Thiochromenopyridines-II: Antibacterial and antioxidant 9-benzylideneamino-5*H*-thiochromeno[2,3-*b*]pyridin-5-ones.

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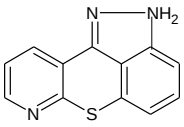
Summary: A series of potential biologically active 9-benzylideneamino-5*H*-thiochromeno[2,3-*b*]pyridin-5-ones were synthesized from 9-amino-5*H*-benzothiopyrano[2,3-*b*]pyridin-5-one and different aromatic aldehydes by using microwave irradiation as well as conventional heating method. The synthesized compounds were characterized through Mass, ^{1}H-NMR, IR spectra and elemental analysis. The synthesized compounds were screened for their antibacterial and antioxidant properties.

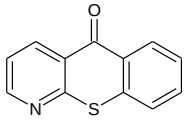
Keywords: Thiochromenopyridine, Antioxidants and antibacterials, Microwave assisted synthesis, Schiff's bases.

Introduction

Synthesis of new heteroaromatic compounds and their derivatives with the aim to enhance their pharmacological properties or to decrease their side effects have received special attention [1,2]. Thiochromones functionalities and their analogues are of considerable importance and have been applied as drugs [3-6]. Some tetracyclic derivatives **(1)** derived from thiochromenopyridines **(2)** are reported to be potent cytotoxic agents [7].



(1)



(2)

On the other hand Schiff's bases, an important class of organic compounds [8], have interesting biological properties [9-12], such as anticancer [13-15], diuretic, antifungal and anticonvulsant. These are also applied as analytical and catalytic reagents [16, 17]. Recently 4-amino-4,5-dihydro-1, 2, 4-triazole-5-thione and 3-amino-1*H*-1,2,4-triazole Schiff's bases were reported to be good fungicides [18, 19]. We had earlier reported the synthesis of some selected thiochromones and biological and antioxidant potential of some of the benzylidene amino compounds prepared in our laboratories [20-26]. During the nitration of 5*H*-1-thiochromeno[2,3-*b*]pyridin-5-one (**3**) a mixture of nitrated products was obtained. We were able to separate the 9-nitro-5*H*-1-thiochromeno[2,3-*b*]pyridin-5-one **(4)** from the 7-nitro-5*H*-1-thiochromeno[2,3-*b*]pyridin-5-one **(4a)** on the basis of their solubilities. The 9-nitro-5*H*-1-thiochromeno[2,3-*b*]pyridin-5-one **(4)** isomer being almost insoluble in glacial acetic acid and was removed by filtration and purified by recrystallization from ethanol. On reduction, 9-nitro-5*H*-1-thiochromeno[2,3-*b*]pyridine-5-one **(4)** gave the corresponding 9-amino-5*H*-1-thiochromeno[2,3-*b*]pyridin-5-one **(5)**. It was condensed with various arylaldehydes to afford respective Schiff's bases (Scheme-1). These Schiff's bases **(6a-6p)** were subjected to their 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging and antibacterial screening.

Experimental

Chemicals and equipments

All chemicals were purchased from E. Merck, BDH or Fluka and used without purification. ^{1}H-NMR spectra were recorded on Bruker DPX instrument at 400 MHz. Chemical shifts are reported in ppm reference to the residual solvent signal. Mass spectra were recorded on Agilent 6890 spectrometer. IR spectra were recorded on a Bruker Tensor 27. Melting points were taken on a Gallenkamp melting point apparatus and are uncorrected. Elemental analysis (C, H, N) was carried out on Elementar by Vario Micro.

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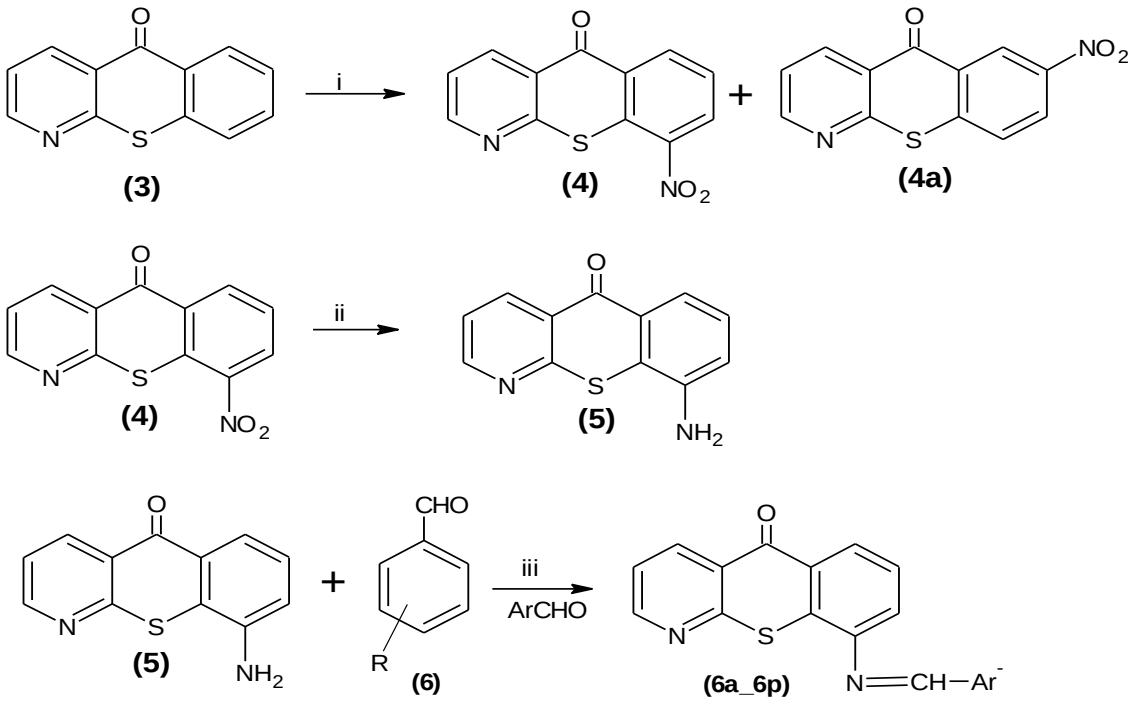

(Scheme-1)

Reaction Conditions:

i) - KNO_3/H_2SO_4, ii**)** - $SnCl_2$/HCl; Fe/HCl or Elemental Sulfur

iii) - Microwave (MW) or Conventional heating

where Ar is defined as follows: **6a** Ar= 4-ClC_6H_4; **6b** Ar= 3',4'$(OMe)_2C_6H_3$; **6c** Ar=2'-$NO_2C_6H_4$; **6d** Ar=2',4'$(OMe)_2C_6H_3$; **6e** Ar= 4'benzyloxy,-3'OMe C_6H_3; **6f** Ar = 4-acetamidobenzaldehyde **6g** Ar= 4'-OHC_6H_4, **6h** Ar= 4'-$N(CH_3)_2C_6H_4$ **6i** Ar=3',4'-methylenedioxybenzaldehyde, **6j** Ar=4'-OH, 3-$OCH_3C_6H_3$ **6k** Ar=3'-$NO_2C_6H_4$ **6l** Ar=4'-$NO_2C_6H_4$ **6m** Ar=4'-$OCH_3C_6H_4$ **6n** Ar=4'-$CH_3C_6H_4$ **6o** Ar=2'-$CH_3C_6H_4$ **6p** Ar=3'-$CH_3C_6H_4$

9-Amino- 5H-thiochromeno[2,3-b]pyridin-5-one. **(5)**

A mixture of 5*H*-thiochromeno[2,3-*b*]pyridin-5-one (10.0 g, 0.46 mol), sulfuric acid (30mL) and potassium nitrate (30.0 g, 0.29 mol) was stirred slowly maintaining the reaction temperature between 25-30 ^{0}C. After half an hour the reaction mixture was cooled in an ice bath, and made alkaline by the addition of liquid ammonia. The precipitates thus obtained were filtered, washed with water and dried. The 9-nitro-5*H*-thiochromeno[2,3-*b*]pyridin-5-one **(4)** was isolated (yield 2.90 g, 24% mp.277 ^{0}C) recrystallized from ethyl alcohol and reduced by $SnCl_2$/HCl or Fe/HCl or elemental sulfur [27] to afford 9-amino-5*H*-thiochromeno[2,3-*b*]pyridin-5-one (yield 0.44 g, 50 %, mp. 254-256 ^{0}C) **(5).**

General Procedure for the Synthesis of 9-benzylideneamino-5H-thiochromeno[2,3-b]pyridin-5-one. **(6a-6p)**

Following two methods were used for the synthesis of **(6a-6p)**

Microwave Assisted Method **(A)**

An equimolar mixture of 9-amino-5*H*-thiochromeno[2,3-*b*]pyridine-5-one **(5)** (0.01 mol), an aldehyde (0.01 mol), 10 mL of methanol and few drops of phosphoric acid was irradiated in a modified household microwave oven (900 watt) equipped with the water condenser for the time ranging from 2-5 minutes. On completion (monitored by TLC) the reaction mixture was cooled and the precipitated product was filtered, dried and recrystallised from an appropriate solvent to obtain respective Schiff's bases.

Conventional Method **(B)**

An equimolar mixture of 9-amino-5*H*-thiochromeno[2,3-*b*]pyridine-5-one **(5)** (0.01 mol), an aldehyde (0.01 mol), 10 mL of methanol and few drops of phosphoric acid was heated under reflux for about 30 minutes to 3 hours. On completion (monitored by TLC) the reaction mixture was cooled and the precipitated product was filtered, dried and recrystallised from an appropriate solvent to obtain the following Schiff's bases.

9-(4'-Chlorobenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6a)**

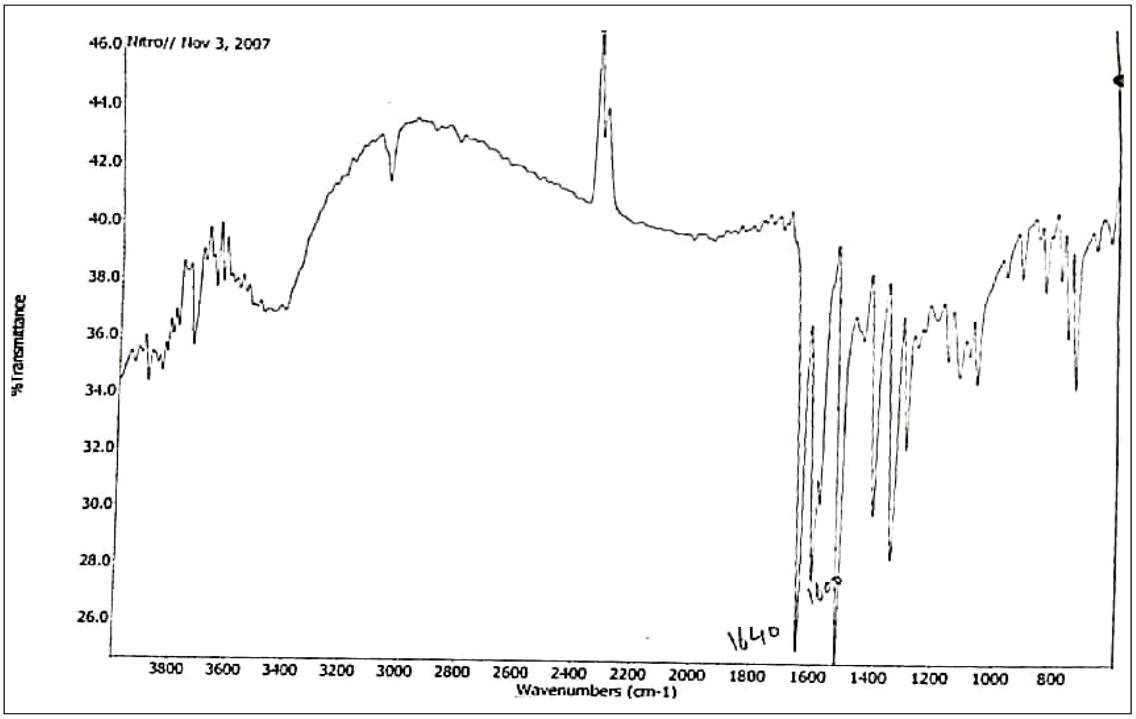

Fig. 1: IR Spectrum of compound **6a**.

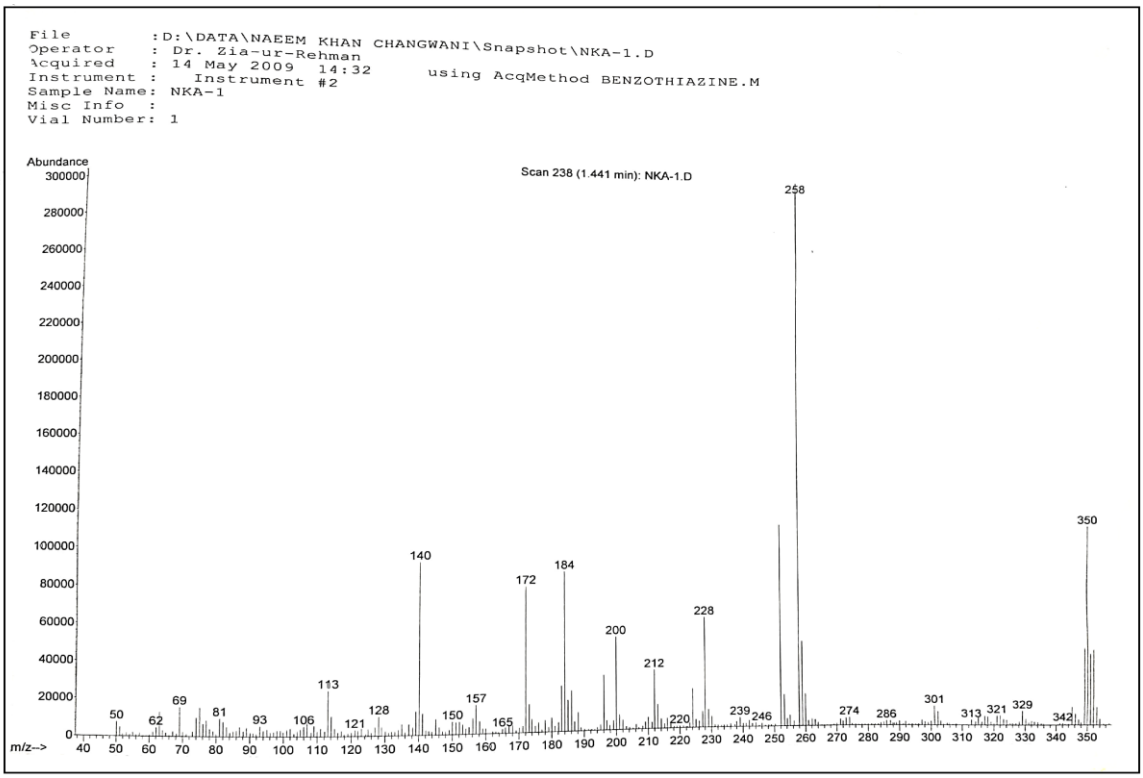

Fig. 2: Mass Spectrum of compound **6a.**

The product obtained by this reaction was yellow. Yield: Method A: (0.665 gm, 70 %), Method B: 0.580 gm, 61 %) mp: 190 ^{0}C ^{1}H-NMR: (DMSO-d_6) δ: 7.56-7.34 (m, 3H, 3', 5', 6'-H) 7.95 (d, J=8.4 Hz, 1H, 2'-H), 8.12 (d, J=8.8 Hz, 1H, 7-H), 8.23 (dd, J=2.4, 8.8 Hz, 1H, 6-H) 8.53 (d, J=8.4 Hz, 1H, 8-H), 8.72 (dd, J=1.8, 4.2 Hz, 1H, 3-H), 8.82 (s, 1H, N=CH), 8.86 (dd, J=1.8, 4.2 Hz, 1H, 4-H), 9.07 (d, J=2.4 Hz, 1H, 2-H), IR: (Neat) cm^{-1} :1600 (N=CH), 1640 (C=O) $C_{19}H_{11}N_2OClS$, MS; m/z 350 [M^+ Cl^{35} 70%, Cl^{37} 30%].

9-(3',4'-dimethoxybenzylideneamino)-5H-thiochromeno[2, 3-b]pyridin-5-one. **(6b)**

The product obtained by this reaction was yellow powder having following analytical data, Yield: Method A: (0.772 gm, 81 %), Method B: (0.591 gm, 62 %), mp: 187 ^{0}C, ^{1}H-NMR: (DMSO-d_6) δ: 3.82 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 7.62 (dd, J=4.8, 8.0 Hz, 1H, 6'-H), 7.73 (dd, J=2.0, 3.6 Hz, 1H, 6-H), 7.94 (d, J=4.8 Hz, 1H, 2'-H), 8.19 (d, J=4.8 Hz, 1H, 5'-H), 8.41 (d, J=2.8 Hz, 1H, 7-H), 8.52 (dd, J=2.8, 4.4 Hz, 1H, 8-H), 8.68 (s, 1H, N=CH), 8.74 (dd, J=2.0, 3.6 Hz, 1H, 6-H), 8.89 (dd, J= 1.6, 4.4, 1H, 3-H), 8.93 (dd, J=1.6, 4.8 Hz, 1H, 4-H), 9.06 (d, J=2.8 Hz, 1H, 2-H), IR: (Neat) cm^{-1}:1590 (N=CH), 1630 (C=O) MS: m/z 376 [M^+]

9-(2'-nitrobenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6c)**

The product obtained by this reaction was yellow powder having following analytical data Yield: Method A: (0.706 gm, 74 %) Method B: (0.678 gm, 71 %) mp:231 ^{0}C ^{1}H-NMR: (DMSO-d_6) δ: 7.65 (dd, J=4.0, 7.6 Hz, 1H, 4'-H), 7.78 (t, J=8.0 Hz, 1H, 7-H), 7.88 (d, J=7.6 Hz, 1H, 8-H), 8.01 (d, J=8.4 Hz, 1H, 5'-H), 8.13 (d, J=8.4 Hz, 1H, 6-H), 8.22 (d, J=7.6 Hz, 1H, 6'-H), 8.30 (s, 1H, 3'-H), 8.76 (d, J=7.6 Hz, 1H, 3-H), 8.91 (d, J=3.6 Hz, 1H, 4-H), 9.05 (s, 1H, N=CH), 9.14 (s, 1H, 2-H), IR (Neat) cm^{-1}: 1540 and 1360 (NO_2), 1610 (C=O), 1660 (N=CH) MS: m/z 361 [M^+]

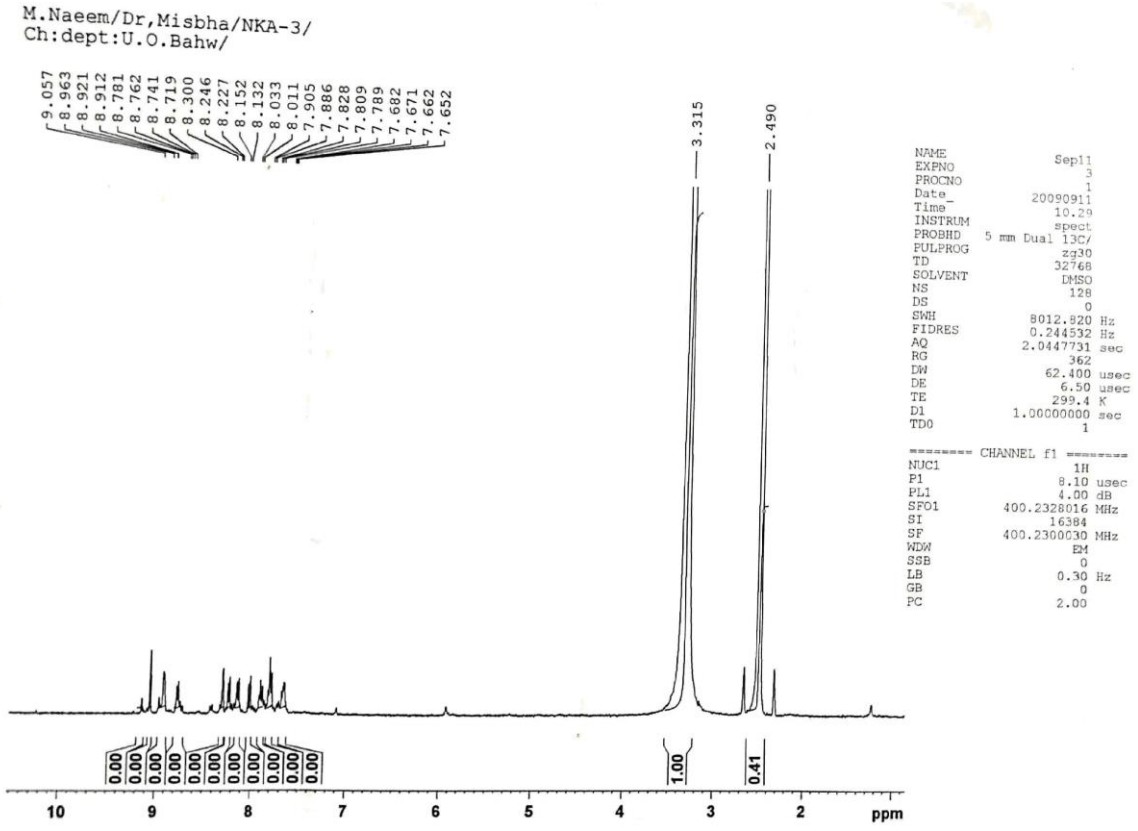

Fig. 3: ^{1}H-NMR Spectrum of compound **6c**.

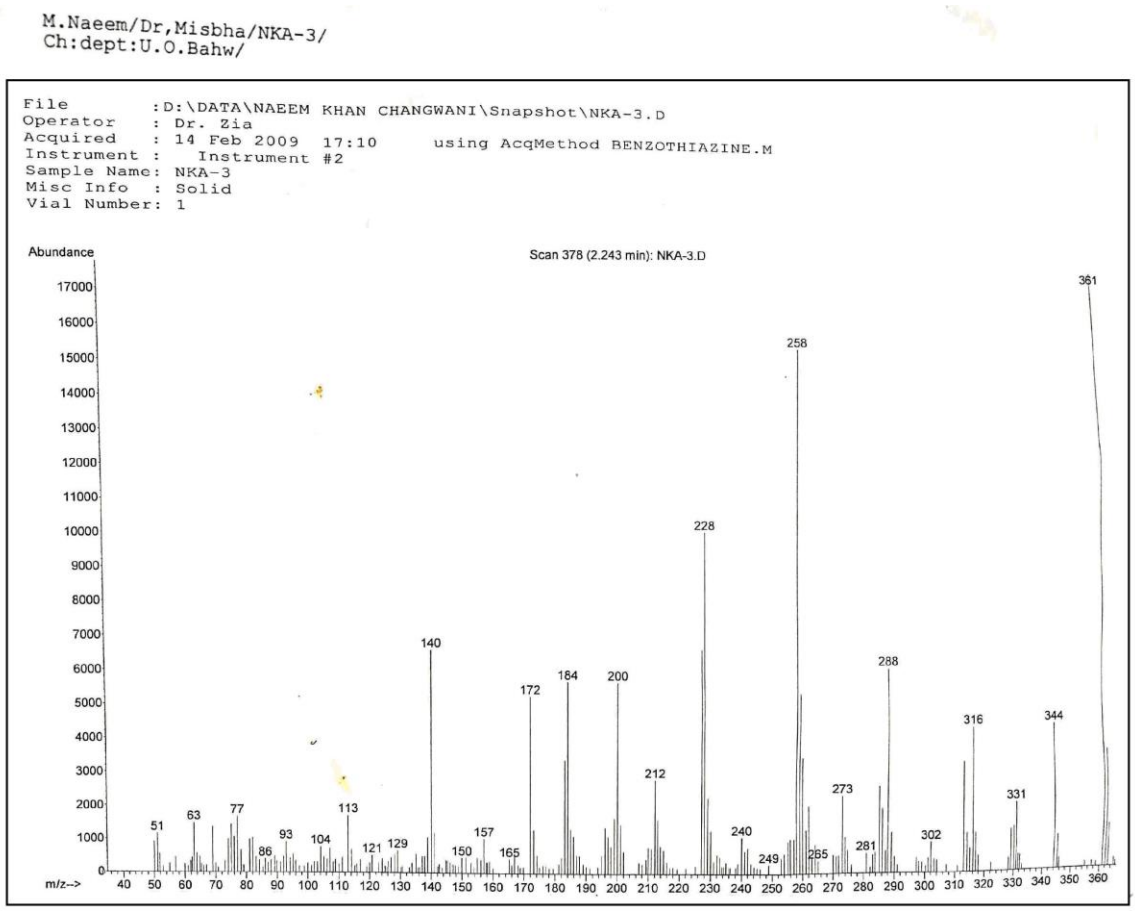

Fig. 4: Mass Spectrum of compound **6c.**

9-(2',4'-dimethoxybenzylideneamino)-5H-thiochromeno[2, 3-b]pyridine-5-one. **(6d)**

The product obtained by this reaction was yellow powder having following analytical data, Yield: Method A: (0.686 gm, 72 %), Method B: (0.667 gm, 70 %), mp:< 360 ^{0}C, **^{1}H-NMR**: (DMSO-d_6) δ: 3.89 (s, OCH_3, 3**H**), 3.92 (s, OCH_3, 3**H**), 7.71 (dd, J=4.4, 8.4 Hz, 1H, 3'-**H**), 7.90 (d, J=4.4 Hz, 1H, 5'-**H**), 8.03 (d, J=7.6 Hz, 1H, 6'-**H**), 8.23 (d, J=8.4 Hz, 1H, 7-**H**), 8.74 (d, J=1.2 Hz, 1H, 6-**H**), 8.76 (dd, J=1.6, 8.4 Hz, 1H, 3-**H**), 8.85 (s, 1H, N=C**H**), 8.92 (dd, J=1.6, 4.4 Hz, 1H, 4-**H**), 9.08 (d, J=2.4 Hz, 1H, 2-**H**), **IR** (Neat) cm^{-1}: 1100 (OCH_3), 1590 (N=CH), 1640 (C=O), **MS**: m/z 376 [M$^+$]

9-(4'-(benzyloxy)-3'-methoxybenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one **(6e)**

The product obtained by this reaction was yellow powder having following analytical data, Yield: Method A: (0.672 gm, 70 %), Method B: (0.586 gm, 61 %), mp: < 350 ^{0}C,**^{1}H-NMR**: (DMSO-d_6) δ: 3.83 (s, 3H, OCH_3), 5.20 (s, 2H, CH_2), 7.22-7.57 (m, 5H, 2''-6''-**H**), 7.64-7.76 (m, 3H, 2', 5',6'-**H**), 7.95 (d, J=8.4 Hz, 1H, 6-**H**), 8.23 (s, 1H, N=C**H**), 8.33 (d, J=7.6 Hz, 1H, 8-**H**), 8.69 (d, J=1.6 Hz, 1H, 7-**H**), 8.75 (d, J=6.8 Hz, 1H, 3-**H**), 8.90 (s, 1H, 4-**H**), 9.83 (s, 1H, 2-**H**), **IR** (Neat) cm^{-1}: 1600 (N=CH), 1660 (C=O), **MS**: m/z 452 [M$^+$].

N-(4'-(5'-oxo-5H-thiochromeno[2,3-b]pyridin-9-ylimino)methyl) phenyl)acetamide. **(6f)**

The product obtained by this reaction was dark brown powder, Yield: Method A: (0.676 gm, 71 %), Method B: (0.600 gm, 63 %), mp:273 ^{0}C, **^{1}H-NMR**: (DMSO-d_6): δ 2.01-2.09 (d, 3H, CH_3) 7.58-7.71 (m, 3H, 2', 5', 6'-**H**), 7.90 (d, J=8.0 Hz, 1H, 3'-**H**), 8.14 (d, J=2.4 Hz, 1H, 6-**H**), 8.21 (d, J=8.4 Hz, 1H, 7-**H**), 8.51 (dd, J=2.4, 8.4 Hz, 1H, 8-**H**) 8.73 (s, 1H, N=C**H**), 8.75, (dd, J=1.6, 8.0, 1H, 3-**H**), 8.91 (dd, J=2.0, 4.8 Hz, 1H, 4-**H**), 9.07 (d, J=2.8 Hz, 1H, 2-**H**), 10.68 (s, 1H, N**H**), **IR** (Neat) cm^{-1}: 1420 (CH_3), 1600 (N=CH), 1610 (C=O), **MS**: m/z 373 [M$^+$]

9-(4'-hydroxybenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6g)**

Yield: Method A: (0.606 gm, 64 %), Method B: (0.568 gm, 60 %), mp: 273 ^{0}C, **^{1}H-NMR**: (DMSO-d_6) δ: 6.87 (d, J=8.0 Hz, 1H, O**H**), 7.65-7.72 (m, 2H, 3',5'-**H**), 7.81(d, J=8.0 Hz, 2H, 2',6'-**H**), 7.90 (d, J=8.4 Hz, 1H, 8-**H**), 8.16 (d, J=2.8 Hz, 1H, 6-**H**) 8.47 (dd, J=2.0, 8.4 Hz, 1H, 8-**H**) 8.61 (s, 1H, N=C**H**), 8.71 (d, J=6.2 Hz, 1H, 3-**H**) 8.93 (d, J=4.4 Hz, 1H, 4-**H**), 9.07 (d, J=2.4 Hz, 1H, 2-**H**), **IR** (Neat) cm^{-1}: 1640 (C=O), 1700 (N=CH), 3610 (-OH), **MS**: m/z 332 [M$^+$]

9-(benzo[d][1,3]dioxol-5-ylmethyleneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6h)**

The product obtained was reddish brown powder, Yield: Method A: (0.666 gm, 70 %), Method B: (0.580 gm, 61 %), mp: 211 ^{0}C, **^{1}H-NMR**: (DMSO-d_6) δ: 6.09 (s, 2H, C**H**$_2$), 7.09 (d, J=8.4 Hz, 5'-**H**), 7.51 (t, J=8.8 Hz, 6'-**H**), 7.73 (dd, J=4.0, 8.4 Hz, 2'-**H**), 8.19 (d, J=3.6 Hz, 1H, 7-**H**), 7.93 (d, J=8.4 Hz, 1H, 8-**H**) 8.54 (dd, J=2.0, 8.4 Hz, 1H, 6-**H**), 8.69 (s, 1H, N=C**H**), 8.73 (dd, J=1.6, 8.4 Hz, 1H, 3-**H**), 8.92 (dd, J=2.0, 4.8 Hz, 1H, 4-**H**), 9.07 (d, J=2.4 Hz, 1H, 2-**H**). **IR** (Neat) cm^{-1}: 1470 (-CH_2), 1600 (C=O), 1630 (N=CH), **MS**: m/z 360 [M$^+$]

9-(4'-hydroxy-3'-methoxybenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6i)**

The product obtained was yellow powder, Yield: Method A: (0.599 gm, 63 %), Method B: (0.561 gm, 59 %) mp: 211 ^{0}C, **^{1}H-NMR**:(DMSO-d_6) δ: 3.82 (s, 3H, OC**H**$_3$), 6.94 (s, 1H, OH), 8.27 (d, J=3.9 Hz, 1H, 7-**H**), 8.49 (dd, J=2.4, 8.4 Hz, 1H, 8-**H**), 8.57 (s, 1H, N=C**H**), 8.63 (d, J=1.5 Hz, 1H, 6-**H**), 8.71 (m, 2H, 2', 5', 6'-**H**), 8.83 (dd, J=1.5, 4.5 Hz, 1H, 3-**H**) 8.87 (dd, J=1.8, 4.5 Hz, 1H, 4-**H**), 9.03 (d, J=1.8 Hz, 1H, 2-**H**). **IR** (Neat) cm^{-1}:1100 (OCH_3), 1600 (N=CH), 1680 (C=O), 3640 (OH), **MS**: m/z 362 [M$^+$]

9-(3'-nitrobenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6j)**

Yield: Method A: (0.694 gm, 73 %), Method B: (0.561 gm, 59 %), mp: 260 ^{0}C, **^{1}H-NMR**: (DMSO-d_6) δ: 7.69 (dd, J=4.8, 8.4 Hz, 1H, 5'-**H**), 7.82 (dd, J=4.5, 8.7 Hz, 1H, 7-**H**), 8.06 (d, J=2.7 Hz, 1H, 4'-**H**) 8.24 (d, J=2.7 Hz, 1H, 8-**H**), 8.46 (s, 1H, N=C**H**), 8.59 (d, J=2.4 Hz, 1H, 6'-**H**), 8.63 (d, J=1.8 Hz, 1H, 2'-**H**), 8.79 (dd, J=3.0, 8.2 Hz, 1H, 6-**H**), 8.88 (dd, J=2.4, 3.9 Hz, 1H, 3-**H**), 8.97 (dd, J=2.1, 5.1 Hz, 1H, 4-**H**), 9.05 (d, J=2.7 Hz, 1H, 2-**H**), **IR** (Neat) cm^{-1}:1525 and 1350 (NO_2), 1580 (N=CH), 1660 (C=O). **MS**: m/z 361 [M$^+$]

9-(4'-nitrobenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6k)**

Yield: Method A: (0.571 gm, 60 %), Method B: (0.552 gm, 58 %), mp: 225 ^{0}C, **^{1}H-NMR**: (DMSO-d_6) δ: 7.64 (dd, J=4.4, 8.0 Hz, 1H, 5'-**H**), 7.75 (d, J=8.4 Hz, 1H, 8-**H**), 7.88 (t, J=7.6 Hz, 1H, 3'-**H**), 8.02 (d, J=4.8 Hz, 1H, 7-**H**), 8.48 (d, J=8.4 Hz, 1H, 2', 6'-**H**), 8.28 (d, J=2.0 Hz, 1H, 6-**H**), 8.75 (d, J=4.8 Hz, 1H, 3-**H**), 8.94 (dd, J=1.6, 4.4 Hz, 1H, 4-**H**), 9.05 (s, 1H, N=C**H**), 9.07 (d, J=2.4 Hz, 1H, 2-**H**), **IR** (Neat) cm^{-1}:1540 and 1360 (NO_2), 1600 (N=CH), 1640 (C=O), **MS**: m/z 361 [M$^+$]

*9-(benzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one***. (6l)**

Yield: Method A: (0.652 gm, 69 %), Method B: (0.539 gm, 57 %), mp: 221 ^{0}C, **^{1}H-NMR** (DMSO-d_6) δ: 7.29 (dd, J=2.0, 6.0 Hz, 1H, 8-**H**), 7.46 (d, J=2.4 Hz, 1H, 7-**H**), 7.53 (dd, J=4.0, 7.6 Hz, 1H, 4'-**H**), 7.55 (dd, J=4.2, 7.8 Hz, 2H, 3',5'-**H**), 7.64 (dd, J=2.4, 8.7 Hz, 1H, 2',6'-**H**), 7.71 (d, J=2.8 Hz, 1H, 6-**H**), 7.97 (dd, J=8.4 Hz, 1H, 3-**H**), 8.46 (s, 1H, N=C**H**), 8.79 (d, J=6.6 Hz, 1H, 4-**H**), 8.90 (d, J=1.8 Hz, 1H, 2-**H**). **IR** (Neat) cm^{-1}:1580 (N=CH), 1680 (C=O), **MS**: m/z 316 [M$^+$]

9-(4'-methoxybenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6m)**

The product obtained was brown powder, Yield: Method A: (0.705 gm, 74 %), Method B: (0.674 gm, 71 %), mp: 255 ^{0}C, **^{1}H-NMR**: (DMSO-d_6) δ: 3.84 (s, 3H, OC**H**$_3$), 7.08 (dd, J=8.7 Hz, 2H, 3',5'-**H**), 7.61 (d, J=2.4 Hz, 1H, 8-**H**), 7.68 (dd, J=2.4, 8.2 Hz, 1H, 6-**H**), 7.79 (dd, J=2.4, 8.2 Hz, 1H, 7-**H**), 7.94 (d, J=2.0 Hz, 1H, 6'-**H**), 7.97 (d, J=1.2 Hz, 1H, 2'-**H**), 8.71 (s, 1H, N=C**H**), 8.76 (d, J=1.2 Hz, 1H, 3-**H**), 8.75 (dd, J=1.8, 4.5 Hz, 1H, 4-**H**), 8.87 (dd, J=1.5, 4.8 Hz, 1H, 2-**H**), **IR**: (Neat) cm^{-1}:1140 (-OCH_3), 1600 (N=CH), 1660 (C=O), **MS**: m/z 346 [M$^+$]

9-(4'-methylbenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6n)**

The product obtained was pale yellow powder, Yield: Method A: (0.729 gm, 77 %), Method B: (0.597gm, 63 %), mp: 219 ^{0}C, **^{1}H-NMR**: (DMSO-d_6) δ: 3.10 (s, 3H, -C**H**$_3$), 7.24 (d, J=7.2 Hz, 2H, 3',5'-**H**), 7.73 (dd, J=2.1, 8.4 Hz, 1H, 6'-**H**), 7.81 (d, J=7.5 Hz, 1H, 2'-**H**), 7.91 (d, J=8.4 Hz, 1H, 7-**H**) 8.26 (d, J=2.4 Hz, 1H, 8-**H**), 8.61 (d, J=2.5 Hz, 1H, 6-**H**), 8.75 (s, 1H, N=C**H**), 8.83 (dd, J=2.1, 4.2 Hz,

1H, 3-**H**) 8.89 (dd, J=1.5, 4.2 Hz, 1H, 4-**H**), 8.98 (dd, J=2.1, 4.8 Hz, 1H, 2-**H**). **IR**: (Neat) cm^{-1}: 1375 (-CH_3), 1660 (C=O), 1670 (N=CH), **MS**: m/z 330 [M^+]

9-(2'-methylbenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6o)**

Yield: Method A: (0.692 gm, 73 %), Method B: (0.568 gm, 60 %), mp 231 ^{0}C, **^{1}H-NMR**: (DMSO-d_6) δ: 2.91 (s, 3H, -C**H**$_3$), 7.31 (d, J=7.5 Hz, 2H, 3',5'-**H**), 7.65 (dd, J=1.8, 8.1 Hz, 1H, 6'-**H**), 7.83 (d, J=7.2 Hz, 1H, 4'-**H**), 7.93 (d, J=8.1 Hz, 1H, 7-**H**) 8.21 (d, J=2.1 Hz, 1H, 8-**H**), 8.56 (d, J=2.8 Hz, 1H, 6-**H**), 8.73 (s, 1H, N=C**H**), 8.81 (dd, J=2.1, 3.9 Hz, 1H, 3-**H**) 8.83 (dd, J=1.5, 4.2 Hz, 1H, 4-**H**), 8.96 (dd, J=2.1, 4.5 Hz, 1H, 2-**H**). **IR**: (Neat) cm^{-1}: 1375 (-CH_3), 1660 (C=O), 1670 (N=CH), **MS**: m/z 330 [M^+]

9-(3'-methylbenzylideneamino)-5H-thiochromeno[2,3-b]pyridin-5-one. **(6p)**

The product obtained was reddish brown powder, Yield: Method A: (0.654 gm, 69 %), Method B: (0.549 gm, 58 %), mp: 245 ^{0}C, **^{1}H-NMR**: (DMSO-d_6) δ: 3.45 (s, 3H, C**H**$_3$), 7.09 (dd, J=2.7, 8.7 Hz, 1H, 2'-**H**), 7.53 (dd, J=3.0, 8.4 Hz, 1H, 5'-**H**), 7.70 (dd, J=4.5, 8.4 Hz, 1H, 6'-**H**), 7.96 (d, J=8.7 Hz, 1H, 7-**H**) 8.23 (d, J=3.9 Hz, 1H, 8-**H**), 8.53 (dd, J=2.4, 9.0 Hz, 1H, 6-**H**), 8.69 (s, 1H, N=C**H**), 8.76 (d, J=1.8 Hz, 1H, 3-**H**), 8.94 (dd, J=1.8, 4.5 Hz, 1H, 4-**H**), 9.08 (d, J=2.7 Hz, 1H, 2-**H**). **IR** (Neat) cm^{-1}: 1375 (-CH_3), 1610 (N=CH), 1700 (C=O), **MS**: m/z 330 [M^+]

Results and Discussion

Synthesis

Scheme-1 gives method for the synthesis of target compounds. Nitration of 5*H*-thiochromeno[2,3-*b*]pyridin-5-one **(3)** with KNO_3 in conc. H_2SO_4 afforded a mixture of 7- and 9-nitro-5*H*-thiochromeno[2,3-*b*]pyridin-5-one. The 9-nitro-5*H*-thiochromeno[2,3-*b*]pyridin-5-one **(4)** was isolated and reduced by **a**)- $SnCl_2$/HCl or **b**)- Iron/HCl or **c**)- using elemental sulfur and mild base [27] to afford 9-amino-5*H*-thiochromeno[2,3-*b*]pyridin-5-one **(5)**. The product **(5)** was treated with different aldehydes by means of microwave irradiation and by conventional method of heating to afford the respective Schiff's bases (**6a-6p**) (**Scheme-1**).

Synthesis of Schiff's bases is generally carried out by refluxing the reaction mixture in presence of an acid as a catalyst [28]. Microwave assisted organic synthesis (MAOS) has been intensively used in different reactions due to its benign environmental impacts and efficiency [29]. In present work, it was observed that reaction time in most of the reaction was considerably decreased and yield of product was found to be somewhat better. An overall comparison between reaction time and yield of these two techniques is given in **Table-1**.

Spectral characterization of synthesized compounds

^{1}H-NMR spectra of compounds have shown the presence of a double doublet at δ 8.89-9.08 and 8.81-8.94 due to a single proton at 2 and 4 position of the pyridine ring respectively. The signals appearing at δ 8.46-9.86 as a singlet was due to N=CH, while all the aromatic protons signals are observed between δ 7.34-8.74 as multiplets and double doublets.

The IR spectra of compounds have shown absorption band at 1620-1690 cm^{-1}, typical for the stretching vibrations of N=CH. The absorbance at 1630-1660 cm^{-1} are due to the presence of C=O group of the thiochromone moiety. Elemental analysis of compounds also confirms their structures.

Table-1: Reaction parameters and CHN analysis of 9-benzylideneamino-5*H*-thiochromeno[2,3-*b*]pyridin-5-one **(6a-6p)**.

Product	Reaction time (minutes)		Yield (%)		CHN Analysis: calculated (found)
	M. W.	Conv.	M. W.	Conv.	C H N
6a	**03**	**60**	**70**	**61**	**65.14(64.97), 3.14(2.94), 8.00(7.88)**
6b	**03**	**75**	**81**	**62**	**67.02(66.72), 4.25(4.05), 7.44(7.08)**
6c	**02**	**45**	**74**	**71**	**63.15(63.01), 3.04(2.71), 11.63(11.14)**
6d	**05**	**90**	**72**	**70**	**67.02(66.81), 4.25(4.01), 7.44(7.10)**
6e	**04**	**75**	**70**	**61**	**71.68(71.27), 4.43(4.23), 6.19(6.03)**
6f	**02**	**90**	**71**	**63**	**67.56(67.19), 4.02(3.83), 11.26(11.04)**
6g	**02**	**180**	**64**	**60**	**68.67(68.27), 3.62(3.19), 8.42(8.12)**
6h	**03**	**150**	**70**	**61**	**66.66(66.29), 3.33(3.01), 7.77(7.03)**
6i	**02**	**105**	**63**	**59**	**66.30(66.01), 3.87(3.32), 7.73(7.23)**
6j	**04**	**45**	**73**	**59**	**63.15(62.79), 3.04(2.71), 11.63(11.31)**
6k	**02**	**60**	**60**	**58**	**63.15(62.90), 3.04(2.84), 11.63(11.38)**
6l	**03**	**90**	**69**	**57**	**72.15(71.83), 3.79(3.11)8.86(7.69)**
6m	**04**	**120**	**74**	**71**	**69.36(69.01), 4.05(3.83), 8.09(7.81)**
6n	**02**	**150**	**77**	**63**	**72.73(72.29), 4.24(3.29), 8.48(8.13)**
6o	**02**	**90**	**73**	**60**	**72.73(72.27), 4.24(4.04), 8.48(8.09)**
6p	**03**	**60**	**69**	**58**	**72.73(72.31), 4.24(4.06), 8.48(7.93)**

The mass spectra of all the compounds were consistent with the calculated values thus showing unambiguously the formation of these Schiff's bases.

Biological activities

DPPH radical scavenging activities

2, 2-diphenyl-1-picrylhydrazyl (DPPH) assay is a well known technique used for the analysis of free radical scavenging activity of different antioxidant compounds. Compounds **6a-6p** were subjected to their 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity using the procedure of Shaheen *et al.* [30] and Mahajan *et al.* [31]. A stock solution of 2,2-diphenyl-1-picrylhydrazyl (DPPH) 0.1 mM was prepared by dissolving 3.94 mg in 100 ml of methanol: water (50:50), sample and standard antioxidant butylated hydroxyanisole (BHA) in DMSO (50 mg). Absorbance was recorded at 517 nm after 30 minutes incubation. Percent radical scavenging activity was determined by comparison with DMSO containing standard butylated hydroxyanisole (BHA). Results of studies have revealed significant activity for 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging, especially **6e** and **6h** (Table-2). As far as the structure-activity relationship (SAR) is concerned, it has been reported that the free radical scavenging activity may increase by an increase in number and strength of electron donating groups such as hydroxyl and methoxy [32].

Table-2: Percent radical scavenging activity (**6a-6p).**

Compound	% Radical scavenging activity
6a	0.21
6b	7.70
6c	8.49
6d	8.27
6e	53.26
6f	27.11
6g	37.13
6h	50.15
6i	4.22
6j	8.67
6k	4.49
6l	5.69
6m	5.45
6n	19.20
6o	22.13
6p	26.23
BHA (Std. antioxidants)	40.97

Antibacterial Screening

Compounds **6a-6p** was also subjected to antibacterial screening using the Agar Well Diffusion method [33, 34]. The *in vitro* antimicrobial activity of compounds against gram negative and gram positive bacteria *Escerichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis* was checked by preparing suspensions of microorganism which contain approximately 10^5-10^6 colony forming units/well (CFU). These compounds were applied to the wells of 6.0 mm diameter at 1.0 mg/mL of DMSO in addition to zero (control) and the standard tetracycline (20.0 µg per disc). The inoculated plates were placed in an incubator at 37 ^{0}C for 24 hrs. and growth was assessed by visual inspection. The inhibition zones were measured in mm and compared with the standard drug.

Results show (Table-3) that the compound **6j** (containing -OH and -OCH_3 groups) was found to be the most active against *P. aeruginosa* (33.2 mm), *E. coli*, (32.0 mm), *S. aureus* (29.0 mm) and *B. subtilis* (23.0 mm). Compounds **6n** and **6d** have also shown moderate activities against *P. aeruginosa* (25.1 mm), and *E. coli*, (22.1 mm), *S. aureus* (24.2 mm) and *B. subtilis* (15.7 mm). The remaining compounds were also found somewhat active against these bacteria. Keeping in view the structure-activity relationship, it was noted that compounds with electron donating groups are generally found to be more active as compared to compounds having electron withdrawing groups.

Table-3: Antibacterial activity of compounds **6a-6p.** (Zone of inhibition in mm).

Compound.	*P. aeruginosa*	*E. coli*	*S. aureus*	*B. subtilis*
6a	–	–	17.5	13.6
6b	21.3	20.2	15.6	13.8
6c	12.5	18.3	–	–
6d	20.2	19.0	23.5	15.7
6e	17.8	33.0	22.0	25.4
6f	–	–	12.8	21.7
6g	18.0	22.5	21.3	15.0
6h	17.0	13.0	22.5	18.2
6i	25.3	–	21.0	–
6j	33.2	32.0	29.0	23.0
6k	17.3	24.0	20.0	22.0
6l	31.0	26.2	25.0	23.5
6m	20.0	14.0	16.3	20.2
6n	23.2	28.3	21.5	22.3
6o	21.3	25.4	13.0	17.3
6p	22.2	–	–	25.3
Tetracycline	24.0	29.0	32.0	24.0

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