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Modelling One-Pot Method for Synthesis of 2,3-Dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine 5,5-Dioxides and Their Homologues

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ABSTRACT

A facile method for synthesis of 2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazines by interaction of methylenactive (2-fluorophenyl)sulfones with homologues of either 5-methoxy-3,4-dihydro-2*H*-pyrrole or 5-(methylthio)-3,4-dihydro-2*H*-pyrrole has been developed.

Keywords: Sulfones; Lactims; Cyclization; Heterocycles; Nucleophilic Aromatic Substitution

1. Introduction

In recent years a substantial number of 1,1-dioxo-4*H*-1,4-benzothiazines have been reported to possess pharmacological activity. They were mentioned as glycine-NMDA receptor antagonists [1] and protein kinase inhibitors, which can be used to treat cancer and hyperproliferative disorders [2]. Similar compounds were patented as potent antivirals [3], potassium channel openers [4], antiischemics to cure heart diseases [5], 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors [6], some of them were reported to be diuretics [7]. Also they were known as highly effective antimicrobial agents against Streptococcus and Klebsiella [8].

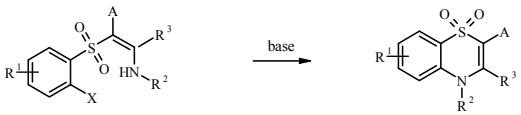
1,1-Dioxo-4*H*-1,4-benzothiazines can be readily synthesized by the oxidation of 4*H*-1,4-benzothiazines [9-13], intramolecular cyclization of *N*-[(2-alkylsulfonyl)-phenyl]amides of carboxylic acids [14-17], spontaneous cyclization of 1-[(2-nitrophenyl)sulfonyl]ketones during reduction [18,19].

The promising approach is also the cyclization of 2-[(2-halogenophenyl)sulfonyl]ethylenamines containing electronwithdrawing group A in the presence of bases [20-26] (**Figure 1**).

The last synthetic approach for 1,1-dioxo-4*H*-1,4-benzothiadiazines is the most convenient for the achievement of high range molecular diversity due to the variability of radicals in the aromatic ring (R^1) and the positions 2, 3, 4 of 1,4-benzothiadiazine moiety (A, R^3, R^2). The most significant limitation of this method is mainly concerned with the leaving halogen (X) activity. For instance, the cyclization of orto-chloroderivatives (X = Cl) could be successfully carried out only in the presence of strong bases [20], silver nitrate [22,23], potassium carbonate-crown-ether [21] or requires the application of microwave technology [24,25]. In the case of fluoroderivatives (X = F), the cyclization proceeds readily [26].

Though the cyclization of 2-[(2-halogenophenyl)sulfonyl]ethylenamines is a versatile methodology for 1,1-dioxo-4*H*-1,4-benzothiadiazines obtaining, the synthesis of the heterocyclic systems where R^2 and R^3 are the parts of the same cycle was not reported yet.

The purpose of this paper is to develop the convenient synthetic way for 2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]-benzothiazine 5,5-dioxides and their homologues, which could be interesting objects for further pharmacological



R^1 = H, Hal; R^2 = Alkyl, Aryl; R^3 = H, Alkyl, SAlkyl, $NAlkyl_2$ A = CN, COOAlkyl, Acyl; X = F, Cl

Figure 1. Cyclization of 2-[(2-halogenophenyl)sulfonyl]ethylenamines.

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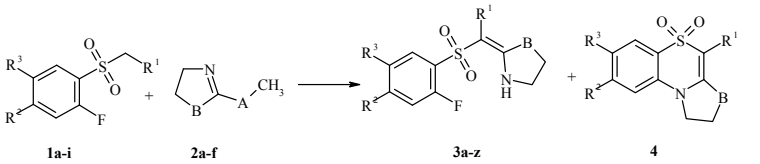
screening.

It was reported that the interaction of asymmetrical methylene active compounds with either 5-methoxy-3,4-dihydro-2*H*-pyrrole or 5-(methylthio)-3,4-dihydro-2*H*-pyrrole and their homologues led to formation of mixture E,*Z*-isomers of enamine-type products [27-29]. With regard to this fact, the interaction between (2-fluorophenyl)sulfones 1a-i and lactims 2a-f (**Figure 2**) should produce 2-{[(2-fluorophenyl)sulfonyl]methylene}-pyrrolidines and their homologues 3a-z (**Figure 1**).

The heating of sulfones 1 with excess of lactims 2 (30% for sulfonylacetonitriles 1a, d-i and 50% for other compounds 1) at 90˚C has been chosen as the standard reaction conditions. The reaction for acetonitriles 1a, d-i was held in DMF media, for other compounds 1 was carried out solvent-free. The process was monitored by TLC and disappearance of starting sulfone 1 spot has been controlled. The results of experiment demonstrated that the interaction of sulfones 1 with 5-methoxy-3,4-dihydro-2*H*-pyrrole and its homologues 2a-c in chosen conditions did not produces solely products 3. In some cases the products of further cyclization 4 were also present in the reaction mixture. The lactims 2 having larger cycle required more reaction time. Experimental data (**Table 1**)



1a-i **2a-f** **3a-z** **4**

1a: R^1 = CN, R^2 = R^3 = H; **1b**: R^1 = Ac, R^2 = R^3 = H; **1c**: R^1 = COOMe, R^2 = R^3 = H; **1d**: R^1 = CN, R^2 = H, R^3 = Me; **1e**: R^1 = CN, R^2 = H, R^3 = F; **1f**: R^1 = CN, R^2 = H, R^3 = Cl; **1g**: R^1 = CN, R^2 = Me, R^3 = H; **1h**: R^1 = CN, R^2 = F, R^3 = H; **1i**: R^1 = CN, R^2 = Cl, R^3 = H; **2a**: A = O, B = CH_2; **2b**: A = O, B = $(CH_2)_2$; **2c**: A = O, B = $(CH_2)_3$; **2d**: A = S, B = CH_2; **2e**: A = S, B = $(CH_2)_2$; **2f**: A = S, B = $(CH_2)_3$.

Figure 2. Interaction of sulfones 1 with lactims 2.

Table 1. 2-{[(2-Fluorophenyl)sulfonyl]methylene}pyrrolidines and their homologues 3a-z.

Cmpd.	Formula	M.W.	A	B	R^1	R^2	R^3	Time, h	Yield 3 (4), %
3a	$C_{12}H_{11}FN_2O_2S$	266.29	O	CH_2	CN	H	H	4	82
3b	$C_{13}H_{13}FN_2O_2S$	280.32	O	$(CH_2)_2$	CN	H	H	4	72 (14)
3c	$C_{14}H_{15}FN_2O_2S$	294.34	O	$(CH_2)_3$	CN	H	H	8	54 (18)
3d	$C_{13}H_{14}FNO_3S$	283.32	O	CH_2	Ac	H	H	10	73
3d	$C_{13}H_{14}FNO_3S$	283.32	S	CH_2	Ac	H	H	4	80
3e	$C_{14}H_{16}FNO_3S$	297.35	S	$(CH_2)_2$	Ac	H	H	6	31
3f	$C_{13}H_{14}FNO_4S$	299.32	O	CH_2	CO_2Me	H	H	10	57
3f	$C_{13}H_{14}FNO_4S$	299.32	S	CH_2	CO_2Me	H	H	10	85
3g	$C_{14}H_{16}FNO_4S$	313.36	S	$(CH_2)_2$	CO_2Me	H	H	20	42
3h	$C_{15}H_{18}FNO_4S$	327.37	S	$(CH_2)_3$	CO_2Me	H	H	20	48
3i	$C_{13}H_{13}FN_2O_2S$	280.32	O	CH_2	CN	H	Me	4	92
3j	$C_{12}H_{10}F_2N_2O_2S$	284.28	O	CH_2	CN	H	F	4	84 (7)
3k	$C_{12}H_{10}ClFN_2O_2S$	300.74	O	CH_2	CN	H	Cl	4	76 (13)
3l	$C_{13}H_{13}FN_2O_2S$	280.32	O	CH_2	CN	Me	H	4	96
3m	$C_{12}H_{10}F_2N_2O_2S$	284.28	O	CH_2	CN	F	H	4	32 (62)
3n	$C_{12}H_{10}ClFN_2O_2S$	300.74	O	CH_2	CN	Cl	H	4	81 (9)
3o	$C_{14}H_{15}FN_2O_2S$	294.34	O	$(CH_2)_2$	CN	H	Me	4	89
3p	$C_{13}H_{12}F_2N_2O_2S$	298.31	O	$(CH_2)_2$	CN	H	F	4	60 (16)
3q	$C_{13}H_{12}ClFN_2O_2S$	314.76	O	$(CH_2)_2$	CN	H	Cl	4	45 (45)
3r	$C_{14}H_{15}FN_2O_2S$	294.34	O	$(CH_2)_2$	CN	Me	H	4	94
3s	$C_{13}H_{12}F_2N_2O_2S$	298.31	O	$(CH_2)_2$	CN	F	H	4	18 (74)
3t	$C_{13}H_{12}ClFN_2O_2S$	314.76	O	$(CH_2)_2$	CN	Cl	H	4	50 (42)
3u	$C_{15}H_{17}FN_2O_2S$	308.37	O	$(CH_2)_3$	CN	H	Me	8	76
3v	$C_{14}H_{14}F_2N_2O_2S$	312.34	O	$(CH_2)_3$	CN	H	F	8	48 (26)
3w	$C_{14}H_{14}ClFN_2O_2S$	328.79	O	$(CH_2)_3$	CN	H	Cl	8	49 (9)
3x	$C_{15}H_{17}FN_2O_2S$	308.37	O	$(CH_2)_3$	CN	Me	H	8	64 (16)
3y	$C_{14}H_{14}F_2N_2O_2S$	312.34	O	$(CH_2)_3$	CN	F	H	8	0 (73)
3z	$C_{14}H_{14}ClFN_2O_2S$	328.79	O	$(CH_2)_3$	CN	Cl	H	8	0 (53)

show that the compounds 3 with R^1 = CN are the most susceptible for cyclization. Thus, they were chosen as the model objects to study the influence of the substituent in benzene ring on the cyclization of compounds 3. It was established that electrondonating groups interdict formation of 1,4-benzothiadiazine ring, at the same time electronwithdrawing groups (halogens) promote cyclization of enamines 3. For example, the combination of O-methyllactim 2c with sulfonylacetonitriles 1h, i, where R^2 = Cl and F, only gave the product of cyclization 8,9,10,11-tetrahydro-7*H*-azepino[2,1-*c*][1,4]benzothiazine-6-carbonitrile 5,5-dioxides 4y, z. The reaction of sulfonylacetone 1b (R^1 = Ac) with O-methyllactim 2a resulted in selectively (1*E*)-1-[(2-fluorophenyl)sulfonyl]-1-(pyrrolidin-2-ylidene)acetone 3d, and its interaction with lactims 2b and 2c allowed us to isolate only 2-methyl-1,4-benzoxathiine 4,4-dioxide 5 (**Figure 3**). Probably in the case of sterically hindered lactims 2b, c, the competing reaction of intramolecular cyclization to 2-methyl-1,4-benzoxathiine-4,4-dioxide 5 became the preferable process.

To prove the formation of compound 5 in this reaction, we performed its alternative synthesis by heating of sulfonylacetone 1b in 1,4-dioxane at 90˚C in the presence of equimolar amount DBU for 4 hours.

The reaction of sulfonylacetone 1b (R^1 = Ac) with S-methyllactims 2d and 2e lead to formations of enamine type products 3d and 3e, and S-methyllactim 2f (2*Z*)-2-{[(2-fluorophenyl)sulfonyl]methylidene}azepane 6 has been isolated with the yield 25% as mixture of *E*- and *Z*-isomers.

The interaction of methyl [(2-fluorophenyl)sulfonyl]-acetate 1c with O-methyllactim 2a requires more time than interaction with sulfones 1a and 1b and results in the mixture of *E*- and *Z*- isomers of enamine 3f. The reaction of sulfone 1c with larger O-methyllactims 2b, c is failed.

The only reaction of methyl [(2-fluorophenyl)sulfonyl]-acetate 1c with S-methyllactims 2d-f allowed us to obtain methyl (2*E*,*Z*)-[(2-fluorophenyl)sulfonyl](pyrrolidin-2-ylidene)acetate 3f and its homologues 3g and 3h with moderate yields.

The cyclization of enamines 3 to 2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine 5,5-dioxides and their homologues 4 has been performed by heating in 1,4-ioxane with equimolar amount of DBU at 50˚C - 60˚C according to **Figure 4**.

Since 2-fluorophenylsulfones 1 interaction with O- or S-methyllactims 2 was a satisfactory approach for enamines 3, and further cyclization of the condensation products 3 to the 2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]-benothiazine 5,5-dioxides and their homologues 4 occurred in numerous cases, it was interesting to develop "one-pot" method for synthesis of the products 4. For this purpose O-methyllactims 2a-c were chosen as the starting material for interaction with [(2-fluorophenyl)-sulfonyl]acetonitriles 1a, d-i, S-methyllactims 2d-f were used for condensation with 1-[(2-fluorophenyl)sulfonyl] acetone 1b and methyl [(2-fluorophenyl)sulfonyl] acetate 1c.

According to the proposed "one-pot", procedure enamines 3 were not isolate. When the reaction of sulfones 1 with lactims 2 was complete, to the cool reaction mixture (20˚C) 1,4-dioxane and equimolar amount of DBU were added and the reaction mixture was heated at 60˚C for 2 - 4 hours. After dilution of reaction mixture with 2-propanol, the precipitate formed was filtered and crystallized from DMF-2-propanol mixture. The yields and some properties of obtained compounds are given in **Table 2**.

2. Experimental Section

The melting points (˚C) were measured with a Buchi B-520 melting point apparatus and were not corrected. IR spectra were recorded on FT-IR Bruker Tensor-27 spectrometer in KBr. Thin-layer chromatography (TLC) was performed on aluminum sheets precoated with silica gel (Merck, Kieselgel 60 F-254). LC/MS spectra were recorded with PE SCIEX API 150EX liquid chromatograph equipped with a UV detector (λ_{max} 215 and 254 nm) and using a C_{18} column (100 × 4 mm). Elution started with water and ended with acetonitrile/water (95:5, v/v) and used a linear gradient at a flow rate of 0.15 mL/min and an analysis cycle time of 25 min. ^{1}H NMR-spectra were

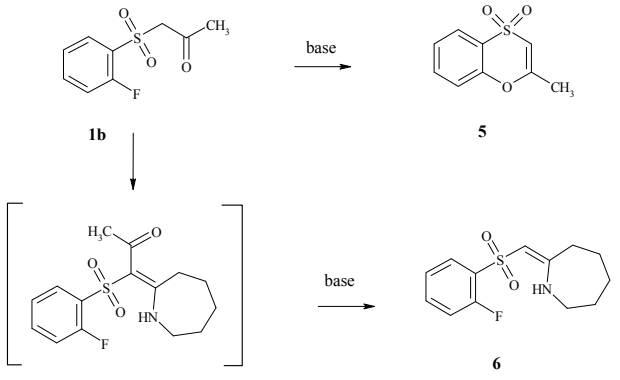


Figure 3. Transformations of sulfonylacetone 1b.

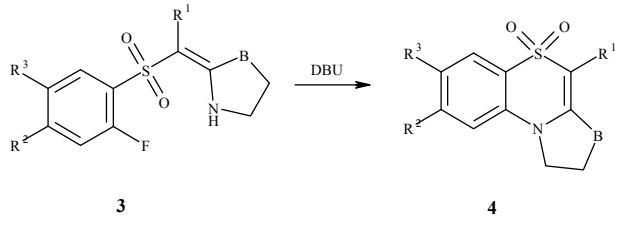


Figure 4. Cyclization of enamines 3 to 2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine 5,5-dioxides and their homologues 4.

Table 2. 2,3-Dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine 5,5-dioxides and their homologues 4.

Cmpd.	Formula	M.w.	A	B	R^1	R^2	R^3	Yield (two-steps), %	Yield (one-pot), %	m. p., ˚C
4a	$C_{12}H_{10}N_2O_2S$	246.29	O	CH_2	CN	H	H	81	93	>300
4b	$C_{13}H_{12}N_2O_2S$	260.31	O	$(CH_2)_2$	CN	H	H	76	85	232 - 233
4c	$C_{14}H_{14}N_2O_2S$	274.34	O	$(CH_2)_3$	CN	H	H	66	78	213 - 216
4d	$C_{13}H_{13}NO_3S$	263.32	O	CH_2	Ac	H	H	61	66	220 - 224
4d	$C_{13}H_{13}NO_3S$	263.32	S	CH_2	Ac	H	H	67	77	220 - 224
4e	$C_{14}H_{15}NO_3S$	277.34	S	$(CH_2)_2$	Ac	H	H	25	42	179 - 181
4f	$C_{13}H_{13}NO_4S$	279.32	O	CH_2	CO_2Me	H	H	46	59	238 - 241
4f	$C_{13}H_{13}NO_4S$	279.32	S	CH_2	CO_2Me	H	H	68	73	238 - 241
4g	$C_{14}H_{15}NO_4S$	293.34	S	$(CH_2)_2$	CO_2Me	H	H	33	53	191 - 196
4h	$C_{15}H_{17}NO_4S$	307.37	S	$(CH_2)_3$	CO_2Me	H	H	68	64	215 - 219
4i	$C_{13}H_{12}N_2O_2S$	260.31	O	CH_2	CN	H	Me	88	93	265 - 268
4j	$C_{12}H_9FN_2O_2S$	264.28	O	CH_2	CN	H	F	67	72	273 - 275
4k	$C_{12}H_9ClN_2O_2S$	280.73	O	CH_2	CN	H	Cl	83	87	288 - 292
4l	$C_{13}H_{12}N_2O_2S$	260.31	O	CH_2	CN	Me	H	95	97	>300
4m	$C_{12}H_9FN_2O_2S$	264.28	O	CH_2	CN	F	H	88	93	>300
4n	$C_{12}H_9ClN_2O_2S$	280.73	O	CH_2	CN	Cl	H	88	91	>300
4o	$C_{14}H_{14}N_2O_2S$	274.34	O	$(CH_2)_2$	CN	H	Me	77	84	181 - 184
4p	$C_{13}H_{11}FN_2O_2S$	278.30	O	$(CH_2)_2$	CN	H	F	67	78	198 - 201
4q	$C_{13}H_{11}ClN_2O_2S$	294.75	O	$(CH_2)_2$	CN	H	Cl	68	80	215 - 218
4r	$C_{14}H_{14}N_2O_2S$	274.34	O	$(CH_2)_2$	CN	Me	H	90	97	210 - 212
4s	$C_{13}H_{11}FN_2O_2S$	278.30	O	$(CH_2)_2$	CN	F	H	78	85	195 - 198
4t	$C_{13}H_{11}ClN_2O_2S$	294.75	O	$(CH_2)_2$	CN	Cl	H	89	94	188 - 190
4u	$C_{15}H_{16}N_2O_2S$	288.37	O	$(CH_2)_3$	CN	H	Me	69	72	160 - 164
4v	$C_{14}H_{13}FN_2O_2S$	292.33	O	$(CH_2)_3$	CN	H	F	66	61	195 - 198
4w	$C_{14}H_{13}ClN_2O_2S$	308.78	O	$(CH_2)_3$	CN	H	Cl	46	48	205 - 206
4x	$C_{15}H_{16}N_2O_2S$	288.37	O	$(CH_2)_3$	CN	Me	H	73	89	191 - 195
4y	$C_{14}H_{13}FN_2O_2S$	292.33	O	$(CH_2)_3$	CN	F	H	-	73	163 - 165
4z	$C_{14}H_{13}ClN_2O_2S$	308.78	O	$(CH_2)_3$	CN	Cl	H	-	53	215 - 217

recorded on Varian Mercury (200 MHz) spectrometer in DMSO-d_6 using TMS as an internal standard (chemical shifts are reported in ppm). ^{13}C NMR-spectra were recorded on Bruker DRX-300 (75 MHz) spectrometer in DMSO-d_6 using TMS as an internal standard (chemical shifts are reported in ppm).

Starting (2-halogenophenyl)sulfones 1a-j [30-32], O- and S-methyl 2a-f [33,34] have been obtained as commercial substances similarly to the previously reported methods.

[(2-Fluorophenyl)sulfonyl](pyrrolidin-2-ylidene) acetonitriles and their homologues 3a-c, i-z; typical procedure.

To the solution of [(2-fluorophenyl)sulfonyl]acetonetrile 1a,d-i (10 mmol) in DMF (4 mL) the correspondent O-methyllactim 2a-c (13 mmol) had been added and the mixture was additionally heated for 4 to 8 hours (monitored by TLC, eluent—$CHCl_3$) at 90˚C. The reaction mixture was diluted with 2-propanol after cooling. The precipitate formed was filtered and used for further trans-

formation without any additional purification. The compounds were isolated as the mixture of *E* and *Z* isomers. The compounds 3b, c, j, k, m, n, p, q, s, t, v, w, x contained a great amount of the correspondent cyclized products 4b, c, j, k, m, n, p, q, s, t, v, w, x as inseparable mixtures, and their analytical samples were not isolated. The compounds 3y, z were not isolated but only the products of their further cyclization 4y, z.

1) (2*E*,*Z*)-[(2-fluorophenyl)sulfonyl](pyrrolidin-2-ylidene)acetonitrile (3a)

Yield: 8.2 mmol (82%); cream coloured solid.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{12}H_{11}FN_2O_2S$: 266.29; found: 266.3.

2) (2*E*,*Z*)-[(2-fluoro-5-methylphenyl)sulfonyl](pyrrolidin-2-ylidene)acetonitrile (3i)

Yield: 9.2 mmol (92%); cream coloured solid.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{13}FN_2O_2S$: 280.32; found: 280.4.

3) (2*E*,*Z*)-[(2-fluoro-4-methylphenyl)sulfonyl](pyrrolidin-2-ylidene)acetonitrile (3l)

Yield: 9.6 mmol (96%); cream coloured solid.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{13}FN_2O_2S$: 280.32; found: 280.4.

4) (2*E*,*Z*)-[(2-fluoro-5-methylphenyl)sulfonyl](piperidin-2-ylidene)acetonitrile (3o)

Yield: 8.9 mmol (89%); cream coloured solid.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{15}FN_2O_2S$: 294.35; found: 294.2.

5) (2*E*,*Z*)-[(2-fluoro-4-methylphenyl)sulfonyl](piperidin-2-ylidene)acetonitrile (3r)

Yield: 9.4 mmol (94%); cream coloured solid.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{15}FN_2O_2S$: 294.35; found: 294.2.

6) (2*E*,*Z*)-azepan-2-ylidene[(2-fluoro-5-methylphenyl)-sulfonyl]acetonitrile (3u)

Yield: 7.6 mmol (76%); cream coloured solid.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{15}H_{17}FN_2O_2S$: 308.37; found: 308.4.

(1*E*)-1-[(2-Fluorophenyl)sulfonyl]-1-(pyrrolidin-2-ylidene)acetone (3d) and (1e)-1-[(2-fluorophenyl) sulfonyl]-1-(piperidin-2-ylidene)acetone (3e); typical procedure.

The mixture of 1-[(2-fluorophenyl)sulfonyl]acetone 1b (10 mmol) with the corresponding S-methyllactim 2d,e (15 mmol) was heated at 90˚C for 6 to 8 hours (monitored by TLC, eluent—$CHCl_3$). The reaction mixture was diluted with 2-propanol after cooling. The precipitate formed was filtered and used for further transformation without any additional purification. The interaction of the starting ketone 1b with 7-(methylthio)-3,4,5,6-tetrahydro-2*H*-azepine 2f resulted 2-methyl-1,4-benzoxathiine-4,4-dioxide 5.

1) (1*E*)-1-[(2-fluorophenyl)sulfonyl]-1-(pyrrolidin-2-ylidene)acetone (3d)

Yield: 6.8 mmol (68%); cream coloured solid (This compound has been also obtained according to the similar procedure by the interaction between 1-[(2-fluorophenyl)sulfonyl]acetone 1b and 5-methoxy-3,4-dihydro-2*H*-pyrrole 2a. Yield: 7.3 mmol (73%)).

IR (KBr): 3203, 2980, 2953, 2891, 1595, 1667, 1473, 1454, 1411, 1261, 1235, 1145, 1122, 1076, 994, 820, 761, 690, 595, 573, 529 cm^{-1}.

^1H NMR (200 MHz DMSO-d_6): δ = 1.81 - 1.96 (m, 2 H, CH_2), 2.15 (s, 3 H, $COCH_3$), 3.09 (t, J = 8.0 Hz, 2 H, CH_2), 3.58 (t, J = 7.2 Hz, 2 H, CH_2), 7.35 - 7.44 (m, 2 H, CH), 7.63 - 7.74 (m, 1 H, CH), 7.85 - 7.94 (m, 1 H, CH), 11.50 (br s, 1 H, NH).

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{14}FNO_3S$: 283.32; found: 283.4.

2) (1*E*)-1-[(2-fluorophenyl)sulfonyl]-1-(piperidin-2-ylidene)acetone (3e)

Yield: 3.1 mmol (31%); cream coloured solid.

IR (KBr): 2975, 2940, 2873, 1606, 1580, 1466, 1444, 1304, 1216, 1152, 1111, 1018, 972, 867, 820, 765, 730, 688, 622, 598, 573, 531, 456 cm^{-1}.

^1H NMR (200 MHz DMSO-d_6): δ = 1.49 - 1.71 (m, 4 H, CH_2), 2.23 (s, 3 H, $COCH_3$), 2.73 (t, J = 6.1 Hz, 2 H, CH_2), 3.42 (t, J = 5.9 Hz, 2 H, CH_2), 7.35 - 7.46 (m, 2 H, CH), 7.63 - 7.74 (m, 1 H, CH), 7.83 - 7.92 (m, 1 H, CH), 13.00 (br s, 1 H, NH).

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{16}FNO_3S$: 297.35; found: 297.4.

Methyl (2*E*,*Z*)-[(2-fluorophenyl)sulfonyl](pyrrolidin-2-ylidene)acetate and its homologues 3f-h; typical procedure.

The mixture of methyl 1-[(2-fluorophenyl)sulfonyl] acetate 1c (10 mmol) with the corresponding S-methyllactim 2d-f (15 mmol) was heated at 100˚C for 10 to 20 hours (monitored by TLC, eluent—$CHCl_3$). The reaction mixture was diluted with 2-propanol after cooling. The precipitate formed was filtered and used for further transformation without any additional purification. The compounds were isolated as the mixture of *E* and *Z* isomers.

1) Methyl (2*E*,*Z*)-[(2-fluorophenyl)sulfonyl] (pyrrolidin-2-ylidene)acetate (3f)

Yield: 8.5 mmol (85%); cream coloured solid. (This compound has been also obtained according to the similar procedure by the interaction between methyl 1-[(2-fluorophenyl)sulfonyl]acetate 1c and 5-methoxy-3,4-dihydro-2*H*-pyrrole 2a. Yield: 5.7 mmol (57%)).

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{14}FNO_4S$: 299.32; found: 299.4.

2) Methyl (2*E*,*Z*)-[(2-fluorophenyl)sulfonyl](piperidin-2-ylidene)acetate (3g)

Yield: 4.2 mmol (42%); cream coloured solid.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{16}FNO_4S$: 313.36; found: 313.4.

3) Methyl (2*E*,*Z*)-azepan-2-ylidene[(2-fluorophenyl)-sulfonyl]acetate (3h)

Yield: 4.8 mmol (48%); cream coloured solid.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{15}H_{18}FNO_4S$: 327.37; found: 327.4.

General procedure for synthesis of compounds 4a-x (cyclization of compounds 3).

The mixture of the correspondent compound 3 (10 mmol), 1,4-dioxane (6 ml) and DBU (10 mmol) was heated at 60˚C for 2 to 4 hours (for R^1 = CN 50˚C, 1 - 2 hours) (monitored by TLC, eluent—2-propanole-$CHCl_3$, 1:30). In the case when the compound 3 contained the admixture of cyclization product 4, the ratio of 3 and 4 in the mixture was calculated on the basis of integral intensity of specific peaks in ^{1}H NMR-spectra of mixture. The reaction mixture was diluted with 2-propanol after cooling. The precipitate formed was filtered and crystallized from 2-propanol-DMF mixture. The compounds 4y, z were formed at the first stage of reaction between 7-(methylthio)-3,4,5,6-tetrahydro-2*H*-azepine 2f and corresponding sulfones 1h, i.

General procedure for synthesis of compounds 4a-z ("one-pot" method).

To the solution of 1 (10 mmol) in DMF (4 mL) the correspondent lactim 2 (13 mmol) had been added and the mixture was additionally heated for 4 to 8 hours (monitored by TLC, eluent—$CHCl_3$) at 90˚C. After the reaction mixture was cooled to room temperature, 1,4-dioxane and equimolar amount of DBU were added and the reaction mixture was heated additionally at 60˚C for 2 - 4 hours. The precipitate formed after dilution of reaction mixture with 2-propanol, was filtered and crystallized from DMF-2-propanol mixture.

1) 2,3-Dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine-4-carbonitrile 5,5-dioxide (4a)

Yield: 8.1 mmol (81%), 9.3 mmol (93%) ("one-pot" method); cream coloured solid.

IR (KBr): 2206, 1609, 1591, 1554, 1481, 1419, 1279, 1152, 1132, 1074, 769, 607, 575 cm^{-1}.

^{1}H NMR (200 MHz DMSO-d_6): δ = 2.16 - 2.31 (m, 2 H, CH_2), 3.23 (t, J = 7.8 Hz, 2 H, CH_2), 4.26 (t, J = 7.2 Hz, 2 H, CH_2), 7.51 - 7.59 (m, 2 H, CH), 7.82 (m, 1 H, CH), 8.02 (d, J = 8.1 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 19.59, 33.74, 53.40, 81.92, 112.63, 117.91, 122.61, 125.13, 126.00, 133.73, 134.25, 161.32.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{12}H_{10}N_2O_2S$: 246.29; found: 246.1.

2) 7,8,9,10-Tetrahydropyrido[2,1-*c*][1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4b)

Yield: 7.6 mmol (76%), 8.5 mmol (85%) ("one-pot" method); cream coloured solid.

IR (KBr): 2957, 2881, 2203, 1581, 1533, 1469, 1350, 1278, 1139, 1073, 767, 609, 572 cm^{-1}.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.73 - 2.01 (m, 4 H, CH_2), 3.02 (t, J = 6.7 Hz, 2 H, CH_2), 4.09 (t, J = 5.9 Hz, 2 H, CH_2), 7.55 - 7.66 (m, 1 H, CH), 7.78 - 7.85 (m, 2 H, CH), 8.01 (d, J = 8.0 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 17.40, 21.56, 29.84, 48.07, 84.63, 112.65, 117.98, 121.78, 126.05, 126.36, 133.50, 138.13, 159.89.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{12}N_2O_2S$: 260.31; found: 260.1.

3) 8,9,10,11-Tetrahydro-7*H*-azepino[2,1-*c*][1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4c)

Yield: 6.6 mmol (66%), 7.8 mmol (78%) ("one-pot" method); cream coloured solid.

IR (KBr): 2940, 2862, 2204, 1580, 1535, 1457, 1415, 1299, 1215, 1167, 1073, 777, 717, 636, 588 cm^{-1}.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.72 (br s, 4 H, CH_2), 1.83 (br s, 2 H, CH_2), 3.18 (br s, 2 H, CH_2), 4.31 - 4.35 (m, 2 H, CH_2), 7.54-7.62 (m, 1 H, CH), 7.75 - 7.88 (m, 2 H, CH), 7.98 (d, J = 8.1 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 24.97, 26.14, 27.44, 34.37, 50.84, 86.61, 112.73, 118.29, 121.69, 125.76, 126.02, 133.72, 138.62, 164.44.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{14}N_2O_2S$: 274.34; found: 274.2.

4) 1-(5,5-Dioxido-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]-benzothiazin-4-yl)ethanone (4d)

Yield: 6.1 mmol (61%), 7.7 mmol (77%) ("one-pot" method); cream coloured solid.

IR (KBr): 3077, 2954, 2885, 1659, 1587, 1525, 1472, 1360, 1338, 1283, 1261, 1239, 1201, 1136, 1100, 995, 954, 933, 759, 593, 558 cm^{-1}.

^{1}H NMR (200 MHz DMSO-d_6): δ = 2.07 - 2.22 (m, 2 H, CH_2), 2.52 (s, 3 H, $COCH_3$), 3.34 (t, J = 7.8 Hz, 2 H, CH_2), 4.15 (t, J = 7.3 Hz, 2 H, CH_2), 7.45 - 7.53 (m, 2 H, CH), 7.60 (t, J = 7.9 Hz, 1 H, CH), 8.01 (d, J = 7.8 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 20.22, 30.78, 35.10, 51.74, 110.13, 117.29, 122.88, 125.26, 127.10, 133.22, 134.48, 159.63, 189.73.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{13}NO_3S$: 263.32; found: 263.0.

5) 1-(5,5-Dioxido-7,8,9,10-tetrahydropyrido[2,1-*c*][1,4]-benzothiazin-6-yl)ethanone (4e)

Yield: 2.5 mmol (25%), 4.2 mmol (42%) ("one-pot" method); cream coloured solid.

IR (KBr): 2968, 1665, 1582, 1520, 1467, 1404, 1356, 1274, 1155, 1137, 1110, 1004, 911, 767, 625, 595, 564, 511 cm^{-1}.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.70 - 1.89 (m, 4 H, CH_2), 2.52 (s, 3 H, $COCH_3$), 3.04 (t, J = 7.0 Hz, 2 H, CH_2), 4.10 (t, J = 5.7 Hz, 2 H, CH_2), 7.45 - 7.53 (m, 1 H, CH), 7.70 - 7.80 (m, 2 H, CH), 7.94 (d, J = 7.5 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 17.35, 21.23,

26.33, 32.15, 46.15, 113.10, 117.76, 121.72, 125.11, 126.91, 132.86, 138.97, 158.53, 191.56.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{15}NO_3S$: 277.34; found: 277.1.

6) Methyl 2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine-4-carboxylate 5,5-dioxide (4f)

Yield: 6.8 mmol (68%), 7.3 mmol (73%) ("one-pot" method); cream coloured solid.

IR (KBr): 3087, 3017, 2954, 1696, 1590, 1542, 1482, 1282,1242, 1113, 765, 595, 555, 502 cm^{-1}.

^1H NMR (200 MHz DMSO-d_6): δ = 2.09 - 2.24 (m, 2 H, CH_2), 3.36 (t, J = 7.8, 2 H, CH_2), 3.75 (s, 3 H, $COOCH_3$), 4.16 (t, J = 7.3 Hz, 2 H, CH_2), 7.42 - 7.49 (m, 2 H, CH), 7.73 (m, 1 H, CH), 7.95 (d, J = 7.4 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 20.02, 34.78, 51.72, 52.03, 100.92, 117.17, 123.07, 125.13, 127.43, 132.96, 134.25, 159.67, 162.77.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{13}NO_4S$: 279.32; found: 279.1.

7) Methyl 7,8,9,10-tetrahydropyrido[2,1-*c*][1,4]benzothiazine-6-carboxylate 5,5-dioxide (4g)

Yield: 3.3 mmol (33%), 5.3 mmol (53%) ("one-pot" method); cream coloured solid.

IR (KBr): 3073, 2955, 2877, 1696, 1585, 1521, 1467, 1293, 1250, 1124, 976, 911, 867, 772, 584, 569, 517 cm^{-1}.

^1H NMR (200 MHz DMSO-d_6): δ = 1.69 - 1.97 (m, 4 H, CH_2), 3.08 (t, J = 6.9, 2 H, CH_2), 3.75 (s, 3 H, $COOCH_3$), 4.08 (t, J = 5.8 Hz, 2 H, CH_2), 7.43 - 7.51 (m, 1 H, CH), 7.68 - 7.79 (m, 2 H, CH), 7.92 (d, J = 7.5 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 17.37, 21.28, 26.69, 46.19, 52.12, 104.47, 117.44, 121.94, 124.98, 127.04, 132.70, 138.91, 157.68, 162.39.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{15}NO_4S$: 293.34; found: 293.2.

8) Methyl 8,9,10,11-tetrahydro-7*H*-azepino[2,1-*c*]-[1,4]benzothiazine-6-carboxylate 5,5-dioxide (4h)

Yield: 6.8 mmol (68%), 6.4 mmol (64%) ("one-pot" method); cream coloured solid.

IR (KBr): 3072, 2941, 2861, 1698, 1583, 1528, 1463, 1465, 1403, 1298, 1238, 1162, 1120, 986, 959, 905, 849, 774, 691, 589, 564, 546, 509, 464 cm^{-1}.

^1H NMR (200 MHz DMSO-d_6): δ = 1.65 (br s, 4 H, CH_2), 1.84 (br s, 2 H, CH_2), 3.06 (br s, 2 H, CH_2), 3.76 (s, 3 H, $COOCH_3$), 4.25 - 4.29 (m, 2 H, CH_2), 7.44 - 7.51 (m, 1 H, CH), 7.65 - 7.79 (m, 2 H, CH), 7.90 (d, J = 7.7 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 25.27, 26.31, 26.85, 31.68, 49.32, 52.42, 105.65, 117.58, 121.91, 124.81, 126.92, 132.86, 139.24, 159.65, 162.56.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{15}H_{17}NO_4S$: 307.37; found: 307.2.

9) 7-Methyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine-4-carbonitrile 5,5-dioxide (4i)

Yield: 8.8 mmol (88%), 9.3 mmol (93%) ("one-pot" method); cream coloured solid.

^1H NMR (200 MHz DMSO-d_6): δ = 2.14 - 2.30 (m, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.20 (t, J = 7.9 Hz, 2 H, CH_2), 4.23 (t, J = 7.2 Hz, 2 H, CH_2), 7.44 (d, J = 8.7 Hz, 1 H, CH), 7.63 (d, J = 8.3 Hz, 1 H, CH), 7.82 (s, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 19.56, 20.33, 33.69, 53.37, 81.55, 112.76, 117.84, 121.97, 125.08, 132.10, 134.54, 136.10, 160.82.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{12}N_2O_2S$: 260.31; found: 260.1.

10) 7-Fluoro-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine-4-carbonitrile 5,5-dioxide (4j)

Yield: 6.7 mmol (67%), 7.2 mmol (72%) ("one-pot" method); cream coloured solid.

^1H NMR (200 MHz DMSO-d_6): δ = 2.16 - 2.31 (m, 2 H, CH_2), 3.22 (t, J = 7.8 Hz, 2 H, CH_2), 4.26 (t, J = 7.2 Hz, 2 H, CH_2), 7.60 - 7.79 (m, 2 H, CH), 7.93 (dd, J(1) = 7.7 Hz, J(2) = 2.6 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 19.43, 33.66, 53.73, 80.85, 108.75, 109.01, 112.36, 120.87, 120.95, 121.40, 121.63, 125.92, 125.99, 131.13, 157.45, 159.91, 161.21.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{12}H_9FN_2O_2S$: 264.28; found: 264.3.

11) 7-Chloro-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine-4-carbonitrile 5,5-dioxide (4k)

Yield: 8.3 mmol (83%), 8.7 mmol (87%) ("one-pot" method); cream coloured solid.

^1H NMR (200 MHz DMSO-d_6): δ = 2.16 - 2.31 (m, 2 H, CH_2), 3.22 (t, J = 7.8 Hz, 2 H, CH_2), 4.25 (t, J = 7.3 Hz, 2 H, CH_2), 7.59 (d, J = 9.2 Hz, 1 H, CH), 7.89 (dd, J(1) = 9.0 Hz, J(2) = 2.4 Hz, 1 H, CH), 8.65 (d, J = 2.5 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 19.58, 33.81, 53.74, 82.18, 112.28, 120.42, 121.91, 126.21, 129.89, 133.30, 133.68, 161.61.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{12}H_9ClN_2O_2S$: 280.73; found: 280.3.

12) 8-Methyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine-4-carbonitrile 5,5-dioxide (4l)

Yield: 9.5 mmol (95%), 9.7 mmol (97%) ("one-pot" method); cream coloured solid.

^1H NMR (200 MHz DMSO-d_6): δ = 2.15 - 2.30 (m, 2 H, CH_2), 2.45 (s, 3 H, CH_3), 3.21 (t, J = 7.8 Hz, 2 H, CH_2), 4.23 (t, J = 7.3 Hz, 2 H, CH_2), 7.37 (d, J = 8.3 Hz, 1 H, CH), 7.38 (s, 1 H, CH), 7.89 (d, J = 8.6 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 19.58, 21.35, 33.70, 53.33, 82.05, 112.71, 117.70, 122.54, 122.73, 126.89, 134.29, 144.46, 161.15.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{12}N_2O_2S$: 260.31; found: 260.1.

13) 8-Fluoro-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine-4-carbonitrile 5,5-dioxide (4m)

Yield: 8.8 mmol (88%), 9.3 mmol (93%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 2.16 - 2.31 (m, 2 H, CH_2), 3.23 (t, J = 7.8 Hz, 2 H, CH_2), 4.22 (t, J = 7.2 Hz, 2 H, CH_2), 7.36 - 7.55 (m, 2 H, CH), 8.11 (dd, J(1) = 8.9 Hz, J(2) = 5.8 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 19.61, 33.83, 53.78, 82.87, 105.03, 105.39, 112.30, 113.70, 114.01, 121.77, 121.81, 125.90, 126.05, 136.48, 136.64, 161.83, 162.64, 165.97.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{12}H_9FN_2O_2S$: 264.28; found: 264.5.

14) 8-Chloro-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazine-4-carbonitrile 5,5-dioxide (4n)

Yield: 8.8 mmol (88%), 9.1 mmol (91%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 2.15 - 2.30 (m, 2 H, CH_2), 3.23 (t, J = 7.8 Hz, 2 H, CH_2), 4.25 (t, J = 7.3 Hz, 2 H, CH_2), 7.60 (d, J = 8.6 Hz, 1 H, CH), 7.69 (s, 1 H, CH), 8.05 (d, J = 8.6 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 19.51, 33.72, 53.60, 82.66, 112.14, 117.67, 123.69, 124.62, 125.91, 135.49, 138.28, 161.76.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{12}H_9ClN_2O_2S$: 280.73; found: 280.3.

15) 3-Methyl-7,8,9,10-tetrahydropyrido[2,1-*c*][1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4o)

Yield: 7.7 mmol (77%), 8.4 mmol (84%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.70 - 1.99 (m, 4 H, CH_2), 2.42 (s, 3 H, CH_3), 3.00 (t, J = 6.7 Hz, 2 H, CH_2), 4.05 (t, J = 5.8 Hz, 2 H, CH_2), 7.64 (d, J = 9.3 Hz, 1 H, CH), 7.73 (d, J = 9.2 Hz, 1 H, CH), 7.81 (s, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 17.45, 20.15, 21.59, 29.80, 48.06, 66.44, 84.17, 112.82, 117.92, 121.15, 126.00, 134.32, 135.96, 136.50, 159.31.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{14}N_2O_2S$: 274.34; found: 274.2.

16) 3-Fluoro-7,8,9,10-tetrahydropyrido[2,1-*c*][1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4p)

Yield: 6.7 mmol (67%), 7.8 mmol (78%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.72 - 1.99 (m, 4 H, CH_2), 3.02 (t, J = 6.7 Hz, 2 H, CH_2), 4.08 (t, J = 5.7 Hz, 2 H, CH_2), 7.69 - 7.79 (m, 1 H, CH), 7.86 - 7.97 (m, 2 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 17.29, 21.42, 29.73, 48.45, 83.48, 107.73, 107.99, 112.41, 120.99, 121.26, 127.04, 134.94, 157.66, 159.88, 160.13.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{11}FN_2O_2S$: 278.30; found: 278.3.

17) 3-Chloro-7,8,9,10-tetrahydropyrido[2,1-*c*][1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4q)

Yield: 6.8 mmol (68%), 8.0 mmol (80%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.73 - 2.01 (m, 4 H, CH_2), 3.02 (t, J = 6.6 Hz, 2 H, CH_2), 4.08 (t, J = 5.8 Hz, 2 H, CH_2), 7.88 - 7.89 (m, 2 H, CH), 8.01 - 8.03 (m, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 17.25, 21.35, 29.77, 48.31, 84.60, 112.25, 120.52, 120.87, 126.94, 130.29, 133.25, 136.97, 160.13.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{11}ClN_2O_2S$: 294.75; found: 294.3.

18) 2-Methyl-7,8,9,10-tetrahydropyrido[2,1-*c*][1,4]-benzothiazine-6-carbonitrile 5,5-dioxide (4r)

Yield: 9.0 mmol (90%), 9.7 mmol (97%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.73 - 2.00 (m, 4 H, CH_2), 2.47 (s, 3 H, CH_3), 3.01 (t, J = 6.7 Hz, 2 H, CH_2), 4.07 (t, J = 6.0 Hz, 2 H, CH_2), 7.41 (d, J = 8.3 Hz, 1 H, CH), 7.68 (s, 1 H, CH), 7.88 (d, J = 8.1, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 17.31, 21.42, 29.71, 47.86, 84.66, 112.65, 117.76, 121.60, 123.52, 127.08, 138.04, 144.09, 159.60.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{14}N_2O_2S$: 274.34; found: 274.2.

19) 2-Fluoro-7,8,9,10-tetrahydropyrido[2,1-*c*][1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4s)

Yield: 7.8 mmol (78%), 8.5 mmol (85%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.72 - 2.00 (m, 4 H, CH_2), 3.02 (t, J = 6.7 Hz, 2 H, CH_2), 4.03 (t, J = 6.0 Hz, 2 H, CH_2), 7.42 - 7.52 (m, 1 H, CH), 7.78 (dd, J(1) = 12.1 Hz, J(2) = 2.2 Hz, 1 H, CH), 8.06 - 8.13 (m, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 17.22, 21.28, 29.76, 48.26, 85.53, 105.35, 105.63, 112.25, 113.97, 114.21, 122.47, 124.88, 124.99, 140.14, 140.25, 160.26, 162.97, 165.45.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{11}FN_2O_2S$: 278.30; found: 278.3.

20) 2-Chloro-7,8,9,10-tetrahydropyrido[2,1-*c*][1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4t)

Yield: 8.9 mmol (89%), 9.4 mmol (94%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.72 - 1.99 (m, 4 H, CH_2), 3.02 (t, J = 6.7 Hz, 2 H, CH_2), 4.08 (t, J = 5.9 Hz, 2 H, CH_2), 7.66 (dd, J(1) = 8.6 Hz, J(2) = 1.7 Hz, 1 H, CH), 7.96 (d, J = 1.6 Hz, 1 H, CH), 8.03 (d, J = 8.6 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 17.22, 21.28, 29.80, 49.22, 85.38, 112.20, 117.98, 123.74, 124.50,

126.31, 138.24, 139.24, 160.36.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{13}H_{11}ClN_2O_2S$: 294.75; found: 294.6.

21) 3-Methyl-8,9,10,11-tetrahydro-7*H*-azepino[2,1-*c*]-[1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4u)

Yield: 6.9 mmol (69%), 7.2 mmol (72%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.71 (br s, 4 H, CH_2), 1.81 (br s, 2 H, CH_2), 2.42 (s, 3 H, CH_3), 3.16 (br s, 2 H, CH_2), 4.28 - 4.32 (m, 2 H, CH_2), 7.60 - 7.70 (m, 2 H, CH), 7.78 (s, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 20.02, 24.87, 26.01, 27.34, 34.14, 50.60, 85.91, 112.81, 118.13, 120.86, 125.47, 134.43, 136.07, 136.30, 163.94.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{15}H_{16}N_2O_2S$: 288.37; found: 288.1.

22) 3-Fluoro-8,9,10,11-tetrahydro-7*H*-azepino[2,1-*c*][1,4]-benzothiazine-6-carbonitrile 5,5-dioxide (4v)

Yield: 6.6 mmol (66%), 6.1 mmol (61%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.71 (br s, 4 H, CH_2), 1.82 (br s, 2 H, CH_2), 3.18 (br s, 2 H, CH_2), 4.31 - 4.35 (m, 2 H, CH_2), 7.68 - 7.78 (m, 1 H, CH), 7.82 - 7.90 (m, 2 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 24.72, 25.90, 27.33, 34.22, 51.08, 85.57, 107.62, 107.87, 112.51, 121.23, 121.45, 126.61, 126.68, 135.36, 157.45, 159.92, 164.47.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{13}FN_2O_2S$: 292.33; found: 292.3.

23) 3-Chloro-8,9,10,11-tetrahydro-7*H*-azepino[2,1-*c*]-[1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4w)

Yield: 4.6 mmol (46%), 4.8 mmol (48%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.70 (br s, 4 H, CH_2), 1.77 - 1.81 (m, 2 H, CH_2), 3.18 (br s, 2 H, CH_2), 4.30 - 4.34 (m, 2 H, CH_2), 7.78 - 8.01 (m, 3 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 24.7, 25.82, 27.30, 34.28, 50.96, 86.66, 112.36, 120.81, 126.60, 129.92, 133.45, 137.45, 164.67.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{13}ClN_2O_2S$: 308.78; found: 308.3.

24) 2-Methyl-8,9,10,11-tetrahydro-7*H*-azepino[2,1-*c*]-[1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4x)

Yield: 7.3 mmol (73%), 8.9 mmol (89%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.71 (br s, 4 H, CH_2), 1.83 (br s, 2 H, CH_2), 2.48 (s, 3 H, CH_3), 3.17 (br s, 2 H, CH_2), 4.29 - 4.33 (m, 2 H, CH_2), 7.40 (d, J = 8.0 Hz, 1 H, CH), 7.58 (s, 1 H, CH), 7.86 (d, J = 7.9 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 21.45, 24.91, 26.10, 27.35, 34.25, 50.57, 86.56, 112.73, 117.96, 121.48, 123.21, 126.81, 138.53, 144.39, 164.19.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{15}H_{16}N_2O_2S$: 288.37; found: 288.3.

25) 2-Fluoro-8,9,10,11-tetrahydro-7*H*-azepino[2,1-*c*]-[1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4y)

Yield: 7.3 mmol (73%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.71 (br s, 4 H, CH_2), 1.78 - 1.81 (m, 2 H, CH_2), 3.18 (br s, 2 H, CH_2), 4.28 - 4.32 (m, 2 H, CH_2), 7.41 - 7.50 (m, 1 H, CH), 7.69 (dd, J(1) = 11.7 Hz, J(2) = 2.2 Hz, 1 H, CH), 8.03 - 8.11 (m, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 24.92, 25.91, 27.39, 34.43, 51.03, 87.65, 105.59, 105.96, 112.46, 113.80, 114.11, 122.26, 124.89, 125.04, 140.62, 140.78, 162.89, 164.81, 166.21.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{13}FN_2O_2S$: 292.33; found: 292.4.

26) 2-Chloro-8,9,10,11-tetrahydro-7*H*-azepino[2,1-*c*]-[1,4]benzothiazine-6-carbonitrile 5,5-dioxide (4z)

Yield: 5.3 mmol (53%) ("one-pot" method); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 1.71 (br s, 4 H, CH_2), 1.80 - 1.82 (m, 2 H, CH_2), 3.16 - 3.19 (m, 2 H, CH_2), 4.31 - 4.35 (m, 2 H, CH_2), 7.63 (dd, J(1) = 8.4 Hz, J(2) = 1.6 Hz, 1 H, CH), 7.84 (d, J = 1.5 Hz, 1 H, CH), 8.00 (d, J = 8.6 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 24.73, 25.80, 27.32, 34.36, 50.84, 87.36, 112.32, 118.10, 123.66, 124.17, 126.03, 138.43, 139.65, 164.83.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_{14}H_{13}ClN_2O_2S$: 308.78; found: 308.3.

2-Methyl-1,4-benzoxathiine 4,4-dioxide (5).

The mixture of 10 mmol [(2-fluorophenyl)sulfonyl] acetone 1b, 10 mmol DBU and 2 mL of 1,4-dioxane were heated 80˚C - 90˚C for 3 - 4 hours (monitored by TLC, eluent—$CHCl_3$). The reaction mixture was diluted with 2-propanol after cooling. The precipitate formed was filtered and crystallized from 2-propanol-DMF mixture.

Yield: 5.5 mmol (55%); cream coloured solid.

^{1}H NMR (200 MHz DMSO-d_6): δ = 2.23 (s, 3 H, CH_3), 6.82 (s, 1 H, CH), 7.43 - 7.53 (m, 2 H, CH_2), 7.68 - 7.77 (m, 1 H, CH), 7.93 (d, J = 7.9 Hz, 1 H, CH).

^{13}C NMR (75 MHz DMSO-d_6): δ = 20.37, 103.44, 118.73, 122.43, 124.54, 126.09, 133.96, 149.90, 158.08.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_9H_8O_3S$: 196.22; found: 196.3.

(2*E*,*Z*)-2-{[(2-fluorophenyl)sulfonyl]methylidene}azepane (6).

The mixture of 1-[(2-fluorophenyl)sulfonyl]acetone 1b (10 mmol) with S-methyllactim 2f (15 mmol) was heated at 90˚C for 6 to 8 hours (monitored by TLC, eluent—$CHCl_3$). The reaction mixture was diluted with 2-propanol after cooling. The precipitate formed was filtered

and crystallized from 2-propanol-DMF mixture.

Yield: 2.5 mmol (25%); cream coloured solid.

LC/MS: *m/z* $[M + H]^+$ calcd for $C_9H_8O_3S$: 269.34; found: 269.5.

3. Conclusion

The reaction of different methylene active (2-fluorophenyl)sulfones with O- and S-methylactims has been studied. A facile one-pot method for synthesis of 2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzothiazines and their homologues by interaction of methylenactive (2-fluorophenyl)sulfones with homologues of either 5-methoxy-3,4-dihydro-2*H*-pyrrole or 5-(methylthio)-3,4-dihydro-2*H*-pyrrole has been developed.

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