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Tetrahedron 59 (2003) 4979–4992

TETRAHEDRON

# A one-pot, two step synthesis of 2,2-disubstituted 1-nitroalkenes

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Received 10 March 2003; accepted 8 May 2003

**Abstract**—The reactions of ketones **1a–o**, nitromethane **2**, and a stoichiometric amount of piperidine **3a** or ethylenediamine **3b** in the presence of mercaptan **6a** in THF or $CH_3CN$ solution give high yields of β-nitrosulfides **7a–o**. The latter can be oxidized by **8a** (*m*-CPBA or *m*-CPBA/AcOH) at 0°C, **8b** ($H_2O_2$/AcOH), or **8c** ($H_2O_2$) at room temperature, thus generating β-nitroalkylsulfoxides **9a–o**, which then undergo elimination to produce medium to high yields of 2,2-disubstituted-1-nitroalkenes **5a–o**, when refluxed in a solution of $ClCH_2CH_2Cl$ (1,2-dichloroethane). After preparation from **1a–o**, **2**, **3**, and **6a**, **7a–o** were oxidized with **8a**, **8b**, or **8c** in a mixture of $CH_3CN$ and $ClCH_2CH_2Cl$ to generate β-nitrosulfoxides **9a–o**, which then underwent elimination under refluxing under one-pot conditions. Compounds **14** and **15g** were also prepared using **13**, **2**, **3b**, and **6**, in a similar manner. © 2003 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

Nitro-olefins are useful intermediates and important structural units in organic synthesis.[1–6] Nitroalkenes are typically prepared by a nitro-aldol approach by reacting nitroalkanes with carbonyl compounds, such as aldehydes, followed by dehydration of the 2-nitroalcohols.[7–12] Unfortunately, the Henry reaction is impractical for the preparation of 2,2-disubstituted-1-nitroalkenes because it is reversible when ketones are used.[13,14] Tamura et al. employed *N*,*N*-dimethylethylenediamine to drive the condensation of ketones with nitroalkanes, but the major products were β,γ-unsaturated tautomers.[15] Our previous study[16] reported that some 2,2-disubstituted-1-nitroalkenes can be prepared by the reaction of ketones **1**, nitromethane **2**, piperidine **3a**, a mercaptan **6**, and *m*-chloroperoxybenzoic acid (*m*-CPBA) **8a-1**, which is an amalgamation of Carroll's[17] and Trost's[18,19] work, involving a nitro-aldol addition to generate the intermediate tertiary β-nitro alcohols **4**, the dehydration of **4** to give nitroalkenes **5** (reversible), the conjugate addition of the mercaptan **6** to **5** to yield β-nitrosulfides **7**, the oxidation of **7** with *m*-CPBA **8a-1** to form β-nitrosulfoxides **9** and, finally, a β-elimination to give **5**. Although medium to high yields of intermediate **7** can be prepared by the reaction of **1** with **2**, **6**, and a catalytic amount of **3a** using benzene as the solvent,[16,17] this method is not only lengthy but also requires a Dean–Stark trap to continuously remove water during the refluxing. In addition, unreacted ketones **1** are sometimes recovered, because they are not consumed completely due to the reversibility of the reaction. In this paper, we wish to report on an alternate, improved, facile, and useful method for preparing **7** without the need for a Dean–Stark apparatus, and develop an extension of the earlier study, in which an improved methodology for the one-pot synthesis of nitroalkenes **5** was described. The overall synthesis involves the use of ketones **1**, nitromethane **2**, various bases **3**, mercaptans **6**, and various oxidization reagents **8**, using a number of solvents such as DMF (dimethylformamide), $ClCH_2CH_2Cl$ (1,2-dichloroethane), THF (tetrahydronfuran), or $CH_3CN$ (acetonitrile) or a mixture of $CH_3CN$–$ClCH_2CH_2Cl$ under similar reaction conditions (Scheme 1).

## 2. Results and discussion

In some preliminary tests, a variety of solvents such as DMF, $ClCH_2CH_2Cl$, THF, and $CH_3CN$ and bases such as piperidine **3a** and ethylenediamine **3b** were examined. Only 43% yield of **7f** and small amounts of unreacted ketone were observed when cyclopentanone **1f** was reacted with **2** and **3a** in the presence of benzyl mercaptan **6a** in DMF solution at 100°C (oil bath temperature) for 3 h (entry 11 of Table 1). The solution became black in color and only traces of **7f** remained when the reaction time was increased to 8 h under similar conditions (entry 12). Similarly, a 64% yield of **7f** and traces of unreacted **1f** were observed when the same

*Keywords*: ketone; mercaptan; nitro-olefin; hydrogen peroxide; one-pot.

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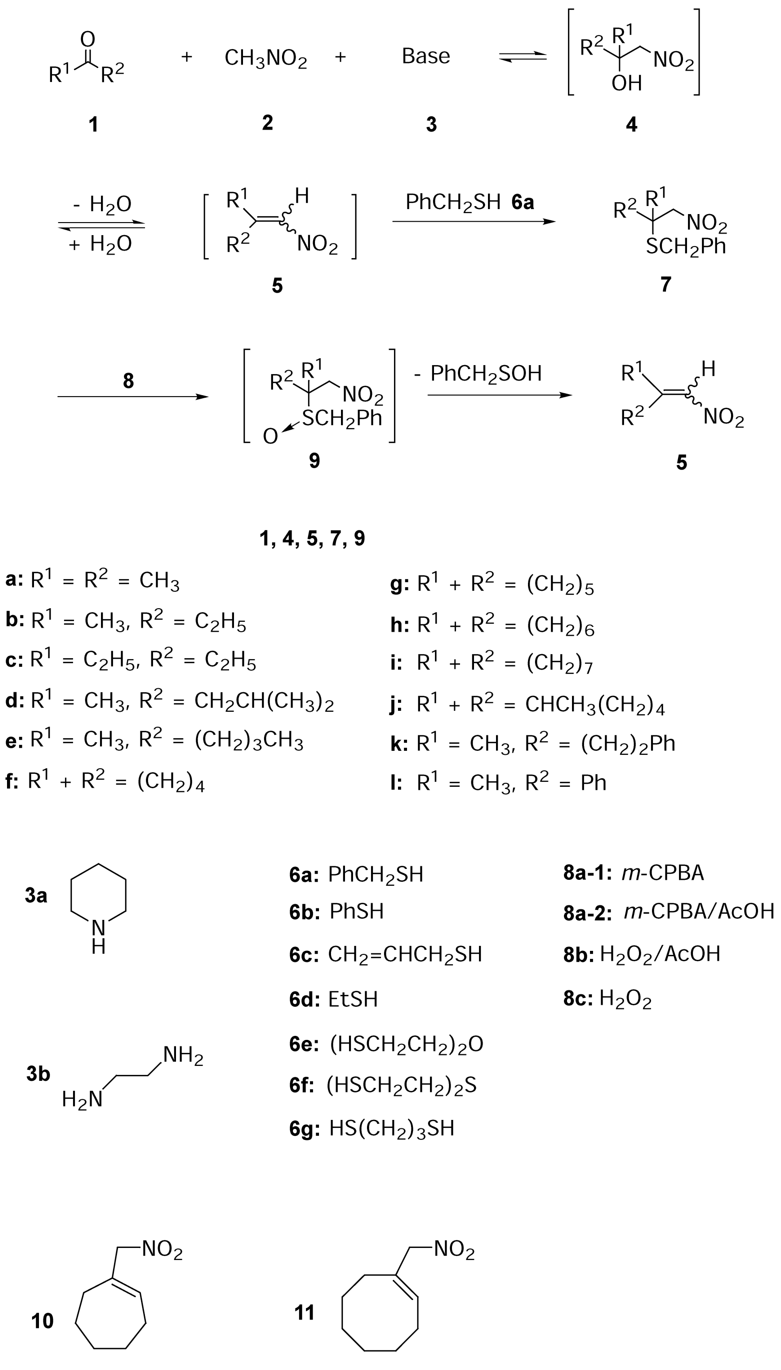
doi:10.1016/S0040-4020(03)00754-3




**Scheme 1.**

reaction was conducted in $ClCH_2CH_2Cl$ solution at reflux for 36 h (entry 13). However, **7f** was produced in 94% yield when refluxing THF or $CH_3CN$ was used as the solvent for a period of 12 h (entry 14) or 4 h (entry 15). These results indicate that the use of THF or $CH_3CN$ as a solvent in preparing intermediate **7** is desirable, compared to benzene, DMF, or $ClCH_2CH_2Cl$. Based on the above observation, ketones **1a–e** and **1g–l**, respectively, were also reacted with **2** and **6a** in the presence of **3a** or **b** in THF or $CH_3CN$ solution under similar conditions, using different reaction times to give **7a–e** and **7g–l**. The complete experimental data are shown in Table 1.

Solvents frequently play an important role in chemical reactions. Different solvents may affect the same reaction to different extents even under similar reaction conditions. In comparing the data in Table 1 to our previous study in which benzene was used as a solvent,[16] we conclude that both THF and $CH_3CN$ are superior solvents for the preparation of **7** and the use of a base, such as **3a** or **b** also leads to dramatically improved yields. According to Table 1, similar and different characteristics are also observed when THF or $CH_3CN$ is used as a solvent. Concerning the similarities, the first observation is that high yields of **7** can be obtained within a few hours under gentle reflux. As a result, this reaction is best controlled by an appropriate choice of solvent. The second observation is the reaction rate. For example, the use of $CH_3CN$ and THF as a solvent results in a

**Table 1**. The preparation of β-nitrosulfides **7** from the reaction of keontes **1**, nitromethane **2**, base **3**, and mercaptan **6a** (4 equiv.) in THF, $CH_3CN$, DMF, or $ClCH_2CH_2Cl$ solution under refluxing condition

| Entry | 1 (equiv.) | 2 (equiv.) | Base (equiv.) | Solvent | Time (h) | 7 | Yield (%)[a] |
|---|---|---|---|---|---|---|---|
| 1 | **1a**[b] | 1.0 | **3a** (2.0) | THF | 12 | **7a** | 96 |
| 2 | **1a**[b] | 1.0 | **3a** (2.0) | $CH_3CN$ | 5 | **7a** | 97 |
| 3 | **1b** (1.0) | 10 | **3b** (1.0) | THF | 18 | **7b** | 82 |
| 4 | **1b** (1.0) | 10 | **3b** (1.0) | $CH_3CN$ | 8 | **7b** | 95 |
| 5 | **1c** (1.0) | 10 | **3b** (2.0) | THF | 60 | **7c** | 42 |
| 6 | **1c** (1.0) | 10 | **3b** (2.0) | $CH_3CN$ | 12 | **7c** | 44 |
| 7 | **1d** (1.0) | 10 | **3b** (2.0) | THF | 60 | **7d** | 52 |
| 8 | **1d** (1.0) | 10 | **3b** (1.5) | $CH_3CN$ | 13 | **7d** | 59 |
| 9 | **1e** (1.0) | 10 | **3b** (1.0) | THF | 24 | **7e** | 94 |
| 10 | **1e** (1.0) | 10 | **3b** (1.0) | $CH_3CN$ | 14 | **7e** | 95 |
| 11 | **1f** (1.0) | 10 | **3a** (1.0) | DMF | 3 | **7f** | 43 |
| 12 | **1f** (1.0) | 10 | **3a** (1.0) | DMF | 8 | **7f** | Trace[c] |
| 13 | **1f** (1.0) | 10 | **3a** (1.0) | $ClCH_2CH_2Cl$ | 36 | **7f** | 64 |
| 14 | **1f** (1.0) | 10 | **3a** (2.0) | THF | 12 | **7f** | 94 |
| 15 | **1f** (1.0) | 10 | **3a** (2.0) | $CH_3CN$ | 4 | **7f** | 94 |
| 16 | **1g** (1.0) | 10 | **3a** (2.0) | THF | 12 | **7g** | 71 |
| 17 | **1g** (1.0) | 10 | **3a** (2.0) | $CH_3CN$ | 4 | **7g** | 96 |
| 18 | **1h** (1.0) | 10 | **3b** (2.0) | THF | 15 | **7h** | 68 |
| 19 | **1h** (1.0) | 10 | **3b** (2.0) | $CH_3CN$ | 12 | **7h** | 83 |
| 20 | **1i** (1.0) | 10 | **3b** (2.0) | THF | 51 | **7i** | 67 |
| 21 | **1i** (1.0) | 10 | **3b** (1.0) | $CH_3CN$ | 8 | **7i** | 51 |
| 22 | **1j** (1.0) | 10 | **3b** (2.0) | THF | 12 | **7j** | 98[d] |
| 23 | **1j** (1.0) | 10 | **3b** (2.0) | $CH_3CN$ | 12 | **7j** | 98[d] |
| 24 | **1k** (1.0) | 10 | **3b** (1.25) | THF | 24 | **7k** | 97 |
| 25 | **1k** (1.0) | 10 | **3b** (1.25) | $CH_3CN$ | 16 | **7k** | 98 |
| 26 | **1l** (1.0) | 10 | **3b** (3.0) | THF | 60 | **7l** | 5 |
| 27 | **1l** (1.0) | 10 | **3b** (3.0) | $CH_3CN$ | 12 | **7l** | 23 |

[a] Isolated yield.
[b] Excess amount.
[c] Messy result.
[d] *E*+*Z* isomers.

decrease in the reaction time from a few days to a few hours, compared to the use of benzene. A possible explanation for these two features, high yield and high reaction rate, is the superior water-solvation ability of these two solvents. In the reaction process, when the intermediate **4** dehydrates to form the intermediate **5** and one water molecule, these two water-soluble solvents can solvate this water molecule well, separate it from **5** and prevent the occurrence of retro-Henry reaction. At this stage, the mercaptan **6** will trap the intermediate **5** without any difficulty to produce high yield of **7**. Concerning the differences between $CH_3CN$ and THF, the yields are always higher and the reaction rate is also much faster when the reaction is conducted in $CH_3CN$. A possible explanation is that $CH_3CN$ is a more polar solvent with an empirical solvent polarity of $E_T$ (30) (46.7) and a dielectric constant of $\varepsilon(38)$ compared to THF, with a polarity of $E_T(30)$ (37.4) and a dielectric constant of $\varepsilon(7.6)$.[20] Solvent polarity is important in terms of the solubility of the reactants, but also because they have an effect on the nucleophilicity of anions that are involved in nucleophilic additions.

In addition to the above advantages, this improved method is also useful for preparing steric β-nitro sulfides, such as **7** with a bulky group in the molecule which is not easily prepared in benzene solution. For example, when cycloheptanone **1h** was reacted with **2** and thiophenol in the presence of **3a** in benzene under reflux for 70 h, no product was generated, and only 22% of the product was obtained when allyl mercaptan was used for 70 h under similar conditions.[16] However, 68 or 83% of **7h** was generated when **1h** was reacted with **2**, **3b**, and **6a** in THF or $CH_3CN$ solution under refluxing for only 15 or 12 h (entries 18 and 19). For cyclooctanone **1i**, 67 or 51% (entries 20 and 21) of **7i** was generated in THF or $CH_3CN$ solution under similar conditions and only traces were observed when benzene was used. Using acetophenone **1l**, although only 5 or 23% of the expected product **7l** was generated in THF or $CH_3CN$ for 60 or 12 h (entries 26 and 27 of Table 1), no product was detected when the reaction was conducted in benzene or 1,2-dichloroethane. A possible explanation for this is that the presence of steric hindrance between the ketone and nucleophiles inhibits the reaction, especially in the case of benzene or 1,2-dichloroethane.

Our previous study found that **7** can be oxidized by *m*-CPBA **8a-1** in $CH_2Cl_2$ and then undergo elimination in a $CCl_4$ solution to give product **5**.[16] However, the experimental procedures are tedious and the reaction is incomplete under these conditions. Then we examined the use of 1,2-dichloroethane $ClCH_2CH_2Cl$ (bp 83–84°C) as the solvent.[16] β-Nitrosulfides **7** was oxidized by **8a-1** at 0°C for 0.5–1 h and then underwent elimination after refluxing for 3–4 h in a $ClCH_2CH_2Cl$ solution to give high yields of **5**. Compared to our previous report,[16] the use of $ClCH_2CH_2Cl$ is actually superior to the use of $CH_2Cl_2$ or $CCl_4$ at certain steps. The change in solvent not only simplifies the experimental procedures but also increases the yields dramatically, as shown in Table 2.

It has been reported that sulfide compounds can be oxidized by peroxy acid[21,22] or by hydrogen peroxide $H_2O_2$ in certain solvents in the presence of acid and a catalyst or by various other oxidizing agents to generate a sulfoxide.[23–28] According to literature reports[21,22] and the results in Table 2, peroxyacetic acid, generated from acetic acid and hydrogen peroxide,[29] could be used to replace **8a-1** (*m*-CPBA). When **7g** was reacted with **8b**, prepared from 14 equiv. of acetic acid and 5 equiv. of 35% $H_2O_2$, in $ClCH_2CH_2Cl$ solution at room temperature for 1 h, followed by refluxing for 4 h, 90% of the expected product **5g** and traces of unidentified products were obtained (entry 7 of Table 3). This indicates that acetic acid is first oxidized by $H_2O_2$ to generate peroxyacetic acid[29] and then oxidizes **7g** to produce intermediate **9g** which finally undergoes

**Table 2**. The preparation of 2,2-disubstituted-1-nitroalkenes **5** from β-nitrosulfides **7** and **8a-1** (1.1 equiv. of *m*-CPBA) in 1,2-dichloroethane solution at 0°C and then under refluxing condition

| Entry | 7 | 0°C Time (h) | Reflux time (h) | 5 | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | **7a** | 0.5 | 3 | **5a** | 85 |
| 2 | **7b** | 0.5 | 3 | **5b** | 95[b] |
| 3 | **7c** | 0.5 | 3 | **5c** | 96 |
| 4 | **7d** | 0.5 | 3 | **5d** | 87[b] |
| 5 | **7e** | 0.5 | 3 | **5e** | 94[b] |
| 6 | **7f** | 0.5 | 3 | **5f** | 94 |
| 7 | **7g** | 0.5 | 3 | **5g** | 96 |
| 8 | **7h** | 0.5 | 3 | **5h** | 95 |
| 9 | **7i** | 0.5 | 3 | **5i** | 91 |
| 10 | **7j** | 1 | 4 | **5j** | 98[b] |
| 11 | **7k** | 1 | 4 | **5k** | 94[b] |
| 12 | **7l** | 1 | 4 | **5l** | 93 |

[a] Isolated yield.
[b] *E*+*Z* isomers.

**Table 3**. The preparation of 2,2-disubstituted-1-nitroalkenes **5** from β-nitrosulfides **7** and **8b** [$H_2O_2$ (5 equiv.)/AcOH (14 equiv.)] in 1,2-dichloroethane solution at room temperature (1 h) and then under refluxing condition (4 h)

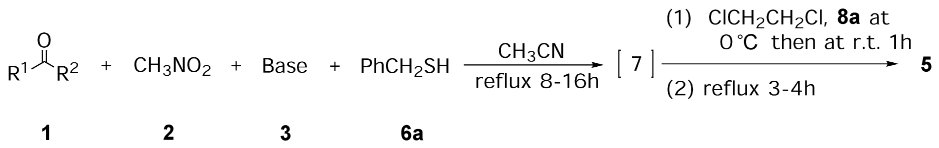
| Entry | 7 | 5 | Yield (%)[a] | Entry | 7 | 5 | Yield (%)[a] |
|---|---|---|---|---|---|---|---|
| 1 | **7a** | **5a** | 97 | 7 | **7g** | **5g** | 90 |
| 2 | **7b** | **5b** | 60[b] | 8 | **7h** | **5h** | 91 |
| 3 | **7c** | **5c** | 94 | 9 | **7i** | **5i** | 88 |
| 4 | **7d** | **5d** | 96[b] | 10 | **7j** | **5j** | 96[b] |
| 5 | **7e** | **5e** | 47[b] | 11 | **7k** | **5k** | 49[b] |
| 6 | **7f** | **5f** | 36 | 12 | **7l** | **5l** | 70 |

[a] Isolated yield.
[b] *E*+*Z* isomers.

elimination to yield **5g** as described above. In addition to substrate **7g**, other substrates such as **7a–f** and **7h–l** were also reacted with **8b** to yield **5a–f** and **5h–l** under similar conditions, as shown in Table 3.

Although **8a** or **b** is able to oxidize **7** to **9** efficiently, organic acid by-product generated, such as *m*-chlorobenzoic acid which is environmentally harmful or acetic acid remained in the mixture and this increases a difficulty in the purification of the final nitroalkenes **5**. To avoid these disadvantages, hydrogen peroxide **8c** (5 equiv.) was used to oxidize **7** directly in $ClCH_2CH_2Cl$ solution under similar conditions. Fortunately, a nearly quantitative yield of **9** was produced in most cases and the end products were very clean compared to the use of **8a** or **b**. These results also suggest that the presence of *m*-chlorobenzoic acid or acetic acid is actually undesirable in the final product, as shown in Table 4.

Based on the results in Tables 1–4, we conclude that the use of pure **7** and oxidization agent **8** in $ClCH_2CH_2Cl$ solution generate high yields of **5**. However, one serious problem was found during the column purification of **7**, the unpleasant odor of traces of mercaptan **6** that remained in the crude mixture. To solve this problem, we combined the first step in the generation of **7** and the second step in the oxidization of **7** by **8** to develop an alternate methodology. The strategy of this involved preparing **5** from **1**, **2**, **3**, **6a**, and **8** in a one-pot synthesis and without the isolation of **7**. Ketones **1g** and **k** were chosen as cyclic and acyclic examples to test this methodology. After generating **7g** from the reaction of **1g**, **2**, **3**, and **6a** in THF solution as shown in Eq. (1), 4 equiv. of **8a-1** was directly added to the solution at 0°C and the temperature was then increased to room temperature for 1 h followed by refluxing for 4 h to give 20% of **5g** and only minor amounts of unreacted **7g** (entry 15 of Table 5). Similarly, 36% of **5g** and negligible unreacted **7g** were also observed when the same reaction was conducted in $CH_3CN$ solution (entry 16 of Table 5). Only traces of product **5k** were generated and unreacted **7k** was largely recovered when **1k** was conducted in THF or $CH_3CN$ solution (entries 25 and 26 of Table 5). Based on the results shown in Tables 2–4 in which the oxidation of **7** with **8** in $ClCH_2CH_2Cl$ solution gave high yields of **5**, $ClCH_2CH_2Cl$ was added to the $CH_3CN$ solution at a volume ratio of $CH_3CN$ to $ClCH_2CH_2Cl$ of 3 to 4. The yield of **5g** was increased to 95% and that of **5k** was also improved and increased to 24% and no intermediate **7g** or **k** remained in the solution (entries 14 and 24 of Table 5). Given the low yield of **5k**, it is possible that some **5k** might have been destroyed by base **3b** after its formation. To prove this assumption, after **7k** was generated from the first step, 14 equiv. of acetic acid AcOH was added to the solution to neutralize **3b** and **8a-1** was then added to the solution to oxidize **7k** in the $CH_3CN$–$ClCH_2CH_2Cl$ mixture, as described above. As expected, the yield of product **5k** was increased to 97% (entry 23 of Table 5). Based on this result, either *m*-CPBA or *m*-CPBA/AcOH was used as an oxidant in subsequent experiments. In addition to **5g** and **k**, nitroalkene **5** were also prepared from ketone **1** under similar procedures and conditions, as shown in Table 5.



(1)

As shown in Table 5, the yields of **5c** (30 and 17%), **5d** (51 and 47%), **5i** (21 and 5%), and **5l** (11 and 4%) were all not high when *m*-CPBA or *m*-CPBA/AcOH were used as oxidants, but these results can be explained by the low yields of **7c** (44%), **7d** (59%), **7i** (51%), and **7l** (23%) in the first step (entries 6, 8, 21, 27 of Table 1) so that the total yields are low to medium (entries 5–8, 19, 20, 27, and 28 of Table 5). Another possibility is that the presence of other compounds in the mixture also underwent side reactions thus decreasing the yield of **5**.

After the use of **8a** as an oxidization reagent to obtain the figures shown in Table 5, the next trial was to use **8b** ($AcOH/H_2O_2$) in the cosolvent of $CH_3CN$–$ClCH_2CH_2Cl$ solution (Eq. (2)). As expected, 5–90% yields of **5** were generated under similar procedures and conditions (Table 6). Although the yields of **5c** (24%), **5d** (37%), **5i** (38%), and **5l** (5%) were, again, not high (entries 3, 4, 9, 12 of Table 6) and are similar to Table 5, these results also can be explained by the rationale as above.

**Table 4**. The preparation of 2,2-disubstituted-1-nitroalkenes **5** from β-nitrosulfides **7** and **8c** (5 equiv. of $H_2O_2$) in 1,2-dichloroethane solution at room temperature (1 h) and then under refluxing condition (4 h)

| Entry | 7 | 5 | Yield (%)[a] | Entry | 7 | 5 | Yield (%)[a] |
|---|---|---|---|---|---|---|---|
| 1 | **7a** | **5a** | 97 | 7 | **7g** | **5g** | 97 |
| 2 | **7b** | **5b** | 93[b] | 8 | **7h** | **5h** | 95 |
| 3 | **7c** | **5c** | 94 | 9 | **7i** | **5i** | 95 |
| 4 | **7d** | **5d** | 96[b] | 10 | **7j** | **5j** | 96[b] |
| 5 | **7e** | **5e** | 90[b] | 11 | **7k** | **5k** | 97[b] |
| 6 | **7f** | **5f** | 95 | 12 | **7l** | **5l** | 70 |

[a] Isolated yield.
[b] *E*+*Z* isomers.

**Table 5**. One-pot synthesis of **5** from **1**, **2**, **3**, and **6a** in $CH_3CN$ or THF and then reaction with *m*-CPBA/AcOH or *m*-CPBA after adding $ClCH_2CH_2Cl$ as a cosolvent if necessary

| Entry | 1 | 3 (equiv.) | Solvent | AcOH (equiv.) | *m*-CPBA (equiv.) | Reflux (h) | 5 | Yield (%)[a] |
|---|---|---|---|---|---|---|---|---|
| 1 | **1a** | **3a** (2.0) | $CH_3CN/ClCH_2CH_2Cl$ | 14 | 4 | 4 | **5a** | 98 |
| 2 | **1a** | **3a** (2.0) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5a** | 80 |
| 3 | **1b** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | 14 | 4 | 4 | **5b** | 89[b] (1.4:1)[c] |
| 4 | **1b** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5b** | 39[b] (1.5:1)[c] |
| 5 | **1c** | **3b** (3.0) | $CH_3CN/ClCH_2CH_2Cl$ | 35 | 4 | 3 | **5c** | 30 |
| 6 | **1c** | **3b** (3.0) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 3 | **5c** | 17 |
| 7 | **1d** | **3b** (1.5) | $CH_3CN/ClCH_2CH_2Cl$ | 14 | 4 | 4 | **5d** | 51[b] (1.1:1)[c] |
| 8 | **1d** | **3b** (1.5) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5d** | 47[b] (1.1:1)[c] |
| 9 | **1e** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | 14 | 4 | 4 | **5e** | 92[b] (1.9:1)[c] |
| 10 | **1e** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5e** | 28[b] (1.8:1)[c] |
| 11 | **1f** | **3a** (0.5) | $CH_3CN/ClCH_2CH_2Cl$ | 14 | 4 | 4 | **5f** | 85 |
| 12 | **1f** | **3a** (0.5) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5f** | 83 |
| 13 | **1g** | **3a** (0.5) | $CH_3CN/ClCH_2CH_2Cl$ | 14 | 4 | 4 | **5g** | 96 |
| 14 | **1g** | **3a** (0.5) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5g** | 95 |
| 15 | **1g** | **3a** (0.5) | THF | – | 4 | 4 | **5g** | 20[d] |
| 16 | **1g** | **3a** (0.5) | $CH_3CN$ | – | 4 | 4 | **5g** | 36[d] |
| 17 | **1h** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | 14 | 4 | 4 | **5h** | 70 |
| 18 | **1h** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5h** | 47 |
| 19 | **1i** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | 14 | 4 | 4 | **5i** | 21[e] |
| 20 | **1i** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5i** | 5[f] |
| 21 | **1j** | **3b** (1.5) | $CH_3CN/ClCH_2CH_2Cl$ | 18 | 5 | 4 | **5j** | 60[b] (1.6:1)[c] |
| 22 | **1j** | **3b** (1.5) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5j** | 54[b] (1.6:1)[c] |
| 23 | **1k** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | 14 | 4 | 4 | **5k** | 97[b] (1:1)[c] |
| 24 | **1k** | **3b** (1.0) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5k** | 24[b] (1:1)[c] |
| 25 | **1k** | **3b** (1.0) | THF | – | 4 | 4 | **5k** | Trace[d] |
| 26 | **1k** | **3b** (1.0) | $CH_3CN$ | – | 4 | 4 | **5k** | Trace[d] |
| 27 | **1l** | **3b** (2.0) | $CH_3CN/ClCH_2CH_2Cl$ | 21 | 6 | 4 | **5l** | 11[b] (1.2:1)[c] |
| 28 | **1l** | **3b** (2.0) | $CH_3CN/ClCH_2CH_2Cl$ | – | 4 | 4 | **5l** | 4[b] (1.1:1)[c] |

Volume ratio of $CH_3CN-ClCH_2CH_2Cl=3:4$.
[a] Isolated yield.
[b] *E*+*Z* isomers.
[c] Ratio between *E* and *Z* isomers measured by the crude NMR before purification.
[d] Unreacted β-nitrosulfides **7** were recovered.
[e] 65% of **11**.
[f] 57% of **11**.

**Table 6**. One-pot synthesis of 2,2-disubstituted-1-nitroalkenes **5** from **1**, **2**, **3**, and **6a** in $CH_3CN$ and then reaction with **8b** ($H_2O_2$/AcOH) in a mixture of $CH_3CN$ and $ClCH_2CH_2Cl$

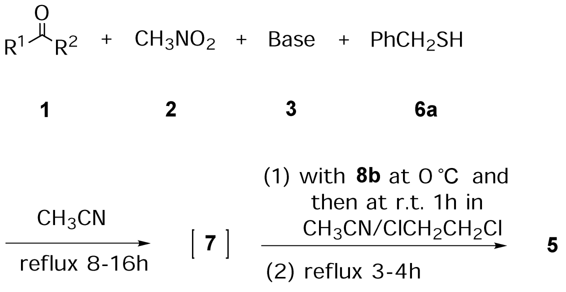
| Entry | 1 | Base 3 (equiv.) | AcOH (equiv.) | $H_2O_2$ (equiv.) | Reflux (h) | 5 | Yield (%)[a] |
|---|---|---|---|---|---|---|---|
| 1 | **1a** | **3a** (2.0) | 14 | 10 | 3 | **5a** | 90 |
| 2 | **1b** | **3b** (0.5) | 18 | 13 | 3 | **5b** | 69[b] (1.5:1)[c] |
| 3 | **1c** | **3b** (3.0) | 35 | 15 | 3 | **5c** | 24 |
| 4 | **1d** | **3b** (1.5) | 21 | 10 | 4 | **5d** | 37[b] (1.1:1)[c] |
| 5 | **1e** | **3b** (1.0) | 21 | 15 | 3 | **5e** | 70[b] (1.9:1)[c] |
| 6 | **1f** | **3a** (0.5) | 14 | 10 | 3.5 | **5f** | 76 |
| 7 | **1g** | **3a** (0.5) | 14 | 10 | 3.5 | **5g** | 73 |
| 8 | **1h** | **3b** (1.0) | 21 | 15 | 3 | **5h** | 53 |
| 9 | **1i** | **3b** (1.0) | 14 | 5.0 | 4 | **5i** | 38 |
| 10 | **1j** | **3b** (1.5) | 18 | 13 | 4 | **5j** | 18[b] (1.6:1)[c] |
| 11 | **1k** | **3b** (1.0) | 21 | 15 | 3 | **5k** | 73[b] (1:1)[c] |
| 12 | **1l** | **3b** (2.0) | 21 | 15 | 4 | **5l** | 5[b] (1.1:1)[c] |

Volume ratio of $CH_3CN-ClCH_2CH_2Cl=3:4$.
[a] Isolated yield.
[b] *E*+*Z* isomers.
[c] Ratio between *E* and *Z* isomers measured by the crude NMR before purification.

**Table 7**. One-pot synthesis of 2,2-disubstituted-1-nitroalkenes **5** from **1**, **2**, **3**, and **6a** in $CH_3CN$ and then reaction with **8c** ($H_2O_2$) in a mixture of $CH_3CN$ and $ClCH_2CH_2Cl$

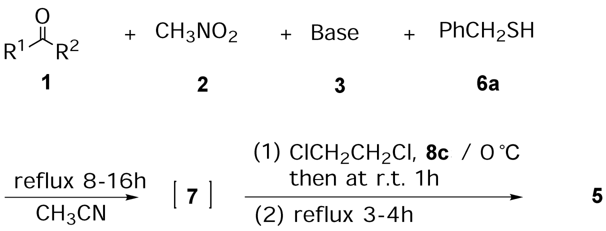
| Entry | 1 | Base 3 (equiv.) | $H_2O_2$ (equiv.) | Reflux (h) | 5 | Yield (%)[a] |
|---|---|---|---|---|---|---|
| 1 | **1a** | **3a** (2.0) | 10 | 3 | **5a** | 70 |
| 2 | **1b** | **3b** (0.5) | 13 | 3 | **5b** | 90[b] (1.6:1)[c] |
| 3 | **1c** | **3b** (3.0) | 15 | 3 | **5c** | 35 |
| 4 | **1d** | **3b** (1.5) | 10 | 4 | **5d** | Trace |
| 5 | **1e** | **3b** (1.0) | 15 | 3 | **5e** | 96[b] (1.8:1)[c] |
| 6 | **1f** | **3a** (0.5) | 10 | 3.5 | **5f** | 91 |
| 7 | **1g** | **3a** (0.5) | 10 | 3.5 | **5g** | 87 |
| 8 | **1h** | **3b** (1.0) | 15 | 3 | **5h** | 23[d] |
| 9 | **1i** | **3b** (1.0) | 5.0 | 4 | **5i** | Trace[d] |
| 10 | **1j** | **3b** (1.5) | 13 | 4 | **5j** | 31[b] (1.5:1)[c] |
| 11 | **1k** | **3b** (1.0) | 15 | 3 | **5k** | 56[b] (1:1)[c] |
| 12 | **1l** | **3b** (2.0) | 15 | 4 | **5l** | 15[b] (1.1:1)[c] |

Volume ratio of $CH_3CN-ClCH_2CH_2Cl=3:4$.
[a] Isolated yield.
[b] *E*+*Z* isomers.
[c] ratio between *E* and *Z* isomers measured by the crude NMR before purification.
[d] β,γ-Unsaturated tautomer is the major products.



(2)

After using **8a** (*m*-CPBA or *m*-CPBA/AcOH) or **8b** ($H_2O_2$/AcOH), the use of **8c** in a one-pot synthesis was attempted (Eq. (3)). As expected, **5** was generated and these findings are shown in Table 7. Although the procedure for the addition of **8c** to the reaction mixture is simpler than **8a** and **b**, however, the experimental conditions are very critical and difficult to control especially with respect to temperature compared to Tables 5 and 6. Sometimes, unreacted **7** was recovered and only traces of **5** were detected if the reaction temperature was kept too low during the addition of **8c** to the mixture. Usually, the temperature increased sharply when **8c** was added to the solution too rapidly and this temperature effect always had a negative impact on the generation of **5**. A possible explanation for this is that **8c** might have reacted with **3a** or **b** before it reacted with **7**.[30,31] To prove this assumption, **8c** was added to the $CH_3CN$–$ClCH_2CH_2Cl$ solution which contained base **3a** or **b** and the temperature of the solution increased sharply. In addition to the above side reaction, some products such as **5h** and **i** also underwent isomerization, generating the *endo*-products **10** and **11** in the presence of base (entries 8 and 9 in Table 7) consistent with other reports.[15]



(3)

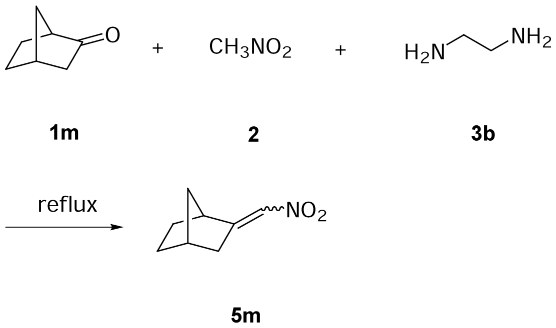
It has been reported that 2-nitromethyleneadamantane can be prepared from the reaction of 2-adamantanone with nitromethane in the presence of **3b** under refluxing conditions and the mechanism for this is proposed in Scheme 2.[32]

**Table 8**. The preparation of 2,2-disubstituted-1-nitroalkenes **5m**, **n**, and **12** from **1m–o** according to Barton's methodology

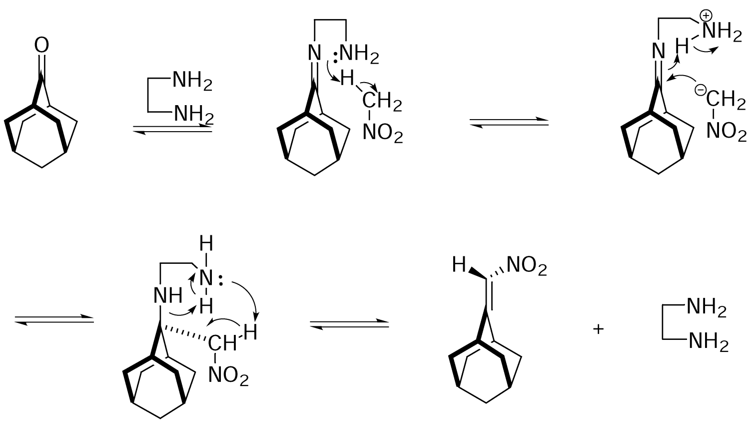
| Entry | 1 | Reflux (h) | Product | Yield (%)[a] |
|---|---|---|---|---|
| 1 | **1m** | 24 | **5m** | 15[b] |
| 2 | **1m** | 36 | **5m** | 24[b] |
| 3 | **1n** | 24 | **5n** | 27[b] |
| 4 | **1n** | 36 | **5n** | 9[b] |
| 5 | **1o** | 24 | **12** | 51[c] |

[a] Isolated yield.
[b] Some unreacted starting material was recovered and the products are *E*+*Z* isomers.
[c] The reaction was completed and **1o** was consumed.

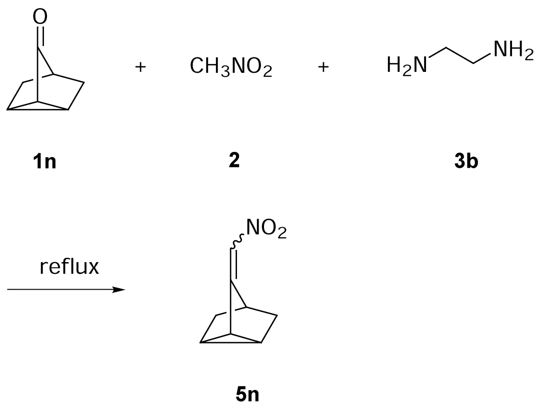
Based on this report,[32–35] steric ketone **1m–o** was reacted with nitromethane **2** in the presence of **3b** under reflux according to the literature procedure (Eqs. (4)–(6)).[32] Although products **5m** and **n** were generated as expected, the yields were low and the reaction rates were also very slow even when the reaction time was increased from 24 to 36 h. Large amounts of unreacted ketones **1m** and **n** were recovered (entries 1–4 of Table 8). In the case of ketone **1o**, all the starting ketone was consumed completely, but the only product was the *endo*-product **12** and *exo*-product **5o** was not observed (entry 5 of Table 8). These results indicate that some *exo*-nitroalkenes actually can be prepared and some products easily undergo isomerization to generate *endo*-nitroalkenes in the presence of base **3b**.[36]



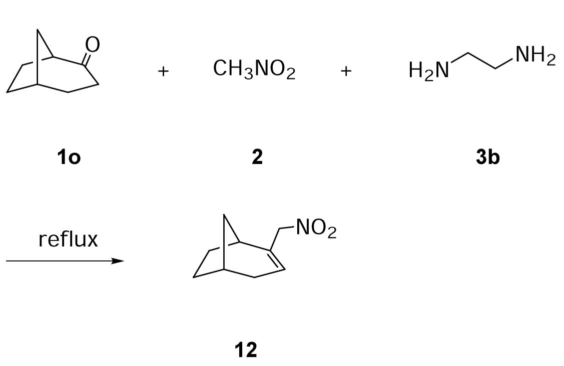
(4)



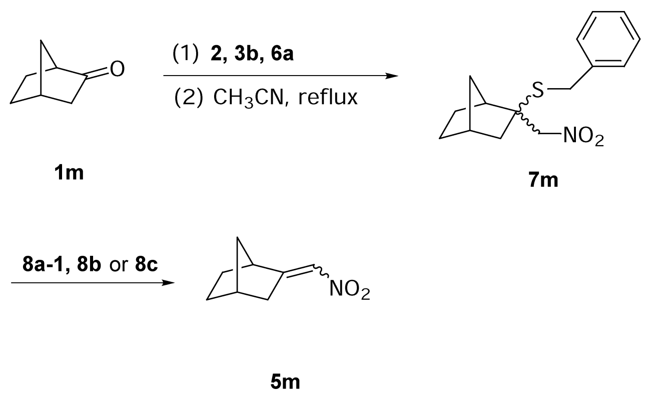
**Scheme 2.**



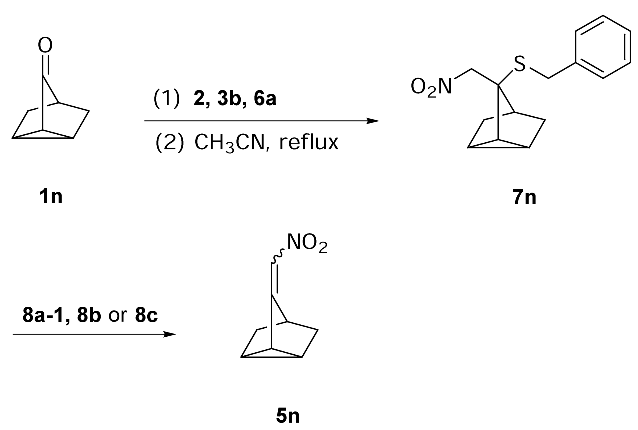

(5)




(6)

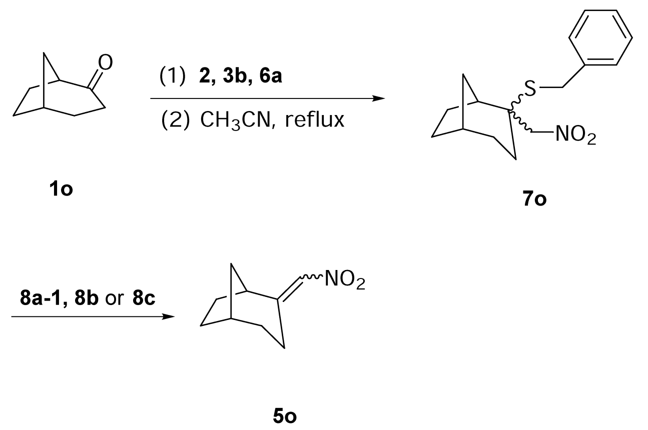



(7)




(8)

To improve these reactions, **7m–o** were first prepared from the reaction of **1m–o**, respectively, with **2**, **3b**, and **6a** as described above (Eqs. (7)–(9)). After the isolation of **7m–o**, oxidizing reagents **8a–c** were used to oxidize **7m–o** in $ClCH_2CH_2Cl$ as shown in Tables 2–4. High yields of products **5m–o** were generated, as shown in Table 9.




(9)

**Table 9**. The preparation of 2,2-disubstituted-1-nitroalkenes **5m–o** from rigid cyclicketones **1m–o**, **2** (10 equiv.), and **6a** (4 equiv.) by using different oxidation reagents **8a-1**, **8b**, or **8c**

| Entry | **1** (equiv.) | Base (equiv.) | Reflux (h) | **7** (Yield, %)[a] | **8**[b] | **5** (Yield, %)[a] |
|---|---|---|---|---|---|---|
| 1 | **1m** (1.0) | **3b** (1.5) | 14 | **7m** (95)[c] | **8a-1** | **5m** (87)[d] |
| 2 | **1m** (1.0) | **3b** (1.5) | 14 | **7m** (95)[c] | **8b** | **5m** (88)[d] |
| 3 | **1m** (1.0) | **3b** (1.5) | 14 | **7m** (95)[c] | **8c** | **5m** (93)[d] |
| 4 | **1n** (1.0) | **3b** (1.0) | 8 | **7n** (97) | **8a-1** | **5n** (94)[d] |
| 5 | **1n** (1.0) | **3b** (1.0) | 8 | **7n** (97) | **8b** | **5n** (94)[d] |
| 6 | **1n** (1.0) | **3b** (1.0) | 8 | **7n** (97) | **8c** | **5n** (94)[d] |
| 7 | **1o** (1.0) | **3b** (1.0) | 8 | **7o** (94) | **8a-1** | **5o** (95)[d] |
| 8 | **1o** (1.0) | **3b** (1.0) | 8 | **7o** (94) | **8b** | **5o** (95)[d] |
| 9 | **1o** (1.0) | **3b** (1.0) | 8 | **7o** (94) | **8c** | **5o** (95)[d] |

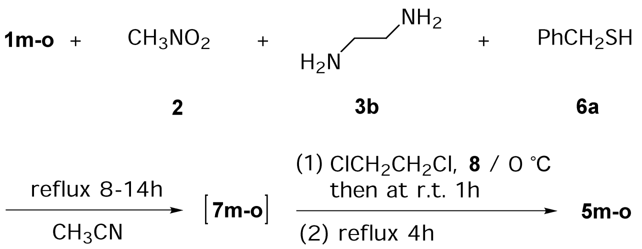
[a] Isolated yield.
[b] **8a-1**:1.1 equiv. of *m*-CPBA in $ClCH_2CH_2Cl$ at room temperature for 1 h and then under refluxing condition for 4 h; **8b**: 5 equiv. of $H_2O_2$ and 14 equiv. of AcOH in $ClCH_2CH_2Cl$ at room temperature 1 h and then under refluxiong condition for 4 h; **8c**: 5 equiv. of $H_2O_2$ in $ClCH_2CH_2Cl$ at 0°C and stirring for 1 h at room temperature and then under refluxing condition for 4 h.
[c] Two isomers were isolated.
[d] *E*+*Z* isomers.

After the preparation **5m–o** using **7m–o**, a one-pot reaction was attempted as shown in Eq. (10). Fortunately, **5m–o** were generated when solutions of **7m–o** were treated with **8a–c**, respectively (Table 10). Based on these results, we found that the use of **8a** (*m*-CPBA or *m*-CPBA/AcOH) or **8b** ($AcOH/H_2O_2$) consistently produced **5** in higher yields than that of **8c** ($H_2O_2$) and these phenomena are in agreement with Tables 5–7 and also prove that the addition of AcOH neutralizes the base, thus increasing product yields.

**Table 10**. One-pot synthesis of 2,2-disubstituted-1-nitroalkenes **5m–o** from **1m–o**, **2** (10 equiv.), **3** and **6a** (4 equiv.) in $CH_3CN$ and then reaction with **8** in $CH_3CN$ and $ClCH_2CH_2Cl$ solution

| Entry | **1** (equiv.) | **3b** (equiv.) | Reflux (h) | **8** (Oxidant)[a] | **5** Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | **1m** (1.0) | 1.5 | 14 | **8a-1** (*m*-CPBA) | **5m** (41)[c] |
| 2 | **1m** (1.0) | 1.5 | 14 | **8a-2** (*m*-CPBA/AcOH)[d] | **5m** (60)[c] |
| 3 | **1m** (1.0) | 1.5 | 14 | **8b** ($H_2O_2$/AcOH) | **5m** (77)[c] |
| 4 | **1m** (1.0) | 1.5 | 14 | **8c** ($H_2O_2$) | **5m** (39)[c,e] |
| 5 | **1n** (1.0) | 1.0 | 8 | **8a-1** (*m*-CPBA) | **5n** (66)[c] |
| 6 | **1n** (1.0) | 1.0 | 8 | **8a-2** (*m*-CPBA/AcOH)[d] | **5n** (96)[c] |
| 7 | **1n** (1.0) | 1.0 | 8 | **8b** ($H_2O_2$/AcOH) | **5n** (93)[c] |
| 8 | **1n** (1.0) | 1.0 | 8 | **8c** ($H_2O_2$) | **5n** (20)[c,e] |
| 9 | **1o** (1.0) | 1.0 | 8 | **8a-1** (*m*-CPBA) | **5o** (31)[c] |
| 10 | **1o** (1.0) | 1.0 | 8 | **8a-2** (*m*-CPBA/AcOH)[d] | **5o** (64)[c] |
| 11 | **1o** (1.0) | 1.0 | 8 | **8b** ($H_2O_2$/AcOH) | **5o** (97)[c] |
| 12 | **1o** (1.0) | 1.0 | 8 | **8c** ($H_2O_2$) | **5o** (25)[c,e] |

Volume ratio of $CH_3CN–ClCH_2CH_2Cl$=3:4.
[a] **8a**: 4 equiv. of *m*-CPBA; **8b**: 21 equiv. of AcOH and 13 equiv. of $H_2O_2$; **8c**: 13 equiv. of $H_2O_2$.
[b] Isolated yield.
[c] *E*+*Z* isomers.
[d] 21 equiv. of AcOH were added before adding *m*-CPBA.
[e] Some unreacted β-nitrosulfides **7** were recovered.




(10)

Only ketones **1a–o**, which contain a mono carbonyl group were used to prepare **5a–o**. It would be interesting to use a dicarbonyl ketone as well. The preparation of compound **5p** was originally proposed from the reaction of 1,4-cyclohexanedione **13** with **2**, **3b**, and mercaptan **6** (Eq. (11)). However, **14a**, **c–g** were obtained in only low to medium (17–81%) yields and small amounts (5–7%) of **15g** could be isolated when mercaptans such as **6g** were used (Table 11).

**Table 11**. The preparation of **14** and **15** from the reaction of **13**, **2** (10 equiv.), **3b** (1 equiv.), and **6** under refluxing conditions (13 h)

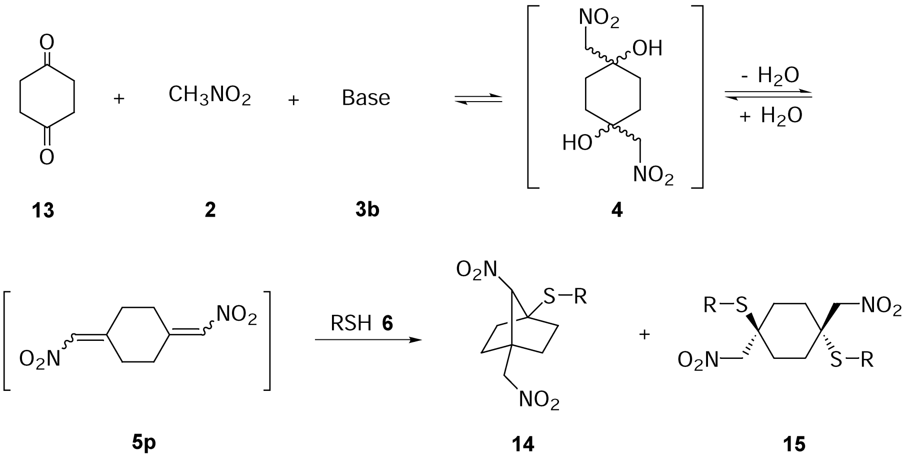
| Entry | **6** (equiv.) | Yield (%)[a] | |
|---|---|---|---|
| | | **14** | **15** |
| 1 | **6a** (4.0) | **14a** (53) | **15a** (–)[b] |
| 2 | **6b** (4.0) | **14b** (–)[c] | **15b** (–)[b] |
| 3 | **6c** (4.0) | **14c** (52) | **15c** (–)[b] |
| 4 | **6d** (4.0) | **14d** (17) | **15d** (–)[b] |
| 5 | **6e** (5.0) | **14e** (44) | **15e** (–)[b] |
| 6 | **6f** (3.5) | **14f** (56) | **15f** (–)[b] |
| 7 | **6g** (2.5) | **14g** (42) | **15g** (7) |
| 8 | **6g** (5.0) | **14g** (81) | **15g** (5) |

[a] Isolated yield.
[b] No product **15** was detectable in the crude $^1H$ NMR or GC–MS analysis.
[c] No product **14** was detectable in the crude $^1H$ NMR or GC–MS analysis.

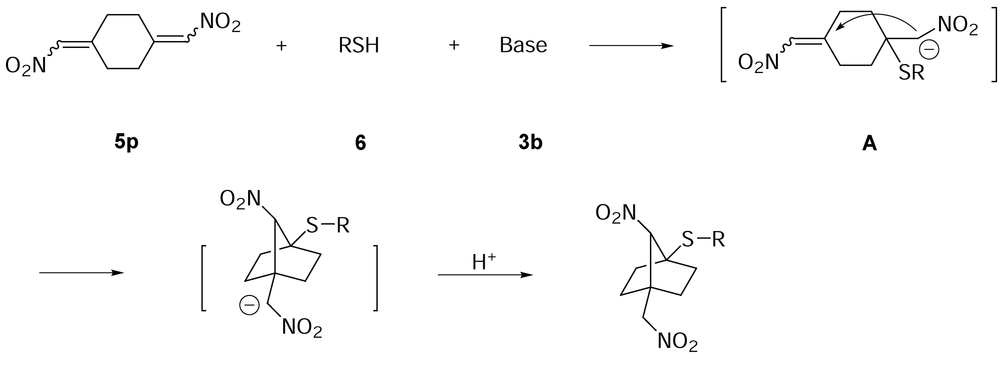
The generation of **14** and **15** provides indirect evidence to support the hypothesis that intermediate **5p** is formed during the reaction. A possible mechanism for the formation of product **14** is shown in Scheme 3, which proceeds through the intermolecular 1,4-addition of 1 equiv. of **6** to one of the nitroalkene groups in **5p** to form nitronate **A** and then nitronate **A** undergoes an intramolecular 1,4-addition to the second nitroalkene group to generate **B** and finally accepts a proton to generate **14**. The generation of **15g** in a similar manner is proposed in Scheme 4. The mechanism involves the intermolecular 1,4-addition of 2 equiv. of **6g** to the two nitroalkene groups of **5p** at the same time to produce **C**, which then accepts a proton to give **15**. Compared to **15**, the yields of product **14** are much higher because only one equiv. of mercaptan **6** is needed in the reaction. The low yield of **15g** can be explained by a steric effect between the anion of **6** and **5p** and the low probability of a simultaneous addition of the 2 equiv. of anion **6** to substrate **5p**.

## 3. Conclusion

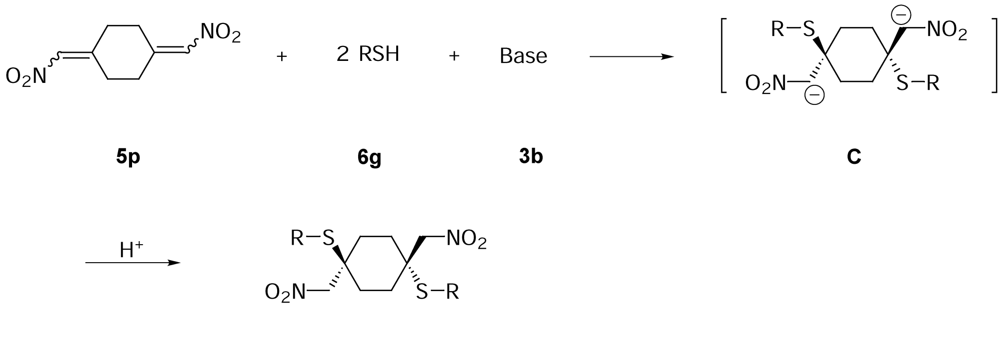
In conclusion, we report on improvements in an earlier method for the preparation of 2,2-disubstituted-1-nitroalkenes by oxidizing β-nitrosulfides **7a–o** with **8a** (*m*-CPBA or *m*-CPBA/AcOH), **8b** ($H_2O_2$/AcOH), or **8c** ($H_2O_2$) in 1,2-dichloroethane solution efficiently. A similar




(11)




Scheme 3.




Scheme 4.

product **5a–o** also can be synthesized by using **1a–o**, **2**, **3**, **6a**, and **8** under one-pot conditions. The generation of **14** and **15** provides indirect evidence to support the formation of intermediate **5p** during the reaction.

## 4. Experimental

### 4.1. General remarks

All reactions were performed in flame or oven-dried glassware under a positive pressure of nitrogen. THF, $CH_3CN$, DMF, and $ClCH_2CH_2Cl$ were used directly without purification. Analytical thin layer chromatography was performed with E. Merck silica gel 60F glass plates and flash chromatography used E. Merck silica gel 60 (230–400 mesh). MS or HRMS were measured by JEOL JMS-D300 or JEOL JMS-HX110 spectrometer. $^1$H and $^{13}$C NMR spectra were recorded with a Varian Gemini-200. All NMR data were obtained in $CDCl_3$ solution and chemical shifts ($\delta$) were given in ppm relative to TMS. Elemental analysis was performed on a Perkin–Elmer 2400 instrument.

### 4.2. Materials

Ketones **1a–l**, **1m**, **1o**, nitromethane **2**, piperidine **3a**, ethylenediamine **3b**, mercaptan **6a–g**, *m*-chloroperoxybenzoic acid **8a**, 1,4-cyclohexanedione **13** were purchased from Aldrich Chemical Co. and other commercially available reagents were used directly without further purification.

### 4.3. Typical experimental procedures for the preparation of the β-nitrosulfides 7a–o from the reaction of ketones 1a–o, nitromethane 2, and benzyl mercaptan 6a in the presence of piperidine 3a or ethylenediamine 3b as base in different solvents (Tables 1 and 9)

In a 100 ml round-bottomed flask were placed ethyl methyl ketone **1b** (5 mmol), nitromethane **2** (50 mmol), ethylenediamine **3b** (5 mmol), and benzyl mercaptan **6a** (20 mmol) in 15 ml of $CH_3CN$ and the solution was refluxed for 8 h. After cooling, the solvent was evaporated and the crude was purified by flash column chromatography using hexane–ethyl acetate (200:1) as the eluent to give pure **7b** (95% isolated yield). Similar procedures were used when other ketones **1c–l** were used to prepare intermediates **7c–l** in different solvents. Due to the low boiling point of **1a**, **2** was used as the limiting reagent and an excess of **1a** was continuously added to the solution during the reaction until all the nitromethane **2** was consumed. All the experimental data concerning the reaction, the solvents used, and the yields of product **7a–l** can be found in Table 1. When ketones **1m–o** were used, similar procedures and conditions were used and the experimental data concerning **7m–o** are shown in Table 9.

**4.3.1. 2-Benzylthio-2-nitromethylpropane (7a).**[5,6] $^1$H NMR (200 MHz, $CDCl_3$) 7.37–7.23 (m, 5H), 4.43 (s, 2H), 3.81 (s, 2H), 1.50 (s, 6H). $^{13}$C NMR (50 MHz, $CDCl_3$) 137.1, 129.0, 128.8, 127.5, 85.0, 44.4, 33.5, 26.4. MS *m/z* (relative intensity) 225 ($M^+$, 0.5), 123 (4.5), 91 (100). HRMS calcd for $C_{11}H_{15}NO_2S$ ($M^+$) 225.0824, found 225.0822. Anal. calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22. Found: C, 58.56; H, 6.83; N, 6.42.

**4.3.2. 2-Benzylthio-2-nitromethylbutane (7b).**[5,6] $^1$H NMR (200 MHz, $CDCl_3$) 7.36–7.31 (m, 5H), 4.51 (d, $J$=11 Hz, 1H), 4.44 (d, $J$=11 Hz, 1H), 3.77 (d, $J$=12.1 Hz, 1H), 3.70 (d, $J$=12.1 Hz, 1H), 1.78 (q, $J$=7.2 Hz, 2H), 1.44 (s, 3H), 1.05 (t, $J$=7.3 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.9, 129.0, 128.7, 127.4, 83.5, 48.6, 32.8, 30.5, 23.5, 8.2. MS $m/z$ (relative intensity) 239 ($M^+$, 45), 193 (100), 179 (45). HRMS calcd for $C_{12}H_{17}NO_2S$ ($M^+$) 239.0980, found 239.0981.

**4.3.3. 3-Benzylthio-3-nitromethylpentane (7c).** $^1$H NMR (200 MHz, $CDCl_3$) 7.34–7.18 (m, 5H), 4.50 (s, 2H), 3.67 (s, 2H), 1.68 (q, $J$=7.4 Hz, 2H), 1.03 (t, $J$=7.4 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.7, 129.1, 128.6, 127.3, 80.1, 52.8, 32.1, 27.1, 7.6. MS $m/z$ (relative intensity) 253 ($M^+$, 2), 223 (5), 207 (5), 205 (7), 91 (100). HRMS calcd for $C_{14}H_{21}NO_2S$ ($M^+$) 253.1137, found 253.1128.

**4.3.4. 2-Benzylthio-2-nitromethyl-4-methylpentane (7d).** $^1$H NMR (200 MHz, $CDCl_3$) 7.34–7.18 (m, 5H), 4.49 (d, $J$=11 Hz, 1H), 4.42 (d, $J$=11 Hz, 1H), 3.77 (d, $J$=12 Hz, 1H), 3.70 (d, $J$=12 Hz, 1H), 1.96 (m 1H), 1.68 (dd, $J$=15, 4.8 Hz, 1H), 1.58 (dd, $J$=15, 4.8 Hz, 1H), 1.47 (s, 3H), 1.01 (d, $J$=6.4 Hz, 3H), 0.98 (d, $J$=6.2 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.8, 129.0, 128.7, 127.4, 84.3, 48.6, 46.1, 32.9, 24.9, 24.8, 24.2, 24.1. MS $m/z$ (relative intensity) 267 ($M^+$, tr), 139 (5), 91 (100), 55 (20). HRMS calcd for $C_{14}H_{21}NO_2S$ ($M^+$) 267.1283, found 267.1283.

**4.3.5. 2-Benzylthio-2-nitromethylhexane (7e).** $^1$H NMR (200 MHz, $CDCl_3$) 7.35–7.19 (m, 5H), 4.50 (d, $J$=10.8 Hz, 1H), 4.43 (d, $J$=10.8 Hz, 1H), 3.77 (d, $J$=12.4 Hz, 1H), 3.70 (d, $J$=12.4 Hz, 1H), 1.71–1.25 (m, 6H), 1.45 (s, 3H), 0.91 (t, $J$=6.8 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 137.0, 129.0, 128.7, 127.4, 83.7, 48.2, 37.5, 32.9, 25.8, 24.0, 22.7, 13.8. MS $m/z$ (relative intensity) 267 ($M^+$, tr),139 (5), 91 (100), 55 (20). HRMS calcd for $C_{14}H_{21}NO_2S$ ($M^+$) 267.1289, found 267.1289.

**4.3.6. 1-Benzylthio-1-nitromethylcyclopentane (7f).**[5,6] $^1$H NMR (200 MHz, $CDCl_3$) 7.37–7.19 (m, 5H), 4.55 (s, 2H), 3.76 (s, 2H), 1.97–1.65 (m, 8H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.7, 128.8, 128.3, 126.9, 82.1, 54.9, 36.3, 33.6, 23.4. MS $m/z$ (relative intensity) 251 ($M^+$, 9), 205 (17), 203 (78), 124 (15), 123 (71), 91 (100). HRMS calcd for $C_{13}H_{17}NO_2S$ ($M^+$) 251.0980, found 251.0981. Anal. calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.58. Found: C, 62.22; H, 6.85; N, 5.82.

**4.3.7. 1-Benzylthio-1-nitromethylcyclohexane (7g).**[5,6] $^1$H NMR (200 MHz, $CDCl_3$) 7.35–7.16 (m, 5H), 4.46 (s, 2H), 3.65 (s, 2H), 1.85–1.12 (m, 10H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.8, 129.0, 128.5, 127.2, 84.5, 49.4, 33.2, 31.9, 25.1, 21.2. MS $m/z$ (relative intensity) 265 ($M^+$, 0.5), 219 (1.5), 91 (100). HRMS calcd for $C_{14}H_{19}NO_2S$ ($M^+$) 265.1137, found 265.1138. Anal. calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.35; H, 7.48; N, 5.37.

**4.3.8. 1-Benzylthio-1-nitromethylcycloheptane (7h).**[5,6] $^1$H NMR (200 MHz, $CDCl_3$) 7.39–7.19 (m, 5H), 4.47 (s, 2H), 3.74 (s, 2H), 2.09–1.38 (m, 12H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.9, 129.1, 128.7, 127.3, 84.5, 52.4, 36.6, 33.0, 29.6, 22.5. MS $m/z$ (relative intensity) 279 ($M^+$, 170), 233 (20), 123 (27), 91 (100). HRMS calcd for $C_{15}H_{21}NO_2S$ ($M^+$) 279.1293, found 279.1290.

**4.3.9. 1-Benzylthio-1-nitromethylcyclooctane (7i).** $^1$H NMR (200 MHz, $CDCl_3$) 7.32–7.19 (m, 5H), 4.44 (s, 2H), 3.67 (s, 2H), 1.78–1.52 (m, 14H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.6, 129.0, 128.4, 127.0, 82.6, 52.6, 32.4, 31.2, 28.5, 27.7, 24.6, 22.1. MS $m/z$ (relative intensity) 293 ($M^+$, tr), 154 (10), 123 (24), 91 (100), 81 (36), 67 (18). HRMS calcd for $C_{16}H_{23}NO_2S$ ($M^+$) 293.1450, found 293.1456.

**4.3.10. (*E*)-1-Benzylthio-1-nitromethyl-2-methylcyclohexane (7j).** The stereochemistry of this compound was assigned based on the NOE analysis. $^1$H NMR (200 MHz, $CDCl_3$) 7.35–7.18 (m, 5H), 4.67 (d, $J$=11.4 Hz, 1H), 4.56 (d, $J$=11.4 Hz, 1H), 3.72 (s, 2H), 2.12–1.18 (m, 9H), 1.08 (d, $J$=7 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.8, 129.3, 128.6, 127.2, 80.0, 52.3, 37.3, 32.2, 31.5, 29.8, 22.5, 21.8, 15.5. MS $m/z$ (relative intensity) 279 ($M^+$, 1.3), 249 (8.3), 231 (11),137 (47.8), 109 (75), 91 (100), 67 (28). HRMS calcd for $C_{15}H_{21}NO_2S$ ($M^+$) 279.1278, found 279.1278.

**4.3.11. (*Z*)-1-Benzylthio-1-nitromethyl-2-methylcyclohexane (7j).** The stereochemistry of this compound was assigned based on the NOE analysis. $^1$H NMR (200 MHz, $CDCl_3$) 7.36–7.21 (m, 5H), 4.89 (d, $J$=10.6 Hz, 1H), 4.36 (d, $J$=10.6 Hz, 1H), 3.66 (d, $J$=12 Hz, 1H), 3.56 (d, $J$=12 Hz, 1H), 2.09–1.20 (m, 9H), 1.03 (d, $J$=6.4 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.9, 129.0, 128.6, 127.3, 82.6, 54.1, 36.8, 32.0, 31.3, 29.9, 25.4, 21.3, 15.9. MS $m/z$ (relative intensity) 279 ($M^+$, 1.3), 249 (8.3), 231 (11),137 (47.8), 109 (75), 91 (100), 67 (28). HRMS calcd for $C_{15}H_{21}NO_2S$ ($M^+$) 279.1281, found 279.1281.

**4.3.12. 2-Benzylthio-2-nitromethyl-4-phenylbutane (7k).** $^1$H NMR (200 MHz, $CDCl_3$) 7.36–7.12 (m, 10H), 4.53 (d, $J$=11 Hz, 1H), 4.45 (d, $J$=11 Hz, 1H), 3.80 (d, $J$=11.6 Hz, 1H), 3.73 (d, $J$=11.6 Hz, 1H), 2.95–2.63 (m, 2H), 1.97 (d, $J$=7.8 Hz, 1H), 1.93 (d, $J$=7.8 Hz, 1H), 1.50 (s, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 140.1, 136.8, 129.0, 128.8, 128.5, 128.4, 127.5, 126.1, 83.4, 48.0, 39.8, 32.9, 30.2, 24.0. MS $m/z$ (relative intensity) 315 ($M^+$, 0.5), 145 (50), 91 (100). HRMS calcd for $C_{18}H_{21}NO_2S$ ($M^+$) 315.1296, found 315.1297.

**4.3.13. 1-Benzylthio-1-nitromethyl-1-phenylethane (7l).** $^1$H NMR (200 MHz, $CDCl_3$) 7.56–7.12 (m, 10H), 4.96 (d, $J$=11.8 Hz, 1H), 4.72 (d, $J$=11.8 Hz, 1H), 3.54 (d, $J$=12.8 Hz, 1H), 3.47 (d, $J$=12.8 Hz, 1H), 1.98 (s, 6H). $^{13}$C NMR (50 MHz, $CDCl_3$) 140.1, 136.7, 129.0, 128.7, 127.9, 127.3, 126.6, 83.9, 50.6, 34.4, 25.1. MS $m/z$ (relative intensity) 287 ($M^+$, 0.5), 148 (10), 118 (85), 91 (100). HRMS calcd for $C_{11}H_{15}NO_2S$ ($M^+$) 287.0976, found 287.0977.

**4.3.14. 2-Benzylthio-2-nitromethyl-bicyclo[2.2.1]heptane (7m—major product).** $^1$H NMR (200 MHz, $CDCl_3$) 7.32–7.20 (m, 5H), 4.69 (d, $J$=12.2 Hz, 1H), 4.63 (d,

$J$=12.2 Hz, 1H), 3.83 (d, $J$=11.6 Hz, 1H), 3.75 (d, $J$=11.6 Hz, 1H), 2.49–1.13 (m, 10H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.9, 129.2, 128.6, 127.2, 80.5, 54.3, 45.2, 43.7, 37.9, 37.1, 33.7, 28.4, 24.7. MS $m/z$ (relative intensity) 277 ($M^+$, 0.5), 107 (15), 91 (100). HRMS calcd for $C_{15}H_{19}NO_2S$ ($M^+$) 277.1131, found 277.1130.

**4.3.15. 2-Benzylthio-2-nitromethyl-bicyclo[2.2.1]heptane (7m—minor product).** $^1$H NMR (200 MHz, $CDCl_3$) 7.37–7.23 (m, 5H), 4.64 (d, $J$=11.4 Hz, 1H), 4.51 (d, $J$=11.4 Hz, 1H), 3.80 (d, $J$=11.4 Hz, 1H), 3.69 (d, $J$=11.4 Hz, 1H), 2.39–1.17 (m, 10H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.8, 129.1, 128.6, 127.3, 82.0, 55.1, 44.2, 43.4, 37.5, 37.2, 34.6, 28.0, 25.9. MS $m/z$ (relative intensity) 277 ($M^+$, 0.5), 107 (15), 91 (100). HRMS calcd for $C_{15}H_{19}NO_2S$ ($M^+$) 277.1131, found 277.1132.

**4.3.16. 3-Benzylthio-3-nitromethyl-tricyclo[2.2.1.0$^{2,6}$]-heptane (7n).** $^1$H NMR (200 MHz, $CDCl_3$) 7.37–7.17 (m, 5H), 4.55 (s, 2H), 3.82 (s, 2H), 2.33–1.29 (m, 8H). $^{13}$C NMR (50 MHz, $CDCl_3$) 137.5, 129.0, 128.5, 127.1, 79.3, 59.0, 37.4, 34.1, 32.3, 30.9, 19.1, 12.2, 12.0. MS $m/z$ (relative intensity) 275 ($M^+$, 0.5), 245 (10), 136 (25), 123 (15), 106 (47), 91 (100). HRMS calcd for $C_{15}H_{17}NO_2S$ ($M^+$) 275.0981, found 275.0982.

**4.3.17. 2-Benzylthio-2-nitromethyl-bicyclo[3.2.1]octane (7o).** There are two isomers were observed after reaction and these two isomers are inseparable and still contain trace of impurity even purified by HPLC. The spectral data of these two isomers are $^1$H NMR (200 MHz, $CDCl_3$) 7.37–7.23 (m), 4.78 (dd, $J$=11.2 Hz), 4.53 (dd, $J$=11.2 Hz), 3.77 (s), 3.72 (s), 2.45–2.18 (m), 2.00–1.20 (m). $^{13}$C NMR (50 MHz, $CDCl_3$) 137.0, 136.7, 129.3, 129.2, 128.59, 128.56, 127.24, 127.16, 82.8, 79.8, 52.9, 52.8, 41.7, 41.0, 34.22, 34.15, 34.0, 33.6, 32.5, 31.9, 29.0, 28.3, 28.1, 27.9, 27.8, 27.3, 26.5, 26.2.

### 4.4. Typical experimental procedures for the synthesis of nitroalkenes 5 from the oxidation of β-nitrosulfides 7 with 8a (*m*-CPBA or *m*-CPBA/AcOH), 8b ($H_2O_2$/AcOH), or 8c ($H_2O_2$) in $ClCH_2CH_2Cl$ solution and undergoing elimination under refluxing conditions (Tables 2–4, and 9)

At 0°C, 1 mmol of **7a** and 1.1 mmol of *m*-CPBA **8a-1** were dissolved in 20 ml of $ClCH_2CH_2Cl$ and stirred for few minutes. The temperature was then increased to room temperature and the solution was stirred for an additional 0.5 h. After the reaction was complete, as evidenced by TLC, the solution was refluxed for 3 h, cooled, and the solvent was evaporated. The purification of the mixture was carried out by flash column chromatography using hexane–ethyl acetate (400:1) to give **5a**. All experimental data using **8a-1** (*m*-CPBA) as oxidization reagent to generate product **5** is shown in Table 2, using **8b** ($H_2O_2$/AcOH) at room temperature, in Table 3, using **8c** ($H_2O_2$) at room temperature, in Table 4. When **7m–o** were used, the yields of products **5m–o** are shown in Table 9.

**4.4.1. 2-Methyl-1-nitropropene (5a).**[5] $^1$H NMR (200 MHz, $CDCl_3$) 6.98 (m, 1H), 2.27 (d, $J$=1.4 Hz, 3H), 1.96 (d, $J$=1.4 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 149.9, 135.2, 24.1, 19.9. MS $m/z$ (relative intensity) 101 ($M^+$, 10), 84 (100), 67 (2). HRMS calcd for $C_4H_8NO_2$ ($M^+$) 102.0555, found 102.0560.

**4.4.2. (*E*)-2-Methyl-1-nitrobutene (5b).**[5,6] $^1$H NMR (200 MHz, $CDCl_3$) 6.98–6.96 (m, 1H), 2.31–2.18 (m, 2H), 2.26–2.24 (m, 3H), 1.14 (t, $J$=7.6 Hz, 3H) $^{13}$C NMR (50 MHz, $CDCl_3$) 154.8, 134.8, 31.2, 18.5, 11.6. MS $m/z$ (relative intensity) 115 ($M^+$, 16), 98 (100), 81 (14), 72 (19). HRMS calcd for $C_5H_9NO_2$ ($M^+$) 115.0633, found 115.0633.

**4.4.3. (*Z*)-2-Methyl-1-nitrobutene (5b).**[5,6] $^1$H NMR (200 MHz, $CDCl_3$) 6.92–6.88 (m, 1H), 2.63 (q, $J$=7.6 Hz, 2H), 2.23 (t, $J$=10.6 Hz, 3H), 1.93 (d, $J$=1.2 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 155.1, 134.3, 26.0, 21.4, 11.4. MS $m/z$ (relative intensity) 115 ($M^+$, 16), 98 (100), 81 (14), 72 (19). HRMS calcd for $C_5H_9NO_2$ ($M^+$) 115.0633, found 115.0633.

**4.4.4. 2-Ethyl-1-nitrobutene (5c).** $^1$H NMR (200 MHz, $CDCl_3$) 6.89 (s, 1H), 2.64 (q, $J$=7.6 Hz, 2H), 2.26 (qd, $J$=7.6, 1.4 Hz, 2H), 1.16 (t, $J$=7.4 Hz, 3H), 1.13 (t, $J$=7.4 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 160.0, 134.3, 28.6, 24.9, 12.2, 11.6. Anal. calcd for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 55.61; H, 8.78; N, 10.46.

**4.4.5. (*E*)-2-Nitromethylene-4-methylpentane (5d).** $^1$H NMR (200 MHz, $CDCl_3$) 6.93 (s, 1H), 2.23 (d, $J$=1.2 Hz, 3H), 2.04 (d, $J$=7 Hz, 2H), 1.98–1.82 (m, 1H), 0.93 (d, $J$=6.4 Hz, 6H). $^{13}$C NMR (50 MHz, $CDCl_3$) 152.6, 135.9, 47.1, 26.2, 22.2, 18.4. MS $m/z$ (relative intensity) 143 ($M^+$, 2.5), 126 (15), 101 (20), 84 (100), 55 (52). Anal. calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.47; H, 9.05; N, 10.07.

**4.4.6. (*Z*)-2-Nitromethylene-4-methylpentane (5d).** $^1$H NMR (200 MHz, $CDCl_3$) 6.98 (s, 1H), 2.61 (dd, $J$=7.4, 0.8 Hz, 2H), 2.03–1.90 (m, 1H), 1.91 (d, $J$=1.4 Hz, 3H), 0.96 (d, $J$=6.6 Hz, 6H). $^{13}$C NMR (50 MHz, $CDCl_3$) 152.5, 135.6, 40.8, 27.4, 22.6, 18.3. MS $m/z$ (relative intensity) 144 ($M^+$, 1.5), 126 (13), 101 (22), 84 (100), 59 (42), 56 (40), 53 (22). Anal. calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.50; H, 9.07; N, 10.08.

**4.4.7. (*E*)-2-Nitromethylenehexane (5e).** $^1$H NMR (200 MHz, $CDCl_3$) 6.96 (q, $J$=1.2 Hz 1H), 2.24 (d, $J$=1.4 Hz, 3H), 2.19 (t, $J$=7 Hz, 2H), 1.58–1.26 (m, 4H), 0.93 (t, $J$=7.2 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 153.6, 135.2, 37.7, 29.1, 22.1, 18.5, 13.6. MS $m/z$ (relative intensity) 144 ($M^+$, 1.5), 126 (26), 100 (30), 84 (36), 71 (60), 55 (100). HRMS calcd for $C_5H_9NO_2$ ($M^+$) 143.0947, found 143.0920.

**4.4.8. (*Z*)-2-Nitromethylenehexane (5e).** $^1$H NMR (200 MHz, $CDCl_3$) 6.93 (s, 1H), 2.65 (t, $J$=6.8 Hz, 2H), 1.92 (d, $J$=1.6 Hz, 3H), 1.58–1.26 (m, 4H), 0.95 (t, $J$=6.8 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) $^{13}$C NMR (50 MHz, $CDCl_3$) 153.6, 135.2, 37.7, 29.1, 22.1, 18.5, 13.6. MS $m/z$ (relative intensity) 144 ($M^+$, 1.5), 126 (26), 100 (30), 84 (36), 71 (60), 55 (100). HRMS calcd for $C_5H_9NO_2$ ($M^+$) 143.0947, found 143.0922.

**4.4.9. Nitromethylenecyclopentane (5f).**[5] $^1$H NMR

(200 MHz, $CDCl_3$) 7.17–7.10 (m, 1H), 3.06–2.93 (m, 2H), 2.59–2.47 (m, 2H), 1.91–1.67 (m, 4H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 163.7, 132.2, 33.9, 33.3, 25.9, 25.4. MS *m/z* (relative intensity) 127 ($M^+$, 2), 111 (11), 81 (68), 79 (100). HRMS calcd for $C_6H_9NO_2$ ($M^+$) 127.0597, found 127.0615.

**4.4.10. Nitromethylenecyclohexane (5g).**[5,6,14] $^1H$ NMR (200 MHz, $CDCl_3$) 6.94–6.89 (m, 1H), 2.89–2.83 m, 2H), 2.24–2.18 (m, 2H), 1.77–1.59 (m, 6H), $^{13}C$ NMR (50 MHz, $CDCl_3$) 155.8, 132.4, 34.4, 28.9, 28.2, 27.3, 25.8. MS *m/z* (relative intensity) 141 ($M^+$, 3), 109 (15), 95 (3), 81 (100). HRMS calcd for $C_7H_{11}NO_2$ ($M^+$) 141.0790, found 141.0788.

**4.4.11. Nitromethylenecycloheptane (5h).**[5] $^1H$ NMR (200 MHz, $CDCl_3$) 6.99 (s, 1H), 3.00–2.92 (m, 2H), 2.42–2.35 (m, 2H), 1.85–1.50 (m, 8H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 160.2, 134.8, 35.4, 32.1, 29.5, 28.8, 27.9, 25.5. MS *m/z* (relative intensity) 155 ($M^+$, 4), 139 (64), 109 (11), 91 (100). HRMS calcd for $C_8H_{13}NO_2$($M^+$) 155.0946, found 155.0937.

**4.4.12. Nitromethylenecyclooctane (5i).** $^1H$ NMR (200 MHz, $CDCl_3$) 7.04 (s, 1H), 2.82 (t, *J*=6 Hz, 2H), 2.33 (t, *J*=6 Hz, 2H), 1.89–1.77 (m, 4H), 1.60–1.41 (m, 6H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 161.9, 134.8, 35.6, 30.0, 27.3, 27.2, 25.9, 25.5, 24.3. MS *m/z* (relative intensity) 169 ($M^+$, tr), 149 (10), 123 (25), 81 (100), 67 (50). HRMS calcd for $C_9H_{15}NO_2$($M^+$) 169.1103, found 169.1095.

**4.4.13. 2-Methyl-1-nitromethylenecyclohexane (5j).** Two isomers were observed after the reaction, but only the major isomer could be isolated after column and HPLC purification. The spectral data of the major isomer are $^1H$ NMR (200 MHz, $CDCl_3$) 6.85 (s, 1H), 3.42–3.32 (m, 1H), 2.39–2.19 (m, 2H), 1.98–1.22 (m, 6H), 1.12 (d, *J*=6.6 Hz, 3H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 159.1, 132.0, 38.0, 36.6, 28.3, 27.8, 24.5, 18.0. GCMS of the two isomers are *m/z* (relative intensity) 155 ($M^+$, tr), 138 (17), 112 (29), 97 (38), 79 (52), 67 (64), 55 (53), 43 (100), 41 (66) and *m/z* (relative intensity) 155 ($M^+$, tr), 138 (55), 110 (30), 97 (40), 79 (75), 67 (96), 55 (95), 43 (98), 41 (100).

**4.4.14. (*E*)-2-Nitromethylene-4-phenylbutane (5k).** $^1H$ NMR (200 MHz, $CDCl_3$) 7.36–7.12 (m, 5H), 6.90 (q, *J*=1.4 Hz, 1H), 2.87–2.79 (m, 2H), 2.53–2.45 (m, 2H), 2.29 (d, *J*=1.2 Hz, 3H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 152.1, 139.8, 135.7, 128.7, 128.3, 126.6, 39.7, 33.4, 18.6. MS *m/z* (relative intensity) 191 ($M^+$, tr), 145 (85), 117 (34), 91 (100), 41 (26). HRMS calcd for $C_{11}H_{13}NO_2$($M^+$) 191.0951, found 191.0952.

**4.4.15. (*Z*)-2-Nitromethylene-4-phenylbutane (5k).** $^1H$ NMR (200 MHz, $CDCl_3$) 7.36–7.18 (m, 5H), 6.97 (s, 1H), 2.99–2.78 (m, 4H), 1.89 (d, *J*=1.4 Hz, 3H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 152.9, 140.5, 135.3, 128.6, 128.4, 126.4, 35.0, 33.7, 22.6. MS *m/z* (relative intensity) 191 ($M^+$, tr), 145 (85), 117 (34), 91 (100), 41 (26). HRMS calcd for $C_{11}H_{13}NO_2$($M^+$) 191.0932, found 191.0933.

**4.4.16. 2-Nitromethylene-bicyclo[3.2.1]octane (5o).** Two isomers were observed after the reaction and are inseparable and still contain traces of impurity even after purification by HPLC. The spectral data of these two isomers are $^1H$ NMR (200 MHz, $CDCl_3$) 6.88 (d, *J*=2.4 Hz), 6.77 (d, *J*=2.0 Hz), 4.26 (s), 3.59 (dd, *J*=16.4, 5.8 Hz), 2.68–1.52 (m).

### 4.5. Typical experimental procedures for the synthesis of 5m, n, and 18 from the reactions of ketones 1m–o, nitromethane 2, and ethylenediamine 3b under refluxing condition according to Barton's methodology (Table 8)[12a]

Ketone **1m** (1 mmol), nitromethane **2** (90 mmol), and ethylenediamine **3b** (0.1 mmol) were placed in a 10 ml round-bottomed flask and the solution refluxed for 24 h under a nitrogen atmosphere. After the solvent was evaporated in vacuo, the residue was further purified by flash column chromatography using hexane–ethyl acetate (200:1) to give pure **5m** (15% isolated yield). When the same reaction was repeated and the reaction time was increased to 36 h, only 24% yield of **5m** was found. For substrate **1o**, the only product was a 51% (isolated yield) of **12** under similar procedures and conditions. All the experimental data are shown in Table 8.

**4.5.1. 2-Nitromethylene-bicyclo[2.2.1]heptane (5m—major product).** $^1H$ NMR (200 MHz, $CDCl_3$) 7.11 (t, *J*=2.2 Hz, 1H), 2.95–2.55 (m, 4H), 1.87–1.31 (m, 6H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 165.7, 129.9, 44.7, 40.1, 39.2, 35.6, 28.0, 27.2. MS *m/z* (relative intensity) 153 ($M^+$, 1.3), 125 (25), 109 (40), 91 (70), 79 (100), 67 (90), 55 (50), 41 (73). HRMS calcd for $C_8H_{12}NO_2$ ($M^+$) 153.0790, found 153.0782.

**4.5.2. 2-Nitromethylene-bicyclo[2.2.1]heptane (5m—minor product).** $^1H$ NMR (200 MHz, $CDCl_3$) 6.90 (s, 1H), 4.13 (d, *J*=4.2 Hz, 1H), 2.51–1.21 (m, 9H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 163.7, 130.6, 43.4, 39.3, 38.9, 35.2, 27.8, 26.8. MS *m/z* (relative intensity) 153 ($M^+$, 1.3), 125 (25), 109 (40), 91 (70), 79 (100), 67 (90), 55 (50), 41 (73). HRMS calcd for $C_8H_{12}NO_2$ ($M^+$) 153.0790, found 153.0765.

**4.5.3. (*E*)-3-Nitromethylene-tricyclo[2.2.1.0$^{2,6}$]heptane (5n).** The stereochemistry of this compound was assigned based on NOE analysis. $^1H$ NMR (200 MHz, $CDCl_3$) 6.85 (s, 1H), 3.79 (d, *J*=0.6 Hz, 1H), 1.96–1.85 (m, 4H), 1.66–1.60 (m, 3H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 165.6, 127.0, 35.1, 33.3, 19.5, 17.7. MS *m/z* (relative intensity) 151 ($M^+$, 11), 122 (7), 103 (26), 91 (32), 77 (100). HRMS calcd for $C_8H_9NO_2$ ($M^+$) 151.0638, found 151.0638.

**4.5.4. (*Z*)-3-Nitromethylene-tricyclo[2.2.1.0$^{2,6}$]heptane (5n).** The stereochemistry of this compound was assigned based on NOE analysis. $^1H$ NMR (200 MHz, $CDCl_3$) 7.14 (s, 1H), 2.84 (t, *J*=5.2 Hz, 1H), 2.40 (d, *J*=1 Hz, 1H), 2.03 (d, *J*=5.2 Hz, 2H), 1.87–1.81 (m, 2H), 1.65–1.60 (m, 2H). $^{13}C$ NMR (50 MHz, $CDCl_3$) 165.3, 128.0, 35.6, 34.6, 20.5, 17.6. MS *m/z* (relative intensity) 151 ($M^+$, tr), 122 (13), 104 (34), 91 (36), 77 (100). HRMS calcd for $C_8H_9NO_2$ ($M^+$) 151.0638, found 151.0638.

**4.5.5. 2-Nitromethyl-bicyclo[3.2.1]oct-2-ene (12).** $^1H$ NMR (200 MHz, $CDCl_3$) 5.61 (s, 1H), 4.83 (d, *J*=13.4 Hz, 1H), 4.76 (d, *J*=13.4 Hz, 1H), 2.30–2.52 (m, 3H), 2.00–1.32 (m, 7H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.1, 129.5, 81.4, 37.5, 36.8, 35.3, 34.9, 32.3, 30.5. MS *m/z* (relative intensity) 167 ($M^+$, 5), 166 (35), 136 (37), 119 (32), 107 (28), 91 (100), 79 (62), 77 (29), 67 (27). HRMS calcd for $C_8H_9NO_2$ ($M^+$) 167.0946, found 167.0920.

### 4.6. Typical experimental procedures for the preparation of 14 and 15g from the reaction of 1,4-cyclohexanedione 13, nitromethane 2, and mercaptan 6 in the presence of ethylenediamine 3b as base in $CH_3CN$ solution (Table 11)

In a 50 ml round-bottomed flask were placed the 1,4-cyclohexanedione **13** (5 mmol), nitromethane **2** (50 mmol), ethylenediamine **3b** (5 mmol), and benzyl mercaptan **6a** (20 mmol) in 15 ml of $CH_3CN$ and the solution refluxed for 13 h. After cooling, the solvent was evaporated and the crude mixture was purified by flash column chromatography using hexane–ethyl acetate (100:1) to give pure **14a** (53% isolated yield). When mercaptan **6g** was used, not only the major product **14g** but also the minor product **15g** was isolated from the reaction mixture. All the experimental data concerning the generation of **14** and **15** are shown in Table 11.

**4.6.1. 1-Benzylthio-7-nitro-4-nitromethyl-bicyclo[2.2.1]-heptane (14a).** $^1$H NMR (200 MHz, $CDCl_3$) 7.38–7.23 (m, 5H), 4.71 (d, $J$=12.6 Hz, 1H), 4.63 (s, 1H), 4.51 (d, $J$=12.6 Hz, 1H), 3.91 (d, $J$=12 Hz, 1H), 3.80 (d, $J$=12 Hz, 1H), 2.42–1.60 (m, 8H). $^{13}$C NMR (50 MHz, $CDCl_3$) 136.8, 128.9, 128.6, 127.4, 92.3, 76.7, 57.4, 48.9, 34.0, 33.7, 32.0, 31.9, 30.3. MS *m/z* (relative intensity) 322 ($M^+$, 1.0), 216 (17), 107 (30), 91 (100). HRMS calcd for $C_{15}H_{18}N_2O_4S$ ($M^+$) 322.0978, found 322.0779.

**4.6.2. 1-Allylthio-7-nitro-4-nitromethyl-bicyclo[2.2.1]-heptane (14c).** $^1$H NMR (200 MHz, $CDCl_3$) 5.99–5.79 (m, 1H), 5.29–5.10 (m, 1H), 4.72 (d, $J$=12.2 Hz, 1H), 4.70 (s, 1H), 4.53 (d, $J$=12.2 Hz, 1H), 3.40–3.18 (m, 2H), 2.44–1.69 (m, 8H). $^{13}$C NMR (50 MHz, $CDCl_3$) 134.5, 117.9, 92.6, 76.8, 57.2, 49.0, 34.3, 32.4, 32.0, 31.8, 30.4. MS *m/z* (relative intensity) 272 ($M^+$, tr), 216 (15), 155 (18), 105 (45), 91 (47), 79 (45), 41 (100).

**4.6.3. 1-Ethylthio-7-nitro-4-nitromethyl-bicyclo[2.2.1]-heptane (14d).** $^1$H NMR (200 MHz, $CDCl_3$) 4.72 (d, $J$=12.2 Hz, 1H), 4.56 (s, 1H), 4.53 (d, $J$=12.2 Hz, 1H), 2.70–1.69 (m, 10H), 1.25 (t, $J$=7.4 Hz, 3H). $^{13}$C NMR (50 MHz, $CDCl_3$) 92.8, 76.8, 57.2, 49.1, 34.1, 32.3, 32.1, 30.4, 22.9, 14.3. MS *m/z* (relative intensity) 260 ($M^+$, 15), 140 (27), 105 (100), 91 (60), 79 (80), 41 (40). HRMS calcd for $C_{10}H_{16}N_2O_4S$ ($M^+$) 260.0841, found 260.0840.

**4.6.4. 1-(2,2′-Oxydiethanethio)-7-nitro-4-nitromethyl-bicyclo[2.2.1]heptane (14e).** $^1$H NMR (200 MHz, $CDCl_3$) 4.72 (d, $J$=12.4 Hz, 1H), 4.72 (s, 1H), 4.52 (d, $J$=12.4 Hz, 1H), 3.74–3.55 (m, 4H), 2.94–2.65 (m, 4H), 2.39–1.26 (m, 8H) 1.59 (t, $J$=8 Hz, 1H). $^{13}$C NMR (50 MHz, $CDCl_3$) 92.8, 76.8, 72.5, 70.3, 56.9, 49.0, 34.2, 32.1, 32.0, 30.3, 28.8, 24.6. MS *m/z* (relative intensity) 337 ($M^+$, 2), 207 (5), 72 (65), 59 (100), 41 (36). HRMS calcd for $C_{12}H_{20}N_2O_5S_2$ ($M^+$) 336.8810, found 336.0811.

**4.6.5. 1-(2,2′-Thiodiethanethio)-7-nitro-4-nitromethyl-bicyclo[2.2.1]heptane (14f).** $^1$H NMR (200 MHz, $CDCl_3$) 4.73 (d, $J$=12.6 Hz, 1H), 4.72 (s, 1H), 4.53 (d, $J$=12.6 Hz, 1H), 2.94–2.65 (m, 8H), 2.42–1.70 (m, 9H). $^{13}$C NMR (50 MHz, $CDCl_3$) 92.7, 76.7, 57.3, 49.1, 36.2, 34.0, 32.4, 32.1, 31.8, 30.3, 29.0, 24.6. MS *m/z* (relative intensity) 352 ($M^+$, 6), 91 (13), 64 (100). HRMS calcd for $C_{12}H_{20}N_2O_4S_3$ ($M^+$) 352.0572, found 352.0572.

**4.6.6. 1-(Propane-1,3-dithio)-7-nitro-4-nitromethyl-bi-cyclo[2.2.1]heptane (14g).** $^1$H NMR (200 MHz, $CDCl_3$) 4.72 (d, $J$=12.6 Hz, 1H), 4.76 (s, 1H), 4.53 (d, $J$=12.6 Hz, 1H), 2.76–2.59 (m, 6H), 1.95–1.76 (m, 8H), 1.40 (t, $J$=8 Hz, 1H). $^{13}$C NMR (50 MHz, $CDCl_3$) 92.7, 76.8, 57.2, 49.1, 34.1, 33.0, 32.2, 32.1, 30.4, 27.0, 23.3. MS *m/z* (relative intensity) 306 ($M^+$, 40), 259 (37), 105 (100), 91 (99), 74 (95). HRMS calcd for $C_{11}H_{18}N_2O_4S_2$ ($M^+$) 306.0707, found 306.0708.

**4.6.7. 1,4-Bis(nitromethyl)-1,4-bis(propane-1,3-dithio)-cyclohexane (15g).** $^1$H NMR (200 MHz, $CDCl_3$) 4.52 (s, 4H), 2.70–2.54 (m, 8H), 2.23 (s, 2H), 2.17 (s, 2H), 1.94–1.71 (m, 8H), 1.38 (t, $J$=8 Hz, 2H). $^{13}$C NMR (50 MHz, $CDCl_3$) 84.8, 48.0, 32.3, 28.3, 25.2, 23.4.


## Acknowledgements

Financial support by the National Science Council of the Republic of China is gratefully acknowledged.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