New Synthesis of 1,2-Thiazetidines of *anti*- and *syn*-9,9′-Bibenzonorbornenylidenes

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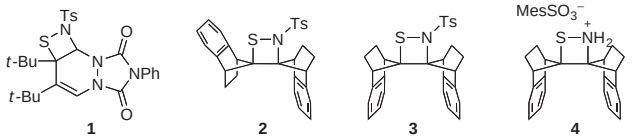
1,2-Thiazetidines **2** and **3** were synthesized by the reactions of *anti*- and *syn*-9,9′-bibenzonorbornenylidenes with TsNSO, followed by deimination with SmI_2. Heating **2** and **3** neat produced a mixture containing aziridines, thiiranes, and alkenes.

Much attention has been paid to the synthesis, structure, reactions, and synthetic applications of small-membered heterocycles that contain some heteroatoms at vicinal positions in their ring, because such heterocycles are very reactive by electrostatic repulsion among lone-pair electrons of the heteroatoms.[1] In four-membered saturated heterocycles with two heteroatoms, one of which is a nonoxidized sulfur atom, 1,2-oxathietane and 1,2-dithietane have been synthesized,[2,3] whereas 1,2-thiazetidine had not been obtained until we succeeded in isolating 1,2-thiazetidine **1** for the first time (Figure 1).[4,5] Compound **1** was unexpectedly formed by the reaction of *N*-tosyl-3,4-di-*t*-butylthiophene 1-imide and PTAD. Recently, we have reported another method for forming 1,2-thiazetidines **2** and **3** and 1,2-thiazetidin-2-ium salt **4** from *N*-tosylthiirane 1-imides and *S*-aminothiiranium salt, respectively.[6,7] Compounds **1**–**4** seemed to be stabilized by both the steric effect of bulky substituents and the electronic effect of a substituent on their nitrogen atom. To better understand the chemistry of 1,2-thiazetidines, both development of this new synthesis and a study of their chemical properties are of crucial importance. We report here the synthesis of 1,2-thiazetidines by using reactions of *anti*- and *syn*-9,9′-bibenzonorbornenylidenes with TsNSO and their thermal decomposition.

N-Sulfinylamide (RNSO) is known to react with enol ether, ketene, and ketenimine yielding 3-alkoxy-, 3-oxo-, and 3-imino-1,2-thiazetidine 1-oxides, respectively.[8–10] It, therefore, seems to be a convenient reagent for constructing a 1,2-thiazetidine skeleton. Reaction of sterically congested alkene with RNSO, followed by deoxygenation of the resulting 1,2-thiazetidine 1-oxide would give 1,2-thiazetidine. Hence, we examined the reactions of alkenes, **5**–**7** and **15**, with TsNSO (Table 1 and Figure 2). Alkene **5** did not react with TsNSO in refluxing CH_2Cl_2 (Entry 1). When the reaction was performed in refluxing $(CH_2Cl)_2$, 1,2-thiazetidine 1-imide **8** was formed together with a small quantity of 1,2-thiazetidine 1-oxide **11** (Entry 2).[11] Further reaction of **11** with TsNSO must form **8**.[12] The same procedure for **6** gave **9** (Entry 3), whereas that for **7**[13] yielded aziridine **13** and thiirane **14** (Entry 4). Decreasing the reaction temperature resulted in the formation of **10**,[11] which decreased the yield of **13**, and increased



1 2 3 4

Figure 1.

Table 1. Reactions of alkenes with TsNSO

alkene (**5**–**7**) —TsNSO→ 1,2-thiazetidine 1-imide (**8**—**10**)

Entry	Alkene	Conditions	Products (yield/%)
1[a]	**5**	CH_2Cl_2, reflux, 48 h	**5** (quant.)
2[a]	**5**	$(CH_2Cl)_2$, reflux, 48 h	**8** (72), **11** (4), **5** (6)
3[a]	**6**	$(CH_2Cl)_2$, reflux, 48 h	**9** (70), **12** (1), **6** (2)
4[b]	**7**	$(CH_2Cl)_2$, reflux, 74 h	**13** (78), **14** (2)
5[b]	**7**	$(CH_2Cl)_2$, 60 °C, 74 h	**10** (22), **13** (43), **14** (6), **7** (24)
6[b]	**7**	CH_2Cl_2, reflux, 126 h	**10** (52), **13** (6), **14** (1), **7** (34)
7[b]	**7**	$(CH_2Cl)_2$, rt, 312 h	**10** (12), **13** (4), **7** (61)[c]

[a]TsNSO (5.0 mol equiv). [b]TsNSO (3.5 mol equiv). [c]A trace amount of **14** was detected.

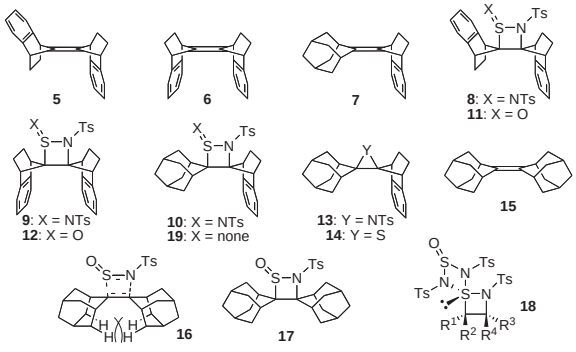


Figure 2.

the recovery of **7** (Entries 5 and 6). The reaction in refluxing CH_2Cl_2 resulted in an improved yield of **10**. The reaction at room temperature slowed and gave a small quantity of **10** (Entry 7). Regio- and π-face selectivity in the reaction is caused by both the homoconjugation interaction between the central C=C bond and the benzene ring,[13] which results in the polarization of the C=C bond, and steric repulsion among the tosyl group in TsNSO and the substituents in **10**. On the other hand, the reaction of **15** with TsNSO gave a quantitative recovery of **15**, suggesting that steric repulsive interaction among hydrogens of the substituents in the transition state such as **16** prevents the formation of **17**.[14]

Compound **10** seemed to transform into **13**, **14**, and **7** under the reaction conditions; hence, heating a solution of **10** in the presence or absence of TsNSO or $TsNH_2$, which is probably formed by hydrolysis of TsNSO, was investigated (Table 2). Most of **10** transformed into **13** in the presence of TsNSO (Entry 1), whereas the proportion of **13** in the reaction with $TsNH_2$ was reduced to almost half (Entry 2). In the absence of both reagents, decomposition proceeded but slowed (Entry 3). As a result, TsNSO was found to accelerate the decomposition more than $TsNH_2$. Ring opening of **10** with its C–S bond cleavage may be the first step in the transformaton into **13**[15] and is probably promoted by the reaction of TsNSO at the sulfimino moiety

Table 2. Decomposition of **10** in the presence or absence of TsNSO or $TsNH_2$

10 $\xrightarrow[(CH_2Cl)_2,\ 60\ °C,\ 48\ h]{\text{TsNSO or } TsNH_2}$ **13** + **14** + **7**

Entry	Mol equiv of TsNSO	Mol equiv of $TsNH_2$	Yield/%			
			13	**14**	**7**	**10**
1	2.5	none	73	trace	N	18
2	none	2.5	31	trace	4	65
3	none	none	14	1	2	78

Table 3. Reactions of thiazetidine 1-imides with reductants

Thiazetidine 1-imide (**8**–**10**) $\xrightarrow[THF]{\text{reductant}}$ Thiazetidine or Aziridine (**2**, **3**) (**21**, **13**)

Entry	Thiazetidine 1-imide	Reductant (mol equiv)	Conditions	Products (yield/%)
1	**8**	SmI_2 (5.0)[a]	rt, 3 h	**2** (63), **11** (6)
2	**9**	SmI_2 (7.0)[a]	rt, 96 h	**3** (45)
3	**9**	SmI_2 (7.0)[a]	reflux, 96 h	**21** (34)
4	**10**	SmI_2 (5.0)[a]	rt, 72 h	**13** (84)
5	**8**	$TiCl_4$/Zn (10)[b]	reflux, 96 h	**2** (87)
6	**10**	$TiCl_4$/Zn (10)[b]	rt, 32 h	**13** (80)
7	**10**	$TiCl_4$/Zn (10)[b]	−40 °C, 156 h	**13** (40), **10** (52)

[a]A 0.1 M THF solution. [b]A low-valent titanium reagent was prepared by reaction of $TiCl_4$ (10 mol equiv) and Zn (10 mol equiv) in refluxing THF for 1 h.

(>S=NTs) in **10** forming tetracoordinate 1,2-thiazetidine **18**. A pathway through the ligand coupling of **18**, which gives **13**, is also possible.[16]

SmI_2 was used successfully for deimination of **8** and **9** (Table 3).[17] The reaction of **8** with SmI_2 in THF at room temperature, followed by purification by silica-gel column chromatography gave **2** together with **11** (Entry 1). A similar procedure for **9** yielded **3** (Entry 2). Although intermediates were observed in both reactions before chromatographic separation, their structure unfortunately could not be confirmed because of difficulty in isolating them. The reaction of **9** in refluxing THF gave aziridine **21**, and no formation of **3** was observed (Entry 3). On the other hand, **10** reacted with SmI_2 to give **13** at room temperature (Entry 4). A low-valent titanium reagent, which was prepared by the reaction of $TiCl_4$ and Zn in refluxing THF, also deiminated **8** to give **2**, whereas it reacted with **10** to yield **13** even at −40 °C (Entries 5–7).[18] The steric effect of the substituents in 1,2-thiazetidine **19** may be less effective than that in **2** and **3**, and hence further reaction of **19** with the reductant probably forms **13** even at low temperature.

Both **2** and **3** decomposed on heating neat to form a mixture of aziridines, thiiranes, and alkene(s) (Figure 3). Thus, heating **2** above 172 °C for 30 min gave **20** (20%), **21** (5%), **22** (31%), **23** (11%), **5** (21%), **6** (5%), **8** (2%), and **2** (6%). Thiazetidine 1-imide **8** was probably formed by the reaction of **2** with tosylnitrene or its equivalent. Further reactions of **2** and these products with a non-volatile reactive species, such as tosylnitrene and Ts–N=S, which form as a by-product, may complicate the decomposition. Heating **3** above 165 °C for 30 min produced **20** (58%), **21** (7%), **22** (7%), **23** (17%), **6** (5%), and **3** (7%). It is noteworthy that the total yield of *anti*-products (**20**, **22**, and **5**) was higher than that of *syn*-products (**21**, **23**, and **6**) in both reactions.[19] There would be a number of pathways through the N–S, C–S, and C–N bond cleavages of **2** and **3** in the first step

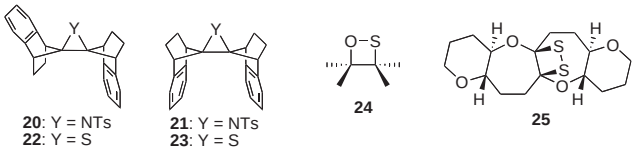


Figure 3.

of the decomposition. These results are in contrast with 1,2-oxathietane **24**, which decomposes to form acetone and thioacetone in solution above −20 °C,[2] and 1,2-dithietane **25**, which extrudes two sulfur atoms to form the corresponding alkene on heating neat.[3]

In summary, we not only developed a synthetic method for 1,2-thiazetidines by the reactions of sterically congested alkenes with TsNSO, followed by deimination with SmI_2 or a low-valent titanium reagent but also observed thermolysis of 1,2-thiazetidines giving a mixture of aziridine, thiiranes, and alkenes. Further investigation into the chemistry of 1,2-thiazetidines is in progress.

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