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Synthesis of 7-chloro-5-trifluoromethyl/7-fluoro/7-trifluoromethyl-4*H*-1,4-benzothiazines as antimicrobial agents

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Abstract—7-Chloro-5-trifluoromethyl/7-fluoro/7-trifluoromethyl-4*H*-1,4-benzothiazines have been synthesized by 2-amino-5-fluoro/5-trifluoromethyl/5-chloro-3-trifluoromethyl benzenethiols condensed with β-diketone/β-ketoesters in the presence of DMSO involving oxidative cyclization. Pharmacological activities have also been included.

1. Introduction

4*H*-1,4-Benzothiazines are structural analogs of 10*H*-phenothiazines.[1–3] 4*H*-1,4-Benzothiazines possess a wide spectrum of biological and pharmacological activities due to presence of a fold along the nitrogen and sulfur axis, which is considered to be responsible as one of the structural features to impart their activities. They are used as antihistaminics,[4] antipsychotics,[5] antiemetics,[6] neuroleptics,[7] tranquilizers,[8] sedatives,[9] etc. Significant activity against cancer has also been shown by phenothiazines.[10–12] With the aim of developing a new class of effective drugs embracing certain characteristic structural features for effective drug–receptor interaction, we have synthesized 7-chloro-5-trifluoromethyl/5-fluoro/5-trifluoromethyl-4*H*-1,4-benzothiazines to make them available for screening of wide ranging pharmacological and biological activities.

2. Results and discussion

2-Amino-5-fluoro/5-trifluoromethyl/5-chloro-3-trifluoromethyl-benzenethiols **5a**–**c** were obtained by the hydrolytic cleavage of 6-fluoro/6-trifluoromethyl/6-chloro-4-trifluoromethyl-2-aminobenzothiazoles **3a**–**c**, which in turn were prepared by the bromination of 4-fluoro/4-trifluoromethyl/4-chloro-2-trifluoromethyl-phenylthioureas **2a**–**c** in chloroform. 4-Fluoro/4-trifluoromethyl/4-chloro-2-trifluoromethylphenylthioureas were obtained by the action of ammonium thiocyanate on 4-fluoro/trifluoromethyl/4-chloro-2-trifluoromethyl anilines **1a**–**c**.

7-Chloro-5-trifluoromethyl/7-fluoro/7-trifluoromethyl-4*H*-1,4-benzothiazines **10a**–**m** have been synthesized by the condensation and oxidative cyclization of 2-amino-5-fluoro/trifluoromethyl/5-chloro-3-trifluoromethylbenzenethiols[13] **5a**–**c** with active methylene compounds in the presence of dimethylsulfoxide. The reaction is considered to proceed through the formation of an enaminoketone intermediate (Scheme 1).

In IR spectra, the synthesized 2-amino-5-fluoro/5-trifluoromethyl/5-chloro-3-trifluoromethyl-benzenethiols **5a**–**c** exhibit two sharp bands in the region 3483–3410 cm^{-1} and 3362–3310 cm^{-1} due to the asymmetric and symmetric stretching vibrations of the primary amino group.

In the region 2587–2550 cm^{-1} a weak absorption band is observed due to S–H stretching vibrations. In compound **5b** strong absorption band is observed in the region 1165 cm^{-1} due to C–F stretching. In compounds **5a**, **c** two bands are observed in the region 1345–1340 cm^{-1} and 1183–1180 cm^{-1} due to asymmetric and symmetric C–F stretching vibrations of CF_3 group. The absorption band at 724 cm^{-1} is observed in compound **5a** due to C–Cl stretching vibrations.

IR spectra of 2-aminobenzenethiols **5a**–**c** exhibit a multiplet in the region δ 8.48–6.53 ppm due to aromatic protons. The broad signal observed in the region δ 4.95–3.61 ppm is attributed to $-NH_2$ protons. The singlet

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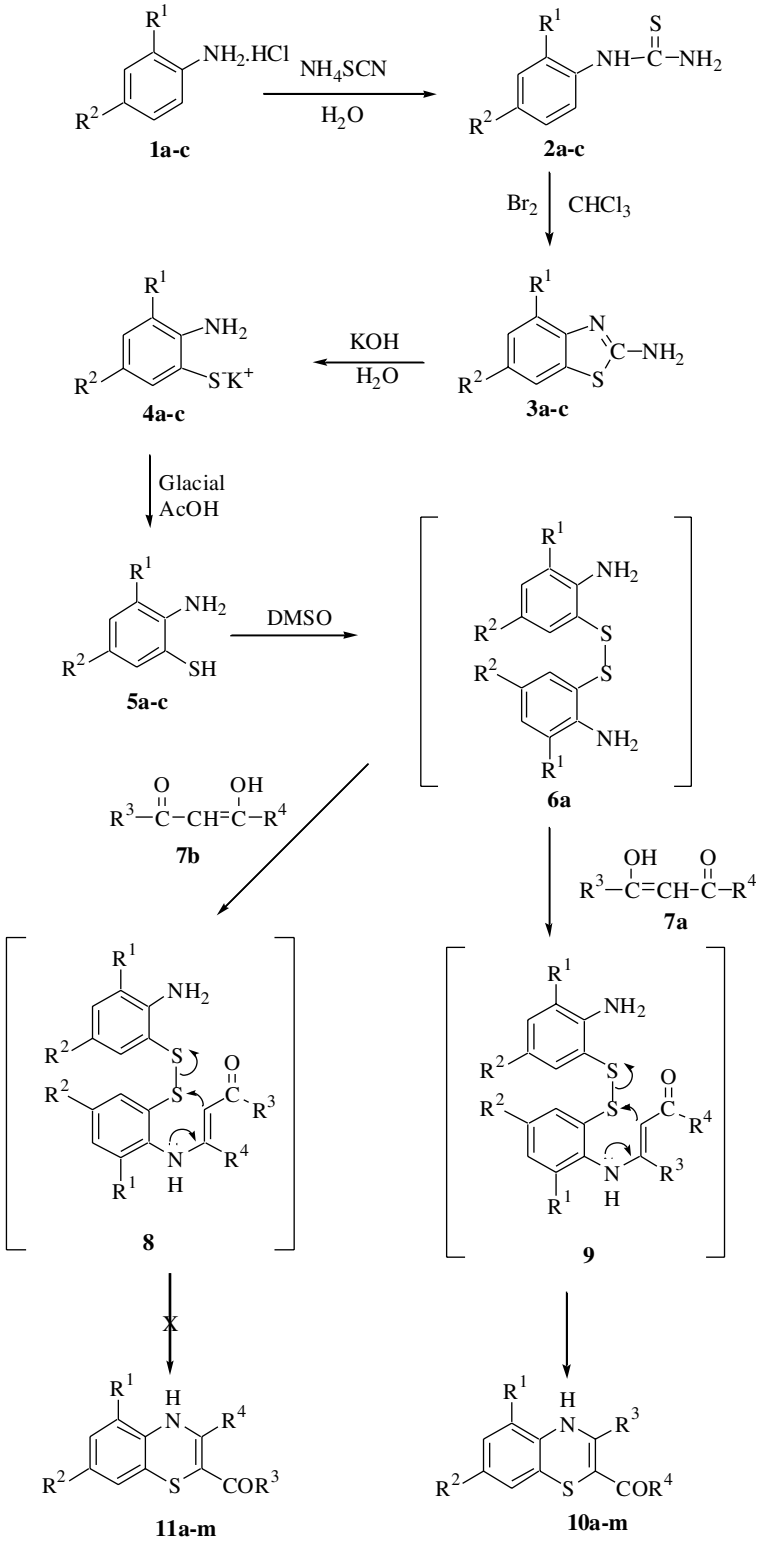

Scheme 1.

observed at δ 1.27–1.23 ppm can be assigned to –SH proton.

In all the 7-chloro-5-trifluoromethyl/7-fluoro/7-trifluoromethyl-4*H*-1,4-benzothiazines **10a**–**m** a sharp intense band is observed in the region 3465–3248 cm^{-1} due to N–H stretching vibrations. In the region 1740–1610 cm^{-1}, an intense band is observed due to C=O stretching vibrations. In the regions 1327–1120 cm^{-1} and 1187–1026 cm^{-1} two sharp bands are observed due to asymmetric and symmetric C–F stretching vibrations of CF_3 group **10d**–**m**. In the regions 1485–

1433 cm^{-1} and 1383–1350 cm^{-1} two sharp bands are observed due to asymmetric and symmetric C–H deformation vibrations of CH_3 group in compounds **10c**, **j**, **m**. An absorption band in the region 640–569 cm^{-1} is attributed to C–Br stretching vibrations in compounds **10b**, **g**, **k**. Compounds **10a**, **e**, **h**, **i**–**m** containing chlorine atom exhibit absorption band in the region 790–752 cm^{-1} due to C–Cl stretching vibrations. Compounds **10a**, **b**, **c** show an absorption band in the region 1070–1050 cm^{-1} due to C–F stretching vibrations.

A single sharp peak observed in the region δ 10.43–8.62 ppm in all 4*H*-1,4-benzothiazines **10a**–**m** is due to N–H proton. Allylic proton (–C═C–CH_3) at C-3 in all 4*H*-1,4-benzothiazines appear in the region δ 2.79–2.21 ppm. Aromatic protons show multiplet in the region δ 8.64–6.11 ppm. In compounds **10c**, **j** a triplet is observed in the region δ 1.44–1.28 ppm due to CH_3 protons of –C_2H_5(p) and a quartet observed in the region δ 2.67–2.31 ppm is due to CH_2 protons of –C_2H_5(p) group at C-2. ^{13}C NMR spectra of **10c**, **f** and **i** as representative and ^{19}F NMR of **10a**–**m** have also been recorded. In mass spectra of 7-chloro-5-trifluoromethyl/5-fluoro/5-trifluoromethyl-4*H*-1,4-benzothiazines **10a**–**m**, the molecular ion peak is in accordance to their molecular weight.

3. Pharmacological activity

All the synthesized compounds (**10a**–**m**) were screened for antibacterial activity[14,15] against *Bacillus subtilis* (**A**), *Bacillus mega* (**B**) (Gram +ve), *Escherichia coli* (**C**), *Aspergillus arogens* (**D**) (Gram −ve), and antifungal activity against *Aspergillus awamori* (**E**) at a concentration of 30 μg/ml using $CHCl_3$ as a solvent by standard method. After 24 h of incubation at 37 °C, the zones of inhibition were measured in millimeter (Table 1).

4. Conclusion

It has been noted that all the compounds **10b**, **c**, **h**, and **j** show strong activities against microbes, whereas compounds **10a**, **d**, **e**, **g**, **i**, **k**, and **l** show moderate activity compounds **10f** and **m** shows weak activity as compared to references. The standard drugs used for references were chloramphenicol (30 μg/ml) and griseofulvin (30 μg/ml).

5. Experimental

Melting points of all the synthesized compounds are uncorrected. The purity of synthesized compounds was checked by thin-layer chromatography. The IR spectra have been recorded on FT IR spectrophotometer Magna IR 550 Nicolet using KBr discs. ^1H NMR and ^{13}C NMR spectra were scanned at 90 MHz/300 MHz on Jeol FX 90Q FT NMR spectrophotometer in DMSO-d_6/$CDCl_3$ using TMS as an internal standard. ^{19}F NMR spectra were scanned with respect to hexafluorobenzene with ^{19}F signal at δ162.9 ppm.

5.1. Preparation of 4-chloro-2-trifluoromethyl-/4-fluoro-/4-trifluoromethyl-phenylthioureas (2a–c)

4-Chloro-2-trifluoromethyl-/4-fluoro-/4-trifluoromethyl-anilines (I; 0.1 mol), hydrochloric acid (9 ml), and water (25 ml) were taken and refluxed for 30 min in a round-bottomed flask. The contents were cooled down to room temperature and then ammonium thiocyanate (0.1 mol) was added. The reaction mixture was again refluxed for 4 h. The solid obtained was cooled down, filtered, washed well with water, dried, and crystallized from ethanol.

5.2. Preparation of 2-amino-6-chloro-4-trifluoromethyl-/2-amino-6-fluoro-/2-amino-6-trifluoromethyl-benzothiazoles (3a–c)

In a round-bottomed flask equipped with a mechanical stirrer and a dropping funnel, 4-chloro-2-trifluoromethyl-/4-fluoro-/4-trifluoromethyl-phenylthioureas (II; 0.1 mol) and chloroform (100 ml) were taken. A solution of bromine (0.1 mol) in chloroform (100 ml) was added with stirring for a period of two hours. Temperature of reaction mixture remains below 5 °C during the reaction.

Table 1. Pharmacological data of substituted 4*H*-1,4-benzothiazines **10a**–**m**

Compound	R^1	R^2	R^3	R^4	Antimicrobial and antifungal activity (zones of inhibition in mm)				
					A	B	C	D	E
10a	H	F	CH_3	–C_6H_4Cl (*m*)	16	14	15	19	14
10b	H	F	CH_3	–C_6H_4Br (*m*)	20	18	19	21	17
10c	H	F	CH_3	–$C_6H_4C_2H_5$ (*p*)	18	16	16	18	15
10d	H	CF_3	CH_3	–C_6H_5	15	13	14	15	14
10e	H	CF_3	CH_3	–C_6H_4Cl (*m*)	16	14	17	19	16
10f	H	CF_3	C_6H_5	–C_6H_5	15	13	16	18	14
10g	H	CF_3	CH_3	–C_6H_4Br (*p*)	16	19	18	20	20
10h	H	CF_3	CH_3	–C_6H_4Cl (*p*)	19	17	18	19	18
10i	CF_3	Cl	CH_3	–C_6H_5	16	15	16	18	16
10j	CF_3	Cl	CH_3	–$C_6H_4C_2H_5$ (*p*)	18	16	17	19	17
10k	CF_3	Cl	CH_3	–C_6H_4Br (*p*)	17	19	21	20	18
10l	CF_3	Cl	C_6H_5	–C_6H_5	16	17	17	20	18
10m	CF_3	Cl	CH_3	–$C_6H_4CH_3$ (*o*)	14	15	16	18	15

Stirring was continued for a period of 4 h. After the addition of bromine, contents of round-bottomed flask were refluxed for about 4 h till the evolution of HBr ceased. Chloroform was removed by filtration and resulting solid was treated with SO_2 water and filtered. The filtrate was neutralized with aqueous ammonia solution. The precipitate was filtered, washed well with water, and crystallized from ethanol.

5.3. Synthesis of 2-amino-5-fluoro/5-trifluoromethyl-/5-chloro-3-trifluoromethyl benzenethiols (5a–c)

2-Amino-6-fluoro-/trifluoromethyl-/6-chloro-4-trifluoromethyl-benzothiazoles obtained, KOH (5 times by weight of thiazole) and water (10 times by weight of thiazole) were taken in a R.B. flask and refluxed until evolution of ammonia ceased. The reaction mixture was cooled, filtered and distilled with cold water. The filtrate was neutralized by acetic acid (5N) with vigorous stirring. During neutralization the temperature of mixture was maintained below 10 °C by adding ice otherwise a decomposed greenish mass is obtained instead of desired 2-aminobenzenethiol. The resulting mixture was extracted 2 or 3 times with ether, ether was evaporated and yellow solid obtained was crystallized from ethanol.

5.4. Preparation of 7-chloro-5-trifluoromethyl/7-fluoro/7-trifluoromethyl-4*H*-1,4-benzothiazines (10a–m)

In a R.B. flask 2-amino-5-fluoro/5-trifluoromethyl/5-chloro-3-trifluoromethyl benzenethiol (0.01 mol) was added to a stirred suspension of β-diketone/β-ketoester (0.01 mol) in dimethylsulfoxide (5 ml). The resulting mixture was refluxed for about 30–40 min, concentrated and cooled. The solid separated out was filtered, washed well with petroleum ether, and crystallized from methanol/acetone (Scheme 1).

Physical, IR, and NMR data of the 2-amino-5-fluoro/5-trifluoromethyl/5-chloro-3-trifluoromethyl-benzenethiols **5a–c** and 7-chloro-5-trifluoromethyl/7-fluoro/7-trifluoromethyl-4*H*-1,4-benzothiazines **10a–m** are as follows:

5.4.1. 2-Amino-5-chloro-3-trifluoromethylbenzenethiol (5a). $C_7H_5ClF_3NS$; mp 186; yield 53.0%; found: C, 36.93; H, 2.21; N, 6.17; Calcd: C, 36.89; H, 2.25; N, 6.10; IR KBr (ν cm^{-1}) 3483, 3362 (NH_2), 2587 (SH), 1345, 1183 (CF_3), 724 (C–Cl); ^1H NMR (DMSO-d_6, δ, ppm) 3.62 (2H, s, NH_2), 8.49–6.91 (2H, m, Ar), 1.29 (1H, s, SH).

5.4.2. 2-Amino-5-fluorobenzenethiol (5b). C_6H_6FNS; mp 98; yield 55.0%; found: C, 50.32; H, 4.23; N, 9.79; Calcd: C, 50.20; H, 4.22; N, 9.77; IR KBr (ν cm^{-1}) 3410, 3310 (NH_2), 2540 (SH), 1065 (CF); ^1H NMR (DMSO-d_6, δ, ppm) 4.15 (2H, s, NH_2), 7.32–6.53 (3H, m, Ar), 1.23 (1H, s, SH).

5.4.3. 2-Amino-5-trifluoromethylbenzenethiol (5c). $C_7H_6F_3NS$; mp 198; yield 49.0%; found: C, 43.51; H, 3.11; N, 7.25; Calcd: C, 42.98; H, 3.10; N, 7.23; IR KBr (ν cm^{-1}) 3470, 3360 (NH_2), 2550 (SH), 1340, 1180 (CF_3), 724 (C–Cl); ^1H NMR (DMSO-d_6, δ, ppm) 4.95 (2H, s, NH2), 8.48–6.49 (3H, m, Ar), 1.24 (1H, s, SH).

5.4.4. 2-(3-Chlorobenzoyl)-3-methyl-7-fluoro-4*H*-1,4-benzothiazine (10a). $C_{16}H_{11}ClFNOS$; mp 155; yield 53.9%; found: C, 60.07; H, 3.48; N, 4.37; Calcd: C, 60.09; H, 3.47; N, 4.38; IR KBr (ν cm^{-1}) 3250 (N–H), 1740 (>C=O), 1040 (C–F), 1471–1350 (C–H of CH_3), 752 (C–Cl); ^1H NMR (DMSO-d_6, δ, ppm) 9.16 (1H, s, NH), 8.15–6.40 (7H, m, Ar), 2.60 (3H, s, CH_3); ^{19}F NMR (DMSO-d_6, δ, ppm) −113.2 (F at C_7).

5.4.5. 2-(3-Bromobenzoyl)-3-methyl-7-fluoro-4*H*-1,4-benzothiazine (10b). $C_{16}H_{11}BrFNOS$; mp 160; yield 84.36%; found: C, 52.75; H, 3.05; N, 3.83; Calcd: C, 52.76; H, 3.04; N, 3.85; IR KBr (ν cm^{-1}) 3248 (N–H), 1620 (>C=O), 1070 (C–F), 1485–1378 (C–H of CH_3), 630 (C–Br); ^1H NMR (DMSO-d_6, δ, ppm) 9.26 (1H, s, NH), 8.08–6.59 (7H, m, Ar), 2.59 (3H, s, CH_3); ^{19}F NMR (DMSO-d_6, δ, ppm) −112.8 (F at C_7).

5.4.6. 2-(4-Ethylbenzoyl)-3-methyl-7-fluoro-4*H*-1,4-benzothiazine (10c). $C_{18}H_{16}FNOS$; mp 110; yield 55.07%; found: C, 68.98; H, 5.13; N, 4.48; Calcd: C, 68.99; H, 5.15; N, 4.47; IR KBr (ν cm^{-1}) 3280 (N–H), 1610 (>C=O), 1050 (C–F), 1485–1385 (C–H of CH_3); ^1H NMR (DMSO-d_6, δ, ppm) 9.36 (1H, s, NH), 8.37–6.72 (7H, m, Ar), 2.79 (3H, s, CH_3), 2.67–2.31 (2H, q, CH_2), 1.14–1.44 (3H, t, CH_3); ^{13}C NMR (DMSO-d_6, δ, ppm) 15.8 (CH_3), 16.5 (CH_2CH_3), 28.6 (CH_2CH_3), 117.9–140.2 (14 aromatic carbons), 152.8 (*C*–F), 178.9 (*C*=O); ^{19}F NMR (DMSO-d_6, δ, ppm) −109.75 (F at C_7).

5.4.7. 2-Benzoyl-3-methyl-7-trifluoromethyl-4*H*-1,4-benzothiazine (10d). $C_{17}H_{12}F_3NOS$; mp 230; yield 68.59%; found: C, 60.88; H, 3.62; N, 4.16; Calcd: C, 60.89; H, 3.61; N, 4.18; IR KBr (ν cm^{-1}) 3390 (N–H), 1620 (>C=O), 1125–1080 (C–F), 1433–1383 (C–H of CH_3); ^1H NMR (DMSO-d_6, δ, ppm) 10.00 (1H, s, NH), 8.64–6.76 (8H, m, Ar), 2.25 (3H, s, CH_3); ^{19}F NMR (DMSO-d_6, δ, ppm) −55.6 (F at C_7).

5.4.8. 2-(3-Chlorobenzoyl)-3-methyl-7-trifluoromethyl-4*H*-1,4-benzothiazine (10e). $C_{17}H_{11}ClF_3NOS$; mp 190; yield 78.48%; found: C, 55.23; H, 2.99; N, 3.77; Calcd: C, 55.22; H, 3.00; N, 3.79; IR KBr (ν cm^{-1}) 3370 (N–H), 1625 (>C=O), 1120–1070 (C–F), 1466–1390 (C–H of CH_3); ^1H NMR (DMSO-d_6, δ, ppm) 9.33 (1H, s, NH), 8.48–6.12 (7H, m, Ar), 2.55 (3H, s, CH_3); ^{19}F NMR (DMSO-d_6, δ, ppm) −54.7 (F at C_7).

5.4.9. 2-Benzoyl-3-phenyl-7-trifluoromethyl-4*H*-1,4-benzothiazine (10f). $C_{22}H_{14}F_3NOS$; mp 130; yield 69.55%; found: C, 66.50; H, 3.53; N, 3.51; Calcd: C, 66.49; H, 3.55; N, 3.52; IR KBr (ν cm^{-1}) 3396 (N–H), 1689 (>C=O), 1327–1026 (C–F); ^1H NMR (DMSO-d_6) δ 8.64 (1H, s, NH), 8.17–6.11 (13H, m, Ar); ^{13}C NMR (DMSO-d_6, δ, ppm) 108.4 (C–CF_3), 118.4 (CCF_3), 107.9–143.2 (20 aromatic carbons), 178.2 (*C*=O); ^{19}F NMR (DMSO-d_6) −53.57 (F at C_7).

5.4.10. 2-(4-Bromobenzoyl)-3-methyl-7-trifluoromethyl-4*H*-1,4-benzothiazine (10g). $C_{17}H_{11}BrF_3NOS$; mp 168; yield 74.16%; found: C, 49.27; H, 2.69; N, 3.36; Calcd: C, 49.29; H, 2.68; N, 3.38; IR KBr (ν cm^{-1}) 3465 (N–H), 1690 (>C=O), 1250–1140 (C–F), 1475–1375 (C–H of CH_3), 569 (C–Br); ^1H NMR (DMSO-d_6, δ, ppm) 9.43 (1H, s, NH), 8.19–6.11 (7H, m, Ar), 2.36 (3H, s, CH_3); ^{19}F NMR (DMSO-d_6, δ, ppm) −53.7 (F at C_7).

5.4.11. 2-(4-Chlorobenzoyl)-3-methyl-7-trifluoromethyl-4*H*-1,4-benzothiazine (10h). $C_{17}H_{11}ClF_3NOS$; mp 180; yield 81.97%; found: C, 55.20; H, 2.98; N, 3.80; Calcd: C, 55.22; H, 3.00; N, 3.79; IR KBr (ν cm^{-1}) 3293 (N–H), 1689 (>C=O), 1260–1125 (C–F), 1466–1383 (C–H of CH_3), 793 (C–Cl); ^1H NMR (DMSO-d_6, δ, ppm) 9.38 (1H, s, NH), 8.47–6.19 (7H, m, Ar), 2.31 (3H, s, CH_3); ^{19}F NMR (DMSO-d_6, δ, ppm) −55.8 (F at C_7).

5.4.12. 2-Benzoyl-7-chloro-3-methyl-5-trifluoromethyl-4*H*-1,4-benzothiazine (10i). $C_{17}H_{11}ClF_3NOS$; mp 167; yield 47.39%; found: C, 55.21; H, 3.01; N, 3.76; Calcd: C, 55.22; H, 3.00; N, 3.79; IR KBr (ν cm^{-1}) 3410 (N–H), 1675 (>C=O), 1210–1140 (C–F), 1479–1371 (C–H of CH_3); ^1H NMR (DMSO-d_6, δ, ppm) 10.43 (1H, s, NH), 8.35–6.83 (7H, m, Ar), 2.6 (3H, s, CH_3); ^{13}C NMR (DMSO-d_6, δ, ppm) 16.9 (CH_3), 107.8 (C–CF_3), 118.9 (C–CF_3), 117.9–138.6 (14 aromatic carbons), 124.8 (*C*–Cl), 180.2 (*C*=O); ^{19}F NMR (DMSO-d_6, δ, ppm) −115.37 (F at C_5).

5.4.13. 2-(4-Ethylbenzoyl)-7-chloro-3-methyl-5-trifluoromethyl-4*H*-1,4-benzothiazine (10j). $C_{19}H_{15}ClF_3NOS$; mp 110; yield 93.25%; found: C, 57.34; H, 3.81; N, 3.51; Calcd: C, 57.36; H, 3.80; N, 3.52; IR KBr (ν cm^{-1}) 3420 (N–H), 1680 (>C=O), 1255–1187 (C–F), 1483–1383 (C–H of CH_3), 790 (C–Cl); ^1H NMR (DMSO-d_6, δ, ppm) 9.13 (1H, s, NH), 8.40–6.91 (6H, m, Ar), 2.66 (3H, s, CH_3), 2.64–2.34 (2H, q, CH_3), 1.25–1.28 (3H, t, CH_3); ^{19}F NMR (DMSO-d_6, δ, ppm) −118.68 (F at C_5).

5.4.14. 2-(4-Bromobenzoyl)-7-chloro-3-methyl-5-trifluoromethyl-4*H*-1,4-benzothiazine (10k). $C_{17}H_{10}BrClF_3NOS$; mp 109; yield 67.25%; found: C, 45.49; H, 2.28; N, 3.10; Calcd: C, 45.51; H, 2.25; N, 3.12; IR KBr (ν cm^{-1}) 3465 (N–H), 1225 (>C=O), 1260–1180 (C–F), 1467–1384 (C–H of CH_3), 640 (C–Br), 787 (C–Cl); ^1H NMR (DMSO-d_6, δ, ppm) 8.62 (1H, s, NH), 8.24–6.97 (6H, m, Ar), 2.22 (3H, s, CH_3); ^{19}F NMR (DMSO-d_6, δ, ppm) −53.7 (F at C_5).

5.4.15. 2-Benzoyl-7-chloro-3-phenyl-5-trifluoromethyl-4*H*-1,4-benzothiazine (10l). $C_{22}H_{13}ClF_3NOS$; mp 140; yield 60.65%; found: C, 61.18; H, 3.01; N, 3.22; Calcd: C, 61.19; H, 3.03; N, 3.24; IR KBr (ν cm^{-1}) 3360 (N–H), 1615 (>C=O), 1316–1170 (C–F), 760 (C–Cl); ^1H NMR (DMSO-d_6, δ, ppm) 9.04 (1H, s, NH), 8.27–6.88 (12H, m, Ar); ^{19}F NMR (DMSO-d_6, δ, ppm) −136.39 (F at C_5).

5.4.16. 2-(4-Methylbenzoyl)-7-chloro-3-methyl-5-trifluoromethyl-4*H*-1,4-benzothiazine (10m). $C_{18}H_{13}ClF_3NO_2S$; mp 102; yield 74.76%; found: C, 54.05; H, 3.30; N, 3.49; Calcd: C, 54.07; H, 3.28; N, 3.50; IR KBr (ν cm^{-1}) 3370 (N–H), 1735 (>C=O), 1240–1130 (C–F), 1483–1366 (C–H of CH_3), 755 (C–Cl); ^1H NMR (DMSO-d_6, δ, ppm) 9.1 (1H, s, NH), 7.67–6.4 (7H, m, Ar), 2.1 (3H, s, CH_3), 1.14 (3H, s, CH_3); ^{19}F NMR (DMSO-d_6, δ, ppm) −124.42 (F at C_5).

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