Chinese Journal of Chemistry, **2004**, *22*, 290—295 **Article**

An Efficient Synthesis of [1,2,4]Triazolo[3,2-*d*][1,5]benzoxazepin-2-thiones, a Kind of Novel Tricyclic *O*,*N*-Heterocycles

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A series of novel tricyclic *O*,*N*-heterocycles, [1,2,4]triazolo[3,2-*d*][1,5]benzoxazepin-2-thiones **7** were achieved via acid-induced ring closure of the geminal arylazo isothiocyanate compounds **5** which were derived from substituted chroman-4-ones, followed by feasible ring expansion with simultaneous insertion of the nitrogen atom into the carbon skeleton. The X-ray crystal structure of **7d** was also described.

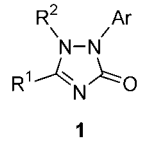
Keywords geminal arylazo isothiocyanate, ring closure, rearrangement, [1,2,4]triazolo[3,2-*d*][1,5]benzoxazepin-2-thiones

Introduction

Many [1,2,4]triazolobenzoheteroazepine heterocycles show important biological activities.[1-4] They have been used as drugs or candidates for antipsychotic agents, as carrageenin-induced edema inhibitors, for inhibiting phospholipase A_2, and also for treatment of osteoporosis. The attachment of a triazolo ring to the heptatomic ring provides the potentiality to enhance the pharmacological activity and/or offer more interesting properties.[5,6] It is not surprising therefore that there has been a significant and ever increasing interest in the design and synthesis of this class of heterocycles.[7,8]

We have previously established an efficient synthetic pathway to obtain [1,2,4]triazolo[3,2-*d*][1,5]benzoxazepines and their chalcogen analogues starting from chroman-4-ones and respectively thiochroman-4-ones.[9,10] In general, the reaction involves the cycloaddition of 1-aza-2-azoniaallenium ions, a kind of positively charged 1,3-dipoles, to the triple bond of nitriles. We have also successfully expanded the reaction sequence to the synthesis of novel thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepines by starting from 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one.[11] However, some drawbacks have been incurred with our approaches: (1) the majority of our products was restricted to the hexachloroantimonate salts, which are unsuitable for evaluating their pharmaceutical usefulness. (2) For obtaining the neutral triazolo fused heterocycles the ethoxy carbonylhydrazones instead of the readily accessible arylhydrazones have to act as the substrate but the stoichiometric amount of antimony(V) chloride used as a Lewis acid does not appear in the final molecule, thus lowering the synthetic efficiency.

Gstach and co-workers[12,13] have reported a convenient synthesis of 1,5-disubstituted 2-aryl-1,2-dihydro-3*H*-1,2,4-triazol-3-ones **1** by acid-induced ring closure-rearrangement of α-(arylazo)alkyl isocyanates (Figure 1). Our continuous interests in the synthesis of tricyclic compounds spurred us to test the possibility of extending Gstach's work to the synthesis of novel 1,2,4-triazolo fused benzoxazepine ring systems. We now show that a kind of novel [1,2,4]triazolo[3,2-*d*][1,5]-benzoxazepin-2-thiones can be furnished by employment of chroman-4-ones that are readily accessible from substituted phenols.



1

Figure 1 Structure of 1,5-disubstituted 2-aryl-1,2-dihydro-3*H*-1,2,4-triazol-3-one (**1**).

Results and discussion

The synthesis of novel [1,2,4]triazolo[3,2-*d*][1,5]-benzoxazepin-2-thiones **7** is shown in Scheme 1. The required chroman-4-ones **2** were readily attainable according to literature[14-16] via the initial Michael-type addition of the respective aryloxide ion to the double bond of acrylonitrile followed by acid-catalyzed hydrolysis of the nitrile group to carboxylic acid and final in-

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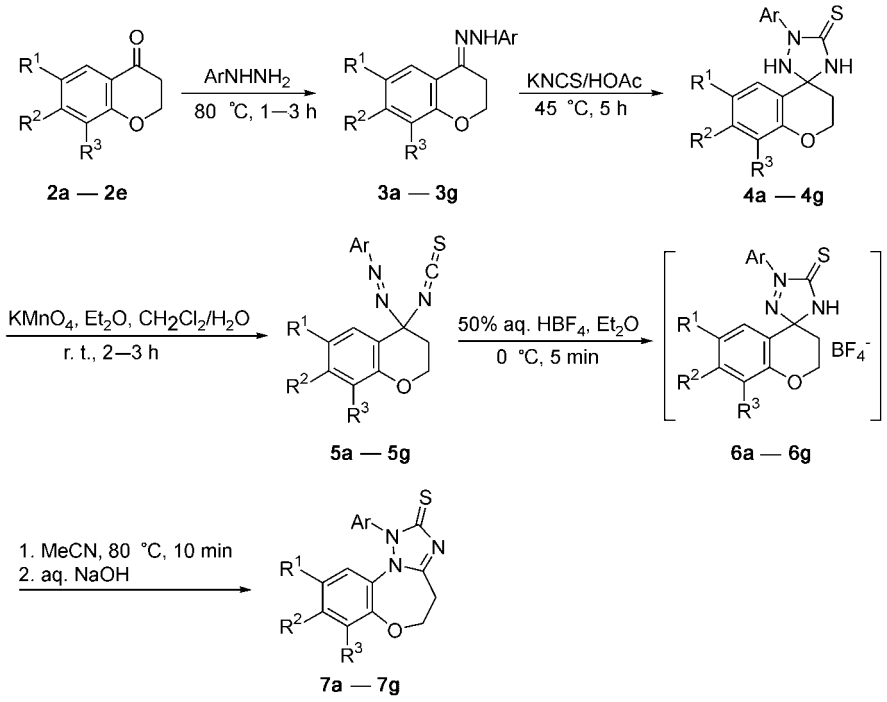
tramolecular ring closure. Substituted chroman-4-ones **2a**—**2e** reacted with arylhydrazine produced the arylhydrazones **3a—3g** in nearly quantitative yield, which were pure enough (^{1}H NMR) for the next step. Arylhydrazone of chromanone **3a**—**3g** reacted with a slight excess of potassium thiocyanate in acetic acid at 45 ℃, and are readily transformed into the corresponding compounds **4a**—**4g**. The reaction features a 1,3-dipolar cycloaddition with the hydrazone moiety as the 1,3-dipole and isothiocyanic acid (generated *in situ*) as the dipolarophile. Oxidative ring cleavage of **4** was accomplished efficiently using 1.2 equivalents of potassium permanganate in a two phase system (H_2O/1∶1 mixture of Et_2O and CH_2Cl_2) to give the bicyclic geminal arylazo isothiocyanates **5** in excellent yield (mostly ＞90%). The IR spectrum of **5** exhibited strong absorptions at 2000 cm^{-1} corresponding to the C＝N＝S group.

The acid-induced ring closure and rearrangement of the isothiocyanates **5** took place with ring expansion to yield [1,2,4]triazolo[3,2-*d*][1,5]benzoxazepin-2-thiones (**7a**—**7g)** via intermediates **6**. Compounds **6** were formed by simply stirring of **5** in Et_2O with 50% aqueous solution of tetrafluoroboric acid at 0 ℃. They were generally highly reactive, capable of existence only as short-lived intermediates, thus precluding their isolation from the reaction mixture. Under mild conditions, intermediates **6** underwent fast 1,2-migration with concurrent ring expansion and insertion of the nitrogen atom into the carbon skeleton to yield the salt of compounds **7a**—7**g.** The neutral free tricyclic heterocycles **7a**—7**g** have been prepared after basic work-up. In all instances, the ring expansion of the benzannulated **6** occurs exclusively with migration of the aromatic side of the ring, yielding **7** as the sole products. This is just what we expected on the basis of our closely related counterparts.

The structure of the tricyclic heterocycles **7** was proved by the analysis of spectroscopic data and X-ray structural investigation. Strong absorption at about 1685 cm^{-1} in IR spectra and ^{13}C NMR signal at about δ 180 are all proofs for the C＝S function. The structure of **7d** was determined by X-ray diffraction analysis. Pale yellow crystals of compound **7d**, suitable for X-ray investigation, were obtained by slow cooling of a methanol solution. The X-ray crystallographic structure analysis provides affirmative evidence for the migration selectivity mentioned above. The X-ray structure of **7d** is shown in Figure 2 and selected bond lengths and bond angles are listed in the Table 1 and Table 2.

Scheme 1



2—7	Ar	R^1	R^2	R^3
a	Ph	H	H	H
b	Ph	Me	H	H
c	Ph	MeO	H	H
d	Ph	H	Me	H
e	Ph	H	H	Me
f	4-ClC_6H_4	H	H	H
g	4-ClC_6H_4	H	H	Me

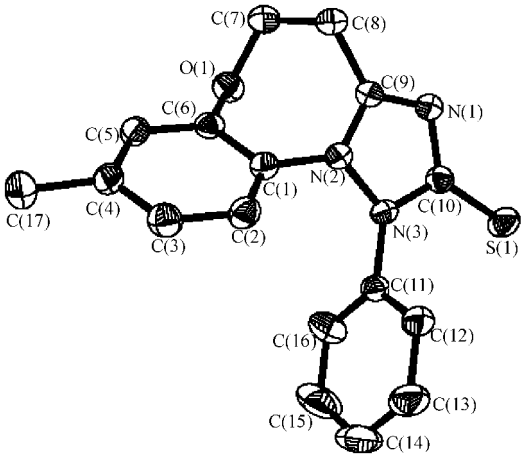


Figure 2 Molecule structure of compound **7d.**

Table 1 Selected bond lengths for compound **7d** (10^{-1} nm)

S(1)—C(10)	1.668(3)	N(3)—C(11)	1.426(3)
C(9)—N(1)	1.310(3)	O(1)—C(6)	1.371(3)
C(9)—N(2)	1.339(3)	O(1)—C(7)	1.434(3)
C(9)—C(8)	1.479(4)	C(4)—C(17)	1.494(4)
N(2)—N(3)	1.384(3)	C(7)—C(8)	1.503(4)
N(2)—C(10)	1.419(3)	N(1)—C(10)	1.364(3)
N(3)—C(10)	1.363(3)	O(2)—C(18)	1.334(9)

Table 2 Selected bond angles for compound **7d** (°)

N(1)-C(9)-C(8)	128.1(3)	O(1)-C(6)-C(5)	120.2(2)
N(2)-C(9)-C(8)	119.6(2)	O(1)-C(6)-C(1)	120.3(2)
C(9)-N(2)-C(1)	127.1(2)	C(5)-C(6)-C(1)	119.4(3)
N(3)-N(2)-C(1)	125.6(2)	O(1)-C(7)-C(8)	113.4(2)
C(10)-N(3)-C(11)	129.4(2)	C(9)-C(8)-C(7)	112.1(2)
N(2)-N(3)-C(11)	123.1(2)	C(9)-N(1)-C(10)	106.4(2)
C(6)-O(1)-C(7)	117.0(2)	N(3)-C(10)-N(1)	108.6(2)
C(2)-C(1)-N(2)	123.1(2)	N(3)-C(10)-S(1)	124.4(2)
C(6)-C(1)-N(2)	117.1(2)	N(1)-C(10)-S(1)	126.9(2)
C(5)-C(4)-C(17)	121.5(3)	C(16)-C(11)-N(3)	119.6(3)
C(3)-C(4)-C(17)	120.5(3)	C(12)-C(11)-N(3)	118.8(3)

In summary, we have successfully developed a new method for the synthesis of [1,2,4]triazolo[3,2-d][1,5]-benzoxazepin-2-thiones, which represent a kind of novel tricyclic heterocycles under ambient conditions. Both spectral data and the X-ray crystallographic analysis confirmed the structural elucidation. Incorporation of a triazolo ring onto the seven-membered ring and the obvious structural relationship with literature precedents render these novel tricyclic heterocycles to be of considerable potential pharmaceutical interests.

Experimental

Melting points are uncorrected and expressed in degree Celsius. IR spectra were recorded on a Mattson Alpha-centauri FT-IR spectrometer, for solids in potassium bromide discs and for liquids by placing a thin lay of the CCl_4 solution between two sodium chloride discs. ^{1}H NMR spectra were acquired on a Brucker AMX 500 spectrometer at 500 MHz (^{1}H NMR) and are reported in ppm (δ) downfield relative to TMS as internal standard, and ^{13}C NMR spectra were recorded at 125 MHz and assigned in ppm (δ). Mass spectra and high-resolution mass spectra were performed on a Varian MAT 44S with EI ionization. All other commercially available compounds were used as received. Solvents and reagents were purified and dried by standard methods prior to use.

2-Arylspiro[1,2,4-triazolidine-5,4'-chroman]-3-thiones (4a—4g)

General procedures Arylhydrazine (10 mmol) was added to a solution of the appropriate chroman-4-one (10 mmol) **2** in EtOH (30 mL). The mixture containing a catalytic amount of AcOH (*ca*. 0.5 mL) was heated under reflux for 1—3 h [TLC control, EtOAc/petroleum ether (60—90 ℃) 1∶5/*V*∶*V*]. Reduced pressure rotary evaporation at 30 ℃ gave the corresponding chroman-4-one arylhydrazone **3** that was employed as the substrate without further purification.

To a 45 ℃ stirred solution of the hydrazone **3** in AcOH (40 mL) and water (3 mL), potassium thiocyanate (9.73 g, 12 mmol) was added. The mixture was stirred for further 8 h. Subsequently, ice-cold water (50 mL) was added carefully and the resulting suspension was kept at 0 ℃ for 1 h. The crude product was filtered, washed with water until neutral, and dried *in vacuo* (P_2O_5). The unreacted hydrazone was removed by refluxing a suspension of the crude product in Et_2O (20 mL) for 10 min. The desired 2-arylspiro[1,2,4-triazolidine-5,4'-chroman]-3-thione (**4)**, which is scarcely soluble in Et_2O was filtered, washed with Et_2O (2×10 mL), and dried *in vacuo* over $CaCl_2$.

2-Phenylspiro[1,2,4-triazolidine-5,4'-chroman]-3-thione (4a)

From **2a** and phenylhydrazine according to the general procedure afforded **4a** as white powders (2.14 g, 72%). m.p. 164—166 ℃. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.06—2.11 (m, 1H, CH_2), 2.39 (d, J=13.9 Hz, 1H, CH_2), 4.40 (d, J=11.2 Hz, 1H, OCH_2), 4.50 (dd, J= 11.2, 11.2 Hz, 1H, OCH_2), 5.17 (s, 1H, NH), 6.47 (s, 1H, CSNH), 6.88—8.00 (m, 9H, ArH); IR (KBr) ν: 3447, 3146, 2974, 1597 cm^{-1}.

11-Methyl-2-phenylspiro[1,2,4-triazolidine-5,4'-chroman]-3-thione (4b)

From **2b** and phenylhydrazine according to the general procedure afforded **4b** as white powders (2.39 g, 77%). m.p. 180—182 ℃. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.02—2.11 (m, 1H, CH_2), 2.31 (s, 3H, CH_3), 2.35—2.41 (m, 1H, CH_2), 4.35—4.40 (m, 1H, OCH_2), 4.43—4.51 (m, 1H, OCH_2), 5.16 (s, 1H, NH), 6.32 (s,

1H, CSNH), 6.79—8.00 (m, 8H, ArH); IR (KBr) *v*: 3433, 3152, 2964, 2928, 1618, 1598 cm^{-1}.

11-Methoxy-2-phenylspiro[1,2,4-triazolidine-5,4'-chroman]-3-thione (4c)

From **2c** and phenylhydrazine according to the general procedure afforded **4c** as white powders (2.22 g, 68%). m.p. 181—183 ℃. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.03—2.10 (m, 1H, CH_2), 2.38 (d, J=9.1 Hz, 1H, CH_2), 3.79 (s, 3H, OCH_3), 4.35 (d, J=9.0 Hz, 1H, OCH_2), 4.44—4.48 (m, 1H, OCH_2), 5.17 (s, 1H, NH), 6.24 (s, 1H, CSNH), 6.92—8.01 (m, 8H, ArH); IR (KBr) *v*: 3419, 3177, 3068, 2958, 2889, 1597 cm^{-1}.

12-Methyl-2-phenylspiro[1,2,4-triazolidine-5,4'-chroman]-3-thione (4d)

From **2d** and phenylhydrazine according to the general procedure afforded **4d** as white powders (2.08 g, 67%); m.p. 179—181 ℃. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.02—2.11 (m, 1H, CH_2), 2.33 (s, 3H, CH_3), 2.38 (d, J=13.9 Hz, 1H, CH_2), 4.39 (d, J=11.1 Hz, 1H, OCH_2), 4.48 (dd, J=11.1, 11.1 Hz, 1H, OCH_2), 5.13 (s, 1H, NH), 6.71 (s, 1H, CSNH), 6.84—8.00 (m, 8H, ArH); IR (KBr) *v*: 3413, 3162, 3039, 2919, 1595 cm^{-1}.

13-Methyl-2-phenylspiro[1,2,4-triazolidine-5,4'-chroman]-3-thione (4e)

From **2e** and phenylhydrazine according to the general procedure afforded **4e** as white powders (2.21 g, 71%). m.p. 174—176 ℃. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.04—2.10 (m, 1H, CH_2), 2.20 (s, 3H, CH_3), 2.38 (d, J=13.7 Hz, 1H, CH_2), 4.43—4.53 (m, 2H, OCH_2), 5.16 (s, 1H, NH), 6.49 (s, 1H, CSNH), 6.92—7.80 (m, 8H, ArH); IR (KBr) *v*: 3413, 3140, 2916, 1597 cm^{-1}.

2-(4-Chlorophenyl)spiro[1,2,4-triazolidine-5,4'-chroman]-3-thione (4f)

From **2f** and *p*-chlorophenylhydrazine according to the general procedure afforded **4f** as white powders (2.00 g, 60%). m.p. 158—160 ℃. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.03—2.14 (m, 1H, CH_2), 2.33—2.39 (m, 1H, CH_2), 4.38—4.43 (m, 1H, OCH_2), 4.45—4.54 (m, 1H, OCH_2), 5.15 (s, 1H, NH), 6.40 (s, 1H, CSNH), 6.91—8.01 (m, 8H, ArH); IR (KBr) *v*: 3370, 3144, 3038, 2983, 1608,1582 cm^{-1}.

2-(4-Chlorophenyl)-13-methylspiro[1,2,4-triazolidine-5,4'-chroman]-3-thione (4g)

From **2g** and *p*-chlorophenylhydrazine according to the general procedure afforded **4g** as white powders (1.90 g, 55%). m.p.177—179 ℃. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.05—2.09 (m, 1H, CH_2), 2.20 (s, 3H, CH_3), 2.35 (d, J=13.8 Hz, 1H, CH_2), 4.47 (m, 2H, OCH_2), 5.14 (s, 1H, NH), 6.36 (s, 1H, CSNH), 6.92—8.01 (m, 7H, ArH); IR (KBr) *v*: 3392, 3165, 2921, 1596 cm^{-1}.

4-(Aryldiazenyl)chroman-4-isothiocyanates 5a—5g

General procedure A solution or suspension of the appropriate 2-arylspiro[1,2,4-triazolidine-5,4'-chroman]-3-thione **4** (10 mmol) in a mixture of Et_2O/CH_2Cl_2 (1∶1, 80 mL) was treated with an aqueous solution of potassium permanganate (50 mL, 2%, 12 mmol), the mixture was vigorously stirred for 2—3 h at room temperature. At the finish of the oxidation process as indicated by TLC [EtOAc/PE (60—90 ℃) 1∶7], the MnO_2 formed was removed by filtration with diatomaceous silica to avoid the formation of emulsions during the extraction process. The aqueous layer was separated and extracted with ether (3×20 mL). The combined organic layers were dried ($MgSO_4$), filtered through a plug of silica gel and concentrated *in vacuo*. The residue was pure (^1H NMR) isocyanate **5** which was dried *in vacuo* over $CaCl_2$ and used without further processing.

4-(Phenyldiazenyl)chroman-4-isothiocyanate (5a)

From **4a** following the general procedure a 98% yield of **5a** was obtained as a yellow oil. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.40—2.43 (m, 1H, CH_2), 2.68—2.72 (m, 1H, CH_2), 4.45—4.48 (m, 1H, OCH_2), 4.65—4.70 (m, 1H, OCH_2), 6.91—7.88 (m, 9H, ArH); IR (film) *v*: 3064, 2926, 2004, 1606 cm^{-1}.

6-Methyl-4-(phenyldiazenyl)chroman-4-isothiocyanate (5b)

From **4b** following the general procedure a 95% yield of **5b** was obtained as a yellow oil. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.22 (s, 3H, CH_3), 2.36—2.43 (m, 1H, CH_2), 2.63—2.71 (m, 1H, CH_2), 4.40—4.46 (m, 1H, OCH_2), 4.60—4.68 (m, 1H, OCH_2), 6.76—7.88 (m, 8H, ArH); IR (film) *v*: 3061, 2925, 2014, 1587 cm^{-1}.

6-Methoxy-4-(phenyldiazenyl)chroman-4-isothiocyanate (5c)

From **4c** following the general procedure a 95% yield of **5c** was obtained as a yellow oil. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.40—2.42 (m, 1H, CH_2), 2.65—2.69 (m, 1H, CH_2), 3.69 (s, 3H, OCH_3), 4.40—4.44 (m, 1H, OCH_2), 4.61—4.65 (m, 1H, OCH_2), 6.49—7.88 (m, 8H, ArH); IR (film) *v*: 3066, 2931, 2011, 1638 cm^{-1}.

7-Methyl-4-(phenyldiazenyl)chroman-4-isothiocyanate (5d)

From **4d** following the general procedure a 97% yield of **5d** was obtained as a yellow oil. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.30 (s, 3H, CH_3), 2.36—2.41 (m, 1H, CH_2), 2.66—2.71 (m, 1H, CH_2), 4.42—4.46 (m, 1H, OCH_2), 4.63—4.67 (m, 1H, OCH_2), 6.73—7.86 (m, 8H, ArH); IR (film) *v*: 3064, 2923, 2009, 1623 cm^{-1}.

8-Methyl-4-(phenyldiazenyl)chroman-4-isothiocyanate (5e)

From **4e** following the general procedure a 97% yield of **5e** was obtained as a yellow oil. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.25 (s, 3H, CH_3), 2.38—2.42 (m, 1H, CH_2), 2.68—2.72 (m, 1H, CH_2), 4.47—4.51 (m, 1H, OCH_2), 4.69—4.72 (m, 1H, OCH_2), 6.82—7.86 (m, 8H, ArH); IR (film) *v*: 3063, 2924, 2002, 1597 cm^{-1}.

4-[(4-Chlorophenyl)diazenyl]chroman-4-isothiocyanate (5f)

From **4f** following the general procedure, a 90% yield of **5f** was obtained as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.39—2.45 (m, 1H, CH_2), 2.67—2.74 (m, 1H, CH_2), 4.43—4.50 (m, 1H, OCH_2), 4.63—4.71 (m, 1H, OCH_2), 6.92—7.81 (m, 8H, ArH); IR (film) ν: 3066, 2970, 2933, 2011, 1585 cm^{-1}.

4-[(4-Chlorophenyl)diazenyl]-8-methylchroman-4-isothiocyanate (5g)

From **4g** following the general procedure, a 90% yield of **5g** was obtained as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.25 (s, 3H, CH_3), 2.26—2.44 (m, 1H, CH_2), 2.65—2.72 (m, 1H, CH_2), 4.45—4.52 (m, 1H, OCH_2), 4.66—4.73 (m, 1H, OCH_2), 6.81—7.81 (m, 7H, ArH); IR (film) ν: 3088, 2923, 1977, 1598 cm^{-1}.

1-Aryl-1,2,4,5-tetrahydro-[1,2,4]triazolo[3,2-*d*][1,5]-benzoxazepin-2-thiones 7a—7g

General procedure To an ice-cooled, stirred solution of compound **5** (5 mmol) in Et_2O (40 mL) was added dropwise 50% aq. HBF_4 (5 mL) over a period of 5 min. The reaction mixture was stirred at 0 ℃ for a few minutes, after which it was diluted with CH_3CN (10 mL). Then ether was removed under reduced pressure. To ensure complete ring expansion, the remaining solution was refluxed for 10 min and then cooled to room temperature. After removal of the major part of CH_3CN under reduced pressure, a 2 mol•L^{-1} NaOH solution was added with stirring until enduringly basic. The reaction mixture was then diluted with water (30 mL) and extracted with CH_2Cl_2 (4×20 mL). The combined organic layers were washed with water, dried ($MgSO_4$), and concentrated. The solvent was evaporated under reduced pressure and the residue was purified by recrystallization or flash chromatography on silica gel (EtOAc) to give the pure title compound.

1-Phenyl-1,2,4,5-tetrahydro-[1,2,4]triazolo[3,2-*d*]-[1,5]benzoxazepin-2-thione (7a)

From **5a** following the general procedure, Crystallization from MeOH afforded **7a** as pale-yellow crystals in 83% yield. m.p. > 237 ℃ (decomp.). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 3.12 (t, J=11.0 Hz, 2H, CH_2), 4.75 (t, J=11.0 Hz, 2H, OCH_2), 6.63—7.46 (m, 9H, ArH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 180.9 (C=S), 157.4 (C=N), 149.3, 134.0, 130.2, 130.0, 129.7, 127.6, 125.3, 124.3, 123.4 (Ar), 74.8 (OCH_2), 26.3 (CH_2); IR (KBr) ν: 3080, 1686, 1602, 1492 cm^{-1}; MS (70 eV) *m/z* (%): 295 (M^+, 100), 146 (32), 93(25), 77(30); HRMS (EI) calcd for $C_{16}H_{13}N_3OS$ 295.0779, found 295.0776.

9-Methyl-1-phenyl-1,2,4,5-tetrahydro-[1,2,4]triazolo-[3,2-*d*][1,5]benzoxazepin-2-thione (7b)

From **5b** following the general procedure, column chromatography (EtOAc) provided **7b** as pale-yellow powders in 80% yield. m.p. 186—188 ℃. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.08 (s, 3H, CH_3), 3.10 (t, J=6.5 Hz, 2H, CH_2), 4.75 (t, J = 6.5 Hz, 2H, OCH_2), 6.40—7.46 (m, 8H, ArH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 180.4 (C=S), 157.3 (C=N), 146.9, 135.4, 133.9, 130.8, 129.9, 129.5, 127.0, 126.9, 123.63, 123.60 (Ar), 74.6 (OCH_2), 26.2 (CH_2), 20.6 (CH_3); IR (KBr) ν: 3059, 2958, 2923, 1686, 1618 cm^{-1}; MS (70 eV) *m/z* (%): 309 (M^+, 97), 160 (100), 93(45), 77(94); HRMS (EI) calcd for $C_{17}H_{15}N_3OS$ 309.0936, found 309.0943.

9-Methoxy-1-phenyl-1,2,4,5-tetrahydro-[1,2,4]triazolo[3,2-*d*][1,5]benzoxazepin-2-thione (7c)

From **5c** following the general procedure, column chromatography (EtOAc) provided **7c** as pale-yellow powders in 77% yield. m.p. 179—181 ℃. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 3.10 (t, J=6.5 Hz, 2H, CH_2), 3.45 (s, 3H, OCH_3), 4.69 (t, J=6.5 Hz, 2H, OCH_2), 6.10—7.19 (m, 8H, Ar); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 180.6 (C=S), 157.5 (C=N), 156.4, 142.6, 134.0, 130.0, 129.7, 127.9, 127.6, 124.6, 116.2, 108.1 (Ar), 74.7 (OCH_2), 55.7 (CH_3), 26.3 (CH_2) ; IR (KBr) ν: 3066, 2958, 2926, 1685, 1593 cm^{-1}; MS (70 eV) *m/z* (%): 325 (M^+, 59), 175 (100), 160 (57), 93 (8), 65 (6); HRMS (EI) calcd for $C_{17}H_{15}N_3O_2S$ 325.0885, found 325.0879.

8-Methyl-1-phenyl-1,2,4,5-tetrahydro-[1,2,4]triazolo-[3,2-*d*][1,5]benzoxazepin-2-thione (7d)

From **5d** following the general procedure, crystallization from MeOH afforded **7d** as pale-yellow crystals in 79% yield. m.p. 173—175 ℃. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.31 (s, 3H, CH_3), 3.10 (t, J=6.5 Hz, 2H, CH_2), 4.72 (t, J=6.5 Hz, 2H, OCH_2), 6.49—7.47 (m, 8H, ArH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 180.2 (C=S), 157.2 (C=N), 149.2, 141.3, 133.9, 130.1, 129.7, 128.0, 126.0, 124.64, 124.60, 123.2 (Ar), 74.9 (OCH_2), 26.2 (CH_2), 21.2 (CH_3) ; IR (KBr) ν: 3059, 2923, 1682; 1615 cm^{-1}; MS (70 eV) *m/z* (%): 309 (M^+, 100), 160 (70), 93 (13), 77 (34); HRMS (EI) calcd for $C_{17}H_{15}N_3OS$ 309.0936, found 309.0940.

7-Methyl-1-phenyl-1,2,4,5-tetrahydro-[1,2,4]triazolo-[3,2-*d*][1,5]benzoxazepin-2-thione (7e)

From **5e** following the general procedure, crystallization from MeOH afforded **7e** as pale-yellow crystals in 85% yield. m.p. 191—193 ℃. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.37 (s, 3H, CH_3), 3.10 (t, J=6.6 Hz, 2H, CH_2), 4.73 (t, J=6.6 Hz, 2H, OCH_2), 6.46—7.45 (m, 8H, ArH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 180.5 (C=S), 157.2 (C=N), 147.3, 134.1, 134.0, 131.6, 129.9, 129.6, 127.8, 127.6, 124.6, 121.0 (Ar), 73.5 (OCH_2), 26.4 (CH_2), 15.8 (CH_3); IR (KBr) ν: 3059, 2924, 1687; 1598 cm^{-1}; MS (70 eV) *m/z* (%): 309 (M^+, 24), 160 (100), 93 (9), 77 (26); HRMS (EI) calcd for $C_{17}H_{15}N_3OS$ 309.0936, found 309.0937.

1-(4-Chlorophenyl)-1,2,4,5-tetrahydro-[1,2,4]triazolo-[3,2-*d*][1,5]benzoxazepin-2-thione (7f)

From **5f** following the general procedure, column chromatography (EtOAc) provided **7f** as pale-yellow

powders in 86% yield. m.p.＞191 ℃ (decomp.). ^{1}H NMR ($CDCl_3$, 500 MHz) δ:3.12 (t, J=6.6 Hz, 2H, CH_2), 4.75 (t, J=6.6 Hz, 2H, OCH_2), 6.67—7.43 (m, 8H, ArH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 181.0 (C=S), 157.7 (C=N), 149.2, 135.8, 132.3, 130.3, 129.8, 128.8, 127.3, 125.4, 124.3, 123.2 (Ar), 74.7 (OCH_2), 26.2 (CH_2) ; IR (KBr) ν: 3064, 2924, 1686, 1603 cm^{-1}; MS (70 eV) *m/z* (%): 329 (M^+, 93), 146 (100), 93 (14), 65 (16); HRMS (EI) calcd for $C_{16}H_{12}ClN_3OS$ 329.0389, found 329.0385.

1-(4-Chlorophenyl)-7-methyl-1,2,4,5-tetrahydro-[1,2,4]triazolo[3,2-*d*][1,5]benzoxazepin-2-thione (7g)

From **5g** following the general procedure, column chromatography (EtOAc) provided **7g** as pale-yellow powders in 85% yield. m.p. 174—176 ℃. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.37 (s, 3H, CH_3), 3.10 (t, J=6.6 Hz, 2H, CH_2), 4.73 (t, J = 6.6 Hz, 2H, OCH_2), 6.48—7.41 (m, 7H, ArH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 180.7 (C=S), 157.5 (C=N), 147.1, 135.7, 134.1, 132.4, 131.6, 129.8, 128.8, 127.4, 124.7, 120.8 (Ar), 73.4 (OCH_2), 26.3 (CH_2), 15.7 (CH_3) ; IR (KBr) ν: 3053, 2924, 1686, 1599 cm^{-1}; MS (70 eV) *m/z* (%): 343 (M^+, 88), 160 (100), 77 (23); HRMS (EI) calcd for $C_{17}H_{14}ClN_3OS$ 343.0546, found 343.0549.

Crystal structure determination of compound 7d

Data were acquired on a Brucker SMART APEX CCD diffractometer. All intensity measurements were performed using graphic monochromated Mo Kα radiation (λ=0.071073 nm). Single crystal of compound **7d** was obtained directly from the analytical samples.

Crystal data $C_{17}H_{15}N_3OS$, M_r=309.40; monoclinic, $C2/c$; a=2.0286(4) nm, b=0.6860(3) nm, c=2.5122(5) nm, U=3.2647(1) nm^3; Z=8, D_c=1.324 g•cm^{-3}, μ=0.209 mm^{-1}; F(000)=1368.0. 6582 reflections were measured, 2870 unique of which were used in all least square calculations, R_{int}=0.0347.

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