SYNTHESIS AND STEREOSPECIFIC FRAGMENTATION OF 3-THIABICYCLO[3.1.0]HEXANE 3,3-DIOXIDES

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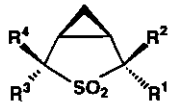
Abstract–Synthesis of new stereoisomeric 3-thiabicyclo[3.1.0]hexane 3,3-dioxides and experimental proof of their fragamentation to 1,4-dienes by a concerted, disrotatory process are described.

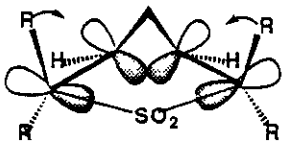
Stereospecific formation of 1,3-dienes by thermal desulfonylation of 3-sulfolenes is now well established.[1] A similar extrusion of sulfur dioxide from 3-thiabicyclo[3.1.0]hexane 3,3-dioxides (**1a**, **1b**, and **1c**) to give corresponding 1,4-dienes was also previously reproted.[2] The ring-opening stereochemistry of the bicyclic sulfones is believed to proceed stereospecifically by a concerted, disrotatory process. Preparation of the bicyclic



1 a	$R^1 = R^2 = R^3 = R^4 = H$	**f**	R^1 = TMS, $R^2 = R^3 = R^4 = H$
b	R^1 = Me, $R^2 = R^3 = R^4 = H$	**g**	R^1 = SPh, $R^2 = R^3 = R^4 = H$
c	$R^1 = R^3$ = Me, $R^2 = R^4 = H$	**h**	R^2 = SPh, $R^1 = R^3 = R^4 = H$
d	$R^1 = R^4$ = Me, $R^2 = R^3 = H$	**i**	R^1 = COOEt, $R^2 = R^3 = R^4 = H$
e	$R^2 = R^4$ = Me, $R^1 = R^3 = H$	**j**	R^2 = COOEt, $R^1 = R^3 = R^4 = H$

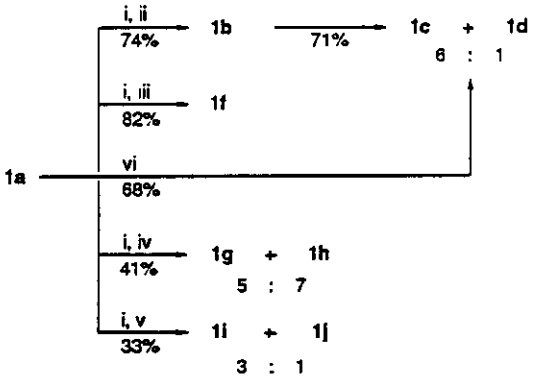
sulfones as stable precursors of 1,4-dienes thus was considered to be of value in orgnic synthesis. So far, because of the shortage of stereoisomers of **1d** and **1e** for comparison, clear-cut experimental proof of concertedness of their fragmentation through a transition state in Figure 1 has not been accomplished. Furthermore, the limited accessibility of various α-substituted 3-thiabicyclo[3.1.0]hexane 3,3-dioxides has impeded this potential method for terminally substituted 1,4-dienes synthesis. In this communication, we wish to describe a new route to sulfone analogues (**1d–e**) and (**1g–j**), and demonstrate their fragmentation proceeding in a concerted, disrotatory mode even in the face of the steric crowdedness formed in the transition state.[3]

Figure 1



First, we found that compound (**1a**) in tetrahydrofuran (THF) at -90 °C could be easily deprotonated without occurrence of the anionic cycloreversion process.[4] By treatment of **1a** with Bu^{n}Li (1 equiv.) followed by MeI, TMSCl, PhSSPh, and ClCOOEt (1.2 equiv.) respectively, compounds (**1b**, **1f** and **1g–j**) were produced smoothly as in Scheme I.[5] Further methylation of **1b** with MeI or dimethylation of **1a** in one flask by sequential addition of Bu^{n}Li (2 euqiv.) and MeI (3 equiv.) under the same conditions allowed generation of 2,4-

Scheme I

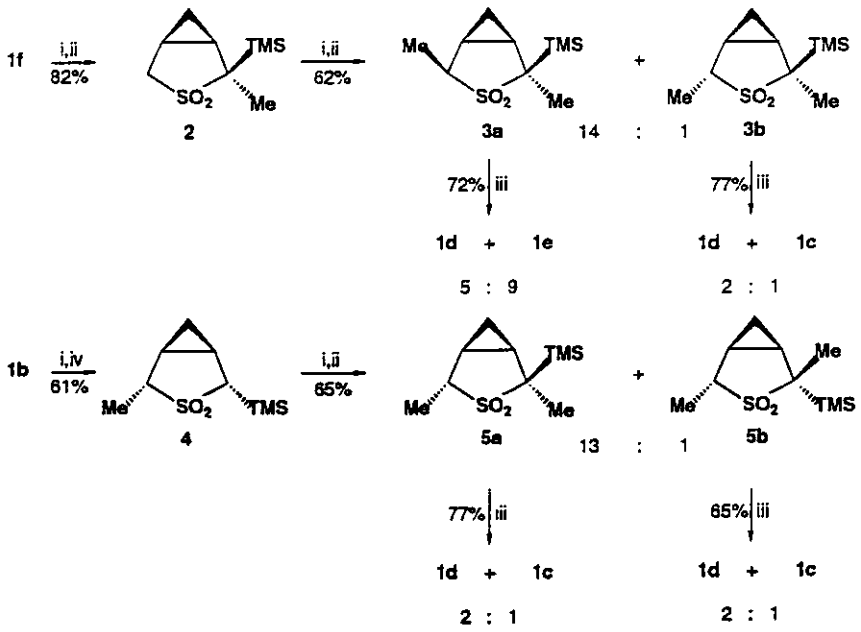


i) Bu^{n}Li, THF -90 °C; ii) MeI; iii) TMSCl; iv) PhSSPh;
v) ClCOOEt; vi) 2 equiv. Bu^{n}Li, THF -90 °C, 3 equiv. MeI.

dimethylated 3-thiabicyclo[3.1.0]hexane 3,3-dioxides (**1c**) and (**1d**) in 6:1 ratio. However, both simple deprotonation/substitution processes failed to give stereoisomer (**1e**) in any significant quantity. The raito of **1c** and **1d** was not able to be altered by refluxing the mixture in NaOH/EtOH. Later, we found that synthesis of **1e** and **1d** as major product could be achieved by a substitution and desilylation sequence starting from **1f** or **1b** (Scheme II). When **1f** in THF was treated with Bu^{n}Li and MeI sequentially at –90 °C followed by aqueous workup at room temperature, compound (**2**) was generated regio- and stereoselectively in good yield. Methylation of **2** afforded two dimethyl stereoisomers (**3a**) and (**3b**) in 14:1 ratio. Treatment of the major product (**3a**) in trifluoroacetic acid with tetrabutylammonium fluoride at room temperature selectively produced the *exo,exo*- dimethyl stereoisomer (**1e**) along with the *exo,endo*- isomer (**1d**) in 9:5 ratio The alternative production of isomer (**1d**) as the major component was accomplished by silylation followed by substitution and

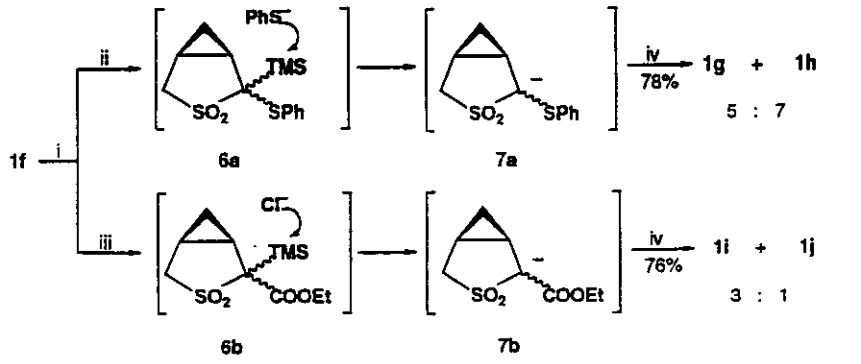
desilylaiton starting from **1b**. Two stereoisomers (**5a**) and (**5b**) in 13:1 ratio were given by way of silylation and methylation of **1b** through 4. Desilylation of both products then afforded **1d** and **1c** in a ratio of 2:1.

Scheme II



i) Bu^nLi, THF, – 90 °C; ii) MeI; iii) Bu^n_4F, CF_3COOH, room temperature; iv) TMSCl.

Scheme III



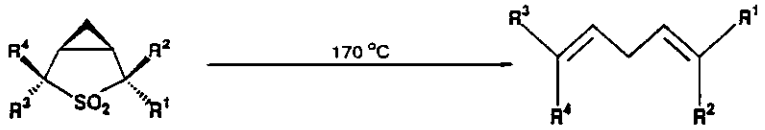
i) Bu^nLi, THF, – 90 °C; ii) PhSSPh; iii) ClCOOEt; iv) H_2O, room temperature.

Noteworthy is that compounds (**1g–j**) were obtained in one flask by treatment of **1f** with Bu^nLi at -90 °C followed by addition of PhSSPh or ClCOOEt (Scheme III). The overall yields of the two-step synthesis of 1g–j from **1a** are superior to those of direct deprotonation/substitution of **1a**. This one-flask formation of **1g–j** could

be from the protonation of anion (**7**), which was generated by the counterion of electrophile attacking on the trimethylsily group of intermediate (**6**).[6]

Experiments on fragmentation of bicyclic sulfones (**1d–e**) and (**1g–j**) thus obtained were carried out in the injection port (170 °C) of a preparative gas chromatography machine fitted with a SE-30 column (2-m).[7] The pyrolysis product was collected with a dry-ice trap. In addition to sulfur dioxide, only one peak was detectable by gas chromatography for each substrate. Both ^{1}H and ^{13}C nmr spectral data of collected products (**8a-f**) confirmed that only one 1,4-dienyl stereoisomer was formed (Scheme IV). The conversion of sulfones to 1,4-dienes is cleanly stereospecific.

Scheme IV



1d	$R^1 = R^4 = Me$, $R^2 = R^3 = H$	**8a**
1e	$R^2 = R^4 = Me$, $R^1 = R^3 = H$	**8b**
1g	$R^1 = SPh$, $R^2 = R^3 = R^4 = H$	**8c**
1h	$R^2 = SPh$, $R^1 = R^3 = R^4 = H$	**8d**
1i	$R^1 = COOEt$, $R^2 = R^3 = R^4 = H$	**8e**
1j	$R^2 = COOEt$, $R^1 = R^3 = R^4 = H$	**8f**

The results can be explained by the retro 2 + 2 + 2 concerted mechanism.[8] The requirement for the diene formation between the fused cyclopropyl and substituent-bearing carbons would result in a disrotatory mode shown in Figure 1. The exclusive formation of dienes (**8a-f**)[9] clearly indicated that the orbital overlap by synchronous rupture of three sigama bonds is more important than steric crowdedness in the transition state.

In summary, a general route for synthesis of new 3-thiabicyclo[3.1.0]hexane 3,3-dioxides (**1d–e**)[9] and (**1g–j**)[9] and experimental proof of thier fragmentation to 1,4-dienes in a concerted, disrotatory manner are provided. The selective synthesis of 2,4-*exo,exo*- and *exo,endo*-dialkylated 3-thiabicyclo[3.1.0]hexane 3,3-dioxides would be expected to be useful in synthesis of natural product containing 1,4-diene moiety.

We thank the National Science Council of the Republic of China for financial support.

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1 (a) W. L. Mock, *J. Am. Chem. Soc.*, 1966, **88**, 2857. (b) S. D. McGregor and D. M. Lemal, *J. Am. Chem. Soc.*, 1966, **88**, 2858. (c) R. M. Kellogg and W. L. Prins, *J. Org. Chem.*, 1974, **39**, 2366. (d) W. L. Mock, *J. Am. Chem. Soc.*, 1975, **97**, 3666.

2 W. L. Mock, *J. Am. Chem. Soc.*, 1970, **92**, 6918.

3 The same conclusion has been reached in an analogous tetrahydrodiazo bicyclic system. see J. A. Berson and S. S. Olin, *J. Am. Chem. Soc.*, 1969, **91**, 777.

4 Y. Gaoni, *Tetrahedron Lett.*, 1977, 4521.

5 Products (**1b**) and (**1f**) were contaminated by their *endo*- stereoisomer in 9% and 8% respectively, and were unseparable by column chromatography or hplc.

6 For a similar example of desilylation by counterion attack process, see H. H. Tso, T. S. Chou and W. C. Lee, *J. Chem. Soc., Chem. Commun.*, 1987, 934.

7 Fragmentation of compounds (**1g–j**) were also performed by heating the dry benzene solution of the bicyclic sulfones in a sealed tube at 170 °C. The yields are between 85–90%.

8 R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 1969, **8**, 781.

9 All products gave satisfactory spectroscopic (nmr, ir, and mass) and analytical data.

Received, 6th September, 1993