An Easy Approach to the Synthesis of New Fused 3-Aryl-5-trifluoromethyl-7,8-dihydro-6*H*-thieno [2,1-*f*] [1,2] thiazine 1-Oxide System

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Abstract: A new series of 4-alkyl(aryl)-4-tetramethylenesulfoximide-1,1,1-trifluoroalk-3-en-2-ones has been prepared from the *O*,*N*-exchange reactions of 4-alkyl(aryl)-4-alkoxy-1,1,1-trifluoroalk-3-en-2-ones with the cyclic *S*,*S*-tetramethylenesulfoximide in absence of solvent, in good yields. Subsequently, the easy preparation of a new series of a fused heterocyclic system of 3-aryl-5-trifluoromethyl-7,8-dihydro-6*H*-thieno[2,1-*f*][1,2]thiazine 1-oxide derivatives (60-85% yields) from intramolecular cyclization reactions of sulfoximide enones employing potassium *t*-butoxide in diethyl ether at reflux is also reported.

Keywords: Sulfoximides, trifluoromethyl ketones, 1,2-thiazines, enaminoketones.

1. INTRODUCTION

Piroxicam, an *N*-heterocyclic carboxamide of 1,2-benzothiazine 1,1-dioxide, was the first member of the family of NSAIDs (Non-steroidal anti-inflammatory drugs) used as an inhibitor of prostaglandin biosynthesis, but, as the other NSAIDs, it showed gastrointestinal and renal toxicity. Also, it is known that several 1,2-thiazines and their benzo derivatives have been used as anti-pyretic and anti-inflammatory agents [1]. Other 3,6-dihydrothiazines are precursors for the stereoselective synthesis of vicinal amino alcohols, diamines and highly functionalized amines [2, 3]. Sulfoximides, important from the biological view, can be also employed as precursors for the synthesis of 1,2-thiazines 1-oxide [4]. Moreover, many patents have been issued claiming the use of sulfoximides as defoliant, herbicide, antifungal agent, antihypertensive, and CNS (Central nervous system) depressant [5]. On the other hand, the introduction of a trifluoromethyl group into many bioactive molecules has sometimes resulted in significant enhancement of their potency and duration of their action due to the increase of lipophilicity [6].

The synthesis of 1,2-thiazines has been relatively well explored *via* [4+2] cycloadditions. In general, the most common 1,2-thiazines either have an alkyl, aryl, acyl or a sulfonyl moiety at the 2 position (N-substituents) and a very stable hexavalent sulfur at the ring, as for example 1,1-dioxides [7]. Examples of 1,2-thiazines 1-oxide have been synthesized by intramolecular cyclization [8], however, the reactions are usually carried out in dimethylsulfoxide or *N*,*N*-dimethylformamide and sodium hydride under argon or nitrogen [7-11] or in sodium methoxide/ethanol [12] with low yields in both cases.

In a previous study, a series of 4-dimethylsulfoximide-1,1,1-trifluorobut-3-en-2-ones was prepared by the direct reaction of 4-alkyl(aryl)-4-alkoxy-1,1,1-trifluorobut-3-en-2-ones with *S*,*S*-dimethylsulfoximide, in 50 – 95 % yields. In the same study, six 5-trifluoromethylated 3-alkyl or 3-aryl-1-methyl-1,2-thiazines 1-oxide derivatives were synthesized in 40 – 76 % yields, by intramolecular cyclization reaction of the respective dimethylsulfoximido enones when the reactions were carried out in presence of sodium methoxide or ethoxide in methanol or ethanol, respectively [13]. However this method only allows the attainment of non fused-bicyclic 1,2-thiazines.

In 1993, several fused *N*-substituted thieno[1,2]thiazines were reported to be very potent carbonic anhydrase inhibitors, useful for treating conditions which derive from the restriction of blood flow to the brain [14]. Thus, for biological evaluations it seemed desirable to develop a general method for the synthesis of new fused thieno[1,2] thiazines, which allow for the introduction of trifluoromethyl, alkyl or aryl substituents to this interesting aza heterocyclic family with the isolation of enaminoketone intermediates (new acyclic sulfoximides).

2. RESULTS AND DISCUSSION

In this study, an efficient method for the synthesis of a series of new 4-alkyl(aryl)-4-tetramethylenesulfoximide-1,1,1-trifluoroalk-3-en-2-ones (**2a-k**) from β-trifluoroacetylated enol ethers [15] or acetals [16, 17], and an interesting synthetic application using intramolecular cyclization reactions to give new cycloalkane geminated 1,2-thiazines 1-oxide (**3c-j**), is reported (Scheme **1**).

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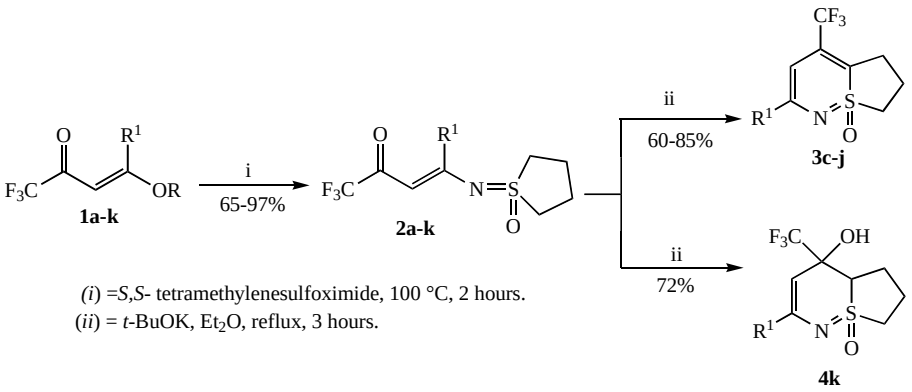

1-4	a	b	c	d	e	f	g	h	i	j	k
R	Et	Me	Me	Me	Me	Me	Me	Me	Me	Me	Me
R^1	H	Me	Ph	4-MePh	4-OMePh	4-FPh	4-ClPh	4-BrPh	4-NO_2Ph	4-4'-Biphenyl	1-Naphthyl

Scheme 1. Synthetic Route for thieno-thiazine system.

As a general procedure, firstly the trifluoromethyl enones (**1a-k**) were treated with *S,S*-tetramethylenesulfoximide in absence of solvent at 100 °C giving the new 4-alkyl(aryl)-4-tetramethylene-sulfoximide-1,1,1-trifluoroalk-3-en-2-ones (**2a-k**) in 65% to 95% yield. These new compounds (**2a-k**) have been employed to obtain 3-aryl-5-trifluoromethyl-7,8-dihydro-6*H*-thieno[2,1-*f*][1,2]thiazines 1-oxide (**3c-j**) by intramolecular cyclization reaction, in good yields. The innovation in this synthetic route was the use of commercially available potassium *t*-butoxide to substitute sodium methoxide or ethoxide in methanol or ethanol under reflux, respectively, or to substitute sodium hydride in dimethylsulfoxide or *N*,*N*-dimethylformamide under argon or nitrogen [7-12]. The reactions described here were easily carried out in the presence of potassium *t*-butoxide in refluxing diethyl ether without an argon or nitrogen atmosphere (Scheme **1**). Surprisingly, using this simple reaction condition, tetrahydrothiazine **4k** was isolated as a pure compound from **2k**.

One can see that the problematic step in this synthetic route, as outlined in the Scheme **1**, was the intramolecular cyclization of **2** to give respective thiazines **3** when the compounds **2** are non-substituted or alkyl-substituted at carbon-4 (**2a-b**).

Unfortunately, poor yields or unidentified dark products were obtained by NMR experiments when the intramolecular cyclization reaction of the respective dimethylsulfoximido enones **2a** and **2b** were carried out in presence of sodium methoxide or ethoxide in methanol or ethanol under reflux, respectively. Attempts to accomplish the synthesis of **2a-b** failed even when potassium hydroxide or sodium hydride was used as base.

The unambiguous ^1H and ^{13}C NMR chemical shift assignments of enones **2a-k** and the thiazines **3c-j** were obtained with the help of 1D- and DEPT 135-NMR experiments and by comparison with NMR data of other 1,2-thiazines 1-oxide formerly synthesized in our laboratory [13].

The aryl-tetramethylenesulfoximide enones (**2b-k**), showed ^1H NMR chemical shifts, in $CDCl_3$, of the olefinic protons (H-3) as a singlet in the range of 5.88-6.75 ppm. The ^1H NMR spectrum for **2a** showed a doublet at 8.27 ppm for the olefenic proton H-4 and another doublet at 5.96 ppm for the other olefinic proton H-3. The analysis of the ^1H NMR spectrum for **2a** gives a coupling constant of 12 Hz for the olefinic protons, which suggests an *E* configuration at the olefinic bond [13, 18]. However, in the case of compounds **2i** and **2k**, which have substituents $R^1 = NO_2$ and 1-naphthyl, respectively, there was a mixture of isomers *E* and *Z* at the olefinic bond, with double signals in the ^1H NMR and ^{13}C NMR spectra. In addition, compounds **2a-k** showed the signals for the tetramethylene hydrogens H-5 and H-8 together as a multiplet in the range of 3.31 - 3.64 ppm, and tetramethylene protons H-6 and H-7 also together as a multiplet in the range of 2.16 - 2.35 ppm. The ^{13}C NMR spectra for compounds **2a-k** showed the carbonyl carbon (C-2) at an average of 176.5 ppm as a quartet with J_{CF} = 32 - 33 Hz, C-4 quaternary in the range of 155.8 - 189.2 ppm, CF_3 group in the range of 117.0 - 118.5 ppm as a quartet with J_{CF} = 292 Hz, C-3 chemical shifts at an average of 97.7 ppm and tetramethylene carbons at an average of 56 ppm (C-5 and C-8), 23.5 ppm (C-5 and C-8).

The 1,2-thiazines 1-oxide (**3c-j**) showed ^1H NMR chemical shifts of the aromatic proton (H-4) as a singlet at an average of 6.52 - 6.71 ppm, tetramethylene protons as a multiplet at an average of 3.75 ppm (H-8a), 3.47 ppm (H-8b), 3.35 ppm (H-6a), 3.20 ppm (H-6b), 2.57 ppm (H-7a) and 2.31 ppm (H-7b). The ^{13}C NMR spectra of compounds **3c-j** showed chemical shifts of C-3 at an average of 152 ppm, C-5 at an average of 133 ppm as a quartet with J_{CF} =33 Hz, CF_3 in the range of 121.4 - 122.8 ppm as a quartet with J_{CF} = 276 Hz, C-5a at an average of 105 ppm, C-4 at an average of 95 ppm, tetramethylene carbons at an average of 53.5 ppm (C-8), 26.2 ppm (C-6) and 20.1 ppm (C-7).

3. CONCLUSION

In summary, the methodology described in this work allows attainment in a single structure of the strong electron withdrawing effect of the CF_3 group, the high bioactive-

versatility of the sulfoximide group and a large scope for aryl substituents in cyclic and acyclic new interesting molecules.

4. EXPERIMENTAL

Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial suppliers without further purification. All melting points were determined on a Reichert Thermovar apparatus and were uncorrected. ^{1}H and ^{13}C NMR spectra were acquired on a Bruker DPX 400 spectrometer (^{1}H at 400.13 MHz and ^{13}C at 100.62 MHz), 5 mm sample tubes, 298 K, digital resolution ±0.01 ppm, in $CDCl_3$ or DMSO-d_6 (**4k**) using TMS as internal reference. Mass spectra were recorded in a HP 5973 MSD connected to a HP 6890 GC and interfaced by a Pentium PC. The GC was equipped with a split-splitless, injector, auto sampler, cross-linked HP-5 capillary column (30m 0.32 mm of internal diameter), and helium was used as the carrier gas. Infrared spectra were recorded as KBr discs using a Bruker Tensor 27 spectrometer over the range 4000-400 cm^{-1}. The CHN elemental analyses were performed on a Perkin Elmer 2400 CHN elemental analyzer (São Paulo University-USP/Brazil).

General Procedure for the Preparation of 4-Alkyl(aryl)-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-ones (2a-k)

A stirred mixture of 4-alkoxy-1,1,1-trifluoro-3-buten-2-ones (**1a-k**) (10 mmol) and *S*,*S*-tetramethylenesulfoximide (10 mmol) was heated in an oil bath in absence of solvent for 2 h at 100 °C for **2b-k** or 30 min for **2a**. After cooling, the solid residues **2a-k** were recrystallized from ethanol.

(E)-4-Tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2a)

This compound was obtained as white solid; yield 65%; Mp.106-108 °C. ^{1}H NMR ($CDCl_3$) δ = 8.27 (d, 1H, *J* =12, H-4), 5.96 (d, 1H, *J* =12, H-3), 3.37 (m, 4H, H-5, H-8), 2.37 (m, 4H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 179.4 (q, ^2J = 33, C-2), 155.8 (C-4), 117.1 (q, ^1J = 292, CF_3), 103.3 (C-3), 54.1 (C-5, C-8), 23.5 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_8H_{10}NO_2SF_3$ (241.04): 241 (M^+, 16), 172 (100), 105 (39), 55 (60). IR (KBr, ν cm^{-1}): 1666 (C=O), 1077 (S=O). Anal. Calcd. for $C_8H_{10}NO_2SF_3$ (241.04): C, 39.83; H, 4.18; N, 5.81%. Found: C, 39.71; H, 3.83; N, 5.69%.

4-Tetramethylenesulfoximide-1,1,1-trifluoropent-3-en-2-one (2b)

This compound was obtained as white solid; yield 71%; Mp.109-111 °C. ^{1}H NMR ($CDCl_3$) δ = 5.88 (s, 1H, H-3), 3.54 (m, 2H, H-5), 3.35 (m, 2H , H-8), 2.45 (s, 3H, CH_3), 2.33 (m, 4H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 177.1 (q, ^2J = 32, C-2), 173.3 (C-4), 117.2 (q, ^1J = 292, CF_3), 98.4 (C-3), 53.3 (C-5, C-8), 24.6 (CH_3), 23.7 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_9H_{12}NO_2SF_3$ (255.05): 255 (M^+, 6), 55 (100), 186 (55), 82 (15). IR (KBr, ν cm^{-1}): 1660 (C=O), 1096 (S=O). Anal. Calcd. for $C_9H_{12}NO_2SF_3$ (255.05): C, 42.35; H, 4.74; N, 5.49%.Found: C, 42.23; H, 4.77; N, 5.44%.

4-Phenyl-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2c)

This compound was obtained as yellow solid; yield 97%; Mp. 136-138 °C. ^{1}H NMR ($CDCl_3$) δ = 7.73 (m, 2H, Ar), 7.42 (m, 2H, Ar), 6.21 (s, 1H, H-3), 3.59 (m, 4H, H-5, H-8), 2.32 (m, 4H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 176.4 (q, ^2J = 32, C-2), 164.5 (C-4), 139.8, 130.9; 128.3; 128.2; (6C, Ar), 117.1 (q, ^1J = 292, CF_3), 97.7 (C-3), 56.6 (C-5, C-8), 23.4 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{14}NO_2SF_3$ (317.07): 317 (M^+, 20), 55 (100), 248 (90), 116 (87), 77(60), 146 (40). IR (KBr, ν cm^{-1}): 1675 (C=O), 1060 (S=O). Anal. Calcd. for $C_{14}H_{14}NO_2SF_3$ (317.07): C, 52.99; H, 4.45; N, 4.41%. Found: C, 52.59; H, 4.33; N, 4.45%.

4-(4-Tolyl)-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2d)

This compound was obtained as yellow solid; yield 74%; Mp. 121-123 °C. ^{1}H NMR ($CDCl_3$) δ = 7.58 (m, 2H, Ar), 7.22 (m, 2H, Ar), 6.18 (s, 1H, H-3), 3.55 (m, 4H, H-5, H-8), 2.39 (s, 3H, CH_3), 2.33 (m, 4H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 176.1 (q, ^2J =32.5, C-2), 164.6 (C-4), 141.5; 136.7; 128.9; 128.3 (6C, Ar), 117.2 (q, ^1J =292, CF_3), 97.0 (C-3), 56.3 (C-5, C-8), 23.3 (C-6, C-7), 21.3 (CH_3). GC/MS (EI, 70 eV): *m/z* (%) for $C_{15}H_{16}NO_2SF_3$ (331.09): 331 (M^+, 25), 55 (100), 262 (100), 130 (95), 146 (56), 158 (43). IR (KBr, ν cm^{-1}): 1682 (C=O), 1063 (S=O). Anal. Calcd. for $C_{15}H_{16}NO_2SF_3$ (331.09): C, 54.37; H, 4.87; N, 4.23%. Found: C, 53.97; H, 4.68; N, 4.37%.

4-(4-Methoxyphenyl)-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2e)

This compound was obtained as yellow solid; yield 71%; Mp. 114-116 °C. ^{1}H NMR ($CDCl_3$) δ = 7.82 (m, 2H, Ar), 6.91 (m, 2H, Ar), 6.17 (s, 1H, H-3), 3.87 (s, 3H, OCH_3), 3.58 (m, 4H, H-5, H-8), 2.32 (m, 4H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 175.3 (q, ^2J =32, C-2), 164.3 (C-4), 161.9 (1C, Ar), 117.5 (q,^1J =292, CF_3), 130.2, 113.2 (5C, Ar), 95.4 (C-3), 55.5 (C-5, C-8), 54.9 (OCH_3), 23.0 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{15}H_{16}NO_3SF_3$ (347.08): 347 (M^+, 24), 146 (100), 278 (55), 174 (33), 55 (35). IR (KBr, ν cm^{-1}): 1664 (C=O), 1059 (S=O). Anal. Calcd. for $C_{15}H_{16}NO_3SF_3$ (347.08): C, 51.87; H, 4.64; N, 4.03%. Found: C, 51.39; H, 4.18; N, 3.93%.

4-(4-Fluorophenyl)-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2f)

This compound was obtained as yellow solid; yield 70%; Mp.112-113 °C. ^{1}H NMR ($CDCl_3$) δ = 7.71 (m, 2H, Ar), 7.08 (m, 2H, Ar), 6.17 (s, 1H, H-3), 3.58 (m, 4H, H-5, H-8), 2.29 (m, 4H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 176.3 (q, ^2J =33, C-2), 166.9 (C-4), 161.9, 135.4, 130.7, 115.0, (6C, Ar), 117.2 (q, ^1J =292, CF_3), 97.2 (C-3), 56.2 (C-5, C-8), 23.4 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{13}NO_2SF_4$ (335.06): 355 (M^+, 32), 55 (100), 266 (92), 134 (80), 146 (65), 162 (29). IR (KBr, ν cm^{-1}): 1666 (C=O), 1065 (S=O). Anal. Calcd. for $C_{14}H_{13}NO_2SF_4$ (335.06): C, 50.15; H, 3.91; N, 4.18%. Found: C, 50.07; H, 3.56; N, 4.21%.

4-(4-Chlorophenyl)-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2g)

This compound was obtained as yellow solid; yield 90%; Mp. 148-150 °C. ^{1}H NMR ($CDCl_3$) δ = 7.66 (m, 2H, Ar), 7.35 (m, 2H, Ar), 6.16 (s, 1H, H-3), 3.59 (m, 4H, H-5, H-8), 2.29 (m, 4H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 176.5 (q, ^2J =32, C-2), 162.7 (C-4), 138.3, 137.1, 129.6, 129.3, 128.8, 128.3 (6C, Ar), 117.1 (q, ^1J =292, CF_3), 97.3 (C-3), 56.7 (C-

5), 54.5 (C-8), 23.4 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{13}ClNO_2SF_3$ (351.03): 351 (M^+, 18), 55 (100), 282 (77), 150 (53) 146 (55), 178 (16). IR (KBr, ν cm^{-1}): 1670 (C=O), 1063 (S=O). Anal. Calcd. for $C_{14}H_{13}ClNO_2SF_3$ (351.03): C, 47.80; H, 3.42; N, 3.98%. Found: C, 47.69; H, 3.44; N, 3.98%.

4-(4-Bromophenyl)-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2h)

This compound was obtained as yellow solid; yield 73%; Mp. 159-161 °C. ^{1}H NMR ($CDCl_3$) δ = 7.54 (m, 4H, Ar), 6.17 (s, 1H, H-3), 3.59 (m, 4H, H-5, H-8), 2.30 (m, 4H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 176.6 (q, ^2J =32, C-2), 162.7 (C-4), 138.9, 131.4, 129.8 (6C, Ar), 117.1 (q, ^1J =292, CF_3), 97.6 (C-3), 56.7 (C-5, C-8), 23.5 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{13}BrNO_2SF_3$ (396.98): 397 (M^+, 10), 55 (100), 328 (53), 196 (30), 146 (52), 224 (10). Anal. Calcd. for $C_{14}H_{13}BrNO_2SF_3$ (396.98): C, 42.44; H, 3.31; N, 3.54%. Found: C, 41.94; H, 3.12; N, 3.69%.

4-(4-Nitrophenyl)-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2i)

This compound was obtained as brown solid; yield 80%; Mp.130-132 °C. Data is from the mixture of isomers *E* and *Z* (1: 0.7, from NMR). ^{1}H NMR ($CDCl_3$) δ = 8.22 (m, 4H, Ar), 7.88 (m, 2H, Ar), 7.53 (m, 2H, Ar), 6.22, 6.13 (s, 2H, H-3), 3.64 (m, 8H, H-5, H-8), 2.35 (m, 8H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 176.6 (q, ^2J =33, C-2), 167.9, 160.8 (C-4), 149.0, 148.2, 145.3, 144.8, 129.3, 129.0, 123.4, 123.1 (12C, Ar), 117.1 (q, ^1J =292, CF_3), 98.7, 98.1 (C-3), 56.9, 53.3 (C-5, C-8), 23.8, 23.4 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{13}N_2O_4SF_3$ (362.05): 362 (M^+, 10), 55 (100), 293(84), 189 (5), 161 (18), 146 (24). IR (KBr, ν cm^{-1}): 1658 (C=O), 1060 (S=O). Anal. Calcd. for $C_{14}H_{13}N_2O_4SF_3$ (362.05): C, 46.41; H, 3.62; N, 7.73%. Found: C, 46.55; H, 3.37; N, 7.59%.

4-(4,4'-Biphenyl)-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2j)

This compound was obtained as yellow solid; yield 81%; Mp.98-100 °C. ^{1}H NMR ($CDCl_3$) δ = 8.00 (m, 2H, Ar), 7.64 (m, 4H, Ar), 7.42 (m, 3H, Ar), 6.75 (s, 1H, H-3), 3.52 (m, 4H, H-5, H-8), 2.24 (m, 4H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 189.2 (C-4), 177.2 (q, ^2J =32, C-2), 145.2, 139.8, 136.9, 128.8, 128.7, 128.0, 127.1, 127.0 (12C, Ar), 121.2 (q, ^1J =278, CF_3), 104.3 (C-3), 55.8 (C-5, C-8), 23.1 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{20}H_{18}NO_2SF_3$ (393.1): 393 (M^+, 28), 181 (100), 324 (1), 289 (28), 152 (67), 55 (62). Anal. Calcd. for $C_{20}H_{18}NO_2SF_3$ (393.10): C, 61.06; H, 4.61; N, 3.56%. Found: C, 61.43; H, 4.48; N, 3.54%.

4-(1-Naphthyl)-4-tetramethylenesulfoximide-1,1,1-trifluorobut-3-en-2-one (2k)

This compound was obtained as white solid; yield 84%; Mp.134-136 °C. Data is from the mixture of isomers E and Z (1: 0.5). ^{1}H NMR ($CDCl_3$) δ = 7.85 (m, 6H, Ar), 7.44 (m, 8H, Ar), 6.37, 5.93 (s, 2H, H-3), 3.31-3.05 (m, 8H, H-5, H-8), 2.16 (m, 8H, H-6, H-7). ^{13}C NMR ($CDCl_3$) δ = 176.1 (q, ^2J =32, C-2), 168.9, 165.5 (C-4), 137.4, 136.6, 133.2, 130.3, 129.9, 129.7, 128.8, 128.3, 126.7, 126.5, 126.2, 125.9, 125.2, 124.7, 124.5, 124.0 (20C, Ar), 113.9 (q, ^1J =293, CF_3), 102.9, 101.2 (C-3), 55.3, 53.3 (C-5, C-8), 23.2, 23.0 (C-6, C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{18}H_{16}NO_2SF_3$ (367.09): 367 (M^+, 20), 166 (100), 298 (38), 270 (20), 194 (25), 146 (35), 127 (50), 55 (45). IR (KBr, ν cm^{-1}): 1676 (C=O), 1059 (S=O). Anal. Calcd. for $C_{18}H_{16}NO_2SF_3$ (367.09): C, 58.85; H, 4.39; N, 3.81%. Found: C, 58.78; H, 4.20; N, 3.62%.

General Procedure for the Preparation of 3-Aryl-5-trifluoromethyl-7,8-dihydro-6*H*-thieno [2,1-*f*] [1,2] thiazines 1-oxide (3c-j) and 3-(1-Naphthyl)-5-trifluormethyl-5-hidroxy-5a,6,7,8-tetrahydro-5*H*-thieno [2,1-*f*] [1,2] thiazine 1-oxide (4k)

Compounds 4-aryl-4-tetramethylenesulfoximide-1,1,1-trifluoro- but-3-en-2-ones (**2c-j**) (2 mmol) were dissolved in 15 ml of dry diethyl ether. Potassium *t*-butoxide (2.2 mmol) was added in one portion. The resulting slurry solutions were stirred under reflux for 3 h. The products were acidified by the addition of 1 ml of acetic acid followed by 10 ml of water. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The solid residues (**3c-j**) and (**4k**) were recrystallized from ethanol.

3-Phenyl-5-trifluoromethyl-7,8-dihydro-6H-thieno [2,1-f] [1,2] thiazine 1-oxide (3c)

This compound was obtained as brown solid; yield 85%; Mp.107-109 °C. ^{1}H NMR ($CDCl_3$) δ = 7.91 (m, 2H, Ar), 7.43 (m, 3H, Ar), 6.65 (s, 1H, H-4), 3.78 (m, 1H, H-8a), 3.49 (m, 1H, H-8b), 3.35 (m, 1H, H-6a), 3.20 (m, 1H, H-6b), 2.57 (m, 1H, H-7a), 2.32 (m, 1H, H-7b). ^{13}C NMR ($CDCl_3$) δ = 152.9 (C-3), 137.4 (1C, Ar), 133.0 (q, ^2J=33, C-5), 129.8, 128.5, 127.3 (5C, Ar), 122.8 (q, ^1J =276, CF_3), 105.9 (C-5a), 95.7 (C-4), 53.6 (C-8), 26.2 (C-6), 20.2 (C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{12}NOSF_3$ (299.06): 299 (M^+, 73), 237 (100), 224 (72), 251 (60), 154 (55), 77 (40), 51 (46). IR (KBr, ν cm^{-1}): 1049 (S=O). Anal. Calcd. for $C_{14}H_{12}NOSF_3$ (299.06): C, 56.18; H, 4.04; N, 4.68%. Found: C, 56.09; H, 3.91; N, 4.63%.

3-(4-Tolyl)-5-trifluoromethyl-7,8-dihydro-6H-thieno [2,1-f] [1,2] thiazine 1-oxide (3d)

This compound was obtained as brown solid; yield 73%; Mp.117-119 °C. ^{1}H NMR ($CDCl_3$) δ = 7.80 (m, 2H, Ar), 7.22 (m, 2H, Ar), 6.62 (s, 1H, H-4), 3.75 (m, 1H, H-8a), 3.47 (m, 1H, H-8b), 3.35 (m, 1H, H-6a), 3.18 (m, 1H, H-6b), 2.56 (m, 1H, H-7a), 2.30 (m, 1H, H-7b). ^{13}C NMR ($CDCl_3$) δ = 152.9 (C-3), 140.1, 134.6 (2C, Ar), 132.9 (q, ^2J =33, C-5), 129.2, 127.1 (4C, Ar), 121.5 (q, ^1J =276, CF_3), 105.4 (C-5a), 95.2 (C-4), 53.6 (C-8), 26.2 (C-6), 21.2 (CH_3), 20.1 (C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{15}H_{14}NOSF_3$ (313.07): 313 (M^+, 57), 251 (100), 238 (48), 264 (44), 168 (28), 91 (18). IR (KBr, ν cm^{-1}): 1098 (S=O). Anal. Calcd. for $C_{15}H_{14}NOSF_3$ (313.07): C, 57.50; H, 4.50; N, 4.47%. Found: C, 57.40; H, 4.32; N, 4.46%.

3-(4-Methoxyphenyl)-5-trifluoromethyl-7,8-dihydro-6H-thieno [2,1-f] [1,2] thiazine 1-oxide (3e)

This compound was obtained as brown solid; yield 70%; Mp.122-124 °C. ^{1}H NMR ($CDCl_3$) δ = 7.85 (m, 2H, Ar), 6.93 (m, 2H, Ar), 6.57 (s, 1H, H-4), 3.85 (s, 3H, OCH_3), 3.75 (m, 1H, H-8a), 3.46 (m, 1H, H-8b), 3.31 (m, 1H, H-6a), 3.18 (m, 1H, H-6b), 2.57 (m, 1H, H-7a), 2.31 (m, 1H, H-7b). ^{13}C NMR ($CDCl_3$) δ = 161.0 (1C, Ar), 152.6 (C-3), 132.9 (q,

^2J=33, C-5), 129.9, 128.7 (3C, Ar), 122.8 (q, ^1J =275, CF_3), 113.8 (2C, Ar), 104.8 (C-5a), 94.6 (C-4), 55.2 (OCH_3), 53.5 (C-8), 26.1 (C-6), 20.1 (C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{15}H_{14}NO_2SF_3$ (329.07): 329 (M^+, 85), 267 (100), 253(66), 280 (35), 184 (18). IR (KBr, ν cm^{-1}): 1035 (S=O). Anal. Calcd. for $C_{15}H_{14}NO_2SF_3$ (329.07): C, 54.70; H, 4.28; N, 4.25%. Found: C, 54.90; H, 4.08; N, 4.29%.

3-(4-Fluorophenyl)-5-trifluoromethyl-7,8-dihydro-6H-thieno [2,1-f] [1,2] thiazine 1-oxide (3f)

This compound was obtained as brown solid; yield 82%; Mp.122-124 °C. ^{1}H NMR ($CDCl_3$) δ = 7.89 (m, 2H, Ar), 7.01 (m, 2H, Ar), 6.58 (s, 1H, H-4), 3.77 (m, 1H, H-8a), 3.47 (m, 1H, H-8b), 3.31 (m, 1H, H-6a), 3.19 (m, 1H, H-6b), 2.57 (m, 1H, H-7a), 2.32 (m, 1H H-7b). ^{13}C NMR ($CDCl_3$) δ = 161.4 (1C, Ar), 151.8 (C-3), 133.6 (1C, Ar), 132.6 (q, ^2J =33, C-5), 129.3, 115.6 (4C, Ar), 122.8 (q, ^1J=276, CF_3), 106.1 (C-5a), 95.4 (C-4), 53.6 (C-8), 26.2 (C-6), 20.2 (C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{11}FNOSF_3$ (317.05): 317 (M^+, 58), 255 (100), 243 (67), 172 (62), 270 (49), 95 (33). IR (KBr, ν cm^{-1}): 1098 (S=O). Anal. Calcd. for $C_{14}H_{11}NOSF_4$ (317.05): C, 52.99; H, 3.49; N, 4.41%. Found: C, 51.55; H, 3.47; N, 4.26%.

3-(4-Chlorophenyl)-5-trifluoromethyl-7,8-dihydro-6H-thieno [2,1-f] [1,2] thiazine 1-oxide (3g)

This compound was obtained as brown solid; yield 81%; Mp.113-115 °C. ^{1}H NMR ($CDCl_3$) δ = 7.76 (m, 2H, Ar), 7.30 (m, 2H, Ar), 6.52 (s, 1H, H-4), 3.68 (m, 1H, H-8a), 3.37 (m, 1H, H-8b), 3.25 (m, 1H, H-6a), 3.07 (m, 1H, H-6b), 2.47 (m, 1H, H-7a), 2.21 (m, 1H, H-7b). ^{13}C NMR ($CDCl_3$) δ = 151.5 (C-3), 132.8 (q, ^2J =33, C-5), 135.8, 128.6, 128.4, (6C, Ar), 122.7 (q, ^1J =276, CF_3), 106.6 (C-5a), 95.6 (C-4), 53.5 (C-8), 26.2 (C-6), 20.1 (C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{11}ClNOSF_3$ (333.02): 333 (M^+, 58), 271 (100), 259 (58), 287 (57), 111 (12). IR (KBr, ν cm^{-1}): 1085 (S=O). Anal. Calcd. for $C_{14}H_{11}ClNOSF_3$ (333.02): C, 50.38; H, 3.32; N, 4.20%. Found: C, 50.36; H, 3.24; N, 4.15%.

3-(4-Bromophenyl)-5-trifluoromethyl-7,8-dihydro-6H-thieno [2,1-f] [1,2] thiazine 1-oxide (3h)

This compound was obtained as brown solid; yield 80%; Mp.123-125 °C. ^{1}H NMR ($CDCl_3$) δ = 7.78 (m, 2H, Ar), 7.55 (m, 2H, Ar), 6.61 (s, 1H, H-4), 3.81 (m, 1H, H-8a), 3.48 (m, 1H, H-8b), 3.36 (m, 1H, H-6a), 3.18 (m, 1H, H-6b), 2.59 (m, 1H, H-7a), 2.35 (m, 1H, H-7b). ^{13}C NMR ($CDCl_3$) δ = 151.6 (C-3), 136.3 (1C, Ar), 132.9 (q, ^2J=33, C-5), 131.6, 128.7, 124.3 (5C, Ar), 122.7 (q, ^1J =276, CF_3), 106.6 (C-5a), 95.7 (C-4), 53.6 (C-8), 26.2 (C-6), 20.2 (C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{11}BrNOSF_3$ (378.21): 378 (M^+, 49), 315 (100), 75 (78), 51 (68), 303 (61), 330 (60). IR (KBr, ν cm^{-1}): 1073 (S=O). Anal. Calcd. for $C_{14}H_{11}BrNOSF_3$ (378,21): C, 44.46; H, 2.93; N, 3.70%. Found: C, 44.75; H, 2.81; N, 3.71%.

3-(4-Nitrophenyl)-5-trifluoromethyl-7,8-dihydro-6H-thieno [2,1-f] [1,2] thiazine 1-oxide (3i)

This compound was obtained as brown solid; yield 60%; Mp.124-126 °C. ^{1}H NMR ($CDCl_3$) δ = 8.24 (m, 2H, Ar), 8.07 (m, 2H, Ar), 6.71 (s, 1H, H-4), 3.86 (m, 1H, H-8a), 3.53 (m, 1H, H-8b), 3.39 (m, 1H, H-6a), 3.23 (m, 1H, H-6b), 2.63 (m, 1H, H-7a), 2.38 (m, 1H, H-7b). ^{13}C NMR ($CDCl_3$) δ =149.7 (C-3), 148.2, 143.3 (2C, Ar), 132.6 (q, ^2J =33, C-5), 127.7, 123.6 (4C, Ar), 122.5 (q, ^1J =276, CF_3), 108.9 (C-5a), 97.3 (C-4), 53.4 (C-8), 26.2 (C-6), 20.2 (C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{14}H_{11}N_2O_3SF_3$ (344.04): 344 (M^+, 49), 295 (100), 222 (77), 283 (53), 269 (32), 249 (27), 153 (22). IR (KBr, ν cm^{-1}): 1068 (S=O). Anal. Calcd. for $C_{14}H_{11}N_2O_3SF_3$ (344.04): C, 48.84; H, 3.22; N, 8.14%. Found: 48.60; H, 3.16; N, 7.92%.

3-(4,4'-Biphenyl)-5-trifluoromethyl-7,8-dihydro-6H-thieno [2,1-f] [1,2] thiazine 1-oxide (3j)

This compound was obtained as brown solid; yield 77%; Mp.168-170 °C. ^{1}H NMR ($CDCl_3$) δ = 7.71-7.42 (m, 9H, Ar), 6.57 (s, 1H, H-4), 3.68 (m, 2H, H-8a e H-8b), 3.39 (m, 1H, H-6a), 3.05 (m, 1H, H-6b), 2.48 (m, 1H, H-7a), 2.07 (m, 1H, H-7b). ^{13}C NMR ($CDCl_3$) δ = 142.8 (C-3), 142.5 (1C, Ar), 139.9 (q, ^2J=34, C-5), 139.8, 135.6, 129.3, 128.9, 127.9, 127.4, 127.0 (11C, Ar), 121.4 (q, ^1J =274, CF_3), 111.1 (C-5a), 101.8 (C-4), 54.4 (C-8), 27.7 (C-6), 21.1 (C-7). GC/MS (EI, 70 eV): *m/z* (%) for $C_{20}H_{16}NOSF_3$ (375.09): 375 (M^+, 98), 326 (100), 230 (96), 309 (94), 283 (52), 202 (51), 313 (46), 257 (34), 152 (32). Anal. Calcd. for $C_{20}H_{16}NOSF_3$ (375.09): C, 63.99; H, 4.30; N, 3.73%. Found: C, 63.73; H, 4.15; N, 4.02%.

3-(1-Naphthyl)-5-trifluoromethyl-5-hidroxy-5a,6,7,8-tetrahydro-5H-thieno [2,1-f] [1,2] thiazine 1-oxide (4k)

This compound was obtained as brown solid; yield 72%; Mp.168-170 °C. ^{1}H NMR (DMSO-d_6) δ = 8.32 (m, 1H, Ar), 7.92 (m, 2H, Ar), 7.52 (m, 4H, Ar), 6.67 (s, 1H, H-4), 5.05 (s, 1H, OH), 3.88 (m, 1H, H-5a), 3.51 (m, 1H, H-8a), 3.44 (m, 1H, H-8b), 2.27 (m, 2H, H-6a e H-6b), 2.14 (m, 1H, H-7a), 1.78 (m, 1H, H-7b). ^{13}C NMR (DMSO-d_6) δ = 147.5 (C-3), 138.1, 133.1, 130.3, 128.3, 128.0, 125.8, 125.7, 125.6, 125.1 (10C, Ar), 124.9 (q, ^1J=286, CF_3), 94.3 (C-4), 72.2 (q, ^2J=29, C-5), 57.1 (C-5a), 51.7 (C-8), 24.7 (C-6), 18.4 (C-7). IR (KBr, ν cm^{-1}): 1061 (S=O). Anal. Calcd. for $C_{18}H_{14}NOSF_3$ (367.1): C, 58.85; H, 4.39; N, 3.81%. Found: C, 58.61; H, 4.10; N, 4.18%

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