DOI: 10.1002/ejoc.200701131

Synthesis of Diazaheterocyclic Ring-Fused 1,2,4-Benzothiadiazine 1,1-Dioxides by a Sequential Aza-Wittig/NH-Addition Cyclization/Nucleophilic Ring-Closure Methodology with *N*-Alkenyl-2-carbodiimidobenzenesulfonamides as Key Intermediates

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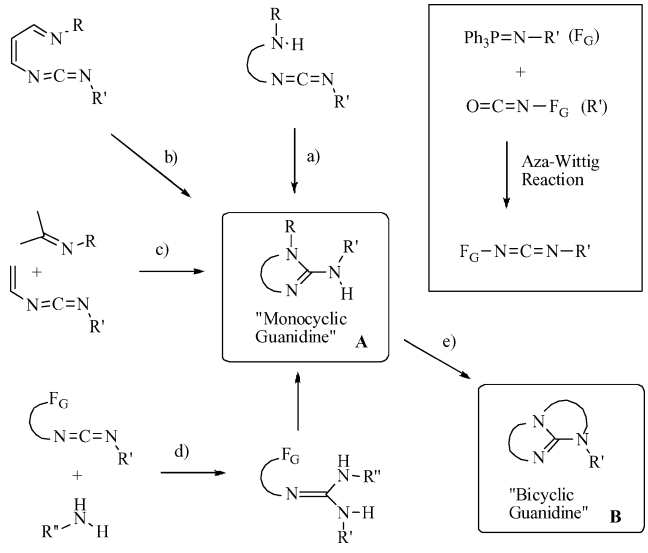
Keywords: Tandem reactions / Carbodiimides / Nitrogen heterocycles / Fused-ring systems / 1,2,4-Benzothiadiazine 1,1-dioxides

Treatment of *N*-alkenyl-2-azidobenzenesulfonamides with triphenylphosphane and subsequent subjection of the resulting iminophosphoranes to aza-Wittig reactions with isocyanates generated functionalized carbodiimides, which spontaneously underwent cyclization to form 2-alkenyl-3-(R^2-substituted amino)-2*H*-1,2,4-benzothiadiazine 1,1-dioxides by internal nucleophilic addition. Subsequent (tandem) cyclizations through iodoamination or hydroamination with $Hg^{II}/NaBH_4$ produced a variety of diazaheterocyclic ring-fused benzothiadiazine dioxides. In one case a methano-bridged benzothiatriazabicyclotridecanone was obtained. The scope and limitations of these cyclizations are reported.

Introduction

Cyclic guanidine moieties are found in a variety of biologically active natural compounds, such as marine alkaloids.[1] One of the most convenient synthetic methods for cyclic guanidines would be nucleophilic addition of a nitrogen species to a functionalized carbodiimide. Many groups (Molina,[2] Wamhoff,[3] Ding,[4] Quintela,[5] Eguchi,[6] Noguchi,[7] Nitta,[8] and Abe[9]), also including our own,[10] have independently developed various (tandem) processes involving aza-Wittig reactions between iminophosphoranes and isocyanates to give functionalized carbodiimides, followed by various types of ring-forming reaction (Scheme 1).[11]

These variously functionalized carbodiimides undergo initial cyclizations onto the cumulene functionality, in the forms of: a) intramolecular addition of a nitrogen nucleophile,[6b,9c,10b] b) electrocyclization,[5a] c) intermolecular [4 + 2] cycloaddition,[8a,8b] or d) intermolecular nucleophilic addition of an amine and various subsequent types of ring-forming reactions between the acyclic guanidine nitrogen and the available inner functional group, to give monocyclic guanidines **A**.[3c,4e,6a,7b–d,10a,12] The second cyclization of the monocyclic guanidines **A**, in which the R group is a functional group reacting with the internal amino group, leads to the formation of the bicyclic guanidines **B** [step (e)]. Indeed, various types of second cyclization reactions with the resulting guanidine nitrogen – including nucleophilic substitution,[6b] nucleophilic addition,[2h,4e,12] Michael addition,[10c] and iodoamination[6,7b–7d] – have been successfully applied. Ring-closing metathesis of **A** was also reported when R and R′ were terminal alkenyl groups.[3d]



Scheme 1. a) Intramolecular nucleophilic addition, b) electrocyclization, c) [4 + 2] cycloaddition, or d) intermolecular nucleophilic addition, followed by various types of ring-forming reaction.

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Thus, synthetic methods for a variety of bicyclic guanidines have been developed by the sequential cyclization methodology with the combined use of a wide range of bond-forming transformations. The utility of this methodology has been shown by the fact that appropriate routes have been applied as key steps in syntheses of mono- and bicyclic guanidine natural products such as the monocyclic guanidines leucettamine B,[2c] isonaanime A,[2d] doriimiazole A,[2d] preclathridine A,[2d] and variolin B,[2e] as well as the bicyclic guanidines (+)-batzelladine A and (–)-batzelladine D.[13]

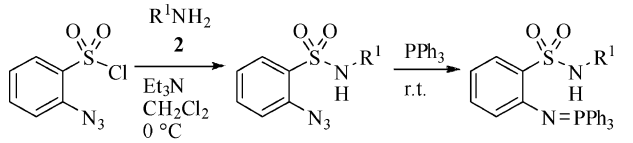
3-Amino-1,2,4-benzothiadiazine 1,1-dioxides are known to possess diverse biological activities, including potassium[14] and calcium[15] channel modulation and adrenergic antagonism effects.[16,17a] Moreover, various azaheterocycle-fused 1,2,4-benzothiadiazine 1,1-dioxide derivatives are expected to display a variety of concomitant bioactivities,[16,17a] so the development of simple synthetic methods to prepare such heterocycles is of value. A survey of the literature showed us that multistep sequences seemed to be necessary in order to gain access to these heterocyclic ring-fused benzothiazine derivatives.[16,17] We therefore started our own study on the synthesis of a variety of diazaheterocyclic ring-fused 1,2,4-benzothiadiazine 1,1-dioxides by a tandem cyclization methodology using 2-(*N*-alkenylsulfamoyl)phenylcarbodiimides as the key intermediates.[18] For the tandem cyclization protocol to produce bicyclic guanidines, we employed iodocyclization[19] and hydroamination[20] with $Hg^{II}/NaBH_4$ (aminomercuration/demercuration) as the second ring-closing reaction between alkenyl and amine groups after the initial cyclization by internal nucleophilic sulfonamide/NH addition onto the cumulene carbon. Although each cyclization is a well documented reaction, it is rare for the cyclizations to be used combinatorially in a tandem methodology for heterocumulene-mediated synthesis of fused heterocycles bearing multicyclic guanidine moieties.[6,7] We report here the novel synthesis of five- to seven-membered aza-heterocyclic ring-fused 1,2,4-benzothiadiazine 1,1-dioxides by this tandem methodology.[18]

Results and Discussion

The prerequisite iminophosphoranes **4** were prepared by treatment of *o*-azidobenzenesulfonyl chloride (**1**) with amines **2** in the presence of triethylamine, followed by Staudinger reactions of the resultant azides **3** with triphenylphosphane (Table 1). The reactions between **4** and various isocyanates **5** proceeded smoothly under the conditions described in Table 2 to produce 3-aminobenzo-1,2,4-thiadiazine 1,1-dioxides **7**[21] in good to excellent yields. The carbodiimides **6** would be the most probable intermediate formed by the initial aza-Wittig reaction.[22] Subsequent intramolecular nucleophilic addition of NH to the cumulene carbon of **6** would provide **7** as the final product.[22]

The benzothiadiazine 1,1-dioxides **7**, bearing substituents with carbon chain lengths of $n = 1, 2, 3$, were subjected to iodocyclization (Method A) and aminomercuration/demercuration (Method B) cyclizations (Scheme 2). *N*-Allyl and *N*-homoallylbenzothiadiazines **7Aa**–**7Ad** ($n = 1$) and **7Ba**–**7Bd** ($n = 2$) underwent iodocyclization smoothly in the presence of threefold molar excesses of molecular iodine and K_2CO_3 at room temperature in CH_2Cl_2 to produce imidazo and pyrimido ring-fused benzothiadiazines **8a**–**d** and **9a**–**d**, respectively, in good to high yields and with excellent selectivity for the *exo-trig* mode (Table 3, Entries 1–8).[23] Similarly, benzothiadiazines **7Ca**–**7Cd** with a chain length

Table 1. Preparation of iminophosphoranes **4**.

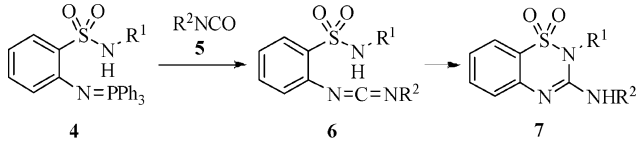


1 **3** **4**

Entry	**2**	R^1	**4**	% Yield[a]
1	**2A**	$CH_2CH=CH_2$	**4A**	94
2	**2B**	$(CH_2)_2CH=CH_2$	**4B**	87
3	**2C**	$(CH_2)_3CH=CH_2$	**4C**	87
4	**2D**	$(CH_2)_4CH=CH_2$	**4D**	96
5	**2E**	*n*Pr	**4E**	92
6	**2F**	Ph	**4F**	87

[a] Conversion from **1**.

Table 2. Preparation of guanidines **7**.

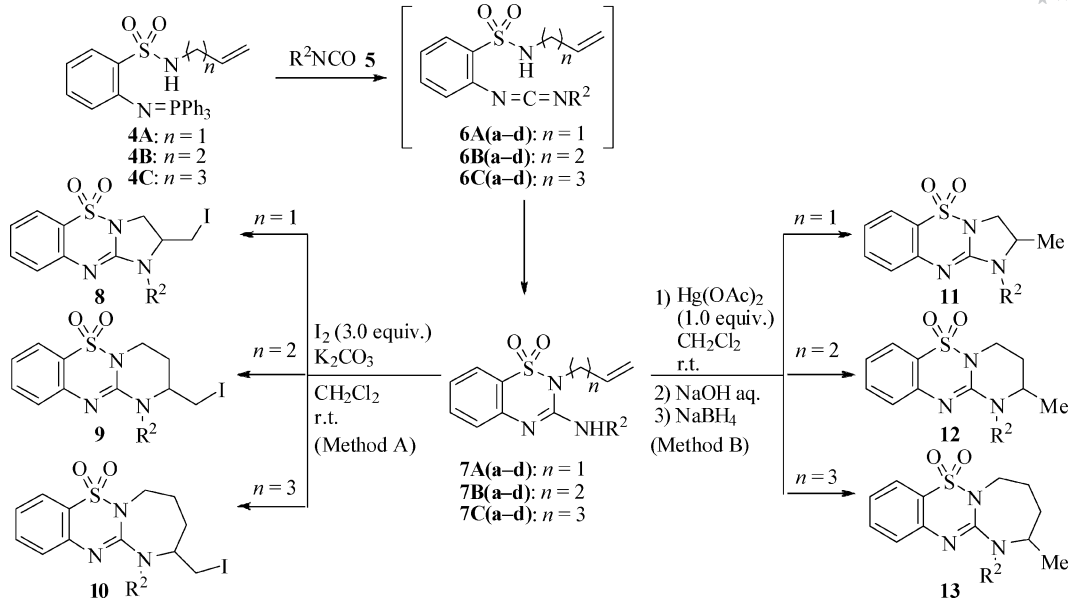


4 **6** **7**

4A: $R^1 = CH_2CH=CH_2$
4B: $R^1 = (CH_2)_2CH=CH_2$
4C: $R^1 = (CH_2)_3CH=CH_2$
4D: $R^1 = (CH_2)_4CH=CH_2$
4E: $R^1 = n$Pr
4F: R^1 = Ph

5a: $R^2 = n$Pr
5b: R^2 = Ph
5c: $R^2 = p$Tol
5d: R^2 = Ts
5e: $R^2 = CH_2CH=CH_2$

Entry	**4**	**5**	Conditions	**7**	% Yield
1	**4A**	**5a**	PhMe, 110 °C, 13 h	**7Aa**	99
2	**4A**	**5b**	PhMe, 110 °C, 2 h	**7Ab**	90
3	**4A**	**5c**	PhMe, 110 °C, 2 h	**7Ac**	90
4	**4A**	**5d**	CH_2Cl_2, room temp., 0.5 h	**7Ad**	99
5	**4A**	**5e**	PhMe, 110 °C, 5 h	**7Ae**	92
6	**4B**	**5a**	PhMe, 110 °C, 6 h	**7Ba**	99
7	**4B**	**5b**	PhMe, 110 °C, 3 h	**7Bb**	89
8	**4B**	**5c**	PhMe, 110 °C, 3 h	**7Bc**	94
9	**4B**	**5d**	CH_2Cl_2, room temp., 0.2 h	**7Bd**	97
10	**4B**	**5e**	PhMe, 110 °C, 6 h	**7Be**	91
11	**4C**	**5a**	PhMe, 110 °C, 4 h	**7Ca**	99
12	**4C**	**5b**	PhMe, 110 °C, 3 h	**7Cb**	97
13	**4C**	**5c**	PhMe, 110 °C, 3 h	**7Cc**	94
14	**4C**	**5d**	CH_2Cl_2, room temp., 0.2 h	**7Cd**	98
15	**4C**	**5e**	PhMe, 110 °C, 5 h	**7Ce**	90
16	**4D**	**5a**	PhMe, 110 °C, 5 h	**7Da**	99
17	**4D**	**5b**	PhMe, 110 °C, 3 h	**7Db**	95
18	**4D**	**5c**	PhMe, 110 °C, 3 h	**7Dc**	93
19	**4D**	**5d**	CH_2Cl_2, room temp., 0.2 h	**7Dd**	99
20	**4D**	**5e**	PhMe, 110 °C, 4 h	**7De**	85
21	**4E**	**5e**	PhMe, 110 °C, 5 h	**7Ee**	94
22	**4F**	**5e**	PhMe, 110 °C, 3 h	**7Fe**	99



Scheme 2. Syntheses of diazaheterocyclic ring-fused benzothiadiazine 1,1-dioxides **8**–**13** by iodoamination (Method A) or hydroamination (Method B) of **7** and by the one-pot method from **4**.

of n = 3 gave diazepine-fused benzothiadiazines **10b**–**d** in high yields (Entries 10–12), except in one case of a 41% yield (Entry 9, **10a**). It is noteworthy that the one-pot method in tandem[24] through three steps starting from iminophosphoranes **4** was efficiently applied to these iodoamination cyclizations to provide the target compounds **8**–**10** in fair to high yields.

Table 3. Syntheses of diazaheterocyclic ring-fused benzothiadiazine 1,1-dioxides **8**–**10** by iodoamination of **7** (Method A) and by the one-pot method from **4**.

Entry	n	R^2	Time [h]	Product	% Yield from **7**	% Yield from **4**
1	1	*n*Pr	1	**8a**	92	97
2	1	Ph	2	**8b**	99	90
3	1	*p*Tol	2	**8c**	97	90
4	1	Ts	15	**8d**	92	99
5	2	*n*Pr	1	**9a**	88	55
6	2	Ph	0.5	**9b**	89	81
7	2	*p*Tol	0.5	**9c**	94	81
8	2	Ts	1	**9d**	96	90
9	3	*n*Pr	26	**10a**	41	35
10	3	Ph	0.5	**10b**	99	92
11	3	*p*Tol	3	**10c**	95	93
12	3	Ts	8	**10d**	99	96

Hydroamination of alkenylbenzothiadiazines **7** with Hg^{II}–$NaBH_4$ (aminomercuration/demercuration, Method B) also proceeded smoothly to afford the corresponding *exo*-mode cyclization products **11**–**13** (Table 4). Thus, treatment of **7** with $Hg(OAc)_2$ in CH_2Cl_2, followed by treatment with aqueous NaOH and $NaBH_4$, yielded five- to seven-membered ring-fused products **11**–**13**, with no *endo*-mode-cyclized products being formed. The one-pot procedure for this tandem cyclization starting from iminophosphoranes **4** was also found to be effective, the results comparing favorably with those of the stepwise methods.

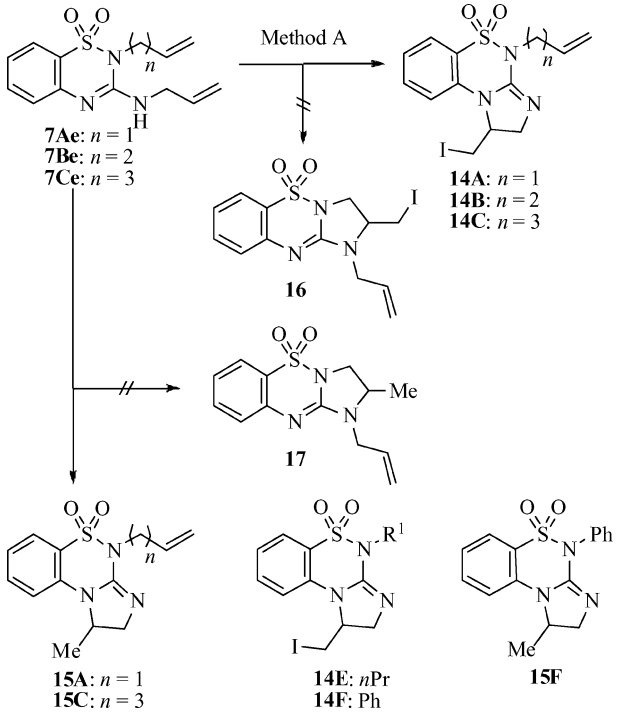
Table 4. Syntheses of diazaheterocyclic ring-fused benzothiadiazine 1,1-dioxides **11**–**13** by hydroamination of **7** (Method B) and by the one-pot method from **4**.

Entry	n	R^2	Time [h]	Product	% Yield from **7**	% Yield from **4**
1	1	*n*Pr	0.1	**11a**	85	80
2	1	Ph	0.5	**11b**	91	88
3	1	*p*Tol	0.5	**11c**	93	88
4	1	Ts	6	**11d**	66	50
5	2	*n*Pr	5	**12a**	86	72
6	2	Ph	2	**12b**	70	72
7	2	*p*Tol	2	**12c**	66	70
8	2	Ts	48	**12d**	57	66
9	3	*n*Pr	12	**13a**	61	47
10	3	Ph	3	**13b**	56	47
11	3	*p*Tol	2	**13c**	64	57
12	3	Ts	48	**13d**	47	37

We next examined the regioselectivities of the two cyclizations – iodoamination (Method A) and hydroamination (Method B) – of 1,2,4-benzothiadiazine 1,1-dioxides **7Ae**–**7Ce** bearing two alkenyl groups, one at the endocyclic *N* at the 2-position (R^1) and the other at the exocyclic *N* at the 3-position. If the alkenyl group at the 2-position (R^1) were involved in cyclizations by either Method A or B, products **16** and **17** would be formed in the same manner as described in Tables 3 and 4, respectively. Alternatively, if the cyclizations were to take place on the *N*-allyl group at the 3-position, then the corresponding products would be compounds **14** and **15**. In fact, compounds **14A** (Method A) and **15A** (Method B) were obtained in 92% and 86% yields, respectively, from **7Ae** (Table 5, Entries 1 and 6). Similarly, the 2-(but-3-enyl)- and 2-(pent-4-enyl)-1,2,4-benzothiadiazine 1,1-dioxides **7Be** and **7Ce** reacted regioselectively to produce the cyclized products **14B** and **14C** (Entries 2 and 3) and **15C** (Entry 7) in moderate to good yields. As expected,

7Ee and **7Fe** also gave **14E** and **14F** (Entries 4 and 5) and **15F** (Entry 8) in good yields. It was of interest that the nitrogen at the 4-position rather than the exocyclic allylamino nitrogen of **7** was a predominant participant as an active nucleophile in both cyclizations to form the [2,1-*c*]-fused imidazoline ring system exclusively.

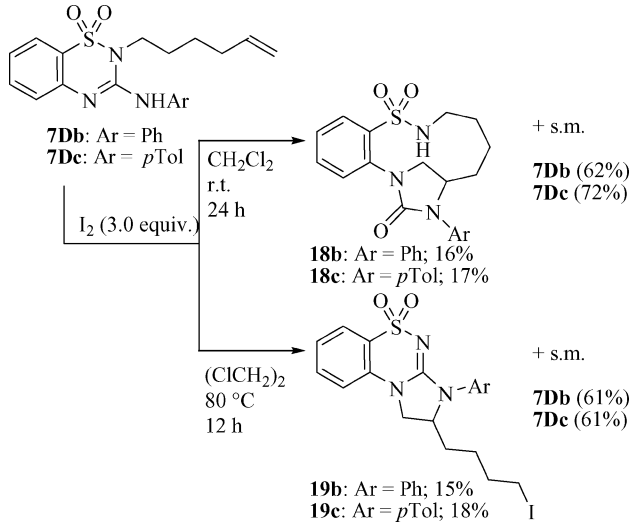
Table 5. Stepwise iodoamination (Method A) and hydroamination (Method B) method for **7Ae**–**7Fe**.



Entry	7	*n*	Method	Time	Product	% Yield
1	**7Ae**	1	A[a]	3	**14A**	92
2	**7Be**	2	A[a]	22	**14B**	44
3	**7Ce**	3	A[a]	0.5	**14C**	42
4	**7Ee**	–	A[a]	0.2	**14E**	96
5	**7Fe**	–	A[a]	4	**14F**	82
6	**7Ae**	1	B[b]	6	**15A**	86
7	**7Ce**	3	B[b]	6	**15C**	60
8	**7Fe**	–	B[b]	5	**15F**	83

[a] Method A: I_2 (3.0 equiv.), CH_2Cl_2, room temp., time stated. [b] Method B: 1) $Hg(OAc)_2$ (1.0 equiv.), CH_2Cl_2, room temp., time stated. 2) $NaBH_4$, NaOH aq. room temp., 1 h.

Further efforts were made to obtain eight-membered ring-fused benzothiadiazines from **7**, bearing a hex-5-enyl group at the 2-position (R^1).[25] Disappointingly, neither the iodoamination nor the aminomercuration of **7Da** (R^2 = *n*Pr) and **7Dd** (R^2 = Ts) proceeded under the above reaction conditions, resulting in quantitative recovery of the starting materials. However, compounds **7Db** (R^2 = Ph) and **7Dc** (R^2 = *p*Tol) did react under the iodocyclization conditions to give the unexpected products **18b** and **18c**, albeit in low yields (**18b**: 16%, **18c**: 17%) with recovery of **7Db** (62%) and **7Dc** (72%) (Scheme 3). The product structures were deduced by various NMR spectroscopy techniques and were unambiguously determined by X-ray structural analysis of **18b** (Figure 1). Interestingly, when the reactions of **7Db** (R^2 = Ph) and **7Dc** (R^2 = *p*Tol) were carried out at 80 °C in 1,2-dichloroethane, compounds **19b** and **19c**, and not **18b** and **18c**, were obtained in 15% and 18% yields, respectively, along with the starting materials (**7Db**: 61%, **7Dc**: 61%). The reaction yielding **18b** and **18c** would be a useful novel synthetic method for novel 12-membered bicyclic thiatriaza heterocycles.



Scheme 3. Iodocyclization of **7Db** and **7Dc**.

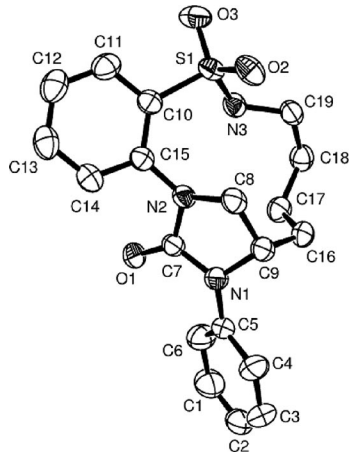
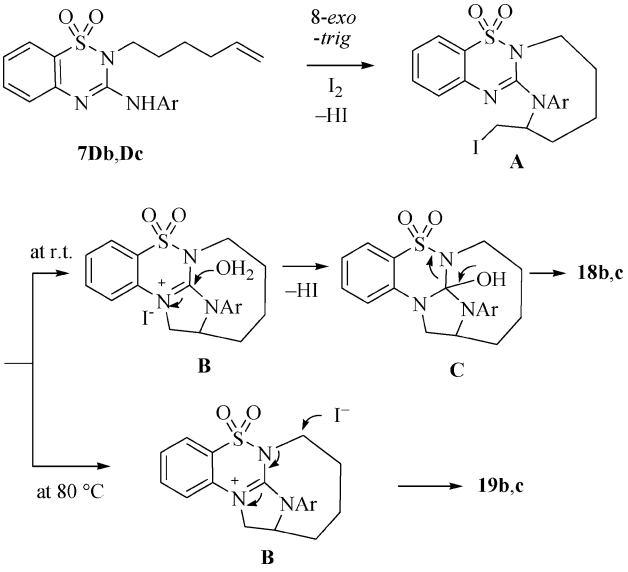


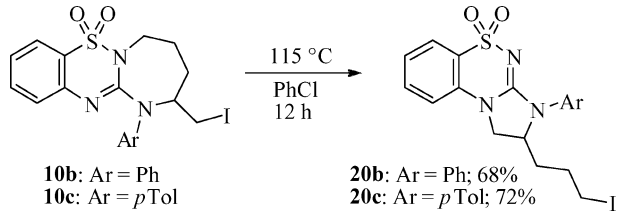
Figure 1. Crystal structure of **18b**.

These results can be explained as shown in Scheme 4. The reaction is initiated by an 8-*exo*-*trig* mode iodocyclization to form the anticipated intermediate **A**, and subsequent intramolecular nucleophilic attack by the proximal nitrogen then leads to the iminium salt **B**. Hydrolysis of salt **B** by a small amount of contaminating water or during workup then takes place at room temperature finally to give **18b** and **18c** via the hemiaminal intermediate **C**, whereas upon heating, nucleophilic attack by an iodide anion in **B** occurs to give **19b** and **19c**. This is probably because the salt **B** has both the more nucleophilic iodide anion and the iminium-sulfonamide group with good leaving ability in a strained bridging structure. The formation of the initial iodocyclization intermediate **A** is supported by the fact that

upon heating **10b** and **10c** (isolated in the case of chain length n = 3, Table 3, Entries 10 and 11) at 115 °C in chlorobenzene, the analogous transformation of **10b** and **10c** to **20b** and **20c** (**b**: 68%, **c**: 72% yield) was observed (Scheme 5).



Scheme 4. Probable pathways for the formation of **18** and **19**.



Scheme 5. Thermal rearrangement of **10b** and **10c**.

Conclusions

In conclusion, we have developed practical syntheses for a variety of diazaheterocyclic ring-fused 1,2,4-benzothiadiazine 1,1-dioxides by a tandem aza-Wittig reaction/intramolecular nucleophilic reaction/iodoamination or hydroamination methodology from iminophosphoranes **4**. Its advantages, such as convenient tandem synthesis and one-pot procedures, good to high yields with highly predictable selectivity, and availability of a broad range of unsaturated alkenylamines, make this protocol attractive. Particularly noticeable is the unexpected formation of the methano-bridged benzothiatriazabicyclo[8.2.1]tridecanones **18b** and **18c** with unique structures. Further applications are currently under investigation in our laboratory.

Experimental Section

General Remarks: All melting points were determined on a Yanaco MP apparatus and are uncorrected. Infrared spectra were recorded on a Hitachi 270–30 or a Horiba FT-710 spectrophotometer. ^{1}H and ^{13}C NMR spectroscopic data were obtained with a JEOL JNM-EX 500, a JEOL JNM-EX 300, or a Bruker AV 600 instrument. Chemical shifts (δ) are quoted in ppm relative to tetramethylsilane (δ = 0) for ^{1}H NMR and $CDCl_3$ (δ = 77.0) for ^{13}C NMR spectroscopy. Mass spectra were measured on a Bruker Daltonics microTOF or a Hitachi double-focusing M-80B spectrometer. Elemental analyses were performed with a Yanaco CHN-CODER MT-6 model. Column chromatography was conducted on silica gel 60 (Kanto Chemical Co.).

Typical Procedure for Preparation of Iminophosphoranes 4: Allylamine (0.38 mL, 5.1 mmol) and triethylamine (1.42 mL, 10.2 mmol) were added at 0 °C with stirring to a solution of **1**[19,26] (1.01 g, 4.64 mmol) in CH_2Cl_2 (10 mL). After the system had been stirred for 15 min, triphenylphosphane (1.22 g, 4.64 mmol) in CH_2Cl_2 (5 mL) was added. The mixture was stirred for 8 h at room temperature and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2 as the eluent to yield **4a** as a colorless solid (2.07 g, 94%).

***N*-(Prop-2-enyl)-2-[(triphenylphosphoranylidene)amino]benzenesulfonamide (4A):** M.p. 171–172 °C (hexane/CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.41 (dddd, J = 1.5, 1.5, 6.0, 6.0 Hz, 2 H, NCH_2), 4.85 [ddt, J = 1.5, 10.2, 1.5 Hz, 1 H, CH=CH_2(*cis*)], 4.91 [ddt, J = 1.5, 17.1, 1.5 Hz, 1 H, CH=CH_2(*trans*)], 5.64 (ddt, J = 10.2, 17.1, 5.8 Hz, 1 H, CH=CH_2), 6.45 (dd, J = 1.1, 8.1 Hz, 1 H, Ar), 6.69 (ddd, J = 1.1, 7.5, 7.7 Hz, 1 H, Ar), 6.86 (t, J = 6.4 Hz, 1 H, NH), 7.01 (ddd, J = 1.7, 7.5, 8.1 Hz, 1 H, Ar), 7.47–7.51 (m, 6 H, PPh_3), 7.55–7.59 (m, 3 H, PPh_3), 7.74–7.79 (m, 6 H, PPh_3), 7.84–7.87 (m, 1 H, Ar) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 46.2 (CH_2), 116.1 (CH_2), 116.5 (CH), 121.9 (d, $^3J_{P,C}$ = 11 Hz, CH), 129.0 (d, $^3J_{P,C}$ = 12 Hz, 6 CH), 129.2 (d, $^1J_{P,C}$ = 100 Hz, 3 C), 129.5 (d, $^4J_{P,C}$ = 3 Hz, CH), 130.2 (d, $^2J_{P,C}$ = 24 Hz, 1 C), 132.3 (d, $^4J_{P,C}$ = 2 Hz, 3 CH), 132.4 (d, $^2J_{P,C}$ = 10 Hz, 6 CH), 132.7 (CH), 133.8 (CH), 148.9 (C) ppm. IR (KBr): $\tilde{\nu}$ = 1155, 1335, 1464, 1585, 3055, 3174 cm^{-1}. HRMS (ESI): calcd. $C_{27}H_{26}N_2O_2PS$ [M + H]$^+$: 473.1447; found 473.1444. $C_{27}H_{25}N_2O_2PS$ (472.54): calcd. C 68.63, H 5.33, N 5.93; found C 69.03, H 5.61, N 5.66.

Typical Procedure for Preparation of Benzo-1,2,4-thiadiazine 1,1-Dioxides 7 by Aza-Wittig Reactions of Iminophosphoranes 4 and Subsequent Cyclization: Phenyl isocyanate (49 μL, 0.45 mmol) was added to a stirred solution of **4B** (200 mg, 0.41 mmol) in toluene (4 mL). The mixture was heated at reflux for 3 h, cooled to room temperature, and quenched with water (2 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (5 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/Hex (1:4) as the eluent to yield **7Bb** as a colorless solid (119 mg, 89%).

2-(But-3-enyl)-3-phenylamino-2*H*-1,2,4-benzothiadiazine 1,1-Dioxide (7Bb): M.p. 133.6–134.3 °C (hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (dt, J = 6.7, 6.7 Hz, 2 H, CH_2), 3.79 (t, J = 6.6 Hz, 2 H, NCH_2), 4.80 [d, J = 17.2 Hz, 1 H, CH=CH_2 (*trans*)], 4.84 [d, J = 10.1 Hz, 1 H, CH=CH_2 (*cis*)], 5.59 (ddt, J = 10.1, 17.2, 6.6 Hz, 1 H, CH=CH_2), 6.79–7.12 (m, 2 H, Ar, NH), 7.23–7.44 (m, 6 H, Ar), 7.55 (dd, J = 7.7, 7.7 Hz, 1 H, Ar), 7.76 (d, J = 7.8 Hz, 1 H, Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.7 (CH_2), 46.9 (CH_2), 118.7 (CH_2), 120.4 (2 CH), 121.2 (CH), 124.1 (CH), 124.2 (CH), 125.7 (CH), 127.6 (C), 129.3 (2 CH), 133.35 (CH), 133.41 (CH), 138.6 (C), 143.3 (C), 147.4 (C) ppm. IR (KBr): $\tilde{\nu}$ = 1173, 1335, 1574, 1613, 3363 cm^{-1}. HRMS (ESI): calcd. $C_{17}H_{17}N_3NaO_2S$ [M + Na]$^+$: 350.0934; found 350.0935.

$C_{17}H_{17}N_3O_2S$ (327.40): calcd. C 62.36, H 5.23, N 12.83; found C 62.01, H 5.38, N 13.19.

Typical Procedure for the Iodocyclization of 7 to Produce 8–10 and 14: K_2CO_3 (136 mg, 0.98 mmol) and I_2 (250 mg, 0.98 mmol) were added to a stirred solution of benzothiadiazine dioxide **7Bb** (108 mg, 0.33 mmol) in CH_2Cl_2 (3 mL). After being stirred for 30 min, the reaction mixture was quenched with saturated aqueous Na_2SO_3 (2 mL). The organic layer was separated, and the aqueous layer was extracted with AcOEt (5 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/Hex (1:4) as the eluent to yield **9b** as a colorless solid (133 mg, 89%).

Typical Procedure for One-Pot Iodoamination from Iminophosphorane 4 to Produce 8–10 and 14: Phenyl isocyanate (37 μL, 0.34 mmol) was added at room temperature to a stirred solution of **4B** (150 mg, 0.31 mmol) in $(CH_2Cl)_2$ (3 mL). The mixture was heated at reflux for 3 h and cooled to room temperature, and then K_2CO_3 (128 mg, 0.92 mmol) and I_2 (234 mg, 0.92 mmol) were added. After being stirred for 30 min, the reaction mixture was quenched with saturated aqueous Na_2SO_3 (2 mL). The organic layer was separated, and the aqueous layer was extracted with AcOEt (5 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/Hex (1:4) as the eluent to yield **9b** as a colorless solid (113 mg, 81%).

2-Iodomethyl-1-phenyl-1,2,3,4-tetrahydropyrimido[1,2-*b*][1,2,4]benzothiadiazine 6,6-Dioxide (9b): M.p. 203–205 °C (hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43–2.57 (m, 1 H, CH_2), 2.70 (dddd, J = 4.3, 4.4, 4.4, 14.1 Hz, 1 H, CH_2), 3.23 (ddd, J = 0.6, 10.4, 10.4 Hz, 1 H, CH_2I), 3.43 (ddd, J = 1.0, 3.4, 10.4 Hz, 1 H, CH_2I), 3.97–4.12 (m, 3 H, NCH, NCH_2), 7.01 (ddd, J = 0.4, 1.0, 8.3 Hz, 1 H, Ar), 7.13 (ddd, J = 1.1, 7.3, 7.9 Hz, 1 H, Ar), 7.30–7.50 (m, 6 H, Ar), 7.73 (ddd, J = 0.4, 1.1, 7.9 Hz, 1 H, Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 5.6 (CH_2), 27.2 (CH_2), 36.1 (CH_2), 58.7 (CH), 121.0 (CH), 122.7 (CH), 123.8 (C), 126.2 (CH), 127.6 (CH), 128.2 (2 CH), 129.4 (2 CH), 133.5 (CH), 141.5 (C), 143.8 (C), 146.8 (C) ppm. IR (KBr): $\tilde{\nu}$ = 569, 690, 1144, 1182, 1329, 1535 cm^{-1}. $C_{17}H_{16}IN_3O_2S$ (453.30): calcd. C 45.04, H 3.56, N 9.27; found C 44.88, H 3.66, N 8.94.

2-Iodomethyl-1-propyl-2,3-dihydro-1*H*-imidazo[1,2-*b*][1,2,4]benzothiadiazine 5,5-Dioxide (8a): Colorless solid. Yield 87 mg (92%) from **7Aa** (65 mg). M.p. 147–149 °C (hexane/CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.4 Hz, 3 H, Me), 1.56–1.76 (m, 2 H, CH_2Me), 3.15 (ddd, J = 5.3, 9.2, 14.3 Hz, 1 H, NCH_2), 3.17 (dd, J = 8.8, 10.6 Hz, 1 H, CH_2I), 3.43 (dd, J = 2.8, 10.6 Hz, 1 H, CH_2I), 3.70 (ddd, J = 6.9, 9.3, 14.3 Hz, 1 H, NCH_2), 3.88 (dd, J = 5.3, 9.7 Hz, 1 H, NCH_2), 3.94–4.00 (m, 1 H, NCH), 4.18 (dd, J = 8.5, 9.7 Hz, 1 H, NCH_2), 7.16 (ddd, J = 1.0, 7.4, 7.9 Hz, 1 H, Ar), 7.27 (dd, J = 1.0, 8.3 Hz, 1 H, Ar), 7.51 (ddd, J = 1.5, 7.4, 8.3 Hz, 1 H, Ar), 7.81 (dd, J = 1.5, 7.9 Hz, 1 H, Ar) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 5.5 (CH_2), 11.2 (CH_3), 20.5 (CH_2), 44.1 (CH_2), 45.3 (CH_2), 55.5 (CH), 122.0 (CH), 122.7 (CH), 123.3 (C), 125.9 (CH), 134.0 (CH), 145.3 (C), 151.6 (C) ppm. IR (KBr): $\tilde{\nu}$ = 579, 1180, 1304, 1581, 1635 cm^{-1}. HRMS (ESI): calcd. $C_{13}H_{16}IN_3NaO_2S$ [M + Na]$^+$: 427.9900; found 427.9918. $C_{13}H_{16}IN_3O_2S$ (405.25): calcd. C 38.53, H 3.98, N 10.37; found C 38.31, H 4.11, N 9.98.

2-Iodomethyl-1-(4-methylphenyl)-2,3,4,5-tetrahydro[1,3]diazepino-[1,2-*b*][1,2,4]benzothiadiazine 7,7-Dioxide (10c): Colorless solid. Yield 103 mg (95%) from **7Cc** (80.1 mg). M.p. 153–154 °C (hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.85–2.12 (m, 3 H, CH_2), 2.37 (s, 3 H, CH_3), 2.33–2.46 (m, 1 H, CH_2), 3.28 (dd, J = 12.4, 12.4 Hz, 1 H, NCH_2), 3.73–3.80 (m, 2 H, CH_2I), 4.26–4.38 (m, 2 H, NCH, NCH_2), 7.11 (dd, J = 0.6, 8.1 Hz, 1 H, Ar), 7.16–7.22 (m, 5 H, Ar), 7.43 (ddd, J = 1.5, 7.4, 8.2 Hz, 1 H, Ar), 7.71 (dd, J = 1.4, 7.9 Hz, 1 H, Ar) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 3.8 (CH_2), 21.0 (CH_3), 23.1 (CH_2), 28.4 (CH_2), 47.8 (CH_2), 65.1 (CH), 121.0 (CH), 123.8 (CH), 126.0 (2 CH), 126.6 (CH), 126.9 (C), 129.8 (2 CH), 133.0 (CH), 136.3 (C), 142.2 (C), 143.8 (C), 151.1 (C) ppm. IR (KBr): $\tilde{\nu}$ = 577, 1180, 1344, 1562 cm^{-1}. LRMS-EI: m/z (%) = 481 (88) [M]$^+$, 354 (46), 340 (100), 207 (29), 91 (42), 28 (43). HRMS (ESI): calcd. $C_{19}H_{20}IN_3O_2S$ [M]$^+$: 481.0321; found 481.0314. $C_{19}H_{20}IN_3O_2S$ (481.35): calcd. C 47.41, H 4.19, N 8.73; found C 47.81, H 4.34, N 8.91.

1-Iodomethyl-4-(prop-2-enyl)-2,4-dihydro-1*H*-imidazo[2,1-*c*][1,2,4]-benzothiadiazine 5,5-Dioxide (14A): Colorless solid. Yield 211 mg (92%) from **7Ae** (158 mg). M.p. 90–91 °C (hexane/CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.31 (dd, J = 9.7, 9.7 Hz, 1 H, CH_2I), 3.41 (dd, J = 2.7, 10.4 Hz, 1 H, CH_2I), 3.80 (dd, J = 4.8, 14.4 Hz, 1 H, CH_2), 4.17 (dd, J = 9.9, 14.3 Hz, 1 H, CH_2), 4.45–4.54 (m, 2 H, CH_2), 4.65–4.70 (m, 1 H, CH), 5.25 [dd, J = 0.6, 10.3 Hz, 1 H, CH=CH_2(*cis*)], 5.37 [dd, J = 0.6, 16.8 Hz, 1 H, CH=CH_2(*trans*)], 6.01 (ddt, J = 10.6, 16.8, 5.8 Hz, 1 H, CH=CH_2), 6.94 (d, J = 8.3 Hz, 1 H, Ar), 7.16 (dd, J = 7.7, 7.7 Hz, 1 H, Ar), 7.59 (ddd, J = 1.0, 8.4, 8.4 Hz, 1 H, Ar), 7.80 (dd, J = 1.0, 7.8 Hz, 1 H, Ar) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 6.5 (CH_2), 45.9 (CH_2), 58.1 (CH_2), 58.7 (CH), 112.4 (CH), 118.8 (CH_2), 121.7 (CH), 123.5 (CH), 124.1 (C), 131.8 (CH), 134.6 (CH), 134.8 (C), 150.1 (C) ppm. IR (KBr): $\tilde{\nu}$ = 581, 752, 1173, 1182, 1342, 1645, 2939 cm^{-1}. LRMS-EI: m/z = 403 (38) [M]$^+$, 338 (39), 212 (100), 171 (48), 170 (53), 41 (27). HRMS (EI): calcd. $C_{13}H_{14}IN_3O_2S$ [M]$^+$: 402.9851; found 402.9844. $C_{13}H_{14}IN_3O_2S$ (403.24): calcd. C 38.72, H 3.50, N 10.42; found C 39.09, H 3.54, N 10.45.

Typical Procedure for Aminomercuration/Demercuration of 7 to Produce 11–13 and 15: $Hg(OAc)_2$ (76.5 mg, 0.24 mmol) was added at room temperature to a stirred solution of benzothiadiazine dioxide **7Bb** (78.6 mg, 0.24 mmol) in CH_2Cl_2 (3 mL). After the system had been stirred for 2 h, aqueous NaOH (3 M, 3 drops) and aqueous $NaBH_4$ (9 mg, 0.2 mmol, in 1 mL) were added to form Hg^0. The precipitated Hg was removed by passing through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/Hex (1:4) as the eluent to give **12b** as a colorless solid (54.6 mg, 70%).

Typical Procedure for One-Pot Aminomercuration/Demercuration from Iminophosphorane 4 to Produce 11–13 and 15: Phenyl isocyanate (30 μL, 0.28 mmol) was added to a stirred solution of **4B** (122 mg, 0.25 mmol) in $(ClCH_2)_2$ (3 mL). The mixture was heated at reflux for 3 h and cooled to room temperature, and $Hg(OAc)_2$ (80 mg, 0.25 mmol) was added. After the system had been stirred for 2 h, aqueous NaOH (3 M, 3 drops) and aqueous $NaBH_4$ (9 mg, 0.2 mmol, in 1 mL) were added to form Hg. Hg particles were removed by passing through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/Hex (1:4) as the eluent to yield **12b** as a colorless solid (58.8 mg, 72%).

2-Methyl-1-phenyl-1,2,3,4-tetrahydropyrimido[1,2-*b*][1,2,4]benzothiadiazine 6,6-Dioxide (12b): M.p. 141–142 °C (hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (dd, J = 0.6, 6.6 Hz, 3 H, Me), 2.05–2.15 (m, 1 H, CH_2), 2.34–2.47 (m, 1 H, CH_2), 3.94–4.14 (m, 3 H, NCH, NCH_2), 6.97 (ddd, J = 0.5, 1.1, 8.3 Hz, 1 H, Ar), 7.06 (ddd, J = 1.1, 7.3, 8.0 Hz, 1 H, Ar), 7.24–7.45 (m, 6 H, Ar), 7.70

(ddd, J = 0.5, 1.5, 8.0 Hz, 1 H, Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8 (CH_3), 29.6 (CH_2), 36.5 (CH_2), 53.9 (CH), 120.9 (CH), 121.9 (CH), 123.6 (C), 125.9 (CH), 126.9 (CH), 128.2 (2 CH), 129.1 (2 CH), 133.3 (CH), 142.2 (C), 144.2 (C), 147.6 (C) ppm. IR (KBr): $\tilde{\nu}$ = 567, 760, 1151, 1331, 1531 cm^{-1}. $C_{17}H_{17}N_3O_2S$ (327.40): calcd. C 62.36, H 5.23, N 12.83; found C 62.08, H 5.44, N 12.67.

2-Methyl-1-phenyl-2,3-dihydro-1*H*-imidazo[1,2-*b*][1,2,4]benzothiadiazine 5,5-Dioxide (11b): Colorless solid. Yield 91 mg (91%) from **7Ab** (100 mg). M.p. 158–160 °C (hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38 (d, J = 6.6 Hz, 3 H, Me), 3.82 (dd, J = 6.6, 9.0 Hz, 1 H, NCH_2), 4.30 (dd, J = 8.6, 9.0 Hz, 1 H, NCH_2), 4.49 (ddq, J = 6.6, 8.6, 6.6 Hz, 1 H, NCH), 7.19 (ddd, J = 1.2, 7.3, 8.0 Hz, 1 H, Ar), 7.25 (dd, J = 8.2, 8.9 Hz, 1 H, Ar), 7.26–7.31 (m, 1 H, Ar), 7.42–7.53 (m, 5 H, Ar), 8.54 (dd, J = 1.6, 7.9 Hz, 1 H, Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.5 (CH_3), 45.5 (CH_2), 52.8 (CH), 121.8 (CH), 123.1 (CH), 123.4 (C), 124.7 (2 CH), 126.2 (CH), 126.3 (CH), 129.1 (2 CH), 133.9 (CH), 136.8 (C), 145.1 (C), 150.4 (C) ppm. IR (KBr): $\tilde{\nu}$ = 1180, 1304, 1581, 1628 cm^{-1}. $C_{16}H_{15}N_3O_2S$ (313.37): calcd. C 61.32, H 4.82, N 13.41; found C 61.39, H 5.01, N 13.45.

2-Methyl-1-phenyl-2,3,4,5-tetrahydro[1,3]diazepino[1,2-*b*][1,2,4]benzothiadiazine 7,7-Dioxide (13b): Colorless solid. Yield 71.6 mg (61%) from **7Cb** (117 mg). M.p. 234–236 °C (hexane/CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.56 (d, J = 6.9 Hz, 3 H, CH_3), 1.80–1.87 (m, 1 H, CH_2), 1.89–1.98 (m, 2 H, CH_2), 2.09–2.20 (m, 1 H, CH_2), 3.42–3.54 (m, 1 H, NCH_2), 4.18–4.30 (m, 1 H, NCH_2), 4.30–4.38 (m, 1 H, NCH), 7.08 (dd, J = 1.0, 8.3 Hz, 1 H, Ar), 7.19 (ddd, J = 1.1, 7.3, 7.9 Hz, 1 H, Ar), 7.23–7.29 (m, 3 H, Ar), 7.38–7.42 (m, 2 H, Ar), 7.43 (ddd, J = 1.5, 7.3, 8.2 Hz, 1 H, Ar), 7.73 (dd, J = 1.4, 7.9 Hz, 1 H, Ar) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 18.6 (CH_3), 23.9 (CH_2), 32.1 (CH_2), 48.0 (CH_2), 59.1 (CH), 121.0 (CH), 123.5 (CH), 126.2 (CH), 126.6 (CH), 126.7 (2 CH), 127.0 (C), 129.1 (2 CH), 132.9 (CH), 144.2 (C), 145.1 (C), 152.3 (C) ppm. IR (KBr): $\tilde{\nu}$ = 1180, 1335, 1558 cm^{-1}. HRMS (ESI): calcd. $C_{18}H_{20}N_3O_2S$ [M + H]$^+$: 342.1271; found 342.1276. $C_{18}H_{19}N_3O_2S$ (341.43): calcd. C 63.32, H 5.61, N 12.31; found C 63.39, H 5.76, N 12.30.

1-Methyl-4-(prop-2-enyl)-2,4-dihydro-1*H*-imidazo[2,1-*c*][1,2,4]benzothiadiazine 5,5-Dioxide (15A): Colorless oil. Yield 191 mg (86%) from **7Ae** (166 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (d, J = 6.2 Hz, 3 H, CH_3), 3.60 (dd, J = 5.6, 13.8 Hz, 1 H, CH_2), 4.15 (dd, J = 10.0, 13.8 Hz, 1 H, CH_2), 4.51 (dd, J = 1.2, 5.7 Hz, 2 H, CH_2), 4.50–4.64 (m, 1 H, CH), 5.24 [dd, J = 0.8, 10.3 Hz, 1 H, CH=CH_2(*cis*)], 5.36 [dd, J = 1.1, 17.1 Hz, 1 H, CH=CH_2(*trans*)], 6.03 (ddt, J = 10.3, 17.1, 5.5 Hz, 1 H, CH=CH_2), 6.96 (d, J = 8.4 Hz, 1 H, Ar), 7.10 (dd, J = 7.7, 7.7 Hz, 1 H, Ar), 7.56 (ddd, J = 1.3, 7.7, 8.1 Hz, 1 H, Ar), 7.76 (dd, J = 1.4, 7.8 Hz, 1 H, Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.1 (CH_3), 45.4 (CH_2), 54.5 (CH), 58.6 (CH_2), 112.7 (CH), 118.2 (CH_2), 120.7 (CH), 122.8 (CH), 123.3 (C), 131.8 (CH), 134.1 (CH), 135.3 (C), 149.8 (C) ppm. IR (NaCl, neat): $\tilde{\nu}$ = 756, 1180, 1342, 1597, 1643, 2970 cm^{-1}. HRMS (ESI): calcd. $C_{13}H_{16}N_3O_2S$ [M + H]$^+$: 278.0958; found 278.0951.

Iodoamination of 7Db to Produce the 11-Membered Ring Compound 18b: I_2 (194 mg, 0.76 mmol) was added to a stirred solution of benzothiadiazine dioxide **7Db** (90.4 mg, 0.25 mmol) in CH_2Cl_2 (3 mL). After being stirred for 24 h, the reaction mixture was quenched with saturated aqueous Na_2SO_3 (2 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (5 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/Hex (1:1) as the eluent to yield **18b** as a colorless solid (14.9 mg, 16%).

8,8-Dioxo-15-phenyl-8λ^6-thia-1,9,15-triazatricyclo[12.2.1.0^{2,7}]heptadeca-2,4,6-trien-16-one (18b): M.p. 222–224 °C (hexane/CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.46–1.52 (m, 1 H, CH_2), 1.64–1.75 (m, 3 H, CH_2), 1.77–1.85 (m, 1 H, CH_2), 2.11–2.18 (m, 1 H, CH_2), 3.21–3.27 (m, 1 H, NCH_2), 3.61–3.67 (m, 1 H, NCH_2), 3.96 (dd, J = 9.1, 9.1 Hz, 1 H, NCH_2), 4.21 (dd, J = 1.0, 9.2 Hz, 1 H, NCH_2), 4.65–4.69 (m, 1 H, NCH), 4.71 (dd, J = 5.7, 5.7 Hz, 1 H, NH), 7.11 (dd, J = 7.4, 7.4 Hz, 1 H, Ar), 7.37 (dd, J = 7.5, 8.5 Hz, 2 H, Ar), 7.42–7.47 (m, 2 H, Ar), 7.61 (d, J = 7.9 Hz, 2 H, Ar), 7.64 (ddd, J = 1.5, 7.8, 7.8 Hz, 1 H, Ar), 8.23 (dd, J = 1.3, 8.0 Hz, 1 H, Ar) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 17.7 (CH_2), 28.8 (CH_2), 29.0 (CH_2), 41.1 (CH_2), 50.4 (CH_2), 53.3 (CH), 120.2 (2 CH), 123.7 (CH), 127.8 (CH), 129.1 (2 CH), 129.9 (CH), 131.2 (CH), 134.3 (CH), 137.3 (C), 138.1 (C), 138.5 (C), 157.4 (C) ppm. IR (KBr): $\tilde{\nu}$ = 602, 1149, 1288, 1404, 1705, 3271 cm^{-1}. HRMS (ESI): calcd. $C_{19}H_{21}N_3NaO_3S$ [M + Na]$^+$: 394.1196; found 394.1202.

Iodoamination of 7db at 80 °C to Produce 19b: I_2 (183 mg, 0.72 mmol) was added to a stirred solution of benzothiadiazine dioxide **7Db** (85 mg, 0.24 mmol) in $(ClCH_2)_2$ (3 mL). The mixture was heated at reflux for 12 h and then cooled to room temperature, and the reaction mixture was quenched with saturated aqueous Na_2SO_3 (2 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (5 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/Hex (1:2) as the eluent to yield **19b** as a colorless solid (18 mg, 15%).

2-(4-Iodobutyl)-3-phenyl-2,3-dihydro-1*H*-imidazo[2,1-*c*][1,2,4]benzothiadiazine 5,5-Dioxide (19b): M.p. 172–174 °C (hexane/CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35–1.47 (m, 2 H, CH_2), 1.48–1.58 (m, 1 H, CH_2), 1.68–1.80 (m, 3 H, CH_2), 3.07–3.14 (m, 2 H, CH_2I), 3.81 (dd, J = 6.4, 9.4 Hz, 1 H, NCH_2), 4.22 (dd, J = 9.4, 9.4 Hz, 1 H, NCH_2), 4.48–4.56 (m, 1 H, NCH), 6.92 (d, J = 8.3 Hz, 1 H, Ar), 7.25–7.32 (m, 2 H, Ar), 7.37–7.44 (m, 4 H, Ar), 7.50 (dd, J = 7.6, 7.6 Hz, 1 H, Ar), 7.94 (d, J = 7.6 Hz, 1 H, Ar) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 6.0 (CH_2), 24.9 (CH_2), 31.1 (CH_2), 32.4 (CH_2), 48.0 (CH_2), 56.7 (CH), 113.3 (CH), 122.7 (C), 124.3 (CH), 124.7 (CH), 124.9 (2 CH), 127.0 (CH), 129.3 (2 CH), 132.7 (CH), 135.0 (C), 135.4 (C), 151.0 (C) ppm. IR (KBr): $\tilde{\nu}$ = 1119, 1288 cm^{-1}. HRMS (ESI): calcd. $C_{19}H_{20}IN_3NaO_2S$ [M + Na]$^+$ 504.0213; found 504.0189.

Synthesis of Imidazo[2,1-*c*][1,2,4]benzothiadiazine 20b: A solution of diazepine-fused benzothiadiazine dioxide **10b** (65.0 mg, 0.14 mmol) in chlorobenzene (2 mL) was heated at 115 °C for 12 h. The mixture was cooled to room temperature and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/Hex (1:2) as the eluent to yield **20b** as a colorless solid (43.9 mg, 68%).

2-(3-Iodopropyl)-3-phenyl-2,3-dihydro-1*H*-imidazo[2,1-*c*][1,2,4]benzothiadiazine 5,5-Dioxide (20b): M.p. 138–139 °C (hexane/CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.71–1.94 (m, 4 H, CH_2), 3.10 (t, J = 6.4 Hz, 2 H, CH_2I), 3.91 (dd, J = 6.2, 9.4 Hz, 1 H, NCH_2), 4.28 (dd, J = 9.4, 9.4 Hz, 1 H, NCH_2), 4.44–4.50 (m, 1 H, NCH), 7.19 (dd, J = 0.9, 8.4 Hz, 1 H, Ar), 7.25 (d, J = 8.2 Hz, 1 H, Ar), 7.29 (dd, J = 7.4, 7.4 Hz, 1 H, Ar), 7.46 (dd, J = 8.4, 8.4 Hz, 2 H, Ar), 7.50 (ddd, J = 1.5, 7.4, 8.2 Hz, 1 H, Ar), 7.52 (dd, J = 0.9, 8.4 Hz, 2 H, Ar), 7.85 (dd, J = 1.5, 7.4 Hz, 1 H, Ar) ppm. ^{13}C

NMR (75 MHz, $CDCl_3$): δ = 4.8 (CH_2), 27.9 (CH_2), 33.0 (CH_2), 43.4 (CH_2), 55.9 (CH), 121.9 (CH), 123.3 (CH), 123.4 (C), 124.7 (2 CH), 126.4 (CH), 126.5 (CH), 129.3 (2 CH), 134.0 (CH), 136.7 (C), 145.0 (C), 150.2 (C) ppm. IR (KBr): $\tilde{\nu}$ = 579, 1173, 1311, 1574, 1628 cm^{-1}. HRMS (ESI): calcd. $C_{18}H_{18}IN_3NaO_2S$ $[M + Na]^+$ 490.0057; found 490.0071.

X-ray Crystal Structure Analysis fo Compound 18b: A single crystal was mounted on a glass capillary, transferred to a Bruker AXS SMART diffractometer equipped with CCD area detector and Mo-K_α (λ = 0.71073 Å) radiation, and centered in the beam at 297 K. The structure was solved and refined with SHELX-97[27] by direct methods and expanded by Fourier techniques. All non-hydrogen atoms were refined anisotropically and hydrogens isotropically. $C_{19}H_{21}N_3O_3S$, M = 371.45, a = 11.2721(9) Å, b = 9.8030(8) Å, c = 15.9351(13) Å, β = 93.8970(10)°, V = 1756.8(2) $Å^3$, monoclinic, space group $P2_1/c$, Z = 4, T = 297(2) K, $\rho_{calcd.}$ = 1.404 $g\,cm^{-3}$, μ = 0.209 mm^{-1}, 10581 reflections measured, 3974 unique (R_{int} = 0.0412), GOF (on F^2) = 1.035, final R_1 ($I > 2\sigma$) = 0.0416, wR_2 ($I > 2\sigma$) = 0.1210, R_1 (all data) = 0.0480, wR_2 (all data) = 0.1269.

CCDC-638254 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see also the footnote on the first page of this article): ^1H and ^{13}C NMR spectra for all new compounds and extended X-ray data of compound **18b**.

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Received: November 29, 2007
Published Online: March 3, 2008

