# Accepted Manuscript


A novel, flexible strategy to construct privileged dibenzo[*b,f*][1,4,5]oxathiazepine 5,5-dioxides and their heterocyclic isosteres

Alexander Sapegin, Valeria Panova, Elena Reutskaya, Alexey V. Smirnov, Mikhail Krasavin

PII: S0040-4020(16)31018-3

DOI: 10.1016/j.tet.2016.10.008

Reference: TET 28149

To appear in: *Tetrahedron*

Received Date: 16 August 2016

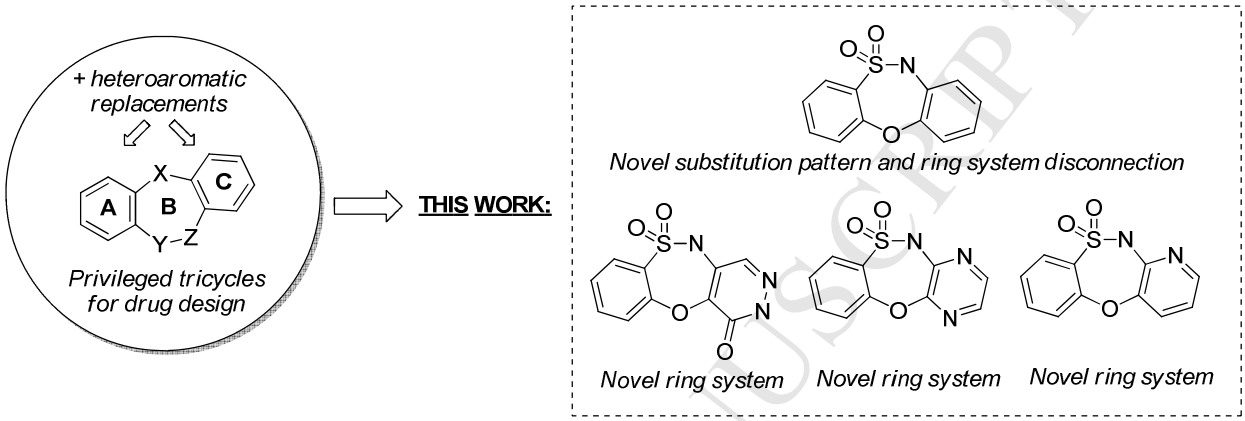
Revised Date: 21 September 2016

Accepted Date: 4 October 2016

Please cite this article as: Sapegin A, Panova V, Reutskaya E, Smirnov AV, Krasavin M, A novel, flexible strategy to construct privileged dibenzo[*b,f*][1,4,5]oxathiazepine 5,5-dioxides and their heterocyclic isosteres, *Tetrahedron* (2016), doi: 10.1016/j.tet.2016.10.008.

# A novel, flexible strategy to construct privileged dibenzo[*b*,*f*][1,4,5]oxathiazepine-5,5-dioxides and their heterocyclic isosteres

Alexander Sapegin, Valeria Panova, Elena Reutskaya, Alexey V. Smirnov, Mikhail Krasavin*



# A novel, flexible strategy to construct privileged dibenzo[*b,f*][1,4,5]oxathiazepine 5,5-dioxides and their heterocyclic isosteres

Alexander Sapegin,[a] Valeria Panova,[b] Elena Reutskaya,[b] Alexey V. Smirnov,[b] Mikhail Krasavin[a,*]

[a]*Institute of Chemistry, Saint Petersburg State University, 26 Universitetskii Prospect, Peterhof, 198504 Russian Federation*

[b]*The Ushinsky Yaroslavl State Pedagogical University, 108 Respublikanskaya St., Yaroslavl, 150000, Russian Federation*

* Corresponding Author; phone: + 7 931 3617872, fax: +7 812 428 6939.

E-mail: m.krasavin@spbu.ru

URL: http://krasavin-group.org

*Keywords:* privileged structures, tricyclic scaffolds, ring-forming process, bis-nucleophiles, bis-electrophiles, aromatic nucleophilic substitution, Smiles rearrangement.

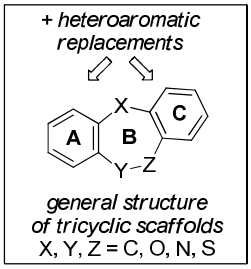
## ABSTRACT

Secondary *o*-hydroxybenzene sulfonamides have been explored as bis-electrophilic partners in a practically simple, atom-economical approach to dibenzo[*b,f*][1,4,5]oxathiazepine-5,5-dioxides and their heterocyclic analogs, which is an underexplored version of privileged tricyclic scaffolds for drug design. The reaction proceeds smoothly and regiospecifically under conventional heating conditions and delivers the target compounds in good to excellent yields. The approach represents a completely new disconnection of the dibenzo[*b,f*][1,4,5]oxathiazepine-5,5-dioxide scaffolds and allows accessing a new chemical space in terms of the substitution pattern. In particular, heterocycles can be conveniently varied within the tricyclic frameworks by altering the nature of the bis-electrophilic aromatic partner in the cyclization. This has been demonstrated by the synthesis of three hitherto uundescribed heterotricyclic scaffolds. The cyclizations were shown to proceed via the Smiles rearrangement, as had been observed by us for a range of similar ring-forming processes.

## 1. Introduction

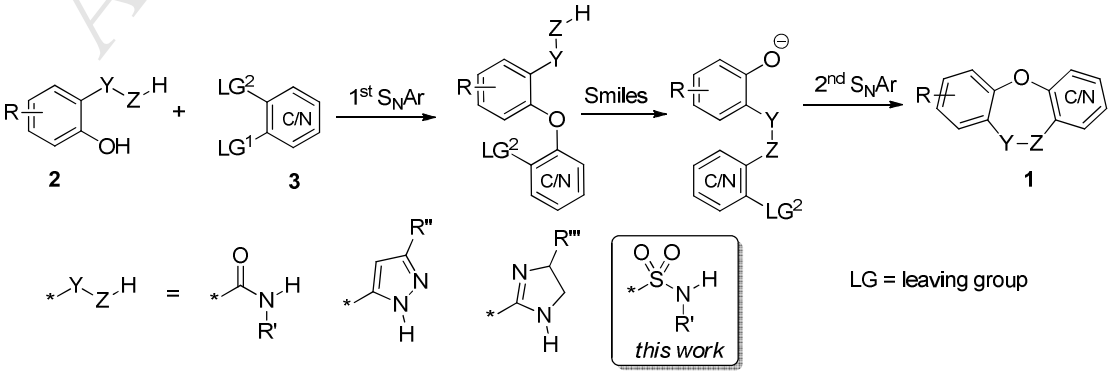
Tricyclic scaffolds (such as **1**) consisting of a seven-membered heterocycle fused to two aromatic or heteroaromatic groups are privileged[1-2] from drug design perspective as they have delivered numerous high-affinity ligands in the central nervous system[3] target area as well of other therapeutically relevant biotargets (Figure 1).[4]

**Figure 1.** Privileged tricycles for the drug design.



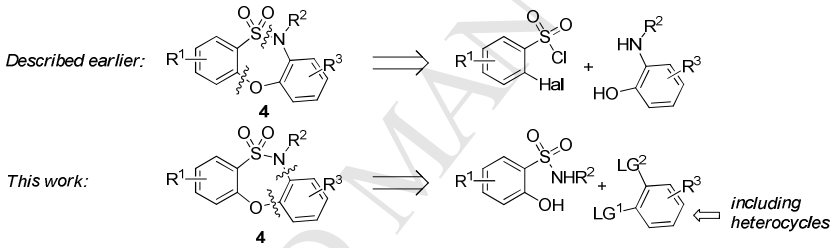

Recently, we have developed a general strategy to constructing such scaffolds that involves the use of phenols **2** containing a second moderately acidic functionality in *ortho*-position, which can react, under basic conditions with bis-electrophilic aromatic and heteroaromatic partners **3**. The process essentially consists of two $S_NAr$ events intermitted, without exception, by a Smiles rearrangement.[5-8] We have shown that the process is triggered by displacement of the most labile leaving group in **3** by the phenoxide anion and cannot be completed before phenoxide anion is liberated again, via the Smile rearrangement, for the substitution of the other less labile leaving group. Thus, the intricate interplay of intramolecular events with nucleophile switch creates an energetically favorable path for the reaction and enables efficient overall ring closing process, in which some of the individual elementary steps would be impossible to realize in practice. The strategy has been realized for such Y-ZH motifs as secondary amides,[5] pyrazoles,[6-7] imidazolines.[8] In this work we investigated a possible involvement of secondary sulfonamide groups that are isosteric to the secondary amides employed earlier (Scheme 1).

**Scheme 1.** Synthetic strategy toward tricycles **1** described by us earlier and pursued in this work.



Dibenzo[*b,f*][1,4,5]oxathiazepine-5,5-dioxide scaffold **4**, which was expected to result from realization of such a methodology, is largely underrepresented in the medicinal chemistry literature (except for a few isolated reports on its employment in the design of antiviral,[9-10] antipsychotic,[11-12] and histone deacetylase inhibitory[13] compounds). Such a void in the bioannotated chemistry space could be due to the absence of reliable and flexible methods to construct **4**. Besides some early reports on electrophilic aromatic cyclization of sulfonyl nitrenes (where compounds containing scaffold **4** were only a part of the total product distribution),[14-15] the literature examples of constructing **4** are limited to reactions of 2-halobenzenesulfonyl chlorides with *o*-aminophenols which involves amino group acylation in the latter followed by intramolecular diphenyl ether formation.[16-18] The alternative disconnection pursued in this work provides access to a vastly different chemical space, including heterocyclic version of the C ring (Figure 2); herein, we present our results in this area.

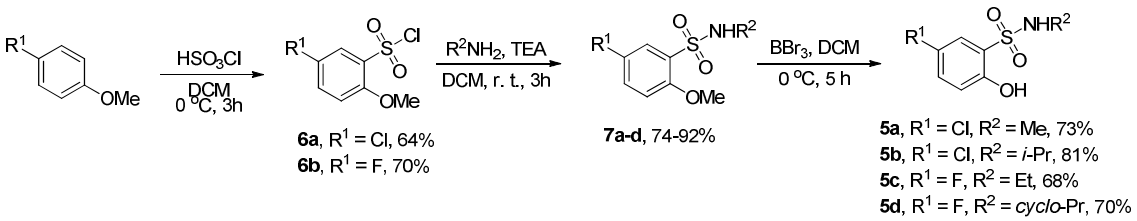
**Figure 2.** Comparison of two alternative disconnections of scaffold **4**.




## 2. Results and discussion

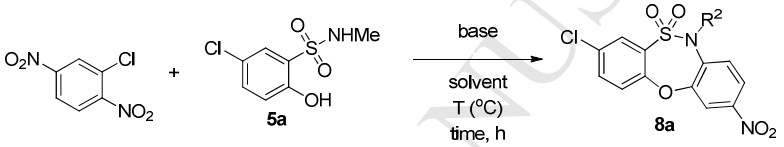
A set of four 2-hydroxybenzenesulfonamides **5a-d** was prepared from 4-chloroanisol and 4-fluoroanisol by regiospecific sulfochlorination at position 3 to deliver sulfonyl chlorides **6a-b** both of which are also available commercially. These reagents were reacted with a set of primary amines ($MeNH_2$, $EtNH_2$, *i*-$PrNH_2$, *cyclo*-$PrNH_2$) to give sulfonamides **7a-d**, all of which are expensive commercially available compounds and one (**7a**) is described in the literature.[19] Cleavage of the methyl ether group in **7a-d** was achieved with $BBr_3$ and the respective phenols **5a-d** were obtained in good yields and purity after a simple reaction workup (Scheme 2).

**Scheme 2.** Preparation of 2-hydroxybenzenesulfonamides **5a-d**.



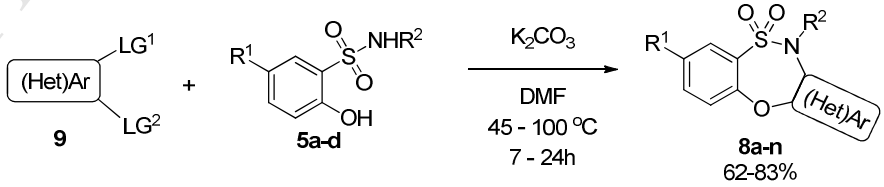
In order to test the applicability of synthons **5a-d** in the formation of dibenzo[*b*,*f*][1,4,5]oxathiazepine-5,5-dioxide scaffold **4**, we investigated a model reaction of **5a** with 1-chloro-2,4-dinitrobenzene under different conditions including variation of the base, solvent and time/temperature regimen (Table 1). In principle, for such a reactive substrate, a reasonable yield of the resulting tricyclic adduct (**8a**) was obtained in all cases. However, the best result was achieved with $K_2CO_3$ in DMF at 50 $^oC$ which is in line with the previously published reports from our group.[5-8] Hence, these conditions were adopted for all combinations of **5a-d** with bis-electrophilic aromatic substrates **9** studied herein for the respective ring-forming reactions leading to **8a-n**, with occasional raising of the reaction time and temperature, as was needed to promote full substrate-to-product conversion for less reactive substrates **9** (Scheme 3).

**Table 1.** Base, solvent and temperature screening for a model dibenzo[*b*,*f*][1,4,5]oxathiazepine-5,5-dioxide formation.




| Experiment | Base | Solvent | T ($^oC$) | Time, h | Yield of **8a** (%) |
|---|---|---|---|---|---|
| 1 | NaH | DMF | 50 | 3 | 51 |
| 2 | *t*-BuOK | DMF | 50 | 3 | 58 |
| 3 | $Na_2CO_3$ | DMF | 100 | 24 | 74 |
| 4 | $K_2CO_3$ | DMF | 50 | 8 | 83 |
| 5 | $K_2CO_3$ | MeCN | reflux | 12 | 79 |
| 6 | $K_2CO_3$ | Acetone | reflux | 36 | 61 |

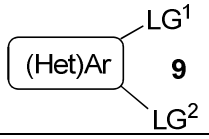
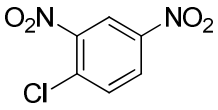
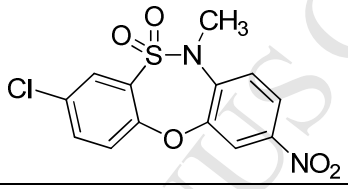
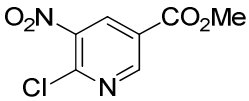
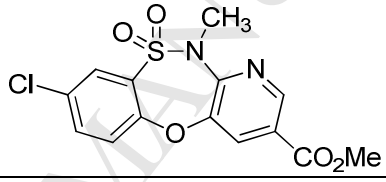
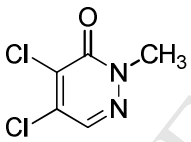
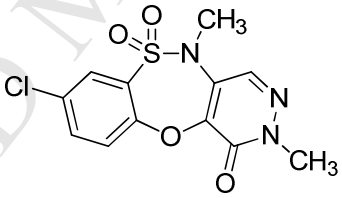
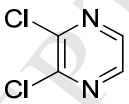
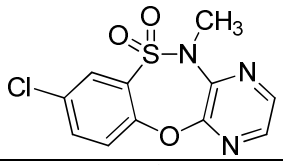
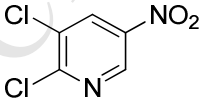
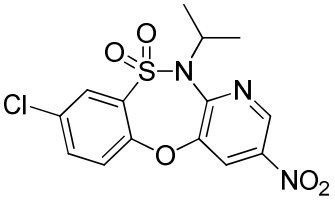
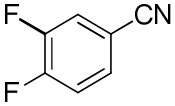
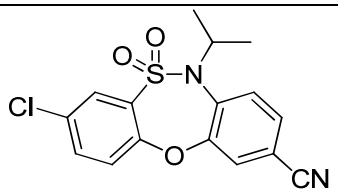
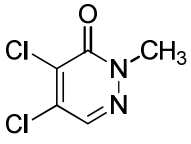
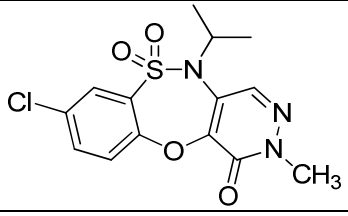
**Scheme 3.** General synthesis of dibenzo[*b*,*f*][1,4,5]oxathiazepine-5,5-dioxides and their heterocyclic analogs **8a-n** investigated in this work (for exact product and substrate structure see Table 2).

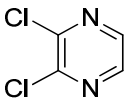
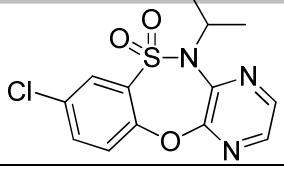
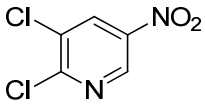
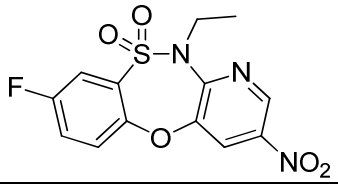
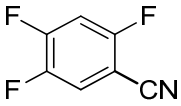
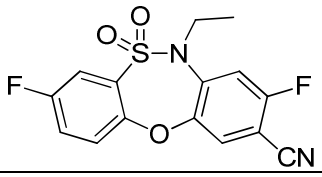
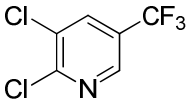
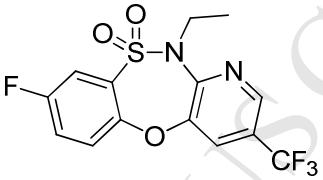
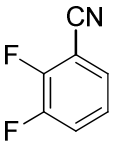
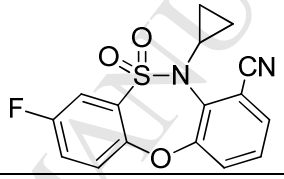
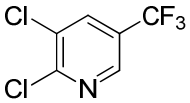
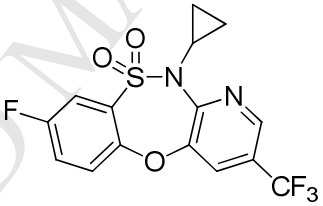
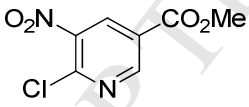
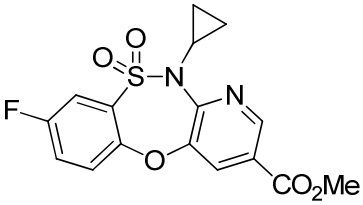



The results presented in Table 3 lead to several generalizations. All the reactions clearly represent an efficient way to construct medicinally important compounds **8** which allows drawing from a broad pool of bis-electrophilic partners **9**: 1-halo-2-nitroaromatic and

heteroaromatic (**8a-b**, **8n**), 1,2-dichloroaromatic and heteroaromatic (**8c-e**, **8g-i**, **8k**, **8m**) and 1,2-difluoroaromatic (**8f**, **8j**, **8l**). The reaction proceeds with a full regioselectivity as only one positional isomer was obtained in each case. This selectivity was particularly striking for the reaction leading **8j** where the potentially labile fluorine atom in *ortho*-position of the benzonitrile moiety is fully preserved and the cyclic product resulting only from the displacement of the *para*-fluoro substituent formed.

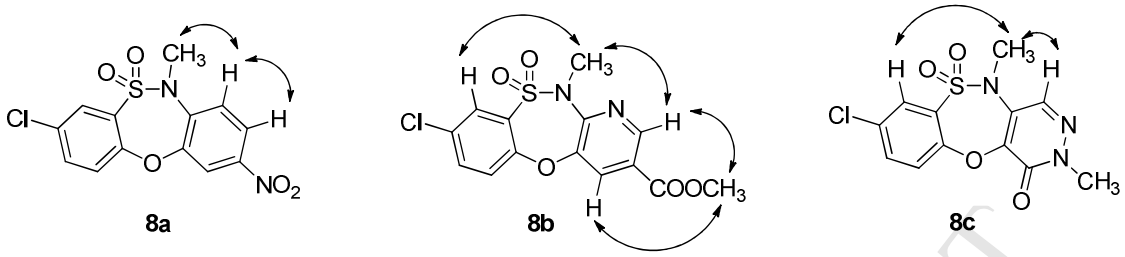
**Table 2.** Compounds **8a-n** prepared in this work.

| Compound | **5** |  | Structure of **8** | Time, h | T, ºC | Isolated yield, % |
|---|---|---|---|---|---|---|
| **8a** | **5a** |  |  | 8 | 50 | 83 |
| **8b** | **5a** |  |  | 16 | 80 | 76 |
| **8c** | **5a** |  |  | 14 | 75 | 73 |
| **8d** | **5a** |  |  | 10 | 50 | 81 |
| **8e** | **5b** |  |  | 7 | 45 | 85 |
| **8f** | **5b** |  |  | 24 | 100 | 63 |
| **8g** | **5b** |  |  | 14 | 75 | 75 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **8h** | **5b** |  |  | 10 | 50 | 68 |
| **8i** | **5c** |  |  | 7 | 45 | 80 |
| **8j** | **5c** |  |  | 16 | 80 | 62 |
| **8k** | **5c** |  |  | 16 | 80 | 65 |
| **8l** | **5d** |  |  | 24 | 100 | 67 |
| **8m** | **5d** |  |  | 16 | 80 | 71 |
| **8n** | **5d** |  |  | 16 | 80 | 69 |

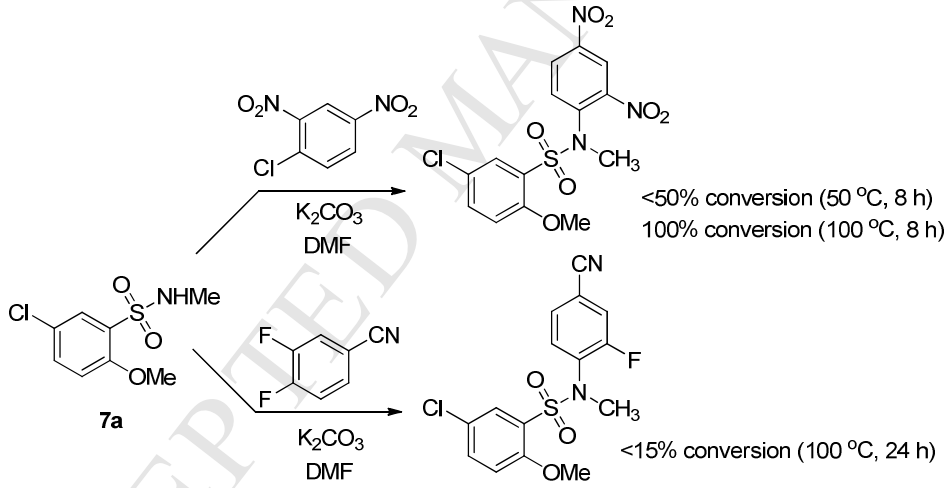
We urge the reader not to be surprised at the regioisomer which is formed in this case. One would expect phenoxide anion formed from **5a-d** under the basic reaction conditions to displace the more labile leaving group in substrates **9** while the less reactive conjugate base of the secondary sulfonamide would perhaps displace the less prone leaving group to complete the cyclization. Yet, the regiochemistry of products was quite the opposite as shown in Table 2 and as was demonstrated by cross-peaks in the NOESY spectra (see Supporting Information) of a representative set of products (**8a-c**, Figure 3).

**Figure 3.** Through-space interactions observed in the NOESY spectra of compounds **8a-c**, confirming their regiochemistry.



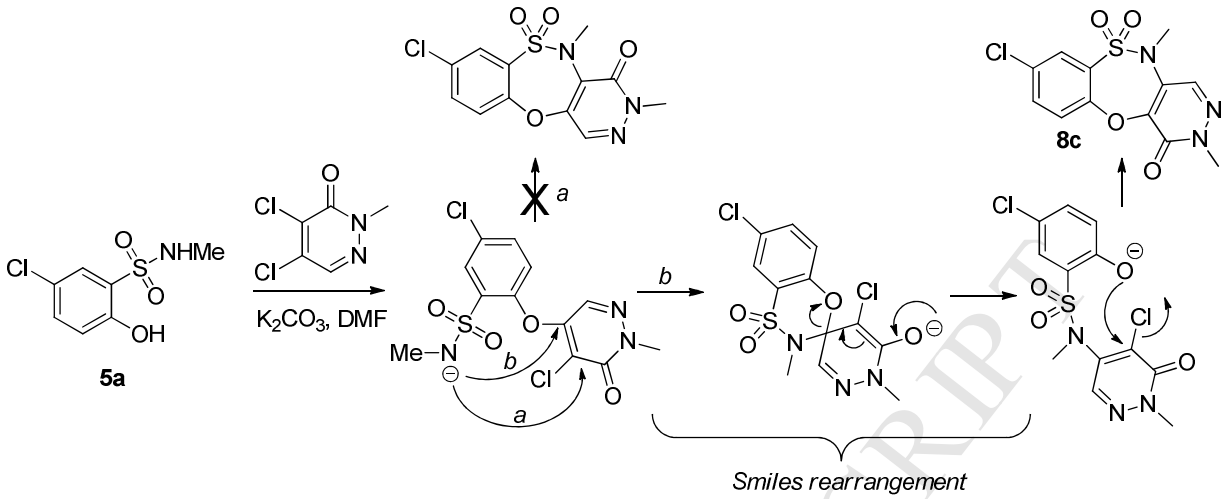

Secondary sulfonamide is, in principle, capable of reacting with some of these substrates directly under similar reaction conditions, as was demonstrated in a control reaction of methyl ether **7a** with 1-chloro-2,4-dinitrobenzene which went to completion albeit under more forcing conditions than the cyclization of the same substrate with **5a** (see Table 1). However, the less reactive 3,4-difluorobenzonitrile did not convert more than 15% of **7a** at 100 °C over 24 h, i.e. under the conditions that led to a complete reaction toward product **8f** (Scheme 4).

**Scheme 4.** Control reactions of methyl ether **7a** with selected substrates **9**.



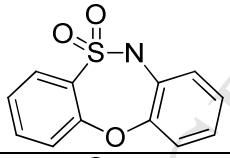
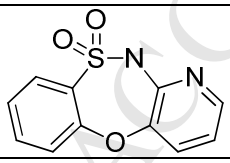
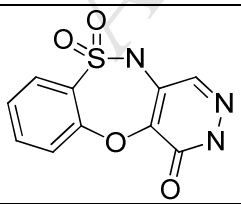
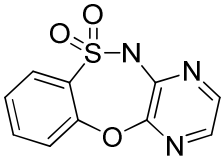

Therefore, the presence of the free phenol in **5a-d** creates a less demanding energy profile for the reaction which results in an efficient displacement of both leaving groups in **9** (one of them being in a non-activated position compared to the other) and a ring-forming process delivering **8a-n**. As mentioned above, we have demonstrated on several occasions[5-8] that such a lower activation barrier reaction path is initiated by the displacement of the more labile leaving group in compound **9** by the phenoxide anion derived from the bis-electrophilic phenol partner. The resulting initial adduct evolved into another phenoxide via a Smiles rearrangement path *b* (as the deprotonated sulfonamide is too weak a nucleophile to displace the less labile leaving group via path *a*, even intramolecularly) and the phenoxide triggers the final ring-closing $S_NAr$, as shown for the formation of product **8c** in Scheme 5.

**Scheme 5.** The $S_NAr^1$-Smiles rearrangement-$S_NAr^2$ reaction path leading to **8c**.




Compounds **8a**, **8f**, **8j**, **8l** contain privileged tricyclic dibenzo[*b*,*f*][1,4,5]oxathiazepine-5,5-dioxide core **4** described earlier which was assembled following a completely novel disconnection, alternative to the ones reported.[16-18] In contrast, compounds **8b**, **8e**, **8i-k**, **8m-n** as well as compounds **8c**, **8g** and **8d**, **8h** are examples of hitherto undescribed (according to the results of SciFinder search[19] summarized in Table 3) tricyclic scaffolds benzo[*b*]pyrido[2,3-*f*][1,4,5]oxathiazepine-10,10-dioxide, benzo[*b*]pyridazino[4,5-*f*][1,4,5]oxathiazepin-1-one-6,6-dioxide and benzo[*b*]pyrazino[2,3-*f*][1,4,5]oxathiazepine-6,6-dioxide, respectively.

**Table 3.** SciFinder novelty analysis for compounds **8a-n** reported herein.

| Scaffold (substructure searched) | Representative compounds | Hits in SciFinder®[19] | Novelty component |
|---|---|---|---|
|  | **8a**, **8f**, **8j**, **8l** | 119 | Novel substitution pattern and ring system disconnection |
|  | **8b**, **8e**, **8i-k**, **8m-n** | 0 | Novel ring system |
|  | **8c**, **8g** | 0 | Novel ring system |
|  | **8d**, **8h** | 0 | Novel ring system |

## 3. Conclusion

In summary, we have described a fundamentally new approach to dibenzo[*b*,*f*][1,4,5]oxathiazepine-5,5-dioxides and their heterocyclic analogs which are representative of a well-known cluster of privileged tricyclic scaffolds. The cyclization of secondary *o*-hydroxybenzene sulfonamides with a range of (hetero)aromatic bis-electrophilic substrates proceeded via a Smiles rearrangement that defined the product regiochemistry. The approach allows for a flexible variation of substituents in both cyclization partners and for streamlined generation of hitherto undescribed heterocyclic versions of dibenzo[*b*,*f*][1,4,5]oxathiazepine-5,5-dioxide scaffold in question. This significantly extends the boundaries of the privileged tricyclic heterocycle chemistry space compared to the earlier described approached. Unveiling the medicinal chemistry potential of the newly synthesized tricycles is underway in our group; the results of these studies will be reported in due course.

## 4. Experimental

### 4.1 General considerations

All reactions were run in oven-dried glassware in atmosphere of nitrogen. Melting points were measured with a Büchi B-520 melting point apparatus and were not corrected. Analytical thin-layer chromatography was carried out on Silufol UV-254silica gel plates using an appropriate mixtures of ethyl acetate and hexane. Compounds were visualized with short-wavelength UV light. $^{1}$H NMR and $^{13}$C NMR spectra were recorded on Bruker MSL-300 spectrometers in DMSO-$d_6$ using TMS as an internal standard. Elemental analyses were obtained at Research Institute for Chemical Crop Protection (Moscow, Russia) using Carlo ErbaStrumentazione 1106 analyzer. IR spectra were recorded on Perkin Elmer Spectrum RX1 FTIR spectrometer. All and reagents were obtained from commercial sources and used without purification. DMF was dried according to the standard procedure[20] and potassium carbonate was dried at 200 $^{o}$C for 5 hours prior to use.

### 4.2 General procedure for preparation of compound 6a,b

A solution of the respective anisole (175 mmol) in $CH_2Cl_2$ (50 mL) was added dropwise to a 0 ºC chlorosulfonic acid (100 mL) so as to maintain the reaction temperature below 5 ºC. After the addition was complete, the reaction mixture was stirred for 3 h and poured over ice. The organic phase was separated, washes with water, dried over anhydrous $Na_2SO_4$, filtered and concentrated

*in vacuo.* The residue was purified by short-path chromatography on silica gel using 10% ethyl acetate in hexanes as eluent to provide the analytically pure target compound.

*4.2.1 4-Chloro-2-methoxybenzene-1-sulfonyl chloride (**6a**).* White solid, (26.9 g, 64%); m.p. 157-160 $^{o}$C; $\delta_H$ (400 MHz, $CDCl_3$) 7.95 (1H, d, *J* 2.7 Hz, $H_{Ar}$), 7.64 (1H, dd, *J* 2.7, 9.0 Hz, $H_{Ar}$), 7.09 (1H, d, *J* 9.0 Hz, $H_{Ar}$), 4.07 (3H, s, $OCH_3$); $\delta_C$ (100.61 MHz, $CDCl_3$) 155.9, 136.9, 132.5, 129.3, 125.5, 114.6, 57.0.

*4.2.2 4-Fluoro-2-methoxybenzene-1-sulfonyl chloride (**6b**).* White solid, (27.4 g, 70%); m.p. 76-79 $^{o}$C; $\delta_H$ (400 MHz, $CDCl_3$) 7.66 (1H, dd, *J* 3.9, 7.3 Hz, $H_{Ar}$), 7.37-7.46 (1H, m, $H_{Ar}$), 7.15 (1H, dd, *J* 3.9, 9.3 Hz, $H_{Ar}$), 4.04 (3H, s, $OCH_3$); $\delta_C$ NMR (100.61 MHz, DMSO-$d_6$) 155.1 (d, *J* 245.0 Hz), 153.7 (d, *J* 2.9 Hz), 131.9 (d, *J* 7.4 Hz), 124.0 (d, *J* 22.8 Hz), 116.5 (d, *J* 27.1 Hz), 114.6 (d, *J* 7.3 Hz), 57.1.

### 4.3 General procedure for preparation of compounds 7a-d

To a solution of the respective sulfonyl chloride **6** (70 mmol) in c a mixture of the respective primary amine (71 mmol) and trimethylamine (9.9 mL, 71 mmol) was added slowly as to maintain the reaction temperature below 25 ºC. After the addition was complete, the reaction mixture was stirred for 3 h and washed with water (3 x 25 mL). The organic phase was dried over anhydrous $Na_2SO_4$, filtered and concentrated *in vacuo.* The crude product was crystallized from ethyl acetate-hexanes to give analytically pure target compounds.

*4.3.1 5-Chloro-2-methoxy-N-methylbenzenesulfonamide (**7a**).* White solid, (14.37 g, 87%); m.p. 115-118 $^{o}$C ($C_6H_{14}$/AcOEt); $\delta_H$ (400 MHz, DMSO-$d_6$) 7.63-7.71 (2H, m, $H_{Ar}$), 7.27 (1H, d, *J* 8.7 Hz, $H_{Ar}$), 7.22 (1H, br s, NH), 3.90 (3H, s, $OCH_3$), 2.42 (3H, d, *J* 5.2 Hz, $NH\underline{CH_3}$); $\delta_C$ (100.61 MHz, DMSO-$d_6$) 155.7, 134.4, 129.5, 128.7, 124.2, 115.4, 57.1, 29.2; HRMS (ESI): $MH^+$, found 237.0043. $[C_8H_{10}ClNO_3S]^+$ requires 237.0040.

*4.3.2 5-Chloro-N-isopropyl-2-methoxybenzenesulfonamide (**7b**).* White solid, (17.00 g, 92%); m.p. 110-113 $^{o}$C ($C_6H_{14}$/AcOEt); $\delta_H$ (400 MHz, DMSO-$d_6$) 7.69-7.62 (2H, m, $H_{Ar}$), 7.36 (1H, d, *J* 7.8 Hz, NH), 7.25 (1H, d, *J* 7.8 Hz, $H_{Ar}$), 3.91 (3H, s, $OCH_3$), 3.23-3.32 (1H, m, $\underline{CH}(CH_3)_2$), 0.95 (6H, d, *J* 6.5 Hz, $CH(\underline{CH_3})_2$); $\delta_C$ (100.61 MHz, DMSO-$d_6$) 155.6, 134.1, 131.1, 128.9, 124.0, 115.3, 56.9, 45.9, 23.5 (2C); HRMS (ESI): $MH^+$, found 265.0349. $[C_{10}H_{14}ClNO_3S]^+$ requires 265.0353.

*4.3.3 N-Ethyl-5-fluoro-2-methoxybenzenesulfonamide (**7c**).* White solid, (12.07 g, 74%); m.p. 111-114 $^{o}$C ($C_6H_{14}$/AcOEt); $\delta_H$ (400 MHz, DMSO-$d_6$) 7.44-7.51 (2H, m, $H_{Ar}$), 7.35 (1H, t, *J* 11.4 Hz, NH), 7.22-7.28 (1H, m, $H_{Ar}$), 3.89 (3H, s, $OCH_3$), 2.79-2.88 (2H, m, $\underline{CH_2}CH_3$), 0.94 (3H, t, *J* 14.4 Hz, $CH_2\underline{CH_3}$); $\delta_C$ (100.61 MHz, DMSO-$d_6$) 155.4 (d, *J* 240.0 Hz), 153.4, 130.0 (d,

*J* 6.4 Hz), 121.0 (d, *J* 22.7 Hz), 116.3 (d, *J* 25.4 Hz), 115.1 (d, *J* 7.3 Hz), 57.1, 38.1, 15.3; HRMS (ESI): $MH^+$, found 234.0558. $[C_9H_{12}FNO_3S]^+$ requires 234.0555.

*4.3.4 N-Cyclopropyl-5-fluoro-2-methoxybenzenesulfonamide* ***(7d)***. White solid, (14.41 g, 84%); m.p. 132-134 $^oC$ ($C_6H_{14}$/AcOEt); $\delta_H$ (400 MHz, DMSO-$d_6$) 7.71 (1H, d, *J* 2.8 Hz, NH), 7.46-7.55 (2H, m, $H_{Ar}$), 7.26 (1H, dd, *J* 2.8, 8.8 Hz, $H_{Ar}$), 3.88 (3H, s, $OCH_3$), 2.10-2.17 (1H, m, $CH_{(cyclopropyl)}$), 0.37-0.47 (4H, m, $2CH_{2\ (cyclopropyl)}$); $\delta_C$ (100.61 MHz, $CDCl_3$) 163.0 (d, *J* 239.5 Hz), 153.4 (d, *J* 1.8 Hz), 129.2 (d, *J* 6.2 Hz), 121.3 (d, *J* 22.74 Hz), 116.8 (d, *J* 26.0 Hz), 115.1 (d, *J* 7.7 Hz), 57.1, 24.4, 5.4 (2C); HRMS (ESI): $MH^+$, found 246.0557. $[C_{10}H_{12}FNO_3S]^+$ requires 246.0555.

**4.4 General procedure for preparation of compounds 5a-d**

A solution of the respective sulfonamide **7** (25 mmol) in $CH_2Cl_2$ (50 mL) was cooled to 0 ºC and treated dropwise with 1M solution of $BBr_3$ in $CH_2Cl_2$ (30 mL, 30 mmol) so that the reaction temperature remained below 5 ºC. After the addition was complete, the reaction mixture was stirred at that temperature for 5 h. Methanol (2 mL) was added, the mixture stirred for 5 min, washed with water (50 mL), dried over anhydrous $Na_2SO_4$, filtered, passed through a short plug of silica gel and concentrated *in vacuo.* The residue was crystallized from the solvent indicated to provide analytically pure target compound.

*4.4.1 5-Chloro-2-hydroxy-N-methylbenzenesulfonamide* ***(5a)***.[19] White solid, (4,052 mg, 73%); m.p. 94-97 $^oC$ ($C_6H_{14}$/AcOEt); $\delta_H$ (400 MHz, DMSO-$d_6$) 11.00 (1H, s, OH), 7.58 (1H, d, *J* 2.7 Hz, $H_{Ar}$), 7.48 (1H, dd, *J* 2.7, 8.7 Hz, $H_{Ar}$), 6.99-7.09 (2H, m, $H_{Ar}$ + NH), 2.42 (3H, d, *J* 4.8 Hz, $CH_3$); $\delta_C$ (100.61 MHz, $CDCl_3$) 154.5, 134.2, 129.1, 126.7, 122.5, 119.4, 29.2; HRMS (ESI): $MNa^+$, found 244.9708. $[C_7H_7ClNNaO_3S]^+$ requires 244.9703.

*4.4.2 5-Chloro-2-hydroxy-N-isopropylbenzenesulfonamide* ***(5b)***. Dark oil, (5,062 mg, 81%); $\delta_H$ (400 MHz, DMSO-$d_6$) 10.96 (s, 1H, OH), 7.59 (1H, d, *J* 2.7 Hz, $H_{Ar}$), 7.47 (1H, dd, *J* 2.7, 8.7 Hz, $H_{Ar}$), 7.18 (1H, d, *J* 7.6 Hz, NH), 7.01 (1H, d, *J* 8.7 Hz, $H_{Ar}$), 3.23-3.36 (1H, m, $\underline{CH}(CH_3)_2$), 0.98 (6H, d, *J* 6.4 Hz, $CH(\underline{CH_3})_2$); $\delta_C$ (100.61 MHz, $CDCl_3$) 154.5, 133.9, 129.1, 128.6, 122.4, 119.4, 45.9, 23.6 (2C); HRMS (ESI): $MNa^+$, found 273.0021. $[C_9H_{11}ClNNaO_3S]^+$ requires 273.0016.

*4.4.3 N-Ethyl-5-fluoro-2-hydroxybenzenesulfonamide* ***(5c)***. Yellow solid, (3,723 mg, 68%); m.p. 54-57 $^oC$ ($C_6H_{14}$); $\delta_H$ (400 MHz, DMSO-$d_6$) 10.63 (1H, s, OH), 7.38 (1H, dd, *J* 3.3, 8.6 Hz, $H_{Ar}$), 7.27-7.33 (1H, m, $H_{Ar}$), 7.19 (1H, t, *J* 11.5 Hz, NH), 6.99 (1H, dd, *J* 4.3, 8.6 Hz, $H_{Ar}$), 2.79-2.88 (2H, m, $\underline{CH_2}CH_3$), 0.96 (3H, t, *J* 14.4 Hz, $CH_2\underline{CH_3}$); $\delta_C$ (100.61 MHz, $CDCl_3$) 154.5 (d, *J* 236.9 Hz), 151.9 (d, *J* 2.2 Hz), 127.4 (d, *J* 6.6 Hz), 121.1 (d, *J* 22.7 Hz), 118.9 (d, *J* 7.3 Hz),

115.6 (d, *J* 25.7 Hz), 38.0, 15.3; HRMS (ESI): $MNa^+$, found 242.0221. $[C_8H_9FNNaO_3S]^+$ requires 242.0218.

*4.4.4 N-Cyclopropyl-5-fluoro-2-hydroxybenzenesulfonamide* ***(5d)****.* Yellow solid, (4,042 mg, 70%); m.p. 118-121 $^oC$ ($C_6H_{14}$); $\delta_H$ (400 MHz, DMSO-$d_6$) 10.63 (1H, s, OH), 7.57 (1H, d, *J* 2.7 Hz, NH), 7.41 (1H, dd, *J* 2.7, 8.7 Hz, $H_{Ar}$), 7.29-7.36 (1H, m, $H_{Ar}$), 7.01 (1H, dd, *J* 4.4, 8.7 Hz, $H_{Ar}$), 2.10-2.17 (1H, m, $CH_{(cyclopropyl)}$), 0.42 (4H, d, *J* 5.2 Hz, $2CH_{2\ (cyclopropyl)}$); $\delta_C$ (100.61 MHz, $CDCl_3$) 154.2 (d, *J* 237.0 Hz), 152.0 (d, *J* 2.2 Hz), 126.7 (d, *J* 6.6 Hz), 121.5 (d, *J* 22.8 Hz), 118.9 (d, *J* 7.3 Hz), 116.1 (d, *J* 25.7 Hz), 24.4, 5.4 (2C); HRMS (ESI): $MNa^+$, found 254.0225. $[C_9H_9FNNaO_3S]^+$ requires 254.0218.

### 4.5 General procedure for preparation of compounds 8a-n

The respective 2-hydroxybenzene sulfonamide **5** (2 mmol) and 1,2-dihaloarene (1-halo-2-nitroarene) partner **9** (2 mmol) were combined in anhydrous DMF (7 mL) with freshly calcinated $K_2CO_3$ (829 mg, 6 mmol) and the mixture was kept, with stirring, at the temperature and for the time period indicated in Table 2. DMF was removed *in vacuo* and the residue was treated with water (10 mL), which caused a viscous oil to separate. It was extracted with $CH_2Cl_2$ (5 mL), the organic layer was separated, dried over anhydrous $Na_2SO_4$, filtered, and concentrated *in vacuo.* The residue was purified by column chromatography on silica gel using an appropriate gradient of $CH_2Cl_2$ in hexanes as eluent.

*4.5.1 3-Chloro-6-methyl-9-nitro-6H-dibenzo[b,f][1,4,5]oxathiazepine 5,5-dioxide* ***(8a)****.* Yellow solid, (564 mg, 83%); m.p. 181-184 $^oC$; [Found: C, 45.69; H, 2.67; N, 8.26; S, 9.43. $C_{13}H_9ClN_2O_5S$ requires C,45.82; H, 2.66; N, 8.22; S, 9.41]; $\delta_H$ (400 MHz, DMSO-$d_6$) 8.25 (1H, d, *J* 2.7 Hz, $H_{Ar}$), 8.11 (1H, dd, *J* 2.7, 8.7 Hz, $H_{Ar}$), 7.87 (1H, dd, *J* 2.7, 8.7 Hz, $H_{Ar}$), 7.83 (1H, d, *J* 2.5 Hz, $H_{Ar}$), 7.76 (1H, d, *J* 8.7 Hz, $H_{Ar}$), 7.67 (1H, d, *J* 8.7 Hz, $H_{Ar}$), 3.26 (3H, s, $CH_3$); $\delta_C$ (100.61 MHz, $CDCl_3$) 150.5, 149.4, 147.1, 138.0, 136.1, 132.4, 130.3, 129.9, 127.3, 125.5, 121.1, 118.4, 39.7.

*4.5.2 Methyl 8-chloro-11-methyl-11H-benzo[b]pyrido[2,3-f][1,4,5]oxathiazepine-3-carboxylate 10,10-dioxide* ***(8b)****.* White solid, (540 mg 76%); m.p. 164-167 $^oC$; [Found: C, 47.26; H, 3.13; N, 7.94; S, 9.05. $C_{14}H_{11}ClN_2O_5S$ requires C, 47.40; H, 3.13; N, 7.90; S, 9.04]; $\delta_H$ (400 MHz, DMSO-$d_6$) 8.72 (1H, d, *J* 1.7 Hz, $H_{Py}$), 8.23 (1H, d, *J* 1.7 Hz, $H_{Py}$), 7.90 (1H, dd, *J* 2.6, 8.7 Hz, $H_{Ar}$), 7.83 (1H, d, *J* 2.6 Hz, $H_{Ar}$), 7.68 (1H, d, *J* 8.7 Hz, $H_{Ar}$), 3.90 (3H, s, $COOCH_3$), 3.39 (3H, s,

$NCH_3$); $\delta_C$ (100.61 MHz, DMSO-$d_6$) 164.3, 149.4, 146.6, 144.9, 142.7, 136.8, 133.8, 131.8, 130.2, 126.1, 125.6, 124.4, 53.1, 35.8.

*4.5.3 8-Chloro-2,5-dimethyl-2,5-dihydro-1H-benzo[b]pyridazino[4,5-f][1,4,5]oxathiazepin-1-one 6,6-dioxide (**8c**).* White solid, (479 mg 73%); m.p. 189-192 $^oC$; [Found: C, 43.84; H, 3.08; N, 12.89; S, 9.80. $C_{12}H_{10}ClN_3O_4S$ requires C, 43.98; H, 3.08; N, 12.82; S, 9.78]; $\delta_H$ (400 MHz, DMSO-$d_6$) 8.00 (1H, s, $H_{pyridazine}$), 7.87 (1H, dd, *J* 2.7, 8.6 Hz, $H_{Ar}$), 7.82 (1H, d, *J* 2.7 Hz, $H_{Ar}$), 7.50 (1H, d, *J* 8.6 Hz, $H_{Ar}$), 3.68 (3H, s, $CH_{3pyridazine}$), 3.12 (3H, s, $NCH_3$); $\delta_C$ (100.61 MHz, DMSO-$d_6$) 148.5, 145.8, 143.7, 139.5, 136.4, 133.8, 129.8, 126.8, 126.4, 125.2, 55.9, 22.3.

*4.5.4 8-Chloro-5-methyl-5H-benzo[b]pyrazino[2,3-f][1,4,5]oxathiazepine 6,6-dioxide (**8d**).* White solid, (423 mg, 71%); m.p. 132-135 $^oC$; [Found: C, 44.24; H, 2.71; N, 14.18; S, 10.79. $C_{11}H_8ClN_3O_3S$ requires C, 44.38; H, 2.71; N, 14.11; S, 10.77]; $\delta_H$ (400 MHz, DMSO-$d_6$) 8.38 (1H, d, *J* 2.2 Hz, $H_{pyrazine}$), 8.28 (1H, d, *J* 2.2 Hz, $H_{pyrazine}$), 7.87 (1H, dd, *J* 2.7, 8.6 Hz, $H_{Ar}$), 7.83 (1H, d, *J* 2.7 Hz, $H_{Ar}$), 7.59 (1H, d, *J* 8.6 Hz, $H_{Ar}$), 3.32 (s, 3H, $NCH_3$); $\delta_C$ (100.61 MHz, DMSO-$d_6$) 149.1, 148.3, 139.8, 139.7, 139.5, 136.5, 132.9, 129.9, 126.2, 125.6, 36.0.

*4.5.5 8-Chloro-11-isopropyl-3-nitro-11H-benzo[b]pyrido[2,3-f][1,4,5]oxathiazepine 10,10-dioxide (**8e**).* Yellow solid, (629 mg, 85%); m.p. 144-147 $^oC$; [Found: C, 48.71; H, 3.56; N, 7.63; S, 8.71. $C_{14}H_{12}ClN_3O_5S$ requires C,48.85; H, 3.55; N, 7.60; S, 8.69]; $\delta_H$ (400 MHz, DMSO-$d_6$) 9.10 (1H, d, *J* 2.5 Hz, $H_{Py}$), 8.60 (1H, d, *J* 2.5 Hz, $H_{Py}$), 7.85-7.93 (2H, m, $2H_{Ar}$), 7.61 (1H, d, *J* 8.7 Hz, $H_{Ar}$), 4.32-4.44 (1H, m, $\underline{CH}(CH_3)_2$), 1.21 (6H, d, *J* 6.9 Hz, $CH(\underline{CH_3})_2$); $\delta_C$ (100.61 MHz, DMSO-$d_6$) 155.9, 148.4, 142.3 (2C), 136.8, 135.7, 131.4, 129.9, 127.8, 127.7, 125.5, 40.1, 39.2 (2C).

*4.5.6 3-Chloro-6-isopropyl-6H-dibenzo[b,f][1,4,5]oxathiazepine-9-carbonitrile 5,5-dioxide (**8f**).* White solid, (438 mg, 63%); m.p. 147-150 $^oC$; [Found: C, 54.93; H, 3.76; N, 8.07; S, 9.21. $C_{16}H_{13}ClN_2O_3S$ requires C, 55.09; H, 3.76; N, 8.03; S, 9.19]; $\delta_H$ (400 MHz, DMSO-$d_6$) 8.05 (1H, d, *J* 1.7 Hz, $H_{Ar}$), 7.77-7.87 (3H, m, $3H_{Ar}$), 7.68 (1H, d, *J* 8.5 Hz, $H_{Ar}$), 7.51 (1H, d, *J* 8.5 Hz, $H_{Ar}$), 4.26-4.38 (1H, m, $\underline{CH}(CH_3)_2$), 1.11 (6H, d, *J* 6.6 Hz, $CH(\underline{CH_3})_2$); $\delta_C$ (100.61 MHz, DMSO-$d_6$) 154.9, 149.8, 135.3, 134.5, 133.2, 132.0, 130.5, 129.2, 127.2, 127.1, 124.8, 117.7, 113.7, 54.7, 22.0 (2C).

*4.5.7 8-Chloro-5-isopropyl-2-methyl-2,5-dihydro-1H-benzo[b]pyridazino[4,5-f][1,4,5]oxathiazepin-1-one 6,6-dioxide (**8g**).* White solid, (533 mg, 75%); m.p. 159-162 $^oC$; [Found: C, 47.12; H, 3.97; N, 11.87; S, 9.03. $C_{14}H_{14}ClN_3O_4S$ requires C, 47.26; H, 3.97; N, 11.81; S, 9.01]; $\delta_H$ (400 MHz, DMSO-$d_6$) $\delta$ 7.87 (1H, d, *J* 2.6 Hz, $H_{Ar}$), 7.59 (1H, s, $H_{pyridazine}$), 7.56 (1H, dd, *J* 2.6, 8.8 Hz, $H_{Ar}$), 7.46 (1H, d, *J* 8.8 Hz, $H_{Ar}$), 4.15-4.27 (1H, m, $\underline{CH}(CH_3)_2$), 3.85 (3H, s, $CH_{3\ pyridazine}$), 1.17 (6H, d, *J* 6.7, $CH(\underline{CH_3})_2$); $\delta_C$ (100.61 MHz, DMSO-$d_6$) $\delta$ 155.9, 148.1, 146.7, 137.7, 136.3, 132.7, 129.5, 127.6, 124.8, 123.6, 55.1, 40.6, 21.8 (2C).

*4.5.8 8-Chloro-5-isopropyl-5H-benzo[b]pyrazino[2,3-f][1,4,5]oxathiazepine 6,6-dioxide (**8h**).* White solid, (442 mg, 68%); m.p. 182-185 $^{o}$C; [Found: C, 47.79; H, 3.72; N, 12.96; S, 9.86. $C_{13}H_{12}ClN_3O_3S$ requires C, 47.93; H, 3.71; N, 12.90; S, 9.84]; $\delta_H$ (400 MHz, DMSO-$d_6$) $\delta$ 8.49 (1H, d, *J* 2.5 Hz, $H_{pyrazine}$), 8.45 (1H, d, *J* 2.5 Hz, $H_{pyrazine}$), 7.84-7.90 (2H, m, $H_{Ar}$), 7.60 (1H, d, *J* 9.0 Hz, $H_{Ar}$), 4.18-4.30 (1H, m, $\underline{CH}(CH_3)_2$), 1.16 (6H, d, *J* 6.8 Hz, $CH(\underline{CH_3})_2$); $\delta_C$ (75 MHz, DMSO-$d_6$) 152.2, 148.3, 142.2, 140.2, 137.0, 136.2, 132.9, 129.4, 126.6, 125.0, 55.2, 22.3 (2C).

*4.5.9 11-Ethyl-8-fluoro-3-nitro-11H-benzo[b]pyrido[2,3-f][1,4,5]oxathiazepine 10,10-dioxide (**8i**).* Yellow solid, (542 mg, 80%); m.p. 149-152 $^{o}$C; [Found: C, 45.88; H, 2.97; N, 12.45; S, 9.47. $C_{13}H_{10}FN_3O_5S$ requires C, 46.02; H, 2.97; N, 12.38; S, 9.45]; $\delta_H$ (400 MHz, DMSO-$d_6$) 9.05 (1H, d, *J* 2.2 Hz, $H_{Py}$), 8.64 (1H, d, *J* 2.2 Hz, $H_{Py}$), 7.71-7.80 (3H, m, $H_{Ar}$), 4.09 (2H, dd, *J* 7.0, 13.9 Hz, $\underline{CH_2}CH_3$), 1.16 (3H, t, *J* 7.0 Hz, $CH_2\underline{CH_3}$); $\delta_C$ (75 MHz, DMSO-$d_6$) 158.8 (d, *J* 248.0 Hz), 147.4, 146.5 (d, *J* 2.9 Hz), 141.8 (d, *J* 11.7 Hz), 140.1, 134.8 (d, *J* 8.1 Hz), 127.2 (2C), 125.9 (d, *J* 8.1 Hz), 124.0 (d, *J* 23.5 Hz), 113.6 (d, *J* 27.1 Hz), 45.1, 15.2.

*4.5.10 6-Ethyl-3,8-difluoro-6H-dibenzo[b,f][1,4,5]oxathiazepine-9-carbonitrile 5,5-dioxide (**8j**).* White solid, (416 mg, 62%); m.p. 143-146 $^{o}$C; [Found: C, 53.41; H, 3.00; N, 8.37; S, 9.55. $C_{15}H_{10}F_2N_2O_3S$ requires C, 53.57; H, 3.00; N, 8.33; S, 9.53]; $\delta_H$ (400 MHz, DMSO-$d_6$) 8.13 (1H, d, *J* 6.4 Hz, $H_{Ar}$), 7.84 (1H, d, *J* 9.5 Hz, $H_{Ar}$), 7.62-7.74 (2H, m, $H_{Ar}$), 7.54-7.60 (1H, dd, *J* 4.4, 9.5 Hz, $H_{Ar}$), 3.76 (2H, dd, *J* 7.1, 13.9 Hz, $\underline{CH_2}CH_3$), 0.99 (3H, t, *J* 7.1 Hz, $CH_2\underline{CH_3}$); $\delta_C$ (75 MHz, DMSO-$d_6$) 160.4 (d, *J* 133.5 Hz), 157.9 (d, *J* 125.4 Hz), 148.8 (d, *J* 2.9 Hz), 147.1 (d, *J* 2.9 Hz), 136.0 (d, *J* 11.0 Hz), 133.7 (d, *J* 6.6 Hz), 127.9, 125.3 (d, *J* 8.1 Hz), 123.1 (d, *J* 22.7 Hz), 118.0 (d, *J* 22.7 Hz), 114.5 (d, *J* 26.4 Hz), 113.2, 101.0 (d, *J* 16.9 Hz), 47.4, 13.8.

*4.5.11 11-Ethyl-8-fluoro-3-(trifluoromethyl)-11H-benzo[b]pyrido[2,3-f][1,4,5]oxathiazepine 10,10-dioxide (**8k**).* Yellow solid, (470 mg, 65%); m.p. 156-159 $^{o}$C; [Found: C, 46.88; H, 2.77; N, 7.45; S, 8.47. $C_{14}H_{10}F_4N_2O_3S$ requires C, 46.41; H, 2.78; N, 7.73; S, 8.85]; $\delta_H$ (400 MHz, DMSO-$d_6$) 8.65 (1H, d, *J* 1.2 Hz, $H_{Py}$), 8.28 (1H, d, *J* 1.2 Hz, $H_{Py}$), 7.64-7.75 (3H, m, $H_{Ar}$), 4.03 (2H, dd, *J* 7.0, 14.0 Hz, $\underline{CH_2}CH_3$), 1.12 (3H, t, *J* 7.0 Hz, $CH_2\underline{CH_3}$); $\delta_C$ (75 MHz, DMSO-$d_6$) 156.2 (d, *J* 247.9 Hz), 146,4 (d, *J* 2.9 Hz), 146.1, 143.0, 141.2 (m), 135.0 (d, *J* 8.0 Hz), 129.3 (m), 125.7 (d, *J* 8.0 Hz), 123.8 (d, *J* 23.5 Hz), 123.3 (d, *J* 272.9 Hz), 123.4, 113.4 (d, *J* 27.2 Hz), 45.1, 15.0.

*4.5.12 6-Cyclopropyl-3-fluoro-6H-dibenzo[b,f][1,4,5]oxathiazipine-7-carbonitrile 5,5-dioxide (**8l**).* White solid, (442 mg, 67%); m.p. 195-197 $^{o}$C; [Found: C, 58.00; H, 3.36; N, 8.52; S, 9.72. $C_{16}H_{11}FN_2O_3S$ requires C, 58.18; H, 3.36; N, 8.48; S, 9.71]; $\delta_H$ (400 MHz, DMSO-$d_6$) 7.60-7.67 (2H, m, $2H_{Ar}$), 7.47-7.57 (2H, m, $2H_{Ar}$), 7.34-7.40 (1H, m, $H_{Ar}$), 7.25-7.32 (1H, m, $H_{Ar}$), 3.08-3.16 (1H, m, $CH_{cyclopropyl}$), 1.31-1.40 (1H, m, $CH_2$ $_{cyclopropyl}$), 0.87-1.04 (2H, m, $CH_2$ $_{cyclopropyl}$), 0.61-0.71 (1H, m, $CH_2$ $_{cyclopropyl}$); $\delta_C$ (75 MHz, DMSO-$d_6$) 158.6 (d, *J* 246.5 Hz), 155.8, 147.7 (d,

*J* 2.9 Hz), 134.4, 132.3 (d, *J* 52.8 Hz), 131.6 (d, *J* 7.0 Hz), 128.6, 125.4 (d, *J* 8.1 Hz), 123.0 (d, *J* 23.5 Hz), 115.9, 115.3 (2C), 115.0, 32.7, 9.5, 5.6.

*4.5.13 11-Cyclopropyl-8-fluoro-3-(trifluoromethyl)-11H-benzo[b]pyrido[2,3-f][1,4,5]oxathiazepine 10,10-dioxide (**8m**).* White solid, (531 mg, 71%); m.p 180-183 $^{o}$C; [Found: C, 47.99; H, 2.70; N, 7.52; S, 8.58. $C_{15}H_{10}F_4N_2O_3S$ requires C, 48.13; H, 2.69; N, 7.48; S, 8.56]; $\delta_H$ (400 MHz, DMSO-$d_6$) $\delta$ 8.73 (1H, s, $H_{Py}$), 8.28 (1H, s, $H_{Py}$), 7.65-7.76 (2H, m, $H_{Ar}$), 7.58 (1H, dd, *J* 4.3, 8.9 Hz, $H_{Ar}$), 3.03-3.10 (1H, m, $CH_{cyclopropyl}$), 0.83-0.91 (2H, m, $CH_{2\ cyclopropyl}$), 0.58-0.66 (2H, m, $CH_{2\ cyclopropyl}$); $\delta_C$ (75 MHz, DMSO-$d_6$) 161.9, 158.6 (d, *J* 248.7 Hz), 152.4, 146.1, 145,3 (d, *J* 2.9 Hz), 144.6, 138.2 (m), 135.0 (d, *J* 8.1 Hz), 125.3 (d, *J* 8.1 Hz), 123.9 (d, *J* 23.2 Hz), 123.3 (d, *J* 272.9 Hz), 113.4 (d, *J* 27.2 Hz), 30.4, 9.4 (2C).

*4.5.14 Methyl 11-cyclopropyl-8-fluoro-11H-benzo[b]pyriddo[2,3-f][1,4,5]oxathiazepine-3-carboxylate 10,10-dioxide (**8n**).* White solid, (502 mg, 69%); m.p. 174-176 $^{o}$C; [Found: C, 52.59; H, 3.60; N, 7.73; S, 8.82. $C_{16}H_{13}FN_2O_5S$ requires C, 52.74; H, 3.60; N, 7.69; S, 8.80]; $\delta_H$ (400 MHz, DMSO-$d_6$) 8.85 (1H, d, *J* 2.0 Hz, $H_{Py}$), 8.44 (1H, d, *J* 2.0 Hz, $H_{Py}$), 7.38-7.46 (2H, m, $H_{Ar}$), 7.02 (1H, dd, *J* 4.3, 9.9 Hz, $H_{Ar}$), 3.90 (3H, s, $COOCH_3$), 2.87-2.94 (1H, m, $CH_{cyclopropyl}$), 0.57-0.79 (4H, m, $CH_{2\ cyclopropyl}$); $\delta_C$ (75 MHz, DMSO-$d_6$) 162.7, 160.0 (d, *J* 249.1 Hz), 151.5, 146.1 (d, *J* 2.9 Hz), 145.9 (d, *J* 33.4 Hz), 136.6, 134.9 (d, *J* 8.1 Hz), 125.1 (d, *J* 8.4 Hz), 124.2 (d, *J* 23.5 Hz), 122.5, 119.7, 113.9 (d, *J* 27.5 Hz), 44.6, 25.3, 15.1.

## Acknowledgement

We gratefully acknowledge support from the Russian Scientific Fund (Project Grant 14-50-00069). NMR studies were performed at the Research Centre for Magnetic Resonance of Saint Petersburg State University Research Park.

## Supplementary data

Supplementary data contains copies of $^{1}$H and $^{13}$C NMR spectra and can be found at http://dx.doi.org/xxx.

## Referenced and notes

1. Evans, B. E.; Rittle, K. E.; Bock, M. G.; DiPardo, R. M.; Freidinger, R. M.; Whitter, W. L.; Lundell, G. F.; Veber D. F.; Anderson, P. S. *J. Med. Chem.* **1988**, *31*, 2235-2246.
2. Welsch, M. E.; Snyder, S. A.; Stockwell, B. R. *Curr. Opin. Chem. Biol.* **2010**, *14*, 347-361.
3. Steiner, G.; Franke, A.; Hadicke, E.; Lenke, D.; Teschendorf, H. J.; Hofmann, H. P.; Kreiskott, H.; Worstmann, W. *J. Med. Chem.* **1986**, *29*, 1877-1888.

4. Fedi, V.; Guidi, A.; Altamura, M. *Mini-Rev. Med. Chem.*, **2008**, *8*, 1464-1484.
5. Sapegin, A. V.; Kalinin, S. A.; Smirnov, A. V.; Dorogov, M. V.; Krasavin, M. *Synthesis* **2012**, *44*, 2401-2407.
6. Sapegin, A.V.; Kalinin, S. A.; Smirnov, A. V.; Dorogov, M. V.; Krasavin, M. *Tetrahedron* **2014**, *70*, 1077-1083.
7. Sapegin, A.V.; Kalinin, S. A.; Smirnov, A. V.; Dorogov, M. V.; Krasavin, M. *Eur. J. Org. Chem.* **2015**, 1333-1340.
8. Karamysheva, K.; Reutskaya, E.; Sapegin, A.; Dorogov, M.; Krasavin, M. *Tetrahedron Lett.* **2015**, *56*, 5632-5636.
9. Tomita, K.; Taoda, Y.; Iwaki, T.; Kawasuji, T.; Akiyama, T.; Sugiyama, S.; Tamura, Y.; Iwatsu, M. International Patent Appl. WO 2014119636A1; *Chem. Abstr.* **2014**, *161*, 320990.
10. Banka, A. L.; Botyanszki, J.; Dickerson, S. H.; Duan, M.; Leivers, M. R.; Mcfadyen, R. B.; Moore, C. B.; Redman, A. M.; Shotwell, J. B.; Tai, V. W.-F.; Tallant, M. D.; Xue, J. International Patent Appl. WO 2012037108A1; *Chem. Abstr.* **2012**, *156*, 450227.
11. Umemoto, S.; Chika, T. Japanese Patent JP46003060B4; *Chem. Abstr.* **1971**, *74*, 125748.
12. Rocher, J.-P. International Patent Appl. WO9730038A1; *Chem. Abstr.* **1997**, *127*, 234329.
13. Shapiro, G.; Moncuso, J.; Pierre, T.; Leit, S.; Deziel, R.; David, S.; Richard, C.; Chantigny, Y. A.; Patrick, B. International Patent Appl. WO2008055068A2; *Chem. Abstr.* **2008**, *148*, 538314.
14. Abramovitch, R. A.; Azogu, C. I.; McMaster, I. T. *J. Am. Chem. Soc.* **1969**, *91*, 1219-1220.
15. Abramovitch, R. A.; Azogu, C. I.; McMaster, I. T.; Vanderpool, D. P. *J. Org. Chem.* **1978**, *43*, 1218-1226.
16. Nagarajan, R.; Ranga, V.; Venkarlu, A.; Shah, R. K. *Indian J. Chem.* **1974**, *12*, 252-254.
17. Bychenkov, A. S.; Tarasov, A. V.; Pisarev, P. K.; Feldblum, V. Sh.; Moskvichev, Yu. A. *Chem. Heterocycl. Compd.* **2008**, *45*, 1391-1395.
18. Altamura, M.; Fedi, V.; Gianotti, D.; Paoli, P.; Rossi, P. *New. J. Chem.* **2009**, *33*, 2219-2231.
19. Blumberg, L. C.; Brown, M. F.; McGlynn, M. A.; Poss, C. S.; Gladue, R. P. PCT International Appl. WO2001072728A2; *Chem. Abstr.* **2001**, *135*, 272991.
20. SciFinder® search performed of August 15, 2016.
21. Varano, F.; Catarzi, D.; Colotta, V.; Cecchi, L.; Filacchioni, G.; Galli, A.; Costagli, C. *Arch. Pharm. Pharm. Med. Chem.***1996**, *329*, 529.