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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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-(R²-substituted amino)-2H-1,2,4-benzothiadiazine 1,1-dioxides by internal nucleophilic addition. Subsequent (tandem)

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 ringforming 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 func-

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 $Ph_3P=N-R'$ (F_G) N=C=N $O=C=N-F_G$ (R') b) a) Aza-Wittig Reaction $F_G - N = C = N - R'$ Ъ "Monocyclic Guanidine" Α e) "Bicyclic Guanidine' В

cyclizations through iodoamination or hydroamination with

Hg^{II}/NaBH₄ 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.

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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.

tional 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]



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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 azaheterocyclefused 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 ringfused 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}/NaBH₄ (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 fiveto 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

Table 1. Preparation of iminophosphoranes 4.

		$\begin{array}{c} R^{1}NH_{2} \\ 2 \\ \hline \\ Et_{3}N \\ CH_{2}Cl_{2} \\ 0 \ ^{\circ}C \end{array} \xrightarrow{O,O} \\ N_{3} \\ \end{array}$	$R^1 - \frac{PPh}{r.t.}$	O O O S N R ¹ H N=PPh ₃
1		3		4
Entry	2	\mathbb{R}^1	4	% Yield ^[a]
1	2A	CH ₂ CH=CH ₂	4 A	94
2	2B	$(CH_2)_2CH=CH_2$	4B	87
3	2 C	$(CH_2)_3CH=CH_2$	4 C	87
4	2D	$(CH_2)_4CH=CH_2$	4D	96
5	2 E	nPr	4 E	92
6	2F	Ph	4F	87

[a] Conversion from 1.

Table 2. Preparation of guanidines 7.



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 K₂CO₃ at room temperature in CH₂Cl₂ 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



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	п	R ²	Time [h]	% Yield		
-				Product	from 7	from 4
1	1	nPr	1	8a	92	97
2	1	Ph	2	8b	99	90
3	1	<i>p</i> Tol	2	8c	97	90
4	1	Ts	15	8d	92	99
5	2	nPr	1	9a	88	55
6	2	Ph	0.5	9b	89	81
7	2	<i>p</i> Tol	0.5	9c	94	81
8	2	Ts	1	9d	96	90
9	3	nPr	26	10a	41	35
10	3	Ph	0.5	10b	99	92
11	3	<i>p</i> Tol	3	10c	95	93
12	3	Ts	8	10d	99	96

Hydroamination of alkenylbenzothiadiazines 7 with Hg^{II} -NaBH₄ (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 NaBH₄, 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	п	R ²	Time [h]	Product	% Yield	
					from 7	from 4
1	1	nPr	0.1	11a	85	80
2	1	Ph	0.5	11b	91	88
3	1	<i>p</i> Tol	0.5	11c	93	88
4	1	Ts	6	11d	66	50
5	2	<i>n</i> Pr	5	12a	86	72
6	2	Ph	2	12b	70	72
7	2	<i>p</i> Tol	2	12c	66	70
8	2	Ts	48	12d	57	66
9	3	<i>n</i> Pr	12	13a	61	47
10	3	Ph	3	13b	56	47
11	3	<i>p</i> 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 (\mathbb{R}^1) and the other at the exocyclic N at the 3-position. If the alkenyl group at the 2-position (\mathbf{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-envl)- and 2-(pent-4-envl)-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.

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





Further efforts were made to obtain eight-membered ring-fused benzothiadiazines from 7, bearing a hex-5-enyl group at the 2-position (\mathbb{R}^1).^[25] Disappointingly, neither the iodoamination nor the aminomercuration of **7Da** ($\mathbb{R}^2 = n\mathbb{P}r$) and **7Dd** ($\mathbb{R}^2 = Ts$) proceeded under the above reaction conditions, resulting in quantitative recovery of the starting materials. However, compounds **7Db** ($\mathbb{R}^2 = Ph$) and **7Dc** ($\mathbb{R}^2 = p$ 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** (\mathbb{R}^2

= Ph) and **7Dc** ($\mathbb{R}^2 = p$ Tol) were carried out at 80 °C in 1,2dichloroethane, 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 methanobridged 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. ¹H

and ¹³C 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 ¹H NMR and CDCl₃ (δ = 77.0) for ¹³C 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 CH₂Cl₂ (10 mL). After the system had been stirred for 15 min, triphenylphosphane (1.22 g, 4.64 mmol) in CH₂Cl₂ (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 CH₂Cl₂ 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/CH₂Cl₂). ¹H NMR $(500 \text{ MHz}, \text{CDCl}_3)$: $\delta = 3.41 \text{ (dddd}, J = 1.5, 1.5, 6.0, 6.0 \text{ Hz}, 2 \text{ H},$ NCH₂), 4.85 [ddt, J = 1.5, 10.2, 1.5 Hz, 1 H, CH=CH₂(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=CH₂), 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, PPh₃), 7.55–7.59 (m, 3 H, PPh₃), 7.74–7.79 (m, 6 H, PPh₃), 7.84–7.87 (m, 1 H, Ar) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 46.2 (CH₂), 116.1 (CH₂), 116.5 (CH), 121.9 (d, ${}^{3}J_{P,C} = 11$ Hz, CH), 129.0 (d, ${}^{3}J_{P,C}$ = 12 Hz, 6 CH), 129.2 (d, ${}^{1}J_{P,C}$ = 100 Hz, 3 C), 129.5 (d, ${}^{4}J_{P,C}$ = 3 Hz, CH), 130.2 (d, ${}^{2}J_{P,C}$ = 24 Hz, 1 C), 132.3 (d, ${}^{4}J_{P,C}$ = 2 Hz, 3 CH), 132.4 (d, ${}^{2}J_{P,C}$ = 10 Hz, 6 CH), 132.7 (CH), 133.8 (CH), 148.9 (C) ppm. IR (KBr): $\tilde{v} = 1155, 1335, 1464, 1585, 3055,$ 3174 cm^{-1} . HRMS (ESI): calcd. $C_{27}H_{26}N_2O_2PS [M + H]^+$: 473.1447; found 473.1444. C27H25N2O2PS (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 μ L, 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 CH₂Cl₂ (5 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried with MgSO₄, 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/CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ = 2.22 (dt, *J* = 6.7, 6.7 Hz, 2 H, CH₂), 3.79 (t, *J* = 6.6 Hz, 2 H, NCH₂), 4.80 [d, *J* = 17.2 Hz, 1 H, CH=CH₂ (*trans*)], 4.84 [d, *J* = 10.1 Hz, 1 H, CH=CH₂ (*cis*)], 5.59 (ddt, *J* = 10.1, 17.2, 6.6 Hz, 1 H, CH=CH₂), 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. ¹³C NMR (75 MHz, CDCl₃): δ = 33.7 (CH₂), 46.9 (CH₂), 118.7 (CH₂), 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{v} = 1173, 1335, 1574, 1613, 3363 cm⁻¹. HRMS (ESI): calcd. C₁₇H₁₇N₃NaO₂S [M + Na]⁺: 350.0934; found 350.0935.

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 $C_{17}H_{17}N_3O_2S$ (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 CH₂Cl₂ (3 mL). After being stirred for 30 min, the reaction mixture was quenched with saturated aqueous Na₂SO₃ (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 MgSO₄, 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 $(37 \ \mu L, 0.34 \ mmol)$ was added at room temperature to a stirred solution of 4B (150 mg, 0.31 mmol) in (CH₂Cl)₂ (3 mL). The mixture was heated at reflux for 3 h and cooled to room temperature, and then K₂CO₃ (128 mg, 0.92 mmol) and I₂ (234 mg, 0.92 mmol) were added. After being stirred for 30 min, the reaction mixture was quenched with saturated aqueous Na₂SO₃ (2 mL). The organic layer was separated, and the aqueous layer was extracted with Ac-OEt (5 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried with MgSO₄, 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/CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ = 2.43–2.57 (m, 1 H, CH₂), 2.70 (dddd, *J* = 4.3, 4.4, 4.4, 14.1 Hz, 1 H, CH₂), 3.23 (ddd, *J* = 0.6, 10.4, 10.4 Hz, 1 H, CH₂I), 3.43 (ddd, *J* = 1.0, 3.4, 10.4 Hz, 1 H, CH₂I), 3.97–4.12 (m, 3 H, NCH, NCH₂), 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. ¹³C NMR (75 MHz, CDCl₃): δ = 5.6 (CH₂), 27.2 (CH₂), 36.1 (CH₂), 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{v} = 569, 690, 1144, 1182, 1329, 1535 cm⁻¹. C₁₇H₁₆IN₃O₂S (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-1H-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/CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): 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, NCH₂), $3.17 (dd, J = 8.8, 10.6 Hz, 1 H, CH_2I), 3.43 (dd, J = 2.8, 10.6 Hz, 10.6 Hz)$ 1 H, CH₂I), 3.70 (ddd, J = 6.9, 9.3, 14.3 Hz, 1 H, NCH₂), 3.88 (dd, J = 5.3, 9.7 Hz, 1 H, NCH₂), 3.94–4.00 (m, 1 H, NCH), 4.18 (dd, *J* = 8.5, 9.7 Hz, 1 H, NCH₂), 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. ¹³C NMR (125 MHz, CDCl₃): δ = 5.5 (CH₂), 11.2 (CH₃), 20.5 (CH₂), 44.1 (CH₂), 45.3 (CH₂), 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): $\tilde{v} = 579, 1180, 1304, 1581, 1635 \text{ cm}^{-1}$. HRMS (ESI): calcd. $C_{13}H_{16}IN_3NaO_2S [M + Na]^+: 427.9900; found 427.9918.$ C₁₃H₁₆IN₃O₂S (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/ CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ = 1.85–2.12 (m, 3 H, CH₂), 2.37 (s, 3 H, CH₃), 2.33–2.46 (m, 1 H, CH₂), 3.28 (dd, *J* = 12.4, 12.4 Hz, 1 H, NCH₂), 3.73–3.80 (m, 2 H, CH₂I), 4.26–4.38 (m, 2 H, NCH, NCH₂), 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. ¹³C NMR (150 MHz, CDCl₃): δ = 3.8 (CH₂), 21.0 (CH₃), 23.1 (CH₂), 28.4 (CH₂), 47.8 (CH₂), 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{v} = 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. C₁₉H₂₀IN₃O₂S [M]⁺: 481.0321; found 481.0314. C₁₉H₂₀IN₃O₂S (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-1H-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/CH₂Cl₂). ¹H NMR (600 MHz, CDCl₃): δ = 3.31 (dd, J = 9.7, 9.7 Hz, 1 H, CH₂I), 3.41 (dd, J = 2.7, 10.4 Hz, 1 H, CH₂I), 3.80 (dd, J = 4.8, 14.4 Hz, 1 H, CH₂), 4.17 (dd, J = 9.9, 14.3 Hz, 1 H, CH₂), 4.45– 4.54 (m, 2 H, CH₂), 4.65–4.70 (m, 1 H, CH), 5.25 [dd, J = 0.6, 10.3 Hz, 1 H, CH=C $H_2(cis)$], 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. ¹³C NMR (150 MHz, CDCl₃): $\delta = 6.5$ (CH₂), 45.9 (CH₂), 58.1 (CH₂), 58.7 (CH), 112.4 (CH), 118.8 (CH₂), 121.7 (CH), 123.5 (CH), 124.1 (C), 131.8 (CH), 134.6 (CH), 134.8 (C), 150.1 (C) ppm. IR (KBr): $\tilde{v} = 581, 752, 1173, 1182, 1342, 1645,$ 2939 cm⁻¹. LRMS-EI: m/z = 403 (38) [M]⁺, 338 (39), 212 (100), 171 (48), 170 (53), 41 (27). HRMS (EI): calcd. C₁₃H₁₄IN₃O₂S [M]+: 402.9851; found 402.9844. C13H14IN3O2S (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 CH₂Cl₂ (3 mL). After the system had been stirred for 2 h, aqueous NaOH (3 M, 3 drops) and aqueous NaBH₄ (9 mg, 0.2 mmol, in 1 mL) were added to form Hg⁰. 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 Ac-OEt/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 μ L, 0.28 mmol) was added to a stirred solution of 4B (122 mg, 0.25 mmol) in (ClCH₂)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 NaBH₄ (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/CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ = 1.25 (dd, *J* = 0.6, 6.6 Hz, 3 H, Me), 2.05–2.15 (m, 1 H, CH₂), 2.34–2.47 (m, 1 H, CH₂), 3.94–4.14 (m, 3 H, NCH, NCH₂), 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. ¹³C NMR (75 MHz, CDCl₃): $\delta = 19.8$ (CH₃), 29.6 (CH₂), 36.5 (CH₂), 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): $\tilde{v} = 567, 760, 1151, 1331, 1531$ cm⁻¹. C₁₇H₁₇N₃O₂S (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/CH₂Cl₂). ¹H NMR (300 MHz, CDCl₃): δ = 1.38 (d, *J* = 6.6 Hz, 3 H, Me), 3.82 (dd, *J* = 6.6, 9.0 Hz, 1 H, NCH₂), 4.30 (dd, *J* = 8.6, 9.0 Hz, 1 H, NCH₂), 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. ¹³C NMR (75 MHz, CDCl₃): δ = 18.5 (CH₃), 45.5 (CH₂), 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), 130.4 (1581, 1628 cm⁻¹. C₁₆H₁₅N₃O₂S (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/CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): $\delta = 1.56$ (d, J = 6.9 Hz, 3 H, CH₃), 1.80-1.87 (m, 1 H, CH₂), 1.89-1.98 (m, 2 H, CH₂), 2.09-2.20 (m, 1 H, CH₂), 3.42–3.54 (m, 1 H, NCH₂), 4.18–4.30 (m, 1 H, NCH₂), 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. ¹³C NMR (125 MHz, CDCl₃): $\delta = 18.6 \text{ (CH}_3), 23.9 \text{ (CH}_2), 32.1 \text{ (CH}_2), 48.0 \text{ (CH}_2), 59.1 \text{ (CH}),$ 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): $\tilde{v} = 1180, 1335, 1558 \text{ cm}^{-1}$. HRMS (ESI): calcd. C₁₈H₂₀N₃O₂S [M + H]⁺: 342.1271; found 342.1276. C₁₈H₁₉N₃O₂S (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-1H-imidazo[2,1-c][1,2,4]benzothiadiazine 5,5-Dioxide (15A): Colorless oil. Yield 191 mg (86%) from **7Ae** (166 mg). ¹H NMR (300 MHz, CDCl₃): δ = 1.43 (d, J = 6.2 Hz, 3 H, CH₃), 3.60 (dd, J = 5.6, 13.8 Hz, 1 H, CH₂), 4.15 (dd, *J* = 10.0, 13.8 Hz, 1 H, CH₂), 4.51 (dd, *J* = 1.2, 5.7 Hz, 2 H, CH₂), 4.50–4.64 (m, 1 H, CH), 5.24 [dd, J = 0.8, 10.3 Hz, 1 H, CH=C $H_2(cis)$], 5.36 [dd, J = 1.1, 17.1 Hz, 1 H, CH=C $H_2(trans)$], 6.03 (ddt, J = 10.3, 17.1, 5.5 Hz, 1 H, CH=CH₂), 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. ¹³C NMR (75 MHz, CDCl₃): δ = 19.1 (CH₃), 45.4 (CH₂), 54.5 (CH), 58.6 (CH₂), 112.7 (CH), 118.2 (CH₂), 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): $\tilde{v} = 756$, 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 CH₂Cl₂ (3 mL). After being stirred for 24 h, the reaction mixture was quenched with saturated aqueous Na₂SO₃ (2 mL). The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (5 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried with MgSO₄, 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-8λ⁶-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/CH₂Cl₂). ¹H NMR (600 MHz, CDCl₃): δ = 1.46–1.52 (m, 1 H, CH₂), 1.64– 1.75 (m, 3 H, CH₂), 1.77–1.85 (m, 1 H, CH₂), 2.11–2.18 (m, 1 H, CH₂), 3.21-3.27 (m, 1 H, NCH₂), 3.61-3.67 (m, 1 H, NCH₂), 3.96 $(dd, J = 9.1, 9.1 Hz, 1 H, NCH_2), 4.21 (dd, J = 1.0, 9.2 Hz, 1 H,$ NCH₂), 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. ¹³C NMR (150 MHz, CDCl₃): δ = 17.7 (CH₂), 28.8 (CH₂), 29.0 (CH₂), 41.1 (CH₂), 50.4 (CH₂), 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): $\tilde{v} = 602$, 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 (ClCH₂)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 Na₂SO₃ (2 mL). The organic layer was separated, and the aqueous layer was extracted with CH₂Cl₂ (5 mL). The combined organic extracts were washed with water (5 mL) and brine (5 mL), dried with MgSO₄, 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/CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): δ = 1.35–1.47 (m, 2 H, CH₂), 1.48– 1.58 (m, 1 H, CH₂), 1.68–1.80 (m, 3 H, CH₂), 3.07–3.14 (m, 2 H, CH₂I), 3.81 (dd, *J* = 6.4, 9.4 Hz, 1 H, NCH₂), 4.22 (dd, *J* = 9.4, 9.4 Hz, 1 H, NCH₂), 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. ¹³C NMR (125 MHz, CDCl₃): δ = 6.0 (CH₂), 24.9 (CH₂), 31.1 (CH₂), 32.4 (CH₂), 48.0 (CH₂), 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{v} = 1119, 1288 cm⁻¹. HRMS (ESI): calcd. C₁₉H₂₀IN₃NaO₂S [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]ben-zothiadiazine 5,5-Dioxide (20b):** M.p. 138–139 °C (hexane/CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃): $\delta = 1.71-1.94$ (m, 4 H, CH₂), 3.10 (t, *J* = 6.4 Hz, 2 H, CH₂I), 3.91 (dd, *J* = 6.2, 9.4 Hz, 1 H, NCH₂), 4.28 (dd, *J* = 9.4, 9.4 Hz, 1 H, NCH₂), 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) H, Ar) ppm. ¹³C

NMR (75 MHz, CDCl₃): δ = 4.8 (CH₂), 27.9 (CH₂), 33.0 (CH₂), 43.4 (CH₂), 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{v} = 579, 1173, 1311, 1574, 1628 cm⁻¹. HRMS (ESI): calcd. C₁₈H₁₈IN₃NaO₂S [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} ($\lambda = 0.71073$ 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, $\beta = 93.8970(10)^\circ$, V = 1756.8(2) Å³, monoclinic, space group $P2_1/c$, Z = 4, T = 297(2) K, $\rho_{calcd.} = 1.404$ gcm⁻³, $\mu = 0.209$ 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 ¹³C NMR spectra for all new compounds and extended X-ray data of compound **18b**.

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