The Mannich reaction in the synthesis of N,S-containing heterocycles
11.* Synthesis of 3,3´-(1,4-phenylene)-bis(8-aryl-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitriles)

V. V. Dotsenko,[a,b] S. G. Krivokolysko,[a] and V. P. Litvinov[c]†*

[a] *"ChemEx" Laboratory Vladimir Dal´ East-Ukrainian National University, 20 a kv. Molodezhnyi, 91034 Lugansk, Ukraine. E-mail: Victor_Dotsenko@bigmir.net*
[b] *Physico-chemical Department, State Enterprise "Luganskstandartmetrology", 50 ul. Timiryazeva, 91021 Lugansk, Ukraine*
[c] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation*

N-Methylmorpholinium 4-aryl-3-cyano-6-oxo-1,4,5,6-tetrahydropyridine-2-thiolates readily undergo the Mannich reaction with *p*-phenylenediamines and excess formaldehyde in the absence of a catalyst to form 3,3´-(1,4-phenylene)-bis(8-aryl-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitriles) in moderate yields (24—56%).

Key words: the Mannich reaction, tetrahydropyridine-2-thiolates, aminomethylation, pyrido[2,1-*b*][1,3,5]thiadiazines, three-component reaction.

One of the most convenient methods for the preparation of 1,3,5-thiadiazine fused ring derivatives is the "double" Mannich reaction of 2-mercaptoazoles (-azines) with formaldehyde and primary amines.[1] Such an approach was used for the synthesis of substituted pyrido[2,1-*b*][1,3,5]thiadiazines[2], bis(pyrido[2,1-*b*][1,3,5]thiadiazin-7-yl)methanes,[3] 1,2,4-triazolo[3,4-*b*][1,3,5]thiadiazines,[4] imidazo[2,1-*b*][1,3,5]thiadiazines,[5,6] 1,2,4-triazino[3,2-*b*][1,3,5]thiadiazines,[5] thiazolo[3´,4´:1,5][1,2,4]-triazolo[3,4-*b*][1,3,5]thiadiazines,[7] 1,3,5-thiadiazino-[3,2-*a*]benzimidazoles,[8] cyclopenta[*g*]pyrido[2,1-*b*][1,3,5]-thiadiazines,[9] pyrimido[2,1-*b*][1,3,5]thiadiazines,[10] and pyrimido[4,3-*b*][1,3,5]thiadiazines.[11]

In continuation of the works in the field of chemistry of partially hydrogenated pyridine-2-chalcogenones,[12] we studied reactions of *N*-methylmorpholinium 4-aryl-3-cyano-6-oxo-1,4,5,6-tetrahydropyridine-2-thiolates (**1**) with formaldehyde and *p*-phenylenediamine. The Mannich reaction involving *p*-phenylenediamine and cyclic S,N-binucleophiles has been studied earlier using 2-mercaptobenzimidazole,[13] 2-thioxo-1,3,4-oxadiazoles,[14] and 4-mercaptoquinazoline[15] as examples. It was noted that in all the cases, only one nucleophilic center of the substrate was involved to form the products of normal aminomethylation at the nitrogen[13,14] or sulfur atom.[15]

We found that a three-component reaction of tetrahydropyridine-2-thiolates **1a—f** with 0.5 equiv. of *p*-phenylenediamine and excess of formaldehyde leads to the products of a "double" S,N-aminomethylation, *i.e.*, 3,3´-(1,4-phenylene)-bis(8-aryl-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitriles) (**2a—f**) in 24—56% yields (Scheme 1). The starting tetrahydropyridine-2-thiolates **1a—f** were synthesized by the condensation of the corresponding aromatic aldehyde, cyanothioacetamide (**3**), and the Meldrum´s acid (**4**) with subsequent cyclization of the stable Michael adduct **5**.

It is necessary to note that, in contrast to the most reactions of the "double" aminomethylation of 2-mercaptoazoles and -azines, the synthesis of compounds **2** does not require acid catalysis. Products **2** are beige or slightly yellowish finely crystalline compounds, virtually insoluble in EtOH and acetone and soluble in warm DMF or DMSO. Compounds **2** were characterized by IR and ^{1}H and ^{13}C NMR spectroscopy. The ^{1}H NMR spectra are distinguished by a double set of signals for the pyrido[2,1-*b*]-[1,3,5]thiadiazine fragment. This fact indicates that the compounds obtained are mixtures of stereoisomers. In fact, as it has been shown earlier,[16] the starting tetrahydropyridine-2-thiolates **1** and their derivatives are mixtures of (4*R*)- and (4*S*)-enantiomers in the ratio close to 1 : 1. Due to the presence of the equivalent chiral centers C(8) and C(8´), bis-pyrido[2,1-*b*][1,3,5]thiadiazines **2** can exist as a mixture of stereoisomers: an enantiomeric pair (8*S*,8´*S*)/(8*R*,8´*R*) (the structures **A** and **B**) and the (8*S*,8´*R*)-*meso*-form **C**. Thus, the double set of signals in the ^{1}H NMR

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† Deceased.

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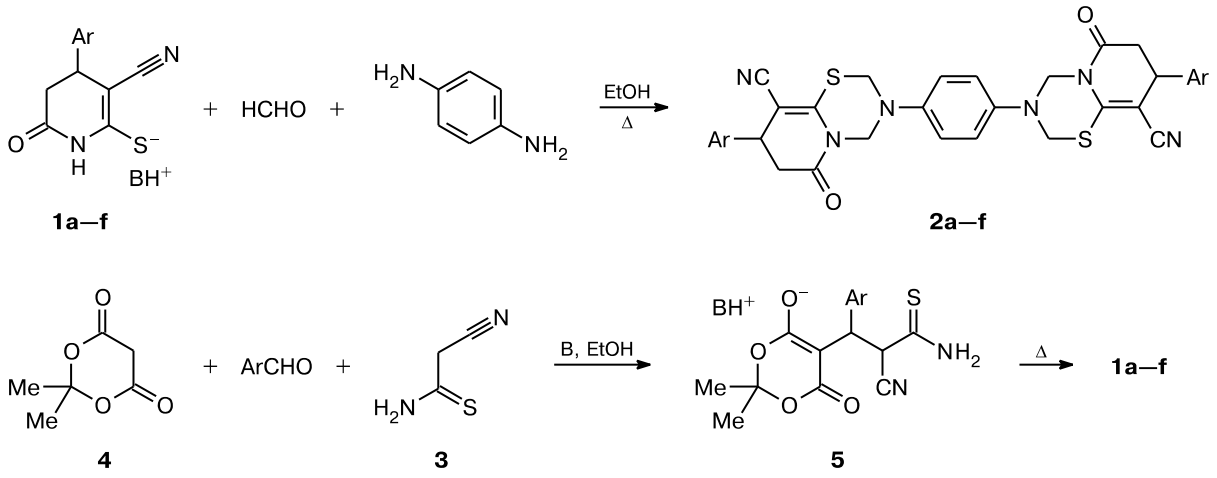
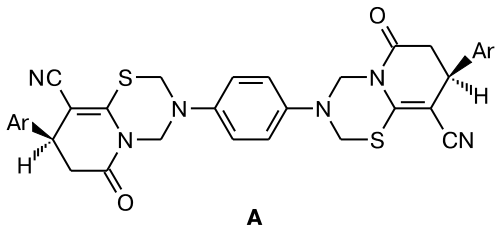
Scheme 1



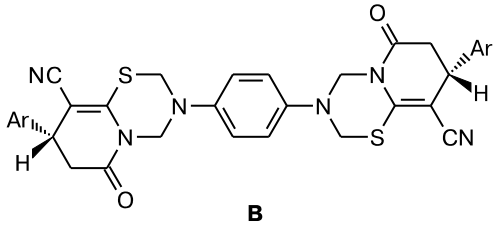
B = *N*-methylmorpholine; Ar = 1-naphthyl (**a**), 2-$MeOC_6H_4$ (**b**), 2-Cl-6-FC_6H_3 (**c**), 2-$NO_2C_6H_4$ (**d**), 4-FC_6H_4 (**e**), 2,4-$(MeO)_2C_6H_3$ (**f**)

spectra of compounds **2** is related to the resonances of the protons of the enantiomeric pair **A**+**B** and the *meso*-form **C** (the ratio ~1 : 1).



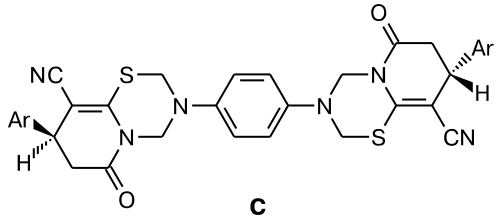
A

(8*S*,8′*S*)



B

(8*R*,8′*R*)



C

meso-(8*S*,8′*R*)

The ^{1}H NMR spectra of bis-pyrido[2,1-*b*][1,3,5]-thiadiazines **2a**—**f** exhibit two doublets of doublets for the diastereotopic protons C(7)H_2 and C(7′)H_2 at δ 2.62—2.84 (*cis*-arrangement with respect to C(8)H, ^2J = 16.0—23.0 Hz, ^3J = 3.0—7.5 Hz) and δ 2.90—3.29 (*trans*-arrangement with respect to C(8)H, ^2J = 16.0—23.0 Hz, ^3J = 7.0—8.5 Hz), as well as a multiplet (pseudotriplet) for the protons C(8)H and C(8′)H at δ 3.88—4.85 (ABX system). The protons of the 1,3,5-thiadiazine fragment produce a complicated pattern in the region δ 5.24—5.65 because of the overlap of the double doublets for the diastereotopic protons N—C(4)H_2—N, N—C(4′)H_2—N, the pair of double doublets for the protons N—C(2)H_2—S, N—C(2′)H_2—S, and the total doubling the number of peaks, corresponding to the signals of the enantiomeric pair **A**+**B** and *meso*-form **C**. It should be noted that chemical shifts of the signals for the protons N—C(4)H_2—N—C(2)H_2—S are in good agreement with the ^{1}H NMR spectroscopic data for the related pyrido[2,1-*b*][1,3,5]thiadiazine structures.[2,3,9] The protons of the 1,4-phenylene spacer (AA′BB′ system) resonate either as a broad singlet, or as a pseudodoublet due to the overlap of two unresolved peaks for the protons (**A**+**B**)/**C** in the region δ 7.07—7.19. The IR spectra of compounds **2a—f** are characterized the presence of the strong absorption bands related to the stretching vibrations of the conjugated cyano group (ν = 2188—2196 cm^{-1}) and the C=O group (ν = 1685—1707 cm^{-1}).

In conclusion, *N*-methylmorpholinium 4-aryl-3-cyano-6-oxo-1,4,5,6-tetrahydropyridine-2-thiolates under the action of *p*-phenylenediamine and formaldehyde in the absence of a catalyst readily undergo *S*,*N*-diaminomethylation to be converted to 3,3′-(1,4-phenylene)-bis(8-aryl-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]-thiadiazine-9-carbonitriles), which exist as mixtures of (8*S*,8′*S*)-, (8*R*,8′*R*)-, and (8*S*,8′*R*)-stereoisomers.

Experimental

^{1}H NMR spectra of compounds **1d**—**f** and **2a**—**d** were recorded on a Bruker DRX-500 spectrometer (500.07 MHz) in

DMSO-d_6, of compounds **2e**,**f** on a Bruker Avance II 400 spectrometer (400.13 MHz), ^{13}C NMR spectrum of compound **2c** on a Bruker DRX-500 spectrometer (125.76 MHz) in DMSO-d_6, using Me_4Si as an internal standard. IR spectra were recorded on a IKS-29 spectrophotometer in Nujol. Elemental analysis were performed on a Perkin—Elmer C,H,N-Analyzer. Purity of compounds was monitored by TLC on Silufol UV-254 plates, using acetone—hexane (1 : 1) as an eluent and visualizing in iodine vapors or under UV light. Melting points of compounds were measured on a Kofler hot-stage microscope and were not corrected. All the solvents (reagent grade) were used without additional purification. The starting *N*-methylmorpholinium tetrahydropyridine-2-thiolates **1a—c** were synthesized according to the known procedures.[17—19] Cyanothioacetamide (**3**) was obtained by the reaction of malononitrile with hydrogen sulfide following the Brunskill method.[20] The Meldrum´s acid (2,2-dimethyl-1,3-dioxane-4,6-dione, **4**) was synthesized according to the procedure described earlier.[21]

***N*-Methylmorpholinium (4*R*/4*S*)-4-aryl-3-cyano-6-oxo-1,4,5,6-tetrahydropyridine-2-thiolates 1d—f** were obtained according to a modified procedure[19] as follows: *N*-methylmorpholine (5 drops) was added to a mixture of the corresponding aromatic aldehyde (20 mmol) and cyanothioacetamide (**3**) (2.0 g, 20 mmol) in EtOH (25—30 mL) with stirring. The reaction mixture was stirred for 1 h at 20 °C, followed by addition of the Meldrum´s acid (**4**) (3.0 g, 20.8 mmol) and *N*-methylmorpholine (3.3 mL, 30 mmol). From the pale yellow solution formed, a white precipitate of the Michael adduct, *N*-methylmorpholinium 5-(3-amino-1-aryl-2-cyano-3-thioxopropyl)-2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-6-olate (**5**), was formed within 5—10 min. A suspension obtained was refluxed for 3—4 h with stirring (accompanied by the adduct dissolution and CO_2 evolution), an orange solution was half concentrated, a crystalline precipitate formed upon cooling and stirring was filtered off, washed with EtOH and acetone. The obtained thiolates **1d—f** were used in the reactions without additional purification.

***N*-Methylmorpholinium (4*R*/4*S*)-3-cyano-6-oxo-4-(2-nitrophenyl)-1,4,5,6-tetrahydropyridine-2-thiolate (1d).** Yellow finely crystalline powder, the yield was 57%, m.p. 146—148 °C. Found (%): C, 54.66; H, 5.37; N, 14.98. $C_{17}H_{20}N_4O_4S$ (M = 376.44). Calculated (%): C, 54.24; H, 5.36; N, 14.88. IR, ν/cm^{-1}: 3160, 3075 (NH, NH^+); 2178 (CN); 1695 (C=O); 1612 (C=C). ^1H NMR, δ: 2.35 (dd, 1 H, C(5)H, ABX system, ^2J = 16.0 Hz, ^3J = 4.0 Hz); 2.80 (s, 3 H, NMe); 2.89 (dd, 1 H, C(5)H, ABX system, ^2J = 16.0 Hz, ^3J = 8.0 Hz); 3.19 (m, 4 H, C$\underline{H_2}$NC$\underline{H_2}$); 3.78 (m, 4 H, C$\underline{H_2}$OC$\underline{H_2}$); 4.06 (m, the overlap of two d, 1 H, C(4)H, ABX system); 7.44 (br.d, 1 H, C(6)H_{Ar}, ^3J = 8.0 Hz); 7.51 (pseudot, the overlap of two d, 1 H, C(4)H_{Ar}, ^3J = 8.0 Hz); 7.72 (pseudot, the overlap of two d, 1 H, C(5)H_{Ar}, ^3J = 8.0 Hz); 7.92 (br.d, 1 H, C(3)H_{Ar}, ^3J = 8.0 Hz); 8.95 (s, 1 H, NH); 9.65 (br.s, 1 H, NH^+).

***N*-Methylmorpholinium (4*R*/4*S*)-3-cyano-4-(4-fluorophenyl)-6-oxo-1,4,5,6-tetrahydropyridine-2-thiolate (1e).** Light yellow finely crystalline powder, the yield was 71%, m.p. 138—142 °C. Found (%): C, 58.06; H, 5.79; N, 12.18. $C_{17}H_{20}FN_3O_2S$ (M = 349.43). Calculated (%): C, 58.43; H, 5.77; N, 12.03. IR, ν/cm^{-1}: 3155, 3075 (NH, NH^+); 2168 (CN); 1698 (C=O); 1602 (C=C). ^1H NMR, δ: 2.35 (dd, 1 H, C(5)H, ABX system, ^2J = 16.0 Hz, ^3J = 3.8 Hz); 2.74 (dd, 1 H, C(5)H, ABX system, ^2J = 16.0 Hz, ^3J = 7.5 Hz); 2.81 (s, 3 H, NCH_3); 3.21 (m, 4 H, C$\underline{H_2}$NC$\underline{H_2}$); 3.67 (m, the overlap of two d, 1 H, C(4)H, ABX system); 3.79 (m, 4 H, C$\underline{H_2}$OC$\underline{H_2}$); 7.11—7.23 (m, 4 H, Ar); 8.66 (s, 1 H, NH); 9.63 (br.s, 1 H, NH^+).

***N*-Methylmorpholinium (4*R*/4*S*)-3-cyano-4-(2,4-dimethoxyphenyl)-6-oxo-1,4,5,6-tetrahydropyridine-2-thiolate (1f).** Pinkish yellow finely crystalline powder, the yield was 82%, m.p. 144—147 °C. Found (%): C, 58.69; H, 6.50; N, 10.88. $C_{19}H_{25}N_3O_4S$ (M = 391.50). Calculated (%): C, 58.29; H, 6.44; N, 10.73. IR, ν/cm^{-1}: 3150, 3080 (NH, NH^+); 2193 (CN); 1683 (C=O); 1618 (C=C). ^1H NMR (DMSO-d_6), δ: 2.27 (dd, 1 H, C(5)H, ABX system, ^2J = 16.1 Hz, ^3J = 2.5 Hz); 2.65 (dd, 1 H, C(5)H, ABX system, ^2J = 16.1 Hz, ^3J = 7.3 Hz); 2.77 (s, 3 H, NCH_3); 3.15 (m, 4 H, C$\underline{H_2}$NC$\underline{H_2}$); 3.74, 3.78 (both s, 3 H each, 2 MeO); 3.75—3.82 (m, 5 H, the overlap of the signals C$\underline{H_2}$OC$\underline{H_2}$ and C(4)H); 6.47 (br.d, 1 H, C(5)H_{Ar}, ^3J = 8.3 Hz); 6.54 (s, 1 H, C(3)H_{Ar}); 6.93 (br.d, 1 H, C(6)H_{Ar}, ^3J = 8.3 Hz); 8.61 (s, 1 H, NH); 9.63 (br.s, 1 H, NH^+).

Synthesis of 3,3´-(1,4-phenylene)-bis(8-aryl-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitriles) 2a—f (general procedure). *p*-Phenylenediamine (65 mg, 0.6 mmol) and excess of 37% aqueous HCHO (1.5 mL, 20 mmol, free of the paraformaldehyde impurities) were added to a suspension of tetrahydropyridine-2-thiolate **1a—f** (1.2 mmol) in EtOH (8—10 mL). The mixture obtained was heated until the homogeneity was reached, refluxed for 3—5 min with vigorous stirring (the product may start to crystallize at this step), stirred for 3 h at 20 °C, and kept for 24—72 h. The crystals were filtered off, sequentially washed with EtOH, acetone, and light petroleum. Compounds **2a—f** were obtained in the analytically pure form.

3,3´-(1,4-Phenylene)-bis[8-(1-naphthyl)-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitrile] (2a). Beige finely crystalline powder, the yield was 24%, m.p. 248—251 °C (decomp.). Found (%): C, 69.90; H, 4.48; N, 11.80. $C_{42}H_{32}N_6O_2S_2$ (M = 716.89). Calculated (%): C, 70.37; H, 4.50; N, 11.72. IR, ν/cm^{-1}: 2196 (C≡N); 1693 (C=O). ^1H NMR, δ: 2.70 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7´)H, ABX system, ^2J = 16.0 Hz, $^3J_{cis}$ = 3.0 Hz); 3.29 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7´)H, ABX system, ^2J = 16.0 Hz, $^3J_{trans}$ = 7.0 Hz); 4.85 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(8)H + C(8´)H, ABX system); 5.43—5.58 (m, the overlap of four dd for stereoisomers (**A**+**B**)/**C**, 2 H each, N—C(4)H_2—N, N—C(4´)H_2—N, N—C(2)H_2—S, N—C(2´)H_2—S); 7.07, 7.09 (both d, 1 H each, C(2)H + + C(2´)$H_{naphthyl}$ stereoisomers (**A**+**B**)/**C**, ^3J = 7.5 Hz); 7.182, 7.189 (both s, 4 H each, phenylene of stereoisomers (**A**+**B**)/**C**); 7.34 (dd, 2 H, C(3)$H_{naphthyl}$, ^3J = 7.5 Hz); 7.59 (m, 4 H, C(6)H + C(6´)$H_{naphthyl}$, C(7)H + C(7´)$H_{naphthyl}$); 7.87 (m, the overlap of two d for stereoisomers (**A**+**B**)/**C**, 2 H each, C(4)H + + C(4´)$H_{naphthyl}$, ^3J = 8.0 Hz); 7.98 (d, 2 H, C(5)$H_{naphthyl}$, ^3J = 7.5 Hz); 8.10 (d, 2 H, C(8)$H_{naphthyl}$, ^3J = 8.0 Hz).

3,3´-(1,4-Phenylene)-bis[8-(2-methoxyphenyl)-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitrile] (2b). Beige finely crystalline powder, the yield was 43%, m.p. 241—243 °C (decomp.). Found (%): C, 63.40; H, 4.80; N, 12.55. $C_{36}H_{32}N_6O_4S_2$ (M = 676.82). Calculated (%): C, 63.89; H, 4.77; N, 12.42. IR, ν/cm^{-1}: 2195 (C≡N); 1690 (C=O). ^1H NMR, δ: 2.62 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7´)H, ABX system, ^2J = 16.0 Hz, $^3J_{cis}$ = 3.5 Hz); 3.08 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7´)H, ABX system, ^2J = 16.0 Hz,

$^3J_{trans}$ = 7.5 Hz); 3.783, 3.787 (both s, 3 H each, MeO of stereoisomers (**A**+**B**)/**C**); 4.07 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(8)H + C(8′)H, ABX system); 5.34—5.55 (m, the overlap of four dd for stereoisomers (**A**+**B**)/**C**, 2 H each, N—C(4)H_2—N, N—C(4′)H_2—N, N—C(2)H_2—S, N—C(2′)H_2—S); 6.80—6.89 (m, 4 H, C(3)H + C(3′)H_{Ar}, C(5)H + + C(5′)H_{Ar}); 7.03 (dd, 2 H, C(4)H + C(4′)H_{Ar}, ^3J = 7.5 Hz, ^3J = 8.0 Hz); 7.10 (pseudos, 4 H, phenylene); 7.28 (m, the overlap of the signals for stereoisomers (**A**+**B**)/**C**, 2 H, C(6)H + + C(6′)H_{Ar}).

3,3′-(1,4-Phenylene)-bis[8-(2-chloro-6-fluorophenyl)-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitrile] (2c). Beige finely crystalline powder, the yield was 53%, m.p. 275—277 °C (decomp.). Found (%): C, 56.25; H, 3.38; N, 11.73. $C_{34}H_{24}Cl_2F_2N_6O_2S_2$ (*M* = 721.64). Calculated (%): C, 56.59; H, 3.35; N, 11.65. IR, ν/cm^{-1}: 2190 (C≡N); 1695 (C=O). ^{1}H NMR, δ: 2.84 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7′)H, ABX system, ^2J = 16.8 Hz, $^3J_{cis}$ = 7.5 Hz); 3.08 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7′)H, ABX system, ^2J = 16.8 Hz, $^3J_{trans}$ = 8.5 Hz); 4.63 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(8)H + C(8′)H, ABX system); 5.34—5.53 (m, the overlap of four dd for stereoisomers (**A**+**B**)/**C**, 2 H each, N—C(4)H_2—N, N—C(4′)H_2—N, N—C(2)H_2—S, N—C(2′)H_2—S); 7.12 (pseudos, 4 H, phenylene); 7.25 (dd, 2 H, C(4)H + C(4′)H_{Ar}, ^3J = 8.3 Hz, ^3J = 8.5 Hz); 7.37 (m, 4 H, C(3)H + C(3′)H_{Ar}, C(5)H + C(5′)H_{Ar}). ^{13}C NMR, δ: 32.31; 34.84; 53.44; 58.62; 86.57; 115.79; 115.97; 117.26; 118.41; 125.71; 125.85; 126.61; 130.96; 134.18; 138.82; 149.71; 160.87; 162.85; 167.13.

3,3′-(1,4-Phenylene)-bis[8-(2-nitrophenyl)-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitrile] (2d). Sand-colored powder, the yield was 28%, m.p. 265—268 °C (decomp.). Found (%): C, 57.50; H, 3.74; N, 16.02. $C_{34}H_{26}N_8O_6S_2$ (*M* = 706.76). Calculated (%): C, 57.78; H, 3.71; N, 15.85. IR, ν/cm^{-1}: 2188 (C≡N), 1698 (C=O). ^{1}H NMR, δ: 2.81 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7′)H, ABX system, ^2J = 23.0 Hz, $^3J_{cis}$ = 6.5 Hz); 3.15 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7′)H, ABX system, ^2J = 23.0 Hz, $^3J_{trans}$ = = 7.5 Hz); 4.39 (pseudot, 2 H, C(8)H + C(8′)H, ABX system, $^3J_{cis}$ = 6.5 Hz, $^3J_{trans}$ = 7.5 Hz); 5.32—5.65 (m, the overlap of four dd for stereoisomers (**A**+**B**)/**C**, 2 H each, N—C(4)H_2—N, N—C(4′)H_2—N, N—C(2)H_2—S, N—C(2′)H_2—S); 7.135, 7.140 (both s, 4 H each, phenylene of stereoisomers (**A**+**B**)/**C**); 7.26, 7.31 (both d, 2 H each, C(6)H + C(6′)H_{Ar} of stereoisomers (**A**+**B**)/**C**, ^3J = 7.5 Hz, ^3J = 6.5 Hz); 7.55—7.61 (m, 4 H, C(4)H + C(4′)H_{Ar}, C(5)H + C(5′)H_{Ar}); 7.98 (br.d, 2 H, C(3)H + C(3′)H_{Ar}, ^3J = 7.0 Hz).

3,3′-(1,4-Phenylene)-bis[8-(4-fluorophenyl)-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitrile] (2e). Greyish beige powder, the yield was 56%, m.p. 252—255 °C (decomp.). Found (%): C, 62.10; H, 4.04; N, 13.02. $C_{34}H_{26}F_2N_6O_2S_2$ (*M* = 652.75). Calculated (%): C, 62.56; H, 4.01; N, 12.87. IR, ν/cm^{-1}: 2193 (C≡N); 1685 (C=O). ^{1}H NMR, δ: 2.67 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7′)H, ABX system, ^2J = 16.2 Hz, $^3J_{cis}$ = = 4.6 Hz); 3.00 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7′)H, ABX system, ^2J = 16.2 Hz, $^3J_{trans}$ = 7.0 Hz); 3.88 (pseudot, 2 H, C(8)H + C(8′)H, ABX system, $^3J_{cis}$ = 4.6 Hz, $^3J_{trans}$ = 7.0 Hz); 5.34 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, N—C(4)H_2—N, N—C(4′)H_2—N or N—C(2)H_2—S, N—C(2′)H_2—S, ^3J = 12.6 Hz); 5.43 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, N—C(2)H_2—S, N—C(2′)H_2—S or N—C(4)H_2—N, N—C(4′)H_2—N, ^3J = 13.8 Hz); 6.99—7.15 (m, 8 H, 2 Ar); 7.063, 7.068 (both s, 4 H each, phenylene of stereoisomers (**A**+**B**)/**C**).

3,3′-(1,4-Phenylene)-bis[8-(2,4-dimethoxyphenyl)-6-oxo-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3,5]thiadiazine-9-carbonitrile] (2f). Beige crystals, the yield was 52%, m.p. 255—258 °C (decomp.). Found (%): C, 62.22; H, 4.96; N, 11.51. $C_{38}H_{36}N_6O_6S_2$ (*M* = 736.88). Calculated (%): C, 61.94; H, 4.92; N, 11.40. IR, ν/cm^{-1}: 2196 (C≡N); 1707 (C=O). ^{1}H NMR, δ: 2.62 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7′)H, ABX system, ^2J = 16.4 Hz, $^3J_{cis}$ = = 3.2 Hz); 2.89 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(7)H + C(7′)H, ABX system, ^2J = 16.4 Hz, $^3J_{trans}$ = 6.8 Hz); 3.760, 3.769 (both s, 3 H each, 2 MeO of stereoisomers (**A**+**B**)/**C**); 3.80 (m, the overlap of two s for stereoisomers (**A**+**B**)/**C**, 3 H each, 2 MeO); 3.95 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, C(8)H + C(8′)H, ABX system, $^3J_{cis}$ = 3.2 Hz, $^3J_{trans}$ = 6.8 Hz); 5.32 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, N—C(4)H_2—N, N—C(4′)H_2—N or N—C(2)H_2—S, N—C(2′)H_2—S, ^3J = 12.4 Hz); 5.41 (m, the overlap of two dd for stereoisomers (**A**+**B**)/**C**, 2 H each, N—C(2)H_2—S, N—C(2′)H_2—S or N—C(4)H_2—N, N—C(4′)H_2—N, ^3J = 13.6 Hz); 6.29 (m, the overlap of two d for stereoisomers (**A**+**B**)/**C**, 2 H each, C(5)H + C(5′)H_{Ar}, ^3J = 8.6 Hz); 6.46 (br.pseudos, 2 H, C(3)H + C(3′)H_{Ar}); 6.66 (m, the overlap of two d for stereoisomers (**A**+**B**)/**C**, 2 H each, C(6)H + C(6′)H_{Ar}, ^3J = 8.6 Hz); 7.08 (pseudos, 4 H, phenylene).

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