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Diels–Alder Reactions with Cyclic Sulfones: VIII.* Organic Catalysis in the Synthesis of Spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′-trione 1,1-Dioxides and 2′-Thioxospiro[1-benzothiophene-4,5′-pyrimidine]-4′,6′-dione 1,1-Dioxides

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Abstract—5-Isopropenyl-2,3-dihydrothiophene 1,1-dioxide reacted with 5-methylidenepyrimidine-2,4,6-triones and 5-methylidene-2-thioxopyrimidine-4,6-diones in the presence of chiral amines or amino acids with high regio- and stereoselectivity to give optically active derivatives of barbituric and thiobarbituric acids spiro-fused at the 5-position to 1-benzothiophene 1,1-dioxide fragment. The reaction of 5-isopropenyl-2,3-dihydrothiophene 1,1-dioxide with 5-(2-methoxybenzylidene)-2-thioxopyrimidine-4,6-dione (generated *in situ* from 2-methoxybenzaldehyde and thiobarbituric acid) in the presence of (–)-ephedrine or L-4-(*tert*-butyldimethylsiloxy)proline gave the corresponding 2-thioxospiro[1-benzothiophene-4,5′-pyrimidine]-4′,6′-dione 1,1-dioxide with an enantiomeric excess of 80%.

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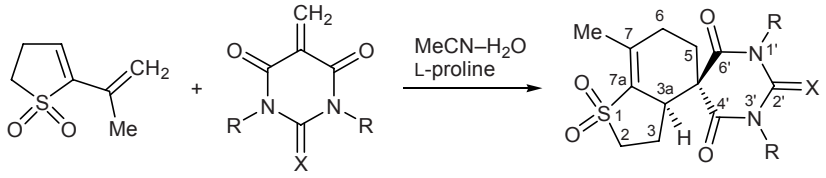
5-Alkyl- and 5,5-dialkylbarbituric acids are widely used as medical agents for the treatment of neurological diseases, depressions, and memory impairment [2], as well as antitumor agents [3, 4]. In the recent time, spiro-fused derivatives of barbituric acid attract increasing attention from the viewpoint of their biological activity [5, 6]. Derivatives of 2-thiobarbituric acids are widely used as antibacterial agents [7], and they inhibit reverse transcriptase and show strong inhibitory activity against HIV-1 *in vitro* [8, 9]. Antiphlogistic [10, 11], antitumor [12–14], and hypocholesteremic agents [15] were found among compounds belonging to the 1-benzothiophene 1,1-dioxide series. The present study was aimed at developing synthetic approaches to hydrogenated 1-benzothiophene 1,1-dioxide derivatives containing spiro-fused barbituric and thiobarbituric acid fragments.

These compounds were synthesized by the Diels–Alder reaction of 5-isopropenyl-2,3-dihydrothiophene 1,1-dioxide (**I**) as diene and 5-methylidenebarbituric and 5-methylidene-2-thiobarbituric acids **II**–**VII** as dienophiles. The reactions of diene **I** with dienophiles **II** and **III** generated *in situ* from barbituric or 1,3-dimethylbarbituric acid and formaldehyde solution were carried out in aqueous acetonitrile in the presence of L-proline (**XIa**) as catalyst. The process was strictly regioselective, and the products were spiro-fused compounds **VIII** and **IX** containing a 2,4,6-trioxopyrimidine fragment fused at the 5-position to C^4 of 1-benzothiophene 1,1-dioxide fragment (yield 70–80%; Scheme 1). Likewise, the reaction of compound **I** with dienophile **VI** generated in a similar way from 5-methylidene-2-thiobarbituric acid gave 52% of thiobarbituric acid derivative **X**. Apart from L-proline, such chiral compounds as L-proline zinc(II) salt (**XIb**), L-4-hydroxyproline (**XIc**), L-4-(*tert*-butyldimethylsiloxy)proline (**XII**), (+)-pseudoephedrine (**XIII**), and 1,3,3-triphenyltetrahydro-3*H*-pyrrolo[1,2-*c*][1,3,2]-oxazaborol-7-ium trifluoromethanesulfonate (**XIV**) [16] were used to catalyze the reactions of diene **I** with

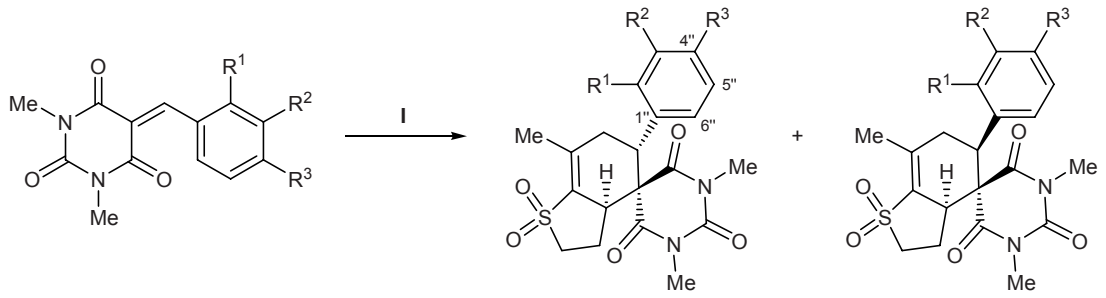
* For communication VII, see [1].

Scheme 1.



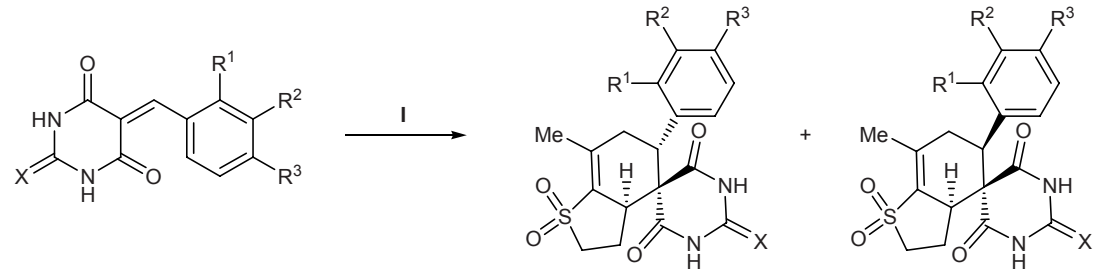
I **II**, **III**, **VI** **VIII–X**

II, **VIII**, X = O, R = Me; **III**, **IX**, X = O, R = H; **VI**, **X**, X = S, R = H.



IVa–IVh **XVa–XVh** **XVIa–XVIh**

IV, **XV**, **XVI**, $R^1 = R^2 = R^3 = H$ (**a**); $R^1 = OMe$, $R^2 = R^3 = H$ (**b**); $R^1 = R^2 = H$, $R^3 = OMe$ (**c**); $R^1 = R^2 = H$, $R^3 = F$ (**d**); $R^1 = OH$, $R^2 = OMe$, $R^3 = H$ (**e**); $R^1 = H$, $R^2 = OH$, $R^3 = OMe$ (**f**); $R^1 = H$, $R^2 = R^3 = OMe$ (**g**); $R^1 = R^2 = R^3 = OMe$ (**h**).



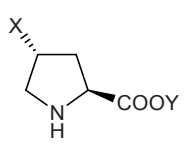
Va–Vc, **VIIa**, **VIIb** **XVIIa–XVIIc**, **XIXa**, **XIXb** **XVIIIa–XVIIIc**, **XXa**, **XXb**

V, **XVII**, **XVIII**, X = O, $R^1 = R^2 = R^3 = H$ (**a**); $R^1 = OMe$, $R^2 = R^3 = H$ (**b**); $R^1 = R^2 = R^3 = OMe$ (**c**); **VII**, **XIX**, **XX**, X = S, $R^1 = R^2 = R^3 = OMe$ (**a**); $R^1 = OMe$, $R^2 = R^3 = H$ (**b**).

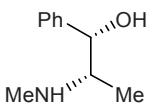
5-arylmethylidenehexahydropyrimidine-2,4,6-triones **IVa**–**IVh**, **Va**, and **Vb** and 5-arylmethylidene-2-thioxohexahydropyrimidine-4,6-dione **VIIa**.

The data in Table 1 show that the cycloaddition of dienophile **IVa** to diene **I** gives a mixture of stereoisomers **XVa** and **XVIa** whose ratio appreciably depends on the catalyst nature. The highest yield of stereoisomer **XVIa** was observed in the reaction catalyzed by L-proline zinc(II) salt (**XIb**). Analogous variation in the ratio of stereoisomers **XVb** and **XVIb** was typical of the reaction of **I** with **IVb** in going from L-proline to its zinc salt as catalyst. Stereoisomer **XVb** was formed as the only product in the reaction catalyzed by 1,3,3-triphenyltetrahydro-3*H*-pyrrolo[1,2-*c*]-[1,3,2]oxazaborol-7-ium trifluoromethanesulfonate (**XIV**). The results of the reactions of **I** with barbituric acid derivatives **IVc**–**IVf** and **IVh** in the presence of zinc salt **XIb** showed that the stereoselectivity depends on the presence of an electron-withdrawing substituent in the arylmethylidene fragment. The yield of stereoisomer **XVd** ($R^1 = R^2 = H$, $R^3 = F$) is considerably larger than the yield of **XVc**, **XVe**, **XVf**, and **XVh**. Dienophiles **Va** and **Vb** prepared from barbituric acid reacted with diene **I** to produce stereoisomer mixtures **XVIIa**/**XVIIIa** and **XVIIb**/**XVIIIb**, respectively. L-Proline derivatives **XI** and **XII** ensured higher stereoselectivity and milder conditions of the cycloaddition. The reaction of **I** with thiobarbituric acid derivative **VIIa** was completely stereoselective, and the only product was stereoisomer **XIXa** (yield 25%).

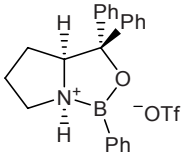
In the recent years, interest in asymmetric catalysis by chiral amines has increased [17, 18]. Catalytic



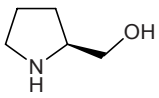
XIa–XIc, **XII**



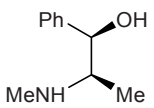
XIII



XIV



XXI



XXII

XI, X = Y = H (**a**); X = H, Y = Zn/2 (**b**); X = HO, Y = H (**c**); **XII**, X = *t*-BuMe$_2$SiO, Y = H.

Diels–Alder reactions with relatively simple dienes and dienophiles have been reported [19–21]. We presumed that Diels–Alder reactions between compounds containing polar groups could involve intermediates formed via interaction with chiral amines and that such intermediates could be converted into optically active final adducts. As catalysts in the Diels–Alder reactions we used L-alanine, L-proline derivatives **XIc** and **XII**, (+)-pseudoephedrine (**XIII**), (*S*)-(+)-prolinol (**XXI**), and (–)-ephedrine (**XXII**). It was found that reactions of diene **I** with 5-arylmethylidenebarbituric acids **IVb**, **IVe**, **Vb**, and **IVc** generated *in situ* are stereoselective and that in some cases these processes may be performed with 100% stereoselectivity (Table 2). Thus organic catalysis of three-component reactions is observed. For example, the reaction of 1,3-dimethylbarbituric acid with 2-methoxybenzaldehyde and diene **I** in the presence of amines or amino acids **XI**–**XIII** and **XXII** yields exclusively 5β-stereoisomer **XVa**. In analogous reaction with 2-hydroxy-3-methoxybenzaldehyde, adduct **XVf** was isolated as the only product. The reactions of diene **I** with barbituric acid and 2-methoxy- or 2,3,4-trimethoxybenzaldehyde afforded optically active adducts **XVIIb** and **XVIIc**. No stereoselectivity was observed in the reactions of diene **I** with dienophiles **IVf** and **VIIb** (generated *in situ*) in the presence of L-proline or (*S*)-(+)-prolinol (**XXI**).

The poor yield of compound **XVe** (45%) formed in the reaction of **I** with **IVe** generated from dimethylbarbituric acid and salicylaldehyde should be noted. Presumably, the formation of 5-arylmethylidenebarbituric acid **IVe** is accompanied by cyclization to produce fused polycyclic compounds [22, 23] which we failed to isolate. For example, our attempt to syn-

Table 1. Reaction conditions, yields, and ratios of spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′-trione 1,1-dioxides **XV**–**XVIII** and 2′-thioxospiro[1-benzothiophene-4,5′-pyrimidine]-4′,6′-dione 1,1-dioxide **XIXa** in the reactions of diene **I** with barbituric and thiobarbituric acid derivatives **IVa**–**IVh**, **Va**, **Vb**, and **VIIa**

Dienophile	Catalyst	Solvent	Temperature, °C	Products	Yield, %	Ratio
IVa	**XIa**	PhH–$CHCl_3$–H_2O	60	**XVa**, **XVIa**	47	5:1
IVa	**XIb**	Dioxane–H_2O	100	**XVa**, **XVIa**	69	2.5:1
IVa	**XII**	Dioxane–H_2O	100	**XVa**, **XVIa**	70	9:1
IVa	**XIII**	Dioxane–H_2O	100	**XVa**, **XVIa**	52	7:1
IVb	**XIa**	PhH–$CHCl_3$–H_2O	60	**XVb**, **XVIb**	35	6:1
IVb	**XIb**	Dioxane–H_2O	100	**XVb**, **XVIb**	55	2.5:1
IVb	**XIV**	CH_2Cl_2	(1) –50; (2) 42	**XVb**	70	–
IVc	**XIb**	Dioxane–H_2O	100	**XVc**, **XVIc**	58	4:1
IVd	**XIb**	Dioxane–H_2O	100	**XVd**, **XVId**	65	8:1
IVe	**XIb**	Dioxane–H_2O	100	**XVe**, **XVIe**	47	3:1
IVf	**XIb**	Dioxane–H_2O	100	**XVf**, **XVIf**	52	3:1
IVg	**XIa**	PhH–$CHCl_3$–H_2O	60	**XVg**, **XVIg**	27	5:1
IVh	**XIa**	PhH–$CHCl_3$–H_2O	60	**XVh**, **XVIh**	32	6:1
IVh	**XIb**	Dioxane–H_2O	100	**XVh**, **XVIh**	67	3:1
Va	**XIc**	Dioxane–H_2O	100	**XVIIa**, **XVIIIa**	58	8:1
Va	**XII**	Dioxane–H_2O	100	**XVIIa**, **XVIIIa**	71	9:1
Vb	**XIa**	DMF–H_2O	130	**XVIIb**, **XVIIIb**	32	3:1
VIIa	**XIa**	DMF–H_2O	130	**XIXa**	25	–

Table 2. Synthesis of optically active spiro-fused barbituric acid derivatives

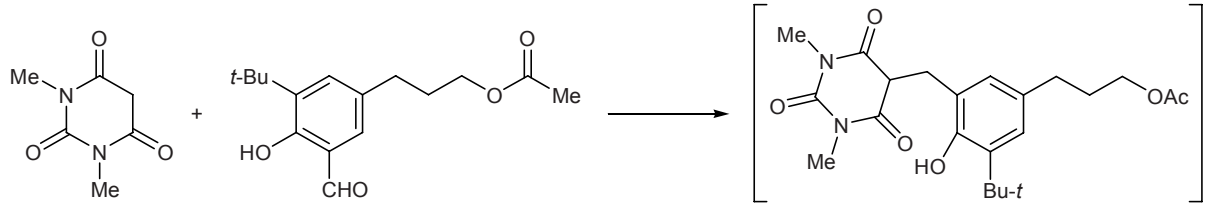
Initial reactants[a]	Catalyst	Product	Yield, %	$[\alpha]_D^{20}$, deg
2-Methoxybenzaldehyde, 1,3-dimethylbarbituric acid, **I**	L-4-Hydroxyproline (**XIc**)	**XVb**	73	+18
2-Methoxybenzaldehyde, 1,3-dimethylbarbituric acid, **I**	(+)-Pseudoephedrine (**XIII**)	**XVb**	60	+35
2-Methoxybenzaldehyde, 1,3-dimethylbarbituric acid, **I**	L-Alanine	**XVb**	66	+30
2-Methoxybenzaldehyde, 1,3-dimethylbarbituric acid, **I**	(–)-Ephedrine (**XXII**)	**XVb**	62	+42
2-Methoxybenzaldehyde, 1,3-dimethylbarbituric acid, **I**	L-4-(*tert*-Butyldimethylsiloxy)-proline (**XII**)	**XVb**	73	+36
2-Hydroxy-3-methoxybenzaldehyde, 1,3-dimethylbarbituric acid, **I**	(+)-Pseudoephedrine (**XIII**)	**XVd**	45	+15
3-Hydroxy-4-methoxybenzaldehyde, 1,3-dimethylbarbituric acid, **I**	L-Proline	**XVf**, **XVIf**, 7 : 1	69	–
2-Methoxybenzaldehyde, barbituric acid, **I**	L-4-Hydroxyproline (**XIc**)	**XVIIb**	75	+18
2,3,4-Trimethoxybenzaldehyde, barbituric acid, **I**	L-4-(*tert*-Butyldimethylsiloxy)-proline (**XII**)	**XVIIc**	72	+37
2-Methoxybenzaldehyde, 2-thiobarbituric acid, **I**	(*S*)-(+)-Prolinol (**XXI**)	**XIXb**, **XXb**, 5 : 1	55	–

[a] Dioxane–water, 4 : 1, 100°C, 21 h.

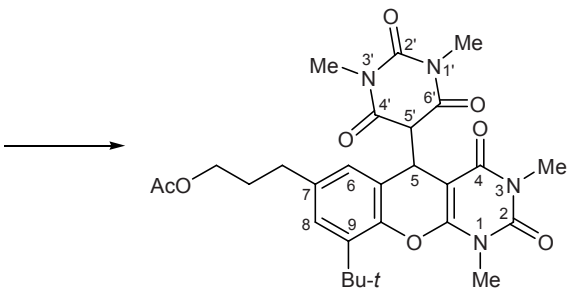
thesize 2-arylmethylidene-4,6-dimethylbarbituric acid from salicylaldehyde derivative **XXIII** resulted in the formation of oxadeazaflavin **XXIV**. The yield of the latter attained 85% when excess dimethylbarbituric acid was taken (Scheme 2).

We performed a series of experiments with diene **I** and 5-(2-methoxybenzylidene)-2-thiobarbituric acid (**VIIb**). The data in Table 3 show how the catalyst affects the optical purity of adduct **XIXb**. It is seen that the Diels–Alder reaction of **I** with thiobarbituric acid

Scheme 2.



XXIII



XXIV

Table 3. Yields and optical purity of (5*R*)-5-(2-methoxyphenyl)-7-methyl-2-thioxo-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-4′,6′(1′*H*,3′*H*)-dione 1,1-dioxide (**XIXb**)[a] in the presence of different chiral catalysts

Solvent	Temperature, °C	Catalyst	Yield of **XIXb**, %		$[\alpha]_D^{20}$, deg
			chemical	ee[b]	
Dioxane–H_2O	100	**XIc**	75	20	+27
Dioxane–H_2O	100	**XII**	68	80	+78
Dioxane–H_2O	100	**XXII**	60	86	+106
DMF–H_2O	130	**XIb**	39	4	+15

[a] 5-(2-Methoxybenzylidene)-2-thioxohexahydropyrimidine-4,6-dione (**VIIb**) was prepared *in situ* from 2-methoxybenzaldehyde and thiobarbituric acid.

[b] According to the chiral HPLC data (Kromasil CHI-DMB).

VIIb could give compound **XIXb** with an ee (enantiomeric excess) value of up to 86%.

(–)-Ephedrine (**XXII**) and L-4-(*tert*-butyldimethylsiloxy)proline (**XII**) ensured high enantio- and diastereoselectivity in the reaction under study. In our experiments organic catalysis involved polyfunctional dienes and dienophiles. We have found no published data on analogous reactions with substrates of similar complexity. The structure of the newly synthesized compounds was determined on the basis of spectral data. The ^{1}H NMR spectra of stereoisomeric adducts displayed characteristic features which allowed us to assign them to (5*R*) or (5*S*) isomers. The configuration of substituents in the adducts was assigned by analyzing vicinal coupling constants between protons on C^5 and C^6. Pseudoequatorial orientation of the aryl substituent in molecules **XVIa–XVIc**, **XVIg**, **XVIh**, **XVIIIa**, **XVIIIb**, and **XXb** followed from the existence of axial–axial coupling between 5-H and 6-H ($J \approx 11$ Hz). In the ^{1}H NMR spectra of (5*S*) isomers **XVIa–XVIc**, **XVIg**, and **XVIh**, singlets from the methyl groups on the nitrogen atoms were displaced downfield (for example, δ 3.13 and 3.27 ppm for **XVa** against δ 2.93 and 3.15 ppm for **XVIa**), presumably due to magnetically anisotropic effect of the benzene ring. The adducts in which the aryl group on C^5 occupies pseudoequatorial position were also characterized by increased nonequivalence of protons on C^6. The

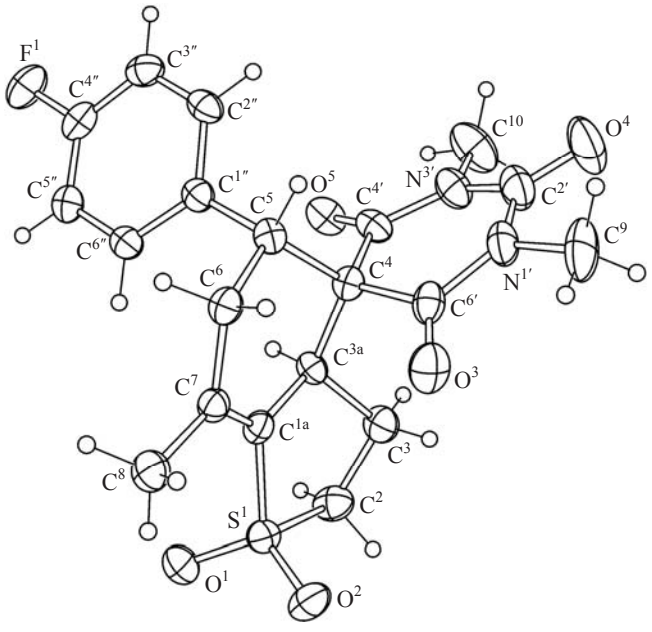


Fig. 1. Structure of the molecule of (5*R*)-5-(4-fluorophenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (**XVd**) according to the X-ray diffraction data.

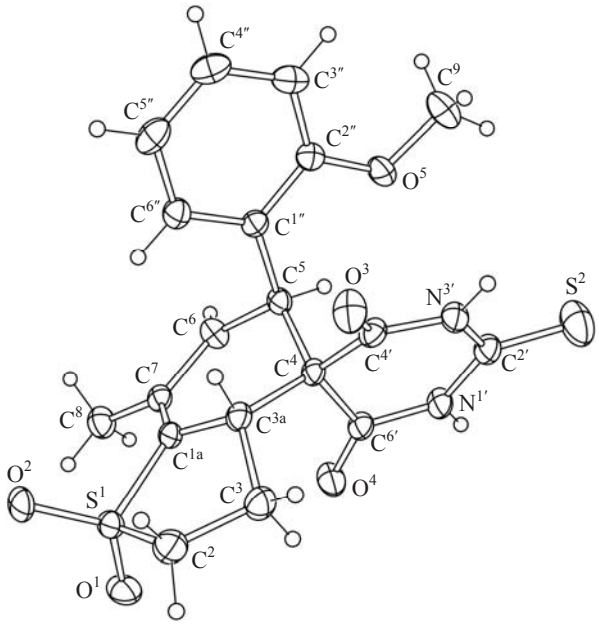


Fig. 2. Structure of the molecule of (5*R*)-5-(2-methoxyphenyl)-7-methyl-2-thioxo-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro-[1-benzothiophene-4,5′-pyrimidine]-4′,6′(1′*H*,3′*H*)-dione 1,1-dioxide (**XIXb**) according to the X-ray diffraction data.

above differences allowed us to estimate ratios of stereoisomeric adducts in the reaction mixtures.

Figures 1 and 2 show the structure of molecules **XVd** and **XIXb** according to the X-ray diffraction data. Molecules **XVd** and **XIXb** have similar steric structures, and their geometric parameters coincide within 3σ. We have found no structures with analogous tetracyclic skeleton in the Cambridge Crystal Structure Database [24]. The geometric parameters of the dioxo-7-thiabicyclo[4.3.0]nonene fragment coincide within 3σ with those in 4-carbamoyl-7-methyl-2,3,3a,4,5,6-hexahydro-1-benzothiophene-4-carboxylic acid 1,1-dioxide [1] and correspond to standard values [25]. Extension of the C^5–C^6 bond to 1.558(5) (**XVd**) and 1.540(4) Å (**XIXb**) against 1.529(4) Å [1] and of the C^5–C^4 bond to 1.589(5) (**XVd**) and 1.600(4) Å (**XIXb**) against 1.545(3) Å should be noted [1]. Most probably, the observed extension of the C^5–C^6 and C^5–C^4 bonds is related to interaction between the aryl substituent and spiro-fused pyrimidine fragment. The cyclohexene ring in both molecules adopts a distorted *sofa* conformation [26] where C^{3a}, C^{1a}, C^7, C^6, and C^5 lie in one plane [the mean-square deviations from that plane are 0.063 (**XVd**) and 0.031 Å (**XIXb**)]; C^4 deviates from that plane by 0.602(6) (**XVd**) and 0.622(5) Å (**XIXb**). The thiophene ring has an *envelope* conformation with the C^3 atom deviating by 0.620(7) (**XVd**) or 0.622(5) Å (**XIXb**) from the plane formed by the remaining four atoms (the mean-square deviations are 0.013 and 0.003 Å, respectively). The benzene ring is almost orthogonal to the plane including five atoms of the cyclohexene fragment: the corresponding dihedral angle is 88.4(2) and 97.8(1)° for compounds **XVd** and **XIXb**, respectively. The hexahydropyrimidine ring in molecules **XVd** and **XIXb** is strongly flattened, the torsion angles (in absolute values) range from 5.4(7) to 20.7(5)° (**XVd**) and from 5.5(5) to 30.6(3)° (**XIXb**). The hexahydropyrimidine ring in **XIXb** has a conformation similar to *envelope*, where the C^4 atom deviates by 0.413(5) Å from the plane formed by the other five atoms in the ring (the mean-square deviation is 0.017 Å). The conformation of analogous fragment in molecule **XVd** resembles *envelope* to a lesser extent: the C^4 atom therein deviates from the plane including the remaining five atoms (the mean-square deviation is 0.060 Å) by only 0.195(6) Å. For comparison, we analyzed geometric parameters of five structurally related spiro-fused dimethylbarbituric acid derivatives, which were taken from the CCSD [27]: DMBART10, LUQJIQ (two independent molecules), OBICOR, and OKOCUM. In all cases, the dimethylbarbituric acid fragment is flattened, and the bond lengths in molecules **XVd** and **XIXb** coincided within 3σ with the corresponding average values for the above five structures. The dihedral angle between the benzene ring and the plane including five atoms of the pyrimidine ring is 34.2(2) and 26.5(1)° for compounds **XVd** and **XIXb**, respectively. Supramolecular architecture of molecules **XIXb** in crystal is set by weak N–H···O hydrogen bonds which give rise to three-dimensional network ($N^{1'}$–$H^{1'A}$···O^2: H···O 2.08, N···O 2.934(3) Å, ∠NHO 173°; $N^{3'}$–$H^{3'A}$···O^{1R}: H···O 1.87, N···O 2.731(4) Å, ∠NHO 174°). No shortened intermolecular contacts were found in the crystalline structure of **XVd**.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded from solutions in $CDCl_3$ on Bruker AC-200 (200.13 MHz for ^{1}H and 50.32 MHz for ^{13}C), AV-300 (300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C), AM-400 (400.13 MHz for ^{1}H and 100.78 MHz for ^{13}C), and Bruker DRX-500 spectrometers (500.13 MHz for ^{1}H and 125.76 MHz for ^{13}C). The molecular weights and elemental compositions were determined from the high-resolution mass spectra (electron impact, 70 eV) which were recorded on a Finnigan MAT-8200 mass spectrometer (vaporizer temperature 270–300°C). The IR spectra were measured in KBr on a Vector-22 instrument. The UV spectra were obtained on an HP 8453 UV-Vis spectrophotometer from solutions in ethanol ($c = 10^{-4}$ M). The optical rotations were measured on a Polar 3005 polarimeter.

The X-ray diffraction data for compounds **XVd** and **XIXb** were acquired using a Bruker P4 diffractometer (MoK_α irradiation, graphite monochromator, 2θ/θ scanning). Correction for absorption was introduced by an empirical method using Ψ-curves. The structures were solved by the direct method with the aid of SHELXS-97 software package [28] and were refined by the least-squares procedure in full-matrix anisotropic approximation using SHELXL-97 software [28]. The parameters of hydrogen atoms were calculated in each iteration cycle from the coordinates of the corresponding carbon atoms. The crystallographic data for compounds **XVd** and **XIXb** and parameters of X-ray diffraction experiments are collected in Table 4. Compound **XIXb** crystallized as solvate with DMSO, and the sulfur atom in the solvate DMSO molecule was disordered by two positions, S^{1R} and S^{1RA} with a population ratio of 0.76 : 0.24. The geometric parameters, conformations, and intermolecular interactions were

analyzed with the aid of PLATON program [29]. The complete sets of crystallographic data for compounds **XVd** and **XIXb** were deposited to the Cambridge Crystallographic Data Centre (entry nos. CCDC 655855 and CCDC 655856, respectively; http://www.ccdc.cam.ac.uk/data_request/cif deposit).

The progress of reactions was monitored by thin-layer chromatography on Silufol UV-254 plates; spots were detected by treatment with iodine vapor. The products were isolated by column chromatography on silica gel using chloroform–ethanol was eluent.

The optical purity of compound **XIXb** was determined by chiral HPLC on a Millikhrom 1 chromatograph; Kromasil CHI-DMB column, 64×2 mm, grain size 10 μm; eluent 10% of isopropyl alcohol in hexane, flow rate 100 μl/min; UV detector, λ 210 nm. The retention time of the (*S*) enantiomer was 8.9 min, and that for the (*R*) enantiomer was 11.4 min.

L-Proline, L-alanine, and L-4-hydroxyproline from Reanal (Hungary), $[\alpha]_D^{20}$ (water) = –84, –23, and –73°, respectively, and (*S*)-(+)-prolinol (**XXI**) from Lancaster ($[\alpha]_D^{20}$ = +31°, toluene) were used. L-4-(*tert*-Butyldimethylsiloxy)proline (**XII**) was synthesized according to the procedure reported in [30]. 1,3,3-Triphenyltetrahydro-3*H*-pyrrolo[1,2-*c*][1,3,2]oxazaborol-7-ium trifluoromethanesulfonate (**XIV**) [31] was prepared as described in [32]. L-Proline zinc(II) salt was synthesized according to [33]. (+)-Pseudoephedrine {**XIII**, (1*S*,2*S*)-2-methylamino-1-phenylpropan-1-ol, mp 118–119°C; sublimed at 100°C (12 mm) after recrystallization from benzene; $[\alpha]_{578}^{20}$ = +53° (*c* = 3, EtOH)} was isolated from *Ephedra equisetina Bunge* [34]. (–)-Ephedrine [**XXII**, (1*R*,2*S*)-2-methylamino-1-phenylpropan-1-ol, mp 38–39°C (from hexane)] was isolated from the corresponding hydrochloride {mp 216–217°C (from EtOH), $[\alpha]_{578}^{20}$ = –36° (*c* = 2, H_2O)} which was isolated from alkaloids of *Ephedra equisetina Bunge* [34, 35]}.

5-Arylmethylideneperhydropyrimidine-2,4,6-triones IVa–IVh, Va, and Vb and 2-thioxo-5-(2,3,4-trimethoxybenzylidene)perhydropyrimidine-4,6-dione (VIIa) were synthesized by the Knoevenagel condensation of *N*,*N*-dimethylbarbituric, barbituric, or thiobarbituric acid with the corresponding aromatic aldehyde in water in the presence of a phase-transfer catalyst. A mixture of 10 mmol of aromatic aldehyde, 10 mmol of 1,3-dimethylbarbituric acid, and 0.17 g of benzyl(trimethyl)ammonium chloride in 40 ml of water was stirred for 4–5 h at 90°C. The mixture was cooled, and the precipitate was filtered off and recrystallized from ethyl acetate. Yield 83–99%; **IVa**, mp 250–252°C (for spectral parameters, see [36]); **IVb**, mp 161–162°C (cf. [36]); **IVc**, mp 134–135°C (cf. [36]); **IVe**, mp 180–181°C (cf. [37]); **Va**, mp 270–272°C (cf. [38]); **Vb**, mp 267–268°C (cf. [38]).

Table 4. Crystallographic data for compounds **XVd** and **XIXb** and parameters of X-ray diffraction experiments

Parameter	**XVd**	**XIXb**·DMSO
Formula	$C_{20}H_{21}N_2O_5FS$	$C_{19}H_{17}N_2O_5S_2 \cdot C_2H_6OS$
Temperature, °C	23	23
Molecular weight	420.45	497.64
Crystal system	Rhombic	Triclinic
Space group	*Pbca*	*P*-1
θ range, deg	2.1–25.5	2.1–26.0
Unit cell parameters:		
a, Å	11.043(2)	9.231(1)
b, Å	17.902(3)	10.045(1)
c, Å	19.484(3)	12.782(1)
α, deg	90	83.590(10)
β, deg	90	82.072(9)
γ, deg	90	79.443(9)
V, Å^3	3852(1)	1149.5(2)
Z	8	2
d_{calc}, g/cm^3	1.450	1.438
μ, mm^{-1}	0.214	0.150
Crystal habit, mm	1.00×0.12×0.04	0.76×0.42×0.21
Total number of reflections	3578	4807
Number of independent reflections	3677	4509
Correction for absorption	Empirical	Empirical
Transmission	0.52–0.85	0.66–0.90
Number of reflections with $I > 2\sigma(I)$	1712	3551
Number of refined parameters	262	299
R_1 [reflections with $F > 4\sigma(F)$]	0.0573	0.0588
wR_2 (all reflections)	0.1944	0.1749
Goodness of fit	0.950	1.08

5-(4-Fluorobenzylidene)-1,3-dimethylhexahydropyrimidine-2,4,6-trione (IVd). Yield 95%, mp 153–156°C. IR spectrum, ν, cm^{-1}: 759, 793, 851, 980, 1152, 1170, 1359, 1663, 1730. UV spectrum, λ_{max}, nm

(log ε): 203 (3.35), 254 (3.19), 331 (2.64). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.36 s (3H, CH_3N), 3.39 s (3H, CH_3N), 7.11 d and 7.14 d (1H each, 2′-H, 6′-H), 8.16 d and 8.18 d (1H each, 3′-H, 5′-H), 8.49 s (1H, CH=). ^{13}C NMR spectrum, δ_C, ppm: 28.23 q (CH_3), 28.91 q (CH_3), 115.33 d and 115.54 d ($C^{3'}$, $C^{5'}$), 116.79 s ($C^{1'}$), 128.68 s (C^5), 136.52 d and 136.61 d ($C^{2'}$, $C^{6'}$), 151.00 s (C^2), 157.54 d (CH=), 160.32 s ($C^{4'}$), 162.31 s and 163.95 s (C^4, C^6). Found: *m*/*z* 261.06849 $[M]^+$. $C_{13}H_{10}FN_2O_3$. Calculated: *M* 261.06754.

5-(3-Hydroxy-4-methoxybenzylidene)-1,3-dimethylhexahydropyrimidine-2,4,6-trione (IVf). Yield 90%, mp 214–215°C (from ethyl acetate). IR spectrum, ν, cm^{-1}: 791, 812, 900, 989, 1015, 1134, 1153, 1273, 1511, 1576, 1654, 1727, 3126. UV spectrum, λ_{max}, nm (log ε): 231 (3.23), 262 (3.16), 315 (2.84), 401 (2.61). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.37 s (3H, CH_3N), 3.39 s (3H, CH_3N), 3.98 s (3H, OCH_3), 5.70 br.s (1H, OH), 6.92 d (1H, 5′-H, *J* = 8.2 Hz), 7.79 d.d (1H, 6′-H, *J* = 1.8, 8.2 Hz), 8.05 d (1H, 2′-H, *J* = 1.8 Hz), 8.44 s (1H, CH=). ^{13}C NMR spectrum, δ_C, ppm: 28.23 q (CH_3), 28.91 q (CH_3), 57.06 q (OCH_3), 109.90 d ($C^{2'}$), 114.93 s ($C^{1'}$), 120.13 d ($C^{6'}$), 126.28 s (C^5), 131.05 d ($C^{5'}$), 145.05 s ($C^{3'}$), 151.35 s (C^2), 158.94 d (CH=), 160.72 s ($C^{4'}$), 162.98 s and 164.28 s (C^4, C^6).

5-(3,4-Dimethoxybenzylidene)-1,3-dimethylhexahydropyrimidine-2,4,6-trione (IVg). Yield 83%, mp 208–210°C (from ethyl acetate). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.38 s (3H, CH_3N), 3.40 s (3H, CH_3N), 3.95 s (3H, OCH_3), 3.99 s (3H, OCH_3), 6.92 d (1H, 5′-H, *J* = 8.2 Hz), 7.78 d.d (1H, 6′-H, *J* = 8.2, 1.8 Hz), 8.37 d (1H, 2′-H, *J* = 1.8 Hz), 8.47 s (1H, CH=). ^{13}C NMR spectrum, δ_C, ppm: 28.18 s (NCH_3), 28.67 s (NCH_3), 58.67 s (OCH_3), 60.28 s (OCH_3), 109.62 d ($C^{2'}$), 110.51 d ($C^{5'}$), 120.88 d ($C^{6'}$), 121.57 s ($C^{1'}$), 127.81 s (C^5), 147.16 s and 150.48 s ($C^{3'}$, $C^{4'}$), 151.51 s (C^2), 155.12 d (CH=), 160.69 s (C=O), 162.81 s (C=O).

1,3-Dimethyl-5-(2,3,4-trimethoxybenzylidene)-hexahydropyrimidine-2,4,6-trione (IVh). Yield 96%, mp 218–221°C. IR spectrum, ν, cm^{-1}: 702, 736, 755, 927, 991, 1090, 1151, 1289, 1308, 1551, 1590, 1670, 1680, 1723. UV spectrum, λ_{max}, nm (log ε): 226 (2.92), 257 (2.81), 388 (3.48). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.32 s (3H, CH_3N), 3.37 s (3H, CH_3N), 3.82 s (3H, OCH_3), 3.92 s (3H, OCH_3), 3.96 s (3H, OCH_3), 6.70 d (1H, *J* = 8.2 Hz), 8.27 d (1H, *J* = 8.2 Hz), 8.82 s (1H, CH=). ^{13}C NMR spectrum, δ_C, ppm: 28.17 s (CH_3), 28.77 s (CH_3), 56.05 s (OCH_3), 60.76 s (OCH_3), 61.92 s (OCH_3), 106.17 s ($C^{5'}$), 117.27 d ($C^{1'}$), 119.58 s (C^5), 129.57 d ($C^{6'}$), 141.02 s ($C^{3'}$), 151.35 s (C^2), 154.01 d (CH=), 155.95 s ($C^{4'}$), 158.76 s ($C^{2'}$), 160.69 s (C=O), 162.81 s (C=O).

2-Thioxo-5-(2,3,4-trimethoxybenzylidene)hexahydropyrimidine-4,6-dione (VIIa). Yield 96%, mp 220–222°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.76 s (3H, OCH_3), 3.86 s (3H, OCH_3), 3.90 s (3H, OCH_3), 6.92 d (1H, 5′-H), 8.41 d (1H, 6′-H), 8.50 s (1H, CH=), 11.50 br.s (2H, NH). Found, %: C 52.66; H 4.43; N 8.92; S 9.48. $C_{14}H_{14}N_2O_5S$. Calculated, %: C 52.17; H 4.34; N 8.69; S 9.94.

1′,3′,7-Trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (VIII). An aqueous formaldehyde solution, 2.5 ml, was added to a mixture of 0.79 g (5 mmol) of *N*,*N*′-dimethylbarbituric acid, 0.76 g (4.8 mmol) of diene **I**, 0.10 g of L-proline, 7 ml of acetonitrile, and 1.5 ml of water. The mixture was stirred for 4 h at 20°C, diluted with 10 ml of water, and extracted with chloroform, the extract was evaporated, and the residue was recrystallized from ethyl acetate. Yield 1.25 g (80%), mp 265–266°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.80 m (1H, 3-H), 1.90–2.10 m (2H, 3-H, 5-H), 2.11 d (3H, CH_3, *J* = 2.2 Hz), 2.21 m (1H, 5-H), 2.38 m (2H, 6-H), 2.92 m (1H, 2-H), 3.12 m (1H, 2-H), 3.24 s (3H, CH_3N), 3.31 s (3H, CH_3N), 3.52 m (1H, 3a-H). ^{13}C NMR spectrum, δ_C, ppm: 17.87 s (CH_3), 21.60 t (C^3), 28.55 s (CH_3), 29.19 s (CH_3), 29.96 t (C^5), 32.91 t (C^6), 41.25 d (C^{3a}), 50.33 t (C^2), 52.23 s (C^4), 131.47 s (C^{1a}), 139.91 s (C^7), 150.54 s ($C^{2'}$), 167.06 s ($C^{4'}$), 170.42 s ($C^{6'}$). Mass spectrum, *m*/*z* (I_{rel}, %): 326 (100) $[M]^+$, 262 (34), 247 (78), 234 (54), 207 (30), 181 (49), 169 (71), 147 (46), 120 (56), 94 (94). $C_{14}H_{18}N_2O_5S$. Calculated: *M* 326.09363.

7-Methyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (IX) was synthesized in a similar way. Yield 70%, mp 240–241°C (from ethanol). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 17.34 s (CH_3), 21.69 t (C^3), 29.06 t (C^5), 30.97 t (C^6), 40.95 d (C^{3a}), 51.12 t (C^2), 53.02 s (C^4), 131.64 s (C^{1a}), 138.67 s (C^7), 150.77 s ($C^{2'}$), 168.26 s ($C^{4'}$), 170.42 s ($C^{6'}$). Found: *m*/*z* 298.06464 $[M]^+$. $C_{12}H_{14}N_2O_5S$. Calculated: *M* 298.06234.

7-Methyl-2′-thioxo-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-4′,6′(1′*H*,3′*H*)-dione 1,1-dioxide (X). Yield 52%, mp 226–229°C (from ethyl acetate). ^{13}C NMR spec-

trum (DMSO-d_6), δ_C, ppm: 17.34 s (CH_3), 21.52 t (C^3), 29.96 t (C^5), 30.51 t (C^6), 41.33 d (C^{3a}), 50.03 t (C^2), 51.22 s (C^4), 131.27 s (C^{1a}), 139.09 s (C^7), 166.36 s ($C^{4'}$), 170.06 s ($C^{6'}$) 178.54 s ($C^{2'}$). Mass spectrum, *m*/*z* (I_{rel}, %): 314 (6) $[M]^+$, 167 (5), 149 (13), 44 (100). $C_{12}H_{14}N_2O_4S_2$. Calculated: *M* 314.03949.

Reactions of 5-benzylidenebarbituric and -2-thiobarbituric acids with 5-isopropenyl-2,3-dihydrothiophene 1,1-dioxide (I) (*general procedures*). *a*. A mixture of 5 mmol of compound **IVa**, **IVb**, **IVg**, **IVh**, **Vb**, or **VIIa**, 4.8 mmol of diene **I**, 0.10 g of L-proline, and 0.08 g of benzyl(trimethyl)ammonium chloride in benzene–chloroform–water (5:3:1 by volume) or in aqueous dimethylformamide (1:10 by volume) was heated for 32–36 h under reflux. The mixture was evaporated, and the residue was subjected to column chromatography on silica gel using chloroform–ethanol as eluent to isolate (in order of elution) unreacted dienophile **IVa**, **IVb**, **IVg**, **IVh**, **Vb**, or **VIIa**, stereoisomer mixture **XVa**/**XVIa**, **XVb**/**XVIb**, or **XVh**, **XVIh**), (5*S*) isomer **XVIa**, **XVIg**, or **XVIIIb**, and (5*R*) isomer **XVa**, **XVg**, **XVIIb**, or **XIXa**.

b. A mixture of 3 mmol of 5-benzylidene-1,3-dimethylperhydropyrimidine-2,4,6-trione **IVa**–**IVf**, **IVh**, or **Va**, 2.7 mmol (0.43 g) of 5-isopropenyl-2,3-dihydrothiophene 1,1-dioxide (**I**), and 0.06 mmol of chiral catalyst **XIb**, **XIc**, **XII**, or **XIII** in aqueous dioxane (10:3 by volume) was heated for 20–38 h under reflux. When the reaction was complete (TLC), the mixture was cooled, and the precipitate was filtered off and recrystallized from ethyl acetate to isolate compound **XVa**, **XVIIa**, or **XVIIIa**. The mother liquor was combined with the filtrate and evaporated, and the residue was subjected to column chromatography on silica gel to isolate (in order of elution) unreacted dienophile, (5*S*) isomer **XVIb**, **XVIc**, or **XVIh**, and (5*R*) isomer **XVb** or **XVh**.

c. A solution of 0.13 g (0.04 mmol) of compound **XIV** (prepared *in situ* [31]) in 10 ml of methylene chloride was cooled to –50°C, a solution of 0.73 g (3 mmol) of pyrimidine-2,4,6-trione **IVb** and 0.43 g (2.7 mmol) of diene **I** in 10 ml of methylene chloride was added dropwise, and the mixture was stirred for 4 h at –50°C, for 2 h at 20°C, and for 40 h on heating under reflux (TLC). The resulting solution was cooled, diluted with water, and extracted with methylene chloride, the extract was washed with water, dried over $MgSO_4$, and evaporated, and the residue was subjected to chromatography on silica gel. The product was additionally recrystallized from ethanol. Yield of **XVb** 0.82 g (70%).

d. A mixture of 3 mmol of barbituric, thiobarbituric, or *N*,*N*′-dimethylbarbituric acid, 3.2 mmol of the corresponding aromatic aldehyde, 0.6 mmol of catalyst (see Tables 2, 3), and 0.43 g (2.7 mmol) of diene **I** in aqueous dioxane (15:3 by volume) was heated in a sealed ampule for 21 h at a bath temperature of 130°C. The ampule was cooled and opened, and the mixture was poured on a Petri dish and allowed to evaporate in air. The dry residue was dissolved in a minimal amount of chloroform, and the solution was applied to a column charged with silica gel. After chromatographic separation, the product (compound **XVb** or **XVf**) was recrystallized from ethanol. To isolate compounds **XVIIb**, **XVIIc**, **XIXb**, and **XXb**, the dry residue was dissolved in ethanol, and the undissolved material was filtered off and additionally purified by recrystallization. The yields and optical rotations of the products are given in Tables 2 and 3.

(5*R*)-1′,3′,7-Trimethyl-5-phenyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVa). mp 223–225°C (from ethyl acetate). IR spectrum, ν, cm^{-1}: 704, 740, 852, 1070, 1128, 1287, 1300, 1500, 1630, 1676, 1747. UV spectrum: λ_{max} 206 nm (log ε 3.29). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.05 m (2H, 3-H), 2.19 d (3H, CH_3, J = 2.2 Hz), 2.59 m (2H, 6-H, J = 2.6, 2.8, ^2J = 18.6 Hz), 2.98 m (1H, 2-H), 3.13 s (3H, CH_3), 3.20 d.d.d (1H, 2-H, J = 2.6, 6.7, 13.0 Hz), 3.27 s (3H, CH_3), 3.35 d.d (1H, 5-H, J = 2.8, 5.9 Hz), 3.47 m (1H, 3a-H), 6.93 m (2H, H_{arom}), 7.27 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 17.99 q (CH_3), 21.87 t (C^3), 29.50 q (CH_3), 29.54 q (CH_3), 36.17 d (C^{3a}), 36.52 t (C^6), 49.72 d (C^5), 50.70 t (C^2), 58.70 s (C^4), 128.58 ($C^{2''}$, $C^{6''}$), 128.72 d ($C^{4''}$), 129.22 d ($C^{3''}$, $C^{5''}$), 133.01 s (C^{7a}), 137.92 s ($C^{1''}$), 138.73 s (C^7), 150.60 s ($C^{2'}$), 168.10 s and 168.41 s ($C^{4'}$, $C^{6'}$). Mass spectrum, *m*/*z* (I_{rel}, %): 402 (10) $[M]^+$, 338 (29), 309 (100), 247 (32), 165 (29), 142 (37), 91 (51). $C_{20}H_{22}N_2O_5S$. Calculated: *M* 402.12493.

(5*S*)-1′,3′,7-Trimethyl-5-phenyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIa). mp 251–253°C (from ethyl acetate). IR spectrum, ν, cm^{-1}: 1449, 1677 (C=C_{arom}); 1131, 1294 (SO_2); 1745 (C=O). UV spectrum: λ_{max} 206 nm (log ε 3.30). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.78 m and 2.00 m (1H each, 3-H), 2.20 d (3H, CH_3, J = 2.2 Hz), 2.53 d.d.d (1H, 6-H, J = 0.6, 2.1, 5.4, 19.0 Hz), 2.85 m (1H, 6-H, ^2J = 19.0 Hz), 2.93 s (3H, CH_3), 3.00 t (1H, 2-H, J = 13.1, 6.8 Hz), 3.15 s (3H, CH_3), 3.17 m (1H,

2-H, J = 1.5, 6.8, 13.1 Hz), 3.52 m (1H, 5-H, J = 5.4, 11.7 Hz), 3.89 m (1H, 3a-H), 6.94 m (2H, H_{arom}), 7.25 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 17.89 q (CH_3), 21.97 t (C^3), 28.02 q (CH_3), 28.49 q (CH_3), 36.55 t (C^6), 43.80 d (C^{3a}), 50.14 d (C^5), 50.96 t (C^2), 57.62 s (C^4), 127.20 d ($C^{2''}$, $C^{6''}$), 128.73 d ($C^{3''}$, $C^{5''}$), 128.92 d ($^{4''}$), 131.44 s (C^{7a}), 136.18 s ($C^{1''}$), 140.41 s (C^7), 149.68 s ($C^{2'}$), 166.33 s and 169.87 s ($C^{4'}$, $C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 402 (71) $[M]^+$, 338 (25) 309 (100), 298 (35), 247 (34), 91 (46). $C_{20}H_{22}N_2O_5S$. Calculated: M 402.12493.

(5*R*)-5-(2-Methoxyphenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVb). mp 278–280°C (from ethanol). IR spectrum, ν, cm^{-1}: 727, 754, 1113, 1125, 1291, 1488, 1682, 1746. UV spectrum, λ_{max}, nm (logε): 206 (3.25), 278 (1.07). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.99 m (2H, 3-H), 2.22 d (3H, CH_3, J = 2.5 Hz), 2.43 d.d.d (1H, 6-H, J = 2.4, 3.3, 18.3 Hz), 2.58 m (1H, 6-H, ^2J = 18.3 Hz), 3.0 m (1H, 2-H), 3.07 s (3H, CH_3), 3.20 m (1H, 2-H), 3.32 s (3H, CH_3), 3.54 m (1H, 3a-H), 3.73 s (3H, OCH_3), 4.15 m (1H, 5-H, J = 3.3, 6.0 Hz), 6.75 d (1H, 3″-H, J = 8.2 Hz), 6.90 t (1H, 4″-H, J = 8.0, 8.2 Hz), 7.12 t (1H, 5″-H, J = 7.5, 8.0 Hz), 7.30 d (1H, 6″-H, J = 7.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.94 q (CH_3), 21.09 t (C^3), 28.85 q (CH_3), 29.01 q (CH_3), 36.61 d (C^{3a}), 37.37 t (C^6), 39.96 d (C^5), 50.52 t (C^2), 55.68 q (OCH_3), 57.92 s (C^4), 109.89 d ($C^{3''}$), 121.55 d ($C^{6''}$), 126.13 s ($C^{1''}$), 127.66 d and 129.37 d ($C^{4''}$, $C^{5''}$), 132.95 s (C^{7a}), 138.73 s (C^7), 150.81 s ($C^{2'}$), 156.16 s ($C^{2''}$), 167.70 s and 168.82 s ($C^{4'}$, $C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 432 (46) $[M]^+$, 340 (100), 298 (68), 121 (95), 91 (69). 432.13501. $C_{21}H_{24}N_2O_6S$. Calculated: M 432.13550.

(5*S*)-5-(2-Methoxyphenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIb). mp 188–205°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.75 m and 1.90 m (1H each, 3-H), 2.13 d (3H, CH_3, J = 2.2 Hz), 2.50 m (1H, 6-H), 2.86 s (3H, CH_3), 2.88–3.16 m (3H, 2-H, 6-H), 3.05 s (3H, CH_3), 3.50 m (1H, 5-H), 3.70 s (3H, OCH_3), 3.90 m (1H, 3a-H), 6.60 d (1H, 3″-H, J = 8.0 Hz), 6.80 m (2H, 4″-H, 5″-H), 7.16 d (1H, 6″-H, J = 7.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.79 q (CH_3), 21.01 t (C^3), 27.98 q (CH_3), 29.13 q (CH_3), 36.21 t (C^6), 39.87 d (C^{3a}), 43.04 d (C^5), 50.99 t (C^2), 56.71 q (OCH_3), 60.17 s (C^4), 110.73 d ($C^{3''}$), 120.41 d ($C^{6''}$), 124.35 s ($C^{1''}$), 127.56 d and 129.29 d ($C^{4''}$, $C^{5''}$), 131.59 s (C^{7a}), 139.99 s (C^7), 150.54 s ($C^{2'}$), 156.92 s ($C^{2''}$), 167.08 s and 170.43 s ($C^{4'}$, $C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 432 (43) $[M]^+$, 340 (87), 298 (53), 247 (33), 121 (100), 119 (32), 91 (89). $C_{21}H_{24}N_2O_6S$. Calculated: M 432.13550.

(5*R*)-5-(4-Methoxyphenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVc). mp 215–217°C (from ethyl acetate). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.09 m (2H, 3-H), 2.19 d (3H, CH_3, J = 2.6 Hz), 2.52 d.d (1H, 6-H, J = 2.4, 3.4, 18.2 Hz), 2.58 m (1H, 6-H), 2.99 m (1H, 2-H), 3.16 s (3H, CH_3), 3.20 m (1H, 2-H), 3.28 s (3H, CH_3), 3.34 d.d (1H, 5-H, J = 3.4, 6.0 Hz), 3.42 m (1H, 3a-H), 3.75 s (3H, OCH_3), 6.79 d (2H, 3″-H, 5″-H, J = 8.2 Hz), 6.86 d (2H, 2″-H, 6″-H, J = 8.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.07 q (CH_3), 21.36 t (C^3), 28.95 q (CH_3), 29.85 q (CH_3), 35.76 d (C^{3a}), 36.79 t (C^6), 49.04 d (C^5), 50.66 t (C^2), 55.09 q (OCH_3), 58.76 s (C^4), 114.58 d ($C^{3''}$, $C^{5''}$), 128.68 d ($C^{2''}$, $C^{6''}$), 129.69 s ($C^{1''}$), 132.89 s (C^{7a}), 140.62 s (C^7), 150.73 s ($C^{2'}$), 159.52 s ($C^{4''}$), 168.05 s and 168.43 s ($C^{4'}$, $C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 432 (46) $[M]^+$, 340 (100), 298 (68), 121 (95), 91 (69). $C_{21}H_{24}N_2O_6S$. Calculated: M 432.13550.

(5*S*)-5-(4-Methoxyphenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIc). mp 198–202°C. IR spectrum, ν, cm^{-1}: 733, 754, 839, 1032, 1113, 1127, 1302, 1515, 1584, 1610, 1675, 1750, 3546, 3627. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.78 m and 2.01 m (1H each, 3-H), 2.19 d (3H, CH_3, J = 2.6 Hz), 2.48 d.d.d (1H, 6-H, J = 2.2, 3.6, 18.8 Hz), 2.82 m (1H, 6-H, ^2J = 18.8 Hz), 2.95 s (3H, CH_3), 2.98 m (1H, 2-H), 3.14 s (3H, CH_3), 3.20 m (1H, 2-H), 3.68 d.d (1H, 5-H, J = 3.6, 11.2 Hz), 3.85 m (1H, 3a-H), 3.73 s (3H, OCH_3), 6.73 d (2H, 3″-H, 5″-H, J = 8.0 Hz), 6.86 d (2H, 2″-H, 6″-H, J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.84 q (CH_3), 21.97 t (C^3), 28.00 q (CH_3), 28.91 q (CH_3), 36.79 t (C^6), 43.84 d (C^{3a}), 49.29 d (C^5), 50.95 t (C^2), 55.14 q (OCH_3), 57.75 s (C^4), 114.00 d ($C^{3''}$, $C^{5''}$), 127.95 s ($C^{1''}$), 128.31 d ($C^{2''}$, $C^{6''}$), 131.35 s (C^{7a}), 140.54 s (C^7), 149.72 s ($C^{2'}$), 159.73 s ($C^{4''}$), 166.42 s and 170.01 s ($C^{4'}$, $C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 432 (43) $[M]^+$, 340 (87), 298 (53), 247 (33), 121 (100), 119 (32), 91 (89). $C_{21}H_{24}N_2O_6S$. Calculated: M 432.13550.

(5*R*)-5-(4-Fluorophenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVd). mp 199–200°C (from ethyl

acetate). IR spectrum, ν, cm^{-1}: 733, 758, 842, 1108, 1127, 1284, 1302, 1511, 1604, 1677, 1700, 1749. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.02 m (2H, 3-H), 2.21 d (3H, CH_3, J = 2.5 Hz), 2.58 m (2H, 6-H), 3.06 m (1H, 2-H), 3.16 s (3H, CH_3), 3.20 m (1H, 2-H), 3.29 s (3H, CH_3), 3.38 d.d (1H, 5-H, J = 3.0, 6.0 Hz), 3.43 m (1H, 3a-H), 6.91–7.01 m (4H, FC_6H_4). ^{13}C NMR spectrum, δ_C, ppm: 18.01 q (CH_3), 21.44 t (C^3), 28.94 q (CH_3), 30.71 q (CH_3), 35.93 d (C^{3a}), 36.59 t (C^6), 48.64 d (C^5), 50.62 t (C^2), 58.42 s (C^4), 115.84 d and 116.05 d ($C^{3''}$, $C^{5''}$), 129.06 d and 129.14 d ($C^{2''}$, $C^{6''}$), 132.98 s (C^{7a}), 133.72 s ($C^{1''}$), 138.47 s (C^7), 150.73 s ($C^{2'}$), 161.23 s ($C^{4''}$), 167.87 s and 168.31 s ($C^{4'}$, $C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 420 (36) $[M]^+$, 356 (23), 327 (100), 297 (75), 247 (32), 109 (55). $C_{20}H_{21}FN_2O_5S$. Calculated: M 420.11551.

(5*R*)-5-(2-Hydroxy-3-methoxyphenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVe). mp 228–231°C (from ethyl acetate). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.02 m (2H, 3-H), 2.20 d (3H, CH_3, J = 2.5 Hz), 2.40 d.d (1H, 6-H, J = 2.9, 18.4 Hz), 2.61 d.d.d (1H, 6-H, J = 0.6, 2.0, 6.7, 18.4 Hz), 2.98 m (1H, 2-H), 3.13 s (3H, CH_3), 3.18 m (1H, 2-H), 3.31 s (3H, CH_3), 3.54 m (1H, 3a-H), 3.86 s (3H, OCH_3), 3.89 d.d (1H, 5-H, J = 2.9, 6.7 Hz), 5.79 s (1H, OH), 6.71 d (2H, 4″-H, J = 8.0 Hz), 6.79 t (1H, 5″-H, J = 8.2, 8.0 Hz). 6.84 d (1H, 6″-H, J = 8.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.83 q (CH_3), 21.01 t (C^3), 28.98 q (CH_3), 29.17 q (CH_3), 36.06 d (C^{3a}), 37.06 t (C^6), 39.88 d (C^5), 50.46 t (C^2), 55.91 q (OCH_3), 57.68 s (C^4), 110.05 d ($C^{5''}$), 119.29 d ($C^{4''}$), 120.54 d ($C^{5''}$), 123.95 s ($C^{1''}$), 132.99 s (C^{7a}), 138.71 s (C^7), 142.99 s ($C^{3''}$), 145.79 d ($C^{2''}$), 150.81 s ($C^{2'}$), 167.58 s ($C^{4'}$), 168.46 s ($C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 448 (100) $[M]^+$, 356 (82), 298 (61). $C_{21}H_{24}N_2O_7S$. Calculated: M 448.13041.

(5*R*)-5-(3-Hydroxy-4-methoxyphenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVf). mp 208–211°C (from ethanol). IR spectrum, ν, cm^{-1}: 733, 756, 1050, 1129, 1287, 1511, 1589, 1681, 1700, 1752, 3501. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.05 m (2H, 3-H), 2.19 d (3H, CH_3, J = 2.5 Hz), 2.52 d.d (1H, 6-H, J = 2.5, 18.5 Hz), 2.61 d.d.d (1H, 6-H, J = 2.5, 6.0, 18.5 Hz), 3.01 m (1H, 2-H), 3.18 s (3H, CH_3), 3.20 m (1H, 2-H), 3.28 s (3H, CH_3), 3.36 d.d (1H, 5-H, J = 2.5, 6.0 Hz), 3.48 m (1H, 3a-H), 3.84 s (3H, OCH_3), 5.81 s (1H, OH), 6.43 d.d (1H, 6″-H, J = 2.1, 8.1 Hz), 6.48 d (1H, 2″-H, J = 2.1 Hz). 6.73 d (1H, 5″-H, J = 8.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.06 q (CH_3), 21.49 t (C^3), 28.92 q (CH_3), 29.01 q (CH_3), 35.90 d (C^{3a}), 36.75 t (C^6), 49.27 d (C^5), 50.68 t (C^2), 55.77 q (OCH_3), 58.78 s (C^4), 110.82 d ($C^{5''}$), 113.91 d ($C^{2''}$), 118.76 d ($C^{6''}$), 130.87 s ($C^{1''}$), 132.89 s (C^{7a}), 138.53 s (C^7), 145.86 s and 146.60 s ($C^{3''}$, $C^{4''}$), 150.73 s ($C^{2'}$), 168.10 s ($C^{4'}$), 168.51 s ($C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 448 (51) $[M]^+$, 356 (56), 298 (56), 188 (51), 137 (100). $C_{21}H_{24}N_2O_7S$. Calculated: M 448.13041.

(5*R*)-5-(3,4-Dimethoxyphenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVg). mp 249–251°C (from ethanol). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.01 m (2H, 3-H), 2.21 d (3H, CH_3, J = 2.1 Hz), 2.58 m (2H, 6-H), 2.98 m (1H, 2-H), 3.18 s (3H, CH_3), 3.25 m (1H, 2-H), 3.28 s (3H, CH_3), 3.43 d.d (1H, 5-H, J = 2.8, 6.2 Hz), 3.48 m (1H, 3a-H), 3.77 s (3H, OCH_3), 3.83 s (3H, OCH_3), 6.48 d (1H, 2″-H, J = 2.0 Hz), 6.50 d.d (1H, 6″-H, J = 2.0, 8.2 Hz), 6.75 d (1H, 5″-H, J = 8.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.03 q (CH_3), 21.48 t (C^3), 28.94 q (CH_3), 29.04 q (CH_3), 36.15 d (C^{3a}), 36.17 t (C^6), 49.38 d (C^5), 50.83 t (C^2), 55.72 q (OCH_3), 55.75 q (OCH_3), 58.71 s (C^4), 110.36 d ($C^{2''}$), 111.15 d ($C^{5''}$), 119.82 d ($C^{6''}$), 130.00 s ($C^{1''}$), 133.16 s (C^{7a}), 138.56 s (C^7), 149.06 s and 149.08 s ($C^{3''}$, $C^{4''}$), 150.71 s ($C^{2'}$), 168.06 s ($C^{4'}$), 168.39 s ($C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 462 (71) $[M]^+$, 369 (30), 202 (37), 191 (86), 151 (100). $C_{22}H_{26}N_2O_7S$. Calculated: M 462.14606.

(5*S*)-5-(3,4-Dimethoxyphenyl)-1′,3′,7-trimethyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIg). mp 205–208°C (from ethanol). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.75 m and 2.00 m (1H each, 3-H), 2.20 d (3H, CH_3, J = 2.3 Hz), 2.50 d.d (1H, 6-H, J = 3.9, 18.2 Hz), 2.80 m (1H, 6-H), 2.90 m (1H, 2-H), 3.00 s (3H, CH_3), 3.20 m (1H, 2-H), 3.18 s (3H, CH_3), 3.30 m (1H, 5-H, J = 3.9, 11.3 Hz), 3.48 m (1H, 3a-H), 3.80 s (6H, OCH_3), 6.43 d (1H, 2″-H, J = 2.2 Hz), 6.47 d.d (1H, 6″-H, J = 2.2, 8.0 Hz), 6.78 d (1H, 5″-H, J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.12 q (CH_3), 23.07 t (C^3), 28.00 q (CH_3), 28.60 q (CH_3), 36.99 t (C^6), 40.18 d (C^{3a}), 49.54 d (C^5), 50.90 t (C^2), 55.81 q and 55.84 q (OCH_3), 57.68 s (C^4), 110.80 d ($C^{2''}$), 114.51 d ($C^{5''}$), 120.21 d ($C^{6''}$), 130.12 s (C^{7a}), 134.08 s ($C^{1''}$), 139.12 s (C^7), 146.42 s ($C^{3''}$), 149.08 s ($C^{2'}$), 151.15 s ($C^{4''}$), 164.99 s and 169.12 s ($C^{4'}$, $C^{6'}$). Found: m/z 462.14660 $[M]^+$. $C_{22}H_{26}N_2O_7S$. Calculated: M 462.14606.

(5*R*)-1′,3′,7-Trimethyl-5-(2,3,4-trimethoxyphenyl)-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVh). mp 280–281°C (from ethyl acetate). IR spectrum, ν, cm^{-1}: 720, 728, 748, 1040, 1092, 1128, 1295, 1495, 1597, 1688, 1700, 1748. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.98 m (2H, 3-H), 2.20 d (3H, CH_3, J = 2.0 Hz), 2.44 d.d (1H, 6-H, J = 2.7, 18.6 Hz), 2.61 d.d.d (1H, 6-H, J = 4.2, 6.5, 18.6 Hz), 3.01 d.d.d (1H, 2-H, J = 7.7, 11.9, 13.2 Hz), 3.12 s (3H, CH_3), 3.18 m (1H, 2-H, J = 2.7, 6.2, 13.2 Hz), 3.30 s (3H, CH_3), 3.39 m (1H, 3a-H), 3.73 d.d (1H, 5-H, J = 2.7, 6.5 Hz), 3.76 s (3H, OCH_3), 3.77 s (3H, OCH_3), 3.81 s (3H, OCH_3), 6.63 d (1H, 5″-H, J = 8.4 Hz), 6.80 d (1H, 6″-H, J = 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.97 q (CH_3), 20.92 t (C^3), 29.05 q (CH_3), 29.08 q (CH_3), 36.37 d (C^{3a}), 37.26 t (C^6), 40.97 d (C^5), 50.47 t (C^2), 55.71 q (CH_3), 58.01 s (C^4), 60.56 q (CH_3), 60.95 q (CH_3), 107.23 d ($C^{5''}$), 121.79 d ($C^{6''}$), 123.30 s ($C^{1''}$), 132.88 s (C^{7a}), 138.99 s (C^7), 141.14 s ($C^{4''}$), 150.85 s ($C^{2'}$), 151.29 s and 153.39 s ($C^{2''}$, $C^{3''}$), 167.76 s ($C^{4'}$), 168.65 s ($C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 492 (65) $[M]^+$, 400 (36), 337 (40), 298 (48), 221 (90), 181 (100). $C_{23}H_{28}N_2O_8S$. Calculated: M 492.15662.

(5*S*)-1′,3′,7-Trimethyl-5-(2,3,4-trimethoxyphenyl)-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIh). mp 185–187°C (from ethanol). IR spectrum, ν, cm^{-1}: 728, 754, 1099, 1131, 1288, 1302, 1498, 1599, 1681, 1746. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.82 m and 2.01 m (1H each, 3-H), 2.19 d (3H, CH_3, J = 2.7 Hz), 2.40 d.d (1H, 6-H, J = 3.7, 19.0 Hz), 2.81 m (1H, 6-H), 2.98 m (1H, 2-H), 2.96 s (3H, CH_3), 3.17 m (1H, 2-H), 3.20 s (3H, CH_3), 3.77 s (3H, OCH_3), 3.81 s (3H, OCH_3), 3.82 s (3H, OCH_3), 3.89 d.d (1H, 5-H, J = 3.7, 11.5 Hz), 3.94 m (1H, 3a-H), 6.49 d (1H, 6″-H, J = 8.7 Hz), 6.52 d (1H, 5″-H, J = 8.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.89 q (CH_3), 21.85 t (C^3), 28.28 q (CH_3), 28.72 q (CH_3), 37.25 t (C^6), 40.12 d (C^{3a}), 43.67 d (C^5), 51.05 t (C^2), 55.88 q (OCH_3), 56.21 s (C^4), 60.68 q (OCH_3), 61.32 q (OCH_3), 106.95 d ($C^{5''}$), 121.95 d ($C^{6''}$), 122.56 s ($C^{1''}$), 131.63 s (C^{7a}), 140.38 s (C^7), 142.22 s ($C^{4''}$), 150.19 s ($C^{2'}$), 151.97 s and 153.79 s ($C^{2''}$, $C^{3''}$), 166.55 s ($C^{4'}$), 169.41 s ($C^{6'}$). Found: m/z 492.15630 $[M]^+$. $C_{23}H_{28}N_2O_8S$. Calculated: M 492.15662.

(5*R*)-7-Methyl-5-phenyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIIa). mp 248–250°C (decomp.; from ethanol). IR spectrum, ν, cm^{-1}: 817, 1034, 1095, 1123, 1294, 1496, 1599, 1685, 1715, 1753, 3093, 3214, 3436. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.96 m (2H, 3-H), 2.06 d (3H, CH_3, J = 1.7 Hz), 2.53 m (2H, 6-H), 3.05 m (1H, 2-H), 3.22 m (1H, 2-H), 3.42 m (1H, 3a-H), 3.62 d (1H, 5-H, J = 2.8, 6.0 Hz), 7.12 m (2H, H_{arom}), 7.32 m (3H, H_{arom}), 11.12 br.s (2H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 17.69 q (CH_3), 21.55 t (C^3), 35.42 d (C^{3a}), 36.05 t (C^6), 46.73 d (C^5), 50.66 t (C^2), 56.82 s (C^4), 127.67 d ($C^{4''}$), 127.85 d ($C^{2''}$, $C^{6''}$), 128.50 d ($C^{3''}$, $C^{5''}$), 133.36 s (C^{7a}), 137.95 s ($C^{1''}$), 139.19 s (C^7), 149.83 s ($C^{2'}$), 169.57 s and 169.97 s ($C^{4'}$, $C^{6'}$). Found: m/z 374.09357 $[M]^+$. $C_{18}H_{18}N_2O_5S$. Calculated: M 374.09363.

(5*S*)-7-Methyl-5-phenyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIIIa). mp 196–200°C (decomp.; from ethanol). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.68 m and 1.92 m (1H each, 3-H), 2.04 d (3H, CH_3, J = 2.5 Hz), 2.53 m and 2.80 m (1H each, 6-H), 3.09 m and 3.20 m (1H each, 2-H), 3.54 m (1H, 5-H, J = 5.8, 11.8 Hz), 3.70 m (1H, 3a-H), 7.12 m (2H, H_{arom}), 7.32 m (3H, H_{arom}), 11.12 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 17.51 q (CH_3), 21.93 t (C^3), 36.80 t (C^6), 44.21 d (C^{3a}), 47.03 d (C^5), 50.26 t (C^2), 56.71 s (C^4), 127.25 d ($C^{2''}$, $C^{6''}$), 127.76 d ($C^{4''}$), 128.89 d ($C^{3''}$, $C^{5''}$), 131.44 s (C^{7a}), 137.55 s ($C^{1''}$), 140.11 s (C^7), 149.14 s ($C^{2'}$), 168.57 s and 171.34 s ($C^{4'}$, $C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 374 (26) $[M]^+$, 179 (19), 153 (23), 91 (100). $C_{18}H_{18}N_2O_5S$. Calculated: M 374.09363.

(5*R*)-5-(2-Methoxyphenyl)-7-methyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIIb). mp 208–211°C (decomp.; from ethanol). IR spectrum, ν, cm^{-1}: 757, 1026, 1052, 1122, 1294, 1493, 1600, 1615, 1678, 1716, 1753, 3024, 3202, 3397. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.08 m (2H, 3-H), 2.22 d (3H, CH_3, J = 2.0 Hz), 2.53 d.d (1H, 6-H, J = 3.2, 18.6 Hz), 2.75 m (1H, 6-H, ^2J = 18.6 Hz), 3.10 m and 3.22 m (1H, 2-H), 3.42 m (1H, 3a-H), 3.68 s (3H, CH_3), 4.04 d (1H, 5-H, J = 5.8, 3.2 Hz), 6.72 d (1H, 3″-H, J = 8.2 Hz), 6.83 t (1H, 5″-H, J = 8.0, 8.6 Hz), 7.00 d (1H, 6″-H, J = 8.6 Hz), 7.16 t (1H, 4″-H, J = 8.0, 8.2 Hz), 10.82 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 18.08 q (CH_3), 21.56 t (C^3), 37.66 d (C^{3a}), 38.44 t (C^6), 40.32 d (C^5), 51.89 t (C^2), 56.01 q (OCH_3), 58.08 s (C^4), 111.45 d ($C^{3''}$), 122.04 d ($C^{5''}$), 127.27 d ($C^{6''}$), 128.55 s ($C^{1''}$), 130.19 d ($C^{4''}$), 133.12 s (C^{7a}), 139.70 s (C^7), 149.86 s ($C^{2'}$), 158.18 s ($C^{2''}$), 169.94 s and 170.48 s ($C^{4'}$, $C^{6'}$). Found: m/z 404.10370 $[M]^+$. $C_{19}H_{20}N_2O_6S$. Calculated: M 404.10420.

(5*S*)-5-(2-Methoxyphenyl)-7-methyl-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIIIb). mp 228–232°C (decomp.; from ethanol). IR spectrum, ν, cm^{-1}: 759, 1026, 1120, 1289, 1340, 1492, 1589, 1601, 1698, 1724, 1751, 3104, 3219, 3431. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.86 m and 2.06 m (1H each, 3-H), 2.09 d (3H, CH_3, J = 2.0 Hz), 2.43 m (2H, 6-H), 3.05 m and 3.20 m (1H each, 2-H), 3.42 m (1H, 3a-H), 3.62 d (1H, 5-H, J = 4.0, 11.2 Hz), 3.78 s (3H, CH_3), 6.79 m (2H, 3″-H, 5″-H), 6.90 d (1H, 6″-H, J = 8.5 Hz), 7.16 t (1H, 4″-H, J = 8.2, 8.2 Hz), 11.32 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 17.81 q (CH_3), 21.85 t (C^3), 36.19 d (C^{3a}), 36.92 t (C^6), 40.13 d (C^5), 50.58 t (C^2), 55.21 q (OCH_3), 56.71 s (C^4), 110.11 d ($C^{3''}$), 120.38 d ($C^{5''}$), 127.27 d ($C^{6''}$), 128.88 s ($C^{1''}$), 131.54 d ($C^{4''}$), 132.04 s (C^{7a}), 139.51 s (C^7), 150.08 s ($C^{2'}$), 156.88 s ($C^{2''}$), 169.27 s and 172.28 s ($C^{4'}$, $C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 404 (24) $[M]^+$, 311 (21), 172 (22), 161 (22), 121 (100). $C_{19}H_{20}N_2O_6S$. Calculated: M 404.10420.

(5*R*)-7-Methyl-5-(2,3,4-trimethoxyphenyl)-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-2′,4′,6′(1′*H*,3′*H*)-trione 1,1-dioxide (XVIIc). mp 229–232°C (decomp.). IR spectrum, ν, cm^{-1}: 700, 742, 1064, 1121, 1286, 1496, 1500, 1605, 1705, 1740, 1752, 3102, 3198, 3427. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.96 m (2H, 3-H), 2.05 d (3H, CH_3, J = 2.0 Hz), 2.41 d.d (1H, 6-H, J = 2.8, 18.7 Hz), 2.55 m (1H, 6-H, ^2J = 18.7 Hz), 3.08 m and 3.15 m (1H each, 2-H), 3.50 m (1H, 3a-H), 3.69 s (OCH_3), 3.79 s (3H, OCH_3), 3.81 s (3H, OCH_3), 3.81 d.d (1H, 5-H, J = 2.8, 5.8 Hz), 6.71 d and 6.73 d (1H each, 5″-H, 6″-H, J = 8.6 Hz), 12.7 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 17.45 q (CH_3), 20.97 t (C^3), 36.55 d (C^{3a}), 36.90 t (C^6), 39.90 d (C^5), 50.46 t (C^2), 56.69 q (OCH_3), 56.40 s (C^4), 60.11 q (OCH_3), 60.49 q (OCH_3), 107.62 d ($C^{5''}$), 121.62 d ($C^{6''}$), 124.44 s ($C^{1''}$), 132.88 s (C^{7a}), 138.61 s (C^7), 140.71 s ($C^{3''}$), 149.68 s ($C^{4''}$), 151.10 s ($C^{2'}$), 152.78 s ($C^{2''}$), 169.32 s and 170.17 s ($C^{4'}$, $C^{6'}$). Mass spectrum, m/z (I_{rel}, %): 464 (3) $[M]^+$, 306 (18), 275 (100), 232 (54). $C_{21}H_{24}N_2O_8S$. Calculated: M 464.12532.

(5*R*)-7-Methyl-2-thioxo-5-(2,3,4-trimethoxyphenyl)-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-4′,6′(1′*H*,3′*H*)-dione 1,1-dioxide (XIXa). mp 249–252°C (decomp.). IR spectrum, ν, cm^{-1}: 1096, 1121, 1134, 1295, 1524, 1599, 1650, 1675, 1718, 3185, 3235, 3415. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.95 m (2H, 3-H), 2.03 d (3H, CH_3, J = 2.0 Hz), 2.33 m (1H, 6-H, ^2J = 18.5 Hz), 2.50 m (1H, 6-H), 3.09 m and 3.22 m (1H each, 2-H), 3.48 m (1H, 3a-H), 3.69 s (3H, OCH_3), 3.76 s (3H, OCH_3), 3.78 s (3H, OCH_3), 3.82 d.d (1H, 5-H, J = 5.6, 2.8 Hz), 6.69 d and 6.75 d (1H each, 5″-H, 6″-H, J = 8.2 Hz), 12.3 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 17.54 q (CH_3), 20.88 t (C^3), 35.60 d (C^{3a}), 36.78 t (C^6), 39.90 d (C^5), 50.43 t (C^2), 55.70 q (OCH_3), 57.09 s (C^4), 60.27 q (OCH_3), 60.79 q (OCH_3), 107.49 d ($C^{5''}$), 121.42 d ($C^{6''}$), 123.92 s ($C^{1''}$), 133.09 s (C^{7a}), 138.18 s (C^7), 140.51 s ($C^{3''}$), 151.11 s ($C^{2''}$), 152.89 s ($C^{4''}$), 167.24 s and 167.93 s ($C^{4'}$, $C^{6'}$), 178.63 s ($C^{2'}$). Mass spectrum, m/z (I_{rel}, %): 480 (55) $[M]^+$, 337 (59), 291 (41), 232 (43), 221 (82), 194 (65), 181 (100). $C_{21}H_{24}N_2O_7S_2$. Calculated: M 480.10248.

(5*R*)-5-(2-Methoxyphenyl)-7-methyl-2-thioxo-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-4′,6′(1′*H*,3′*H*)-dione 1,1-dioxide (XIXb). mp 213–220°C (decomp.; from EtOH–DMSO, 1:1). IR spectrum, ν, cm^{-1}: 728, 756, 1006, 1095, 1116, 1128, 1291, 1297, 1300, 1495, 1548, 1609, 1665, 1706, 3183, 3280, 3391. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.99 m (2H, 3-H), 2.07 d (3H, CH_3, J = 2.0 Hz), 2.33 m (1H, 6-H, ^2J = 18.8 Hz), 2.55 m (1H, 6-H), 2.99 m and 3.20 m (1H each, 2-H), 3.60 m (1H, 3a-H), 3.68 s (3H, OCH_3), 4.02 d.d (1H, 5-H, J = 6.0, 2.8 Hz), 6.86 m (3H, 3″-H, 4″-H, 6″-H), 7.32 t (1H, 5″-H, J = 8.6, 8.0 Hz), 9.5 br.s and 11.12 br.s (1H each, NH). ^{13}C NMR spectrum, δ_C, ppm: 17.63 q (CH_3), 21.62 t (C^3), 35.32 d (C^{3a}), 36.48 t (C^6), 44.60 d (C^5), 50.38 t (C^2), 55.11 q (OCH_3), 57.09 s (C^4), 109.83 d ($C^{3''}$), 120.63 d ($C^{6''}$), 126.48 s ($C^{1''}$), 127.69 d ($C^{4''}$), 128.80 d ($C^{5''}$), 132.74 s (C^{7a}), 138.36 s (C^7), 156.52 s ($C^{2''}$), 166.87 s and 167.76 s ($C^{4'}$, $C^{6'}$), 178.27 s ($C^{2'}$). Found: m/z 420.08004 $[M]^+$. $C_{19}H_{20}N_2O_5S_2$. Calculated: M 420.08136.

(5*S*)-5-(2-Methoxyphenyl)-7-methyl-2-thioxo-3,3a,5,6-tetrahydro-2*H*,2′*H*-spiro[1-benzothiophene-4,5′-pyrimidine]-4′,6′(1′*H*,3′*H*)-dione 1,1-dioxide (XXb). mp 232–238°C (decomp.; from ethanol). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.64 m and 1.92 m (1H each, 3-H), 2.02 d (3H, CH_3, J = 2.2 Hz), 2.40 m (1H, 6-H, ^2J = 18.5 Hz), 2.80 m (1H, 6-H), 3.15 m (1H, 2-H), 3.50 m (2H, 2-H, 3a-H), 3.88 s (3H, OCH_3), 3.92 d.d (1H, 5-H, J = 11.6, 5.8 Hz), 6.70 d (1H, 3″-H, J = 8.2 Hz), 6.80 t (1H, 4″-H, J = 8.6, 8.2 Hz), 6.86 d (1H, 6″-H, J = 8.0 Hz), 7.22 t (1H, 5″-H, J = 8.6, 8.0 Hz), 12.05 br.s and 12.25 br.s (1H each, NH). ^{13}C NMR spectrum, δ_C, ppm: 17.47 q (CH_3), 20.74 t (C^3), 36.54 t (C^6), 37.95 d (C^{3a}), 43.16 d (C^5), 50.80 t (C^2), 55.24 s (C^4), 55.59 q (OCH_3), 111.05 d ($C^{3''}$), 120.35 d ($C^{6''}$), 125.19 s ($C^{1''}$), 126.92 d

($C^{4''}$), 129.09 d ($C^{5''}$), 131.36 s (C^{7a}), 140.71 s (C^{7}), 157.04 s ($C^{2''}$), 166.28 s and 169.16 s ($C^{4'}$, $C^{6'}$), 177.81 s ($C^{2'}$). Mass spectrum, *m*/*z* (I_{rel}, %): 420 (12) $[M]^+$, 328 (31), 121 (39), 91 (30), 66 (100). $C_{19}H_{20}N_2O_5S_2$. Calculated: *M* 420.08136.

3-[9-*tert*-Butyl-1,3-dimethyl-2,4-dioxo-5-(1,3-dimethyl-2,4,6-trioxohexahydropyrimidin-5-yl)-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidine-7-yl]propyl acetate (XXIV). A mixture of 0.25 g (0.9 mmol) of aldehyde **XXIII**, 0.2 g (1.3 mmol) of 1,3-dimethylbarbituric acid, 0.14 g (0.89 mmol) of diene **I**, and 0.024 g (0.18 mmol) of L-4-hydroxyproline in 10 ml of dioxane–water (8:2) was heated for 8 h under reflux, an additional 0.12 g of 1,3-dimethylbarbituric acid was added, and the mixture was heated for 12 h more under reflux. The mixture was then evaporated, and the residue was subjected to chromatography on silica gel to isolate (in order of elution) 0.12 g of unreacted diene **I** and 0.42 g (85%) of compound **XXIV** with mp 175–177°C (from ethyl acetate). IR spectrum, ν, cm^{-1}: 754, 1035, 1110, 1123, 1180, 1213, 1227, 1377, 1493, 1595, 1600, 1660, 1670, 1676, 1680, 1700, 1720, 1747. ^{1}H NMR spectrum, δ, ppm: 1.41 s (9H, Bu-*t*), 1.85 m (2H, CH_2), 2.03 s (3H, CH_3), 2.57 m (2H, 7-CH_2), 2.97 s (3H, 1′-CH_3), 3.22 s (3H, 3′-CH_3), 3.35 s (3H, 1-CH_3), 3.57 s (3H, 3-CH_3), 3.92 d (1H, 5-H, *J* = 1.2 Hz), 4.00 m (2H, CH_2C=O), 4.99 d (1H, 5′-H, *J* = 1.2 Hz), 6.78 d (1H, 6-H, *J* = 1.8 Hz), 7.07 d (1H, 8-H, *J* = 1.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.47 q (CH_3), 27.65 q (CH_3N), 27.69 q (CH_3N), 27.88 q (CH_3N), 29.33 q [(**C**H_3)$_3$C], 29.65 t (CH_2), 29.85 s (1′-CH_3), 31.18 t (CH_2), 34.25 s [(CH_3)$_3$**C**], 37.85 d (C^5), 53.89 d ($C^{5'}$), 62.96 t (CH_2), 85.29 s (C^{4a}), 119.24 s (C^{5a}), 125.14 d (C^6), 126.99 d (C^8), 137.37 d (C^9), 138.14 s (C^7), 146.38 s (C^{9a}), 150.14 s (C^2), 150.69 s ($C^{2'}$), 154.05 s (C^{10a}), 161.25 s (C^4), 166.52 s and 166.77 s ($C^{4'}$, $C^{6'}$), 170.52 s (C=O). Mass spectrum, *m*/*z* (I_{rel}, %): 554 (2) $[M]^+$, 552 (5), 342 (10), 312 (16), 43 (14). $C_{28}H_{34}N_4O_8$. Calculated: *M* 554.23764.

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