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EFFICIENT SYNTHESIS AND CHARACTERIZATION OF SOME NOVEL PHENOTHIAZINE SULFONAMIDES

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ABSTRACT

A coherent, methodical and practical technique has been developed for the synthesis of novel *N*-[3-(Trifluoromethyl)-10*H*-phenothiazin-1-yl] sulfonamides **9** by the reaction of 3-(Trifluoromethyl)-10*H*-phenothiazin-1-amine **8** with different sulfonylchlorides in the presence of pyridine and DCM under stirring conditions. Melting points of the compounds are evaluated utilizing cintex melting point apparatus. The compounds are purified using thin-layer chromatography and column chromatography and the derivatives are specified by IR, ^{1}H NMR and Mass spectral data. Elemental analyses are conducted on a Carlo Erba 106 and Perkin Elmer model 240 analyzers. The compounds yields are good in shorter reaction time.

Keywords: Phenothiazine, Sulfonamide, Palladium Catalyst, Buchwald-Hartwig type Reactions, Pharmacophores.

INTRODUCTION

Heterocyclic compounds[1] containing nitrogen and sulphur have manifested in many biologically active compounds. A large number of biologically[2] and pharmacologically active compounds contain phenazine entirely represent an important class of compounds and have enchanted a great deal of heed in recent years such as antifungal, antibacterial[3], anticonvulsant[4], anticancer[5], antileukemia[6], antiherpes [7],anti-inflammatory [8], anticytotoxic[9], antiparasitic[10] and antitubercular.[11]

Phenothiazine is formed by the amalgamation of two benzene nuclei at 2, 3 and 5, 6 positions of thiazine. It is contrarily called as thiodiphenyl amine.[12] It has antipsychotic, antiemetic, antihypertensive, antihistaminic[13] antimicrobial, antimalarial, antihelmintic, analgesic, anti-inflammatory [14] and human cholinesterase inhibition[15] therapeutic activities.

Sulfonamides[16] (sulfa drugs) are a group of drugs procured from sulphanilamide that avert the proliferation of bacteria by inhibiting p-amino benzoic acid in the binding site of enzyme dihydropteroate synthase.[17] These are the best chemotherapeutic agents.[18] Derivatives of the sulfonamide have been delineate with manifold structural features and proficient biological properties such as antiplasmodial [19], carbonic anhydrase inhibitors [20], antioxidant, anti glucoma agents[21]anticholinesterase[22], antitumor, and antiproliferative [23] activities. These are also pronounced as most comprehensively used second veterinary medicine [24]. These derivatives are stupendously used to treat gastrointestinal and urinary tract infections because of their palliate of orchestration and non interference with host defence mechanism [25].

Fluorine incorporated organic compounds inaugurate an area of promptly growing interest because of their idiosyncratic physical and biological properties.[26, 27] Palladium engendered Buchwald-Hartwig type reactions are the conservative methods to congregate these compounds implicate emergence of carbon-carbon and carbon-heteroatom bonds [28]. These reactions substantially incriminate heating the substrate at high temperature for a lengthy period of time in which many functional groups are influenced, and therefore their usage is greatly limited. In the present study, it is observed that considerable progress in

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the improvement of Buchwald-Hartwig reactions,[29-35] by a cost-effective catalyst system for the production of phenothiazinyl sulfonamides with best results.

To intensify pharmacological activity two active pharmacophores if linked together, would generate new molecular templates. Biologically potent substituted phenothiazines and sulfonamides already well established as the key epicenter in medicinal chemistry. Keeping in view the pharmacological potential of phenothiazines and sulfonamides, the title compounds containing these nuclei N-[3-(Trifluoromethyl)-phenothiazin-1-yl] sulfonamides 9 have been synthesized.

EXPERIMENTAL

Materials and Methods

Melting points are determined using a Cintex melting point apparatus and these are uncorrected. Merck silica gel 60 F254 precoated plates (0.25 mm) and Silica gels (particle size 100-200 mesh) are utilized to conduct Thin-layer chromatography (TLC) and column chromatography. Perkin-Elmer BX series FTIR spectrometer is employed to record IR spectra (KBr). ^{1}H NMR spectra are accomplished on a Bruker AMX 400 MHz spectrometer. Chemical shift values are given in ppm (δ) with TMS as an internal standard. Mass spectra are determined on Agilent LC-1100 (LC-MS) series instrument. Elemental analyses are done on a Carlo Erba 106 and Perkin Elmer model 240 analyzers. Anhydrous DMF is purchased and is used without further purification. Tris (dibenzylidene-acetone) dipalladium (0) and X-Phos are commercially available. These are used as such lacking further purification. All the chemicals and reagents used in present exploration are bought from Sigma Aldrich chemical company.

General Procedure

To a solution of 2-bromoaniline **1** in DCM triethylamine is added, followed by acetyl chloride and stirred at room temperature to result in *N*-(2-bromophenyl) acetamide **2.** To the stirred mixture of **2, 2**-ethyl heptyl 3-mercaptopropanoate **3** in DIPEA, Pd_2 (dba) $_3$ and X-Phos are added under reflux conditions at 100˚C to obtain the 2-ethylhexyl 3-((2-acetamido- phenyl) thio) propanoate **4.** Then sodiumethoxide is added to a mixture of **4** and stirred in ethanol at room temperature to afford sodium 2-acetamidobenzenethiolate **5**.

To 2-chloro-1, 3-dinitro-5-(trifluoromethyl) benzene **6,** a solution of **5** in DMF is added to furnish 1-nitro-3-(trifluoromethyl)-10*H*-phenothiazine 7 by undergoing Smiles rearrangement. Ammonium chloride and zinc are added a lot wise to a solution of **7** in 1, 4-dioxane and water to form 3-(trifluoromethyl)-10*H*-phenothiazin-1-amine **8** to undergo reduction reaction.

Treatment of **8** with various sulfonylchlorides in the presence of pyridine in DCM under stirring conditions at 0˚C obtained the corresponding *N*-[3-(trifluoromethyl)-10*H*-phenothiazin-1-yl] sulfonamides **9a-j**.

RESULTS AND DISCUSSION

Characterization of Synthesized Compounds

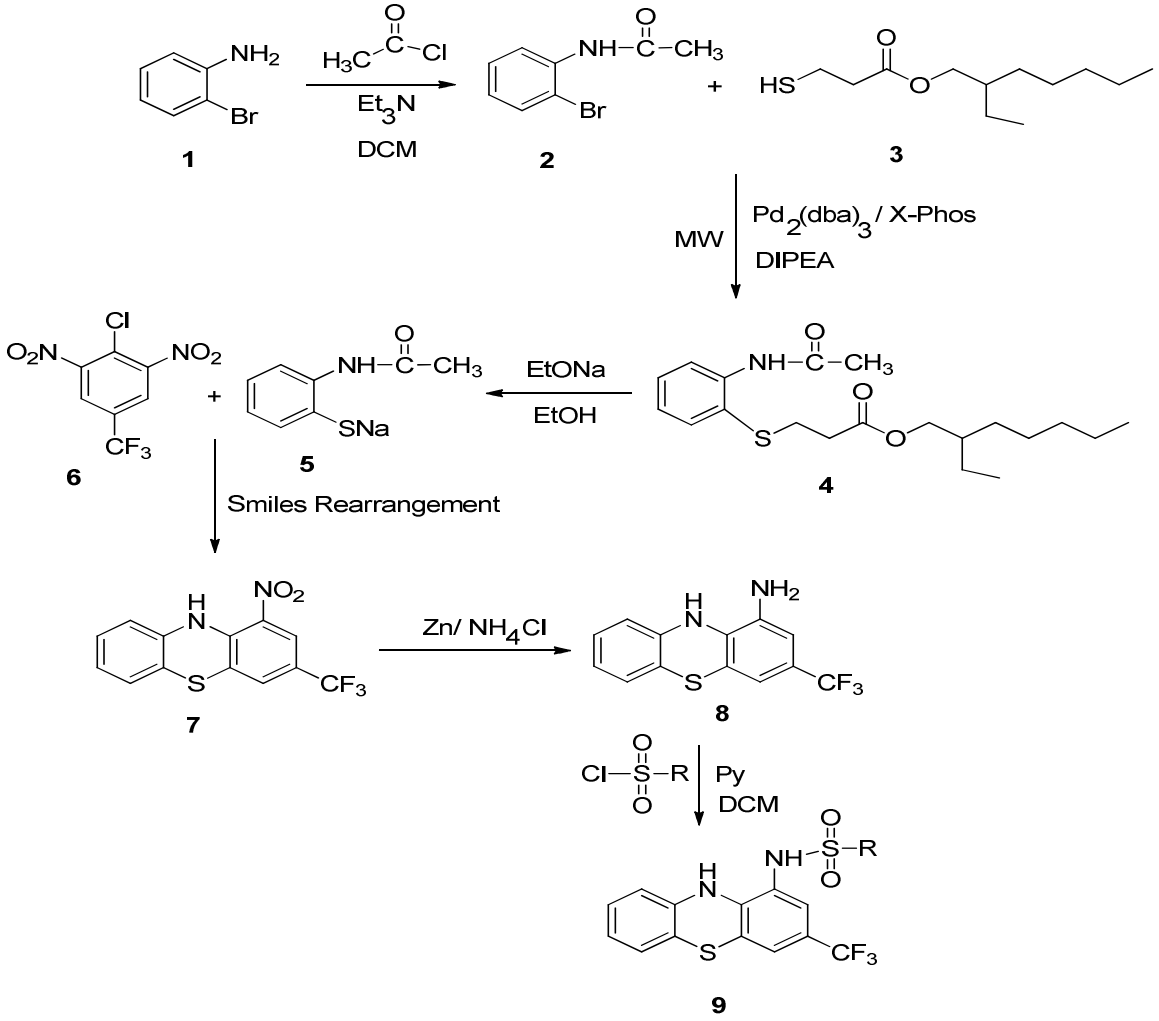
N-(2-Bromophenyl) acetamide (2)

To a solution of 2-bromoaniline (0.01 mol) **1** in DCM, triethylamine (0.02 mol) is added and then followed by acetyl chloride (10 ml)**.** The developed reaction mixture is agitated at room temperature for 10 hr. After the achievement of the reaction (monitored by TLC), the reaction blended is diluted with DCM (100 ml). The organic layer is cleaned with saturated aqueous sodium bicarbonate and brine solution. The separated organic layer dried over anhydrous Na_2SO_4 and the solvent is evaporated under reduced pressure, crude is refined by column chromatography on 100-200 silica gel by eluting with 50% ethyl acetate in n-hexane. Then the white colored solid is obtained **2**. Yield: 90%; m. p121-123^{o}C. IR (KBr) υ (cm^{-1}) 3236, 3162, 3116, 3068, 2946, 1612, 1597, 1538, 1513, 1416,, 1129; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 2.3(s, 3H, CH_3), 7.75 (brs, 1H, NH),8.37-8.43 (m, 3H, Ar-H), 8.63 (s, 1H, Ar-H); LC-MS: *m/z* 214[M+H]$^+$. Calculated analysis percentage for C_8H_8BrNO: C 44.89%, H 3.77%, N 6.54%. Found: C 44.99%, H 4.02%, N 6.59%.

2-Ethylhexyl 3-((2-acetamidophenyl) thio) propanoate (4)

To a agitated solution of **2** and 2-ethylheptyl 3-mercaptopropanoate **3** in benzene is added DIPEA (0.04 mol) at room temperature and degassed with argon for 15 min and then Tris (dibenzylidene-acetone)

dipalladium(0) (0.01 eq.) and X-Phos (0.04 eq.) are added at room temperature .The reaction mixture is subjected to microwave irradiation (Biotage Microwave, 300 Watt) at 150˚C for 15 min.



Scheme-1: Synthetic Route of The *N*-[3-(Trifluoromethyl)-10*H*-Phenothiazin-1-yl] Sulfonamides

The reaction mixture is seived through celite pad and cleansed with DCM. Filtrate is intensed under reduced pressure. The obtained crude is purged by silica gel column chromatography (eluted with 5-6% methanol in DCM) to get white coloured solid **4,** Yield: 88%; b.p. 104-105^{o}C. IR (KBr) υ (cm^{-1}): 3292, 3142, 2968, 2907, 1747, 1631, 1552, 1513, 1459, 1448, 1363, 1228; ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 0.87(t, 6H, 2XCH_3), 1.2-1.4(m, 9H, 3XCH_3), 2.3 (s, 3H, CH_3), 2.58 (t, 2H, -CH_2-), 2.98 (t, 2H, -CH_2-), 4.02 (m, 2H, -CH_2-), 8.4-8.5 (m, 3H, Ar-H), 8.68 (s, 1H, Ar-H), 8.98 (brs, 1H, NH); LC-MS: *m/z* 352.0$[M+H]^{+}$. Calculated percentage for $C_{19}H_{29}NO_3S$: C, 64.92; H, 8.32; N, 3.98. Found: C, 65.10; H, 8.37; N, 4.03%.

2-Acetamidobenzenethiolate (5)

Sodium ethoxide (21%) is added to a solution of 2-ethylhexyl 3-((2-acetamidophenyl) thio) propanoate (0.01 mol) **4** in ethanol (10 ml) .The resulting reaction mixture is stirred at room temperature for 2 hr. On conclusion of the reaction (monitored by TLC), the reaction mixture is cooled to room temperature. The obtained product is strained and refined by recrystallization from ethanol to obtain **5**. Yield is 84%.

1-Nitro-3-(trifluoromethyl)-10H-phenothiazine (7)

To a stirred solution of 2-acetamidobenzenethiolate 5 (0.01 mol) in DMF 2-chloro-1, 3-dinitro-5-(trifluoromethyl) benzene **6** (0.01 mol) *is a*dded**.** The reaction mixture is refluxed at 110˚C for 12 hr, strained through celite pad and cleansed with DCM. Filtrate is concentrated under reduced pressure. The

obtained crude is purged by silica gel column chromatography (eluted with 5-6% methanol in DCM). All the pure fractions are intensified to obtain pale brown product **7.** Yield: 89%; m.p:187-189°C. IR (KBr) υ (cm^{-1}): 3419, 3161, 3044, 2981, 1598, 1537, 1512, 1416, 1319, 1129; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.90-701(m, 4H, Ar-H), 7.60 (brs, 1H, NH), 8.10 (s, 1H, Ar-H), 9.85 (s, 1H, Ar-H); LC-MS: *m/z* 314[M]$^+$. Percentage calculation for $C_{13}H_9F_3N_2O_2S$: C, 49.68; H, 2.89; N, 8.91 Found: C, 49.75; H, 3.03; N, 8.96.

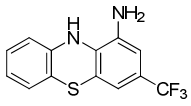
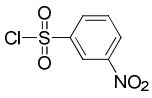
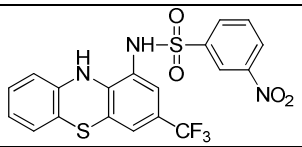
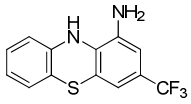
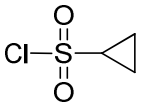
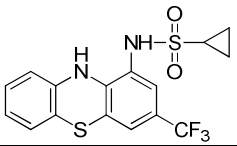
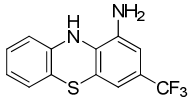
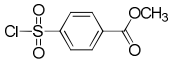
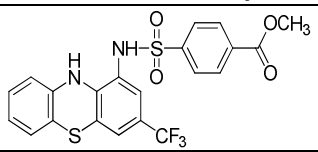
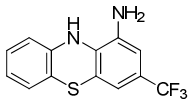
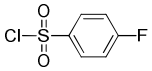
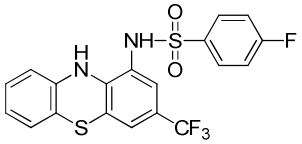
3-(Trifluoromethyl)-10H-phenothiazin-1-amine (8)

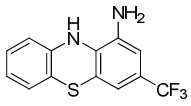
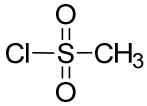
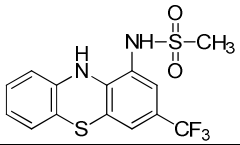
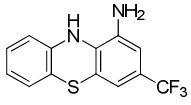
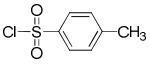
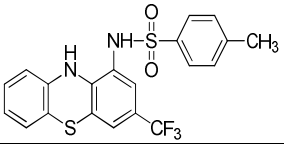
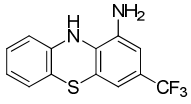
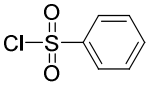
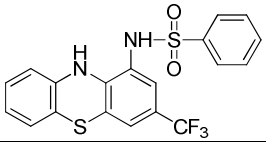
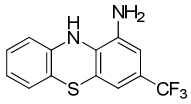
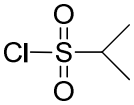
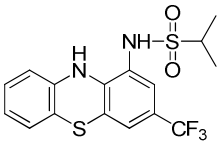
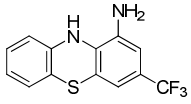
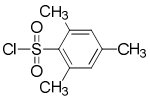
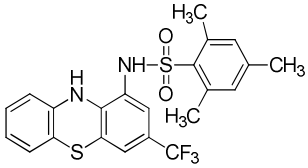
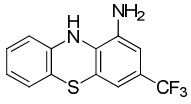
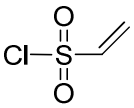
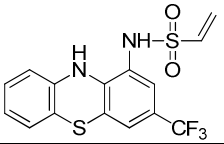
Ammonium chloride (3.20g, 0.06 mol) and Zinc (3.9g, 0.06 mol) are added lot wise at 0˚C to a solution of 1-nitro-3-(trifluoromethyl)-10H-phenothiazine **7** (0.01 mol) in 1,4-dioxane: water (8:2, 25 ml) at 0˚C . This reaction mixture is agitated at room temperature for 4.0 hr. After achievement of the reaction as indicated by TLC, reaction mixture is sieved through celite pad and wiped with ethylacetate and saturated with sodium bicarbonate solution. The organic layer is 6 dried over anhydrous Na_2SO_4 and the solid is chromatographed on silica gel to give pale yellow solid **8,** Yield: 90%; m.p. 122-124°C. IR (KBr) υ (cm^{-1}): 3422, 3243, 3162, 3069, 1612, 1597, 1568, 1538, 1513, 1417, 1129 ; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.45 (brs, 2H, NH_2), 6.5 (brs, 1H, NH), 6.65-6.9 (m, 3H, Ar-H), 6.92 (m, 1H, Ar-H), 7.02 (m, 1H, Ar-H), 7.82 (s, 1H, Ar-H); LC-MS: *m/z* 282.0[M]$^+$. Calculation of percentage for $C_{13}H_9F_3N_2S$: C, 55.31; H, 3.21; N, 9.92. Found: C, 55.42; H, 3.24; N, 9.98%.

N-[3-(Trifluoromethyl)-10H-phenothiazin-1-yl] sulfonamides (9)

Treatment of 3-(Trifluoromethyl)-10*H*-phenothiazin-1-amine **8**(0.01 mol) with various sulfonylchlorides in the presence of pyridine in DCM under stirring conditions at 0˚C obtained the corresponding *N*-[3-(trifluoromethyl)-10*H*-phenothiazin-1-yl] sulfonamides. Completion of reaction is monitored by TLC. The reaction mixture is seived and scrubbed with DCM. The filtrate is concentrated under reduced pressure. The obtained crude is decontaminated by silica gel column chromatography (eluted with 5-6% methanol in DCM). All the pure fractions are concentrated to obtain the products **9a-j.**

Table-1: Physical Data of Compounds 9a-j

S. No.	Amine	Sulfonyl chloride	Product	Time (h)	M.P (˚C)	*Yield (%)
9a				1.5	152	85%
9b				2.0	182	88%
9c				1.5	210	93%
9d				2.0	248	91%

9e				2.5	151	80%
9f				2.0	174	83%
9g				1.5	141	88%
9h				2.0	175	91%
9i				2.5	193	87%
9j				2.0	187	86%

The phenothiazine sulfonamides 9c, 9d and 9h are produced with high yield i.e. above 90%. 9c Yield is very high with a shorter reaction time. All the other products are produced with a yield greater than 80%. The yields are isolated after column purification.

The emergence of compound **2** is concluded by the study of different spectra. The IR spectrum of the compound **2** confirm single absorption band due to NH functional group at 3236 cm^{-1} and did not show two absorption bands due to NH_2 functional group present in its precursor **1**, exhibited the formation of the compound **2**. Similarly, the formation of **2** is supported by the ^1H NMR spectrum accomplished a signal with one proton at δ 7.75 ppm as a broad singlet which corresponds to the NH proton that is absent in its precursor **1**. The mass spectrum of the product **2** also concurs with the structure showed $[M+H]^+$ ion peak at m/z 214.

Development of compound **4** is characterized by its IR band at 1747 cm^{-1} due to ester C=O. Similarly, the formation of **4** is assisted by the ^1H NMR spectrum exhibited signals for different protons in between δ 0.87 to 4.02 ppm which corresponds to the methyl, methylene protons those are absent in its precursor **2**. The mass spectrum of **4** entrenched the structure by exhibiting $[M+H]^+$ ion peak at m/z 352.

The structure of compound 7 is determined by the study of different spectra. The IR spectrum of the compound **7** show single absorption band due to NH functional group at 3419 cm^{-1}, establishing the formation of the compound **7**. Similarly, the formation of **7** is aided by the ^1H NMR spectrum exhibited a signal with one proton at δ 7.60 ppm as a broad singlet which corresponds to the NH proton that is observed at δ 8.98 ppm in its precursor **4**. The mass spectrum of the product **7** also obeys with the structure displayed $[M+H]^+$ ion peak at m/z 314.

The construction of compound **8** is identified by its three characteristic absorption bands in the IR spectra at 3422, 3243 and 3162 cm^{-1} due to NH, NH_2 groups and did not display absorption bands due to $–NO_2$ functional group present in its precursor **7**, confirming the formation of compound **8**. The ^1H NMR

spectrum showed a broad singlet with establishing two protons at δ 7.60 ppm corresponds to the NH_2 protons. The mass spectrum of the product **8** also agrees the structure showed (M^+) ion peak at m/z 282.
The structure of compound **9** is established by the study of different spectra. The IR spectrum of the compound **9a** showed two characteristic absorption bands at 3483 and 3326 cm^{-1} due to the NH functional groups and did not entrench absorption bands due to NH_2 functional group present in its precursor **8**, confirming the formation of the compound **9a**. Similarly, the formation of **9a** is supported by the ^1H NMR spectrum presented a signal with one proton at δ 9.83 ppm as a broad singlet which corresponds to the NH proton that is absent in its precursor **8**. The mass spectrum of the product **9a** also agrees with the structure exhibited $(M)^+$ ion peak at m/z 467.0. The chemical structures of the remaining compounds **9b-j** are identified with the same protocol.
The structures of products **2-9** have been elucidated based on IR, ^1H NMR and MS spectral data. Elemental analyses are satisfactory and confirmed the elemental composition and purity of newly synthesized compounds **2-9.**

Spectral Data

3-Nitro-N-[3-(trifluoromethyl)-10H-phenothiazin-1-yl] benzenesulfonamide (9a): Yellow solid. IR (KBr) υ (cm^{-1}): 3483, 3367, 3184, 3093, 3025,1685, 1646, 1607, 1585, 1466, 1303, 1145 ; ^1H NMR (400 MHz, DMSO-d6): δ 6.63-6.73 (m, 2H, Ar-H), 6.82 (m, 1H, Ar-H), 6.90-6.98 (m, 2H, Ar-H), 7.23 (brs, 1H, NH), 7.80 (m, 1H, Ar-H), 8.00 (m, 1H, Ar-H), 8.22 (s, 1H, Ar-H), 8.39 (s, 1H, Ar-H), 9.83 (brs, 1H, NH); LC-MS: m/z 467.0[M]+. Calculation of percentage for $C_{19}H_{12}F_3N_3O_4S_2$: C, 48.82; H, 2.59; N, 8.99. Found: C, 48.92; H, 2.61; N, 9.04%.

N-[3-(Trifluoromethyl)-10H-phenothiazin-1-yl] cyclopropanesulfonamide(9b): Yellow solid. IR (KBr) υ (cm^{-1}): 3428, 3334, 3161, 3044, 2973, 2945, 1609, 1598, 1537,1512, 1498, 1477, 1416, 1360, 1320, 1129; ^1H NMR (400 MHz, DMSO-d6): δ 0.78 (m, 2H, -CH2-), 0.88 (m, 2H, -CH2-), 2.76 (m, 1H, CH), 6.84-6.90 (m, 1H, Ar-H), 6.95-6.99 (m, 2H, Ar-H), 7.03-7.08 (m, 1H, Ar-H), 7.28 (m, 2H, Ar-H), 8.23 (brs, 1H, NH), 9.20 (brs, 1H, NH); LC-MS: m/z 386.12[M]+. Calculation of percentage for $C_{16}H_{13}F_3N_2O_2S_2$: C, 49.73; H, 3.39; N, 7.25. Found: C, 49.85; H, 3.40; N, 7.31%.

Methyl 4-{[3-(trifluoromethyl)-10H-phenothiazin-1-yl] sulfamoyl} benzoate (9c): Yellow solid. IR (KBr) υ (cm^{-1}): 3456, 3191, 3091, 2983, 2937, 1741,1620, 1593, 1464, 1419, 1338, 1219, 1181; ^1H NMR (400 MHz, DMSO-d6): δ 3.85 (s, 3H, CH3), 6.67(m, 2H, Ar-H), 6.83 (m, 1H, Ar-H), 6.90-6.98 (m, 2H, Ar-H), 7.30 (brs, 1H, NH), 7.75 (d, 2H, Ar-H), 8.05 (d, 2H, Ar-H), 8.10 (s, 1H, Ar-H), 9.98 (brs, 1H, NH); LC-MS: m/z 478.99[M]+. Calculated analysis percentage for $C_{21}H_{15}F_3N_2O_4S_2$: C, 52.49; H, 3.15; N, 5.83. Found: 52.59; H, 3.16; N, 5.87%.

4-Fluoro-N-[3-(trifluoromethyl)-10H-phenothiazin-1-yl] benzenesulfonamide (9d): Yellow solid. IR (KBr) υ (cm^{-1}): 3374, 3300, 3034, 2974, 1607, 1575, 1498, 1462, 1326, 1249, 1155; ^1H NMR (400 MHz, DMSO-d6): δ 6.65 (s, 1H, Ar-H), 6.78-6.90(m, 2H, Ar-H), 6.95 (m, 1H, Ar-H), 7.02 (m, 2H, Ar-H), 7.18 (brs, 1H, NH), 7.35 (d, 2H, Ar-H), 7.62 (d, 2H, Ar-H), 8.10 (s, 1H, Ar-H), 9.80 (brs, 1H, NH); LC-MS: m/z 439.0[M-H]+. Calculated analysis percentage for $C_{19}H_{12}F_4N_2O_2S_2$: C, 51.81, H, 2.75; N, 6.36. Found: C, 51.94, H, 2.77; N, 6.39%.

N-[3-(trifluoromethyl)-10H-phenothiazin-1-yl] methanesulfonamide (9e): Pale brownish solid. IR (KBr) υ (cm^{-1}): 3438, 3088, 3054, 3007, 2945, 2923, 2878, 1625, 1587, 1541, 1433, 1390, 1248, 1201, 1177; ^1H NMR (400 MHz, DMSO-d6): δ 3.04 (s, 3H, CH3), 6.85 (s, 1H, Ar-H), 6.97-7.09(m, 3H, Ar-H), 7.28 (brs, 2H, NH, Ar-H), 8.20 (s, 1H, Ar-H), 9.17 (brs, 1H, NH); LC-MS: m/z 360.08[M]+. Calculated analysis percentage for $C_{14}H_{11}F_3N_2O_2S_2$: C, 46.66, H, 3.08; N, 7.77. Found: C, 46.86, H, 3.10; N, 7.82%.

4-Methyl-N-[3-(trifluoromethyl)-10H-phenothiazin-1-yl] benzenesulfonamide (9f): Pale yellow solid. IR (KBr) υ (cm^{-1}): 3433, 1625, 1585, 1514, 1473, 1395; ^1H NMR (400 MHz, DMSO-d6): δ 6.18 (s, 1H, NH), 6.82-7.05(m, 4H, Ar-H), 7.42 (brs, 1H, NH), 7.63 (m, 4H, Ar-H), 7.82 (m, 3H, Ar-H); LC-MS: m/z

435[M-H]+. Calculated analysis percentage for $C_{19}H_{13}F_3N_2O_2S_2$: C, 54.02, H, 3.10; N, 6.63. Found: C, 54.14, H, 3.12; N, 6.67%.

N-[3-(Trifluoromethyl)-10H-phenothiazin-1-yl] benzenesulfonamide (9g): Yellow solid. IR (KBr) υ (cm^{-1}): 3417, 3268, 3181, 3074, 2979, 1606, 1573, 1533, 1512, 1477, 1412, 1127; ^{1}H NMR (400 MHz, DMSO-d6): δ 2.26 (s, 3H, CH3), 6.87 (s, 1H, Ar-H), 6.71(m, 1H, Ar-H), 6.85 (m, 2H, Ar-H), 6.93 (m, 1H, Ar-H), 7.17(brs, 1H, NH), 7.31 (d, 2H, Ar-H), 7.53 (d, 2H, Ar-H), 8.05 (s, 1H, Ar-H), 9.55 (brs, 1H, NH); LC-MS: m/z 421[M-H]+. Calculated analysis percentage for $C_{20}H_{15}F_3N_2O_2S_2$: C, 55.04, H, 3.46; N, 6.42. Found: C, 55.14, H, 3.49; N, 6.47%.

N-[3-(Trifluoromethyl)-10H-phenothiazin-1-yl] propanesulfonamide (9h): Dark brown solid. IR (KBr) υ (cm^{-1}): 3415, 3318, 2964, 2914, 2901, 2854, 1532, 1494,1450, 1368, 1299, 1227, 1178; ^{1}H NMR (400 MHz, DMSO-d6): δ 1.20 (d, 6H, 2XCH3), 3.32 (m, 1H, CH), 6.87(m, 2H, Ar-H), 7.01-7.10 (m, 2H, Ar-H), 7.22 (s, 1H, Ar-H), 7.33(brs, 1H, NH), 8.15 (s, 1H, Ar-H), 9.25 (brs, 1H, NH); LC-MS: m/z 388.1[M]+. Calculated analysis percentage for $C_{16}H_{15}F_3N_2O_2S_2$: C, 49.47, H, 3.89; N, 7.21. Found: C, 49.59, H, 3.91; N, 7.27%.

2,4,6-Trimethyl-N-[3-(trifluoromethyl)-10H-phenothiazin-1-yl] benzenesulfonamide(9i): Pale green solid. IR (KBr) υ (cm^{-1}): 3425, 3342, 3021, 2973., 2927, 2872, 1617, 1605, 1522, 1476, 1425, 1372, 1216; ^{1}H NMR (400 MHz, DMSO-d6): δ 2.20 (s, 3H, CH3), 2.40 (s, 6H, 2XCH3), 6.41 (s, 1H, CH), 6.85-7.01(m, 6H, Ar-H), 7.17 (brs, 1H, NH), 8.10 (s, 1H, Ar-H), 9.53 (brs, 1H, NH); LC-MS: m/z 464.1[M]+. Calculated analysis percentage for $C_{22}H_{19}F_3N_2O_2S_2$: C, 56.88, H, 4.12; N, 6.03. Found: C, 56.99, H, 4.14; N, 6.08%.

N-[3-(Trifluoromethyl)-10H-phenothiazin-1-yl] ethenesulfonamide (9j): Dark yellow solid. IR (KBr) υ (cm^{-1}): 3418, 3236, 3162, 3067, 2981, 2946, 1611, 1598, 1538, 1514, 1415, 1320, 1130; ; ^{1}H NMR (400 MHz, DMSO-d6): δ 6.62 (d, 1H, Ar-H), 6.57 (d, 2H, Ar-H), 6.87 (s, 1H, Ar-H), 6.97-7.11(m, 3H, Ar-H), 7.30 (brs, 2H, NH, Ar-H), 8.22 (s, 1H, Ar-H), 9.12 (brs, 1H, NH); LC-MS: m/z 372.0[M]+. Calculated analysis percentage for $C_{15}H_{11}F_3N_2O_2S_2$: C, 48.38, H, 2.98; N, 7.52. Found: C, 48.49, H, 3.01; N, 7.58%.

CONCLUSION

An elementary, methodical method has been developed for the synthesis of novel *N*-[3-(Trifluoromethyl)-10*H*-phenothiazin-1-yl] sulfonamides **9**. This method offers several advantages: mild reaction conditions, intensified reaction rates, easy isolation of products and operational simplicity. The extent and generality of this protocol are illustrated with respect to 3-(Trifluoromethyl)-10*H*-phenothiazin-1-amine **8** with various sulfonyl chlorides.

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