Aryl Ring Migration Reaction in the Synthesis of 2,4-Diaryl-4*H*-3,1-benzothiazines

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Abstract: A new rearrangement of 1-(diarylmethyl)-2-isothiocyanatobenzenes into 2,4-diaryl-4*H*-3,1-benzothiazine derivatives is described. Treatment of the starting compounds with aluminum trichloride under Friedel–Crafts conditions leads to migration of an aryl substituent by an electrophilic *ipso*-substitution mechanism, followed by cyclization to form a 3,1-benzothiazine ring. The expected intramolecular thiocarbamoylation reaction also takes place, and 5,11-dihydro-6*H*-dibenzo[*b*,*e*]azepine-5-thiones are isolated as byproducts. Factors influencing the mechanism and selectivity of the reaction are discussed. The corresponding 1-(arylmethyl)-2-isothiocyanatobenzene derivatives were also synthesized, and their behavior under Friedel–Crafts reaction conditions was investigated to confirm the crucial role of the stability of the intermediate benzhydryl/benzyl cations in determining the course of the reaction.

Key words: 1-(diarylmethyl)-2-isothiocyanatobenzenes, Friedel–Crafts, rearrangement, aryl migration, 3,1-benzothiazines

Among 3,1-benzothiazine derivatives, many are biologically active as cardiac stimulants,[1] antiischemic agents,[2] inotropic drugs,[3] medications for treatment of anaphylactic reactions and allergies,[4] cAMP phosphodiesterase inhibitors,[5] antibacterial agents,[6] plant-disease-controlling agents,[7] and medicines for treating bone-deficit conditions.[8] 3,1-Benzothiazin-4-ones have shown activity in chymotrypsin inactivation,[9] and are candidates as anthelmintic drugs.[10] 3,1-Thiazine derivatives have also been patented for use as color formers in a wide range of copying systems.[11]

In contrast to the isomeric 1,3-benzothiazines, little research has been devoted to the chemistry of 3,1-benzothiazines, largely because the synthetic precursors of these compounds are less accessible. There are few general approaches among the known methods for the synthesis of 3,1-benzothiazines. Besides some special methods, such as the synthesis of 4-aryl- or 4,4-diaryl-4*H*-3,1-benzothiazines through cycloaddition reactions of keteneimines and thiones,[12] or by oxygen–sulfur exchange in aryl-substituted 4*H*-3,1-benzoxazines using phosphorus pentasulfide,[13] the most general route to the 3,1-benzothiazine heterocyclic system involves a combination of sulfur atom alkylation with an electrophilic carbon compound followed by 3,1-benzothiazine ring closure. 2-Aminobenzyl alcohols are the substrates that are most frequently used for the synthesis of 3,1-benzothiazines. 2-Amino-4-aryl-4*H*-3,1-benzothiazines can be obtained easily in high yields by refluxing 2-aminobenzhydrols with thiourea in ethanol in the presence of concentrated hydrobromic acid.[4,14] In this reaction, the generated benzhydryl bromide alkylates thiourea, and the resulting isothiuronium salt cyclizes with elimination of ammonia. 2-Aminobenzyl alcohol reacts in the same way.[15] The reaction can be also carried out with preformed benzyl halides, as in the case of 2-aminobenzyl chloride hydrochloride, which gives 2-aryl-substituted 4*H*-3,1-benzothiazines and benzoic acid thioamides.[16]

The formation of a nucleophilic sulfur-containing function can precede the cyclization stage. By this route, unlike the cyclization of 2-aminobenzhydrols in acidic media, the reaction with carbon disulfide in the presence of an aqueous alkali gives 4*H*-3,1-benzothiazines in which the amino group is attacked before cyclization occurs.[10b,17a,b] The same approach can be implemented in a solid-phase synthesis of amino-3,1-benzothiazine through treatment of 2-aminocinnamic acid with aryl isothiocyanates, followed by an intramolecular Michael addition.[18] A similar method involves the intramolecular cyclization of carbodiimides and isothiocyanates having an α,β-unsaturated ketone function in the *ortho*-position through treatment with carbon disulfide and fluoride anion.[19] An interesting bifunctional synthon, 1-(bromomethyl)-2-isothiocyanatobenzene[20] or the quaternary salt generated by its reaction with pyridine,[21] gives substituted 4*H*-3,1-benzothiazines on treatment with amines or phenols. Lawesson's reagent is widely used for introduction of a thioamide function. On treatment with this reagent, 2-(acylamino)benzyl alcohols can be transformed into 2-aryl-, 4-aryl-, or 2,4-diaryl-4*H*-3,1-benzothiazines,[22] although the method is not, in general, selective and often gives 3,1-benzoxazines and thiazolines as byproducts. Xanthates can be also used as sulfur donors.[1,5] Interaction of 2-aminobenzyl alcohols with 4,5-dichloro-1,2,3-dithiazolium chloride (Appel's salt) gives the corresponding

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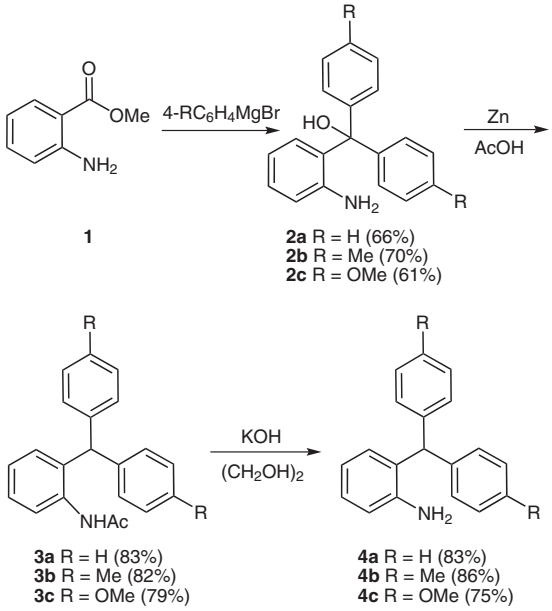
imines, which can be transformed into benzothiazine derivatives by treatment with sodium cyanoborohydride,[23] sodium hydride,[24] or triphenylphosphine.[25] An original method for the synthesis of 2-aryl(hetaryl)-4*H*-3,1-benzothiazine-4-ones involves the acid-catalyzed acylation of aromatic/heteroaromatic substrates with 2-isothiocyanobenzoate, followed by intramolecular cyclization of the intermediate amides.[26]

This analysis of the available synthetic approaches to 4*H*-3,1-benzothiazine derivatives shows that almost all require sequential generation of a sulfur nucleophile and a carbon electrophile as reactive centers. This leads to a reduced yields and the formation of various isomeric byproducts. Benzyl or benzhydryl halides prepared from the corresponding alcohols, as well as activated double bonds or carboxyl functions, have been used as electrophiles. However, we have previously discovered a rearrangement of 1-(difurylmethyl)-2-isothiocyanatobenzenes into 3,1-benzothiazine derivatives[27] that overcomes this limitation, as the electrophilic benzhydryl cation and the thioamide function are generated simultaneously under the reaction conditions; the generation of a benzhydryl cation by transfer of a hetaryl group from the sterically overloaded triaryl(hetaryl)methyl center was used for the first time in the synthesis of 3,1-benzothiazine derivatives.

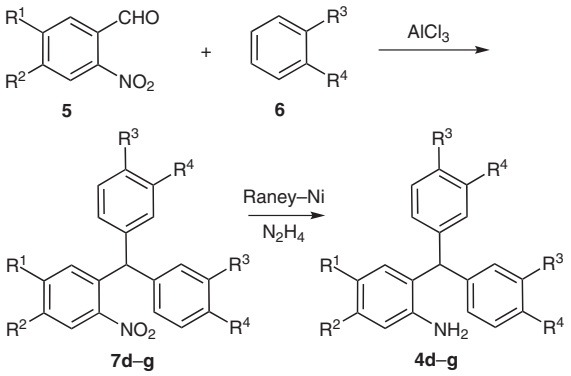
We initially supposed that this reaction might be specific to aryl(difuryl)methyl derivatives, because the furan ring is prone to react with electrophiles at its α-position, a reaction that is well documented in the literature.[28] However, some preliminary studies with 1-(diarylmethyl)-2-isothiocyanatobenzenes showed, to our surprise, that these compounds also reacted to form 3,1-benzothiazine derivatives as the main products.[29] In contrast, seven-membered azepinethiones, which might be expected to form as a result of an intramolecular cyclization reaction that is typical of many aromatic or heteroaromatic isocyanates,[30] were observed only as minor byproducts in a few cases.[29] Here, we describe our detailed investigations of synthesis of 2,4-diaryl-4*H*-3,1-benzothiazines and the scope of this reaction.

The 2-(diarylmethyl)aniline derivatives used as starting compounds in this work were prepared in two ways. Treatment of methyl 2-aminobenzoate (**1**) with arylmagnesium bromides[31] gave the corresponding triarylcarbinols **2a–c**. These products were reduced by zinc in acetic acid to give the corresponding *N*-[2-(diarylmethyl)phenyl]acetamides **3a–c**, which were subsequently hydrolyzed with alkali to give the free amines **4a–c** (Scheme 1).

Alternatively, condensation of 2-nitrobenzaldehydes **5** with 1,2-dialkoxybenzenes **6** in the presence of anhydrous aluminum trichloride gave the 1-(diarylmethyl)-2-nitrobenzenes **7d–g**, which were reduced with hydrazine and Raney nickel to give the corresponding amino derivatives **4d–g** (Scheme 2, Table 1).



Scheme 1 Synthesis of carbinols **2a–c**, acetamides **3a–c**, and amines **4a–c**



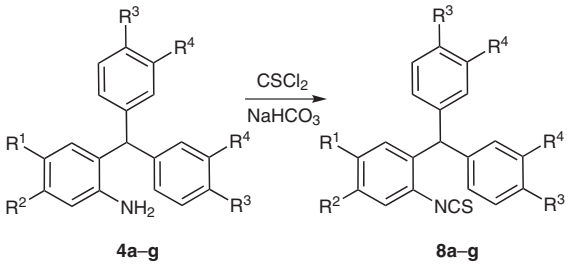
Scheme 2 Synthesis of starting amines **4d–g**

Table 1 Yields of Nitro Compounds **7d–g** and Amines **4d–g**

	R^1	R^2	R^3	R^4	Yield (%)	
					7	**4**
d	H	H	OMe	OMe	57	84
e	OMe	OMe	OMe	OMe	27	91
f	OMe	OMe	OEt	OEt	50	78
g	H	H	OCH_2CH_2O		76	75

The 1-(diarylmethyl)-2-isothiocyanatobenzenes **8a–g** were synthesized by treatment of the corresponding amines **4** with thiophosgene and aqueous sodium bicarbonate (Scheme 3, Table 2).

Treatment of isothiocyanates **8** with aluminum trichloride in 1,2-dichloroethane gave the corresponding benzothiazines **9a–g** in moderate yields (Scheme 4, Table 3). Formation of azepinethiones **10** as byproducts was observed in all cases except for isothiocyanate **8b**, which gave the benzothiazine **9b** as the sole product. The side products



Scheme 3 Synthesis of isothiocyanates **8a–g**

Table 2 Yields of Isothiocyanates **8a–g**

	R^1	R^2	R^3	R^4	Yield of **8** (%)
a	H	H	H	H	97
b	H	H	Me	H	87
c	H	H	OMe	H	50
d	H	H	OMe	OMe	77
e	OMe	OMe	OMe	OMe	78
f	OMe	OMe	OEt	OEt	65
g	H	H	OCH_2CH_2O		89

10a, **10d**, and **10f** were isolated chromatographically and fully characterized by spectral methods. X-ray analysis of a single crystal of **10d** gave unambiguous proof of its structure (Figure 1). Note that benzothiazine derivatives **9** prevail over the azepinethiones **10** as the main reaction products in all cases except for isothiocyanate **8a**, which gave azepinethione **10a** in 25% yield and the corresponding benzothiazine **9a** in 9% yield (Scheme 4, Table 3).

A plausible mechanism for the reaction is shown in the Scheme 5. In the case of the products **10** (path B), a classic intramolecular electrophilic substitution with the aluminum trichloride-activated isothiocyanate group takes place at the C2 position of the aromatic ring; this is a well-documented intramolecular cyclization reaction under

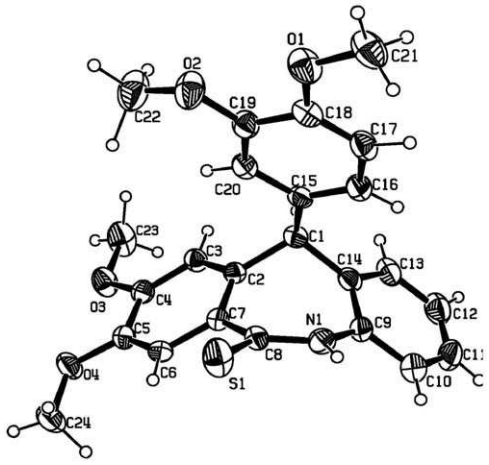
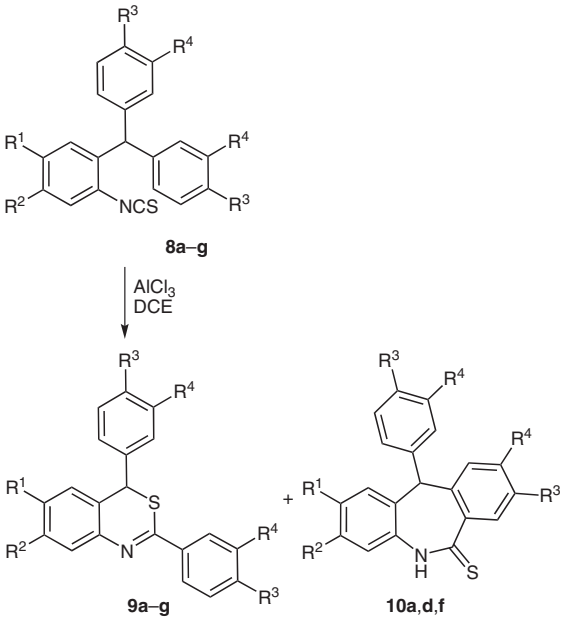


Figure 1 X-ray crystallographic structure of azepinethione **10d**



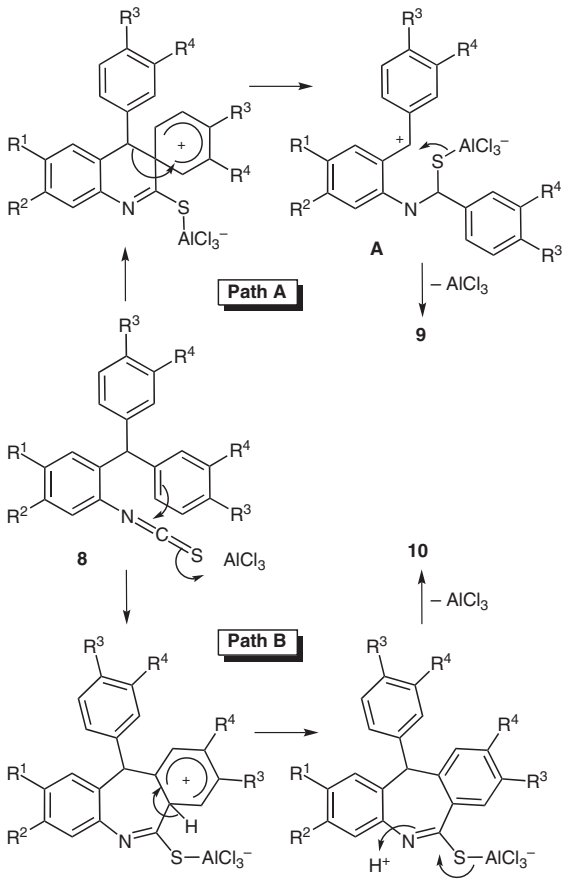
Scheme 4 Synthesis of 2,4-diaryl-4*H*-3,1-benzothiazines **9a–g** and azepinethiones **10a**, **10d**, and **10f**

Table 3 Yields of 2,4-Diaryl-4*H*-3,1-Benzothiazines **9a–g** and Azepinethiones **10a**, **10d**, and **10f**

	R^1	R^2	R^3	R^4	Yield (%)	
					9	**10**
a	H	H	H	H	9	25
b	H	H	Me	H	60	–
c	H	H	OMe	H	19	–
d	H	H	OMe	OMe	37	7
e	OMe	OMe	OMe	OMe	30	–
f	OMe	OMe	OEt	OEt	26	5
g	H	H	OCH_2CH_2O		61	–

Friedel–Crafts conditions.[30] In the case of the products **9**, however, the activated isothiocyanate group attacks the aromatic ring at the position connected to the *meso*-carbon to form a σ-complex (path A). Interestingly, the second route predominates even when the *ipso*-attack is strongly disfavored sterically, because the formation of the six-membered thiazine ring is energetically more favored than formation of an azepinethione.

In the case of isothiocyanate **8c**, along with the expected rearrangement product **9c**, the product of demethylation at the methoxy group **11** was also isolated in 15% yield (Scheme 6); the structure of this compound was confirmed by single-crystal X-ray crystallography (Figure 2). It appeared that the methoxy group at the 2-position of the aromatic ring the benzothiazine cycle had been demethylated. Although aluminum chloride is a common reagent for demethylation, it usually requires refluxing of the reaction mixture for several hours to achieve complete con-

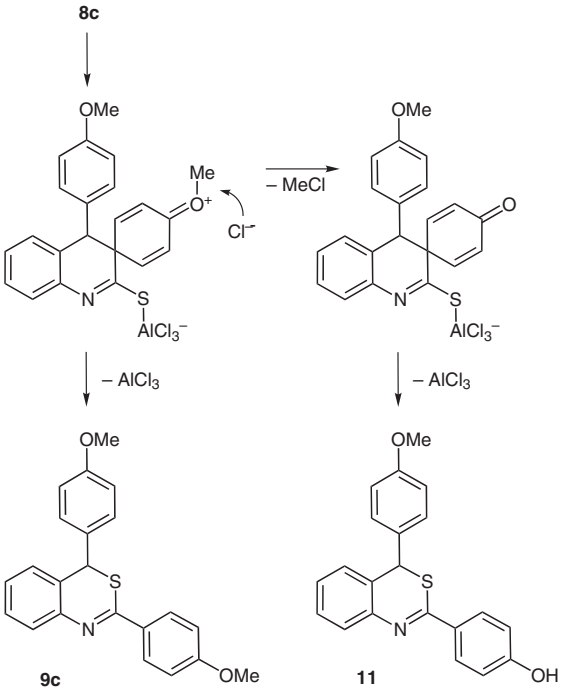


Scheme 5 Probable mechanism of formation of 2,4-diaryl-4*H*-3,1-benzothiazines **9** and azepinethiones **10**

version. Surprisingly in this case, however, the reaction was easily accomplished at room temperature.[32] This ready elimination of a methyl group from the 2-position of the aryl ring of the ring strongly supports the assumption that demethylation occurred at the stage of the spiro complex (Scheme 6). The absence of demethylation products in the cases of compounds **9d–f** can be rationalized in terms of steric hindrance from the second alkoxy group retarding attack by the nucleophile.

Obviously, the driving force of the reaction is the generation of the stable carbocation **A** (Scheme 5) as an intermediate. Its stability is a prerequisite for aromatic ring migration to form the benzothiazine heterocycle. This explains, in particular, why intramolecular cyclization dominates in the case of isothiocyanate **8a**, which is much less prone to formation of carbocation **A** because of the absence of stabilizing electron-donor substituents on the aromatic rings of the benzhydryl cation, in contrast to the other substrates. We therefore believed that migration of an aryl would be less favored in the case of the corresponding diarylmethane derivatives and that the same reaction would lead to intramolecular cyclization to give corresponding azepinethiones.

Intrigued by this possibility, we focused our efforts on the synthesis of isothiocyanates **16a–c** (Scheme 7). The sequence begins with Friedel–Crafts acylation of 1,2-



Scheme 6 Probable mechanism of the demethylation reaction

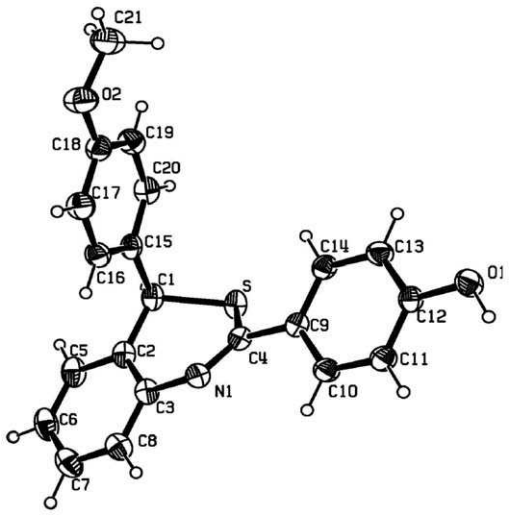
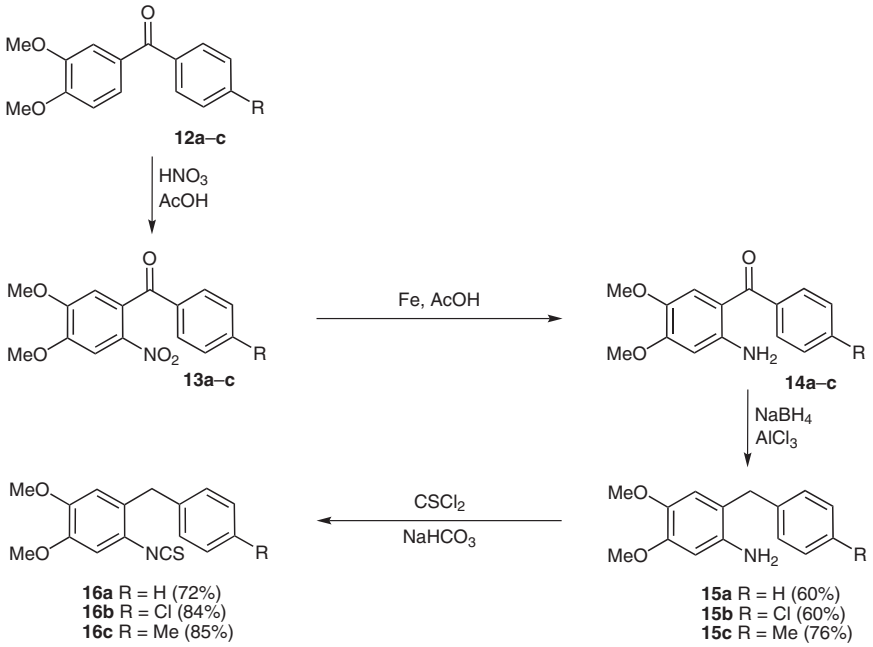


Figure 2 X-ray crystallographic structure of the demethylated derivative **11**

dimethoxybenzene (veratrole) by benzoyl chlorides to give the corresponding benzophenones **12a–c**, which, without additional purification, were nitrated with concentrated nitric acid in acetic acid to give the 2-nitro compounds **13a–c**. These were reduced with iron and acetic acid to give the corresponding 2-aminobenzophenones **14a–c**.[33] Further, reduction of 2-aminobenzophenones **14a–c** with sodium borohydride and aluminum chloride in boiling tetrahydrofuran gave the 2-benzylanilines **15a–c**, which, without purification or characterization, were converted directly into isothiocyanates **16a–c** through treatment with thiophosgene using the standard procedure.



Scheme 7 Synthesis of isothiocyanates **16a–c**

Surprisingly, treatment of compound **16a** or **16b** with aluminum trichloride in 1,2-dichloroethane gave a mixture of unstable products that could not be separated chromatographically. Only in the case of isothiocyanate **16c** was the azepinethione **17** isolated from the reaction mixture in 38% yield (Scheme 8). Unfortunately we failed in our attempts to grow a single crystal of azepinethione **17** that was suitable for X-ray analysis, and instead we used a two-dimensional NMR technique ([D_6]-DMSO, 323K) to confirm its structure.

The ^{1}H NMR spectrum of azepinethione **17** contains the ten expected signals; three signals corresponding to protons H12 (7.76 ppm), H14 (7.22 ppm), and H15 (7.14 ppm) are in the aromatic region, and clearly arise from the trisubstituted (*m*, *p*) benzene ring. It was easy to assign the NH proton signal H1 of the thioamide group at 12.25 ppm. The signal of the methylene group H5 (3.67 ppm) was assigned on the basis of the integral intensities of the corresponding peaks. The remaining ^{1}H signals in the spectrum were assigned by means of ^{1}H–^{1}H nuclear Overhauser effect spectroscopy (NOESY), and the critical NOE contacts are shown in Figure 3.

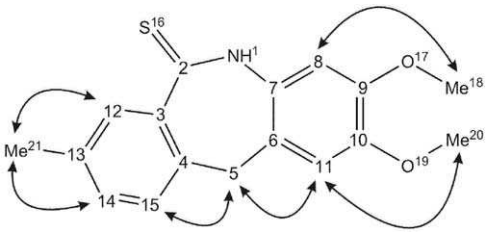


Figure 3 Key NOESY correlations of azepinethione **17**

The assignments of the NMR signals of the carbon atoms were made by means of two-dimensional ^{1}H–^{13}C heteronuclear single quantum coherence (HSQC) experiments, and ^{1}H–^{13}C heteronuclear multiple bond correlation (HMBC) spectroscopy for the quaternary carbons. The main correlations are shown in Figure 4. Results of the assignments are listed in Table 4.

We observed a dynamic effect in the ^{1}H NMR spectrum of azepinethione **17** in deuteriochloroform (Figure 5). Signals from the methylene group C5, which usually form a broad singlet at room temperature, appeared as a singlet upon heating to 45 °C, and split into two doublets at –10 °C. At the same time we did not observe any significant

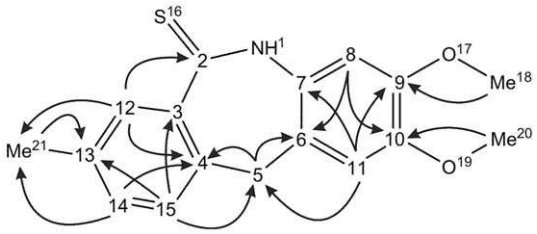
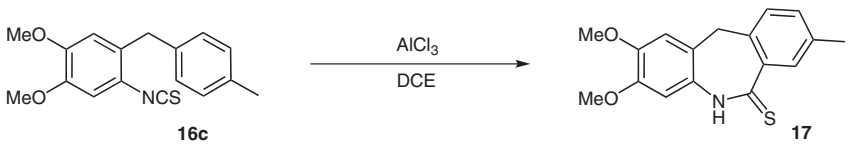


Figure 4 Key HMBC (H → C) correlations for azepinethione **17**



Scheme 8 Synthesis of azepinethione **17**

Table 4 ^{1}H and ^{13}C Chemical Shifts (ppm) for Azepinethione **17**

	^{13}C (ppm)	^{1}H (ppm)		^{13}C (ppm)	^{1}H (ppm)
N1-H		12.25	C10	147.2	
C2	198.0		C11-H	111.1	6.95
C3	137.2		C12-H	132.4	7.76 (d, *J* = 1.6 Hz)
C4	137.0		C13	135.1	
C5-H	36.3	3.67 (2 H)	C14-H	132.2	7.22 (dd, *J* = 1.6, 7.7 Hz)
C6	128.2		C15-H	126.1	7.14 (d, *J* = 7.7 Hz)
C7	130.2		C18-H	55.7	3.70 (3 H)
C8-H	106.4	6.89	C20-H	55.7	3.75 (3 H)
C9	147.2		C21-H	20.2	2.27 (3 H)

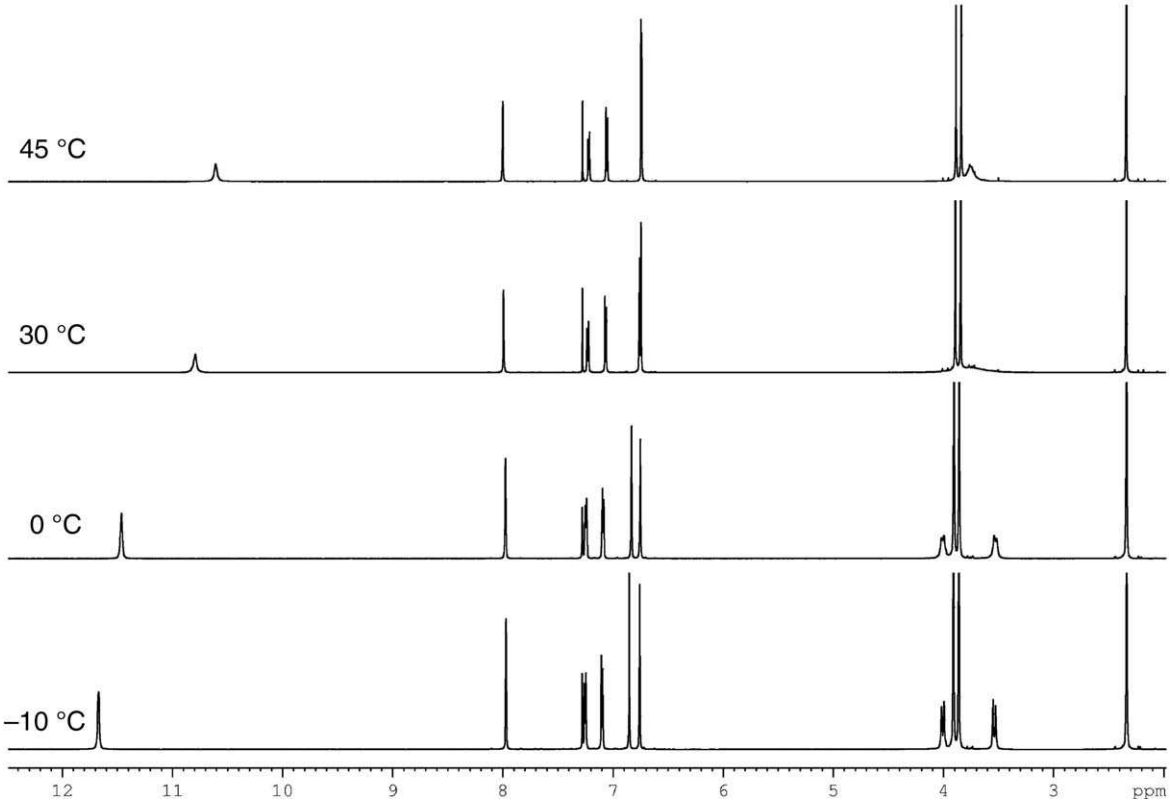


Figure 5 Temperature effects on the ^{1}H NMR spectrum of azepinethione **17** in $CDCl_3$

changes in the other signals. Because the molecule has a butterfly conformation (Figure 6), we believe that the temperature dependence of the spectrum is probably associated with a rapid conformational change (like the flapping of a butterfly's wings).

In conclusion, we investigated a novel rearrangement of 1-(diarylmethyl)-2-isothiocyanatobenzenes into 3,1-benzothiazines. The key step in the mechanism of this reaction is a nontrivial electrophilic C–C bond breakage with formation of a benzhydryl cation and migration of an aryl group. In the case of corresponding diarylmethane derivatives, rearrangement does not take place because of the

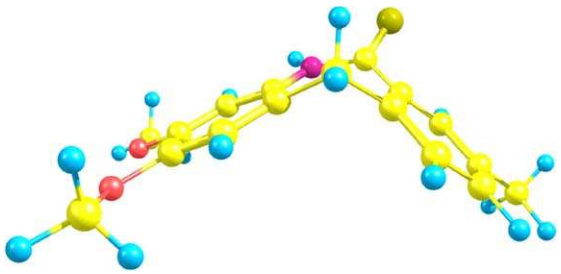


Figure 6 Conformation of azepinethione **17** optimized by MM2 calculations (ChemOffice Chem3D view)

much lower stability of the benzyl carbocation intermediates, even when electron-donor stabilizing groups are present.

The microanalyses were carried out at the Laboratory of Physico-Chemical Methods of Research, Department of Chemistry, M.V. Lomonosov Moscow State University. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 on Bruker AC 200, WM 250, DPX 300, and Avance 600 spectrometers. Chemical shifts are reported in ppm relative to TMS as an internal standard; coupling constants (J) are quoted in Hz. Two-dimensional spectra of azepinethione **17** were recorded on a Bruker Avance 600 spectrometer using standard Bruker software, and the XWINNMR 3.5 program (Bruker) was used to acquire and store the NMR data. A mixing time of 800 ms was used in the gNOESY experiment. The gHMBC experiment was optimized for the coupling constant $^nJ_{H-C}$ = 8 Hz. Mass spectra were recorded on a Kratos MS-30 instrument with 70-eV electron-impact ionization at 200 °C. IR spectra were recorded on InfraLUM FT-02 and FT-801 instruments. Column chromatography was carried out using silica gel KSK (50–160 μm; Sorbpolymer, Russia).

Crystallographic data for compound **11** and **10d** have been deposited at the Cambridge Crystallographic Data Centre with the accession numbers CCDC-693283 and CCDC-693284, respectively. The data can be obtained free of charge from www.ccdc.cam.ac.uk/data_request/cif.

Anilines **4a–c** were obtained according to the literature procedure[31] as yellow oils, and used in the next step as prepared. Compounds **14** were prepared according to the literature procedure.[33]

1-(Diarylmethyl)-2-nitrobenzenes 7d–g; General Procedure

$AlCl_3$ (1.9 g, 14.2 mmol) was added in small portions to a stirred soln of 2-nitrobenzaldehyde **5** (9.5 mmol) and 1,2-dialkoxybenzene **6** (19.9 mmol) in CH_2Cl_2 (80 mL) at 5 °C, and the mixture was stirred at 5 °C for 2.5 h. The cooling bath was then removed, and stirring was continued at r.t. until full conversion was achieved (TLC). The mixture was poured into H_2O (300 mL) and extracted with CH_2Cl_2 (3 × 70 mL). The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The residue was dissolved in PE and the soln was filtered through the pad of silica gel and then concentrated under reduced pressure.

Compounds **7d** and **7f** were recrystallized, whereas compounds **7e** and **7g** were used at the next step as prepared.

1-[Bis(3,4-dimethoxyphenyl)methyl]-2-nitrobenzene (7d)

Pale yellow solid; yield: 57%; mp 95–96 °C (PE–CH_2Cl_2).

IR (KBr): 1528, 1508, 1464, 1440, 1360, 1272, 1244, 1236, 1140, 1028, 860, 816, 760, 728 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.91–7.88 (m, 1 H, H_{Ar}), 7.64–7.60 (m, 1 H, H_{Ar}), 7.52–7.48 (m, 1 H, H_{Ar}), 7.12–7.10 (m, 1 H, H_{Ar}), 6.88 (d, 2 H, J = 8.2 Hz, H_{Ar}), 6.68 (d, J = 1.6 Hz, 2 H, H_{Ar}), 6.48 (dd, J = 1.6, 8.2 Hz, 2 H, H_{Ar}), 6.00 (s, 1 H, CH), 3.73 (s, 6 H, OCH_3), 3.64 (s, 6 H, OCH_3).

Anal. Calcd for $C_{23}H_{23}NO_6$: C, 67.47; H, 5.66; N, 3.42. Found: C, 67.19; H, 5.45; N, 3.37.

1-[Bis(3,4-diethoxyphenyl)methyl]-4,5-dimethoxy-2-nitrobenzene (7f)

Yellow solid; yield: 50%; mp 103–104 °C (MeOH).

IR (KBr): 1524, 1516, 1472, 1440, 1396, 1336, 1276, 1248, 1212, 1140, 1060, 1048, 992, 796, 756 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 7.60 (s, 1 H, H_{Ar}), 6.87 (d, J = 8.2 Hz, 2 H, H_{Ar}), 6.67 (d, J = 1.7 Hz, 2 H, H_{Ar}), 6.53 (s, 1 H, H_{Ar}), 6.49 (dd, J = 1.7, 8.2 Hz, 2 H, H_{Ar}), 6.09 (s, 1 H, CH), 3.99 (q, J = 7.0 Hz, 4 H, OCH_2CH_3), 3.91 (q, J = 7.0 Hz, 4 H, OCH_2CH_3), 3.85 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 1.31 (t, J = 7.0 Hz, 6 H, OCH_2CH_3), 1.25 (t, J = 7.0 Hz, 6 H, OCH_2CH_3).

Anal. Calcd for $C_{29}H_{35}NO_8$: C, 66.27; H, 6.71; N, 2.66. Found: C, 66.15; H, 6.58; N, 2.75.

2-(Diarylmethyl)anilines 4d–g; General Procedure

A mixture of the nitro compound **7** (4.6 mmol), N_2H_4 H_2O (2 mL), and Raney Ni (1.5 g) in EtOH (40 mL) was stirred under reflux until the reaction was complete (TLC). The catalyst was filtered off and the soln was treated with active charcoal, filtered, and concentrated.

Compounds **4e–g** were obtained as yellow oils and used in the next step as prepared.

2-[Bis(3,4-dimethoxyphenyl)methyl]aniline (4d)

White solid; yield: 84%; mp 163–164 °C (EtOH).

IR (KBr): 3468, 3384, 1516, 1464, 1448, 1416, 1264, 1232, 1136, 1028, 760 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.97–6.91 (m, 1 H, H_{Ar}), 6.87 (d, J = 8.2 Hz, 2 H, H_{Ar}), 6.72 (d, J = 1.6 Hz, 2 H, H_{Ar}), 6.66–6.63 (m, 1 H, H_{Ar}), 6.53 (dd, J = 1.6, 8.2 Hz, 2 H, H_{Ar}), 6.58–6.47 (m, 2 H, H_{Ar}), 5.38 (s, 1 H, CH), 4.56 (s, 2 H, NH_2), 3.73 (s, 6 H, OCH_3), 3.64 (s, 6 H, OCH_3).

Anal. Calcd for $C_{23}H_{25}NO_4$: C, 72.80; H, 6.64; N, 3.69. Found: C, 73.01; H, 6.66; N, 3.76.

1-(Diarylmethyl)-2-isothiocyanatobenzenes 8; General Procedure

A soln of $CSCl_2$ (0.3 mL, 3.9 mmol) in CH_2Cl_2 (4 mL) and a soln of $NaHCO_3$ (0.84 g, 10 mmol) in H_2O (30 mL) were added simultaneously to a stirred soln of amine **4** (3.2 mmol) in CH_2Cl_2 (10 mL) at r.t. When the reaction was complete (TLC), the mixture was poured into H_2O (150 mL) and the mixture was stirred for 6 h. The organic layer was extracted with CH_2Cl_2 (2 × 40 mL), separated, and dried (Na_2SO_4). The solvent was evaporated, and the oily residue was dissolved in hot PE and filtered through a pad of silica gel. The soln was concentrated and the residue was crystallized (PE–CH_2Cl_2).

Compound **8g** was isolated as a yellow oil and used at the next step as prepared.

1-(Diphenylmethyl)-2-isothiocyanatobenzene (8a)

Colorless plates; yield: 97%; mp 97–98 °C (PE–CH_2Cl_2).

IR (KBr): 2139, 1593, 1446, 1076, 1027, 930, 760, 700 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.48–7.44 (m, 1 H, H_{Ar}), 7.37–7.23 (m, 8 H, H_{Ar}), 7.11–7.08 (m, 4 H, H_{Ar}), 6.93–6.90 (m, 1 H, H_{Ar}), 5.81 (s, 1 H, CH).

Anal. Calcd for $C_{20}H_{15}NS$: C, 79.70; H, 5.02; N, 4.65; S, 10.64. Found: C, 79.83; H, 5.06; N, 4.53; S, 10.76.

1-[Bis(4-methylphenyl)methyl]-2-isothiocyanatobenzene (8b)

Pale beige solid; yield: 87%; mp 63–65 °C (PE–CH_2Cl_2).

IR (KBr): 2100, 1512, 1476, 1448, 932, 808, 800, 724 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.24–7.18 (m, 3 H, H_{Ar}), 7.11 (d, J = 7.8 Hz, 4 H, H_{Ar}), 6.98 (d, J = 7.8 Hz, 4 H, H_{Ar}), 7.00–6.97 (m, 1 H, H_{Ar}), 5.73 (s, 1 H, CH), 2.34 (s, 6 H, CH_3).

Anal. Calcd for $C_{22}H_{19}NS$: C, 80.20; H, 5.81; N, 4.25; S, 9.73. Found: C, 80.59; H, 5.92; N, 4.16; S, 9.74.

1-[Bis(4-methoxyphenyl)methyl]-2-isothiocyanatobenzene (8c)

Beige solid; yield: 50%; mp 65–67 °C (PE–CH_2Cl_2).

IR (KBr): 2140, 1588, 1480, 1468, 1448, 1248, 1184, 1108, 1032, 936, 816, 804, 756 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.18 (m, 3 H, H_{Ar}), 7.01 (d, *J* = 8.6 Hz, 4 H, H_{Ar}), 6.97–6.94 (m, 1 H, H_{Ar}), 6.85 (d, *J* = 8.6 Hz, 4 H, H_{Ar}), 5.70 (s, 1 H, CH), 3.81 (s, 6 H, OCH_3).

Anal. Calcd for $C_{22}H_{19}NO_2S$: C, 73.10; H, 5.30; N, 3.87; S, 8.87. Found: C, 72.82; H, 5.37; N, 3.82; S, 8.50.

1-[Bis(3,4-dimethoxyphenyl)methyl]-2-isothiocyanatobenzene (8d)
Pale beige solid; yield: 77%; mp 89–90 °C (PE–CH_2Cl_2).

IR (KBr): 2120, 1592, 1480, 1464, 1264, 1244, 1140, 1028, 756 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.24–7.15 (m, 3 H, H_{Ar}), 6.97–6.92 (m, 1 H, H_{Ar}), 6.80 (d, *J* = 8.3 Hz, 2 H, H_{Ar}), 6.69 (d, *J* = 1.5 Hz, 2 H, H_{Ar}), 6.55 (dd, *J* = 1.5, 8.3 Hz, 2 H, H_{Ar}), 5.66 (s, 1 H, CH), 3.87 (s, 6 H, OCH_3), 3.80 (s, 6 H, OCH_3).

Anal. Calcd for $C_{24}H_{23}NO_4S$: C, 68.39; H, 5.50; N, 3.32; S, 7.61. Found: C, 68.05; H, 5.49; N, 3.09; S, 7.55.

1-[Bis(3,4-dimethoxyphenyl)methyl]-2-isothiocyanato-3,4-dimethoxybenzene (8e)
Pale green cubes; yield: 78%; mp 128–129 °C (PE–CH_2Cl_2).

IR (KBr): 2127, 1589, 1511, 1462, 1344, 1236, 1137, 1109, 1026, 793, 747 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 6.79 (d, *J* = 8.2 Hz, 2 H, H_{Ar}), 6.74 (s, 1 H, H_{Ar}), 6.69 (d, *J* = 1.8 Hz, 2 H, H_{Ar}), 6.56 (dd, 2 H, *J* = 1.8, 8.2, H_{Ar}), 6.43 (s, 1 H, H_{Ar}), 5.61 (s, 1 H, CH), 3.90 (s, 6 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.80 (s, 6 H, OCH_3), 3.67 (s, 3 H, OCH_3).

Anal. Calcd for $C_{26}H_{27}NO_6S$: C, 64.85; H, 5.65; N, 2.91; S, 6.66. Found: C, 65.07; H, 5.89; N, 2.95; S, 6.59.

1-[Bis(3,4-diethoxyphenyl)methyl]-2-isothiocyanato-3,4-dimethoxybenzene (8f)
Beige solid; yield: 65%; mp 117 °C (PE–CH_2Cl_2).

IR (KBr): 2152, 1512, 1476, 1464, 1456, 1436, 1424, 1304, 1256, 1244, 1224, 1204, 1136, 1044, 864 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 6.79 (d, *J* = 8.2 Hz, 2 H, H_{Ar}), 6.73 (s, 1 H, H_{Ar}), 6.66 (d, *J* = 1.8 Hz, 2 H, H_{Ar}), 6.53 (dd, *J* = 1.8, 8.2 Hz, 2 H, H_{Ar}), 6.40 (s, 1 H, H_{Ar}), 5.57 (s, 1 H, CH), 4.07 (q, *J* = 7.0 Hz, 4 H, O*CH*$_2$CH$_3$), 3.99 (q, *J* = 7.0 Hz, 4 H, O*CH*$_2$CH$_3$), 3.85 (s, 3 H, OCH_3), 3.65 (s, 3 H, OCH_3), 1.44 (t, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 1.39 (t, *J* = 7.0 Hz, 6 H, OCH_2CH_3).

Anal. Calcd for $C_{30}H_{35}NO_6S$: C, 67.02; H, 6.56; N, 2.61; S, 5.96. Found: C, 67.29; H, 6.74; N, 2.63; S, 6.08.

Compounds 9–11; General Procedure
$AlCl_3$ (0.3 g, 2.25 mmol) was added to a soln of isocyanate **8** (1.66 mmol) in DCE (5 mL). The mixture was stirred for 24 h at r.t. (TLC monitoring), then poured into H_2O (100 mL) and extracted with CH_2Cl_2 (3 × 40 mL). The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The oily residue was purified by chromatography (silica gel; EtOAc–benzene–PE, 6:5:13 for **9a** and **10a**; acetone–CH_2Cl_2–PE, 3:2:12 for **9c** and **11**; EtOAc–PE, 1:3 for **9d** and **10d**; acetone–CH_2Cl_2–PE, 4:5:14 for **9e**; EtOAc–PE, 1:4 for **9f** and **10f**; acetone–CH_2Cl_2–PE, 3:2:12 for **9g**).

Benzothiazine **9b** was recrystallized from PE–CH_2Cl_2.

2,4-Diphenyl-4*H*-3,1-benzothiazine (9a)
Pale beige solid; yield: 9%; mp 91 °C.

IR (KBr): 1536, 1492, 1448, 1196, 1180, 948, 768, 720 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.06–8.03 (m, 2 H, H_{Ar}), 7.57–7.44 (m, 5 H, H_{Ar}), 7.37–7.33 (m, 1 H, $H_{Ar,}$), 7.29–7.17 (m, 6 H, H_{Ar}), 5.79 (s, 1 H, CH).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 157.7, 143.2, 142.1, 137.3, 131.7, 128.7 (2C), 128.6 (3C), 128.1, 127.6, 127.4 (2C), 127.3 (2C), 126.9 (2C), 122.5, 43.4.

MS (EI, 70 eV): *m/z* (%) = 301 (100) [M^+], 300 (53), 299 (12), 224 (28), 197 (14), 165 (52), 121 (31), 76 (18).

Anal. Calcd for $C_{20}H_{15}NS$: C, 79.70; H, 5.02; N, 4.65; S, 10.64. Found: C, 80.04; H, 5.19; N, 4.49; S, 10.68.

2,4-Bis(4-methylphenyl)-4*H*-3,1-benzothiazine (9b)
Pale yellow solid; yield: 60%; mp 111 °C (PE–CH_2Cl_2).

IR (KBr): 1604, 1534, 1507, 1450, 1195, 1174, 1107, 940, 822, 763, 729 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.93 (d, *J* = 8.0 Hz, 2 H, H_{Ar}), 7.52–7.42 (m, 2 H, H_{Ar}), 7.31 (d, *J* = 8.0 Hz, 2 H, H_{Ar}), 7.34–7.30 (m, 1 H, H_{Ar}), 7.22–7.20 (m, 1 H, H_{Ar}), 7.05 (s, 4 H, H_{Ar}), 5.72 (s, 1 H, CH), 2.37 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 157.7, 143.4, 141.9, 139.1, 136.8, 134.8, 129.3 (2C), 129.1 (2C), 128.4, 127.8, 127.5 (3C), 127.2, 126.9 (2C), 122.9, 43.4, 21.0, 20.5.

MS (EI, 70 eV): *m/z* (%) = 329 (100) [M^+], 297 (11), 238 (16), 197 (12), 193 (11), 180 (12), 179 (56), 178 (30), 165 (26), 135 (12).

Anal. Calcd for $C_{22}H_{19}NS$: C, 80.20; H, 5.81; N, 4.25; S, 9.73. Found: C, 80.53; H, 6.03; N, 4.11; S, 10.09.

2,4-Bis(4-methoxyphenyl)-4*H*-3,1-benzothiazine (9c)
Pale yellow solid; yield: 19%; mp 149 °C.

IR (KBr): 1608, 1540, 1508, 1268, 1260, 1252, 1168, 1028, 844, 832, 772 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.01 (d, *J* = 8.3 Hz, 2 H, H_{Ar}), 7.51–7.49 (m, 1 H, H_{Ar}), 7.44–7.40 (m, 1 H, H_{Ar}), 7.32–7.28 (m, 1 H, H_{Ar}), 7.20–7.18 (m, 1 H, H_{Ar}), 7.08 (d, *J* = 8.2 Hz, 2 H, H_{Ar}), 7.03 (d, *J* = 8.3 Hz, 2 H, H_{Ar}), 6.82 (d, *J* = 8.2 Hz, 2 H, H_{Ar}), 5.68 (s, 1 H, C*H*), 3.81 (s, 3 H, OCH_3), 3.68 (s, 3 H, OCH_3).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 162.2, 158.5, 157.2, 143.5, 134.0, 130.0, 129.2 (2C), 128.5, 128.2 (2C), 127.5, 127.3, 127.0, 123.1, 114.0 (2C), 113.9 (2C), 55.4, 54.9, 43.2.

MS (EI, 70 eV): *m/z* (%) = 361 (100) [M^+], 360 (19), 347 (14), 346 (38), 329 (16), 254 (15), 210 (10), 195 (12), 59 (16), 57 (19).

Anal. Calcd for $C_{22}H_{19}NO_2S$: C, 73.10; H, 5.30; N, 3.87; S, 8.87. Found: C, 73.18; H, 5.16; N, 3.66; S, 8.52.

2,4-Bis(3,4-dimethoxyphenyl)-4*H*-3,1-benzothiazine (9d)
Pale yellow cubes; yield; 37%; mp 121 °C.

IR (KBr): 1596, 1536, 1512, 1464, 1448, 1444, 1416, 1348, 1264, 1236, 1224, 1156, 1140, 1024, 804, 764 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.71 (d, *J* = 1.8, Hz, 1 H, H_{Ar}), 7.62 (dd, *J* = 1.8, 8.5 Hz, 1 H, H_{Ar}), 7.53–7.51 (m, 1 H, H_{Ar}), 7.45–7.40 (m, 1 H, H_{Ar}), 7.33–7.28 (m, 1 H, H_{Ar}), 7.21–7.19 (m, 1 H, H_{Ar}), 7.05 (d, *J* = 8.5 Hz, 1 H, H_{Ar}), 6.94 (d, *J* = 1.6 Hz, 1 H, H_{Ar}), 6.80 (d, *J* = 8.3 Hz, 1 H, H_{Ar}), 6.56 (dd, *J* = 1.6, 8.3 Hz, 1 H, H_{Ar}), 5.56 (s, 1 H, CH), 3.85 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 3.67 (s, 6 H, OCH_3).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 152.1, 148.8, 148.6 (2C), 148.3, 143.5, 134.1, 130.1, 128.3, 127.5, 127.3, 127.0, 123.3, 121.7, 119.4, 111.7, 111.2 (2C), 109.7, 55.6, 55.5, 55.4 (2C), 43.7.

MS (EI, 70 eV): *m/z* (%) = 421 (100) [M^+], 407 (13), 406 (47), 59 (16).

Anal. Calcd for $C_{24}H_{23}NO_4S$: C, 68.39; H, 5.50; N, 3.32; S, 7.61. Found: C, 68.68; H, 5.63; N, 3.15; S, 7.78.

2,4-Bis(3,4-dimethoxyphenyl)-6,7-dimethoxy-4*H*-3,1-benzothiazine (9e)

Pale yellow solid; yield: 30%; mp 194 °C.

IR (KBr): 1595, 1504, 1460, 1415, 1265, 1242, 1141, 1019, 876, 812, 759 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.67 (d, *J* = 1.8 Hz, 1 H, H_{Ar}), 7.55 (dd, *J* = 1.8, 8.5 Hz, 1 H, H_{Ar}), 7.10 (s, 1 H, H_{Ar}), 7.04 (d, *J* = 8.5 Hz, 1 H, H_{Ar}), 6.91 (d, *J* = 1.6 Hz, 1 H, H_{Ar}), 6.83 (s, 1 H, H_{Ar}), 6.78 (d, *J* = 8.3 Hz, 1 H, H_{Ar}), 6.50 (dd, *J* = 1.6, 8.3 Hz, 1 H, H_{Ar}), 5.56 (s, 1 H, CH), 3.86 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 3.67 (s, 6 H, OCH_3).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 154.4, 151.8, 148.8, 148.6, 148.5, 148.2 (2C), 137.3, 135.1, 130.4, 121.3, 119.2, 114.6, 111.6, 111.1, 111.0, 110.7, 110.3, 109.5, 55.7, 55.6 (3C), 55.5 (2C), 43.4.

MS (EI, 70 eV): *m/z* (%) = 481 (97) [M^+], 466 (38), 451 (22), 450 (100), 434 (11), 420 (13), 344 (35), 328 (12), 299 (59), 284 (12), 225 (15), 181 (23), 151 (26).

Anal. Calcd for $C_{26}H_{27}NO_6S$: C, 64.85; H, 5.65; N, 2.91; S, 6.66. Found: C, 64.72; H, 5.51; N, 2.70; S, 6.75.

2,4-Bis(3,4-Diethoxyphenyl)-6,7-dimethoxy-4*H*-3,1-benzothiazine (9f)

Pale yellow solid; yield: 26%; mp 124–125 °C.

IR (KBr): 1605, 1503, 1473, 1422, 1262, 1236, 1140, 1040, 1002, 865, 775 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.64 (d, *J* = 1.9 Hz, 1 H, H_{Ar}), 7.52 (dd, *J* = 1.9, 8.6 Hz, 1 H, H_{Ar}), 7.08 (s, 1 H, H_{Ar}), 7.02 (d, *J* = 8.6 Hz, 1 H, H_{Ar}), 6.86 (d, *J* = 2.0 Hz, 1 H, H_{Ar}), 6.82 (s, 1 H, H_{Ar}), 6.77 (d, *J* = 8.3 Hz, 1 H, H_{Ar}), 6.49 (dd, *J* = 2.0, 8.3 Hz, 1 H, H_{Ar}), 5.53 (s, 1 H, CH), 4.13–4.06 (m, 4 H, OCH_2CH_3), 3.96–3.88 (m, 4 H, OCH_2CH_3), 3.86 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 1.33–1.38 (m, 6 H, OCH_2CH_3), 1.28–1.23 (m, 6 H, OCH_2CH_3).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 154.3, 151.3, 148.5, 148.1, 148.0, 147.8, 147.6, 137.4, 135.1, 130.3, 121.4, 119.3, 114.6, 113.1, 112.6, 112.3, 111.2, 110.7, 110.3, 64.0, 63.8 (2C), 63.7, 55.7, 55.6, 43.3, 14.7 (4C).

MS (EI, 70 eV): *m/z* (%) = 537 (100) [M^+], 508 (11), 507 (45), 506 (98), 328 (14), 327 (21).

Anal. Calcd for $C_{30}H_{35}NO_6S$: C, 67.02; H, 6.56; N, 2.61; S, 5.96. Found: C, 67.45; H, 6.71; N, 2.59; S, 6.12.

2,4-Bis(2,3-dihydro-1,4-benzodioxin-6-yl)-4*H*-3,1-benzothiazine (9g)

Yellow oil; yield: 61%. This compound was obtained with 90% purity, and characterized by spectral methods only.

IR (Nujol): 1612, 1584, 1540, 1500, 1480, 1460, 1428, 1320, 1288, 1260, 1248, 1204, 1164, 1128, 1068, 1052, 920, 888, 820, 768 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 2.0 Hz, 1 H, H_{Ar}), 7.65 (dd, *J* = 2.0, 8.4 Hz, 1 H, H_{Ar}), 7.56–7.54 (m, 1 H, H_{Ar}), 7.42–7.37 (m, 1 H, H_{Ar}), 7.27–7.22 (m, 1 H, H_{Ar}), 7.08–7.06 (m, 1 H, H_{Ar}), 6.92 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 6.77–6.67 (m, 3 H, H_{Ar}), 5.30 (s, 1 H, CH), 4.29–4.26 (m, 4 H, CH_2CH_2), 4.19 (s, 4 H, CH_2CH_2).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 158.7, 147.0, 144.0, 143.5 (2C), 143.3, 134.5, 131.5, 128.6, 127.7, 127.5, 127.3, 123.0, 121.9, 120.7, 117.5 (2C), 117.3, 116.6, 64.7, 64.3 (3C), 45.2.

MS (EI, 70 eV): *m/z* (%) = 417 (100) [M^+], 361 (10), 333 (26), 250 (10), 238 (17), 237 (14), 223 (26), 179 (25), 171 (20), 163 (17), 87 (29), 85 (38), 59 (29), 57 (14).

11-Phenyl-5,11-dihydro-6*H*-dibenzo[*b*,*e*]azepine-6-thione (10a)

Yellow solid; yield: 25%; mp 216 °C.

IR (KBr): 1604, 1528, 1492, 1448, 1388, 1240, 1184, 1160, 1008, 772, 760, 740, 708, 696 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 12.23 (s, 1 H, NH), 8.10–8.08 (m, 1 H, H_{Ar}), 7.61–7.48 (m, 3 H, H_{Ar}), 7.39–7.14 (m, 7 H, H_{Ar}), 6.78–6.76 (m, 2 H, H_{Ar}), 5.47 (s, 1 H, CH).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 198.0, 141.4, 140.0, 137.5, 137.0, 136.6, 133.7, 132.1, 130.0, 128.5, 128.0 (2C), 127.8, 127.1, 126.5 (2C), 126.3 (2C), 122.6, 53.7.

MS (EI, 70 eV): *m/z* (%) = 301 (100) [M^+], 269 (20), 267 (47), 239 (16), 224 (19), 191 (12), 190 (25), 180 (19), 165 (32), 152 (11), 79 (12), 59 (13).

Anal. Calcd for $C_{20}H_{15}NS$: C, 79.70; H, 5.02; N, 4.65; S, 10.64. Found: C, 79.53; H, 5.06; N, 4.61; S, 10.55.

11-(3,4-Dimethoxyphenyl)-8,9-dimethoxy-5,11-dihydro-6*H*-dibenzo[*b*,*e*]azepine-6-thione (10d)

Yellow solid; yield: 7%; mp 100–101 °C.

IR (KBr): 1602, 1512, 1412, 1265, 1235, 1128, 1025, 949, 872, 757 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 12.06 (s, 1 H, NH), 7.72 (s, 1 H, H_{Ar}), 7.56–7.53 (m, 1 H, H_{Ar}), 7.32–7.28 (m, 2 H, H_{Ar}), 7.22–7.19 (m, 1 H, H_{Ar}), 7.09 (s, 1 H, H_{Ar}), 6.77 (d, *J* = 8.0 Hz, 1 H, H_{Ar}), 6.32 (d, *J* = 1.6 Hz, 1 H, H_{Ar}), 6.31 (dd, *J* = 1.6, 8.0 Hz, 1 H, H_{Ar}), 5.32 (s, 1 H, CH), 3.87 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 3.67 (s, 3 H, OCH_3), 3.54 (s, 3 H, OCH_3).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 197.0, 152.1, 148.0, 147.3, 147.0, 137.9, 136.5, 134.9, 132.7, 129.6, 129.2, 127.5, 126.1, 122.5, 119.1, 117.0, 111.6, 111.4, 111.0, 55.8, 55.6, 55.5, 55.3, 53.0.

MS (EI, 70 eV): *m/z* (%) = 421 (100) [M^+], 406 (23), 390 (27), 388 (17), 329 (27), 328 (16), 301 (30), 267 (14), 238 (12), 179 (29), 178 (15), 151 (36), 59 (12).

Anal. Calcd for $C_{24}H_{23}NO_4S$: C, 68.39; H, 5.50; N, 3.32; S, 7.61. Found: C, 68.50; H, 5.48; N, 3.25; S, 7.50.

Crystal data: $C_{24}H_{23}NO_4S$, orthorhombic, space group *P*bca; *a* = 10.108(2) Å, *b* = 16.238(3) Å, *c* = 25.960(5) Å, *V* = 4260.9(14) $Å^3$, Z = 8, D_{calcd} = 1.314 Mg/m^3, *F*(000) = 1776; 3703 reflections collected, 3602 unique (R_{int} = 0.0252); final *R* indices (1307 observed collections $I > 2\sigma I$): R_1 = 0.0350, wR_2 = 0.0875; final *R* indices (all data): R_1 = 0.1700, wR_2 = 0.0980.

11-(3,4-Diethoxyphenyl)-8,9-diethoxy-2,3-dimethoxy-5,11-dihydro-6*H*-dibenzo[*b*,*e*]azepine-6-thione (10f)

Yellow solid; yield: 5%; mp 186–187 °C.

IR (KBr): 1600, 1508, 1476, 1444, 1420, 1396, 1356, 1264, 1244, 1224, 1140, 1104, 1040, 996, 864, 796, 756 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 11.85 (s, 1 H, NH), 7.70 (s, 1 H, H_{Ar}), 7.12 (s, 1 H, H_{Ar}), 7.01 (s, 1 H, H_{Ar}), 6.85 (s, 1 H, H_{Ar}), 6.74 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 6.31 (d, *J* = 1.6 Hz, 1 H, H_{Ar}), 6.29 (dd, *J* = 1.6, 8.4 Hz, 1 H, H_{Ar}), 5.18 (s, 1 H, CH), 4.17–4.09 (m, 2 H, OCH_2CH_3), 4.06–3.97 (m, 2 H, OCH_2CH_3), 3.95–3.87 (m, 2 H, OCH_2CH_3), 3.82 (s, 3 H, OCH_3), 3.83–3.73 (m, 2 H, OCH_2CH_3), 3.71 (s, 3 H, OCH_3), 1.37 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.32 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.26 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.20 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 195.7, 151.5, 147.4, 147.3, 146.8, 146.7, 146.0, 135.4, 133.2, 130.1, 129.7, 129.1, 119.4, 118.6, 113.2, 112.9, 112.7, 112.3, 106.7, 64.0 (2C), 63.8, 63.7, 55.8, 55.6, 52.4, 14.7 (3C), 14.6.

MS (EI, 70 eV): *m/z* (%) = 537 (100) [M$^+$], 522 (71), 509 (24), 506 (43), 478 (15), 462 (13), 328 (18), 193 (14), 179 (36), 151 (30), 123 (31), 59 (27), 57 (27).

Anal. Calcd for $C_{30}H_{35}NO_6S$: C, 67.02; H, 6.56; N, 2.61; S, 5.96. Found: C, 67.11; H, 6.86; N, 2.65; S, 5.80.

4-[4-(4-Methoxyphenyl)-4*H*-3,1-benzothiazin-2-yl]phenol (11)
Pale yellow solid; yield: 15%; mp 226 °C.

IR (KBr): 3459, 1608, 1584, 1540, 1508, 1436, 1292, 1256, 1236, 1188, 1164, 1032, 964, 836, 768 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.09 (s, 1 H, OH), 7.91 (d, *J* = 8.6 Hz, 2 H, H_{Ar}), 7.48–7.39 (m, 2 H, H_{Ar}), 7.31–7.26 (m, 1 H, H_{Ar}), 7.19–7.17 (m, 1 H, H_{Ar}), 7.07 (d, *J* = 8.6 Hz, 2 H, H_{Ar}), 6.88 (d, *J* = 8.6 Hz, 2 H, H_{Ar}), 6.82 (d, *J* = 8.6 Hz, 2 H, H_{Ar}), 5.66 (s, 1 H, CH), 3.68 (s, 3 H, OCH_3).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 160.9, 158.5, 157.3, 143.6, 134.1, 129.4 (2C), 128.5, 128.2 (2C), 127.3 (2C), 127.2, 126.9, 123.1, 115.4 (2C), 113.9 (2C), 55.0, 43.1.

MS (EI, 70 eV): *m/z* (%) = 347 (100) [M$^+$], 332 (29).

Anal. Calcd for $C_{21}H_{17}NO_2S$: C, 72.60; H, 4.93; N, 4.03; S, 9.23. Found: C, 72.73; H, 5.13; N, 3.93; S, 9.02.

Crystal data: $C_{21}H_{17}NO_2S$, monoclinic, space group *P*2(1)/n; *a* = 13.795(3) Å, *b* = 8.128(2) Å, *c* = 15.622(3) Å, β = 96.06(3)°, *V* = 1741.8(7) Å^3, Z = 4, D_{calcd} = 1.325 Mg/m^3, *F*(000) = 728; 3459 reflections collected, 3335 unique (R_{int} = 0.0181); final *R* indices (2105 observed collections $I > 2\sigma I$): R_1 = 0.0288, wR_2 = 0.0827; final *R* indices (all data): R_1 = 0.0622, wR_2 = 0.0877.

2-Benzyl-4,5-dimethoxyanilines 15; General Procedure
Anhydrous $AlCl_3$ (4.5 g, 34 mmol) and $NaBH_4$ (1.3 g, 34 mmol) were added portionwise to a stirred soln of compound **14** (17 mmol) in THF (120 mL) cooled to 0–5 °C. The resulting suspension was stirred at 0–5 °C for 20 min and then refluxed for 1–2 h until the starting compound was consumed (TLC). The mixture was then cooled and poured into H_2O (400 mL). The organic layer was separated and the H_2O layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na_2SO_4), treated with activated charcoal, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2–PE (1:2) and the soln was filtered through the pad of silica gel. The residue was crystallized from CH_2Cl_2–PE (1:4).

Compound **15a** was obtained as a yellow oil and used at the next step as prepared.

2-(4-Chlorobenzyl)-4,5-dimethoxyaniline (15b)
Pale beige plates; yield: 60%; mp 98–99 °C.

IR (KBr): 3420, 3346, 1609, 1522, 1485, 1465, 1414, 1295, 1234, 1127, 1085, 1005, 840, 795, 751 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.2 Hz, 2 H, H_{Ar}), 7.11 (d, *J* = 8.2 Hz, 2 H, H_{Ar}), 6.62 (s, 1 H, H_{Ar}), 6.32 (s, 1 H, H_{Ar}), 3.84 (s, 3 H, OCH_3), 3.82 (s, 2 H, CH_2), 3.80 (s, 3 H, OCH_3), 3.28 (s, 2 H, NH_2).

Anal. Calcd for $C_{15}H_{16}ClNO_2$: C, 64.87; H, 5.81; N, 5.04. Found: C, 64.65; H, 5.95; N, 5.12.

4,5-Dimethoxy-2-(4-methylbenzyl)aniline (15c)
Pale beige needles; yield: 76%; mp 104–105 °C.

IR (KBr): 3420, 3347, 1610, 1521, 1461, 1296, 1234, 1210, 1168, 1127, 1005, 840, 803, 758 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.10 (s, 4 H, H_{Ar}), 6.66 (s, 1 H, H_{Ar}), 6.31 (s, 1 H, H_{Ar}), 3.84 (s, 3 H, OCH_3), 3.83 (s, 2 H, CH_2), 3.81 (s, 3 H, OCH_3), 3.30 (s, 2 H, NH_2), 2.33 (s, 3 H, CH_3).

Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.47; H, 7.48; N, 5.55.

1-Benzyl-2-isothiocyanatobenzenes 16; General Procedure
The procedure used for the synthesis of compounds **8** was also used for the synthesis of compounds **16**.

1-Benzyl-2-isothiocyanato-4,5-dimethoxybenzene (16a)
Pale beige needles; yield: 72%; mp 83–84 °C (CH_2Cl_2–PE).

IR (KBr): 2136, 1612, 1516, 1496, 1464, 1452, 1404, 1348, 1296, 1268, 1228, 1208, 1168, 1124, 1004, 788, 728 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.18 (m, 5 H, H_{Ar}), 6.76 (s, 1 H, H_{Ar}), 6.63 (s, 1 H, H_{Ar}), 4.00 (s, 2 H, CH_2), 3.86 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3).

Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91; S, 11.24. Found: C, 67.39; H, 5.33; N, 4.93; S, 11.01.

1-(4-Chlorobenzyl)-2-isothiocyanato-4,5-dimethoxybenzene (16b)
Pale beige needles; yield: 84%; mp 118–119 °C (CH_2Cl_2–PE).

IR (KBr): 2156, 1604, 1516, 1492, 1460, 1404, 1352, 1288, 1268, 1232, 1208, 1172, 1124, 1008, 864, 844, 788 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 8.3 Hz, 2 H, H_{Ar}), 7.11 (d, *J* = 8.3 Hz, 2 H, H_{Ar}), 6.75 (s, 1 H, H_{Ar}), 6.60 (s, 1 H, H_{Ar}), 3.96 (s, 2 H, CH_2), 3.86 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3).

Anal. Calcd for $C_{16}H_{14}ClNO_2S$: C, 60.09; H, 4.41; N, 4.38; S, 10.03. Found: C, 60.19; H, 4.46; N, 4.36; S, 9.90.

1-Isothiocyanato-4,5-dimethoxy-2-(4-methylbenzyl)benzene (16c)
White solid; yield: 85%; mp 106–107 °C (CH_2Cl_2–PE).

IR (KBr): 2152, 1608, 1520, 1464, 1448, 1404, 1348, 1292, 1268, 1232, 1168, 1124, 1008, 868, 840, 788 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.12 (d, *J* = 8.1 Hz, 2 H, H_{Ar}), 7.08 (d, *J* = 8.1 Hz, 2 H, H_{Ar}), 6.75 (s, 1 H, H_{Ar}), 6.63 (s, 1 H, H_{Ar}), 3.96 (s, 2 H, CH_2), 3.86 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 2.33 (s, 3 H, CH_3).

Anal. Calcd for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68; S, 10.71. Found: C, 68.03; H, 5.68, N, 4.71; S, 10.50.

2,3-Dimethoxy-8-methyl-5,11-dihydro-6*H*-dibenzo[*b*,*e*]azepine-6-thione (17)
Compound **17** was obtained analogously to compounds **9** and **10**, except that the reaction mixture was kept at r.t. for 48 h. See Table 4 for NMR data.

Yellow solid; yield: 38%; mp 186–187 °C (EtOAc–PE).

IR (KBr): 1520, 1508, 1440, 1348, 1280, 1264, 1248, 1124, 1112, 1020, 860 cm^{-1}.

MS (EI, 70 eV): *m/z* (%) = 299 (81) [M$^+$], 284 (28), 266 (26), 256 (17), 165 (20), 104 (19), 101 (100), 82 (58), 58 (78), 57 (37).

Anal. Calcd for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68; S, 10.71. Found: C, 67.01; H, 5.71; N, 4.69; S, 10.48.

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References

(1) Kim, M. Y.; Shin, H. T.; Lee, C. W.; Kim, J. W.; Kim, S. H.; Choi, Y.; Son, M. H. US 5171851, **1992**; *Chem. Abstr.* **1992**, *118,* 213099.

(2) (a) Rieu, J.-P.; Patoiseau, J.-F.; John, G. W.; Legrand, B.; Valentin, J.-P. WO 9705134, **1997**; *Chem. Abstr.* **1997**, *126*, 225308. (b) Rieu, J.-P.; Patoiseau, J.-F.; John, G.; Legrand, B.; Verscheure, Y. WO 0043391, **2000**; *Chem. Abstr.* **2000**, *133*, 135319. (c) Tamada, S.; Fujioka, T.; Ogawa, H.; Teramoto, S.; Kondo, K. JP 1061469, **1989**; *Chem. Abstr.* **1989**, *112*, 118837.

(3) Ogawa, H.; Tamada, S.; Fujioka, T.; Teramoto, S.; Kondo, K.; Yamashita, S.; Yabuuchi, Y.; Tominaga, M.; Nakagawa, K. *Chem. Pharm. Bull.* **1988**, *36*, 2401.

(4) Gauthier, J. A.; Asselin, A. A. CA 1210396, **1986**; *Chem. Abstr.* **1986**, *106*, 176409.

(5) Jones, G. H.; Venuti, M. C.; Alvarez, R.; Bruno, J. J.; Berks, A. H.; Prince, A. *J. Med. Chem.* **1987**, *30*, 295.

(6) Takasaki, T.; Sato, K.; Abe, T. JP 183282, **2003**; *Chem. Abstr.* **2003**, *139*, 85163.

(7) Tsubata, K.; Shimaoka, T.; Nishida, T.; Takagi, K.; Baba, K.; Tajima, S. WO 9854163, **1998**; *Chem. Abstr.* **1998**, *130*, 38384.

(8) Petrie, C.; Orme, M. W.; Baindur, N.; Robbins, K. G.; Harris, S. M.; Kontoyianni, M.; Hurley, L. H.; Kerwin, S. M.; Mundy, G. R. WO 9751308, **1997**; *Chem. Abstr.* **1997**, *127*, 17703.

(9) Neumann, U.; Gütschow, M. *Bioorg. Chem.* **1995**, *23*, 72.

(10) (a) Shridhar, D. R.; Rao, K. S.; Bhopale, K. K.; Tripathi, H. N.; Sai, G. S. T. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1981**, *20*, 471. (b) Pelosi, S. S. Jr. US 4002620, **1977**; *Chem. Abstr.* **1977**, *86*, 140074.

(11) Ishige, S.; Usui, H.; Saeki, K. DE 2704724, **1977**; *Chem. Abstr.* **1977**, *87*, 144134.

(12) (a) Dondoni, A.; Battaglia, A.; Giorgianni, P.; Gilli, G.; Sacerdoti, M. *J. Chem. Soc., Chem. Commun.* **1977**, 43. (b) Dondoni, A.; Battaglia, A.; Giorgianni, P. *J. Org. Chem.* **1980**, *45*, 3766. (c) Dondoni, A.; Battaglia, A.; Giorgianni, P. *J. Org. Chem.* **1982**, *47*, 3998. (d) Carisi, P.; Mazzanti, G.; Zani, P.; Barbaro, G.; Battaglia, A.; Giorgianni, P. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2647.

(13) Gromachevskaya, E. V.; Kosulina, T. P.; Kulnevich, V. G. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1993**, *29*, 460; *Khim. Geterotsikl. Soedin.* **1993**, 537.

(14) Gauthier, J.; Duceppe, J. S. *J. Heterocycl. Chem.* **1984**, *21*, 1081.

(15) Sorkin, E.; Hinden, W. *Helv. Chim. Acta.* **1949**, *32*, 63.

(16) El-Desoky, S. I.; Kandeel, E. M.; Abd-el-Rahman, A. H.; Schmidt, R. R. *J. Heterocycl. Chem.* **1999**, *36*, 153.

(17) (a) Beilenson, B.; Hamer, F. M.; Rathbone, R. J. *J. Chem. Soc.* **1945**, 222. (b) Lednicer, D.; Emmert, D. E. *J. Heterocycl. Chem.* **1971**, *8*, 903.

(18) Hari, A.; Miller, B. L. *Org. Lett.* **2000**, *2*, 3667.

(19) Tarraga, A.; Molina, P.; Lopez, J. L. *Tetrahedron Lett.* **2000**, *41*, 4895.

(20) Gonda, J.; Kristian, P. *Collect. Czech. Chem. Commun.* **1986**, *51*, 2802.

(21) Gonda, J.; Kristian, P. *Collect. Czech. Chem. Commun.* **1986**, *51*, 2810.

(22) (a) Nishio, T.; Sekiguchi, H. *Heterocycles* **2002**, *58*, 203. (b) Nishio, T. *J. Org. Chem.* **1997**, *62*, 1106.

(23) Lee, H.; Kim, K. *Heteroat. Chem.* **1993**, *4*, 263.

(24) Besson, T.; Guillaumet, G.; Lamazzi, C.; Rees, C. W. *Synlett* **1997**, 704.

(25) Besson, T.; Guillaumet, G.; Lamazzi, C.; Rees, C. W.; Thiery, V. *J. Chem. Soc., Perkin Trans. 1* **1998**, 4057.

(26) (a) Dean, W. D.; Papadopoulos, E. P. *J. Heterocycl. Chem.* **1982**, *19*, 1117. (b) Looney-Dean, V.; Lindamood, B. S.; Papadopoulos, E. P. *Synthesis* **1984**, 68. (c) Deck, L. M.; Turner, S. D.; Deck, J. A.; Papadopoulos, E. P. *J. Heterocycl. Chem.* **2001**, *38*, 343.

(27) (a) Butin, A. V.; Abaev, V. T.; Stroganova, T. A.; Gutnov, A. V. *Molecules* **1997**, *2*, 62. (b) Abaev, V. T.; Tsiunchik, F. A.; Gutnov, A. V.; Butin, A. V. *J. Heterocycl. Chem.* **2008**, *45*, 475.

(28) (a) Jones, G.; McKinley, W. H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 599. (b) Schneider, C. S.; Pook, K. H. *J. Chem. Soc., Perkin Trans. 1* **1986**, 877. (c) Abaev, V. T.; Gutnov, A. V.; Butin, A. V.; Zavodnik, V. E. *Tetrahedron* **2000**, *56*, 8933. (d) Butin, A. V.; Tsiunchik, F. A.; Abaev, V. T.; Zavodnik, V. E. *Synlett* **2008**, 1145.

(29) Abaev, V. T.; Tsiunchik, F. A.; Gutnov, A. V.; Butin, A. V. *Tetrahedron Lett.* **2006**, *47*, 4029.

(30) (a) Gittos, M. W.; Robinson, M. R.; Verge, J. P.; Davies, R. V.; Iddon, B.; Suschitzky, H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 33. (b) Davies, R. V.; Iddon, B.; Paterson, T. Mc. C.; Pickering, M. W.; Suschitzky, H.; Gittos, M. *J. Chem. Soc., Perkin Trans. 1* **1976**, 138. (c) Davies, R. V.; Iddon, B.; Suschitzky, H.; Pickering, M. W.; Gallagher, P. T.; Gittos, M. W.; Robinson, M. D. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2357. (d) Molina, P.; Alcantara, J.; Lopez-Leonardo, C. *Tetrahedron* **1996**, *52*, 5833. (e) Duceppe, J. S.; Gauthier, J. *J. Heterocycl. Chem.* **1984**, *21*, 1685.

(31) Tolstay, T. P.; Vanchikov, A. N.; Vinnik, E. V.; Asulyan, L. D. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1999**, *35*, 978; *Khim. Geterotsikl. Soedin.* **1999**, 1112.

(32) Weissman, S. A.; Zewge, D. *Tetrahedron* **2005**, *61*, 7833.

(33) Butin, A. V.; Smirnov, S. K.; Stroganova, T. A.; Bender, W.; Krapivin, G. D. *Tetrahedron* **2007**, *63*, 474.