Intramolecular Pummerer Reaction of γ, δ-Unsaturated Sulfinyl Compounds

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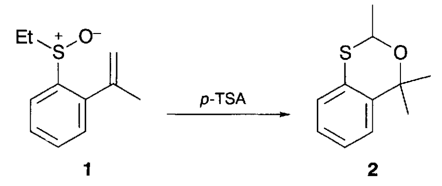
A novel preparation of 1,3-oxathiane derivatives through Pummerer rearrangement of γ,δ-unsaturated sulfinyl compounds and its plausible mechanism are described.

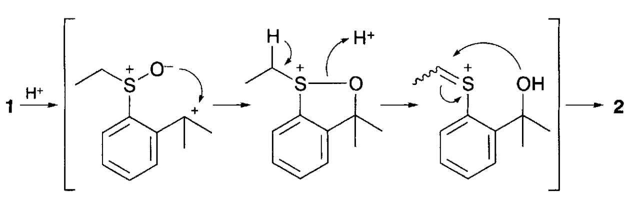
The Pummerer rearrangement[1] is well known as a useful reaction for the formation of an α-acyloxysulfide from a sulfinyl compound by the use of an acid anhydride.[2] Considering the mechanism of this reaction, we supposed that it might be applicable to the formation of the 1,3-oxathiane ring from a certain unsaturated sulfinyl compound. The important synthetic utilities of 1,3-oxathiane as masked acyl anion equivalents have been documented.[3,4] However, few methods[5] other than the hemithioacetalization of carbonyl compounds with mercapto-alcohol for the preparation of 1,3-oxathiane derivatives are known. Here, we report a new method for construction of 1,3-oxathiane derivatives *via* an intramolecular Pummerer reaction of γ,δ-unsaturated sulfinyl compounds with organic acids.

In preliminary experiments we found that toluene-*p*-sulfonic acid (*p*-TSA) was effective for the intramolecular Pummerer reaction of sulfinyl compound **1** rather than other proton acids such as acetic, trifluoroacetic and trifluoromethanesulfonic acids. Thus, the reaction of **1** with *p*-TSA (1.2 equiv.) in refluxing xylene for 50 min afforded 1,3-oxathiane **2** in 53% yield (Scheme 1). This reaction proceeds *via* the formation of a five-membered sulfonium intermediate as shown in Scheme 2.

Next, we examined the reactions with conformationally rigid substrates such as **3**–**7** which were prepared from Diels–Alder reactions between alkylsulfinyl alkenes and cyclopentadiene.[6] As shown in Table 1, the reaction of **3**, a mixture of two inseparable diastereoisomers, afforded 1,3-oxathiane **8** in 50% yield (entry 1). Nitrosulfinyl compounds[7] **4**–**6** gave **9a**–**11a** as major and **9b**–**11b** as minor products (entries 2–4), while **7** decomposed under similar conditions (entry 5). In order to clarify the structure of **9a**, an X-ray diffraction analysis was carried out (Fig. 1).† It was found that the oxathiane ring in **9a** exists in a chair conformation with an equatorial methyl group. On the other hand, the stereostructure of the minor oxathiane **9b** was confirmed by NOE as shown in Fig. 2. Chemical



Scheme 1

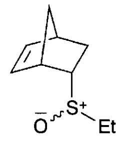


Scheme 2

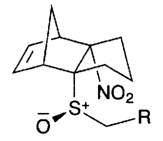
Table 1 Intramolecular Pummerer reaction of γ,δ-unsaturated sulfinyl compounds with *p*-TSA[a]

Entry	Sulfoxide	Product (Yield%)[b]	
1	**3**[c]	**8** (50)[d]	
2	**4**	**9a** (73)	**9b** (4)
3	**5**	**10a** (77)[e]	**10b** (6)[e]
4	**6**	**11a** (82)[e]	**11b** (1)[e]
5	**7**	—[f]	

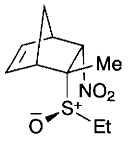
[a] Reactions were carried out in xylene under reflux for 1 h. [b] Isolated yield. [c] Mixture of two diastereoisomers in 3 : 1 ratio was used. [d] No other isomers were detected. [e] Yields were calculated from ^1H NMR integration. [f] Many spots appeared on TLC.



3



4 R = Me
5 R = Et
6 R = Ph



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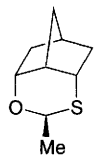

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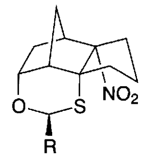
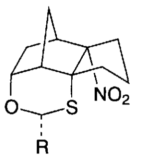


9a R = Me
10a R = Et
11a R = Ph



9b R = Me
10b R = Et
11b R = Ph

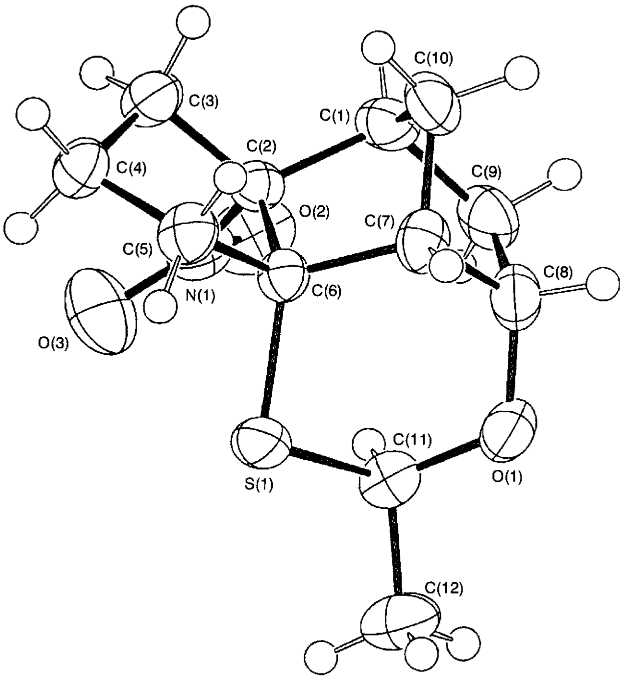


Fig. 1 ORTEP[8] drawing of oxathiane **9a**

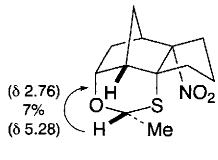
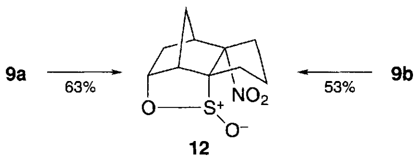


Fig. 2 NOE experiment on **9b**



Scheme 3

correlation between **9a** and **9b** was also achieved by oxidative cleavage of the oxathiane ring: treatment of **9a** and **9b** with NCS–$AgNO_3$[3] produced the sultine **12** (Scheme 3).[‡] The stereostructures of other products were elucidated by comparison of their ^1H NMR data with those of **9a** and **9b**.

In summary, we have demonstrated a novel method for 1,3-oxathiane synthesis through the Pummerer rearrangement of γ,δ-unsaturated sulfinyl compounds. It is notable that the carbenium cation generated by protonation of the alkene could act as an electrophilic species toward the intramolecular sulfoxide. Further studies on the generalization of this reaction are in progress in our laboratories.

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Footnotes

[†] *Crystal data* for **9a**: a colourless prismatic crystal of dimensions 0.25 × 0.10 × 0.45 mm was mounted on a glass fibre. Intensity measurements were made on a Rigaku AFC5R diffractometer with graphite-monochromated Mo-Kα radiation ($\lambda = 0.71073$ Å). $C_{12}H_{17}NO_3S$, $M_r = 255.33$, triclinic, space group $P\bar{1}$, $Z = 2$; $a = 7.081(3)$, $b = 13.380(8)$, $c = 6.764(3)$ Å, $\alpha = 103.46(4)$, $\beta = 105.12(3)$, $\gamma = 89.08(5)°$, $V = 601.0(6)$ Å^3, $D_x = 1.411$ g cm^{-3}, μ(Mo-Kα) = 0.25 mm^{-1}. The data were collected at 295 K using the ω–2θ scan technique to a maximum 2θ value of 52.0° with scan widths (1.26 + 0.30 tan θ)° in ω and scan speed of 6° min^{-1} in ω. Of the 2583 reflections which were collected, 2370 were unique ($R_{int} = 0.008$). The fluctuation of three standard reflections measured after every 97 reflections was within 0.8%. The data were corrected for Lorentz and polarization effects, but not absorption effects. The structure was solved by direct methods.[9] The structure was refined anisotropically for non-hydrogen atoms and isotropically for hydrogen atoms by full-matrix least-squares methods. The quantity minimized was $\Sigma w(|F_o| - |F_c|)^2$, where $w = 1/\sigma^2(F_o)$. The final $R = 0.032$, $wR = 0.028$ for 1771 reflections with $I_o > 3\sigma(I_o)$, $S = 1.53$, $(\Delta/\sigma)_{max} = 0.4$; $\Delta\rho_{max} = 0.19$ e Å^{-3}, $\Delta\rho_{min} = -0.18$ e Å^{-3}. Atom scattering factors were taken from Cromer and Weber.[10] Calculations were performed using the TEXSAN.[11] Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

[‡] Attempts to transform the oxathianes **9a** and **9b** to the corresponding mercaptoalcohols were unsuccessful.

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11 TEXSAN–TEXRAY Structure Analysis Package, Molecular Structure Corporation, 3200 Research Forest Drive, The Woodlands, Texas 77381, USA.