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Synthesis and Chemistry of Benzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-ones and Related Ring Transformations

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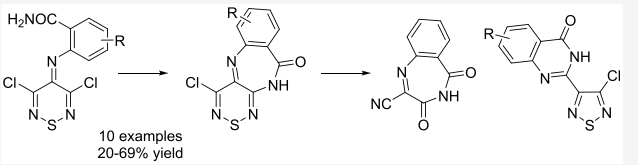
ABSTRACT: 2-[(3,5-Dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)-amino]benzamides are cyclized to benzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-ones via (i) treatment with NaH and via (ii) Pd-catalyzed C-N coupling. The behavior of the latter toward nucleophiles and thermal, oxidative, and reductive conditions revealed unexpected transformations to 3,5-dioxo-4,5-dihydro-3*H*-benzo[*e*][1,4]diazepine-2-carbonitrile and 2-(4-substituted-1,2,5-thiadiazol-3-yl)quinazolin-4(3*H*)-ones.



INTRODUCTION

Benzo[*e*][1,4]diazepines and their hetareno-fused analogues can act as allosteric enhancers of the binding of the neurotransmitter gamma-amino butyric acid (GABA) in the neuronal $GABA_A$ receptors.[1] This behavior has led to uses in pharmaceuticals, in particular, as psychoactive drugs with anxiolytic, sedative, and hypnotic activity, e.g., commercial 1,4-benzodiazepine drugs include diazepam (anxiolytic) and flumazenil (benzodiazepine overdose antidote)[2] (Figure 1).

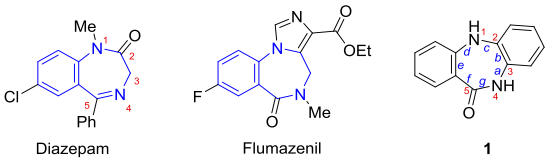


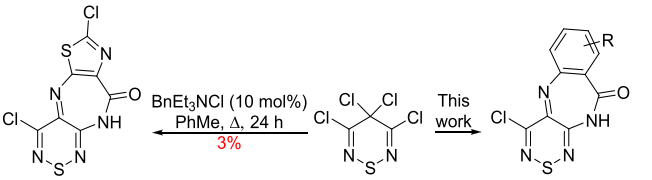
Figure 1. Examples of benzo[*e*][1,4]diazepines.

Di(het)areno[*b*,*e*][1,4]diazepin-11-ones, *e.g.*, compound **1** (Figure 1), are a less explored structural sub-category that act as anticancer agents,[3] HIV non-nucleoside reverse transcriptase inhibitors,[4] and antiarrhythmic agents.[5] Changing the site of the (het)areno fusion can change the biological activity of the system; i.e., novel hetero-[*b*]-fused benzo[*e*][1,4]diazepines can therefore lead to new applications.

Recently, the thiadiazino-fused diazepine **2**, a previously unknown ring system, was isolated in low yield (3%) from the chloride-mediated thermal degradation of tetrachlorothiadiazine **3** (Scheme 1).[6] Intrigued by its formation and our interest in discovering new 1,2,6-thiadiazine chemistry and applications, we targeted the synthesis of analogous benzo-fused systems **4** (Scheme 1).

1,2,6-Thiadiazines are sulfur-nitrogen heterocycles that have broad applications.[7] Non S-oxidized 4*H*-1,2,6-thiadiazines are rare, but have uses in both the biological[8,9] and materials sciences.[10,11] Their chemistry and applications have recently been reviewed.[12] Our interest in thiadiazines is currently focused on 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine (**3**), which can be prepared from dichloromalononitrile and SCl_2,[13] or from *N*-2,2-trichloro-2-cyanoacetimidoyl chloride and S_8.[14] Thiadiazine **3** is used to synthesize aromatic 1,2,6-thiadiazines such as 2-(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)-malononitrile (**5**),[15] *N*-aryl-3,5-dichloro-4*H*-1,2,6-thiadiazin-4-imines **6**,[16] 3,5-dichloro-4*H*-1,2,6-thiadiazin-4-one (**7**),[15] and 3,5-dichloro-4*H*-1,2,6-thiadiazin-4-thione (**8**).[17] Furthermore, it can be used to prepare C(4)-saturated analogues such as 4,4-diamino-,[18] 4,4-dialkoxy-, and 4,4-bis(alkylthio)-3,5-dichloro-4*H*-1,2,6-thiadiazines **9**, **10**, and **11**, respectively[17] (Scheme 2).

Scheme 1. Conversion of Tetrachlorothiadiazine 3 to Diazepines 2 and 4



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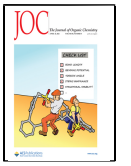

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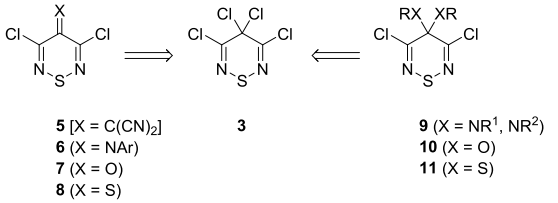
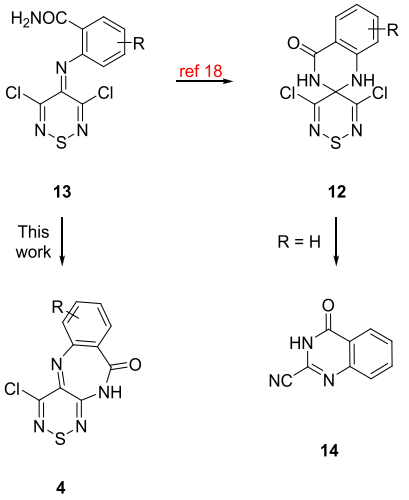
Scheme 2. Selected Transformations of Tetrachlorothiadiazine 3



RESULTS AND DISCUSSION

Recently, we described the 3-step synthesis of 3′,5′-dichloro-1*H*-spiro(quinazoline-2,4′-[1,2,6]thiadiazin)-4(3*H*)-ones **12** starting from tetrachlorothiadiazine **3** (Scheme 3).[18] The cyclization of benzamides **13** on the thiadiazine C(4) position to give spirocycles **12** was enabled by protic solvents and heat. Spirocycle **12** (R = H) can also be decomposed to quinazoline **14** (Scheme 3).[18] An alternative cyclization of benzamides **13** at the thiadiazine C(3/5) position could give the desired thiadiazino-fused benzodiazepines **4**, which are structural analogues to the thiadiazino-fused thiazolodiazepine **2** (Scheme 1). Herein, we present the formation of benzothiadiazinodiazepines **4**, via the cyclization of benzamides **13**, and related chemistry. Other routes to diazepines **4** were also investigated, but with no success [see Supporting Information (SI)].

Scheme 3. Reactions of Benzamides 13



Carboxamide **13a** (R = H) can be prepared in two steps from tetrachlorothiadiazine **3**.[18] Prior stability studies on amide **13a** revealed that acidic conditions, protic solvents, and thermal conditions induce its conversion to spirocycle **12a**.[18] An investigation of its reactivity showed that cyclization on the thiadiazine C(3) position occurred under basic conditions or in the presence of Pd catalysts (see SI for details). Two sets of conditions were promising: the first being treatment with NaH (1 equiv), in THF, at ca. 20 °C, for 15 min that gave a deep orange-colored diazepine **4a** (68%), together with a small amount of the known colorless spirocycle **12a** (2%) (Table 1); the structure of diazepine **4a** was supported by single crystal X-ray studies (Figure 2). For structure elucidation details, see the SI. The second set of conditions involved Superstable Pd(0) (1.25 mol %), DPEphos (0.05 equiv), K_2CO_3 (1.5 equiv), in

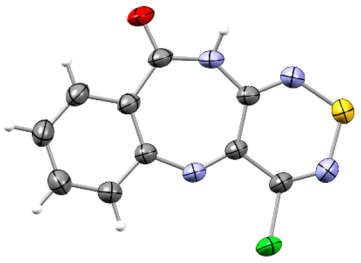
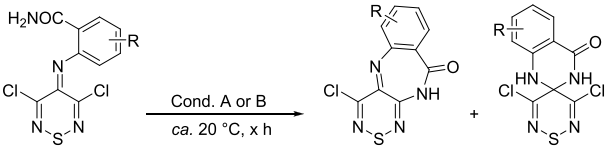


Figure 2. X-ray structure of 4-chlorobenzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-one (**4a**) (CCDC-2052542).

Table 1. Conversion of Thiadiazinimines 13a−j to Diazepines 4a−j and Spirocycles 12a−j



Conditions A: NaH (1 equiv), THF
Conditions B: Pd Superstable (1.25 mol %), DPEphos (0.05 equiv), K_2CO_3 (1.5 equiv)

		conditions A					conditions B			
entry	**13** (R)	time (h)	yield **4** (%)	yield **12** (%)	total (**4**+**12**) (%)	entry	time (h)	yield **4** (%)	yield **12** (%)	total (**4**+**12**) (%)
1	**13a** (H)	0.25	68	2	70	11	24	76	13	89
2	**13b** (4-Me)	0.25	32	10	42	12	96	32	20	52
3	**13c** (5-Me)	0.25	41	30	71	13	30	66	19	85
4	**13d** (6-Me)	24	46	0	46	14	72	67	9	76
5	**13e** (4-Cl)	0.25	44	42	86	15	24	57	34	91
6	**13f** (5-Cl)	0.75	62	31	93	16	12	74	21	95
7	**13g** (6-Cl)	0.50	65	33	98	17	48	67	19	87
8	**13h** (4-Br)	0.16	60	36	96	18	24	56	33	89
9	**13i** (5-Br)	0.16	69	28	97	19	24	62	31	93
10	**13j** (6-Br)	4	20	24	44	20	48	65	28	93

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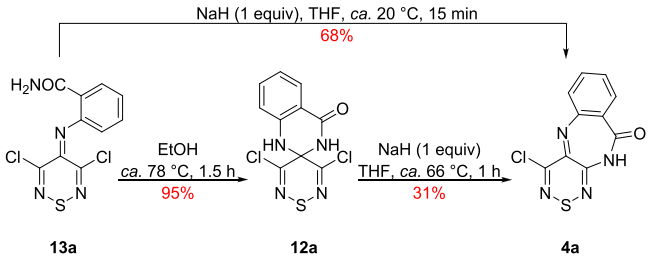
THF, at ca. 20 °C, for 24 h that gave products **4a** and **12a** in 76% and 13% yields, respectively.

Mechanistically, the formation of diazepine **4a** is attributed to a 7-endo-trig cyclization reaction, while the intriguing formation of spirocycle **12a** can be attributed to a competing 6-endo-trig cyclization. Both cyclizations are allowed according to Baldwin's rules.[19] Prior studies support that the formation of spirocycles **12** does not require the deprotonation of starting benzamides as they can be exclusively formed in the absence of base.[18] Despite considerable effort, we failed to prevent their formation during the synthesis of the diazepines **4**.

The possibility that spirocycles **12** were precursors to diazepines **4** was investigated. Treatment of spirocycle **12a** with NaH (1 equiv) in THF at ca. 20 °C led to a slow consumption of the starting material **12a** (24 h) and isolation of diazepine **4a** in 21% yield; no other products were observed. Performing the reaction at ca. 66 °C led to a faster consumption of the spirocycle **12a** (1 h) and a slightly improved yield of diazepine **4a** (31%) (Scheme 4).

Scheme 4. Investigation of the Conversion of Spirocycle 12a into Diazepine 4a



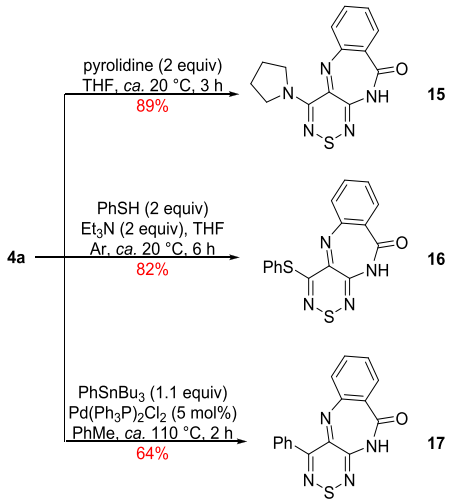
Tentatively, the formation of spirocycle **12a** was thermodynamically favored, and a higher activation energy is required to ring open the spirocycle **12a** than that needed for the cyclization of the starting benzamide **13a** to give the diazepine **4a**.

The reaction scope was then investigated (Table 1) by screening the above two sets of conditions with the known benzamides **13b–j**.[18] The three electron releasing methyl-substituted analogues **13b–d** gave moderate yields of diazepines **4b–d** (32–67%) with 5-methylbenzamide **13c** giving the higher overall yield (71% and 85%) with both sets of conditions (Table 1, entries 3 and 13). The use of conditions B improved the yields of diazepine in both the 5- and the 6-Me analogues, but no improvement was observed with the 4-Me analogue. Chloro-substituted analogues **13e–g** gave moderate yields (44–74%) of diazepines **4e–g** along with 31–42% of spirocycles **12e–g**, totaling to an almost quantitative conversion (Table 1, entries 5–7 and 15–17).

Conditions B gave marginally better yields of diazepines **4e–g** compared to conditions A. Similar results to the chloro-substituted analogues were obtained with 4- and 5-bromo analogues **13h** and **13i**, respectively. The 6-bromo analogue **13j**, however, gave a significantly lower yield (Table 1, entries 8–10 and 18–20), presumably owing to steric effects as the group next to the nucleophilic amide can hinder its ability to attack the thiadiazine C(3) position. Moreover, for 6-substituted analogues, in the case of the large Me (A_{Me} 1.70 kcal/mol),[20] and Br groups (A_{Br} 0.49 kcal/mol),[21] prolonged reaction times were observed, but not with the large Cl group (A_{Cl} 0.51 kcal/mol).[21]

After briefly investigating the reaction scope, we assessed the chemistry of the parent diazepine **4a** starting from the substitution of the C(4) chloride. Nucleophilic displacements with N-, O-, and S-nucleophiles were initially studied. Treatment of diazepine **4a** with pyrrolidine (2 equiv) in THF at ca. 20 °C for 3 h gave 4-(pyrrolidin-1-yl)benzo[*e*]-[1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-one (**15**) in 89% yield (Scheme 5). Reaction with MeONa (2 equiv), in

Scheme 5. Chloride Displacement of Diazepine 4a



MeOH, at ca. 20 °C gave only unreacted starting material, and heating to ca. 65 °C led to a complex mixture of products (TLC), while similar results were also obtained with PhONa. This can potentially be attributed to the acidity of the amide proton of diazepine **4a** that leads to deprotonation in the presence of stronger bases like alkoxides. The deprotonated anion of **4a** was expected to be less reactive due to the electron donation of the anionic nitrogen into the thiadiazine ring. Treatment of diazepine **4a** with PhSH (2 equiv) and Et_3N (2 equiv), in THF, at ca. 20 °C for 6 h led to its complete consumption and formation of phenylsulfide **16** in 82% yield (Scheme 5).

Furthermore, some Pd coupling reactions on the C(4) position were investigated. Stille coupling of diazepine **4a** with $PhSnBu_3$ (1.1 equiv), in PhMe, in the presence of Pd-$(Ph_3P)_2Cl_2$ (5 mol %), at ca. 110 °C, gave the 4-phenyl-thiadiazine **17** in a moderate 64% yield (Scheme 5). Unfortunately, Suzuki couplings were not as effective; $PhB(OH)_2$ (1.5 equiv), in dioxane/H_2O (5:3), in the presence of Na_2CO_3 (1 equiv) and $Pd(Ph_3P)_4$ (5 mol %), at ca. 100 °C gave product **17** in only 4% yield. Alternative anhydrous conditions involving $PhB(OH)_2$ (1.5 equiv), KF (1.7 equiv), 18-crown-6 (0.5 equiv), $Pd(OAc)_2$ (5 mol %), in PhMe, at ca. 110 °C,[22] led to degradation of the starting material.

Nitration of the peripheral arene ring of diazepine **4a** was also attempted to further diversify the functionality of the tricyclic ring system. Pleasingly, treatment of diazepine **4a** with KNO_3 (1 equiv) in concd H_2SO_4, at ca. 0 °C led to rapid consumption of the starting material and isolation of 4-chloro-8-nitrobenzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10-(11*H*)-one (**4k**) (see SI for structure elucidation) in 93% yield (Scheme 6).

Subsequently, we studied the methylation of the N(11) atom of the diazepine **4a**. Reaction with MeI (4 equiv), after

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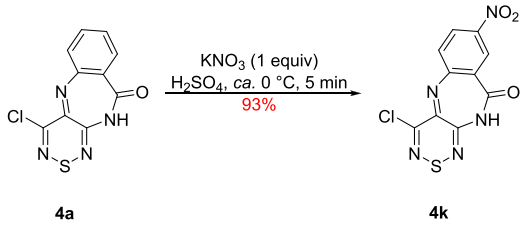
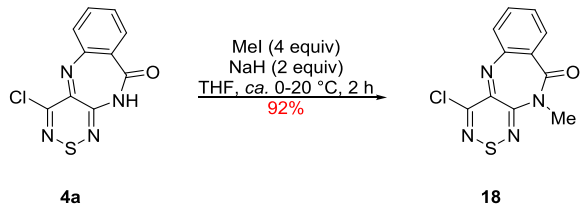
Scheme 6. Nitration of Diazepine 4a



treatment with NaH (2 equiv), in THF, at ca. 0 °C gave a high 92% yield of 4-chloro-11-methylbenzo[*e*][1,2,6]thiadiazino-[3,4-*b*][1,4]diazepin-10(11*H*)-one (**18**) (Scheme 7). The site

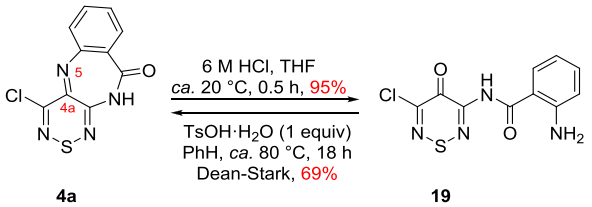
Scheme 7. *N*-Methylation of Diazepine 4a



of methylation is supported by the similarity of the ^{1}H NMR spectra and of the UV−vis absorptions of **4a** (λ_{max} 433 nm, log ε 4.05) vs **18** (λ_{max} 400 nm, log ε 4.09). Further support was provided by the ^{13}C NMR spectra, with a δ_C 166.9 for the carbonyl signal remaining typical of a carboxamide, while the δ_C 36.4 of the methyl supported its attachment to nitrogen. Interestingly, earlier efforts to prepare N-Me diazepine **18** from tetrachlorothiadiazine **3** and 2-amino-*N*-methylbenzamide gave only 3′,5′-dichloro-3-methyl-1*H*-spiro[quinazoline-2,4′-[1,2,6]thiadiazin]-4(3*H*)-one.[23]

The potential for selective ring degradations of the parent diazepine **4a** was then investigated. DSC studies of recrystallized diazepine **4a** showed a mp at 218.7 °C (onset), followed by a decomposition at 251.7 °C (onset), to give polar intractable material (baseline by TLC). In solution, diazepine **4a** was stable to mild thermal (PhCl, ca. 132 °C, 4 d) and basic conditions (Et_3N 5 equiv, THF, ca. 20 °C, 4 d). Treatment of diazepine **4a** with glacial AcOH, at ca. 20 °C, for 48 h led to no reaction, but treatment with 6 M HCl in THF, at ca. 20 °C, led to a rapid consumption (0.5 h) and formation of colorless 2-amino-*N*-(5-chloro-4-oxo-4*H*-1,2,6-thiadiazin-3-yl)benzamide (**19**) in 95% yield (Scheme 8), the structure of which was

Scheme 8. Acid Hydrolysis of Diazepine 4a



supported by X-ray crystallography (Figure 3). Presumably, benzamide **19** forms via the acid-catalyzed hydrolysis of the diazepine C(4a)═N(5) imine bond. Benzamide **19** can be cyclodehydrated to reform the diazepine **4a** in 69% yield using TsOH·H_2O (1 equiv) in hot PhH under Dean−Stark conditions (Scheme 8).

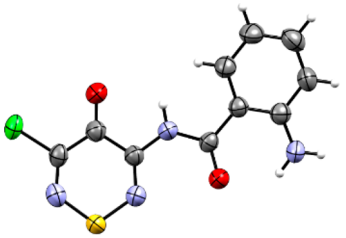
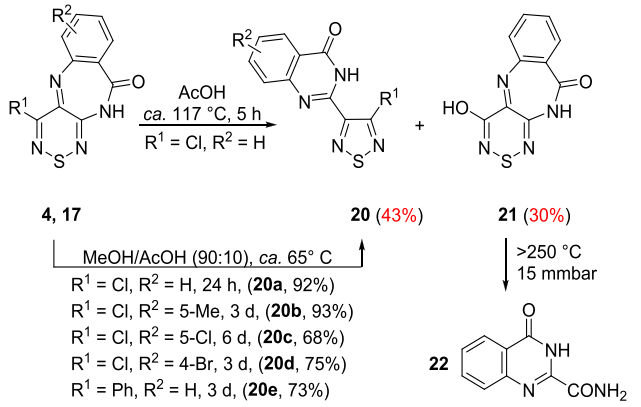


Figure 3. X-ray structure of 2-amino-*N*-(5-chloro-4-oxo-4*H*-1,2,6-thiadiazin-3-yl)benzamide (**19**) (CCDC-2052543).

Surprisingly, heating a solution of diazepine **4a** in AcOH, at ca. 117 °C, for 3 h led to complete consumption of the starting material and isolation of two unexpected products: the colorless 2-(4-chloro-1,2,5-thiadiazol-3-yl)quinazolin-4(3*H*)-one (**20a**) and the pink-colored 4-hydroxybenzo[*e*][1,2,6]-thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-one (**21**) in 43% and 30% yields, respectively (Scheme 9). The structure elucida-

Scheme 9. Conversion of Diazepines 4 into Thiadiazoles 20 and Thiadiazinol 21



tions of both products were supported by single crystal X-ray analysis (see SI). Worthy of note was that, during an attempted sublimation of thiadiazinol **21** under a static vacuum of 15 mbar at 250 °C, it decomposed to give only 4-oxo-3,4-dihydroquinazoline-2-carboxamide (**22**) (see SI). The formation of thiadiazole **20a** was optimized to a 92% yield by use of MeOH/AcOH (90:10) at ca. 65 °C for 24 h (see SI). The scope of the reaction was also briefly investigated using the optimized reaction conditions. Methyl-, chloro-, and bromo-substituted diazepines **4c**, **4f**, and **4h** were converted to thiadiazoles **20b−d** in good yields (Scheme 9). Methyl-substituted diazepine **4c** gave a 93% yield of thiadiazole **20b**, while the bromo analogue **4h** gave a 75% yield of **20d**. Interestingly, the chloro analogue **4f** gave a 68% yield of thiadiazole **20c**, albeit with a prolonged reaction time of 6 d, presumably due to the more electron withdrawing chloride slowing down the reaction. Attempts to convert the 8-nitro analogue **4k** led only to unreacted starting material. Nevertheless, the 4-phenyldiazepine **17** was successfully converted into the phenylthiadiazole **20e** in 73% yield, demonstrating that the ring transformation was not limited to 4-chloro-substituted analogues.

Ring transformations of 1,2,6-thiadiazines into 1,2,5-thiadiazoles are rare with only one example reported for some C(4) saturated systems which was mediated by heat and by Brønsted or Lewis acid catalysis.[24] Tentatively, we propose

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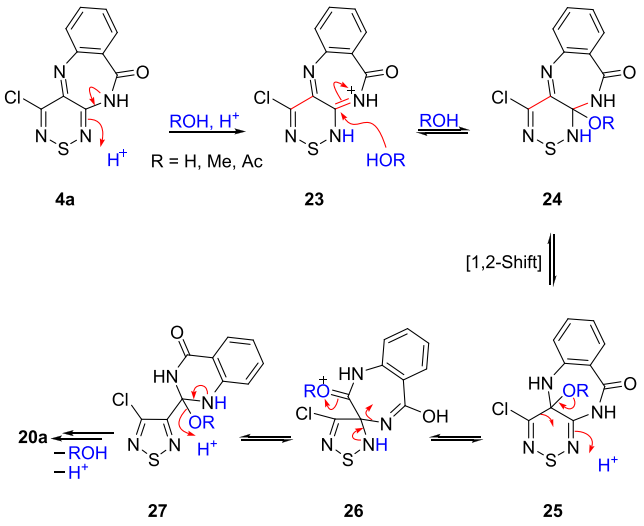
that the mechanism of the formation of thiadiazole **20a** proceeds via an initial protonation of the thiadiazine N(1), as the more basic amidine-like nitrogen site, to give the cationic thiadiazinium **23**, which is then strongly activated to trap an incoming nucleophile (ROH, where R = H, Me, or Ac) at C(11a) to give adduct **24**. A subsequent 1,2-migration of the RO group to the C(4a) position establishes an intermediate **25** that is set up to undergo two consecutive Wagner−Meerwein shifts to give intermediates **26** and then **27**, in an analogous manner to that previously reported for the ring contraction of thiadiazine ketals.[24] A final elimination of the nucleophile gives the final thiadiazole **20a** (Scheme 10).

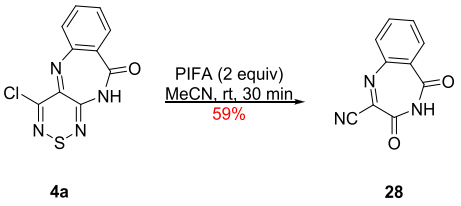
Scheme 10. Proposed Mechanism for the Formation of Thiadiazole 20a



Worthy of note is that a similar migration of methylthio groups was reported during the isomerization of trimethyl α-keto trithioorthocarboxylates into α,α-bis(methylthio) thiolcarboxylates.[25] Similar ring contractions of benzodiazepines to quinazolines have been reported,[26] but this is the only example where this rearrangement occurs on a 1,2,6-thiadiazine bearing a delicate imidoyl chloride moiety.

The stability of diazepine **4a** to reductive and oxidative conditions was also tested. Reaction of diazepine **4a** either with $NaBH_4$ (2 equiv), in MeOH, at ca. 20 °C for 3 d, or with Zn or Sn (2 equiv), in AcOH, at ca. 20 °C for 24 h, led to complete consumption of the starting compound but gave only intractable complex reaction mixtures (TLC). Treatment of diazepine **4a** with MnO_2 (10 equiv) in DCM, at ca. 20 °C, for 24 h led to no reaction, whereas reaction with MCPBA (2 equiv), in DCM, at ca. 20 °C led to a complex mixture of products. However, treatment of diazepine **4a** with PIFA (2 equiv), in MeCN, at ca. 20 °C, for 30 min led to complete consumption of the starting material and isolation of colorless 3,5-dioxo-4,5-dihydro-3*H*-benzo[*e*][1,4]diazepine-2-carbonitrile (**28**) in 59% yield (Scheme 11), the structure of which was supported by X-ray crystallography (Figure 4). The formation of diazepine **28** was attributed to hydrolytic ring cleavage of an initially formed sulfoxide (see SI for further details).

Scheme 11. Reaction of Diazepine 4a with PIFA



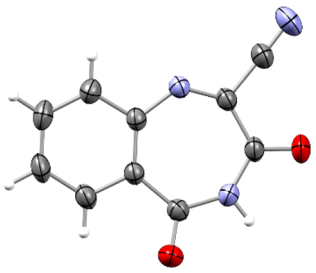


Figure 4. X-ray structure of 3,5-dioxo-4,5-dihydro-3*H*-benzo[*e*][1,4]-diazepine-2-carbonitrile (**28**) (CCDC-2052547).

CONCLUSIONS

In conclusion, we report the first synthesis of benzo[*e*]-[1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-ones **4** starting from 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)-amino]benzamides **13** via two different reactions, treatment with NaH and Pd-catalyzed C-N coupling. Preliminary investigations of the reactivity of diazepine **4a** revealed the mechanistically intriguing ring contraction to quinazoline-thiadiazole **20a** and the PIFA-mediated oxidative degradation of the thiadiazine ring to benzodiazepine **28**.

EXPERIMENTAL SECTION

General Methods and Materials. All chemicals were commercially available except those whose synthesis is described. Anhydrous Na_2SO_4 was used for drying organic extracts, and all volatiles were removed under reduced pressure. Toluene, acetonitrile, and THF were distilled over CaH_2 before use. Thiophenol was distilled before use. Reactions were protected from moisture with $CaCl_2$ drying tubes or an Ar atmosphere. All reaction mixtures and column eluents were monitored by TLC using commercial glass backed thin layer chromatography (TLC) plates (Merck Kieselgel 60 F_{254}). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography was used throughout for all non-TLC scale chromatographic separations using Merck Silica Gel 60 (less than 0.063 mm).[27] Melting points were determined using a PolyTherm-A, Wagner & Munz, Koefler - Hotstage Microscope apparatus or were determined using a TA Instruments DSC Q1000 with samples hermetically sealed in aluminum pans under an argon atmosphere, using heating rates of 5 °C/min (DSC mp listed by *onset* and *peak* values). Solvents used for recrystallization are indicated after the melting point. UV spectra were obtained using a PerkinElmer Lambda-25 UV/vis spectrophotometer, and inflections are identified by the abbreviation "inf". IR spectra were recorded on a Shimadzu FTIR-NIR Prestige-21 spectrometer with a Pike *Miracle* Ge ATR accessory, and strong, medium, and weak peaks are represented by s, m, and w, respectively. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 (at 300 and 75 MHz, respectively), or a 500 machine (at 500 and 125 MHz, respectively). Deuterated solvents were used for homonuclear lock, and the signals are referenced to the deuterated solvent peaks. APT NMR studies identified quaternary and tertiary carbons, which are indicated by (s) and (d) notations, respectively. MALDI-TOF mass spectra were recorded on a Bruker Autoflex III Smartbeam instrument, while ESI-APCI$^+$ mass spectra were recorded on a Model 6110 Quadrupole MSD, Agilent

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Technologies and ES-API spectra on a Model 1260 Infinity II Quadrupole MSD, Agilent Technologies. 3,4,4,5-Tetrachloro-4*H*-1,2,6-thiadiazine (**3**),[13] 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]benzamides **13**,[18] and 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]benzonitrile (**29**)[16] were prepared according to literature procedures.

Initial Attempts to Access Benzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]diazepines 4 (see SI for Discussion Related to Compounds 29, 30, 33, 35, and 37). *2-[(3,5-Dimorpholino-4H-1,2,6-thiadiazin-4-ylidene)amino]benzonitrile (**33**).* A solution of 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]benzonitrile (**29**) (28.3 mg, 0.10 mmol) in neat morpholine (175 μL, 2.00 mmol) was stirred at ca. 20 °C until no starting material remained (by TLC, 24 h). DCM (10 mL) was then added, and the mixture was adsorbed onto silica and chromatographed (DCM/*t*-BuOMe, 90:10) to give the *title compound* **33** (37.3 mg, 97%) as red plates, mp (hotstage) 206−207 °C (EtOH); R_f 0.50 (DCM/*t*-BuOMe, 90:10); (Anal. Calcd for $C_{18}H_{20}N_6O_2S$: C, 56.23; H, 5.24; N, 21.86. Found: C, 56.18; H, 5.39; N, 21.67); λ_{max}(DCM)/nm 248 inf (log ε 4.39), 323 (4.03), 507 (3.62); ν_{max}/cm^{-1} 2978w, 2910w and 2897w (alkyl C-H), 2220m (C≡N), 1580s, 1572s, 1526m, 1443m, 1366m, 1304w, 1273m, 1265m, 1250m, 1217w, 1138m, 1113s, 1065m, 1051w, 1007m, 964w, 939w, 876w, 866m, 851m, 835m, 831m, 793m, 762m, 748m, 743m, 737m; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.65 (dd, 1H, *J* = 7.7, 1.3 Hz), 7.45 (ddd, 1H, *J* = 8.0, 8.0, 1.4 Hz), 7.22 (ddd, 1H, *J* = 7.7, 7.7, 0.8 Hz), 6.69 (d, 1H, *J* = 8.1 Hz), 3.88 (t, 4H, *J* = 4.3 Hz), 3.69 (br s, 4H), 2.87 (br s, 8H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 152.0 (s), 147.3 (s), 137.82 (s), 137.78 (s), 132.1 (d), 132.0 (d), 125.1 (d), 119.9 (d), 117.8 (s), 105.4 (s), 66.5 (t), 65.4 (t), 46.4 (t); *m*/*z* (APCI$^+$) 385 (MH$^+$, 100%), 381 (52), 325 (34), 273 (28), 186 (43).

*(Z)-2-{[3-Chloro-5-(phenylamino)-4H-1,2,6-thiadiazin-4-ylidene]amino}benzonitrile (**35**).* To a stirred solution of 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]benzonitrile (**29**) (28.3 mg, 0.100 mmol) in THF (1 mL) at ca. 20 °C was added aniline (18 μL, 0.20 mmol). The mixture was then stirred at this temperature until no starting material remained (by TLC, 18 h). The reaction mixture was then adsorbed onto silica and chromatographed (*n*-hexane/DCM, 50:50) to give the *title compound* **35** (33.7 mg, 99%) as orange needles, mp (hotstage) 146−147 °C (*c*-hexane); R_f 0.44 (*n*-hexane/DCM, 50:50); (Anal. Calcd for $C_{16}H_{10}ClN_5S$: C, 56.56; H, 2.97; N, 20.61. Found: C, 56.68; H, 2.73; N, 20.57); λ_{max}(DCM)/nm 259 inf (log ε 4.18), 282 inf (4.24), 293 inf (4.34), 310 (4.38), 331 (4.34), 344 inf (4.26), 423 (4.20); ν_{max}/cm^{-1} 3242w (N-H), 2226m (C≡N), 1591m, 1537s, 1530s, 1497m, 1481w, 1454w, 1439m, 1329m, 1321m, 1281w, 1267w, 1248w, 1219w, 1169m, 1101w, 1030w, 1001w, 891s, 837w, 787m, 766m, 748m; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.24 (br s, 1H), 7.66−7.63 (m, 3H), 7.53 (ddd, 1H, *J* = 7.8, 7.8, 1.4 Hz), 7.39 (dd, 1H, *J* = 7.5, 7.5 Hz), 7.20−7.16 (m, 2H), 6.91 (d, 1H, *J* = 8.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 152.1 (s), 148.1 (s), 137.3 (s), 134.0 (s), 132.6 (d), 132.3 (s), 132.2 (d), 129.1 (d), 124.8 (d), 124.0 (d), 120.4 (d), 120.1 (d), 117.2 (s), 103.6 (s); *m*/*z* (ES-API$^+$) 342 (MH$^+$ + 2, 16%), 340 (MH$^+$, 38), 325 (M$^+$ − N, 100).

*Methyl 2-[(3,5-Dichloro-4H-1,2,6-thiadiazin-4-ylidene)amino]-benzoate (**30**).* To a stirred solution of 3,4,4,5-tetrachloro-4*H*-1,2,6-thiadiazine (**3**) (238 mg, 1.00 mmol) in MeCN (4 mL) at ca. 20 °C was added methyl 2-aminobenzoate (454 mg, 3.00 mmol). The mixture was then stirred at this temperature until no starting material remained (by TLC, 1 h). *t*-BuOMe (10 mL) was then added, and the precipitate was filtered and washed with *n*-hexane (5 mL). The filtrate was then adsorbed onto silica and chromatographed (*n*-hexane/DCM, 20:80) to give the *title compound* **30** (297.5 mg, 94%) as orange plates, mp (hotstage) 77−78 °C (*n*-hexane/-60 °C); R_f 0.59 (*n*-hexane/DCM, 20:80); (Anal. Calcd for $C_{11}H_7Cl_2N_3O_2S$: C, 41.79; H, 2.23; N, 13.29. Found: C, 41.87; H, 2.17; N, 13.38); λ_{max}(DCM)/nm 329 (log ε 4.30), 424 (3.10); ν_{max}/cm^{-1} 3071w (aryl C-H), 2951w (alkyl C-H), 1709s (C═O), 1620m, 1595m, 1476m, 1435m, 1300m, 1273m, 1256s, 1233m, 1206m, 1190m, 1165m, 1138m, 1084s, 1049m, 957m, 883m, 872m, 827m, 802s, 773s, 745s, 719m; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.98 (dd, 1H, *J* = 7.9, 1.3 Hz), 7.47 (ddd, 1H, *J* = 7.7, 7.7, 1.4 Hz), 7.13 (ddd, 1H, *J* = 7.6, 7.6, 1.0 Hz), 6.71 (ddd, 1H, *J* = 8.0, 0.5, 0.5 Hz), 3.81 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 166.0 (s), 149.8 (s), 134.0 (s), 132.7 (d), 130.7 (d), 123.6 (d), 118.2 (d), 117.2 (s), 52.0 (q), one C (s) resonance missing; *m*/*z* (MALDI-TOF) 318 (MH$^+$ + 2, 77%), 316 (MH$^+$, 100), 286 (34), 284 (56).

*Reaction of Methyl 2-[(3,5-Dichloro-4H-1,2,6-thiadiazin-4-ylidene)amino]benzoate (**37**) with n-Butylamine.* To a stirred solution of methyl 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)-amino]benzoate (**30**) (158 mg, 0.500 mmol) in DCM (4 mL) at ca. 20 °C was added *n*-butylamine (99 μL, 1.00 mmol). The mixture was then stirred at this temperature until no starting material remained (by TLC, 1 h). The reaction mixture was then adsorbed onto silica and chromatographed (*n*-hexane/DCM, 50:50) to give the methyl (*Z*)-2-{[3-(*n*-butylamino)-5-chloro-4*H*-1,2,6-thiadiazin-4-ylidene]-amino}benzoate (**37**) (81.5 mg, 46%) as orange plates, mp (hotstage) 63−64 °C (*n*-hexane/−40 °C); R_f 0.40 (*n*-hexane/DCM, 50:50); (Anal. Calcd for $C_{15}H_{17}ClN_4O_2S$: C, 51.06; H, 4.86; N, 15.88. Found: C, 50.88; H, 4.75; N, 15.97); λ_{max}(DCM)/nm 271 (log ε 4.02), 326 (3.85), 455 (4.05); ν_{max}/cm^{-1} 3323w and 3320w (N-H), 2957w, 2926w and 2859w (alkyl C-H), 1705s (C═O), 1611m, 1597m, 1560s, 1557s, 1454w, 1435m, 1314m, 1277m, 1250m, 1227w, 1190m, 1157m, 1138w, 1084s, 1067m, 1051w, 966w, 870m, 845m, 826m, 800m, 791m, 760m, 712s; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.96 (dd, 1H, *J* = 8.0, 1.4 Hz), 7.42 (ddd, 1H, *J* = 7.5, 7.5, 1.5 Hz), 7.19 (br s, 1H), 7.09 (ddd, 1H, *J* = 7.7, 7.7, 1.2 Hz), 6.69 (dd, 1H, *J* = 8.0, 0.9 Hz), 3.79 (s, 3H), 3.41 (q, 2H, *J* = 6.8 Hz), 1.64−1.62 (m, 2H), 1.42−1.40 (m, 2H), 0.95 (t, 3H, *J* = 7.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 166.2 (s), 151.4 (s), 151.0 (s), 132.3 (d), 130.8 (s), 130.7 (d), 122.9 (d), 119.8 (d), 118.6 (s), 51.8 (q), 41.1 (t), 31.0 (t), 20.2 (t), 13.8 (q), one C (s) resonance missing; *m*/*z* (MALDI-TOF) 355 (MH$^+$ + 2, 69%), 353 (MH$^+$, 100), 323 (41), 321 (82).

Preparation of Aryl[1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-ones (4). *4-Chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one (**4a**) (Typical Procedure A).* To a stirred solution of 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]-benzamide (**13a**) (30.1 mg, 0.100 mmol) in THF (5 mL) at ca. 20 °C was added NaH (4.0 mg, 0.10 mmol, 60% dispersion in mineral oil). The mixture was then stirred at this temperature until no starting material remained (by TLC, 15 min). Glacial AcOH (10 μL) and DCM (10 mL) were then added, and the mixture was adsorbed onto silica and chromatographed (*n*-hexane/DCM, 20:80) to give the *title compound* **4a** (18.1 mg, 68%) as orange needles, mp (hotstage) 214−215 °C (*c*-hexane); mp (DSC) onset 218.7 °C, peak max 219.6 °C, decomp. onset 251.7 °C, peak max 263.8 °C; R_f 0.44 (*n*-hexane/DCM, 20:80); (Anal. Calcd for $C_{10}H_5ClN_4OS$: C, 45.38; H, 1.90; N, 21.17. Found: C, 45.16; H, 1.82; N, 20.98); λ_{max}(DCM)/nm 247 (log ε 4.49), 282 (4.29), 292 (4.29), 323 (4.19), 355 (4.19), 433 (4.05); ν_{max}/cm^{-1} 3213w and 3159w (N-H), 3080w and 3048w (aryl C-H), 1659s (C═O), 1599m, 1570m, 1530m, 1506m, 1445m, 1431m, 1375s, 1341s, 1300w, 1211w, 1188m, 1155w, 1130m, 1092w, 972w, 937m, 899m, 872s, 826m, 777s, 745s, 735m; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.16 (dd, 1H, *J* = 7.9, 1.6 Hz), 7.74 (br s, 1H), 7.59 (ddd, 1H, *J* = 7.8, 7.8, 1.6 Hz), 7.48 (dd, 1H, *J* = 8.0, 1.2 Hz), 7.33 (ddd, 1H, *J* = 7.8, 7.8, 1.3 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 163.8 (s), 149.6 (s), 143.8 (s), 143.7 (s), 135.6 (d), 134.52 (d), 134.49 (s), 133.3 (d), 129.4 (d), 122.5 (s); *m*/*z* (MALDI-TOF) 267 (MH$^+$ + 2, 32%), 266 (M$^+$ + 2, 37), 265 (MH$^+$, 100), 248 (45), 237 (37). Further elution (DCM) gave 3′,5′-dichloro-1*H*-spiro[quinazoline-2,4′-[1,2,6]thiadiazin]-4(3*H*)-one (**12a**) (0.6 mg, 2%) as colorless needles mp (hotstage) 116−117 °C (*c*-hexane/THF) (lit.,[18] mp 116−117 °C (*c*-hexane/THF); R_f 0.13 (DCM); ^{1}H NMR (DMSO-d_6, 500 MHz) 8.99 (s, 1H), 8.26 (s, 1H), 7.61 (dd, 2H, *J* = 7.8, 1.1 Hz), 7.33 (ddd, 1H, *J* = 7.6, 7.6, 1.5 Hz), 6.73 (dd, 1H, *J* = 7.6, 7.6 Hz), 6.62 (d, 1H, *J* = 8.0 Hz), identical to an authentic sample.[18]

*4-Chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10(11H)-one (**4a**) (Typical Procedure B).* To a stirred solution of 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]benzamide (**13a**) (30.1 mg, 0.100 mmol) in THF (2 mL) at ca. 20 °C were added tris{tris[3,5-bis(trifluoromethyl)phenyl]phosphine}palladium [aka

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Superstable Pd(0)] (2.6 mg, 1.25 mol %), DPEPhos (2.7 mg, 0.0050 mmol), and K_2CO_3 (20.7 mg, 0.150 mmol). The mixture was then stirred at this temperature until no starting material remained (by TLC, 24 h). DCM (10 mL) was then added, and the mixture was adsorbed onto silica and chromatographed (*n*-hexane/DCM, 20:80) to give the *title compound* **4a** (20.2 mg, 76%) as orange needles, mp (hotstage) 214−215 °C (*c*-hexane); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.16 (dd, 1H, J = 7.9, 1.6 Hz), 7.74 (br s, 1H), 7.59 (ddd, 1H, J = 7.8, 7.8, 1.6 Hz), 7.48 (dd, 1H, J = 8.0, 1.2 Hz), 7.33 (ddd, 1H, J = 7.8, 7.8, 1.3 Hz), identical to that reported above. Further elution (DCM) gave 3′,5′-dichloro-1*H*-spiro[quinazoline-2,4′-[1,2,6]-thiadiazin]-4(3*H*)-one (**12a**) (4.0 mg, 13%) as colorless needles mp (hotstage) 116−117 °C (*c*-hexane/THF) (lit.,[18] mp 116−117 °C (*c*-hexane/THF); R_f 0.13 (DCM); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.99 (s, 1H), 8.26 (s, 1H), 7.61 (dd, 2H, J = 7.8, 1.1 Hz), 7.33 (ddd, 1H, J = 7.6, 7.6, 1.5 Hz), 6.73 (dd, 1H, J = 7.6, 7.6 Hz), 6.62 (d, 1H, J = 8.0 Hz), identical to that reported above.

Conversion of Spirocycle ***12a*** *to Diazepine* ***4a***. To a stirred solution of 3′,5′-dichloro-1*H*-spiro[quinazoline-2,4′-[1,2,6]-thiadiazin]-4(3*H*)-one (**12a**) (30.1 mg, 0.100 mmol) in THF (5 mL) at ca. 20 °C was added NaH (4.0 mg, 0.10 mmol, 60% dispersion in mineral oil), and the mixture was then stirred at ca. 66 °C using an oil bath until no starting material remained (by TLC, 1 h). Glacial AcOH (10 μL) and DCM (10 mL) were then added, and the mixture was adsorbed onto silica and chromatographed (*n*-hexane/DCM, 20:80) to give 4-chlorobenzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]-diazepin-10(11*H*)-one (**4a**) (8.2 mg, 31%) as orange needles, mp (hotstage) 214−215 °C (*c*-hexane), R_f 0.44 (*n*-hexane/DCM, 20:80); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.16 (dd, 1H, J = 7.9, 1.6 Hz), 7.74 (br s, 1H), 7.59 (ddd, 1H, J = 7.8, 7.8, 1.6 Hz), 7.48 (dd, 1H, J = 8.0, 1.2 Hz), 7.33 (ddd, 1H, J = 7.8, 7.8, 1.3 Hz); identical to that reported above.

4-Chloro-7-methylbenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one ***(4b)***. Similar treatment (procedure A) of 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]-4-methylbenzamide (**13b**) (31.5 mg, 0.100 mmol) gave after chromatography (DCM) the *title compound* **4b** (8.9 mg, 32%) as orange needles, mp (hotstage) 267−268 °C (*c*-hexane/THF); R_f 0.63 (DCM); (Anal. Calcd for $C_{11}H_7ClN_4OS$: C, 47.40; H, 2.53; N, 20.10. Found: C, 47.16; H, 2.28; N, 20.38); λ_{max}(DCM)/nm 251 (log ε 4.09), 285 (3.94), 296 (3.94), 350 (3.78), 434 (3.62); ν_{max}/cm^{-1} 3219w and 3171w (N-H), 3051w (aryl C-H), 1667s (C═O), 1605m, 1566m, 1510m, 1425w, 1383m, 1325m, 1258w, 1236w, 1194w, 937m, 895m, 876m, 841m, 833m, 756m, 739m; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.00 (s, 1H), 7.89 (d, 1H, J = 7.9 Hz), 7.19 (d, 1H, J = 8.5 Hz), 7.17 (s, 1H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 164.1 (s), 147.6 (s), 145.5 (s), 144.8 (s), 143.3 (s), 136.5 (s), 133.3 (d), 132.4 (d), 129.5 (d), 121.4 (s), 20.4 (q); m/z (MALDI-TOF) 281 (MH$^+$ + 2, 55%), 279 (MH$^+$, 87), 263 (25), 251 (13), 244 (60), 238 (56), 236 (100), 216 (26). Further elution (*n*-hexane/*t*-BuOMe, 50:50) gave 3′,5′-dichloro-7-methyl-1*H*-spiro-[quinazoline-2,4′-[1,2,6]thiadiazin]-4(3*H*)-one (**12b**) (3.2 mg, 10%) as colorless needles, mp (hotstage) 231−232 °C (*c*-hexane/THF) (lit.,[18] mp 231−232 °C (*c*-hexane/THF); R_f 0.57 (DCM/*t*-BuOMe, 90:10); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.89 (d, 1H, J = 1.2 Hz), 8.16 (d, 1H, J = 1.2 Hz), 7.49 (d, 1H, J = 7.9 Hz), 6.55 (d, 1H, J = 7.9 Hz), 6.41 (s, 1H), 2.23 (s, 3H), identical to an authentic sample.[18]

4-Chloro-8-methylbenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one ***(4c)***. Similar treatment (procedure A) of 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]-5-methylbenzamide (**13c**) (31.5 mg, 0.100 mmol) gave after chromatography (*n*-hexane/DCM, 20:80) the *title compound* **4c** (11.4 mg, 41%) as orange needles, mp (hotstage) 203−204 °C (*c*-hexane); R_f 0.42 (*n*-hexane/DCM, 20:80); (Anal. Calcd for $C_{11}H_7ClN_4OS$: C, 47.40; H, 2.53; N, 20.10. Found: C, 47.54; H, 2.26; N, 20.01); λ_{max}(DCM)/nm 254 (log ε 4.56), 285 (4.43), 294 (4.43), 323 (4.28), 359 (4.35), 436 (4.22); ν_{max}/cm^{-1} 3237w and 3190w (N-H), 1678m and 1672s (C═O), 1604m, 1562w, 1514m, 1476w, 1422m, 1371s, 1323s, 1217m, 1186m, 1136m, 1098w, 951w, 908m, 895s, 839s, 799s, 793s, 779s, 758m, 727m; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.98 (s, 1H), 7.81 (d, 1H, J = 1.8 Hz), 7.45 (dd, 1H, J = 8.1, 1.9 Hz), 7.23 (d, 1H, J = 8.0 Hz), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 164.3 (s), 147.6 (s), 144.8 (s), 141.3 (s), 138.9 (s), 135.9 (s), 135.5 (d), 133.2 (d), 132.6 (d), 123.7 (s), 20.5 (q, CH_3); m/z (APCI$^+$) 281 (MH$^+$ + 2, 35%), 279 (MH$^+$, 100), 104 (10). Further elution (DCM/*t*-BuOMe, 90:10) gave 3′,5′-dichloro-6-methyl-1*H*-spiro[quinazoline-2,4′-[1,2,6]thiadiazin]-4(3*H*)-one (**12c**) (9.5 mg, 30%) as colorless needles, mp (hotstage) 217−218 °C (*c*-hexane/THF) (lit.,[18] mp 217−218 °C (*c*-hexane/THF); R_f 0.48 (*n*-hexane/*t*-BuOMe, 50:50); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.92 (d, 1H, J = 1.6 Hz), 8.10 (d, 1H, J = 1.5 Hz), 7.41 (d, 1H, J = 1.6 Hz), 7.14 (ddd, 1H, J = 8.3, 2.2, 0.5 Hz), 6.54 (d, 1H, J = 8.2 Hz), 2.18 (s, 3H), identical to an authentic sample.[18]

4-Chloro-9-methylbenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one ***(4d)***. Similar treatment (procedure B) of 2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]-6-methylbenzamide (**13d**) (31.5 mg, 0.100 mmol) gave after chromatography (*n*-hexane/DCM, 20:80) the *title compound* **4d** (18.7 mg, 67%) as orange needles, mp (hotstage) 199−200 °C (*c*-hexane); R_f 0.80 (*n*-hexane/DCM, 20:80); (Anal. Calcd for $C_{11}H_7ClN_4OS$: C, 47.40; H, 2.53; N, 20.10. Found: C, 47.36; H, 2.39; N, 19.88); λ_{max}(DCM)/nm 247 (log ε 4.27), 281 inf (4.06), 349 (4.07), 414 (3.96); ν_{max}/cm^{-1} 3225w and 3173w (N-H), 3057w (aryl C-H), 2951w and 2936w (alkyl C-H), 1678s (C═O), 1599w, 1547w, 1520w, 1510m, 1447m, 1433m, 1427m, 1393m, 1383m, 1306m, 1281m, 1229m, 1194m, 1126m, 1078w, 1040w, 974m, 937m, 868m, 837m, 814m, 802s, 773m, 739s; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.08 (s, 1H), 7.47 (dd, 1H, J = 7.8, 7.8 Hz), 7.24 (d, 1H, d, J = 7.5 Hz), 7.12 (d, 1H, J = 7.8 Hz), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 166.6 (s), 144.4 (s), 144.0 (s), 143.7 (s), 141.1 (s), 138.6 (s), 132.3 (d), 131.8 (d), 129.1 (d), 125.6 (s), 22.1 (q); m/z (APCI$^+$) 281 (MH$^+$ + 2, 34%), 279 (MH$^+$, 100), 153 (19), 130 (93). Further elution (*n*-hexane/*t*-BuOMe, 50:50) gave 3′,5′-dichloro-5-methyl-1*H*-spiro[quinazoline-2,4′-[1,2,6]thiadiazin]-4(3*H*)-one (**12d**) (2.8 mg, 9%) as colorless needles, mp (hotstage) 228−229 °C (*c*-hexane) (lit.,[18] mp 229−230 °C (*c*-hexane); R_f 0.70 (*n*-hexane/*t*-BuOMe, 50:50); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 8.74 (d, 1H, J = 1.7 Hz), 8.13 (d, 1H, J = 1.8 Hz), 7.16 (dd, 1H, J = 7.8, 7.8 Hz), 6.51 (d, 1H, J = 7.4 Hz), 6.47 (d, 1H, J = 8.1 Hz), 2.52 (s, 3H), identical to an authentic sample.[18]

4,7-Dichlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10-(11H)-one ***(4e)***. Similar treatment (procedure A) of 4-chloro-2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]benzamide (**13e**) (33.6 mg, 0.100 mmol) gave after chromatography (*n*-hexane/DCM, 20:80) the *title compound* **4e** (13.3 mg, 44%) as orange needles, mp (hotstage) 246−247 °C (*c*-hexane); R_f 0.62 (*n*-hexane/DCM, 20:80); (Anal. Calcd for $C_{10}H_4Cl_2N_4OS$: C, 40.15; H, 1.35; N, 18.73. Found: C, 40.10; H, 1.16; N, 18.49); λ_{max}(DCM)/nm 248 (log ε 4.24), 287 (4.09), 297 (4.10), 356 (3.91), 438 (3.78); ν_{max}/cm^{-1} 3227w and 3173w (N-H), 3053w (aryl C-H), 1670s (C═O), 1576w, 1562s, 1508m, 1504m, 1468w, 1422w, 1416s, 1317m, 1304m, 1204m, 1138m, 1109w, 1078m, 934m, 897m, 874m, 808m, 749s, 712s; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.13 (s, 1H), 7.98 (d, 1H, J = 8.5 Hz), 7.43 (dd, 1H, J = 8.5, 2.2 Hz), 7.32 (d, 1H, J = 2.2 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 163.4 (s), 147.7 (s), 144.97 (s), 144.94 (s), 139.0 (s), 137.7 (s), 134.1 (d), 131.7 (d), 128.1 (d), 123.1 (s); m/z (APCI$^+$) 301 (MH$^+$ + 2, 9%), 299 (MH$^+$, 14), 219 (15), 153 (29), 130 (100). Further elution (DCM/*t*-BuOMe, 95:5) gave 3′,5′,7-trichloro-1*H*-spiro[quinazoline-2,4′-[1,2,6]thiadiazin]-4(3*H*)-one (**12e**) (14.1 mg, 42%) as colorless needles, mp (hotstage) 255−256 °C (*c*-hexane) (lit.,[18] mp 255−256 °C (*c*-hexane); R_f 0.80 (DCM/*t*-BuOMe, 95:5); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.14 (s, 1H), 8.52 (s, 1H), 7.62 (d, 1H, J = 8.3 Hz), 6.77 (dd, 1H, J = 8.4, 1.9 Hz), 6.68 (d, 1H, J = 1.9 Hz), identical to an authentic sample.[18]

4,8-Dichlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10-(11H)-one ***(4f)***. Similar treatment (procedure A) of 5-chloro-2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]benzamide (**13f**) (33.6 mg, 0.100 mmol) gave after chromatography (*n*-hexane/DCM, 50:50) the *title compound* **4f** (18.6 mg, 62%) as orange plates, mp (hotstage) 238−239 °C (*c*-hexane); R_f 0.22 (*n*-hexane/DCM, 50:50);

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(Anal. Calcd for $C_{10}H_4Cl_2N_4OS$: C, 40.15; H, 1.35; N, 18.73. Found: C, 40.10; H, 1.23; N, 18.56); λ_{max}(DCM)/nm 259 (log ε 4.19), 281 (4.05), 291 (4.02), 359 (4.03), 444 (3.88); ν_{max}/cm^{-1} 3196w and 3134w (N-H), 3042w (aryl C-H), 1649m and 1643s (C═O), 1595m, 1562m, 1535w, 1503w, 1462m, 1434m, 1433m, 1408w, 1371s, 1362s, 1215w, 1188w, 1142m, 1107w, 947m, 910m, 901m, 885m, 860m, 843m, 835s, 762m, 702s; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.17 (s, 1H), 7.91 (d, 1H, J = 2.6 Hz), 7.68 (dd, 1H, J = 8.5, 2.6 Hz), 7.32 (d, 1H, J = 8.5 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 163.1 (s), 147.8 (s), 144.8 (s), 142.6 (s), 137.0 (s), 134.9 (d), 134.5 (d), 132.6 (s), 131.4 (d), 125.8 (s); m/z (APCI$^+$) 301 (MH$^+$ + 2, 19%), 299 (MH$^+$, 25), 242 (100), 130 (15). Further elution (DCM/*t*-BuOMe, 90:10) gave 3′,5′,6-trichloro-1*H*-spiro-[quinazoline-2,4′-[1,2,6]-thiadiazin]-4(3*H*)-one (**12f**) (10.4 mg, 31%) as colorless plates, mp (hotstage) 164−165 °C (PhH/*c*-hexane) (lit.,[18] mp 164−165 °C (PhH/*c*-hexane); R_f 0.81 (DCM/*t*-BuOMe, 90:10); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.19 (s, 1H), 8.48 (s, 1H), 7.55 (d, 1H, J = 2.6 Hz), 7.37 (dd, 1H, J = 8.7, 2.6 Hz), 6.68 (d, 1H, J = 8.7 Hz), identical to an authentic sample.[18]

*4,9-Dichlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10-(11H)-one (**4g**).* Similar treatment (procedure A) of 2-chloro-6-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]benzamide (**13g**) (33.6 mg, 0.100 mmol) gave after chromatography (*n*-hexane/DCM, 50:50) the *title compound* **4g** (19.5 mg, 65%) as orange plates, mp (hotstage) 195−196 °C (*c*-hexane); R_f 0.22 (*n*-hexane/DCM, 50:50); (Anal. Calcd for $C_{10}H_4Cl_2N_4OS$: C, 40.15; H, 1.35; N, 18.73. Found: C, 39.84; H, 1.62; N, 18.67); λ_{max}(DCM)/nm 319 (log ε 4.08), 351 (4.12), 417 inf (3.76); ν_{max}/cm^{-1} 3154w (N-H), 3053w (aryl C-H), 1659s (C═O), 1599w, 1572m, 1503w, 1435w, 1377m, 1325m, 1267w, 1233w, 1198w, 1180w, 1126w, 957m, 866m, 808m, 802m, 746s; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 11.30 (s, 1H), 7.55 (dd, 1H, J = 8.0, 8.0 Hz), 7.46 (dd, 1H, J = 8.0, 1.4 Hz), 7.21 (dd, 1H, J = 7.9, 1.4 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 75 MHz): δ 164.0 (s), 145.4 (s), 144.1 (s), 143.6 (s), 140.3 (s), 133.7 (s), 133.2 (d), 130.5 (d), 129.7 (d), 125.8 (s); m/z (APCI+) 303 (MH$^+$ + 4, 16%), 301 (MH$^+$ + 2, 72), 299 (MH$^+$, 100), 154 (64), 104 (10). Further elution (*n*-hexane/*t*-BuOMe, 50:50) gave 3′,5,5′-trichloro-1*H*-spiro[quinazoline-2,4′-[1,2,6]thiadiazin]-4(3*H*)-one (**12g**) (11.2 mg, 33%) as colorless needles, mp (hotstage) 231−232 °C (*c*-hexane/THF) (lit.,[18] mp 231−232 °C (*c*-hexane/THF); R_f 0.43 (*n*-hexane/*t*-BuOMe, 50:50); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.00 (d, 1H, J = 1.7 Hz), 8.52 (d, 1H, J = 1.8 Hz), 7.27 (dd, 1H, J = 8.1, 8.1 Hz), 6.75 (dd, 1H, J = 7.9, 1.0 Hz), 6.61 (dd, 1H, J = 8.2, 1.0 Hz), identical to an authentic sample.[18]

*7-Bromo-4-chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one (**4h**).* Similar treatment (procedure A) of 4-bromo-2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]-benzamide (**13h**) (38.0 mg, 0.100 mmol) gave after chromatography (*n*-hexane/DCM, 20:80) the *title compound* **4h** (20.5 mg, 60%) as orange needles, mp (hotstage) 263−264 °C (*c*-hexane/THF); R_f 0.31 (*n*-hexane/DCM, 20:80); (Anal. Calcd for $C_{10}H_4BrClN_4OS$: C, 34.96; H, 1.17; N, 16.31. Found: C, 34.85; H, 1.09; N, 16.24); λ_{max}(DCM)/nm 238 (log ε 4.50), 284 (4.36), 295 (4.37), 362 (4.16), 463 (4.02); ν_{max}/cm^{-1} 3217w and 3167w (N-H), 3080w and 3051w (aryl C-H), 1670s (C═O), 1587w, 1557m, 1504m, 1422m, 1379s, 1315m, 1302w, 1206m, 1138m, 1072w, 943w, 872m, 814m, 746s; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 11.10 (br s, 1H), 7.89 (d, 1H, J = 8.5 Hz), 7.56 (dd, 1H, J = 8.5, 2.1 Hz), 7.46 (d, 1H, J = 2.0 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 75 MHz): δ 163.6 (s), 147.8 (s), 144.99 (s), 144.95 (s), 137.7 (s), 134.7 (d), 134.1 (d), 131.1 (d), 127.9 (s), 123.5 (s); m/z (MALDI-TOF) 345 (MH$^+$ + 2, 91%), 343 (MH$^+$, 100), 302 (42), 300 (41), 264 (10), 113 (10). Further elution (DCM/*t*-BuOMe, 90:10) gave 7-bromo-3′,5′-dichloro-1*H*-spiro[quina-zoline-2,4′-[1,2,6]thiadiazin]-4(3*H*)-one (**12h**) (13.8 mg, 36%) as colorless plates, mp (hotstage) 245−246 °C (*n*-hexane/*t*-BuOMe) (lit.,[18] mp 245−246 °C (*n*-hexane/*t*-BuOMe); R_f 0.57 (DCM/*t*-BuOMe, 90:10); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.15 (d, 1H, J = 1.3 Hz), 8.52 (d, 1H, J = 1.3 Hz), 7.54 (d, 1H, J = 8.2 Hz), 6.91 (dd, 1H, J = 8.3, 1.8 Hz), 6.82 (d, 1H, J = 1.8 Hz), identical to an authentic sample.[18]

*8-Bromo-4-chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one (**4i**).* Similar treatment (procedure A) of 5-bromo-2-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]-benzamide (**13i**) (38.0 mg, 0.100 mmol) gave after chromatography (*n*-hexane/DCM, 50:50) the *title compound* **4i** (23.8 mg, 69%) as orange needles, mp (hotstage) 193−194 °C (*c*-hexane); R_f 0.26 (*n*-hexane/DCM, 50:50); (Anal. Calcd for $C_{10}H_4BrClN_4OS$: C, 34.96; H, 1.17; N, 16.31. Found: C, 34.92; H, 1.08; N, 16.28); λ_{max}(DCM)/nm 261 (log ε 4.04), 282 inf (3.92), 291 inf (3.89), 360 (3.93), 446 (3.77); ν_{max}/cm^{-1} 3196w and 3138w (N-H), 3042w (aryl C-H), 1643s (C═O), 1591m, 1560w, 1530m, 1503w, 1433m, 1402w, 1371s, 1321s, 1213w, 1188w, 1142m, 1096m, 943m, 901m, 878m, 854m, 833s, 752m; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.16 (br s, 1H), 8.04 (d, 1H, J = 2.5 Hz), 7.80 (dd, 1H, J = 8.5, 2.5 Hz), 7.23 (d, 1H, J = 8.5 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 163.0 (s), 147.7 (s), 144.9 (s), 142.9 (s), 137.4 (d), 137.1 (s), 135.0 (d), 134.3 (d), 125.9 (s), 121.0 (s); m/z (APCI$^+$) 347 (MH$^+$ + 4, 18%), 345 (MH$^+$ + 2, 58), 343 (MH$^+$, 46), 242 (100), 130 (58). Further elution (DCM/*t*-BuOMe, 90:10) gave 6-bromo-3′,5′-dichloro-1*H*-spiro-[quinazoline-2,4′-[1,2,6]thiadiazin]-4(3H)-one (**12i**) (10.6 mg, 28%) as colorless needles, mp (hotstage) 206−207 °C ($CHCl_3$) (lit.,[18] mp 206−207 °C ($CHCl_3$); R_f 0.76 (DCM/*t*-BuOMe, 90:10); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.19 (s, 1H), 8.48 (s, 1H), 7.55 (s, 1H), 7.37 (d, 1H, J = 8.9 Hz), 6.68 (d, 1H, J = 8.8 Hz), identical to an authentic sample.[18]

*9-Bromo-4-chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one (**4j**).* Similar treatment (procedure A) of 2-bromo-6-[(3,5-dichloro-4*H*-1,2,6-thiadiazin-4-ylidene)amino]-benzamide (**13j**) (38.0 mg, 0.100 mmol) gave after chromatography (*n*-hexane/DCM, 20:80) the *title compound* **4j** (7.0 mg, 20%) as orange plates, mp (hotstage) 193−194 °C (*n*-hexane/DCM); R_f 0.31 (*n*-hexane/DCM, 20:80); (Anal. Calcd for $C_{10}H_4BrClN_4OS$: C, 34.96; H, 1.17; N, 16.31. Found: C, 35.05; H, 1.16; N, 16.48); λ_{max}(DCM)/nm 252 inf (log ε 4.04), 285 inf (3.82), 335 (3.89), 415 (3.81); ν_{max}/cm^{-1} 3152w (N-H), 3057w (aryl C-H), 1659s (C═O), 1599w, 1566m, 1558m, 1547w, 1503m, 1433m, 1377m, 1325m, 1267w, 1231w, 1196w, 1184w, 1121w, 951m, 864m, 804m, 764m, 741s, 723m; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.32 (br s, 1H), 7.64 (d, 1H, J = 7.9 Hz), 7.45 (dd, 1H, J = 8.0, 8.0 Hz), 7.23 (d, 1H, J = 7.9 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 164.8 (s), 145.4 (s), 144.0 (s), 143.6 (s), 140.3 (s), 133.9 (d), 133.4 (d), 130.2 (d), 127.6 (s), 122.5 (s); m/z (MALDI-TOF) 345 (MH$^+$ + 2, 100%), 343 (MH$^+$, 100), 310 (9), 308 (11), 302 (50), 300 (47), 264 (11), 113 (12). Further elution (*n*-hexane/*t*-BuOMe, 50:50) gave 5-bromo-3′,5′-dichloro-1*H*-spiro[quinazoline-2,4′-[1,2,6]thiadiazin]-4(3*H*)-one (**12j**) (9.2 mg, 24%) as colorless needles, mp (hotstage) 229−230 °C (*c*-hexane/THF) (lit.,[18] mp 229−230 °C (*c*-hexane/THF); R_f 0.70 (*n*-hexane/*t*-BuOMe, 50:50); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.02 (d, 1H, J = 1.5 Hz), 8.52 (d, 1H, J = 1.7 Hz), 7.17 (dd, 1H, J = 8.0, 8.0 Hz), 6.97 (d, 1H, J = 7.8 Hz), 6.65 (d, 1H, J = 8.3 Hz), identical to an authentic sample.[18]

Reactions of 4-Chlorobenzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]-diazepin-10(11*H*)-one (4a). *4-(Pyrrolidin-1-yl)benzo[e][1,2,6]-thiadiazino[3,4-b][1,4]diazepin-10(11H)-one (**15**).* To a stirred solution of 4-chlorobenzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-one (**4a**) (26.5 mg, 0.100 mmol) in THF (0.5 mL) at ca. 20 °C was added pyrrolidine (17 μL, 0.20 mmol), and the mixture was stirred at this temperature until no starting material remained (TLC, 1 h). The reaction mixture was then adsorbed onto silica and chromatographed (DCM) to give the *title compound* **15** (26.8 mg, 89%) as dark red needles, mp (hotstage) 157−158 °C (*c*-hexane); R_f 0.40 (DCM); (Anal. Calcd for $C_{14}H_{13}N_5OS$: C, 56.17; H, 4.38; N, 23.40. Found: C, 56.04; H, 4.26; N, 23.26); λ_{max}(DCM)/nm 255 inf (log ε 4.40), 288 inf (4.12), 321 (4.02), 375 (3.95), 482 (4.00); ν_{max}/cm^{-1} 3179w (N-H), 3115w and 3015w (aryl C-H), 2976w, 2916w and 2872w (alkyl C-H), 1643s (C═O), 1593w, 1551m, 1483m, 1468m, 1441m, 1412s, 1364m, 1337m, 1317m, 1292w, 1246m, 1224w, 1202w, 1148m, 1103w, 1090m, 1034w, 964w, 926m, 903m, 881m, 866m, 856m, 822m, 775m, 764m, 754s; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.10 (dd, 1H, J = 7.9, 1.6 Hz), 7.70 (br s, 1H), 7.51 (ddd,

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1H, J = 7.7, 7.7, 1.7 Hz), 7.28 (dd, 1H, J = 7.9, 1.1 Hz), 7.24 (dd, 1H, J = 7.6, 1.3 Hz), 3.72 (br s, 4H), 1.96−1.93 (m, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 166.2 (s), 150.0 (s), 145.5 (s), 137.9 (s), 137.8 (s), 134.4 (d), 132.9 (d), 131.8 (d), 127.4 (d), 123.7 (s), 49.7 (t), one C (t) resonance missing; m/z (MALDI-TOF) 299 (M^+, 88%), 298 ($M^+ - H$, 95), 281 (16), 269 (75), 257 (58), 252 (29), 230 (63), 203 (15), 69 (100).

*4-(Phenylthio)benzo[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10-(11H)-one (**16**).* To a stirred solution of 4-chlorobenzo[e][1,2,6]-thiadiazino[3,4-b][1,4]diazepin-10(11H)-one (**4a**) (26.5 mg, 0.100 mmol) in THF (1 mL) at ca. 0 °C, under an argon atmosphere, was added thiophenol (21 μL, 0.20 mmol), followed by a dropwise addition of Et_3N (28 μL, 0.20 mmol), and the mixture was stirred at this temperature for 30 min and then warmed to ca. 20 °C and stirred until no starting material remained (TLC, 6 h). The reaction mixture was then adsorbed onto silica and chromatographed (n-hexane/DCM, 20:80) to give the *title compound* **16** (27.7 mg, 82%) as red needles, mp (hotstage) 247−248 °C (c-hexane/DCE); R_f 0.38 (n-hexane/DCM, 20:80); (Anal. Calcd for $C_{16}H_{10}N_4OS_2$: C, 56.79; H, 2.98; N, 16.56. Found: C, 56.95; H, 2.73; N, 16.36); λ_{max}(DCM)/nm 261 (log ε 4.16), 344 (3.82), 367 inf (3.81), 456 (3.72); ν_{max}/cm^{-1} 3196w (N-H), 3115w and 3030w (aryl C-H), 1659m and 1645s (C═O), 1597m, 1566m, 1557m, 1483m, 1466m, 1441m, 1423m, 1381m, 1348m, 1215w, 1177w, 1134m, 1022w, 937w, 887w, 874m, 830w, 779w, 770w, 760m, 746s, 739m; ^1H NMR (DMSO-d_6, 500 MHz): δ 10.86 (s, 1H), 8.02 (dd, 1H, J = 8.4, 1.8 Hz), 7.63 (ddd, 1H, J = 7.6, 7.6, 1.6 Hz), 7.54−7.51 (m, 2H), 7.47−7.46 (m, 3H), 7.36−7.33 (m, 2H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz): δ 163.8 (s), 162.3 (s), 144.0 (s), 142.0 (s), 135.7 (s), 135.4 (d), 135.0 (d), 132.8 (d), 132.6 (d), 129.6 (s), 129.4 (d), 129.3 (d), 128.4 (d), 124.2 (s); m/z (MALDI-TOF) 338 (M^+, 100%), 261 (36), 229 (16), 194 (11), 142 (29).

*4-Phenylbenzo[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10(11H)-one (**17**).* To a stirred solution of 4-chlorobenzo[e][1,2,6]thiadiazino-[3,4-b][1,4]diazepin-10(11H)-one (**4a**) (52.9 mg, 0.200 mmol) in PhMe (1 mL) at ca. 20 °C were added tributylphenylstannane (80.8 mg, 0.220 mmol) and $Pd(Ph_3P)_2Cl_2$ (7.0 mg, 5 mol %). The solution was then deaerated by bubbling into the reaction mixture Ar gas for 10 min. The reaction mixture was then heated at ca. 110 °C using an oil bath, under Ar, until no starting material remained (TLC, 2 h). The reaction mixture was then cooled to ca. 20 °C, t-BuOMe (10 mL) added, and the organic phase was washed with saturated aqueous KF (10 mL), then dried (Na_2SO_4), adsorbed onto silica, and chromatographed (n-hexane/DCM, 80:20) to give the *title compound* **17** (39.0 mg, 64%) as orange needles, mp (hotstage) 172−173 °C (c-hexane); R_f 0.45 (n-hexane/DCM, 20:80); (Anal. Calcd for $C_{16}H_{10}N_4OS$: C, 62.73; H, 3.29; N, 18.29. Found: C, 62.68; H, 3.32; N, 18.14); λ_{max}(DCM)/nm 256 inf (log ε 4.53), 289 inf (4.32), 372 (4.24); ν_{max}/cm^{-1} 3215w (N-H), 3130w and 3042w (aryl C-H), 1672s and 1667s (C═O), 1597w, 1572m, 1558m, 1535m, 1439m, 1377m, 1350s, 1292m, 1250m, 1188w, 1148m, 1121w, 1096w, 959w, 872m, 831m, 785m, 779m, 766m, 748m, 733s, 712m; ^1H NMR (DMSO-d_6, 500 MHz): δ 11.17 (s, 1H), 7.96 (dd, 1H, J = 7.9, 1.6 Hz), 7.94 (dd, 2H, J = 7.8, 1.4 Hz), 7.58 (ddd, 1H, J = 7.7, 7.7, 1.6 Hz), 7.47−7.40 (m, 3H), 7.36 (ddd, 1H, J = 7.9, 7.9, 1.1 Hz), 7.09 (dd, 1H, J = 7.8, 0.8 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 165.8 (s), 157.5 (s), 144.9 (s), 143.0 (s), 139.2 (s), 135.5 (s), 134.9 (d), 133.0 (d), 132.9 (d), 130.2 (d), 128.7 (d), 128.2 (d), 127.9 (d), 123.1 (s); m/z (APCI$^+$) 307 (MH^+, 100%), 153 (15), 130 (46).

*Nitration of 4-Chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one (**4a**).* To a stirred sample of 4-chlorobenzo-[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10(11H)-one (**4a**) (53.0 mg, 0.200 mmol) was added concentrated H_2SO_4 (1 mL), and the mixture was cooled to ca. 0 °C with a water-ice bath. Then, KNO_3 (20.2 mg, 0.200 mmol) was added in one portion and the mixture stirred at this temperature until complete consumption of the starting material (TLC, 5 min). The mixture was then poured onto crushed ice, and the orange precipitate that formed was filtered, washed with H_2O (2 × 10 mL), and dried under vacuum to give *4-chloro-8-nitrobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10(11H)-one (**4k**)* (48.3 mg). The filtrate was then extracted with t-BuOMe (2 × 10 mL), dried over Na_2SO_4, and evaporated to give a further 9.3 mg (total of 57.6 mg, 93%) of **4k** as orange plates, mp (hotstage) 217−218 °C (c-hexane/THF); R_f 0.50 (DCM); (Anal. Calcd for $C_{10}H_4ClN_5O_3S$: C, 38.78; H, 1.30; N, 22.61. Found: C, 38.96; H, 1.44; N, 22.38); λ_{max}(DCM)/nm 247 inf (log ε 4.37), 296 (4.26), 313 inf (4.17), 367 (4.17), 468 (4.20); ν_{max}/cm^{-1} 3235w, 3150w and 3123w (N-H), 1661s, 1612m, 1580m, 1563m, 1518m (NO_2), 1495m, 1460w, 1429m, 1379m, 1337s (NO_2), 1244w, 1217w, 1142m, 1126m, 1074m, 961w, 930w, 897m, 816s, 746m; ^1H NMR (DMSO-d_6, 300 MHz): δ 11.38 (br s, 1H), 8.65 (d, 1H, J = 2.8 Hz), 8.36 (dd, 1H, J = 8.8, 2.8 Hz), 7.49 (d, 1H, J = 8.8 Hz); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 75 MHz): δ 162.7 (s), 149.0 (s), 148.4 (s), 145.6 (s), 145.4 (s), 138.9 (s), 134.4 (d), 129.1 (d), 127.4 (d), 125.2 (s); m/z (MALDI-TOF) 312 (MH^+ + 2, 56%), 310 (MH^+, 100), 265 ($MH^+ - NO_2$, 66), 264 ($M^+ - NO_2$, 36), 263 ($M^+ - NS$, 13).

*4-Chloro-11-methylbenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one (**18**).* To a stirred solution of 4-chlorobenzo-[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10(11H)-one (**4a**) (26.5 mg, 0.100 mmol) in THF (2 mL) cooled to ca. 0 °C via a water/ice bath was added NaH (8.0 mg, 0.20 mmol, 60% dispersion in mineral oil), and the mixture was stirred for 5 min. CH_3I (25 μL, 0.40 mmol) was then added, and the mixture warmed to ca. 20 °C over 30 min and stirred for an additional 1.5 h. The mixture was then adsorbed onto silica and chromatographed (n-hexane/DCM, 30:70) to give the *title compound* **18** (25.6 mg, 92%) as yellow needles, mp (hotstage) 97−98 °C (n-pentane/t-BuOMe/-40 °C); R_f 0.67 (n-hexane/DCM, 30:70); (Anal. Calcd for $C_{11}H_7ClN_4OS$: C, 47.40; H, 2.53; N, 20.10. Found: C, 47.51; H, 2.47; N, 19.95); λ_{max}(DCM)/nm 248 (log ε 4.54), 278 inf (4.25), 352 (4.24), 400 inf (4.09); ν_{max}/cm^{-1} 3065w (aryl C-H), 2957w, 2926w and 2868w (alkyl C-H), 1721m, 1665m, 1659m, 1605m, 1580m, 1493m, 1454m, 1414w, 1346m, 1323s, 1263m, 1217m, 1180w, 1107m, 1086m, 1054m, 1020w, 991m, 893m, 845m, 777m, 754s, 723m; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.06 (dd, 1H, J = 7.9, 1.4 Hz), 7.58 (ddd, 1H, J = 7.8, 7.8, 1.6 Hz), 7.41 (d, 1H, J = 7.9 Hz), 7.36 (dd, 1H, J = 7.7, 7.7 Hz), 3.43 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 166.9 (s), 144.3 (s), 144.2 (s), 143.6 (s), 139.6 (s), 134.0 (d), 133.3 (d), 131.6 (d), 128.9 (d), 126.4 (s), 36.4 (q, CH_3N); m/z (APCI$^+$) 281 (MH^+ + 2, 30%), 279 (MH^+, 100), 236 (25).

*2-Amino-N-(5-chloro-4-oxo-4H-1,2,6-thiadiazin-3-yl)benzamide (**19**).* To a stirred solution of 4-chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]diazepin-10(11H)-one (**4a**) (26.5 mg, 0.100 mmol) in THF (1 mL) at ca. 20 °C was added 6 M aqueous HCl (1 mL), and the solution was stirred at this temperature until no starting material remained (TLC, 30 min). DCM (10 mL) and saturated aqueous Na_2CO_3 (10 mL) were added and the phases separated. The aqueous phase was extracted with DCM (2 × 10 mL), and the combined organic phase was dried (Na_2SO_4), adsorbed onto silica, and chromatographed (DCM) to give the *title compound* **19** (26.9 mg, 95%) as yellow plates, mp (hotstage) 170−171 °C (c-hexane); R_f 0.81 (DCM); (Anal. Calcd for $C_{10}H_7ClN_4O_2S$: C, 42.49; H, 2.50; N, 19.82. Found: C, 42.55; H, 2.46; N, 19.91); λ_{max}(DCM)/nm 303 (log ε 3.86), 314 inf (3.84), 358 (3.99); ν_{max}/cm^{-1} 3466w, 3449w, 3364w and 3333w (N-H), 1682m, 1640m, 1632m, 1612m, 1585m, 1557m, 1493s, 1477s, 1323w, 1223s, 1198m, 1165m, 1059m, 1047m, 999w, 897m, 853w, 799w, 783m, 746m, 729m; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.98 (s, 1H), 7.52 (dd, 1H, J = 8.3, 1.3 Hz), 7.33 (ddd, 1H, J = 7.2, 7.2, 1.4 Hz), 7.75−6.72 (m, 2H), 5.90 (br s, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 165.7 (s), 156.3 (s), 150.9 (s), 148.2 (s), 146.1 (s), 134.8 (d), 127.6 (d), 118.0 (d), 116.9 (d), 112.3 (s); m/z (MALDI-TOF) 284 (M^+ + 2, 33%), 282 (M^+, 100), 120 (16).

*Cyclodehydration of Carboxamide **19** to Diazepine **4a**.* To a stirred solution of 2-amino-*N*-(5-chloro-4-oxo-4*H*-1,2,6-thiadiazin-3-yl)benzamide (**19**) (28.3 mg, 0.100 mmol) in PhH (20 mL) at ca. 20 °C was added $TsOH{\cdot}H_2O$ (19 mg, 0.10 mmol), and the mixture was then stirred at ca. 80 °C using an oil bath under a Dean−Stark condenser until no starting material remained (by TLC, 18 h). The mixture was adsorbed onto silica and chromatographed (n-hexane/DCM, 20:80) to give 4-chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-

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diazepin-10(11*H*)-one (**4a**) (18.3 mg, 69%) as orange needles, mp (hotstage) 214−215 °C (*c*-hexane), R_f 0.44 (*n*-hexane/DCM, 20:80); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.16 (dd, 1H, J = 7.9, 1.6 Hz), 7.74 (br s, 1H), 7.59 (ddd, 1H, J = 7.8, 7.8, 1.6 Hz), 7.48 (dd, 1H, J = 8.0, 1.2 Hz), 7.33 (ddd, 1H, J = 7.8, 7.8, 1.3 Hz); identical to that reported above.

*Reaction of 4-Chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one (**4a**) with AcOH.* A stirred solution of 4-chlorobenzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]-diazepin-10(11*H*)-one (**4a**) (26.5 mg, 0.100 mmol) in glacial AcOH (1 mL) was heated to ca. 117 °C using an oil bath, until no starting material remained (TLC, 3 h). The reaction mixture was left to cool to ca. 20 °C, and *n*-hexane (5 mL) was added, which led to the precipitation of a pink solid. The solid was filtered, washed with *n*-hexane (5 mL), and dried under vacuum to give 4-hydroxybenzo[*e*][1,2,6]thiadiazino[3,4-*b*]-[1,4]diazepin-10(11*H*)-one (**21**) (7.4 mg, 30%) as red needles, mp (hotstage) 263 °C (decomp., AcOH/Et_2O); mp (DSC) decomp. onset 290.4 °C, peak max 294.7 °C; R_f 0.26 (DCM/*t*-BuOMe, 90:10); (Anal. Calcd for $C_{10}H_6N_4O_2S$: C, 48.78; H, 2.46; N, 22.75. Found: C, 48.99; H, 2.31; N, 22.66); λ_{max}(DCM)/nm 274 (log ε 4.11), 390 (3.72), 492 inf (4.02), 524 (4.18), 558 (4.12); ν_{max}/cm^{-1} 3150w and 3113w (N-H), 3053w and 3042w (aryl C-H), 1657m and 1651m (C═O), 1607m, 1593m, 1574m, 1549m, 1491s, 1441w, 1408w, 1358m, 1335m, 1314w, 1292w, 1263m, 1182w, 1169m, 1117w, 1098w, 1063w, 968m, 955w, 872w, 833m, 802w, 777m, 745s; ^{1}H NMR (CF_3CO_2D, 500 MHz): δ 8.23 (d, 1H, J = 7.9 Hz), 7.67 (dd, 1H, J = 7.5, 7.5 Hz), 7.42 (dd, 1H, J = 7.7, 7.7 Hz), 7.31 (d, 1H, J = 7.9 Hz), NH and OH deuterium exchanged; ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 163.5 (s), 159.7 (s), 140.2 (s), 139.7 (s), 134.9 (d), 133.3 (d), 131.7 (s), 124.8 (d), 122.9 (d), 120.5 (s); m/z (MALDI-TOF) 247 (MH$^+$, 100%), 204 (8). Attempted sublimation of hydroxydiazepine **21** under a static vacuum (15 mbar, 250 °C) gave 4-oxo-3,4-dihydroquinazoline-2-carboxamide (**22**) as colorless plates, mp (hotstage) 228−229 °C (lit.,[28] mp 231−233 °C), ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.02 (br s, 1H), 8.37 (br s, 1H), 8.17 (d, 1H, J = 7.3 Hz), 8.08 (br s, 1H), 7.88 (dd, 1H, J = 6.7, 6.7 Hz), 7.77 (d, 1H, J = 7.9 Hz), 7.61 (dd, 1H, J = 7.9, 7.9 Hz), identical to the one reported.[28] The filtrate was then adsorbed onto silica and chromatographed (DCM) to give 2-(4-chloro-1,2,5-thiadiazol-3-yl)quinazolin-4(3*H*)-one (**20a**) (11.4 mg, 43%) as colorless needles, mp (hotstage) 253−254 °C (DCE); R_f 0.35 (DCM); (found: C, 45.23; H, 1.84; N, 20.98. $C_{10}H_5ClN_4OS$ requires C, 45.38; H, 1.90; N, 21.17%); λ_{max}(DCM)/nm 254 (log ε 4.14), 298 inf (4.17), 308 (4.29), 321 (4.28), 332 (4.25), 346 inf (4.00); ν_{max}/cm^{-1} 3231w (N-H), 1682s (C═O), 1601m, 1493w, 1468w, 1441w, 1377w, 1331w, 1315w, 1244w, 1175w, 1134m, 1049w, 1022w, 932m, 881w, 829w, 804m, 775s; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.8 (br s, 1H), 8.21 (dd, 1H, J = 8.0, 1.3 Hz), 7.91 (ddd, 1H, J = 7.3, 7.3, 1.5 Hz), 7.80 (d, 1H, J = 8.0 Hz), 7.65 (ddd, 1H, J = 7.5, 7.5, 1.0 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 161.1 (s), 150.3 (s), 147.6 (s), 145.0 (s), 144.3 (s), 135.0 (d), 128.2 (d), 127.9 (d), 126.1 (d), 122.0 (s); m/z (MALDI-TOF) 267 (MH$^+$ + 2, 75%), 266 (MH$^+$ + 1, 25), 265 (MH$^+$, 91), 245 (100), 192 (28), 150 (13), 120 (10).

*Reaction of 4-Chlorobenzo[e][1,2,6]thiadiazino[3,4-b][1,4]-diazepin-10(11H)-one (**4a**) with MeOH/AcOH 90:10 (Table S3, Entry 10) (Typical Procedure C).* To a stirred mixture of MeOH (0.9 mL) and glacial AcOH (100 μL) at ca. 20 °C was added 4-chlorobenzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-one (**4a**) (26.5 mg, 0.100 mmol), and the mixture was heated to ca. 65 °C until no starting material remained (TLC, 24 h). The reaction mixture was left to cool to ca. 20 °C, then filtered, and the solid was washed with MeOH (5 mL) and dried under vacuum to give 2-(4-chloro-1,2,5-thiadiazol-3-yl)quinazo-lin-4(3*H*)-one (**20a**) (24.4 mg, 92%) as colorless needles, mp (hotstage) 253−254 °C (DCE); R_f 0.35 (DCM); ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.8 (br s, 1H), 8.21 (dd, 1H, J = 8.0, 1.3 Hz), 7.91 (ddd, 1H, J = 7.3, 7.3, 1.5 Hz), 7.80 (d, 1H, J = 8.0 Hz), 7.65 (ddd, 1H, J = 7.5, 7.5, 1.0 Hz); identical to that reported above.

*2-(4-Chloro-1,2,5-thiadiazol-3-yl)-6-methylquinazolin-4(3H)-one (**20b**).* Similar treatment (procedure C) of 4-chloro-8-methylbenzo[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-one (27.9 mg, 0.100 mmol) gave after 3 d the *title compound* **20b** (25.9 mg, 93%) as colorless needles, mp (hotstage) 216−217 °C (MeOH); R_f 0.19 (DCM); (Anal. Calcd for $C_{11}H_7ClN_4OS$: C, 47.40; H, 2.53; N, 20.10. Found: C, 47.23; H, 2.39; N, 19.98); λ_{max}(DCM)/nm 258 (log ε 3.97), 303 inf (3.97), 316 (4.11), 328 (4.10), 339 (4.10), 355 inf (3.85); ν_{max}/cm^{-1} 3267w and 3237w (N-H), 2928w (C-H), 1676s, 1624m, 1605m, 1487m, 1441m, 1371w, 1337w, 1288w, 1250w, 1179w, 1140w, 1101w, 1094w, 1051w, 934m, 909m, 831m, 799m, 782m, 773m; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.00 (br s, 1H), 8.15 (s, 1H), 7.82 (d, 1H, J = 8.3 Hz), 7.66 (d, 1H, J = 7.9 Hz), 2.54 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 75 MHz): δ 161.1 (s), 150.4 (s), 145.6 (s), 144.3 (s), 144.2 (s), 138.3 (s), 136.3 (d), 127.8 (d), 125.5 (d), 121.7 (s), 21.0 (q); m/z (MALDI-TOF) 281 (MH$^+$ + 2, 60%), 279 (MH$^+$, 100).

*6-Chloro-2-(4-chloro-1,2,5-thiadiazol-3-yl)quinazolin-4(3H)-one (**20c**).* Similar treatment (procedure C) of 4,8-dichlorobenzo[*e*]-[1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-one (29.9 mg, 0.100 mmol) with MeOH (4.5 mL) and glacial AcOH (0.50 mL) gave after 6 d the *title compound* **20c** (20.4 mg, 68%) as colorless needles, mp (hotstage) 240−241 °C (MeOH); R_f 0.35 (DCM); (Anal. Calcd for $C_{10}H_4Cl_2N_4OS$: C, 40.15; H, 1.35; N, 18.73. Found: C, 39.76; H, 1.68; N, 18.62); λ_{max}(DCM)/nm 254 (log ε 4.19), 302 inf (4.30), 315 (4.44), 325 inf (4.41), 338 (4.39), 354 inf (4.11); ν_{max}/cm^{-1} 3267w (N-H), 2951w, 2924w and 2853w (C-H), 1686s, 1611m, 1601m, 1485m, 1470m, 1433m, 1416m, 1371w, 1327m, 1306w, 1277m, 1244w, 1225w, 1173w, 1136m, 1111w, 1094w, 1069w, 1047w, 932m, 887m, 839m, 793m, 766m, 746m; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 13.02 (br s, 1H), 8.14 (d, 1H, J = 2.4 Hz), 7.93 (dd, 1H, J = 8.7, 2.5 Hz), 7.82 (d, 1H, J = 8.7 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 160.3 (s), 150.1 (s), 146.4 (s), 145.5 (s), 144.4 (s), 135.1 (d), 132.5 (s), 130.1 (d), 125.2 (d), 123.3 (s); m/z (MALDI-TOF) 301 (MH$^+$ + 2, 63%), 299 (MH$^+$, 100).

*7-Bromo-2-(4-chloro-1,2,5-thiadiazol-3-yl)quinazolin-4(3H)-one (**20d**).* Similar treatment (procedure C) of 7-bromo-4-chlorobenzo-[*e*][1,2,6]thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-one (34.4 mg, 0.100 mmol) with MeOH (4.5 mL) and glacial AcOH (0.50 mL) gave after 3 d the *title compound* **20d** (25.9 mg, 75%) as colorless needles, mp (hotstage) 241−242 °C (DCE); R_f 0.22 (DCM); (Anal. Calcd for $C_{10}H_4BrClN_4OS$: C, 34.96; H, 1.17; N, 16.31. Found: C, 35.13; H, 1.13; N, 16.44); λ_{max}(DCM)/nm 244 (log ε 4.49), 257 (4.31), 317 (4.28), 331 inf (4.21), 346 inf (3.92); ν_{max}/cm^{-1} 3284w (N-H), 3080w and 3032w (C-H), 1672s, 1595m, 1557w, 1497w, 1454w, 1435m, 1416w, 1371w, 1327w, 1296w, 1252w, 1177m, 1138m, 1063w, 1047w, 930m, 901m, 887m, 880m, 866m, 858m, 845m, 785m; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.96 (br s, 1H), 8.11 (d, 1H, J = 8.5 Hz), 8.00 (d, 1H, J = 1.9 Hz), 7.80 (dd, 1H, J = 8.5, 1.9 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 160.9 (s), 150.1 (s), 148.8 (s), 146.4 (s), 144.5 (s), 131.1 (d), 130.0 (d), 125.5 (s), 128.2 (d), 121.2 (s); m/z (MALDI-TOF) 347 (MH$^+$ + 4, 12%), 345 (MH$^+$ + 2, 100), 343 (H$^+$, 73).

*2-(4-Phenyl-1,2,5-thiadiazol-3-yl)quinazolin-4(3H)-one (**20e**).* Similar treatment (procedure C) of 4-phenylbenzo[*e*][1,2,6]-thiadiazino[3,4-*b*][1,4]diazepin-10(11*H*)-one (30.6 mg, 0.100 mmol) gave after 3 d the *title compound* **20e** (22.3 mg, 73%) as colorless plates, mp (hotstage) 176−177 °C (*c*-hexane); R_f 0.67 (DCM/*t*-BuOMe, 90:10); (Anal. Calcd for $C_{16}H_{10}N_4OS$: C, 62.73; H, 3.29; N, 18.29. Found: C, 62.84; H, 3.12; N, 18.15); λ_{max}(DCM)/nm 250 inf (log ε 4.20), 299 inf (4.07), 315 (4.17), 320 (4.13), 332 (4.12), 348 inf (3.88); ν_{max}/cm^{-1} 3204w (N-H), 1688m, 1676s, 1603m, 1562w, 1485w, 1468m, 1445m, 1335w, 1317w, 1306w, 1238w, 1144m, 926m, 897w, 747w, 797s, 754m, 745m, 729m; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.16 (br s, 1H), 8.32 (d, 1H, J = 7.8 Hz), 7.84 (d, 2H, J = 7.2 Hz), 7.73 (dd, 1H, J = 7.0, 7.0 Hz), 7.55−7.48 (m, 5H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 162.7 (s), 161.2 (s), 150.9 (s), 147.8 (s), 144.5 (s), 134.9 (d), 132.6 (s), 130.3 (d), 129.9 (d), 128.6 (d), 128.2 (d), 127.8 (d), 126.7 (d), 122.2 (s); m/z (MALDI-TOF) 308 (MH$^+$ + 1, 16%), 307 (MH$^+$, 100).

*3,5-Dioxo-4,5-dihydro-3H-benzo[e][1,4]diazepine-2-carbonitrile (**28**).* To a stirred solution of 4-chlorobenzo[*e*][1,2,6]thiadiazino[3,4-

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b][1,4]diazepin-10(11*H*)-one (**4a**) (26.5 mg, 0.100 mmol) in MeCN (1 mL) at ca. 20 °C was added phenyliodine bis(trifluoroacetate) (PIFA) (86 mg, 0.200 mmol), and the mixture was stirred at this temperature until no starting material remained (TLC, 30 min). The reaction mixture was then adsorbed onto silica and chromatographed (DCM) to give the *title compound* **28** (11.8 mg, 59%) as colorless needles, mp (hotstage) 221−222 °C (*c*-hexane/DCE); R_f 0.23 (DCM); (Anal. Calcd for $C_{10}H_5N_3O_2$: C, 60.31; H, 2.53; N, 21.10. Found: C, 60.54; H, 2.62; N, 20.87); λ_{max}(DCM)/nm 260 inf (log ε 3.36), 324 (3.42), 375 inf (2.73); ν_{max}/cm^{-1} 3223w (N-H), 3111w (aryl C-H), 2247w (C≡N), 1678s (C═O), 1620w, 1578w, 1562w, 1387m, 1323m, 1252m, 1211w, 1163w, 1134m, 1105w, 986w, 824m, 797m, 783m; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.18 (br s, 1H), 8.25 (dd, 1H, J = 7.9, 1.5 Hz), 7.90 (ddd, 1H, J = 7.7, 7.7, 1.6 Hz), 7.81 (dd, 1H, J = 7.8, 1.4 Hz), 7.78 (ddd, 1H, J = 7.8, 7.8, 1.4 Hz); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 163.2 (s), 157.1 (s), 141.1 (s), 137.3 (s), 135.2 (d), 134.9 (d), 133.1 (d), 132.5 (d), 127.3 (s), 115.7 (s, C≡N); *m*/*z* (MALDI-TOF) 222 (M + Na$^+$, 100%), 200 (MH$^+$, 21), 130 (10).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00206.

Initial investigations leading to compounds **30**, **33**, **35**, and **37**, optimization experiments, mechanistic rationale, structure elucidation, X-ray crystallography studies, and NMR spectra (PDF)

Accession Codes

CCDC 2052542−2052547 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

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