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Bromoallenes as Allyl Dication Equivalents in the Presence or Absence of Palladium(0): Direct Construction of Bicyclic Sulfamides Containing Five- to Eight-membered Rings by Tandem Cyclization of Bromoallenes

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Abstract: A highly regioselective synthesis of bicyclic sulfamides is described. Based on our recent discovery that bromoallenes can act as allyl dication equivalents in the presence of a palladium catalyst and alcohol, we investigated tandem cyclization of bromoallenes bearing a sulfamide group. It is found that some bromoallenes act as allyl dication equivalents even in the absence of a palladium(0) catalyst to afford cyclosulfamides containing five- or six-membered rings. While the palladium-free cyclization is dependent on the substrate structure affording the bicyclic sulfamides through the first cyclization onto the proximal or central carbon atom of the bromoallenes, the palladium-catalyzed reaction strongly promotes the first cyclization onto the central allenic carbon atom to afford bicyclic sulfamides containing a seven- or eight-membered ring. Formation of two types of bicyclic sulfamides from single bromoallenes by simply changing the reaction conditions is also described.

Keywords: allenes · cyclization · heterocycles · palladium · tandem reactions

Introduction

Cyclic sulfamides are an extremely important class of compounds, the structural motifs of which exist in many pharmaceutically useful compounds. It is well documented that cyclic sulfamides are general templates suitable for the design of inhibitors such as HIV[1] and serine protease,[2] and other biologically useful compounds[3] like conformationally restricted, nonhydrolyzable peptidomimetics.[4] As well as their evident importance in the pharmaceutical point of view, some cyclic sulfamides have also been used as effective chiral auxiliaries in asymmetric aldol reactions,[5] condensing agents between alcohols and carboxylic acids or amides in Mitsunobu-like reactions,[6] and useful building blocks within the field of supramolecular chemistry.[7]

In spite of the evident utility of sulfamides, some existing routes for their synthesis are not an ideal process. For example, typical procedures described in previous work for the synthesis of cyclosulfamides rely upon the reaction of a diamine with sulfuryl chloride (SO_2Cl_2) or sulfamide ($H_2NSO_2NH_2$).[8,9] However, those approaches can be limited by the drastic reaction conditions, the formation of polycondensation side products, and the preparation of the diamine itself. Recently, the synthesis of cyclic sulfamides, including medium-ring ones, by ring-closing metathesis have also been reported.[10,11]

Currently, reactions of bromoallenes are attracting much interest due to their interesting chemical properties associated with the cumulated double bonds and bromine substituent.[12] However, except for our recent study on ring-forming reactions,[13,14] all the reactions of bromoallenes reported to date are intermolecular reactions.[15,16,17,18] In our previous work,[14] we found that bromoallenes **A** can act as allyl dication equivalents **B** in the presence of palladium(0) and alcohol, which are extremely useful for the synthesis of medium-

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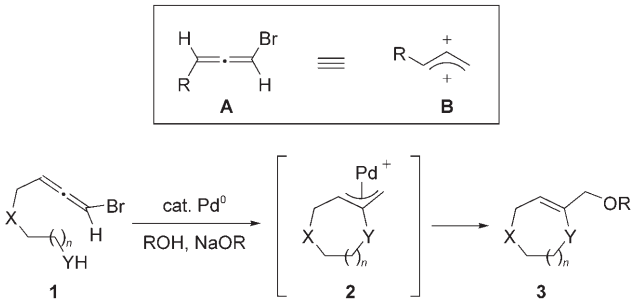
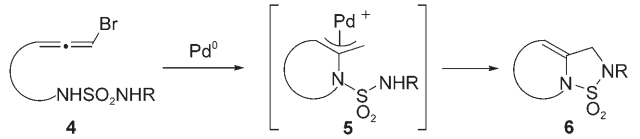
Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author. The Supporting Information contains the synthetic procedures and characterization for **7e**, **8d–8e**, **9b–i**, **19a–c**, **21b–c**, **24–28**, **36**, **37**, **43**, **51**, **52**, **65**, **78**, **79**, and **81**; and ^{1}H NMR spectra for all new compounds.

sized heterocycles (Scheme 1). Thus, reaction of bromoallene **1** with sodium alkoxide in the presence of a palladium(0) catalyst in alcohol affords η^3-allylpalladium(II) intermediate **2** by intramolecular nucleophilic attack at the central carbon atom of the allenic moiety. A second nucleophilic reaction with alkoxide provides **3** in good to high yields. In light of this chemistry, we planned a novel synthesis of bicyclic sulfamides **6** by tandem cyclization of bromoallenes **4** through η^3-allylpalladium(II) intermediate **5** (Scheme 2).



Scheme 1. Palladium(0)-catalyzed medium-ring formation from bromoallenes.

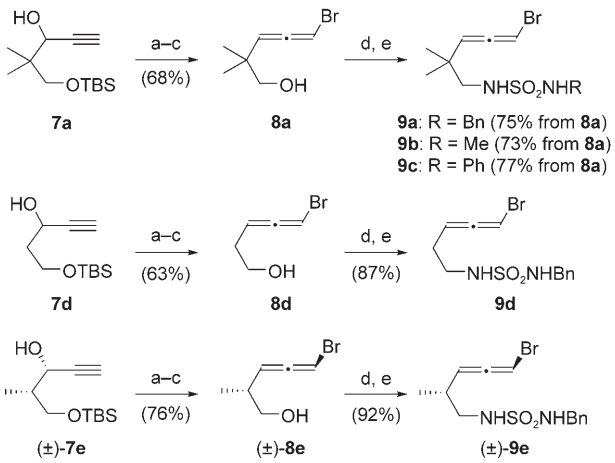


Scheme 2. Synthesis of bicyclic sulfamides.

Herein we describe a highly regioselective construction of bicyclic sulfamides containing five- to eight-membered rings by using bromoallenes that have a sulfamide moiety as nucleophile. Particularly notable is that highly reactive bromoallenes which form five- or six-membered rings in the first cyclization require no palladium catalyst, affording bicyclic sulfamides in high yields.[19] Formation of two types of bicyclic sulfamides from single bromoallenes with a four- or five-atom tether between the sulfamide and bromoallene by simply changing the reaction conditions is also described.

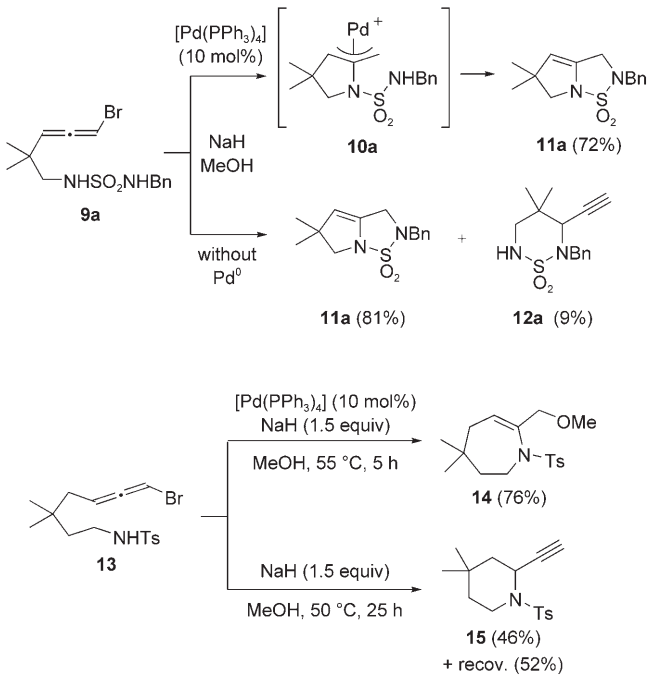
Results and Discussion

Synthesis of bromoallenes bearing a sulfamide group: To investigate the synthesis of bicyclic sulfamides by tandem cyclization of bromoallenes as depicted in Scheme 2, bromoallenes **9**, bearing a sulfamide moiety as nucleophile, were prepared from propargyl alcohols **7** as shown in Scheme 3. Propargyl alcohol **7a**[20] was easily obtained from the corresponding monoprotected diol by oxidation and alkynylation. Treatment of **7a** with MsCl and Et_3N gave the corresponding mesylate, which was then converted to bromoallenol **8a** by the reaction with $CuBr{\cdot}SMe_2$/LiBr[21] followed by desilylation. Condensation of **8a** with $BocNHSO_2NHBn$[22] (Boc = 1,1-dimethylethoxycarbonyl) under the Mitsunobu conditions gave the corresponding *N*-Boc bromoallene, the Boc group of which was removed with 3 N HCl to afford the desired bromoallene **9a** with a benzyl group on the terminal nitrogen atom. Similarly, bromoallene **9b** with a methyl group on the terminal nitrogen atom and **9c** with a phenyl group were prepared from the bromoallenol **8a** by the reaction with $BocNHSO_2NHMe$[22] or $BocNHSO_2NHPh$,[22] respectively. According to this procedure, bromoallenes **9d** and (±)-**9e** were similarly prepared from the corresponding propargyl alcohols **7d**[23] and (±)-**7e**,[24] respectively. Other bromoallenes with a sulfamide group were synthesized in a straightforward manner by use of a similar protocol (see the Supporting Information).



Scheme 3. Synthesis of bromoallenes **9** bearing a sulfamide group. Reagents: a) MsCl, Et_3N; b) $CuBr{\cdot}SMe_2$, LiBr; c) 1% HCl/EtOH; d) $BocNHSO_2NHR$, PPh_3, DEAD; e) 3 N HCl, EtOAc.

Formation of cyclic sulfamides containing a bicyclo[3.3.0]octane skeleton: We first investigated the tandem cyclization of the bromoallene **9a** in the presence of palladium(0). To realize the desired cyclization, selective addition of the internal sulfamide nitrogen atom onto the central allenic carbon atom followed by advantageous reaction of the terminal sulfamide nitrogen over that of alkoxide is essential. As we expected, cyclization of the bromoallene **9a** gave bicyclic sulfamide **11a** (72% yield) as the sole isolable product (Scheme 4), presumably through the intermediate **10a**. Surprisingly, the same reaction also proceeded in the absence of palladium(0) to afford **11a** in better yield (81%) along with a small amount of six-membered ring **12a** (9%), although prolonged reaction time was required. These results demonstrate that bromoallene **9a** can act as allyl dication equivalent even in the absence of palladium(0). However, it should be clearly noted that, in the medium-ring formation,[14] the palladium catalyst is essential for successful conversion. For example, treatment of bromoallene **13** with in situ-generated NaOMe in the presence of $[Pd(PPh_3)_4]$ gave the seven-membered ring **14**[14c] in 76% yield, as a



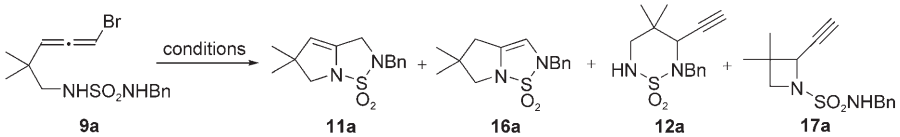
Scheme 4. Cyclization of bromoallenes in the presence or absence of palladium(0).

result of the first intramolecular nucleophilic attack on the central carbon atom of the allene moiety followed by the second nucleophilic reaction by methoxide. However, treatment of the bromoallene **13** with NaH in MeOH in the absence of $[Pd(PPh_3)_4]$ gave the six-membered ring **15** in 46% yield by the S_N2'-type intramolecular nucleophilic attack on the proximal carbon atom of the allene moiety. Thus, the reaction of bromoallenes as an allyl dication in the absence of a palladium catalyst can be applied to highly reactive bromoallenes that easily form the cyclized products such as five-membered rings.

Next, we investigated the cyclization of bromoallene **9a** under some other reaction conditions (Table 1). Treatment of **9a** with Cs_2CO_3 in DMF gave six-membered ring **12a** as a major product, along with the bicyclic sulfamide **11a** (34% yield, entry 2). A similar result was obtained using NaH in DMF, but a small amount of azetidine **17a** (20% yield) was also obtained in this case (entry 3). The reaction of **9a** with K_2CO_3 in MeOH at 60°C gave the bicyclic sulfamide **11a** in 84% yield and monocyclic sulfamide **12a** in 9% yield (entry 4), which is a comparable result to that obtained with NaH/MeOH (entry 1). On the other hand, the reaction of **9a** with lithium diisopropylamide (LDA; 2.5 or 5.0 equiv) in THF at low temperature gave the azetidine **17a** as the sole product in poor yields (2% and 18% yield, respectively, entries 6 and 7). Furthermore, we investigated the reaction of **9a** using tetrabutyl ammonium fluoride (TBAF) in THF to obtain the bicyclic sulfamide **16a** in high yield (92%, entry 8).[25] From these observations, it has been proven that the bromoallene **9a** can effectively act as allyl dication equivalents under appropriate basic conditions such as base/MeOH or TBAF/THF even in the absence of palladium(0).

We next investigated the palladium-free tandem cyclization reaction using various bromoallenes under two reaction conditions (conditions A: NaH in MeOH at 60°C; conditions B: TBAF in THF at 60°C). The results of the cyclization are summarized in Table 2. As we expected, treatment of the bromoallene **9b**, which has a methyl group on the terminal nitrogen atom, gave bicyclic sulfamide **11b** as the major product (65% yield) along with a small amount of monocyclic six-membered ring **12b** (10% yield) under the conditions A (entry 1). On the other hand, under the conditions B, the bromoallene **9b** was converted into the isomerized bicyclic sulfamide **16b** (41%) and the six-membered ring **12b** (56%) in lower selectivity (entry 2). Exposure of the bromoallene **9c**, which has an aniline moiety as the second nucleophile, to conditions A afforded six-membered ring **12c** as a major product (50%, entry 3). This is presumably due to the highly acidic nature of the aniline proton. When the bromoallene **9d**, which has an unsubstituted carbon tether, was allowed to react under conditions A, bi-

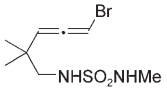
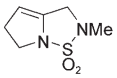
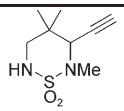
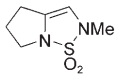
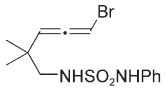
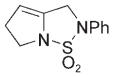
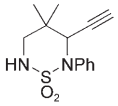
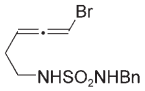
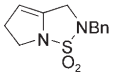
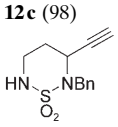
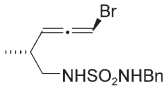
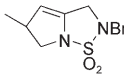
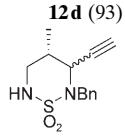
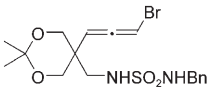
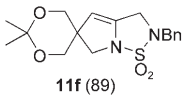
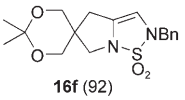
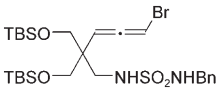
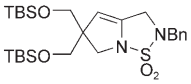
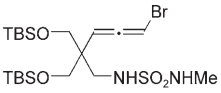
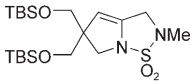
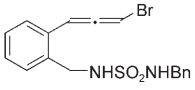
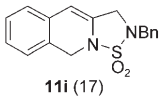
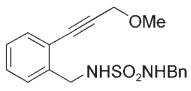
Table 1. Palladium-free cyclization of bromoallene **9a** under various reaction conditions.[a]



Entry	Base	Solvent	T [°C]	t [h]	Yield [%][b] 11a	16a	12a	17a	Recov. [%]
1	NaH	MeOH	60	16	81		9		
2	Cs_2CO_3	DMF	RT	2.5	34		56		10
3	NaH	DMF	RT	2	25		54	20	
4	K_2CO_3	MeOH	60	22	84		9		
5	NaH	THF	RT	6	68			10	
6	LDA	THF	−78 to RT	4				2	67
7[c]	LDA	THF	−78 to RT	8				18	17
8	TBAF	THF	60	1		92			

[a] 2.5 equivalents of base were used. [b] Yields of isolated products. [c] 5.0 equivalents of a base were used.

Table 2. Synthesis of bicyclic sulfamide in the absence of palladium(0).[a]

Entry	Substrate	Conditions[a]	t [h]	Product (Yield [%][b])	
1	 **9b**	A	12	 **11b** (65)	 **12b** (10)
2	**9b**	B	1	 **16b** (41)	**12b** (56)
3	 **9c**	A[c]	24	 **11c** (27)	 **12c** (50)
4	**9c**	B	1		**12c** (98)
5	 **9d**	A	12	 **11d** (50)	 **12d** (24)
6	**9d**	B	1		**12d** (93)
7	 (±)-**9e**	A	10	 **11e** (57)	 **12e** (3,4-*trans*: 9) **12e'** (3,4-*cis*: 5)
8	 **9f**	A	6	 **11f** (89)	
9	**9f**	B	1	 **16f** (92)	
10	 **9g**	A	4.5	 **11g** (91)	
11	 **9h**	A	2	 **11h** (95)	
12	 **9i**	A	19	 **11i** (17)	 **18i** (15)
13	**9i**	B[d]	0.25	**11i** (54)	

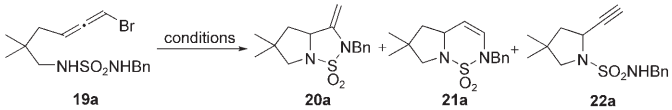
[a] Conditions A: NaH (2.5 equiv), MeOH, 60 °C; Conditions B: TBAF (2.5 equiv), THF, 60 °C, unless otherwise noted. [b] Yields of isolated products. [c] Heated to reflux. [d] Reaction occurred at RT.

cyclic sulfamide **11d** was isolated (50%) along with six-membered ring **12d** (24%; entry 5). Similarly, under conditions A, bicyclic sulfamide **11e** as well as a small amount of six-membered ring (±)-**12e** and (±)-**12e′** (entry 7) were obtained by the reaction of the bromoallene (±)-**9e**, which has a mono-methyl substituent on the carbon atom between the allenyl and sulfamide groups.[26] In sharp contrast, reaction of bromoallenes **9c** and **9d** under the conditions B (entries 4 and 6) afforded six-membered rings **12c** and **12d** selectively in high yields (98% and 93%, respectively). Treatment of the bromoallene **9f**, which has a quaternary carbon center in the carbon tether, gave a tricyclic sulfamide **11f** in 89% yield as the sole isolable product (entry 8). Similarly, the bromoallenes **9g** and **9h** were converted into a bicyclic sulfamide **11g** (91% yield) and **11h** (95% yield) as a single product (entries 10 and 11). Under the conditions B, the bromoallene **9f**, which contains a protected diol, was effectively converted into the isomerized sulfamide **16f** in 92% yield (entry 9). It is worth noting that the bromoallene **9i**, with a phenyl substituent on the three-atom tether between the allenyl and sulfamide groups, was converted into tricyclic sulfamide **11i**[27] in 17% and 54% yield by exposure to the conditions A (entry 12) or B (entry 13), respectively. This is in striking contrast to the results obtained with bromoallenes **19a–c**, bearing a saturated three-atom carbon tether (vide infra), which exclusively form a five-membered ring on the first cyclization.[28] Under the conditions A (entry 12), 15% of alkyne **18i** was also produced as a side product.[29]

From these observations, the conditions A (NaH/MeOH) afforded the desired bicyclic sulfamides **11** in moderate to good selectivities, while the product distribution under the conditions B (TBAF/THF) is highly dependent on the structure of the starting bromoallenes.

Next, we investigated the synthesis of cyclic sulfamide using bromoallene **19a**, which has a three-atom tether between the sulfamide and bromoallene, under the same reaction conditions. Interestingly, the first cyclization regioselectively occurred at the allenic carbon close to the sulfamide group to give **20a** (66%) and **21a** (18%) (Table 3, entry 1).[30] Treatment of **19a** with NaH in DMF[31c] afforded cyclized products **20–22a** in low selectivity (entry 2). Exposure of **19a** to *t*BuOK/THF or pyridine afforded no cyclized product (entries 3 and 4); however,

Table 3. Palladium-free cyclization of bromoallene **19a**, which has a three-atom tether between the sulfamide and bromoallene, under various reaction conditions.[a]



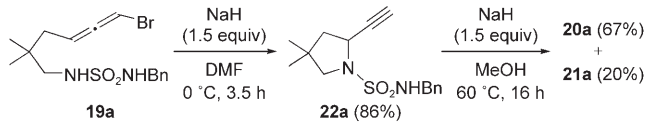
19a **20a** **21a** **22a**

Entry	Base	Solvent	t [h]	Yield [%][b] **20a**	**21a**	**22a**
1	NaH	MeOH	20[c]	66	18	
2	NaH	DMF	6[d]	29	26	11
3	*t*BuOK	THF	2.5	decomp		
4	pyridine	pyridine	15	decomp		
5	TBAF	THF	3	77	18	
6	$(C_4H_9)_4NOH$	THF	2.5	72	13	

[a] Reactions were carried out with a base (2.5 equiv) under reflux. [b] Yields of isolated products. [c] The reaction was conducted at 60 °C. [d] The reaction was conducted at 50 °C.

quaternary ammonium salts such as TBAF (entry 5)[31b] or $(C_4H_9)_4NOH$ (entry 6) gave better results affording **20a** in 72–77% yields along with **21a** (13–18%).

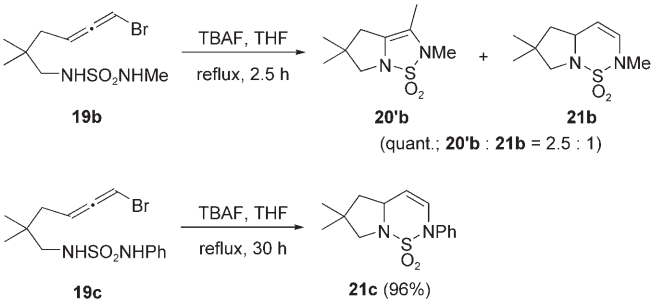
To reveal the intermediate of this tandem cyclization reaction, we investigated stepwise reaction (Scheme 5). Treatment of the bromoallene **19a** with NaH in DMF at 0 °C gave pyrrolidine **22a** in 86% yield. Reaction of **22a** under the reaction conditions shown in entry 1 (Table 3) afforded the *exo*-cyclized product **20a** (67%) and *endo*-cyclized product **21a** (20%) in the essentially same product ratio as the one-pot reaction. These results strongly suggest that the alkyne **22** is a plausible intermediate of the tandem cyclization.[31]



19a **22a** (86%)

Scheme 5. Stepwise reaction of bromoallene **19a**.

Next, we investigated the base-induced tandem cyclization of bromoallenes **19b** and **19c** (Scheme 6). As we expected, the reaction of bromoallene **19b**, which has a methyl group on the terminal nitrogen atom, gave two types of bicyclic sulfamides (quant.; **20′b**/**21b** = 2.5:1).[32,33] It is remarkable that exposure of the bromoallene **19c**, which has an aniline moiety as the second nucleophile, to the same reaction conditions afforded bicyclic sulfamide **21c** as the sole product in 96% yield, through exclusive 6-*endo* reaction on the second cyclization.



19b **20′b** **21b**

19c **21c** (96%)

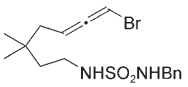
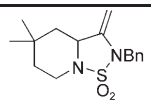
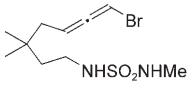
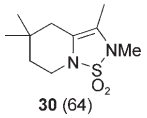
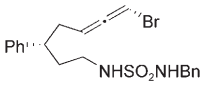
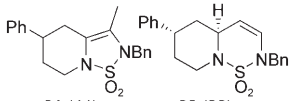
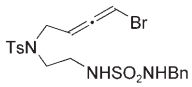
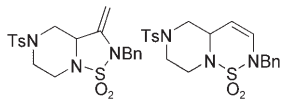
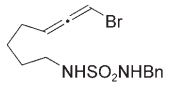
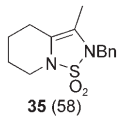
Scheme 6. Base-induced tandem cyclization of bromoallenes **19**, with a three-atom tether between the sulfamide and bromoallene.

The results shown in Table 2 and Scheme 6 revealed that the base-induced cyclization of bromoallenes in the absence of palladium(0) favors five-membered ring formation on the first cyclization, except for the phenylallene derivative **9i**: the bromoallenes **9** that have a two-atom tether prefer the first cyclization onto the central carbon of the allene, while the bromoallenes **19** with a three-atom tether easily undergo S_N2'-type cyclization on the proximal allenic carbon.

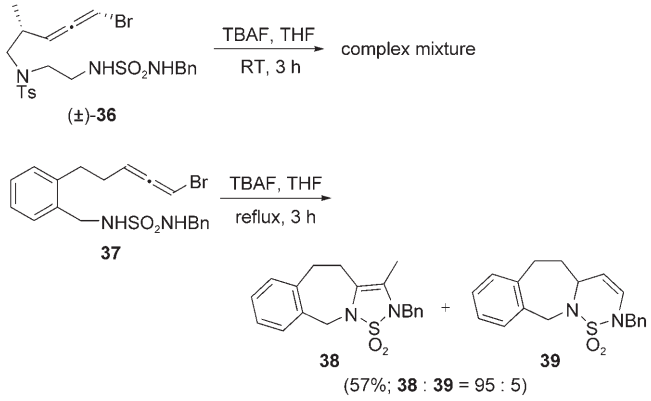
Formation of cyclic sulfamides containing a bicyclo[4.3.0]nonane skeleton: We next investigated the palladium-free cyclization of bromoallenes that have a four-atom tether between the sulfamide and bromoallene (Table 4). Treatment of **24**, which has a benzyl group on the terminal nitrogen atom, with NaH in MeOH gave the bicyclic sulfamide **29** with a bicyclo[4.3.0]nonane skeleton in 79% yield (entry 1). This cyclization would proceed through an alkyne intermediate followed by intramolecular amination of the triple bond.[34] In the reaction of **25**, which has a methyl group on the terminal nitrogen atom, with NaH and MeOH, a mixture of double bond regioisomers was obtained in variable ratios. However, we observed exclusive formation of the isomerized product **30** in 64% yield by washing the diluted reaction mixture with 4% HCl (entry 2). Compound **30** was presumably produced by acid-catalyzed isomerization of the exomethylene of the cyclized product of the type **29** (entry 1). Bromoallene **26**, which has a mono-substituted carbon tether, afforded **31** in 44% yield (entry 3) along with **32**,[35] which has a bicyclo[4.4.0]decane skeleton (20% yield), produced by 6-*endo* cyclization of the alkyne intermediate. The reaction of **26** with TBAF in THF gave a better combined yield of the bicyclic sulfamides **31** and **32** (90%), but the *exo*/*endo* selectivity on the second cyclization was lower (entry 4). Similarly, the reaction of **27**, which has a tosylamide tether, with TBAF yielded the corresponding bicyclic sulfamides **33** and **34** with a piperazine skeleton in 41 and 13% yield, respectively.[36] When the bromoallene **28**, which has an unsubstituted carbon tether, was used, bicyclic sulfamide **35** was obtained in 58% yield (entry 6).

An important limitation of the palladium-free cyclization is shown in Scheme 7. The reaction of bromoallene **36**, which has a five-atom tether, under the same reaction conditions afforded a complex mixture of unidentified compounds, without isolating the desired cyclosulfamide with a bicyclo[5.3.0]decane skeleton. However, the palladium-free tandem cyclization of bromoallene **37**, which has a phenylring tether, with TBAF afforded cyclic sulfamides **38** and **39**[37] containing a seven-membered ring in 57% yield. From these results, we found that the palladium-free tandem cyclization of bromoallenes is useful for the synthesis of cyclic

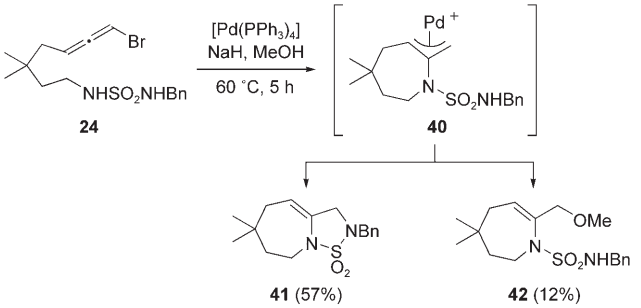
Table 4. Palladium-free tandem cyclization of bromoallenes having a four-atom tether between the sulfamide and bromoallene.[a]

Entry	Substrate	Conditions	Product (Yield [%][b])
1	 **24**	NaH/MeOH 60 °C, 24 h	 **29** (79)
2[c]	 **25**	NaH/MeOH 60 °C, 20 h	 **30** (64)
3	 (±)-**26**	NaH/MeOH reflux, 30 h	 **31** (44) **32** (20)
4	(±)-**26**	TBAF/THF reflux, 3 h	**31** (49), **32** (41)
5	 **27**	TBAF/THF RT, 8 h	 **33** (41) **34** (13)
6	 **28**	TBAF/THF 60 °C, 0.5 h	 **35** (58)

[a] All reactions were carried out with NaH/MeOH or TBAF/THF. [b] Yields of isolated products. [c] The reaction mixture was treated with 4% HCl before purification.



Scheme 7. Palladium-free tandem cyclization of bromoallenes with a five-atom tether between the sulfamide and bromoallene.



Scheme 8. Reaction of bromoallene **24** that has a four-atom tether between the sulfamide and bromoallene in the presence of palladium(0).

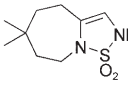
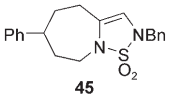
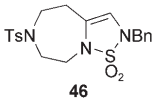
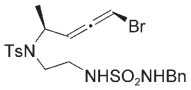
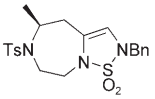
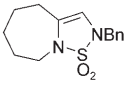
sulfamide containing five- to seven-membered rings, although the seven-membered-ring formation requires conformationally favorable bromoallenes such as **37**.

Palladium-catalyzed tandem cyclization of bromoallenes: Although the above-mentioned palladium-free reactions are extremely useful in that bromoallenes can act as allylic dication equivalents even in the absence of a palladium catalyst, this cyclization is limited to the highly reactive bromoallenes, which easily form cyclized products, and the product distribution and selectivity are dependent on the structure of the starting bromoallenes. We then turned our attention to the palladium-catalyzed reaction, which would facilitate the cyclization at the central carbon atom of allenes forming various cyclic products including medium-sized rings through η^3-allylpalladium(II) intermediate **5**, as depicted in Scheme 2.

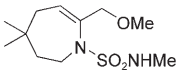
First, we investigated the palladium-catalyzed tandem cyclization reaction of bromoallene **24**, which has a four-atom tether between the sulfamide and bromoallene (Scheme 8). As we expected, treatment of the bromoallene **24** with NaH in MeOH in the presence of palladium(0) gave a bicyclic sulfamide **41**, which contains a seven-membered ring in 57% yield, along with 12% of monocyclized product **42** (Scheme 8). The η^3-allylpalladium intermediate **40** is considered as a plausible intermediate, which can be generated by intramolecular amination of the bromoallene moiety at the central carbon atom. Compared with the palladium-free reaction (Table 4, entry 1), it was proven that the palladium catalyst dramatically changes the cyclization mode, and two types of bicyclic sulfamides **29** and **41** can be selectively obtained from the single bromoallene **24** by simply changing the reaction conditions.

Then, we investigated the palladium-catalyzed cyclization of the same bromoallenes shown in Table 4. The results are summarized in Table 5. As we expected, treatment of bromoallene **25** with NaH/MeOH in the presence of [Pd(PPh_3)$_4$] (10 mol%) afforded the desired product **44** in 50% yield. Similarly, the reaction of all the other bromoallenes

Table 5. Cyclization of bromoallenes in the presence of a palladium catalyst.[a]

Entry	Substrate	Conditions	Product	Yield[b]
1	**25**	60 °C, 4 h then 4% HCl	 **44**	50[c]
2	(±)-**26**	55 °C, 2 h	 **45**	78
3[d]	(±)-**26**	55 °C, 2.5 h	**45**	70
4	**27**	60 °C, 2 h then 4% HCl	 **46**	48[e]
5	 **43**	60 °C, 1 h	 **47**	74
6	**28**	60 °C, 1 h	 **48**	28[f]

[a] Unless otherwise noted, reactions were carried out with $[Pd(PPh_3)_4]$ (10 mol%), NaH (2.5 equiv) in MeOH. [b] Yields of isolated products. [c] 18% of **49** was also obtained. [d] The reaction was carried out with $[Pd(PPh_3)_4]$ (5 mol%) at 55 °C. [e] 4% of **50** was also obtained. [f] Considerable amount of other unidentified products was also obtained.


49

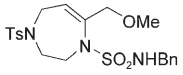
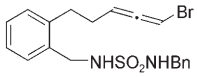
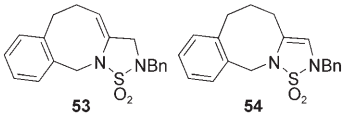
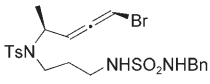
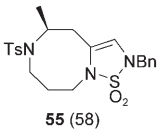
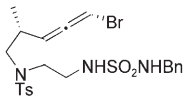
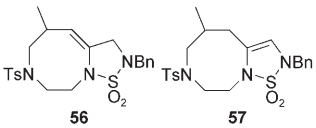
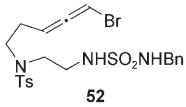

50

Table 6. Cyclization of bromoallenes in the presence of a palladium catalyst.[a]

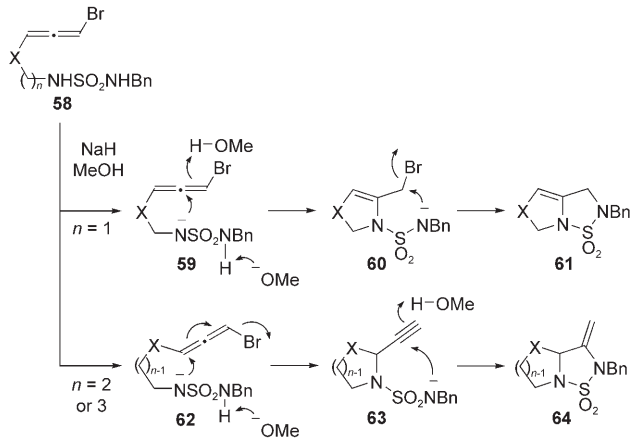
Entry	Substrate	*t* [h]	Product (Yield [%][b])
1	 **37**	1.5	 **53** **54** (57; **53**:**54** = 12:1)
2[c]	 **51**	3	 **55** (58)
3[c]	 (±)-**36**	6	 **56** **57** (52; **56**:**57** = 1:4)
4	 **52**	4	complex mixture

[a] All reactions were carried out with $[Pd(PPh_3)_4]$ (10 mol%), NaH (2.5 equiv) in MeOH at 60 °C. [b] Yields of isolated products. [c] The reaction mixture was treated with 4% HCl before purification.

26–**28** and **43** yielded bicyclic sulfamides **45**–**48** each containing a seven-membered ring. When the reaction was conducted with 5 mol% of $[Pd(PPh_3)_4]$ (entry 3), comparable yield (70%) of the desired bicyclic sulfamide **45** was obtained.[38] We could not isolate the bicyclo[4.3.0] rings from the reaction mixture, which can be formed by the uncatalyzed reaction under the same reaction conditions (Table 4). However, formation of a small amount of such six-membered rings cannot be ruled out. These results revealed that the palladium catalyst strongly promotes the first cyclization at the central carbon atom of the bromoallenes leading to bicyclic sulfamides having a seven-membered ring.

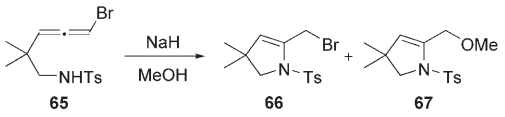
Next, the palladium-catalyzed cyclization of the bromoallenes that have a five-atom tether between the sulfamide and bromoallene was investigated. The results are summarized in Table 6. As we expected, the reaction of bromoallene **37**, which has a phenyl substituent on the carbon atom between the bromoallene and the sulfamide group, in the presence of Pd^0 gave tricyclic sulfamides **53** and **54** (**53**:**54** = 12:1), containing an eight-membered ring in moderate yield (57%) (entry 1). Under the same conditions, bromoallene **51**, bearing a mono-methyl substituent and a tosylamide on the five-atom tether between the bromoallene and sulfamide group, afforded the isomerized product **55** in 58% yield by washing the diluted reaction mixture with 4% HCl (entry 2).[39] Furthermore, the bromoallene **36** effectively yielded bicyclic sulfamides **56** and **57**, containing an eight-membered ring, although the acid treatment caused incomplete isomerization to **57** in this case (**56**:**57** = 1:4, entry 3). In contrast, the reaction of bromoallene **52**, lacking a monomethyl group, resulted in formation of a complex mixture in which the desired bicyclic compound was not isolated (entry 4). This result shows a limitation of the palladium-catalyzed tandem cyclization in eight-membered-ring formation: an appropriate substituent on the carbon tether between the bromoallene and the sulfamide group is required for effective cyclization.[40] However, the palladium catalyst completely controls the regioselectivity on the first cyclization onto the central carbon of the bromoallenes, which is in striking contrast to the base-induced tandem cyclization without a palladium catalyst favoring a five- or six-membered ring formation.

Mechanism of the cyclization: Possible reaction courses of the palladium-free cyclization are shown in Scheme 9. In the reaction of bromoallenes that have a two-atom tether between the sulfamide and bromoallene ($n=1$) without a palladium catalyst, the first intramolecular nucleophilic attack takes place at the central carbon of bromoallene **59** and is followed by protonation by MeOH to produce intermediate **60** bearing a bromomethyl group. The second intramolecular nucleophilic addition affords the bicyclic sulfamide **61**. This reaction pathway through the intermediate **60** is supported by the experimental results shown in Table 7: NaH-mediated cyclization of the bromoallene **65**, which has a tosylamide group, in MeOH at lower reaction temperature (entry 1) yielded dihydropyrrole **66** (8%), which has a bromomethyl group, with a considerable amount of the starting bromoal-



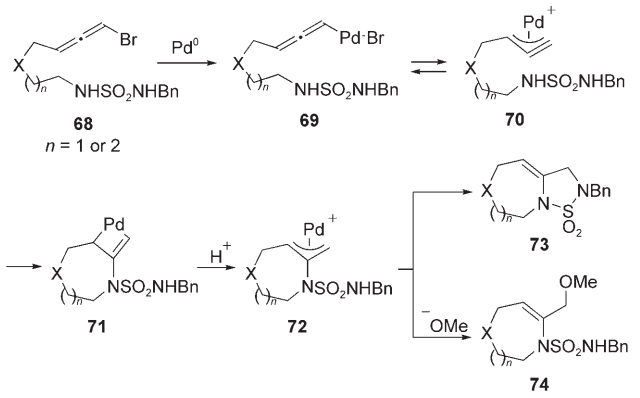
Scheme 9. Possible reaction courses of the palladium-free cyclization.

Table 7. Palladium-free reaction of bromoallene **65**.[a]

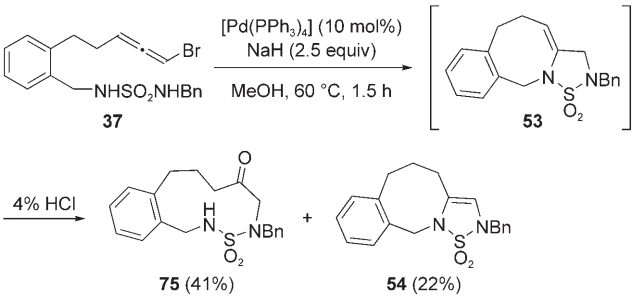


Entry	T [°C]	t [h]	Product	Yield [%][b]
1	RT	20	**66**	8[c]
2	60	7	**67**	94

[a] Reactions were carried out with NaH (1.5 equiv) in MeOH. [b] Yields of isolated products. [c] 71% of **65** was recovered.



Scheme 10. Possible reaction courses of the palladium-catalyzed tandem cyclization.



Scheme 11. Formation of macrocyclic sulfamide **75** through tandem cyclization and subsequent ring-expansion.

lene **65** (71%). In contrast, the same reaction at higher temperature (entry 2) gave the methoxymethyl derivative **67** in 94% yield, which was produced by the nucleophilic substitution of **66** with methoxide.[41]

In the palladium-free tandem cyclization of bromoallenes that have a three- or four-atom tether between the sulfamide and bromoallene ($n=2$ or 3), the first S_N2'-type intramolecular nucleophilic attack of the internal nitrogen at the proximal carbon of bromoallene **62** affords the alkyne intermediate **63** and is followed by intramolecular amination of the triple bond to give bicyclic sulfamide **64**.[31,34]

A possible reaction course for the palladium-catalyzed cyclization of bromoallenes is shown in Scheme 10. Oxidative addition of bromoallene **68** to Pd^0 gives η^1-allenylpalladium complex **69**, which is in a state of equilibrium with η^3-propargylpalladium complex **70**.[42] The first intramolecular nucleophilic addition occurs to the central carbon atom of η^3-propargylpalladium complex **70** to produce palladacyclobutene **71**.[43] This is followed by protonation by MeOH to generate η^3-allylpalladium complex **72**. In many cases, the second intramolecular nucleophilic addition by the terminal nitrogen predominates over that by methoxide to afford the bicyclic sulfamide **73** as the major product, along with a small amount of mono-cyclized product **74**.

It is worth noting that eleven-membered cyclosulfamide **75** as well as **54** were obtained in 41% yield when the bromoallene **37** was treated with NaH and $[Pd(PPh_3)_4]$ in MeOH followed by treatment with 4% HCl (Scheme 11). This reaction would proceed through acid-catalyzed hydrolysis of the relatively unstable tricyclic cyclosulfamide **53** (compare with entry 1, Table 6). This reaction clearly demonstrates the scope of the presented tandem cyclization as a potential tool for the synthesis of macrocyclic cyclosulfamides.

Conclusion

In conclusion, we have developed a novel cyclization of bromoallenes that have a sulfamide moiety as nucleophiles, leading to bicyclic sulfamides depending on the substrate structure and reaction conditions. Highly reactive bromoallenes act as allyl dication equivalents even in the absence of a palladium(0) catalyst to afford cyclosulfamides containing five- or six-membered rings. On the other hand, the palladium-catalyzed cyclization can be applied to a wide variety of bromoallenes and proceeds in a highly regioselective manner, to give bicyclic sulfamides containing a seven- or eight-membered ring. These two reactions of bromoallenes are extremely useful for the synthesis of bicyclic sulfamides and would extend the pharmacological and chemical potentiality of these compounds.

Experimental Section

General methods: Melting points are uncorrected. Nominal (LRMS) and exact mass (HRMS) spectra were recorded on a JEOL JMS-01SG-2 or JMS-HX/HX 110 A mass spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$. Chemical shifts are reported in parts per million downfield from internal Me_4Si (s = singlet, d = doublet, dd = double of doublets, ddd = doublet of doublets of doublets, t = triplet, q = quartet, m = multiplet). Optical rotations were measured in $CHCl_3$ with a JASCO DIP-360 digital polarimeter. For flash chromatography, silica gel 60 H (silica gel for thin-layer chromatography, Merck) or silica gel 60 (finer than 230 mesh, Merck) was employed.

1-Bromo-5-hydroxy-4,4-dimethylpenta-1,2-diene (8a): Methanesulfonyl chloride (2.2 mL, 28 mmol) was added to a stirred mixture of the propargylic alcohol **7a** (4.85 g, 20 mmol) and Et_3N (4.5 mL, 36 mmol) in CH_2Cl_2 (50 mL) at 0 °C under nitrogen, and the resulting mixture was stirred for 15 min at this temperature. The mixture was made acidic with 4% HCl, and the whole was extracted with Et_2O. The extract was washed with water, saturated $NaHCO_3$, water, and brine, and dried over $MgSO_4$. Usual workup followed by rapid filtration through a short pad of SiO_2 with Et_2O gave a crude mesylate, which was used without further purification. A mixture of CuBr·DMS (8.2 g, 40 mmol) and LiBr (3.5 g, 40 mmol) were dissolved in THF (30 mL) at room temperature under nitrogen. After stirring for 2 min, a solution of the above crude mesylate in THF (20 mL) was added to this reagent at room temperature. The mixture was stirred for 19 h at this temperature and 3 h at 50 °C, and quenched with saturated NH_4Cl and 28% NH_4OH. The whole was extracted with Et_2O. The extract was washed with water and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (8:1) to give the protected bromoallene as an oil. This oil was dissolved in a solution of 1% HCl in ethanol (35 mL), which was prepared from conc. HCl and EtOH, and the resulting mixture was stirred for 12 h at room temperature. Water was added to the mixture, and the whole was extracted with EtOAc. The extract was washed with brine and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (3:1) to give **8a** (2.6 g, 68% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.086 (s, 3H; CMe), 1.091 (s, 3H; CMe), 1.58 (br s, 1H; OH), 3.41 (d, J = 10.8 Hz, 1H; 5-C*H*H), 3.46 (d, J = 10.8 Hz, 1H; 5-CH*H*), 5.37 (d, J = 5.7 Hz, 1H; 3-H), 6.04 ppm (d, J = 5.7 Hz, 1H; 1-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.06, 24.11, 38.0, 71.4, 73.8, 107.8, 200.9 ppm; IR (KBr): $\tilde{\nu}$ = 3344 (OH), 1954 cm^{-1} (C=C=C); MS (FAB): m/z (%): 193 (15) [M^++H, ^{81}Br], 191 (10) [M^++H, ^{79}Br], 111 (100); HRMS (FAB): calcd for $C_7H_{11}BrNaO$ [M^++Na, ^{79}Br]: 212.9891; found: 212.9910.

***N*-Benzyl-*N*′-(5-bromo-2,2-dimethylpenta-3,4-dienyl)sulfamide (9a)**: A solution of the bromoallene **8a** (382 mg, 2.0 mmol) in THF (5 mL) and diethyl azodicarboxylate (1.57 g, 3.6 mmol; 40% in toluene solution) were added to a stirred solution of PPh_3 (944 mg, 3.6 mmol) and BocNH-SO_2NHBn (1.03 g, 3.6 mmol) in THF (12 mL) under nitrogen at 0 °C, and the resulting mixture was heated under reflux for 1.5 h. Concentration under reduced pressure gave an oily residue, which was purified by short column chromatography over silica gel with *n*-hexane/EtOAc (4:1) to give the *N*-Boc derivative as an oil. HCl (3 N; 6 mL) was added to a stirred solution of this bromoallene in EtOAc (10 mL) at room temperature. After stirring for 3 h at 60 °C, the mixture was made basic with 28% NH_4OH. The whole was extracted with EtOAc. The extract was washed with water and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (3:1) to give **9a** (540 mg, 75% yield) as colorless crystals. M.p. 76 °C (*n*-hexane/Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (s, 6H; 2×CMe), 2.88 (d, J = 6.9 Hz, 2H; 1-CH_2), 4.20 (t, J = 6.9 Hz, 1H; NH), 4.23 (d, J = 6.0 Hz, 2H; CH_2Ph), 4.56 (t, J = 6.0 Hz, 1H; NH), 5.20 (d, J = 5.7 Hz, 1H; 3-H), 6.04 (d, J = 5.7 Hz, 1H; 5-H), 7.31–7.40 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.3, 25.4, 36.1, 47.3, 52.9, 74.4, 107.5, 128.07 (2C), 128.11, 128.9 (2C), 136.6, 200.8 ppm; IR (KBr): $\tilde{\nu}$ = 3300 ($NHSO_2$), 1955 (C=C=C), 1323 cm^{-1} ($NHSO_2$); elemental analysis calcd (%) for $C_{14}H_{19}BrN_2O_2S$: C 46.80, H 5.33, N 7.80; found: C 46.71, H 5.21, N 7.76.

General procedure for the tandem cyclization of bromoallenes in the absence of palladium—synthesis of 2-benzyl-5,5-dimethyl-2,3,5,6-tetrahydro-1-thia-2,6a-diaza-pentalene-1,1-dioxide (11a) and (±)-2-benzyl-3-ethynyl-4,4-dimethyl-1,2,6-thiadiazinane-1,1-dioxide (12a) (Table 1, entry 1): NaH (60% suspension in mineral oil; 12 mg, 0.3 mmol) was added to MeOH (0.5 mL) at room temperature under nitrogen, and the mixture was stirred for 10 min at this temperature. A solution of the bromoallene **9a** (43.1 mg, 0.12 mmol) in MeOH (0.7 mL) was added to the stirred mixture at room temperature, and the resulting mixture was stirred for 16 h at 60 °C. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (3:1) to give, in order of elution, **11a** (27 mg, 81% yield) and **12a** (3.5 mg, 9% yield).

Compound ***11a***: Colorless solid; m.p. 48 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 6H; 2×CMe), 3.32 (s, 2H; CH_2), 3.73 (d, J = 1.5 Hz, 2H; CH_2), 4.32 (s, 2H; CH_2Ph), 4.79 (t, J = 1.5 Hz, 1H; C=CH), 7.30–7.37 ppm (m, 5H; Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 27.5 (2C), 46.1, 48.4, 51.6, 59.2, 111.6, 128.1, 128.4 (2C), 128.7 (2C), 134.7, 136.3 ppm; IR (KBr): $\tilde{\nu}$ = 1682 (C=C–N), 1317 cm^{-1} (NSO_2); MS (FAB): m/z (%): 279 (89) [M^++H], 91 (100); HRMS (FAB): calcd for $C_{14}H_{19}N_2O_2S$ [M^++H]: 279.1167; found: 279.1169.

Compound ***12a***: Colorless crystals; m.p. 118 °C (*n*-hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (s, 3H; CMe), 1.08 (s, 3H; CMe), 2.56 (d, J = 2.4 Hz, 1H; C≡CH), 2.94 (ddd, J = 14.4, 5.4, 1.8 Hz, 1H; C*H*H), 3.56 (dd, J = 2.4, 1.8 Hz, 1H; 3-H), 3.64 (dd, J = 14.4, 10.8 Hz, 1H; CH*H*), 4.09 (d, J = 14.1 Hz, 1H; PhC*H*H), 4.70–4.76 (m, 1H; NH), 4.78 (d, J = 14.1 Hz, 1H; PhCH*H*), 7.28–7.39 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.16, 23.22, 33.7, 49.4, 52.4, 59.5, 77.0, 77.1, 127.9, 128.6 (2C), 128.9 (2C), 135.2 ppm; IR (KBr): $\tilde{\nu}$ = 3284 ($NHSO_2$), 2114 (C≡C), 1336 cm^{-1} (NSO_2); elemental analysis calcd (%) for $C_{14}H_{18}N_2O_2S$: C 60.40, H 6.52, N 10.06; found: C 60.19, H 6.52, N 10.00.

2-Ethynyl-4,4-dimethyl-1-(4-methylphenylsulfonyl)piperidine (15): NaH (60% suspension of mineral oil; 12 mg, 0.3 mmol) was added to MeOH (1 mL) at room temperature under nitrogen, and the mixture was stirred for 20 min at this temperature. A solution of the bromoallene **13** (74.5 mg, 0.20 mmol) in MeOH (1 mL) was added to the stirred mixture at room temperature, and the resulting mixture was stirred for 25 h at 50 °C. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (6:1) to give **15** (26.8 mg, 46% yield) as colorless crystals. Considerable amount of bromoallene **13** (39.0 mg, 52%) was also recovered.

Compound ***15***: Colorless solid; m.p. 111–112 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (s, 3H; CMe), 1.12 (s, 3H; CMe), 1.39–1.44 (m, 1H; C*H*H), 1.51 (dd, J = 12.8, 6.0 Hz, 1H; C*H*H), 1.63 (dt, J = 13.5, 2.0 Hz, 1H; CH*H*), 1.73 (dd, J = 12.8, 6.0 Hz, 1H; CH*H*), 1.75 (d, J = 2.4 Hz, 1H; C≡CH), 2.42 (s, 3H; CMe), 2.99 (dt, J = 13.5, 2.0 Hz, 1H; 6-C*H*H), 3.60–3.66 (m, 1H; 6-CH*H*), 4.86–4.90 (m, 1H; 2-H), 7.27 (d, J = 8.0 Hz, 2H; Ph), 7.73 ppm (d, J = 8.0 Hz, 2H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 25.4, 29.0, 33.3, 38.3, 38.9, 42.3, 43.7, 74.3, 81.1, 128.0 (2C), 129.1 (2C), 135.7, 143.2 ppm; IR (KBr): $\tilde{\nu}$ = 3267 ($NHSO_2$), 2114 (C≡C), 1346 cm^{-1} ($NHSO_2$); MS (FAB): m/z (%): 292 (100) [M^++H]; HRMS (FAB): calcd for $C_{16}H_{22}NO_2S$ [M^++H]: 292.1371; found: 292.1375.

2-Benzyl-5,5-dimethyl-2,4,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*]-[1,2,5]thiadiazole-1,1-dione (16a) (Table 1, entry 8): TBAF (0.50 mL, 0.50 mmol; 1.0 M solution in THF) was added to a stirred solution of bromoallene **9a** (71.9 mg, 0.20 mmol) in THF (2 mL) at room temperature, and the resulting mixture was stirred for 1 h at 60 °C. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (3:1) to give **16a** (51.1 mg, 92% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (S, 6H; CMe_2), 2.26 (d, J = 1.5 Hz, 2H; CH_2), 3.26 (s, 2H; CH_2N), 4.46 (s, 2H; CH_2Ph), 5.56 (t, J = 1.5 Hz, 1H; C=CH), 7.31–7.38 ppm (m, 5H; Ph); IR (KBr): $\tilde{\nu}$ = 1679 (C=C–N), 1321 cm^{-1} (NSO_2); MS (FAB): m/z (%): 279 (47) [M^++H], 322 (100); HRMS (FAB): calcd for $C_{14}H_{19}N_2O_2S$ [M^++H]: 279.1167; found: 279.1168.

***N*-Benzyl-2-ethynyl-3,3-dimethylazetidine-1-sulfonamide (17a) (Table 1, entry 3)**: Bromoallene **9a** (71.9 mg, 0.200 mmol) was added to a stirred suspension of NaH (60% suspension of mineral oil; 20.0 mg, 0.500 mmol) in DMF (1.0 mL) at 0°C under nitrogen, and the resulting mixture was stirred for 1 h at room temperature. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (4:1) to give, in order of elution, **11a** (13.9 mg, 25% yield), **17a** (11.2 mg, 20% yield), and **12a** (30.1 mg, 54% yield).

*Compound **17a***: Colorless needles; m.p. 81–82°C (*n*-hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.21$ (s, 3H; CMe), 1.38 (s, 3H; CMe), 2.57 (d, $J = 2.4$ Hz, 1H; C≡CH), 3.29 (d, $J = 6.9$ Hz, 1H; C*H*H), 3.64 (d, $J = 6.9$ Hz, 1H; CH*H*), 4.29 (d, $J = 6.0$ Hz, 2H; CH_2Ph), 4.41 (d, $J = 2.4$ Hz, 1H; 2-H), 4.53 ppm (t, $J = 6.0$ Hz, 1H; NH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 23.7$, 26.1, 34.5, 47.6, 60.2, 60.8, 76.1, 79.2, 128.0, 128.1 (2C), 128.7 (2C), 136.6 ppm; IR (KBr): $\tilde{\nu} = 3286$ ($NHSO_2$), 2360 (C≡C), 1333 cm^{-1} ($NHSO_2$); MS (FAB): *m*/*z* (%): 279 (100) [M^++H]; HRMS (FAB): calcd for $C_{14}H_{19}N_2O_2S$ [M^++H]: 279.1167; found: 279.1159.

2,5,5-Trimethyl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*][1,2,5]thiadiazole-1,1-dione (11b) and 3-ethynyl-2,4,4-trimethyl-1,2,6-thiadiazinane-1,1-dioxide (Table 2, entry 1) (12b): By using the procedure described for the preparation of the bicyclic sulfamide **11a** and six-membered ring **12a** from bromoallene **9a**, the bromoallene **9b** (53.0 mg, 0.187 mmol) was converted into **11b** (25 mg, 65% yield) and **12b** (4.0 mg, 10% yield).

*Compound **11b***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.22$ (s, 6H; 2×CMe), 2.84 (s, 3H; NMe), 3.30 (s, 2H; NCH_2), 3.88 (d, $J = 1.8$ Hz, 2H; NCH_2), 4.84 ppm (t, $J = 1.8$ Hz, 1H; C≡CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 27.5$ (2C), 34.5, 48.3, 48.9, 59.2, 111.5, 136.4 ppm; IR (KBr): $\tilde{\nu} = 1680$ (C=C–N), 1319 cm^{-1} ($NHSO_2$); MS (FAB): *m*/*z* (%): 203 (100) [M^++H]; HRMS (FAB): calcd for $C_8H_{15}N_2O_2S$ [M^++H]: 203.0854; found: 203.0856.

*Compound **12b***: Colorless solid; m.p. 144–145°C (*n*-hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.10$ (s, 3H; CMe), 1.20 (s, 3H; CMe), 2.52 (d, $J = 2.4$ Hz, 1H; C≡CH), 2.89 (s, 3H; NMe), 3.14 (dd, $J = 14.4$, 6.0 Hz, 1H; C*H*H), 3.31 (dd. $J = 14.4$, 6.0 Hz, 1H; CH*H*), 3.83 (d, $J = 2.4$ Hz, 1H; 3-H), 4.43 ppm (t, $J = 6.0$ Hz, 1H; NH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.0$, 24.0, 34.1, 34.4, 54.2, 63.4, 76.6, 77.0 ppm; IR (KBr): $\tilde{\nu} =$ 2119 (C≡C), 1332 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 203 (35) [M^++H], 154 (100); HRMS (FAB): calcd for $C_8H_{15}N_2O_2S$ [M^++H]: 203.0854; found: 203.0861; elemental analysis calcd (%) for $C_8H_{14}N_2O_2S$: C 47.50, H 6.98, N 13.85; found: C 47.27, H 6.79, N 13.55.

2,5,5-Trimethyl-2,4,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*][1,2,5]thiadiazole-1,1-dione (16b) (Table 2, entry 2): By using the procedure described for the preparation of the bicyclic sulfamide **16a** from **9a**, the bromoallene **9b** (42 mg, 0.15 mmol) was converted into **16b** (12.5 mg, 41% yield) and **12b** (16.9 mg, 56% yield).

*Compound **16b***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.20$ (s, 6H; CMe_2), 2.31 (d, $J = 1.5$ Hz, 2H; CH_2), 3.00 (s, 3H; NMe), 3.23 (s, 2H; CH_2N), 5.63 ppm (t, $J = 1.5$ Hz, 1H; C=CH); IR (KBr): $\tilde{\nu} = 1651$ (C=C–N), 1321 cm^{-1} ($NHSO_2$); MS (FAB): *m*/*z* (%): 203 (35) [M^++H], 69 (100); HRMS (FAB): calcd for $C_8H_{15}N_2O_2S$ [M^++H]: 203.0854; found: 203.0856.

5,5-Dimethyl-2-phenyl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*]-[1,2,5]thiadiazole-1,1-dioxide (11c) and 3-ethynyl-4,4-dimethyl-2-phenyl-1,2,6-thiadiazinane-1,1-dioxide (12c) (Table 2, entry 3): By using the procedure described for the preparation of the bicyclic sulfamide **11a** and six-membered ring **12a** from bromoallene **9a**, the bromoallene **9c** (51.8 mg, 0.15 mmol) was converted into **11c** (10 mg, 27% yield) and **12c** (18.5 mg, 50% yield).

*Compound **11c***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.27$ (s, 6H; 2×CMe), 3.42 (s, 2H; 6-CH_2), 4.40 (d, $J = 1.8$ Hz, 2H; 3-CH_2), 4.99 (t, $J = 1.8$ Hz, 1H; 4-H), 7.15–7.18 (m, 1H; Ph), 7.20–7.29 (m, 2H; Ph), 7.38–7.42 ppm (m, 2H; Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 27.5$ (2C), 45.8, 48.0, 59.4, 112.3, 119.1 (2C), 124.9, 129.6 (2C), 134.7, 137.6 ppm; IR (KBr): $\tilde{\nu} = 1685$ (C=C–N), 1325 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 265 (21) [M^++H], 136 (100); HRMS (FAB): calcd for $C_{13}H_{17}N_2O_2S$ [M^++H]: 265.1011; found: 265.1011.

*Compound **12c***: Colorless crystals; m.p. 153°C (*n*-hexane/Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.19$ (s, 3H; CMe), 1.30 (s, 3H; CMe), 2.27 (d, $J = 2.7$ Hz, 1H; C≡CH), 3.28 (dd, $J = 15.0$, 6.3 Hz, 1H; 5-C*H*H), 3.46 (dd, $J = 15.0$, 9.9 Hz, 1H; 5-CH*H*), 4.45 (d, $J = 2.7$ Hz, 1H; 3-H), 4.67 (dd, $J = 9.9$, 6.3 Hz, 1H; NH), 7.32–7.46 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.9$, 23.8, 34.8, 54.4, 64.1, 77.0, 77.6, 128.4, 128.90 (2C), 128.94 (2C), 139.3 ppm; IR (KBr): $\tilde{\nu} = 3275$ ($NHSO_2$), 2123 (C≡C), 1338 cm^{-1} ($NHSO_2$); elemental analysis calcd (%) for $C_{13}H_{16}N_2O_2S$: C 59.07, H 6.10, N 10.60; found: C 58.93, H 6.00, N 10.63.

2-Benzyl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*][1,2,5]thiadiazole-1,1-dioxide (11d) and 2-benzyl-3-ethynyl-1,2,6-thiadiazinane-1,1-dioxide (12d) (Table 2, entry 5): By using the procedure described for the preparation of the bicyclic sulfamide **11a** and six-membered ring **12a** from bromoallene **9a**, the bromoallene **9d** (66.2 mg, 0.2 mmol) was converted into **11d** (25 mg, 50% yield) and **12d** (12 mg, 24% yield).

*Compound **11d***: Colorless solid; m.p. 87–89°C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.81$–2.90 (m, 2H; CH_2), 3.63 (t, $J = 8.7$ Hz, 2H; CH_2), 3.73–3.76 (m, 2H; CH_2), 4.33 (s, 2H; CH_2Ph), 4.90 (tt, $J = 2.4$, 2.4 Hz, 1H; C=CH), 7.28–7.41 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 33.3$, 45.9, 46.5, 51.6, 100.8, 128.2, 128.5 (2C), 128.8 (2C), 134.8, 138.9 ppm; IR (KBr): $\tilde{\nu} = 1684$ (C=C–N), 1308 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 251 (51) [M^++H], 136 (100); HRMS (FAB): calcd for $C_{12}H_{15}N_2O_2$ [M^++H]: 251.0854; found: 251.0826.

*Compound **12d***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.83$–2.01 (m, 2H; 4-CH_2), 2.52 (d, $J = 2.4$ Hz, 1H; C≡CH), 3.39–3.49 (m, 1H; 5-C*H*H), 3.79–3.92 (m 1H; 5-CH*H*), 4.11 (d, $J = 14.1$ Hz, 1H; PhC*H*H), 4.15–4.19 (m, 1H; 3-H), 4.52 (dd, $J = 9.9$, 5.1 Hz, 1H; NH), 4.74 (d, $J = 14.1$ Hz, 1H; PhCH*H*), 7.28–7.42 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 30.6$, 42.2, 49.5, 49.6, 75.3, 78.8, 128.0, 128.6 (2C), 129.0 (2C), 135.2 ppm; IR (KBr): $\tilde{\nu} = 3278$ ($NHSO_2$), 2114 (C≡C), 1321 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 251 (100) [M^++H]; HRMS (FAB): calcd for $C_{12}H_{15}N_2O_2S$ [M^++H]: 251.0854; found: 251.0859.

(±)-2-Benzyl-5-methyl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*]-[1,2,5]thiadiazole-1,1-dioxide (11e), (±)-(3*R,4*R**)-2-benzyl-3-ethynyl-4-methyl-1,2,6-thiadiazinane-1,1-dioxide (12e) and its (±)-(3*R**,4*S**)-isomer (12e′) (Table 2, entry 7)**: By using the procedure described for the preparation of the bicyclic sulfamide **11a** and six-membered ring **12a** from bromoallene **9a**, the bromoallene **9e** (69 mg, 0.2 mmol) was converted into **11e** (30 mg, 57% yield), **12e** (5 mg, 9% yield) and **12e′** (2.5 mg, 5% yield).

*Compound **11e***: Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.17$ (d, $J = 6.5$ Hz, 3H; CMe), 3.18 (dd, $J = 9.5$, 8.0 Hz, 1H; C*H*H), 3.28–3.36 (m, 1H; 5-H), 3.70–3.78 (m, 3H; CH*H* and CH_2), 4.29 (d, $J = 14.0$ Hz, 1H; PhC*H*H), 4.36 (d, $J = 14.0$ Hz, 1H; PhCH*H*), 4.85–4.86 (m, 1H; 4-H), 7.30–7.40 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.6$, 41.6, 46.0, 51.6, 53.5, 106.9, 128.2, 128.5 (2C), 128.8 (2C), 134.8, 137.9 ppm; IR (KBr): $\tilde{\nu} = 1682$ (C=C–N), 1315 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 287 (100) [M^++Na]; HRMS (FAB): calcd for $C_{13}H_{16}N_2NaO_2S$ [M^++Na]: 287.0830; found: 287.0836.

*Compound **12e***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.05$ (d, $J = 6.6$ Hz, 3H; CMe), 1.92–2.04 (m, 1H; 4-H), 2.52 (d, $J = 2.4$ Hz, 1H; C≡CH), 3.20 (ddd, $J = 14.4$, 7.2, 7.2 Hz, 1H; 5-C*H*H), 3.69 (ddd, $J = 14.4$, 8.1, 3.9 Hz, 1H; 5-CH*H*), 4.01 (dd, $J = 6.9$, 2.4 Hz, 1H; 3-H), 4.27 (d, $J = 14.4$ Hz, 1H; PhC*H*H), 4.59 (dd, $J = 8.1$, 7.2 Hz, 1H; NH), 4.66 (d, $J = 14.4$ Hz, 1H; PhCH*H*), 7.27–7.44 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 15.0$, 33.2, 48.6, 49.8, 56.7, 75.9, 79.1, 127.8, 128.4 (2C), 128.8 (2C), 136.2 ppm; IR (KBr): $\tilde{\nu} = 3269$ ($NHSO_2$), 2123 (C≡C), 1331 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 265 (100) [M^++H]; HRMS (FAB): calcd for $C_{13}H_{17}N_2O_2S$ [M^++H]: 265.1011; found: 265.1011.

*Compound **12e′***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.97$ (d, $J = 7.2$ Hz, 3H; CMe), 2.05–2.15 (m, 1H; 4-H), 2.57 (d, $J = 2.4$ Hz, 1H; C≡CH), 3.18 (dddd, $J = 14.4$, 3.6, 3.6, 2.1 Hz, 1H; 5-C*H*H), 3.66 (ddd, $J = 14.4$, 11.7, 11.7 Hz, 1H; 5-CH*H*), 3.83 (ddd, $J = 4.5$, 2.4, 2.1 Hz, 1H; 3-H), 4.03 (d, $J = 13.5$ Hz, 1H; PhC*H*H), 4.47 (dd, $J = 11.7$, 3.6 Hz, 1H; NH), 4.82 (d, $J = 13.5$ Hz, 1H; PhCH*H*), 7.30–7.40 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.6$, 34.6, 47.5, 49.4, 54.5, 76.1, 77.1, 128.1, 128.7 (2C), 129.2 (2C), 134.7 ppm; IR (KBr): $\tilde{\nu} = 3269$ ($NHSO_2$), 2112 (C≡C),

1325 cm^{-1} (NSO_2); MS (FAB): *m/z* (%): 265 (100) [M^++H]; HRMS (FAB): calcd for $C_{13}H_{17}N_2O_2S$ [M^++H]: 265.1011; found: 265.1018.

2-Benzyl-5,5-bis(hydroxymethyl)-*O*,*O*-isopropylidene-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*][1,2,5]thiadiazole-1,1-dione (11f) (Table 2, entry 8): By using the procedure described for the preparation of the bicyclic sulfamide **11a** and six-membered ring **12a** from bromoallene **9a**, the bromoallene **9f** (75.3 mg, 0.170 mmol) was converted into **11f** (54.6 mg, 89% yield) as colorless needles. M.p. 149–151 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (s, 3H; CMe), 1.43 (s, 3H; CMe), 3.67 (s, 2H; NCH_2), 3.71–3.86 (m, 6H; NCH_2 and 2×OCH_2), 4.33 (s, 2H; CH_2Ph), 4.75 (s, 1H; C=CH), 7.31–7.37 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8, 26.5, 46.1, 51.7, 52.1, 53.5, 66.7 (2C), 98.0, 102.2, 128.3, 128.5 (2C), 128.9 (2C), 134.5, 140.1 ppm; IR (KBr): $\tilde{\nu}$ = 2999 (C=C), 1672 (C=C−N), 1317 cm^{-1} (NSO_2); elemental analysis calcd (%) for $C_{17}H_{22}N_2O_4S$: C 58.27, H 6.33, N 7.99; found: C 58.30, H 6.28, N 7.85.

2-Benzyl-5,5-bis(hydroxymethyl)-*O*,*O*-isopropylidene-2,4,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*][1,2,5]thiadiazole-1,1-dione (16f) (Table 2, entry 9): By using the procedure described for the preparation of the bicyclic sulfamide **16a** from bromoallene **9a**, the bromoallene **9f** (10 mg, 0.023 mmol) was converted into **16f** (7.5 mg, 92% yield) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (s, 6H; CMe_2), 2.40 (d, *J* = 1.2 Hz, 2H; CH_2), 3.48 (s, 2H; CH_2N), 3.71–3.83 (m, 4H; 2×CH_2O), 4.46 (s, 2H; CH_2Ph), 5.59 (t, *J* = 1.2 Hz, 1H; C=CH), 7.32–7.36 ppm (m, 5H; Ph); IR (KBr): $\tilde{\nu}$ = 3273 (NSO_2), 1614 (C=C−N), 1321 cm^{-1} (NSO_2); MS (FAB): *m/z* (%): 351 (29) [M^++H], 154 (100); HRMS (FAB): calcd for $C_{17}H_{23}N_2O_4S$ [M^++H]: 351.1379; found: 351.1378.

2-Benzyl-5,5-bis[(*tert*-butyldimethylsiloxy)methyl]-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*][1,2,5]thiadiazole-1,1-dione (11g) (Table 2, entry 10): By using the procedure described for the preparation of the bicyclic sulfamide **11a** and six-membered ring **12a** from bromoallene **9a**, the bromoallene **9g** (60.1 mg, 0.097 mmol) was converted into **11g** (47.3 mg, 91% yield) as colorless solids. M.p. 86–87 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.027 (s, 12H; $SiMe_2$), 0.88 (s, 18H; 2×CMe_3), 3.39 (s, 2H; NCH_2), 3.57–3.63 (m, 4H; 2×CH_2OTBS), 3.74 (d, *J* = 1.5 Hz, 2H; CH_2NBn), 4.32 (s, 2H; CH_2Ph), 4.80 (t, *J* = 1.5 Hz, 1H; C=CH), 7.31–7.37 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.55 (2C), −5.52 (2C), 18.2 (2C), 25.8 (6C), 46.1, 50.7, 51.6, 60.3, 63.9 (2C), 104.5, 128.2, 128.5 (2C), 128.8 (2C), 134.7, 139.2 ppm; IR (KBr): $\tilde{\nu}$ = 2929 (C=C), 1680 (C=C−N), 1327 cm^{-1} (NSO_2); MS (FAB): *m/z* (%): 539 (57) [M^++H], 73 (100); HRMS (FAB): calcd for $C_{26}H_{47}N_2O_4SSi_2$ [M^++H]: 539.2795; found: 539.2793.

5,5-Bis[(*tert*-butyldimethylsiloxy)methyl]-2-methyl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*b*][1,2,5]thiadiazole-1,1-dione (11h) (Table 2, entry 11): By using the procedure described for the preparation of the bicyclic sulfamide **11a** and six-membered ring **12a** from bromoallene **9a**, the bromoallene **9h** (48.2 mg, 0.0887 mmol) was converted into **11h** (39.0 mg, 95% yield) as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.04 (s, 12H; 2×$SiMe_2$), 0.88 (s, 18H; 2×CMe_3), 2.84 (s, 2H; CH_2), 3.36 (s, 2H; CH_2), 3.603–3.609 (m, 4H; 2×CH_2), 3.89 (d, *J* = 1.5 Hz, 2H; CH_2), 4.86 ppm (s, 1H; 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.56 (2C), −5.53 (2C), 18.2 (2C), 25.8 (6C), 34.6, 49.0, 50.7, 60.3, 63.9 (2C), 104.3, 139.1 ppm; IR (KBr): $\tilde{\nu}$ = 2929 (C=C), 1682 (C=C−N), 1329 cm^{-1} ($NHSO_2$); MS (FAB): *m/z* (%): 463 (46) [M^++H], 73 (100); HRMS (FAB): calcd for $C_{20}H_{43}N_2O_4SSi_2$ [M^++H]: 463.2482; found: 463.2471.

2-Benzyl-3,9-dihydro[1,2,5]thiadiazolo[2,3-*b*]isoquinoline-1,1(2*H*)-dione (11i) and *N*-benzyl-*N*′-{[2-(3-methoxyprop-1-ynyl)phenyl]methyl}sulfamide (18i) (Table 2, entry 12): By using the procedure described for the preparation of the bicyclic sulfamide **11a** and six-membered ring **12a** from bromoallene **9a**, the bromoallene **9i** (177 mg, 0.45 mmol) was converted into **11i** (24.3 mg, 17%) and **18i** (23.4 mg, 15%).

*Compound **11i***: Colorless crystals; m.p. 156–157 °C (*n*-hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.93 (d, *J* = 1.8 Hz, 2H; 3-CH_2), 4.30 (s, 2H; CH_2), 4.68 (s, 2H; CH_2), 5.52 (t, *J* = 1.8 Hz, 1H; C=CH), 6.93 (dd, *J* = 6.9, 1.8 Hz, 1H; Ph), 7.08–7.21 (m, 3H; Ph), 7.34–7.40 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.7, 48.8, 51.6, 100.0, 124.7, 126.15, 126.24, 126.9, 128.3, 128.4, 128.6 (2C), 128.9 (2C), 130.8, 133.0, 134.3 ppm; IR (KBr): $\tilde{\nu}$ = 1668 (C=CN), 1322 cm^{-1} ($NHSO_2$); MS (FAB): *m/z* (%): 335 (28) [M^++Na], 312 (100); HRMS (FAB): calcd for $C_{17}H_{16}N_2NaO_2Si$ [M^++Na]: 335.0830; found: 335.0814.

*Compound **18i***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.41 (s, 3H; Me), 4.30 (s, 2H; CH_2), 4.08 (d, *J* = 6.0 Hz, 2H; CH_2), 4.31 (s, 2H; CH_2), 4.36 (d, *J* = 6.0 Hz, 2H; CH_2), 4.60 (t, *J* = 6.0 Hz, 1H; NH), 4.86 (t, *J* = 6.0 Hz, 1H; NH), 7.17–7.39 (m, 8H; Ph), 7.34–7.40 ppm (m, 1H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.1, 47.3, 58.0, 60.4, 83.8, 90.5, 121.9, 127.9, 128.0 (3C), 128.7 (2C), 128.8, 129.0, 132.7, 136.5, 138.7 ppm; IR (KBr): $\tilde{\nu}$ = 3292 ($NHSO_2$), 2231 (C≡C), 1327 cm^{-1} ($NHSO_2$); MS (FAB): *m/z* (%): 345 (45) [M^++H], 91 (100); HRMS (FAB): calcd for $C_{18}H_{21}N_2O_3S$ [M^++H]: 345.1273; found: 345.1272.

1,3-Diaza-3-benzyl-7,7-dimethyl-4-methylene-2-thiabicyclo[3.3.0]octane-2,2-dione (20a) and 1,3-Diaza-3-benzyl-8,8-dimethyl-2-thiabicyclo-[4.3.0]non-4-ene-2,2-dione (21a) (Table 3, entry 1): NaH (60% suspension in mineral oil; 15 mg, 0.375 mmol) was added to MeOH (1 mL) at room temperature under nitrogen, and the mixture was stirred for 10 min at this temperature. A solution of bromoallene **19a** (56 mg, 0.15 mmol) in MeOH (1 mL) was added to the stirred mixture at room temperature, and the resulting mixture was stirred for 20 h at 60 °C. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (6:1) to give, in order of elution, **20a** (29 mg, 66% yield) and **21a** (8 mg, 18% yield).

*Compound **20a***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (s, 3H; CMe), 1.17 (s, 3H; CMe), 1.76 (dd, *J* = 12.6, 7.5 Hz, 1H; 6-C*H*H), 2.14 (dd, *J* = 12.6, 8.1 Hz, 1H; 6-CH*H*), 3.19 (d, *J* = 9.9 Hz, 1H; 8-C*H*H), 3.35 (d, *J* = 9.9 Hz, 1H; 8-CH*H*), 3.929 (s, 1H; C=C*H*H), 3.933 (s, 1H; C=CH*H*), 4.30 (d, *J* = 16.2 Hz, 1H; C*H*HPh), 4.65 (dd, *J* = 8.1, 7.5 Hz, 1H; 5-H), 4.72 (d, *J* = 16.2 Hz, 1H; CH*H*Ph), 7.28–7.36 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.0, 26.4, 40.3, 46.92, 46.94, 62.8, 63.2, 83.1, 127.3 (2C), 127.7, 128.6 (2C), 135.0, 145.1 ppm; IR (KBr): $\tilde{\nu}$ = 1664 (C=C−N), 1333 cm^{-1} (NSO_2); MS (FAB): *m/z* (%): 293 (100) [M^++H]; HRMS (FAB): calcd for $C_{15}H_{21}N_2O_2S$ [M^++H]: 293.1324; found: 293.1307.

*Compound **21a***: Colorless solid; m.p. 72 °C (*n*-hexane/Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (s, 3H; CMe), 1.16 (s, 3H; CMe), 1.58 (dd, *J* = 13.2, 3.9 Hz, 1H; 7-C*H*H), 2.12 (dd, *J* = 13.2, 9.3 Hz, 1H; 7-CH*H*), 2.83 (d, *J* = 9.3 Hz, 1H; 9-C*H*H), 3.11 (d, *J* = 9.3 Hz, 1H; 9-CH*H*), 4.35 (d, *J* = 15.0 Hz, 1H; C*H*HPh), 4.65–4.71 (m, 2H; 5-H and 6-H), 4.70 (d, *J* = 15.0 Hz, 1H; CH*H*Ph), 5.79 (dd, *J* = 8.7, 2.1 Hz, 1H; 6-H), 7.28–7.37 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.0, 29.0, 37.9, 46.4, 51.3, 61.3, 61.5, 107.4, 127.1, 128.0, 128.5 (2C), 128.7 (2C), 136.1 ppm; IR (KBr): $\tilde{\nu}$ = 1645 (C=C−N), 1354 cm^{-1} (NSO_2); MS (FAB): *m/z* (%): 293 (100) [M^++H], HRMS (FAB): calcd for $C_{15}H_{21}N_2O_2S$ [M^++H]: 293.1324; found: 293.1335.

***N*-Benzyl-2-ethynyl-4,4-dimethylpyrrolidine-1-sulfonamide (22a)**: A solution of bromoallene **19a** (149 mg, 0.4 mmol) in DMF (2 mL) was added to a stirred suspension of NaH (60% suspension of mineral oil; 40 mg, 1.0 mmol) in DMF (2 mL) at 0 °C under nitrogen at 0 °C. After the mixture was stirred for 3.5 h at this temperature, the mixture was poured into ice-water saturated with NH_4Cl. The mixture was extracted with Et_2O. The extract was washed with water and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (5:1) to give **22a** (101 mg, 86% yield) as colorless crystals. M.p. 92–93 °C (*n*-hexane/Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (s, 3H; CMe), 1.22 (s, 3H; CMe), 1.92 (dd, *J* = 12.3, 6.3 Hz, 1H; 3-C*H*H), 2.11 (dd, *J* = 12.3, 7.8 Hz, 1H; 3-CH*H*), 2.40 (d, *J* = 1.8 Hz, 1H; C≡CH), 3.14 (d, *J* = 9.9 Hz, 1H; 5-C*H*H), 3.27 (d, *J* = 9.9 Hz, 1H; 5-CH*H*), 4.26 (dd, *J* = 13.5, 5.4 Hz, 1H; C*H*HPh), 4.33 (dd, *J* = 13.5, 6.9 Hz, 1H; CH*H*Ph), 4.51 (ddd, *J* = 7.8, 6.3, 1.8 Hz, 1H; 2-H), 4.59 (dd, *J* = 6.9, 5.4 Hz, 1H; NH), 7.28–7.38 ppm (m, 5H; Ph); ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 26.2, 26.4, 38.5, 47.2, 47.4, 49.5, 60.9, 72.1, 83.8, 127.6, 127.9 (2C), 128.5 (2C), 136.7 ppm; IR (KBr): $\tilde{\nu}$ = 3278 ($NHSO_2$), 2116 (C≡C), 1336 cm^{-1} ($NHSO_2$); elemental analysis calcd (%) for $C_{15}H_{20}N_2O_2S$: C 61.61, H 6.89, N 9.58; found: C 61.53, H 6.81, N 9.52.

2,6,6-Trimethyl-4a,5,6,7-tetrahydro-2*H*-pyrrolo[1,2-*b*][1,2,6]thiadiazine-1,1-dione (21b) and 2-acetyl-*N*,4,4-trimethylpyrrolidine-1-sulfonamide

(23b): TBAF (0.635 mL, 0.635 mmol; 1.0 M solution in THF) was added to a stirred solution of the bromoallene **19b** (75.5 mg, 0.254 mmol) in THF (2.5 mL) under nitrogen at room temperature, and the mixture was stirred for 2.5 h under reflux. HCl (3 N; 0.5 mL) was added to the stirred mixture, and the resulting mixture was stirred for 0.5 h at room temperature. The whole was extracted with EtOAc. The extract was washed with water, saturated $NaHCO_3$ and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (2:1) to give, in order of elution, **21b** (6.9 mg, 13% yield) and **23b** (41.5 mg, 70% yield).

Compound ***21b***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.15$ (s, 3H; CMe), 1.17 (s, 3H; CMe), 1.63 (dd, $J = 12.3$, 3.6 Hz, 1H; C*H*H), 2.13 (dd, $J = 12.3$, 9.0 Hz, 1H; CH*H*), 2.95 (d, $J = 9.0$ Hz, 1H; C*H*HN), 3.05 (s, 3H; NMe), 3.14 (d, $J = 9.0$ Hz, 1H; CH*H*N), 4.65–4.68 (m, 1H; CH), 4.70 (dd, $J = 8.7$, 1.8 Hz, 1H; 5-H), 5.75 ppm (dd, $J = 8.7$, 2.1 Hz, 1H; 6-H); ^{13}C NMR (67.5 MHz, $CDCl_3$): $\delta = 27.9$, 28.8, 35.4, 37.8, 46.6, 61.4, 61.5, 107.1, 129.6 ppm; IR (KBr): $\tilde{\nu} = 3315$ ($NHSO_2$), 1645 (C=C–N), 1351 cm^{-1} ($NHSO_2$); MS (FAB): *m*/*z* (%): 217 (100) [M^++H], HRMS (FAB): calcd for $C_9H_{17}N_2O_2S$ [M^++H]: 217.1011; found: 217.1016.

Compound ***23b***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.11$ (s, 3H; CMe), 1.14 (s, 3H; CMe), 1.64 (dd, $J = 12.3$, 9.0 Hz, 1H; C*H*H), 2.10 (ddd, $J = 12.3$, 9.0, 1.0 Hz, 1H; CH*H*), 2.20 (s, 3H; CMe), 2.81 (s, 3H; NMe), 3.14 (d, $J = 9.6$ Hz, 1H; C*H*HN), 3.35 (dd, $J = 9.6$, 1.0 Hz, 1H; CH*H*N), 4.48–4.53 (br s, 1H; NH), 4.50 ppm (t, $J = 9.0$ Hz, 1H; CH); ^{13}C NMR (67.5 MHz, $CDCl_3$): $\delta = 25.76$, 25.82, 26.4, 29.5, 38.9, 43.5, 61.0, 67.6, 207.9 ppm; IR (KBr): $\tilde{\nu} = 3300$ (NSO_2), 1711 (C=O), 1315 cm^{-1} ($NHSO_2$); MS (FAB): *m*/*z* (%): 235 (100) [M^++H], HRMS (FAB): calcd for $C_9H_{19}N_2O_3S$ [M^++H]: 235.1116; found: 235.1119.

6,6-Dimethyl-2-phenyl-4a,5,6,7-tetrahydro-1*H*-pyrrolo[1,2-*b*][1,2,6]thiadiazine-1,1(2*H*)-dione (21c): TBAF (0.363 mL, 0.363 mmol; 1.0 M solution in THF) was added to a stirred solution of the bromoallene **19c** (50.0 mg, 0.145 mmol) in THF (1.4 mL) under nitrogen at room temperature, and the resulting mixture was stirred for 30 h under reflux. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (2:1) to give **21c** (37.0 mg, 96% yield) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.20$ (s, 3H; CMe), 1.21 (s, 3H; CMe), 1.72 (dd, $J = 12.8$, 3.8 Hz, 1H; C*H*H), 2.21 (dd, $J = 12.8$, 8.8 Hz, 1H; CH*H*), 3.07 (d, $J = 9.0$ Hz, 1H; NC*H*H), 3.20 (d, $J = 9.0$ Hz, 1H; NCH*H*), 4.78–4.82 (m, 1H; 4a-H), 4.88 (dd, $J = 8.6$, 1.8 Hz, 1H; 4-H), 6.14 (dd, $J = 8.6$, 1.5 Hz, 1H; 3-H), 7.29–7.48 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 28.1$, 29.0, 38.0, 46.5, 61.41, 61.48, 107.8, 125.8 (2C), 127.1, 128.6, 129.3 ppm (2C); IR (KBr): $\tilde{\nu} = 1643$ (C=C–N), 1363 (NSO_2), 1170 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 279 (100) [M^++H]; HRMS (FAB): calcd for $C_{14}H_{19}N_2O_2S$ [M^++H]: 279.1167; found: 279.1169.

6,8-Diaza-8-benzyl-3,3-dimethyl-9-methylene-7-thiabicyclo[4.3.0]nonane-7,7-dione (29) (Table 4, entry 1): NaH (60% suspension in mineral oil; 10 mg, 0.25 mmol) was added to MeOH (0.5 mL) at room temperature under nitrogen, and the mixture was stirred for 10 min at this temperature. A solution of bromoallene **24** (38.7 mg, 0.10 mmol) in MeOH (0.5 mL) was added to the stirred mixture at room temperature, and the resulting mixture was stirred for 24 h at 60 °C. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (5:1) to give **29** (24.3 mg, 79% yield) as colorless crystals. M.p. 85–87 °C (*n*-hexane/Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.03$ (s, 6H; 2×CMe), 1.44–1.70 (m, 4H; 2-CH_2 and 4-CH_2), 3.01 (ddd, $J = 12.6$, 12.6, 3.0 Hz, 1H; 5-C*H*H), 3.52 (ddd, $J = 12.6$, 5.1, 2.1 Hz, 1H; 5-CH*H*), 3.87 (dd, $J = 2.4$, 2.4 Hz, 1H; C=C*H*H), 3.91 (dd, $J = 2.4$, 2.4 Hz, 1H; C=CH*H*), 3.93–3.99 (m, 1H; 1-H), 4.52 (d, $J = 16.8$ Hz, 1H; PhC*H*H), 4.69 (d, $J = 16.8$ Hz, 1H; PhCH*H*), 7.27–7.39 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 23.5$, 29.5, 32.3, 36.1, 38.8, 40.9, 46.1, 54.6, 81.3, 127.0 (2C), 127.6, 128.6 (2C), 135.1, 142.6 ppm; IR (KBr): $\tilde{\nu} = 1670$ (C=C–N), 1315 cm^{-1} (NSO_2); elemental analysis calcd (%) for $C_{16}H_{22}N_2O_2S$: C 62.71, H 7.24, N 9.14; found: C 62.52, H 7.13, N 9.03.

2,3,5,5-Tetramethyl-4,5,6,7-tetrahydro[1,2,5]thiadiazolo[2,3-*a*]pyridine-1,1(2*H*)-dione (30) (Table 4, entry 2): By using the procedure described for the preparation of the bicyclic sulfamide **29** from bromoallene **24**, the bromoallene **25** (46.7 mg, 0.150 mmol) was converted into **30** (22.2 mg, 64% yield) as colorless solids. M.p. 71–73 °C (*n*-hexane/Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.98$ (s, 6H; 2×CMe), 1.64 (t, $J = 5.4$ Hz, 2H; CH_2), 1.81 (s, 3H; CMe), 2.06 (s, 2H; CH_2), 2.97 (s, 3H; NMe), 3.31 ppm (t, $J = 5.4$ Hz, 2H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 9.32$, 27.2 (2C), 29.0, 29.3, 35.8, 36.3, 40.6, 116.4, 117.5 ppm; IR (KBr): $\tilde{\nu} = 1698$ (C=C–N), 1309 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 231 (100) [M^++H]; HRMS (FAB): calcd for $C_{10}H_{19}N_2O_2S$ [M^++H]: 231.1167; found: 231.1176.

2-Benzyl-3-methyl-5-phenyl-4,5,6,7-tetrahydro-2*H*-[1,2,5]thiadiazolo[2,3-*a*]pyridine 1,1-dioxide (31) and (±)-(4a*R,6*R**)-2-benzyl-6-phenyl-2,4a,5,6,7,8-hexahydropyrido[1,2-*b*][1,2,6]thiadiazine 1,1-dioxide (32) (Table 4, entry 3)**: TBAF (0.375 mL, 0.375 mmol; 1.0 M solution in THF) was added to a stirred solution of the bromoallene **26** (65.3 mg, 0.15 mmol) in THF (1.5 mL) under nitrogen at room temperature, and the resulting mixture was stirred for 3 h under reflux. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (5:1) to give, in the order of elution, **31** (21.8 mg, 41% yield) and **32** (26.2 mg, 49% yield; ca. 90% purity).

Compound ***31***: Colorless crystals; m.p. 117–119 °C (ca. 90% purity, *n*-hexane/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.70$ (s, 3H; CMe), 2.02–2.15 (m, 2H; CH_2), 2.34–2.39 (m, 1H; C*H*H), 2.63–2.71 (m, 2H; CH*H* and 5-H), 3.19 (ddd, $J = 11.5$, 11.5, 4.0 Hz, 1H; 7-C*H*H), 3.68 (ddd, $J = 11.5$, 4.5, 4.5 Hz, 1H; 8-CH*H*), 4.61 (s, 2H; CH_2Ph), 7.18–7.45 ppm (m, 10H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 10.0$, 29.9, 31.0, 40.4, 44.4, 46.5, 116.6, 116.8, 126.6 (2C), 126.9, 127.4 (2C), 127.7, 128.6 (2C), 128.7 (2C), 136.6, 144.0 ppm; IR (KBr): $\tilde{\nu} = 1695$ (C=C–N), 1306 cm^{-1} (NSO_2); MS (EI) *m*/*z* (%): 354 (60) [M^+], 289 (100); HRMS (EI) calcd for $C_{20}H_{22}N_2O_2S$ [M^+]: 354.1402; found: 354.1414.

Compound ***32***: Colorless needles; m.p. 116–119 °C (*n*-hexane/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.75$–1.84 (m, 1H; 7-C*H*H), 1.87–1.91 (m, 1H; 7-CH*H*), 1.96–2.08 (m, 2H; 5-CH_2), 2.66–2.71 (m, 2H; 6-H and 8-C*H*H), 3.51 (ddd, $J = 11.0$, 4.0, 4.0 Hz, 1H; 8-CH*H*), 4.51 (d, $J = 15.0$ Hz, 1H; C*H*HPh), 4.66 (dd, $J = 8.5$, 1.5 Hz, 1H; 4-H), 4.71 (d, $J = 15.0$ Hz, 1H; CH*H*Ph), 4.90–4.91 (m, 1H; 4a-H), 5.99 (dd, $J = 8.5$, 1.5 Hz, 1H; 3-H), 7.18–7.38 ppm (m, 10H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 31.3$, 36.3, 36.8, 43.8, 51.4, 56.2, 102.5, 126.7 (3C), 128.1, 128.4 (2C), 128.6 (2C), 128.8 (2C), 129.7, 136.1, 144.6 ppm; IR (KBr): $\tilde{\nu} = 1635$ (C=C–N), 1356 cm^{-1} (NSO_2); elemental analysis calcd (%) for $C_{20}H_{22}BrN_2O_2S$: C 67.77, H 6.26, N 7.90; found: C 67.78, H 6.25, N 7.89.

3,6,8-Triaza-8-benzyl-9-methylene-3-(4-methylphenylsulfonyl)-7-thiabicyclo[4.3.0]nonane-7,7-dione (33) and 2-benzyl-6-(4-methylphenylsulfonyl)-2,4a,5,6,7,8-hexahydro-1*H*-pyrazino[1,2-*b*][1,2,6]thiadiazine-1,1-dione (34) (Table 4, entry 5): By using the procedure described for the preparation of the bicyclic sulfamides **31** and **32** from bromoallene **26**, the bromoallene **27** (51.4 mg, 0.100 mmol) was converted into **33** (17.9 mg, 41% yield) and **34** (5.7 mg, 13% yield).

Compound ***33***: Colorless solid; m.p. 172–173 °C (*n*-hexane/$CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.45$ (s, 3H; Ph*Me*), 2.54–2.58 (m, 2H; CH_2), 2.70 (dt, $J = 11.7$, 3.0 Hz, 1H; C*H*H), 3.25 (dt, $J = 11.7$, 3.0 Hz, 1H; CH*H*), 3.65–3.75 (m, 2H; CH_2), 3.88 (dd, $J = 10.5$, 2.7 Hz, 1H; C=C*H*H), 4.01–4.06 (m, 2H; C=CH*H* and NCH), 4.56 (d, $J = 3.0$ Hz, 2H; CH_2Ph), 7.28–7.36 (m, 7H; Ph), 7.63 ppm (d, $J = 8.1$ Hz, 2H; Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 21.7$, 41.6, 43.7, 46.3, 47.9, 56.5, 84.2, 127.0 (2C), 127.4 (2C), 127.8, 128.7 (2C), 130.0 (2C), 132.4, 134.2, 138.0, 144.3 ppm; IR (KBr): $\tilde{\nu} = 1597$ (C=C–N), 1356 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 234 (30) [M^++H], 154 (100); HRMS (FAB): calcd for $C_{20}H_{24}N_3O_4S_2$ [M^++H]: 434.1208; found: 434.1225.

Compound ***34***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.45$ (s, 3H; Ph*Me*), 2.51 (dt, $J = 11.7$, 3.0 Hz, 1H; C*H*H), 2.70 (dd, $J = 11.7$, 3.6 Hz, 1H; C*H*H), 2.85 (dt, $J = 11.7$, 3.0 Hz, 1H; CH*H*), 3.25 (dt, $J = 11.7$, 3.6 Hz, 1H; CH*H*), 3.60–3.68 (m, 2H; CH_2), 4.50 (d, $J = 15.3$ Hz, 1H; PhC*H*H), 4.52–4.62 (m, 1H; NCH), 4.64 (d, $J = 15.3$ Hz, 1H; PhCH*H*), 4.77 (dd, $J = 8.1$, 1.5 Hz, 1H; C*H*=CH), 5.99 (dd, $J = 8.1$, 2.7 Hz, 1H; CH=C*H*), 7.32–7.39 (m, 7H; Ph), 7.62 ppm (d, $J = 8.4$ Hz, 2H; Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 21.6$, 42.7, 44.5, 48.4, 51.8, 55.6, 101.6, 127.6 (2C), 128.3, 128.4 (2C), 128.9 (2C), 130.0 (2C), 130.1,

132.3, 135.5, 144.3 ppm; IR (KBr): $\tilde{\nu}$ = 1639 (C=C–N), 1352 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 434 (36) [M^++H], 154 (100); HRMS (FAB): calcd for $C_{20}H_{24}N_3O_4S_2$ [M^++H]: 434.1208; found: 434.1223.

2-Benzyl-3-methyl-4,5,6,7-tetrahydro-1*H*-[1,2,5]thiadiazolo[2,3-*a*]pyridine-1,1(2*H*)-dione (35) (Table 4, entry 6): By using the procedure described for the preparation of the bicyclic sulfamides **31** and **32** from bromoallene **26**, the bromoallene **28** (50.0 mg, 0.139 mmol) was converted into **35** (22.4 mg, 58% yield) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.59 (tt, *J* = 5.7, 5.7 Hz, CH_2), 1.68 (s, 3H; Me), 1.85 (tt, *J* = 5.7, 5.7 Hz, CH_2), 2.30 (t, *J* = 5.7 Hz, 2H; CH_2), 3.28 (t, *J* = 5.7 Hz, 2H; CH_2), 4.57 (s, 2H; CH_2Ph), 7.25–7.42 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.99, 22.1, 22.3, 23.7, 44.5, 46.4, 116.0, 116.9, 127.4 (2C), 127.6, 128.6 (2C), 136.7 ppm; IR (KBr): $\tilde{\nu}$ = 1604 (N-C=C), 1313 (NSO_2), 1166 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 301 (23) [M^++Na], 91 (100); HRMS (FAB): calcd for $C_{14}H_{18}N_2NaO_2S$ [M^++Na]: 301.0987; found: 301.0975.

2-Benzyl-1-methyl-2,4,9,10-tetrahydro-3-thia-2,3a-diazabenzo[*f*]azulene 3,3-dioxide (38) and 3-benzyl-5,10,11,11a-tetrahydro-3*H*-4-thia-3,4a-diazadibenzo[*a*,*d*]cycloheptene 4,4-dioxide (39): TBAF (0.375 mL, 0.375 mmol; 1.0 M solution in THF) was added to a stirred solution of bromoallene **37** (65.3 mg, 0.15 mmol) in THF (1.5 mL) under nitrogen at room temperature, and the resulting mixture was stirred for 3 h under reflux. Concentration under reduced pressure gave an oily residue, which was purified by flash column chromatography over silica gel with *n*-hexane/EtOAc (4:1) to give **38** and **39** (29 mg, 57% yield; **38**:**39** = 95:5).

*Compound **38***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.76 (s, 3H; CMe), 2.56–2.60 (m, 2H; CH_2), 2.90–2.94 (m, 2H; CH_2), 4.36 (s, 2H; CH_2Ph), 4.53 (s, 2H; CH_2Ph), 7.14–7.37 ppm (m, 9H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.6, 25.2, 32.5, 48.0, 51.6, 119.2, 122.3, 126.8, 127.6 (2C), 127.7, 128.45, 128.53 (2C), 129.1, 129.4, 134.8, 136.2, 141.0 ppm; IR (KBr): $\tilde{\nu}$ = 1674 (C=C–N), 1327 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 341 (60) [M^++H], 91 (100); HRMS (FAB): calcd for $C_{19}H_{21}N_2O_2S$ [M^++H]: 341.1324; found: 341.1338.

General procedure for the palladium-catalyzed tandem cyclization of bromoallenes—synthesis of 2-benzyl-6,6-dimethyl-2,3,5,6,7,8-hexahydro-1*H*-1λ^6-[1,2,5]thiadiazolo[2,3-*a*]azepine-1,1-dione (41) and *N*-benzyl-7-(methoxymethyl)-4,4-dimethyl-2,3,4,5-tetrahydro-1*H*-azepine-1-sulfonamide (42): MeOH (1.0 mL) was added to NaH (60% suspension in mineral oil; 20 mg, 0.25 mmol) at 0 °C under nitrogen, and the mixture was stirred for 10 min at room temperature. [$Pd(PPh_3)_4$] (11.6 mg, 0.010 mmol) and a solution of bromoallene **24** (77.0 mg, 0.20 mmol) in MeOH (1.0 mL) were added to the stirred mixture at room temperature, and the resulting mixture was stirred for 6 h at 60 °C. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (3:1) to give, in order of elution, **41** (50.0 mg, 74% yield) and **42** (8.0 mg, 12%).

*Compound **41***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (s, 6H; 2×CMe), 1.73–1.77 (m, 2H; CH_2), 2.00 (d, *J* = 6.0 Hz, 2H; CH_2), 3.42–3.46 (m, 2H; NCH_2), 3.66 (dd, *J* = 3.3, 1.5 Hz, 2H; NCH_2), 4.18 (s, 2H; PhCH_2), 4.60 (tdd, *J* = 6.3, 1.5, 1.5 Hz, 1H; C=CH), 7.32–7.39 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.7 (2C), 32.6, 39.5, 41.4, 42.7, 50.4, 51.3, 102.6, 128.1, 128.7 (2C), 128.7 (2C), 133.6, 134.6 ppm; IR (KBr): $\tilde{\nu}$ = 2956 (C=C), 1691 (C=C–N), 1321 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 307 (100) [M^++H]; HRMS (FAB): calcd for $C_{16}H_{23}N_2O_2S$ [M^++H]: 307.1480; found: 307.1461.

*Compound **42***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (s, 6H; 2×CMe), 1.68–1.72 (m, 2H; CH_2), 2.14 (d, *J* = 6.9 Hz, 2H; CH_2), 3.30 (s, 3H; OMe), 3.42–3.46 (m, 2H; CH_2N), 4.12 (s, 2H; CH_2OMe), 4.27 (d, *J* = 6.3 Hz, 2H; CH_2Ph), 4.95 (t, *J* = 6.3 Hz, 1H; NH), 5.61 (t, *J* = 6.9 Hz, 1H; C=CH), 7.28–7.36 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.4, 29.8 (2C), 39.2, 43.7, 46.3, 47.1, 57.7, 74.0, 126.4, 127.8, 128.0 (2C), 128.7 (2C), 137.1, 140.1 ppm; IR (KBr): $\tilde{\nu}$ = 3298 (NH), 2954 (C=C), 1666 (C=C–N), 1346 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 339 (70) [M^++H], 91 (100); HRMS (FAB): calcd for $C_{17}H_{27}N_2O_3S$ [M^++H]: 339.1742; found: 339.1743.

2-Methyl-6,6-dimethyl-2,3,5,6,7,8-hexahydro[1,2,5]thiadiazolo[2,3-*a*]azepine-1,1-dione (44) and 7-(methoxymethyl)-4,4,*N*′-trimethyl-2,3,4,5-tetrahydro-1*H*-azepine-1-sulfamide (49) (Table 5, entry 1): By using the procedure described for the preparation of the compound **41** and **42** from bromoallene **24**, the bromoallene **25** (62 mg, 0.20 mmol) was converted into **44** (23 mg, 50% yield) and **49** (9.4 mg, 18% yield). This reaction mixture was treated with 4% HCl before purification.

*Compound **44***: Colorless crystals; m.p. 66–67 °C (*n*-hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 (s, 6H; 2×CMe), 1.47–1.51 (m, 2H; CH_2), 1.58–1.62 (m, 2H; CH_2), 2.29–2.33 (m, 2H; CH_2), 2.97 (s, 3H; NMe), 3.49–3.53 (m, 2H; CH_2), 5.52 ppm (t, *J* = 1.2 Hz, 1H; C=CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.4, 28.5 (2C), 31.6, 33.1, 38.2, 41.4, 42.1, 107.4, 127.4 ppm; IR (KBr): $\tilde{\nu}$ = 1658 (C=C–N), 1303 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 231 (81) [M^++H], 154 (100); HRMS (FAB): calcd for $C_{10}H_{19}N_2O_2S$ [M^++H]: 231.1167; found: 231.1167.

*Compound **49***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (s, 6H; 2×CMe), 1.67–1.70 (m, 2H; CH_2), 2.13 (d, *J* = 7.2 Hz, 2H; CH_2), 2.77 (d, *J* = 5.4 Hz, 3H; NMe), 3.35 (s, 3H; OMe), 3.39–3.43 (m, 2H; CH_2), 4.10 (s, 2H; OCH_2), 4.58 (q, *J* = 5.4 Hz, 1H; NH), 5.62 ppm (t, *J* = 7.2 Hz, 1H; C=CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.2, 29.2, 29.8, 39.2 (2C), 43.7, 46.3, 57.7, 74.0, 126.8, 140.0 ppm; IR (KBr): $\tilde{\nu}$ = 3298 ($NHSO_2$), 1666 (C=C–N), 1331 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 263 (64) [M^++H], 231 (100); HRMS (FAB): calcd for $C_{11}H_{23}N_2O_3S$ [M^++H]: 263.1429; found: 263.1431.

2-Benzyl-6-phenyl-2,4,5,6,7,8-hexahydro[1,2,5]thiadiazolo[2,3-*a*]azepine 1,1-dioxide (45) (Table 5, entry 2): By using the procedure described for the preparation of the compound **41** and **42** from bromoallene **24**, the bromoallene **26** (65.3 mg, 0.15 mmol) was converted into **45** (41.7 mg, 78% yield) as colorless crystals. M.p. 88–90 °C (decomp, *n*-hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.57–1.70 (m, 1H; C*H*H), 1.88–2.13 (m, 3H; CH*H* and CH_2), 2.32–2.52 (m, 2H; CH_2), 2.62–2.70 (m, 1H; 6-H), 2.70–3.46 (m, 1H; 8-C*H*H), 3.94–4.01 (m, 1H; 8-CH*H*), 4.45 (d, *J* = 15.0 Hz, 1H; C*H*HPh), 4.51 (d, *J* = 15.0 Hz, 1H; CH*H*Ph), 5.54 (s, 1H; 3-H), 7.15–7.40 ppm (m, 10H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.6, 36.6, 37.2, 42.0, 48.8, 48.9, 105.2, 126.4, 126.6 (2C), 127.0, 128.2, 128.5 (2C), 128.6 (2C), 128.7 (2C), 135.0, 146.4 ppm; IR (KBr): $\tilde{\nu}$ = 1662 (C=C–N), 1302 cm^{-1} (NSO_2); MS (EI) *m*/*z* (%): 355 (1.8) [M^+], 213 (100); HRMS (EI) calcd for $C_{20}H_{22}N_2O_2S$ [M^+]: 354.1402; found: 355.1419.

2-Benzyl-6-(4-methylphenylsulfonyl)-2,4,5,6,7,8-hexahydro-1*H*-[1,2,5]thiadiazolo[2,3-*d*][1,4]diazepine-1,1-dione (46) and *N*-benzyl-7-(methoxymethyl)-4-(4-methylphenylsulfonyl)-2,3,4,5-tetrahydro-1*H*-1,4-diazepine-1-sulfamide (50) (Table 5, entry 4): By using the procedure described for the preparation of the compound **41** and **42** from bromoallene **24**, the bromoallene **27** (77.2 mg, 0.150 mmol) was converted into **46** (31.4 mg, 48% yield) and **50** (2.5 mg, 4% yield). This reaction mixture was treated with 4% HCl before purification.

*Compound **46***: Colorless solid; m.p. 105–106 °C (*n*-hexane/Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (s, 3H; Ph*Me*), 2.56–2.59 (m, 2H; CH_2), 3.28–3.31 (m, 2H; CH_2), 3.41–3.44 (m, 2H; CH_2), 3.76–3.79 (m, 2H; CH_2), 4.41 (s, 2H; CH_2Ph), 5.51 (s, 1H; C=CH), 7.30–7.37 (m, 7H; Ph), 7.62 ppm (d, *J* = 8.4 Hz, 2H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 28.8, 44.2, 48.7, 49.2, 50.0, 106.9, 124.5, 127.0 (2C), 128.3, 128.4 (2C), 128.8 (2C), 130.0 (2C), 134.5, 135.0, 143.9 ppm; IR (KBr): $\tilde{\nu}$ = 1596 (C=C–N), 1309 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 434 (11) [M^++H], 154 (100); HRMS (FAB): calcd for $C_{20}H_{24}N_3O_4S_2$ [M^++H]: 434.1208; found: 434.1219.

*Compound **50***: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (s, 3H; Ph*Me*), 3.25 (s, 3H; OMe), 3.45–3.48 (m, 2H; CH_2), 3.54–3.57 (m, 2H; CH_2), 3.79 (d, *J* = 6.9 Hz, 2H; CH_2), 4.12 (s, 2H; OCH_2), 4.29 (d, *J* = 6.3 Hz, 2H; CH_2Ph), 5.13 (t, *J* = 6.3 Hz, 1H; NH), 5.79 (t, *J* = 6.9 Hz, 1H; C=CH), 7.22–7.36 (m, 7H; Ph), 7.65 ppm (d, *J* = 8.7 Hz, 2H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 45.1, 47.3, 50.4, 50.9, 57.9, 73.2, 122.0, 127.2 (2C), 127.3, 128.0 (2C), 128.8 (2C), 129.9 (2C), 35.3, 36.7, 43.5, 43.8 ppm; IR (KBr): $\tilde{\nu}$ = 1597 (C=C–N), 1333 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 466 (28) [M^++H], 154 (100); HRMS (FAB): calcd for $C_{21}H_{28}N_3O_5S_2$ [M^++H]: 466.1470; found: 466.1483.

(5*S*)-2-Benzyl-5-methyl-6-(4-methylphenylsulfonyl)-2,4,5,6,7,8-hexahydro-1*H*-[1,2,5]thiadiazolo[2,3-*d*][1,4]diazepine-1,1-dione (47) (Table 5, entry 5): By using the procedure described for the preparation of the compound **41** and **42** from bromoallene **24**, the bromoallene **43** (80.0 mg,

0.105 mmol) was converted into **47** (50.0 mg, 74% yield) as colorless crystals. M.p. 96–97°C (*n*-hexane/EtOAc); $[\alpha]_D^{24}=+17.0$ ($c=1.00$ in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.88$ (d, $J=6.9$ Hz, 3H; CMe), 2.29 (dd, $J=15.3$, 4.8 Hz, 1H; C*H*H), 2.43 (s, 3H; Ph*Me*), 2.75–2.80 (m, 1H; CH*H*), 3.18 (dd, $J=15.3$, 4.8 Hz, 1H; C*H*H), 3.52 (dd, $J=15.3$, 4.8 Hz, 1H; CH*H*), 3.88 (dd, $J=15.3$, 4.8 Hz, 1H; C*H*H), 4.07 (dd, $J=15.3$, 4.8 Hz, 1H; CH*H*), 4.37–4.42 (m, 1H; 5-H), 4.45 (d, $J=3.0$ Hz, 2H; PhCH_2), 5.51 (d, $J=1.5$ Hz, 1H; C=CH), 7.28–7.35 (m, 7H; Ph), 7.66 ppm (d, $J=8.1$ Hz, 2H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=14.3$, 21.5, 34.7, 43.2, 44.7, 48.9, 49.8, 108.7, 121.7, 126.8 (2C), 128.3, 128.4 (2C), 128.8 (2C), 129.9 (2C), 134.6, 137.7, 143.6 ppm; $\tilde{\nu}$ = IR (KBr): 1597 (C=C–N), 1323 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 448 (51) [M^++H], 154 (100); HRMS (FAB): calcd for $C_{21}H_{26}N_3O_4S_2$ [M^++H]: 448.1365; found: 448.1363.

2-Benzyl-2,4,5,6,7,8-hexahydro-1*H*-[1,2,5]thiadiazolo[2,3-*a*]azepine-1,1-dione (48) (Table 5, entry 6): By using the procedure described for the preparation of the compound **41** and **42** from bromoallene **24**, the bromoallene **28** (50 mg, 0.14 mmol) was converted into **48** (11 mg, 28% yield) as colorless oil: ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.61$–1.73 (m, 4H; 2×CH_2), 1.79–1.83 (m, 2H; CH_2), 2.28 (m, 2H; CH_2), 3.58 (*t*, $J=5.1$ Hz, 2H; CH_2), 4.45 (s, 2H; CH_2Ph), 5.47 (s, 1H; C=CH), 7.29–7.40 ppm (m, 5H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=27.7$, 28.8, 29.9, 30.5, 43.3, 48.9, 105.0, 127.4, 128.0, 128.4 (2C), 128.6 (2C), 134.9 ppm; IR (KBr): $\tilde{\nu}=1660$ (N-C=C), 1303 (NSO_2), 1172 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 301 (49) [M^++Na], 278 (100); HRMS (FAB): calcd for $C_{14}H_{18}N_2NaO_2S$ [M^++Na]: 301.0987; found: 301.0963.

2-Benzyl-3,5,6,11-tetrahydro[1,2,5]thiadiazolo[2,3-*b*][2]benzazocine-1,1-(2*H*)-dione (53) (Table 6, entry 1): NaH (60% suspension in mineral oil; 20 mg, 0.625 mmol) was added to MeOH (1 mL) at room temperature under nitrogen, and the mixture was stirred for 10 min at this temperature. [$Pd(PPh_3)_4$] (23.1 mg, 0.0200 mmol) and a solution of the bromoallene **37** (84.3 mg, 0.2 mmol) in MeOH (1 mL) were added to the stirred mixture at room temperature, and the resulting mixture was stirred for 1.5 h at 60°C. After the mixture was quenched with saturated NH_4Cl, the whole was extracted with EtOAc. The extract was washed with water, saturated $NaHCO_3$ and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (4:1) to give **53** (containing a small amount of **54**; **53**:**54** = 12:1; 39 mg, 57% yield). Full characterization of the compound **53** was hampered by its instability (the compound **53** is easily isomerized into the double bond isomer **54**).

*Compound **53***: Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): $\delta=2.57$ (dt, $J=7.5$, 7.5 Hz, 2H; CH_2), 3.12 (t, $J=7.5$ Hz, 2H; CH_2), 3.49 (d, $J=1.5$ Hz, 2H; CH_2), 4.08 (s, 2H; CH_2), 4.51 (tt, $J=7.5$, 1.5 Hz, 1H; C=CH), 4.81 (s, 2H; CH_2), 7.09–7.13 (m, 1H; Ph), 7.23–7.36 (m, 7H; Ph), 7.43–7.47 ppm (m, 1H; Ph).

*Compound **54***: Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.75$–1.83 (m, 2H; 5-CH_2), 2.33 (t, $J=6.0$ Hz, 2H; 4-CH_2), 2.80–2.84 (m, 2H; 6-CH_2), 4.10 (s, 2H; PhCH_2), 4.60 (s, 2H; PhCH_2), 5.37 (s, 1H; 3-H), 7.12–7.54 ppm (m, 9H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=27.2$, 31.8, 33.8, 47.3, 50.9, 111.2, 126.7, 127.5, 127.9, 128.4 (2C), 128.5 (2C), 128.9, 129.9, 131.2, 133.2, 134.5, 141.4 ppm; IR (KBr): $\tilde{\nu}=1653$ (C=C–N), 1317 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 340 (40) [M^++Na], 91 (100); HRMS (FAB): calcd for $C_{19}H_{20}N_2NaO_2S$ [M^++Na]: 363.1143; found: 363.1132.

(5*S*)-2-Benzyl-5-methyl-6-(4-methylphenylsulfonyl)-4,5,6,7,8,9-hexahydro[1,2,5]thiadiazolo[2,3-*a*][1,5]diazocine-1,1(2*H*)-dione (55) (Table 6, entry 2): MeOH (0.7 mL) was added to NaH (60% suspension of mineral oil; 15 mg, 0.38 mmol) at 0°C under nitrogen, and the mixture was stirred for 10 min at room temperature. [$Pd(PPh_3)_4$] (17.3 mg, 0.015 mmol) and a solution of the bromoallene **51** (86.2 mg, 0.159 mmol) in MeOH (1.0 mL) were added to the stirred mixture at room temperature, and the resulting mixture was stirred for 6 h at 60°C. 4% HCl (0.5 mL) was added to the mixture at room temperature. The whole was extracted with EtOAc. The extract was washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (4:1) to give **55** (42.5 g, 58% yield) as colorless crystals. M.p. 127–128°C (*n*-hexane/EtOAc); $[\alpha]_D^{26}=+75.0$ ($c=1.00$ in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.75$ (d, $J=6.9$ Hz, 3H; CMe), 1.92–2.00 (m, 1H; C*H*H), 2.07–2.21 (m, 1H; CH*H*), 2.15 (dd, $J=15.6$, 4.2 Hz, 1H; C*H*H), 2.42 (s, 3H; Ph*Me*), 2.74 (dd, $J=15.6$, 4.2 Hz, 1H; CH*H*), 2.92 (ddd, $J=19.2$, 12.3, 3.6 Hz, 1H; C*H*H), 3.45 (dd, $J=15.6$, 4.2 Hz, 1H; C*H*H), 3.72 (ddd, $J=19.2$, 12.3, 3.6, 1H; CH*H*), 3.82 (dd, $J=15.6$, 4.2 Hz, 1H; CH*H*), 4.09–4.23 (m, 1H; 6-H), 4.45 (s, 2H; PhCH_2), 5.45 (s, 1H; C=CH), 7.24–7.40 (m, 7H; Ph), 7.70 ppm (d, $J=8.1$ Hz, 2H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=14.8$. 21.5, 30.5, 33.7, 37.9, 39.1, 48.7, 50.9, 108.2, 120.1, 127.0 (2C), 128.3, 128.4 (2C), 128.7 (2C), 129.8 (2C), 134.7, 136.9, 143.5 ppm; IR (KBr): $\tilde{\nu}=1597$ (C=C–N), 1331 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 462 (34) [M^++H], 154 (100); HRMS (FAB): calcd for $C_{22}H_{28}N_3O_4S_2$ [M^++H]: 462.1521; found: 462.1512.

2-Benzyl-5-methyl-7-(4-methylphenylsulfonyl)-4,5,6,7,8,9-hexahydro-[1,2,5]thiadiazolo[2,3-*d*][1,4]diazocine-1,1(2*H*)-dione (57) (Table 6, entry 3): By using the procedure described for the preparation of the compound **59** from bromoallene **55**, the bromoallene **36** (81.4 mg, 0.150 mmol) was converted into **56** and **57** (36.2 mg, 52% yield, **56**:**57** = 1:4). In this case, it was difficult to isolate and characterize the compound **56**, because **56** was readily converted into compound **57** in $CDCl_3$.

*Compound **57***: Colorless crystals; m.p. 109–110°C (*n*-hexane/EtOAc); ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.80$ (d, $J=6.3$ Hz, 3H; CMe), 2.03 (dd, $J=15.0$, 2.4 Hz, 1H; 4-C*H*H), 2.35–2.41 (m, 2H; 4-CH*H;* and 5-H), 2.44 (s, 3H; Ph*Me*), 2.81–2.90 (m, 2H; CH_2), 3.35–3.39 (m, 1H; C*H*H), 3.60–3.68 (m, 1H; CH*H*), 3.81–3.95 (m, 2H; CH_2), 4.41 (d, $J=14.7$ Hz, 1H; C*H*HPh), 4.48 (d, $J=14.7$ Hz, 1H; CH*H*Ph), 5.50 (s, 1H; C=CH), 7.29 (m, 7H; Ph), 7.66 ppm (d, $J=8.4$ Hz, 2H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=16.6$, 21.5, 28.2, 33.7, 43.8, 49.5, 52.2, 54.6, 108.4, 121.5, 127.0 (2C), 128.3, 128.5 (2C), 128.8 (2C), 129 (2C), 134.7, 135.4, 143.7 ppm; IR (KBr): $\tilde{\nu}=1499$ (C=C–N), 1333 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 462 (17) [M^++H], 154 (100); HRMS (FAB): calcd for $C_{22}H_{28}N_3O_4S_2$ [M^++H]: 462.1521; found: 462.1530.

5-Bromomethyl-3,3-dimethyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-pyrrole (66) (Table 7, entry 1): NaH (6.6 mg, 0.17 mmol) was dissolved in MeOH (0.5 mL) at room temperature under nitrogen, and the mixture was stirred for 10 min at this temperature. A solution of the bromoallene **65** (37.9 mg, 0.110 mmol) in MeOH (0.6 mL) was added to the stirred mixture at room temperature. After the mixture was stirred for 30 min at room temperature, the mixture was poured into ice-water saturated with NH_4Cl. The mixture was extracted with Et_2O. The extract was washed with water and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (7:1) to give **66** (3 mg, 8% yield) and **65** (27.0 mg, 71% yield, recovery).

*Compound **66***: Colorless crystals; m.p. 80–82°C (*n*-hexane); ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.83$ (s, 6H; 2×CMe), 2.43 (s, 3H; Ph*Me*), 3.51 (s, 2H; 2-CH_2), 4.37 (s, 2H; 1′-CH_2), 5.28 (s, 1H; 4-H), 7.32–7.35 (m, 2H; Ph), 7.70–7.72 ppm (m, 2H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=21.6$, 25.4, 27.6 (2C), 40.6, 63.3, 127.0, 127.6 (2C), 129.7 (2C), 134.3, 137.9, 144.0 ppm; IR (KBr): $\tilde{\nu}=1643$ (C=C–N), 1350 cm^{-1} (NSO_2); MS (FAB): *m*/*z* (%): 368 (91) [M^++Na, ^{81}Br], 366 (91) [M^++Na, ^{79}Br], 176 (100); HRMS (FAB): calcd for $C_{14}H_{18}BrNNaO_2S$ [M^++Na, ^{79}Br]: 366.0139; found: 366.0145.

5-Methoxymethyl-3,3-dimethyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-pyrrole (67) (Table 7, entry 2): NaH (60% suspension of mineral oil; 9 mg, 0.225 mmol) was dissolved in MeOH (0.7 mL) at room temperature under nitrogen, and the mixture was stirred for 10 min at this temperature. A solution of the bromoallene **65** (51.6 mg, 0.15 mmol) in MeOH (0.8 mL) was added to the stirred mixture at room temperature, and the resulting mixture was stirred for 7 h at 60°C. Concentration under reduced pressure gave an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (5:1) to give **67** (41.6 mg, 94% yield) as colorless crystals. M.p. 69–71°C (*n*-hexane/Et_2O); ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.85$ (s, 6H; 2×CMe), 2.42 (s, 3H; Ph*Me*), 3.42 (s, 3H; OMe), 3.46 (s, 2H; 2-CH_2), 4.30 (d, $J=1.5$ Hz, 2H; 1′-CH_2), 5.08 (t, $J=1.5$ Hz, 1H; 4-H), 7.31–7.33 (m, 2H; Ph), 7.70–7.73 ppm (m, 2H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=21.5$, 28.1 (2C),

40.5, 58.6, 63.1, 68.4, 122.4, 127.6 (2C), 129.6 (2C), 134.3, 138.0, 143.6 ppm; IR (KBr): $\tilde{\nu}$ = 1655 (C=C–N), 1348 cm^{-1} (NSO_2); MS (FAB): *m/z* (%): 318 (100) [M^++Na]; HRMS (FAB): calcd for $C_{15}H_{22}NO_3S$ [M^++Na]: 296.1320; found: 296.1340.

8-Benzyl-7,7-dioxo-5,6,7,8,9,11,12,13-octahydro-7-thia-6,8-diazabenzocycloundecen-10-one (75) and 2-benzyl-4,5,6,11-tetrahydro-2*H*-1-thia-2,11a-diazabenzo[*a*]cyclopenta[*d*]cyclooctene 1,1-dioxide (54): NaH (60% suspension of mineral oil; 15 mg, 0.375 mmol) was dissolved in MeOH (0.5 mL) at room temperature under nitrogen, and the mixture was stirred for 10 min at this temperature. [$Pd(PPh_3)_4$] (17.3 mg, 0.015 mmol) and a solution of the bromoallene **37** (63.2 mg, 0.15 mmol) in MeOH (1 mL) were added to the stirred mixture at room temperature, and the resulting mixture was stirred for 1.5 h at 60 °C. The mixture was made acidic with 4% HCl, and the whole was extracted with Et_2O. The extract was washed with water and brine, and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with *n*-hexane/EtOAc (4:1) to give **75** (22 mg, 41% yield) and **54** (11.4 mg, 22% yield).

Compound ***75***: Colorless crystals; m.p. 148–149 °C (*n*-hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.10 (tt, *J* = 6.3, 6.3 Hz, 2H; 12-CH_2), 2.42 (t, *J* = 6.3 Hz, 2H; 11-CH_2), 2.65 (t, *J* = 6.3 Hz, 2H; 13-CH_2), 3.61 (s, 2H; 9-CH_2), 4.15 (d, *J* = 5.4 Hz, 2H; 5-CH_2), 4.44 (t, *J* = 5.4 Hz, 1H; NH), 4.70 (s, 2H; CH_2Ph), 7.20–7.37 ppm (m, 9H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.0, 29.7, 40.5, 45.3, 51.1, 53.1, 126.7, 128.0, 128.7 (2C), 128.9 (3C), 130.1, 130.8, 134.0, 135.5, 140.7, 208.6 ppm; IR (KBr): $\tilde{\nu}$ = 3298 ($NHSO_2$), 1716 (C=O), 1321 cm^{-1} ($NHSO_2$); elemental analysis calcd (%) for $C_{19}H_{22}N_2O_3S$: C 63.66, H 6.19, N 7.82; found: C 63.58, H 6.21, N 7.78.

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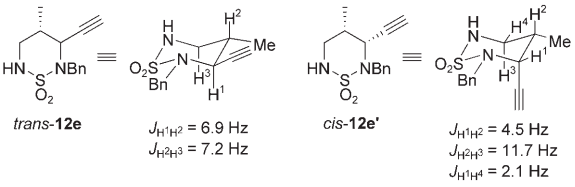
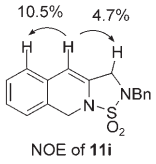
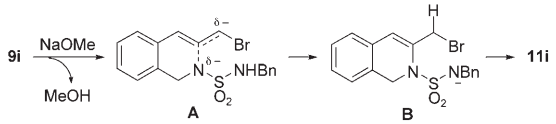
[24] For synthesis of the propargyl alcohol (±)-**7e**, see the Supporting Information.
[25] We observed by ^{1}H NMR spectra that the isomer **16a** is gradually converted into the isomer **11a** in CD_3OD. Therefore, it is apparent that the isomer **11a** is thermodynamically more stable than the isomer **16a**. At the present stage of our understanding, preferential formation of the relatively unstable isomer **16a** by the reaction with TBAF/THF over the isomer **11a** is unclear.
[26] Structure of *trans*-**12e** and *cis*-**12e′** were determined by comparison of *J* values of the ring protons, as shown below.



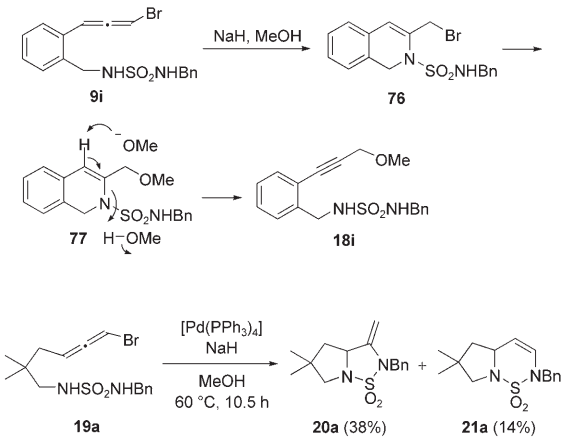
[27] The structure of **11i** was determined by NOE analysis.



[28] The phenyl group of **9i** promotes the regioselective cyclization onto the central allenic carbon, presumably through a highly conjugated anionic transition state **A** and/or intermediate **B**.



[29] Formation of the alkyne **18i** can be rationalized by addition-elimination mechanism. One plausible pathway is shown below.
[30] A similar result was obtained by the cyclization in the presence of palladium(0), although the yield was lower, as shown below.
[31] Related five-membered ring formations by intramolecular amination of carbon–carbon triple bond have been already reported, see: a) Y. Tamaru, M. Kimura, S. Tanaka, S. Kure, Z. Yoshida, *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2838–2849; b) P. A. Jacobi, H. L. Brielmann, S. I.



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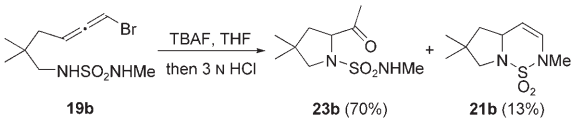
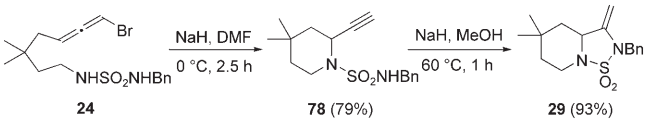
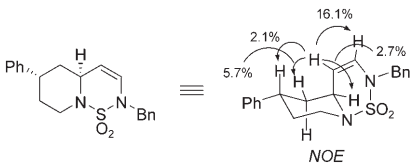
[32] Isolation of **20′b** was extremely difficult due to the hydrolysis during purification, yielding a ring-opening product **23b**. Accordingly, **23b** was isolated in 70% yield after acidic workup and fully characterized.



[33] The ratio of **20′b**/**21b** was determined as follows: concentration of the reaction mixture and rapid filtration with short pad of SiO_2 gave a crude mixture, ^{1}NMR analysis of which showed formation of **20′b** and **21b** (2.5:1) quantitatively, without detecting **23b**.
[34] To reveal the intermediate of this tandem cyclization reaction, we investigated stepwise reaction of the bromoallene **24**. Treatment of the bromoallene **24** with NaH in DMF gave piperidine **78** in 79% yield. Reaction of **78** under the same reaction conditions as the one-pot reaction afforded the *exo*-cyclized product **29** (93%) as a single isomer.



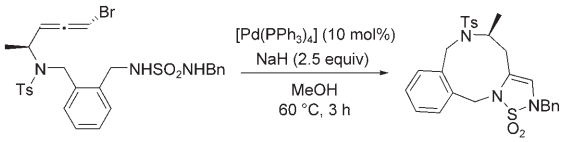
[35] Structure of (±)-**32** was confirmed by NOE analysis as shown below.



[36] The reaction of **27** with NaH in MeOH afforded an inseparable mixture of (*E*)- and (*Z*)-enynes, produced by elimination of HBr under the basic reaction conditions.
[37] A trace amount of **39** was also detected by ^{1}H NMR spectroscopy.
[38] The reaction with 2 mol% $[Pd(PPh_3)_4]$ was ineffective: only 15% of the cyclosulfamide **49** and a trace amount of **32**, produced by the uncatalyzed reaction (Table 5), were obtained.

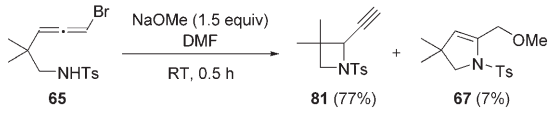
[39] Without treatment with HCl, the ratio of regioisomers (products of the type **53** and **54**) is variable.

[40] The palladium-catalyzed cyclization of bromoallene **79** having a six-atom tether between the sulfamide and allenyl group gave a trace of the desired tricyclic sulfamide **80** containing a nine-membered ring (<5% yield).



79 **80** (< 5%)

[41] Treatment of bromoallene **65** with NaOMe in DMF gave azetidine **81** as a major product and a small amount of dihydropyrrole **67** having a methoxymethyl group. We have already reported the formation of azetidines by NaH-mediated intramolecular amination of bromoallenes: see, reference [13b].



65 **81** (77%) **67** (7%)

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