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Synthesis of novel N-(3,4-dihydro-2H-1,4-benzoxazin-6- yl) Substituted-sulfonamide Derivatives

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Abstract

Oxazine derivatives are important heterocycles compounds. benzo-fused and heterocyclefused [1,4]oxazines in biological activity natural products notice for the synthesis of novel oxazine compounds. Oxazine derivatives are found to be important synthetic intermediates having role in biological applicable. We have developed novel series of N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)Substituted-sulfonamides. This may help for designing new medicines.

Keywords: Oxazine, Sulfonamides, Heterocycles compounds, Benzo-fused.

INTRODUCTION

All worldwide major cause of human illness is due to infection cause by or related to bacteria and the frequency of resistance to the existent antibiotics has risen dramatically over the last few decades. Hence demand for the development of new antibacterial agent is urgent need. Oxazines contains N and O hence are known as heterocyclic compounds [1]. Oxazines herocyclic derivatives which having special concern for the past 3 to 4 decades[2]. Oxazine are found in natural and some non-natural compounds. This types are very useful to study biological activity [3-5]. Oxazines with aromatic properties were first synthesised in by Holly(1944) and Cope(1944) by means of Mannich Method [6]. 1, 4 oxazines are potential leads antibacterial, inhibit cancer[7], antimicrobial, antitubercular and antifungal studies [8-12]. The aim of the research work is to developed novel oxazine base molecules which can have medicinal properties and which can be useful for the treatments of various diseases.

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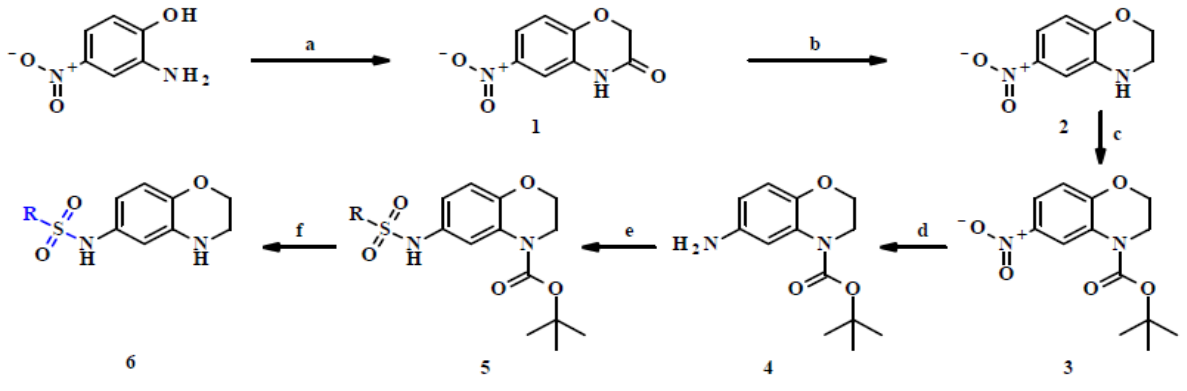
MATERIALS AND METHODS

All the raw materials used for synthesis of desired products were obtained from commercial suppliers and was purified as per requirement. The starting material 2-amino-4- nitro-phenol with 2-chloroacetyl chloride is commercially available and synthesis of this intermediate is also reported in literature. Mass spectra were recorded on „LCMSQp2010s" instrument by direct injection method. Nuclear Magnetic Resonance spectra (^{1}HNMR) were recorded on Bruker advance spectrometer (400 MHz) using DMSO-d_6 or $CDCl_3$ solvent and Tetramethylsilane used as an internal standard. Chemical shift (δ) are reported in parts per million. Reactions were monitored and its purity was checked by Merck pre-coated plate (silica gel 60 F254) Thin Layer Chromatography was visualized with UV light.

RESULT AND DISCUSSIONS

The synthesis of 6-nitro-4*H*-1,4-benzoxazin-3-one**(1)** by reacting 2-amino-4-nitro- phenol with 2-chloroacetyl chloride in DMF solvent at RT and K_2CO_3 was used as base then on reacting with Boron trifluoride etherate (BF_3 Etherate) and NaBH4 in THF solvent at RT yield 6-nitro-3,4-dihydro-2*H*-1,4-benzoxazine**(2)**. Then tert-butyl 6-nitro-2,3- dihydropyrido[3,2-b][1,4]oxazine-4-carboxylate**(3)** isolated by reacting with BOC anhydride and also used as solvent and DMAP as catalyst at 70^{0}C. Compound tert-butyl 6-amino-2,3- dihydro-1,4-benzoxazine-4-carboxylate**(4)** was isolated by reducing nitro group of compound **(3)** with 10% Pd/C in DCM and DMF solvent at RT under hydrogen pressure. Compound **(4)** was reacted with different alkyl or substituted aryl sulphonyl chloride in pyridine as a base and solvent at RT gave different derivatives of tert-butyl 6-(Substituted sulfonamido)-2,3-dihydro-1,4-benzoxazine-4-carboxylate**(5a-h)** which on reacting with conc. HCl solution in methanol at RT gave different derivatives of N-(3,4-dihydro-2H-1,4- benzoxazin-6-yl)Substituted-sulfonamide**(6a-h)**.

Reaction Scheme



Scheme-1

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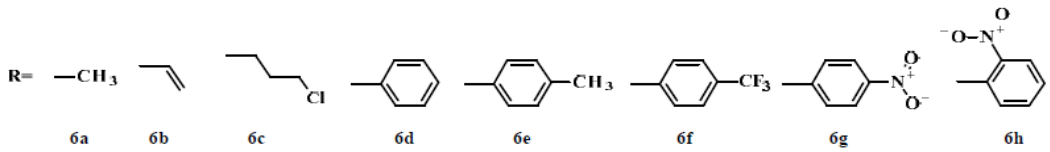

a) 2-amino-4-nitro-phenol, Chloroacetyl chloride, DMF, K_2CO_3, 0^0C, 16 h b) THF, 0^0C, $NaBH_4$, BF_3 . $O(C_2H_5)_2$ c) BOC anhydride, DMAP, 70^0C, 1 h d) 10 % Pd/C, DCM, DMF, H_2 gas e) THF, Pyridine, 0^0C, Alkyl or Aryl sulphonyl chloride f) CH_3OH, Conc.HCl, RT, 16 h.

Procedure

Synthesis of 6-nitro-4*H*-1,4-benzoxazin-3-one (1)

To the solution of 2-amino-4-nitrophenol (1.5 gm, 9.74 mmole) and DMF (40 ml) was mixed at RT for 0.30 hr. Then cooled the reaction mass to 0^0C and K_2CO_3 (4 gm, 29 mmole) was added and stirred for 15 min at 0^0C. Chloroacetyl chloride (1.56 gm, 13.81 mmole) was added drop wise at 0^0C in 30 min. The reaction mass stirred at RT for 16 h (monitored by TLC). DMF was distilled under reduced pressure at 45^0C. Chilled water (150 ml) was added to the reaction mass and stirred at RT for 1 h. Solid obtained was filtered and was washed with water till pH of the cake is neutral. Dry the solid mass under reduced pressure at 45^0C. Colour : yellow solid; Yield 74%; M.P. $>210^0$C;

IR (KBr) (ν max, cm^{-1}) 3176.76, 3068.75, 2976.16, 1714.72, 1608.63, 1525.69, 1409.96, 1340.53, 1292.31, 1234.44;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ 11.079 (s, 1H), 7.860-7.837 (d, 1H, J= 9.2 Hz), 7.747 (s, 1H), 7.163-7.140 (d, 1H, J= 9.2 Hz), 4.774 (s, 2H);

ES-MS: m/z 193.1 $[M+H]^+$.

Synthesis of 6-nitro-3,4-dihydro-2H-1,4-benzoxazine (2)

To the stirred solution of 6-nitro-4H-1,4-benzoxazin-3-one (1) (1.7 gm, 8.85 mmole) in dry THF (50 ml) was added BF_3 etharate (2.8 ml, 22.13 mmole) at 0^0C under inert atmosphere. The reaction mass was stirred for 1 h at RT and then $NaBH_4$ (0.836 gm, 22 mmole) was added lot wise at 0^0C under inert atmosphere. The reaction mixture was stirred for 16 h at RT (monitored by TLC). Reaction mass was quenched with methanol dropwise at RT. THF distilled under reduced pressure. Reaction mass was dissolved in methanol (50 ml) and THF

(50 ml) and stirred at 60^0C for 20 min. Distilled out all THF-Methanol under reduced pressure and dissolved the reaction mass in ethyl acetate (50 ml). Ethyl acetate layer was washed with saturated aq. $NaHCO_3$ solution (25 ml) and then with (2 X 50 ml) water. Dry ethyl acetate layer with anhydrous Na_2SO_4 and distilled under reduced pressure. Crude product isolated was crystalized with diethyl ether.

Colour : Off white solid; Yield 75%;

M.P. 118- 120^0C;

IR (KBr) (ν max, cm^{-1}) 3425.58, 2939.52, 2873.94, 1581.63, 1510.26, 1330.88,

1300.02, 1222.87, 1087.85;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz);δ 7.573- 7.551 (d, 1H, J=8.8 Hz), 7.477 (s, 1H), 6.819-6.797 (d, 1H, J=8.8 Hz), 4.342-4.319 (t, 2H, J=4.8 Hz, J=4.4 Hz), 4.090 (s, 1H), 3.478-3.456 (t, 2H, J=4 Hz, J= 4.8 Hz);

ES-MS: m/z 181.1 [M+H]+.

Synthesis of tert-butyl 6-nitro-2,3-dihydro-1,4-benzoxazine-4-carboxylate (3)

To the solution of 6-nitro-3,4-dihydro-2H-1,4-benzoxazine (2) (4 gm, 22.2 mmole) in Di-tert-butyl dicarbonate (40 ml) at 0^0C followed by DMAP (3.2 gm, 26.65 mmole). Stirred the reaction mass for 1 h 70^0C (monitored by TLC). Distilled out all Di-tert-butyl dicarbonate under reduced pressure at 50^0C. Reaction mass was dissolved in DCM (50 ml) and washed with aq. (2 X 50 ml) saturated NH4Cl solution. Then DCM layer was washed with (2 X 25 ml) water and dried with anhydrous Na_2SO_4. DCM distilled under reduced pressure at 40^0C.

Colour : Orange solid; Yield 88%;

M.P. 106-108^0C;

IR (KBr) (ν max, cm^{-1}) 2988.52, 2929.87, 1705.07, 1587.42, 1512.19, 1348.24, 1321.24, 1248.02, 1163.08;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ 8.799 (s, 1H), 7.899-7.877 (d, 1H, J=8.8 Hz), 6.955-6.933 (d, 1H, J=8.8 Hz), 4.347-4.324 (t, 2H, J= 4.8 Hz, J= 4.4 Hz), 3.920-3.897 (t, 2H, J=4.8 Hz, J=4.4Hz), 1.584 (s, 9H);

ES-MS: m/z No response [M+H]+.

Synthesis of tert-butyl 6-amino-2,3-dihydro-1,4-benzoxazine-4-carboxylate (4)

To the solution of tert-butyl 6-nitro-2,3-dihydro-1,4-benzoxazine-4-carboxylate (3) (1.5 gm, 5.35 mmole) in 100 ml Tetrahydrofuran was added 0.5 gm 10% Pd/C (50% wet wt.). Reaction mass stirred under hydrogen gas pressure (5Kg) for 8 h (monitored by TLC). Filtered the reaction mass through celite bed and Pd/C cake was washed with (2 X 30 ml) THF. Removed solvent under reduced pressure.

Colour : Brown solid; Yield 95%;

M.P. 125-127^{0}C; IR (KBr) (ν max, cm^{-1}) 3437.15, 2954.95, 2924.09, 1701.22, 1502.55, 1375.25, 1246.02, 1161.15;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ 7.399 (s, 1H), 6.512-6.481(d, 1H, J= 8.4 Hz), 6.207-6.186 (d, 1H, J=8.4 Hz), 4.579 (s, 2H), 4.040-4.017 (t, 2H, J= 4 Hz, J= 5.2, J=9.2 Hz), 3.691-3.668(t, 2H, J=4.4 Hz, 4.8 Hz, J=9.2 Hz), 1.456 (s, 9H);

ES-MS: m/z 251.2 [M+H]+.

Synthesis of tert-butyl 6-(Substituted sulfonamido)-2,3-dihydro-1,4-benzoxazine-4-carboxylate (5a-h)

To the solution of tert-butyl 6-amino-2,3-dihydro-1,4-benzoxazine-4-carboxylate (4) (0.1 gm, 0.4 mmole) in pyridine (3 ml) at 0^{0}C was added alkyl or substituted aryl sulphonyl chloride (0.55 mmole) and stirred the reaction mass for 16 h (monitored by TLC). Quench the reaction mass with chilled water (20 ml) and stirred for 1 h. Solid obtained was filtered. Crude product isolated was dissolved in ethyl acetate (50 ml) and washed with aq. (2 X 25 ml) 5% $KHSO_4$ solution. Then ethyl acetate layer was washed with (3 X 25 ml) water and dried with anhydrous Na_2SO_4. Distilled solvent under reduced pressure at 45^{0}C. Crude product was purified by column chromatography (60-120 mesh silica gel) and resulting compound was eluted in 25% ethyl acetate in hexane.

Tert-butyl 6-(methanesulfonamido)-2,3-dihydro-1,4-benzoxazine-4-carboxylate (**5a**)

Colour : Off white solid; Yield 52.6%;

M.P. = 156-158^{0}C;

^{1}H Nuclear Magnetic Resonance in Chloroform (D_3) (400 megahertz): 7.211-7.190 (d, 1H, J= 8.4 Hz), 6.922-6.901 (d, 1H, J= 8.4 Hz), 4.241-4.219 (d, 2H, J= 4.4Hz, J= 4.4 Hz, J= 8.8 Hz), 3.916-3.895 (d, 2H, J= 4.4 Hz, J= 4 Hz, J= 8.4 Hz), 3.414 (s, 1H), 1.540 (s, 9H);

ES-MS: m/z 232.2 [M+H]+.

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Tert-butyl 6-(vinylsulfonylamino)-2,3-dihydro- 1,4-benzoxazine-4-carboxylate (5b)

Colour : Yellow solid; Yield 60.68%;

M.P. = 132-134^{0}C;

^{1}H Nuclear Magnetic Resonance in Chloroform (D_3) (400 megahertz)δ: 7.754 (s, 1H), 6.901-6.879 (d, 1H, J= 8.8 Hz), 6.830-6.809 (d, 1H, J=8.4 Hz), 6.583-6.517 (d,1H, J=6.4 Hz, J=10 Hz, J=10 Hz), 6.261 (s, 1H), 6.232-6.219 (d, 1H, J= 5.2 Hz), 5.949-5.924(d, 1H, J=10 Hz), 4.234-4.211 (t, 2H, J=4.4 Hz, J=4.8 Hz, J=9.2 Hz), 3.853-3.831 (t, 2H, J=4.4 Hz, J=4.4 Hz, J=8.8 Hz) 1.550 (s, 9H);

ES-MS: m/z 339.1[M+H]+.

Tert-butyl6-(3-chloropropylsulfonylamino)-2,3-dihydro-1,4-benzoxazine-4-carboxylate (5c)

Colour : Off white solid; Yield 57.63%;

M.P.= 134-136^{0}C;

^{1}H Nuclear Magnetic Resonance in Chloroform (D_3) (400 megahertz) δ: 7.820 (s, 1H), 6.941-6.919 (d, 1H, J=8.8 Hz), 6.865-6.842 (d, 1H, J=9.2 Hz), 6.282 (s, 1H),4.246-4.224 (t, 2H, J=4.4 Hz, J=4.4 Hz, J=8.8 Hz), 3.867-3.845 (t, 2H, J=4. 4 Hz, 4.4 Hz,J=8.8 Hz), 3.677-3.646 (t, 2H, J=6.4 Hz, J= 6 Hz, J=12.4 Hz), 3.259-3.222 (t, 2H, J=7.6 Hz,7.2 Hz, J=14.8 Hz), 2.341-2.273 (m. 2H), 1.551(s, 9H);

ES-MS: m/z 389.2 [M-H]ˉ.

Tert-butyl 6-(benzenesulfonamido)-2,3-dihydro -1,4-benzoxazine-4-carboxylate (5d)

A Light Brown solid; Yield 71.16%; mp = 146-148^{0}C;

^{1}H Nuclear Magnetic Resonance in Chloroform (D_3) (400 megahertz)δ: 7.768-7.751 (d, 2H, J=6.8 Hz), 7.598 (s, 1H), 7.562-7.526 (t, 1H, J=7.2 Hz, J=7.2 Hz), 7.468-7.429 (t, 2H, J=8 Hz, J=7.6 Hz), 6.738-6.670 (m, 2H), 6.326 (s, 1H), 4.207-4.184 (t, 2H, J=4.4 Hz, J=4.8 Hz, J=9.2 Hz), 3.816-3.793 (t, 2H, J= 4.4 Hz, J=4.8 Hz, J=9.2 Hz), 1.510 (s, 9H);

ES-MS: m/z 389.2 [M-H]ˉ.

Colour : Off white solid; Yield 49.5%;

M.P. = 180-182^{0}C;

^{1}H Nuclear Magnetic Resonance in Chloroform (D_3) (400 megahertz) δ: 7.648-7.627 (d, 2H, J=8. 4 Hz), 7.585 (s, 1H), 7.245-7.224 (d, 2H, J=8.4 Hz), 6.736-6.663(m, 2H), 6.244 (s, 1H), 4.206-4.184 (t, 2H, J=4.4 Hz, J=4.4 Hz, J=8.8 Hz), 3.793 (t, 2H, J=4.8Hz, J=4.8 Hz, J=9.6 Hz), 2.390 (s, 3H), 1.510 (s, 9H);

ES-MS: m/z 403.2 [M-H]$^-$.

Tert-butyl 6-[[4-(trifluoromethyl)phenyl] sulfonyl-amino]-2,3-dihydro-1,4-benzoxazine-4-carboxylate (5f)

Colour : Pale Yellow solid; Yield 76.44%; mp = 184-186^{0}C;

^{1}H Nuclear Magnetic Resonance in Chloroform (D_3) (400 megahertz)δ: 10.130 (s, 1H), 7.961-7.941 (d, 2H, J=8 Hz), 7.902-7.882 (d, 2H, J=8 Hz), 7.503 (s, 1H),6.745 (m, 2H), 4.148-4.126 (t, 2H, J=4 Hz, 4.8 Hz, J=8.8 Hz), 3.712-3.691 (t, 2H, J=4.4 Hz, J=4 Hz, J=8.4 Hz), 1.411 (s, 9H);

ES-MS: m/z 457.2 [M-H]$^-$.

Tert-butyl 6-[(4-nitrophenyl)sulfonylamino]-2,3-dihydro-1,4-benzoxazine-4-carboxylate (5g)

Colour : Pale Yellow solid; Yield 57.13%; mp = 180-182^{0}C;

^{1}H Nuclear Magnetic Resonance in Chloroform (D_3) (400 megahertz)δ: 8.307- 8.284 (d, 2H, J=9.2 Hz), 7.946-7.923 (d, 2H, J= 9.2 Hz), 7.619 (s, 1H), 6.766 (m, 2H), 6.371 (s, 1H), 4.214-4.191 (t, 2H, J=4 Hz, 4.8 Hz, J=8.8 Hz), 3.820-3.797 (t, 2H, J=4.4 Hz, J=4 Hz, J=8.4 Hz), 1.498 (s, 9H);

ES-MS: m/z 434.2 [M-H]$^-$.

Tert-butyl 6-[(2-nitrophenyl)sulfonylamino]-2,3-dihydro-1,4-benzoxazine-4-carboxylate (5h)

Colour : Pale Yellow solid; Yield 93%; mp = 122-124^{0}C;

^{1}H Nuclear Magnetic Resonance in Chloroform (D_3) (400 megahertz)δ: 7.870-7.853 (d, 2H, J=6.8 Hz), 7.721-7.672 (m, 2H), 7.623-7.582 (m, 1H) 7.083 (s, 1H) 6.799-6.728 (m, 2H), 4.211-4.189 (t, 2H, J=4.4 Hz, J=4.4 Hz, J=8.8 Hz), 3.815-3.791 (t, 2H, J=5.2 Hz, J=4.4 Hz, 9.6 Hz), 1.509 (s, 9H);

ES-MS: m/z 434.2 [M-H]$^-$.

Synthesis of N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)Substituted-sulfonamide (6a-h)

To the solution of tert-butyl 6-(Substituted sulfonamido)-2,3-dihydro-1,4- benzoxazine-4-carboxylate (5) (100 mg) in methanol (2ml) at 0^0C was added conc. HCl solution dropwise. Stirred the reaction mass at RT for 5 h (monitored by TLC). Distilled methanol under reduced pressure. 5% aq. Na_2CO_3 solution (10 ml) was added and stirred for 10 min. Reaction mass was extracted with ethyl acetate (50 ml) and washed with (2 X 10 ml) water. Ethyl acetate layer was dried with anhydrous Na_2SO_4 and distilled under reduced pressure. Crude compound isolated was purified by column chromatography (60-120 mesh silica gel) and resulting compound was eluted in 40% ethyl acetate in hexane.

Preparation of compounds (6a-n)

N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl) methanesulfonamide (6a)

A Brown solid; Yield 90%; mp = 130-132^{0}C;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ: 9.112 (s, 1H), 6.579-6.558 (d, 1H, J=8.4 Hz), 6.484 (s, 1H), 6.327-6.306 (d, 1H, J= 8.4 Hz)

5.924 (s, 1H), 4.074-4.054 (t, 2H, J=4 Hz, J=4.4 Hz, J= 8.4 Hz), 3.254-3.243 (t, 2H, J=4.4 Hz), 2.847 (s, 3H);

ES-MS: m/z 229.1 [M+H]+.

N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl) ethenesulfonamide (6b)

Colour : Brown Liquide ; Yield 84.96%;

M.P. = Viscous Liquid so not taken;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ: 9.387 (s, 1H), 6.697-6.631 (d, 1H, J=10 Hz, J=6.4 Hz, J=10 Hz, J=26.4 Hz), 6.540-6.518 (d, 1H, J=8.8 Hz), 6.429 (s, 1H), 6.268-6.241 (d, 1H, J=10.8 Hz),6.022 (s, 1H), 5.980-5.954 (d, 1H, J=10.4 Hz), 5.903 (s, 1H), 4.059-4.037 (t, 2H, J=4 Hz, J=4.8 Hz, J=8.8 Hz), 3.228 (t, 2H);

ES-MS: m/z 241.1 [M+H]+.

3-chloro-N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)propane-1-sulfonamide (6c)

A Brown Liquide; Yield 82%; mp = Viscous Liquid so not taken;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ: 9.313 (s, 1H), 6.577-6.556 (d, 1H, J=8.4 Hz), 6.941(s, 1H), 6.324-6.303(d, 1H, J= 8.4 Hz), 5.944 (s, 1H), 4.072-4.050 (t, 2H, J=4.4 Hz, J=4.4 Hz, 8.8 Hz), 3.737-3.704 (t, 2H, J=6.4 Hz, J=6.8 Hz, J=13.2 Hz), 3.238 (t, 2H), 3.108-3.070 (t, 2H, J=7.6 Hz,J=7.6 Hz, J=15.2 Hz), 2.127-2.057 (m, 2H);
ES-MS: m/z 291.1 [M+H]+.

N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)benzene sulphonamide (6d)

Colour : Brown Liquide; Yield 92%;

M.P. = Viscous Liquid so not taken;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ: 9.697 (s, 1H), 7.712-7.694 (d, 2H, J=7.2 Hz), 7.613-7.514 (m, 3H), 6.447-6.426 (d, 1H, J=8.4 Hz), 6.353 (s, 1H), 6.147-6.126 (d, 1H, J=8.4 Hz), 5.857 (s, 1H), 4.001 (t,2H), 3.177 (t, 2H);

ES-MS: m/z 291.1 [M+H]+.

N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)-4-methyl-benzenesulfonamide (6e)

Colour : Off White solid; Yield 95%;

M.P. = 138-140^{0}C;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ: 9.622 (s, 1H), 7.596-7.576 (d, 2H, J=8 Hz), 7.336-7.317 (d, 2H, J=7.6 Hz), 6.444-6.424 (d,1H, J=8 Hz), 6.354 (s, 1H), 6.146-6.127 (d, 1H, J=7.6 Hz), 5.852 (s, 1H), 4.002 (t, 2H), 3.178 (t, 2H), 2.335 (s, 3H); ES-MS: m/z 305.1 [M+H]+.

N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)-4-(trifluoromethyl)benzenesulfonamide (6f)

Colour : Off White solid; Yield 81%;

M.P. = 162-164^{0}C;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ: 9.938 (s, 1H),7.967-7.947 (d, 2H, J=8 Hz), 7.910-7.888 (d, 2H, J=8.8 Hz), 6.476-6.455 (d,1H, J=8.4 Hz), 6.360-6.353 (s, 1H), 6.146-6.124 (d, 1H, J=8.8 Hz), 5.903 (s, 1H), 4.024- 4.004 (t, 2H, J=4 Hz, J=4 Hz, J-8 Hz), 3.189 (t, 2H);

ES-MS: m/z 359.1 [M+H]+.

N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)-4-nitro-benzenesulfonamide (6g)

Colour : Pale Yellow solid; Yield 90%; M.P.= 185-187^{0}C;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ: 10.016 (s, 1H), 8.389-8.367 (d, 2H, J=8.8 Hz), 7.944-7.823 (d, 2H, J=8.4 Hz), 6.479-6.458(d, 1H, J=8.4 Hz), 6.333 (s, 1H), 6.152-6.130 (d, 1H, J=8.8 Hz), 5.899 (s, 1H), 4.014 (t, 2H), 3.185 (t, 2H);

ES-MS: m/z 336.1 [M+H]+.

N-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)-2-nitro-benzenesulfonamide (6h)

Colour : Pale Yellow solid; Yield 86%;

M.P. = 182-184^{0}C;

^{1}H Nuclear Magnetic Resonance in Dimethyl sulfoxide (D_6) (400 megahertz) δ: 10.118 (s, 1H), 7.965-7.945 (d, 1H, J=8 Hz), 7.895-7.794 (m, 3H), 6.502-6.481 (d, 1H,J=8.4 Hz) 6.390 (s, 1H), 6.216-6.195 (d, 1H, J=8.4 Hz), 5.924 (s, 1H), 4.029-4.009 (t, 2H, J=4 Hz, J=4 Hz, J=8 Hz), 3.193 (t, 2H);

ES-MS: m/z 336.1 [M+H]+.

CONFLICT OF INTEREST

There is no conflict of interest for given article

CONCLUSION

We have synthesized Oxazine and related heterocyclic compounds includes carboxlates, benzenesulfonamide, sulphonamide and Substituted-sulfonamide. These compounds were reported to have antimicobacterial, antibacterial, antifungal, anticoagulant, anticancer, antioxidant, and cytotoxic activities. We have also characterized all compounds to confirm their structure and we have obtained an excellent yield i.e. near to 90%.

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