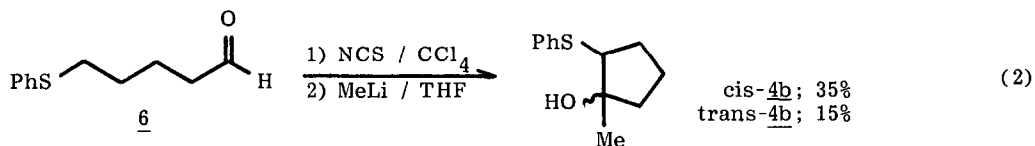


Reactions of (phenylthio)alkyl acetates (1a-h) which have varying lengths of, or substituents on, the alkyl chain were performed under the similar reaction condition. The results are summarized in Table I.

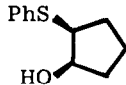
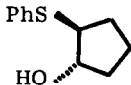
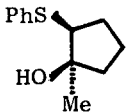
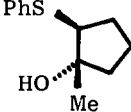
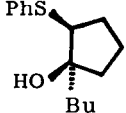
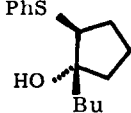
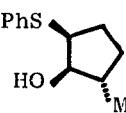
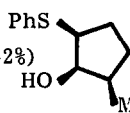
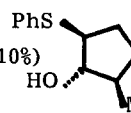
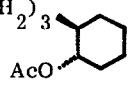
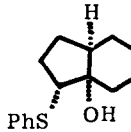
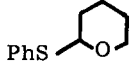
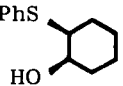
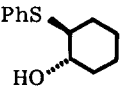
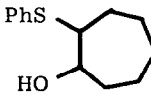
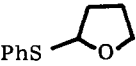
The intramolecular insertion of 4-, 5-, and 6-oxidoalkyl(phenylthio)-carbenes proceeded regioselectively to give the corresponding 2-(phenylthio)-cycloalkanols. Among these, five-membered ring forming reactions proceeded most efficiently, demonstrating a synthetic potential of the present novel cyclization reaction. The directing effect of oxyanionic substitution is manifested not only by the above regioselectivity but also by the completely different course of the reaction for the *tert*-butyldimethylsilyloxy derivative 5 (entry 6) where 2-(phenylthio)tetrahydropyran was obtained but none of 4a. Except the reaction of 3-oxidopropyl(phenylthio)carbene (entry 9), formation of cyclic ethers was not observed.



Alternatively, the oxidoalkyl(phenylthio)carbenes can also be generated by the reaction of chloro(phenylthio)aldehyde with MeLi. 5-(Phenylthio)pentanal (6) was converted first to the chloride and then treated with 2.2 equiv of MeLi in THF to give 1-methyl-2-(phenylthio)cyclopentanol (4b) in 50% yield (eq 2).

There have been a few reports on the stereochemical aspect of the intramolecular C-H insertion of flexible systems.<sup>2,5</sup> In the present study, we determined the stereochemistry of products except entry 8.<sup>6</sup> The intramolecular insertion by 5-oxidoalkyl(phenylthio)carbenes showed a *cis* stereoselectivity with respect to phenylthio and hydroxyl group. On the other hand, the reaction of 5-oxidopentyl(phenylthio)carbene produced the *trans* product selectively. It should be noted that the *cis* selectivity is not based on a simple steric factor because an alkyl substituent at the  $\alpha$  position to the oxido group did not affect the selectivity (see entries 2 and 3). As a possible explanation, we propose that in the transition state as depicted in Figure 1, the oxido group interacts with the carbenic carbon and the insertion proceeds selectively into

Table I Intramolecular Insertion by (Phenylthio)carbenes into  $\alpha$  C-H Bond of Alkoxides<sup>a</sup>

Entry	Starting Material	Products <sup>b</sup> (Isolated Yield) <sup>c</sup>
1	<u>1a</u> ; PhS(CH <sub>2</sub> ) <sub>5</sub> -OAc	<u>4a</u> <sup>d</sup> ;  (45%)  (24%)
2	<u>1b</u> ; PhS(CH <sub>2</sub> ) <sub>4</sub> CH(CH <sub>3</sub> )-OAc	<u>4b</u> ;  (49%)  (26%)
3	<u>1c</u> ; PhS(CH <sub>2</sub> ) <sub>4</sub> CH(CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub> )-OAc	<u>4c</u> ;  (42%)  (21%)
4	<u>1d</u> ; PhS(CH <sub>2</sub> ) <sub>3</sub> CH(CH <sub>3</sub> )CH <sub>2</sub> OAc	<u>4d</u> ;  (42%)  (10%)  (16%) A B C
5 <sup>e</sup>	<u>1e</u> ; PhS(CH <sub>2</sub> ) <sub>3</sub> 	<u>4e</u> ;  (49%)
6 <sup>f</sup>	<u>5</u> ; PhS(CH <sub>2</sub> ) <sub>5</sub> -OSi(Me) <sub>2</sub> <sup>t</sup> Bu	 (30%)
7 <sup>e</sup>	<u>1f</u> ; PhS(CH <sub>2</sub> ) <sub>6</sub> -OAc	<u>4f</u> <sup>g</sup> ;  (7%)  (23%)
8	<u>1g</u> ; PhS(CH <sub>2</sub> ) <sub>7</sub> -OAc	<u>4g</u> <sup>h</sup> ;  (8%)
9	<u>1h</u> ; PhS(CH <sub>2</sub> ) <sub>4</sub> -OAc	 (54%)

a) Unless otherwise noted, reactions were performed by the same procedure described in the text. b) All showed satisfactory spectral (IR, <sup>1</sup>HNMR, and mass) and high resolution mass spectral data. c) Overall yields based on (phenylthio)alkyl acetate 1. d) Reference (4). e) After the addition of MeLi (2 equiv) at -85 °C, n-BuLi (1.1 equiv) was separately added at -85 °C (entry 5) or -40 °C (entry 7). f) 1.3 Equiv of MeLi was used. After the reaction, the crude mixture was treated with n-Bu<sub>4</sub>NF in THF. g) Vebel, J. J.; Miasezewski, R. F.; Arlt, R. E. *J. Org. Chem.* 1977, 42, 585. h) The stereochemistry was not determined.

the proximal pseudo axial  $\alpha$  C-H bond. In entries 2 and 3 where  $R^1$  is an alkyl group, and in entry 4 where  $R^2$  is methyl, the substituent would take the pseudo equatorial position, and hence the major products have the geometry as shown in Table I. The proposed transition state is further supported by the exclusive formation of the *cis* insertion product 4e in entry 5 where  $\alpha$  C-H bond is sterically constrained to take an axial position (see Figure I). The reversal in stereoselectivity in the six-membered ring formation (entry 6) may be explained by a sterically unfavorable interaction between the oxido group and the carbenic carbon.

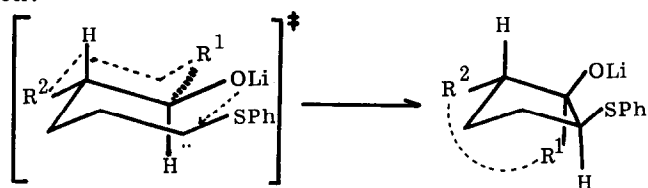


Fig I

## References and Notes

- (1) (a) Kirmse, W. "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971; Chapter 4. (b) Burke, S. D.; Grieco, P. A. *Org. React.* 1971, 26, 361. (c) Taylor, K. G. *Tetrahedron* 1982, 38, 2751.
- (2) A highly selective intramolecular 1,5-insertion by  $\alpha$ -diazo- $\beta$ -ketoesters catalyzed by Rh(II) acetate has been reported recently: (a) Taber, D. F.; Petty, E. H. *J. Org. Chem.* 1982, 47, 4808. (b) Taber, D. F.; Raman, K. *J. Am. Chem. Soc.* 1983, 105, 5935.
- (3) (a) Harada, T.; Oku, A. *J. Am. Chem. Soc.* 1981, 103, 5965. (b) Harada, T.; Akiba, E.; Oku, A. *Ibid.* 1983, 105, 2771. (c) Harada, T.; Nozaki, Y.; Oku, A. *Tetrahedron Lett.* 1983, 24, 5665. (d) Harada, T.; Nozaki, Y.; Yamaura, Y.; Oku, A. *J. Am. Chem. Soc.* 1985, 107, 2189.
- (4) Recently, T. Cohen and his coworkers have reported a formation of 2-(phenylthio)cyclopentanol (36% yield) in the reaction of 4-oxidobutyl (phenylthio)carbene generated from 5,5-diphenylthiopentanol by the action of *sec*-BuLi; Cohen, T.; Ritter, R. H.; Ouellette, D. *J. Am. Chem. Soc.* 1982, 104, 7142.
- (5) Regitz, M.; Ruter, J. *Chem. Ber.* 1969, 102, 3877.
- (6) The *trans* isomer of 4b and 4e were prepared by the reaction of 1,2-epoxy-1-methylcyclopentane and *cis*-6,7-epoxybicyclo[4,3,0]nonane<sup>7</sup> with sodium phenyl thiolate, respectively. The stereochemistry of *cis*- and *trans*-4c was determined by the comparison of their <sup>1</sup>H NMR (200 MHz) spectra with those of *cis*- and *trans*-4b. Protons attached to C-2 are appearing at; *cis*-4b; 3.30 (d,d,  $J = 8.5$  and  $9.8$  Hz), *trans*-4b; 3.48 (m), *cis*-4c; 3.30 (d,d,  $J = 8.0$  and  $9.8$  Hz), and *trans*-4c; 3.50 (m). The relative configuration in the three isomers of 4d with respect to methyl and hydroxyl group was determined after the desulfurization by Raney Ni (W-4). In an epimeric pair of 4d-A and 4d-C, 1-H of 4d-C resonates at an upper field ( $\delta$  3.48) by 0.2 ppm than that of 4d-A does because of the shielding effect of C-1 and C-3 substituents both *cis* to this proton.<sup>8</sup> Moreover, the larger values of  $J_{12}$  (8.0 Hz) and  $J_{15}$  ( $\sim 8$  Hz) in 4d-C than those of 4d-A ( $J_{12} = 5.2$  Hz,  $J_{15} = \sim 5$  Hz) verifies the above assignment. The downfield shift of the resonance of 1-H in 4d-B ( $\delta$  3.77) in comparison with that of 4d-A and 4d-C together with the relatively small values of coupling constants ( $J_{12} = 3.4$  and  $J_{15} = \sim 3$  Hz) supports its *cis*, *cis* configuration.<sup>8</sup>
- (7) Crandall, J. K.; Magaha, H. S.; Henderson, M. A.; Widener, R. K.; Tharp, G. A. *J. Org. Chem.* 1982, 47, 5372.
- (8) (a) Gaudemer, A. In "Stereochemistry"; Kagan, H. B., Ed.; Georg Thieme Publishers: Stuttgart 1977; Vol. I, p 92. (b) Rei, M-H. *J. Org. Chem.* 1978, 43, 2173.

(Received in Japan 16 May 1985)