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CONVENIENT SYNTHESIS OF S-CONTAINING HETEROBICYCLES

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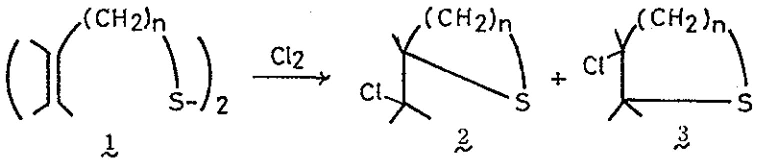
6-*exo*-Chloro-2-thiabicyclo[2.2.1]heptane and its 1-methyl analog, and 4-*exo*-chloro-6-thiabicyclo[3.2.1]octane are synthesized by the intramolecular cyclization of sulfenyl chlorides formed *in situ* from the reaction of the corresponding cycloalkenyl disulfides with chlorine.

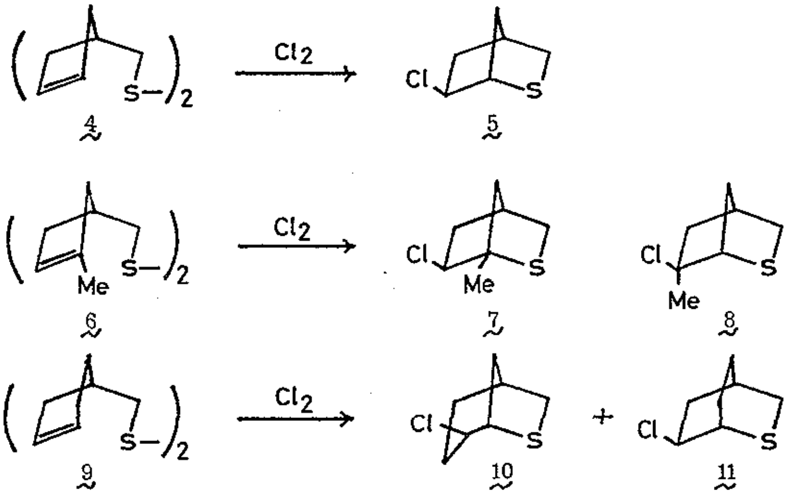
Rapid and stereospecific *trans* addition of sulfenyl halides to olefins[1] provide a powerful utilization to the synthesis of S-containing heterobicycles which usually require a long synthetic pathway. The intramolecular additions of sulfenyl chlorides (**1**) also proceeded smoothly and gave the corresponding cyclic β-chloro sulfides (**2**, **3**) quantitatively (Scheme 1).[2]

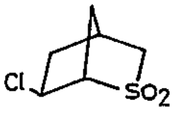
The application of this reaction to the cyclic olefins (**4**, **6**, **9**) resulted in the quantitative formation of the corresponding bicyclic β-chloro derivatives (**5**, **7**, **10**) (Scheme 2). The procedure is very simple; *e.g.* the calculated volume of chlorine gas was introduced to a solution of disulfide in methylene dichloride or chloroform at -30~-50° by the aid of a hypodermic syringe. Careful evaporation of the solvent left the quantitative amount of the corresponding bicyclic chloride which was spectroscopically and gas chromatographically pure.

Scheme 1.



Scheme 2.





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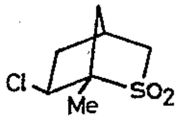

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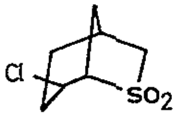

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The disulfide (**4**) yielded a single product, which was identical with a compound prepared by another route.[3] Similarly, **6** gave a single isomer (**7**). No detection of **8** was observed. This result is extremely interesting because one may expect the major formation of **8**. Probably, less stability of **8** than **7** may be due to strong repulsive interaction between 6-*endo*-methyl group and the lone pair electrons of the *endo*-side of the sulfur atom. The reaction of **9** with chlorine gave a mixture of **10** and **11** in a ratio of 69 : 31 as initial products.[4] However, rapid isomerization between both isomers trended toward a single isomer and only **10** was obtained. β-Chloro sulfide is usually so reactive that structural characterization was done as the corresponding β-chloro sulfone after oxidation with *m*-chloroperbenzoic acid: **12**, mp. 99-99.5° ; **13**, mp. 141.5-142.5° ; **14**, mp. 183.5-184.5° ; **14** (Cl = Br), mp. 131.5-132°.[5] Skeletal identification of **10**, moreover, was confirmed by comparison of **14** (Cl = H), mp. 233.5-234.5° with that of reported value.[6]

The β-chloro sulfides (**5**, **7**, **10**) are important as synthetic intermediates because they can be directed to other derivatives easily; for example, hydrolysis (aqueous Na_2CO_3-acetone), methanolysis (MeOH), and acetolysis (AcOH-AcONa) gave the corresponding hydroxy, methoxy, and acetoxy derivatives in quantitative yields.

References and Footnotes

1. As a review: W. H. Mueller, *Angew. Chem. Internat. Edit.*, **8**, 482 (1969).
2. S. Ikegami, J. Ohishi, and Y. Shimizu, *Tetrahedron Letters*, 3923 (1975).
3. 6-*exo*-Chloro-2-thianorbornane (**5**) was also prepared from HCl-addition

to 2-thia-5-norbornene which was synthesized by the cycloaddition of cyclopentadiene with thiophosgene followed by LAH-reduction of the resulting adduct. (S. Ikegami, J. Ohishi, K. Tsuneoka, and S. Akaboshi, Unpublished results).

4. The structure of **11** was determined on the basis of its chemical behavior and its pmr signal; that is, both compounds, **10** and **11**, were mutually interconvertible and the proton of the 6-position of **11** dioxides exhibited a signal at 4.86 ppm, multiplets of doublet, J = 9 Hz.

5. Pmr data (ppm from TMS in $CDCl_3$) and elemental analyses of all β-chloro sulfones are indicated as follows: **12**, pmr; 3.54 (br. s., C_1-H), 4.74 (d. d., $J_{5en,6}$ = 6.5 Hz, $J_{5ex,6}$ = 3 Hz, C_6-H). Anal. Calcd. for $C_6H_9O_2ClS$; C, 39.89; H, 5.02; S, 17.75; Cl, 19.62. Found; C, 39.82; H, 5.11; S, 17.66; Cl, 19.51. **13**, pmr; 4.74 (d. d., $J_{5en,6}$ = 6.5 Hz, $J_{5ex,6}$ = 3 Hz, C_6-H). Anal. Calcd. for $C_7H_{11}O_2ClS$; C, 43.19; H, 5.70; S, 16.47; Cl, 18.21. Found; C, 42.90; H, 5.80; S, 16.28; Cl, 18.22. **14**, pmr; 4.61 (m, C_4-H). Anal. Calcd. for $C_7H_{11}O_2ClS$; C, 43.19; H, 5.70; S, 16.47; Cl, 18.21. Found; C, 42.91; H, 5.80; S, 16.36; Cl, 18.39. **14** (Cl = Br), pmr; 4.74 (m, C_4-H). Anal. Calcd. for $C_7H_{11}O_2BrS$; C, 35.16; H, 4.64; S, 13.41; Br, 33.41. Found; C, 35.16; H, 4.71; S, 13.24; Br, 33.95.

6. S. F. Birch, R. A. Dean, N. J. Hunter, and E. V. Whitehead (*J. Org. Chem.*, **22**, 1590 (1957)) report mp. 236-237° for **14** (Cl = H) and mp. 310° for **11** dioxides (Cl = H).

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