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A novel method for thiiranation of alkenes with 1,1′-dithiobis(1*H*-1,2,4-triazole)

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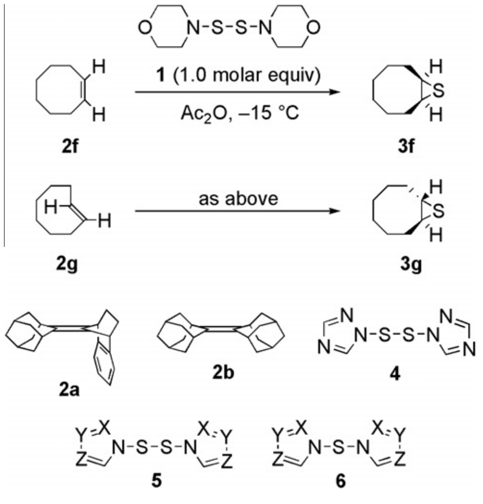
ABSTRACT

Eight alkenes reacted with 1,1′-dithiobis(1*H*-1,2,4-triazole) **4** at −15 °C to form the corresponding thiiranes in moderate to good yields. The thiiranations of *anti*- and *syn*-9,9′-bibenzonorbornenylidenes and *cis*- and *trans*-cyclooctenes with **4** proceeded with retention of configuration of the starting alkenes.

Three-membered heterocycles are good precursors for organic syntheses because relieving their ring strain can accelerate their reactions, and therefore, syntheses of many valuable compounds from oxiranes and aziridines have been reported to date.[1,2] Thiiranes seem to act as superior precursors to oxiranes and aziridines because their sulfur atom facilitates their transformation to other compounds.[2] Although many methods for both oxiranation and aziridination of alkenes (direct syntheses of oxiranes and aziridines from alkenes) have been developed, only a few methods for thiiranation of alkenes with sulfur-atom transfer agents are known,[3] despite much effort being devoted to the development of an efficient method for thiirane production. However, none of the reported thiiranation methods offer a broad preparative scope because they have serious shortcomings such as being limited to alkenes used, using an excess of alkenes or sulfur-atom transfer agents, conducting thiiranations under severe conditions, and further reactions of the resulting thiiranes. The rational reasons for the shortcomings seem to be the lower electrophilic character of the sulfur-atom transfer agents relative to the reagents used in oxiranation or aziridination and a propensity for the formation of a catenated sulfur–sulfur linkage by the reaction between the electrophilic and nucleophilic sulfur atoms in the agent and the thiirane, respectively.[3a] Consequently, two-step synthesis of thiiranes from alkenes via oxiranes is quite popular in laboratories, and many methods for the transformation from oxiranes to thiiranes have been developed.[2a] Recently, we reported that some alkenes underwent thiiranation with a mixture of 4,4′-dithiodimorpholine (**1**) and Brønsted acid or acid anhydride as an activating agent.[4,5] The thiiranation of two tetrasubstituted alkenes **2a** and **2b** and *cis*- and *trans*-cyclooctenes **2f** and **2g** using Ac_2O as a solvent at −15 °C gave the corresponding thiiranes in moderate to good yields (Scheme 1), whereas other disubstituted alkenes, such as dicyclopentadiene and *cis*- and *trans*-stilbenes, did not undergo thiiranation under similar conditions even at elevated temperatures.[5a] We have now found that some tetrasubstituted and cyclic alkenes react with 1,1′-dithiobis(1*H*-1,2,4-triazole) (**4**)



Scheme 1.

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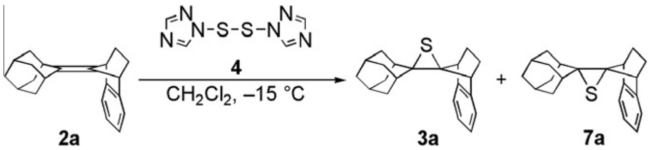
Table 1
Effect of different quantities of **4** on thiiranation of **2a**



Entry	Molar equivalent of **4**	Time	% Yields (% relative yields)[a]		
			3a	**7a**	**2a**
1	1.0	3 h	58 (65)	6 (7)	11
2	0.5	18 h	53(80)	6 (9)	34
3	3.0	30 min	98	Trace	Trace

[a] The relative yield is based on the converted **2a** by normalizing it to 100%.

without an activating agent under mild conditions to give the corresponding thiiranes in moderate to good yields.

Reportedly, *N*,*N*′-dithiobisazole (**5**) and *N*,*N*′-thiobisazole (**6**), which have N–S–S–N and N–S–N linkage, respectively, and their benzazolyl analogs can act as good sulfur-atom transfer agents when reacting with some types of nucleophiles.[6] The disulfide **5** is known to be more reactive than the corresponding sulfide **6**. In a series of these compounds, **4** synthesized by the reaction of *N*-trimethylsilyl-1,2,4-triazole with S$_2$Cl$_2$ has moderate reactivity toward nucleophiles;[6a] hence, it may act as a thiiranation reagent for alkenes.

Surprisingly, alkene **2a**, which seems to be a model alkene suitable for investigating the thiiranation conditions because of the ease of its analysis,[7] reacted with **4** in CH$_2$Cl$_2$ at -15 °C without an activating agent to give the corresponding thiiranes **3a** and **7a** (Table 1). Thus, thiiranation of **2a** with 1.0 molar equiv of **4** afforded **3a** and **7a** in 58% and 6% yields, respectively, together with **2a** in 11% yield. When 0.5 molar equiv of **4** was used, the total yield of **3a** and **7a** exceeded 50%, suggesting that one or more sulfur atoms of **4** were introduced into **2a** in the thiiranation. The reaction with 3.0 molar equiv of **4** resulted in the consumption of **2a** and the exclusive formation of **3a**.

Treatment of **2b** with 1.0 molar equiv of **4** at -15 °C gave **3b** (Table 2, entry 1).[8,9] Thiiranations of **2c** and **2d** proceeded with retention of the stereochemical configuration of alkenes, forming **3c** and a mixture of **3d** and **7d**, respectively (entries 2 and 3).[10] No other product derived from the alkenes **2b**–**d** was observed in their thiiranation, so the relative yield of the thiiranes was approximately quantitative. Compound **2e**,[11] a different type of tetrasubstituted alkene, underwent at room temperature neither thiiranation to form **3e** nor sulfuration to afford pentathiepane **8e**, which is produced exclusively by sulfuration of **2e** with elemental sulfur,[12] resulting in the quantitative recovery of **2e** (Fig. 1). This may be because **3e**, having a strained [3.3.1]propellane skeleton, is not formed due to the high energy barrier of the transition state of the thiiranation,

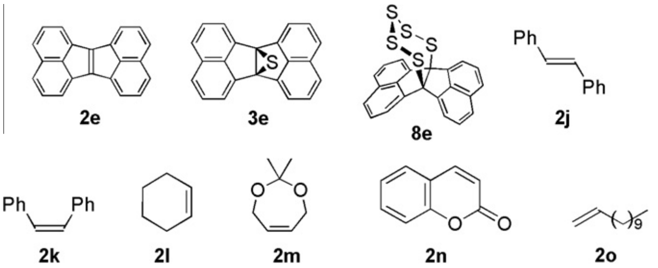
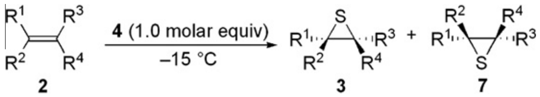
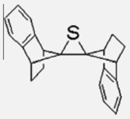
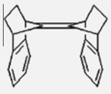
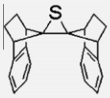
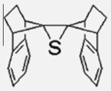
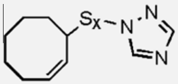
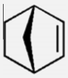
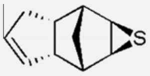


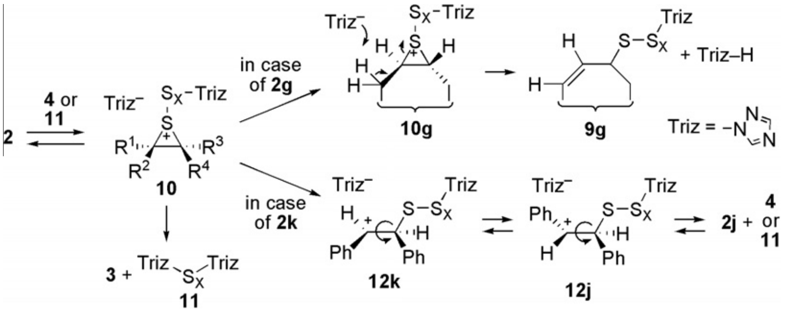
Figure 1.

Table 2
Thiiranation of **2** with **4**[a]



Entry	Solvent	Alkene	Products (yield) [relative yield][b]		Recovery yield **2**
1	CH$_2$Cl$_2$	**2b** 	**3b** (93%)[c] [99%] 		6%[c]
2	CH$_2$Cl$_2$	**2c** 	**3c** (60%)[c] [97%] 		37%[c]
3	CH$_2$Cl$_2$	**2d**	**3d** (19%)[c] [76%]	**7d** (6%)[c] [24%]	75%[c]
4	CDCl$_3$	**2f**	**3f** (50%)[d] [96%]		48%[d]
5	CDCl$_3$	**2g** 	**3g** (58%)[d] [59%] 	**9g** (41%)[d]	ND[e]
6	CDCl$_3$	**2h** 	**3h** (8%)[d] [32%] 		75%[d]
7	CDCl$_3$	**2i**	**3i** (38%)[d] [83%]		54%[d]

[a] Reactions of **2e** and **2j**–**o** with **4** did not afford the corresponding thiiranes.
[b] The relative yield is based on the converted alkene by normalizing it to 100%.
[c] Isolated yield.
[d] Judged from the ^{1}H NMR spectrum of the reaction mixture with triptycene as an internal standard.
[e] Not detected.



Scheme 2.

or if **3e** is produced, the decomposition into **2e** proceeds under the reaction conditions.[13] This thiiranation is also applicable to some cyclic alkenes. Thus, similar treatment of *cis*-and *trans*-cyclooctenes **2f** and **2g** with **4** resulted in the stereospecific formation of **3f** and **3g**,[14] respectively (entries 4 and 5). In the case of the thiiranation of **2g**, both isomerization of **2g** to **2f**, which is thermodynamically more stable than **2g**,[15] and that of **3g** to **3f** were not observed, and a byproduct **9g**, whose structure was speculated by the ^{1}H, ^{13}C, and 2D NMR spectra, including ^{1}H–^{1}H COSY, HMQC, and HMBC, of the reaction mixture,[16–18] was detected. The thiiranation of **2h** proceeded at its *exo*-π-face, affording **3h** (entry 6).[14c,19] When **2i** reacted with 1.0 molar equiv of **4**, one sulfur atom was introduced onto one of the two C=C bonds, forming **3i** (entry 7).[3d] The reaction of *trans*-stilbene **2j** with **4** at room temperature for 4 d resulted in the quantitative recovery of **2j**, whereas that of *cis*-stilbene **2k** for 7 d gave **2k** and **2j** in 37% and 61% yields, respectively. Cyclohexene **2l**, which is slightly less reactive toward electrophilic *m*-CPBA than **2f**,[20] as well as **2m**, **2n**, and **2o**, did not undergo the thiiranation even at room temperature, resulting in the quantitative recovery of the alkenes.

The thiiranation of **2** with **4** may proceed as follows (Scheme 2): 1) the C=C bond in **2** reacts with one of the two sulfur atoms of **4**, the electron density of which seems to be low because of its connection with the electronegative nitrogen atom, to eliminate the triazolyl anion, resulting in the formation of thiiranium salt **10** at the initial stage of the reaction, 2) the triazolyl anion in **10** attacks the sulfur atom, which is connected to the thiiranium sulfur atom, to yield **3** and **11**. Both electron density and angle strain of the C=C bond in **2** seem to control the reactivity toward **4**. In the case of **2g**, triazolyl-anion-induced cleavage of the thiiranium ring of **10g** takes place to relieve the strain of the molecule, forming **9g**. In the case of **2k**, ring cleavage of **10k** results in the formation of **12k**, and then rotation about its central C–C bond followed by elimination of **4** or **11** from the resulting **12j** gives **2j**, which is thermodynamically more stable than **2k**.

In conclusion, we have demonstrated that 1,1′-dithiobis(1*H*-1,2,4-triazole) acts as a good sulfur-atom transfer agent for the thiiranation of some alkenes even without an activating agent under mild reaction conditions. Stereospecific formation of the thiiranes seems to be a characteristic of the present thiiranation.

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References and notes

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9. *A typical experimental procedure for the thiiranation of alkenes is as follows*: To a suspension of **4** (237 mg, 1.2 mmol) and triptycene (75 mg, 0.30 mmol) as an internal standard in $CDCl_3$ (7.0 mL) at −15 °C under argon atmosphere, **2f** (130 mg, 1.2 mmol) was added. After stirring at −15 °C for 23 h, ice water was added into the reaction mixture. The organic layer was separated, washed with water, and dried over $MgSO_4$. Yields of **3f** and **2f** were determined from the ^{1}H NMR spectrum of the resulting solution.
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16. Despite our efforts, **9g** has never been isolated in pure form.
17. Distinctive signals of **9g** in the ^{1}H NMR appeared at $\delta = 4.23–4.35$ (m, 1H) due to $R^1R^2C(SR^3)–H$, at $\delta = 5.41–5.53$ (m, 1H) and 5.78 (ddt, $J = 10.5$, 1.2, and 8.3 Hz, 1H) due to $C(sp^2)–H$, and at $\delta = 8.04$ (s, 1H) and 8.23 (s, 1H) due to triazole-*H*, and those in the ^{13}C NMR at $\delta = 25.3$, 26.1, 26.4, 28.8, 33.0, 49.8, 128.1, 133.3, 151.6, 153.8. Although ESI-HRMS of **9g** gave the $[M+H]^+$ ion peak with a relatively weak intensity at *m*/*z* 242.0754 [calcd for $C_{10}H_{16}N_3S_2$: 242.0780], the observed isotope pattern of the ion peak was slightly different from the theoretical pattern.
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