano-4-3-methoxybiphenyl-4-ol-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulphonamide (3h):

Yield:- 62%; MP: 104-106 ºC; MS: m/z = 620 ;IR (KBr): 2936 cm^{-1} (C-H, str. sym), 2190.8 cm^{-1} (C≡N str.), 1633.5 cm^{-1} (NH def), 1454.9 cm^{-1} (C-H str. asym), 790.2 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 3.85 – 3.90 (s, 3H), 4.17 – 4.24 (dt, 1H), 5.21 – 5.27 (d, 1H), 6.69 – 6.75 (t, 1H), 6.86 – 6.93 (d, 1H), 6.98 – 7.08 (m, 2H), 7.09 – 7.23 (m, 2H), 7.41 – 7.50 (ddd, 3H), 7.59 – 7.75 (m, 4H), 7.94 – 8.00 (d, 1H), 8.14 – 8.19 (s, 2H), 8.56 – 8.61 (s,1H); Elemental Analysis for $C_{31}H_{23}Cl_2N_3O_5S$: Calculated:C(60.00%)H(3.74%)N(6.77%) O(12.89%). Found: C(60.00%)H(3.74%) N(6.77%)O(12.89%).

N-[3-(6-Amino-5-cyano-4-1, 1'-(E)-ethene-1, 2-diyldibenzene-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulfonamide (3i):

Yield:- 66%; MP: 86-88 ºC; MS: m/z = 600 ;IR (KBr): 2938.3 cm^{-1} (C-H, str. sym), 2191 cm^{-1} (C≡N str.), 166.2 cm^{-1} (NH def), 1452.5 cm^{-1} (C-H str. asym), 792.1 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 4.21 – 4.28 (dt, 1H), 5.42 – 5.48 (d, 1H), 6.87 – 6.92 (s, 2H), 6.99 – 7.07 (dt, 1H), 7.10 – 7.19 (t, 1H), 7.26 – 7.36 (m, 2H), 7.42 – 7.75 (m, 9H), 7.80 – 7.88 (ddd, 2H), 7.94 – 8.00 (d, 1H), 8.49 – 8.57 (d, 3H); Elemental Analysis for $C_{32}H_{23}Cl_2N_3O_3S$: Calculated:C(64.00%)H(3.86%)N(7.00%) O(7.99%).Found:C(64.00%)H(3.86%) N(7.00%) O(7.99%).

N-[3-(6-Amino-5-cyano-4-2-phenylfuran-4H-pyran-2-yl) phenyl]-2, 5-dichlorobenzenesulphonamide (3j):

Yield:- 70%; MP: 154-156 ºC; MS: m/z = 564 ;IR (KBr): 2932.7 cm^{-1} (C-H, str. sym), 2192.2 cm^{-1} (C≡N str.), 1634.5 cm^{-1} (NH def), 1455.2 cm^{-1} (C-H str. asym), 790.1 cm^{-1} (C-Cl str.).; ^{1}H NMR (400 MHz, DMSO-d6) δ 4.20 – 4.27 (dt, 1H), 5.35 – 5.42 (d, 1H), 6.57 – 6.65 (t, 1H), 6.85 – 6.93 (dd, 1H), 7.01 – 7.07 (t, 1H), 7.07 – 7.18 (m, 2H), 7.43 – 7.51 (m, 2H), 7.53 – 7.61 (m, 1H), 7.64 – 7.81 (m, 5H), 7.94 –

8.00 (d, 1H), 8.50 – 8.55 (s, 2H), 8.94 – 8.99 (s,1H); Elemental Analysis for $C_{28}H_{19}Cl_2N_3O_4S$: Calculated:C(59.58%)H(3.39%)N(7.44%) O(11.34%). Found: C(59.58%)H(3.39%) N(7.44%)O(11.34%).

N-[3-(6-Amino-5-cyano-4-6-bromo-2-chloro-4-phenylquinoline-4H-pyran-2-yl)phenyl]-2,5-dichlorobenzenesulphonamide(3k):

Yield:- 58%; MP: 120-122 ºC; MS: m/z = 738 ;IR (KBr): 2934.5 cm^{-1} (C-H, str. sym), 2191 cm^{-1} (C≡N str.), 1638.5 cm^{-1} (NH def), 1455.2 cm^{-1} (C-H str. asym), 791.8 cm^{-1}(C-Cl str.).; ^1H NMR (400 MHz, DMSO-d6) δ 4.21 – 4.28 (dd, 1H), 5.40 – 5.47 (d, 1H), 7.01 – 7.09 (dt, 1H), 7.11 – 7.20 (t, 1H), 7.21 – 7.27 (t, 1H), 7.49 – 7.59 (m, 3H), 7.59 – 7.75 (m, 6H), 7.94 – 8.00 (d**,** 1H), 8.02 – 8.10 (dd, 1H), 8.15 – 8.21 (d, 1H), 8.25 – 8.30 (s, 2H), 8.73 – 8.78(s,1H); Elemental Analysis for $C_{33}H_{20}BrCl_3N_4O_3S$: Calculated: C(53.64%)H(2.73%)N(7.58%) O(6.50%). Found: C(53.64%)H(2.73%) N(7.58%)O(6.50%).

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