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STEREOSPECIFIC ALKYLATION OF SULFUR-STABILIZED CARBANION IN DITHIABICYCLO[3.1.0]HEXANE SYSTEMS

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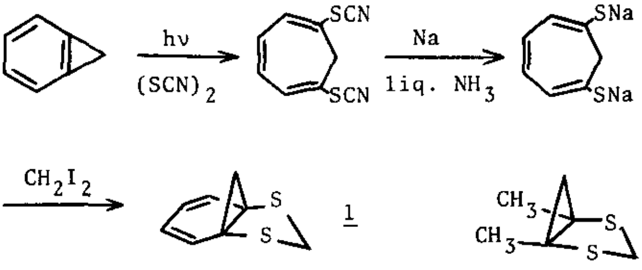
Abstract — The sulfur-stabilized carbanion formed from dithiabicyclo[3.1.0]hexane systems (1) and (2) reacted with various electrophiles to give endo products highly stereospecifically.

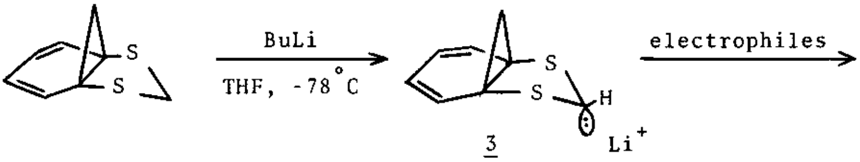
In recent years, sulfur-stabilized carbanions have been attracting attention of synthetic chemists.[1] Dithiane and dithiolane derivatives are especially useful synthetic reagents as a carbonyl synthon.[2] We recently described the synthesis of a dithiolane derivative (1) from benzocylopropene,[3] and became interested in the reactivity of a carbanion derived from 1, since the rigid structure of 1 is useful for the study of stereochemical behavior of dithiolane carbanion.
We now report the high stereospecificity observed for the reactions of carbanion of 1 and closely related compound (2).

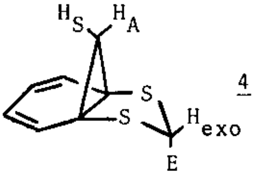


1

2

The reaction of 1 with butyllithium in THF at -78 °C, followed by addition of methyl iodide, resulted in the formation of methylated product (4a). Similarly, the quenching with allyl chloride, trimethylsilyl chloride, benzaldehyde, or deuterium oxide gave 4b, 4c, 4d or 4e, respectively. In each case, the formation of a single product was confirmed by TLC and NMR.

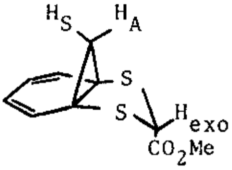




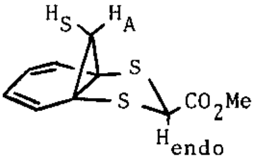
4

a:	E= CH_3	53%
b:	E= $CH_2CH{=}CH_2$	64%
c:	E= Me_3Si	57%
d:	E= PhCH(OH)	53%
e:	E= D	50%

On the contrary, the quenching of 3 with carbon dioxide, followed by acidic work up and methylation with diazomethane, afforded two products 5a (26%) and 5b (14%).

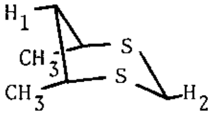


5a



5b

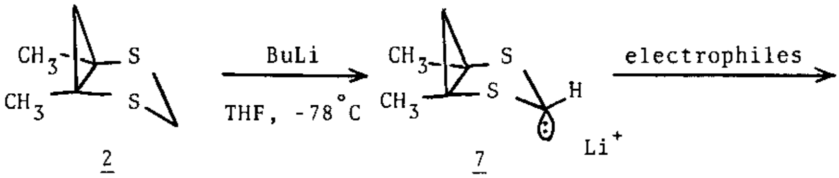
Unequvocal assignment of 5a and 5b was made by the NMR spectra using shift reagent Eu(fod)$_3$. A long range coupling of zig-zag type between H_S and H_{exo} was observed in the spectrum of 5a, as reported also for dithiane (6)[6] (between $H^1$and H^2), while not between H_S and H_{endo} in that of 5b.[8]

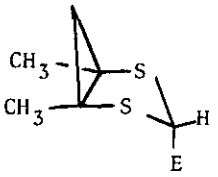


6

The fact that a similar long range coupling is observed for H_{exo} in all of 4 (4a-4e) clearly suggests that the electrophiles entered from the endo side to give the endo product (4).

The endo specificity in quenching of sulfur-stabilized carbanion was also observed for a similar system (2).[4]

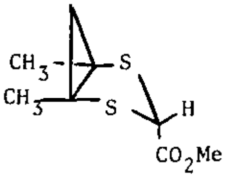




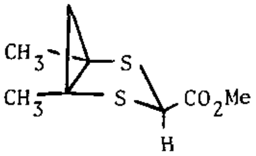
8

a: E= CH_3	97%
b: E= $PhCH_2$	43%
c: E= Me_3Si	39%
d: E= PhCH(OH)	54%
e: E= D	93%

Here again, the reaction of 7 with carbon dioxide (after methylation by diazomethane) gave a mixture of endo (9a) and exo products (9b).[7]



9a



9b

The stereospecificity observed in the reactions of electrophiles with the carbanion derived from 1 and 2 exhibits a sharp contrast with that observed for the carbanion of the dithiane (6) whose structure is very similar to those of 1 and 2; the reaction of 6 with butyllithium, followed by addition of electrophiles, is reported to proceed in a highly stereospecific way giving equatorial products.[5,6] In this case, the preferential equatorial attack is explained in terms of higher thermodynamic stability of the equatorial anion compared with the axial anion.[6] We consider that the specificity found for 1 and 2 is most probably explicable also in terms of higher stability of the endo anion. Detailed analysis of the endo stability must await further study, which is now in progress.

References and Notes

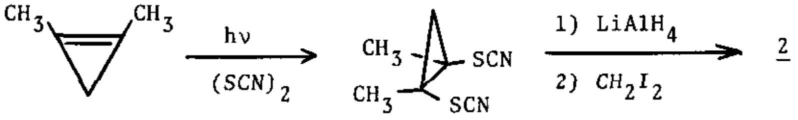
1. E. Block, 'Reactions of Organosulfur Compounds', Academic Press, New York, 1978, Chapter 2.

2. a) D. Seebach and E. J. Corey, J. Org. Chem., 1975, **40**, 231; B.-Th. Gröbel, and D. Seebach, Synthesis, 1977, 357.

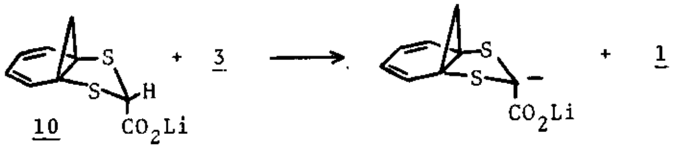
   b) J. Nakayama and M. Hoshino, Yuki Gosei Kagaku Kyokai Shi, 1979, **37**, 655;

S.Ncube, A. Pelter, and K. Smith, Tetrahedron Lett., 1979, 1893; I. Degani, R. Fochi, and V. Regondi, Tetrahedron Lett., 1981, 1821 and references cited therein.

3. R. Okazaki, M. O-oka, N. Tokitoh, Y. Shishido, and N. Inamoto, Angew. Chem. Int. Ed. Engl., **20**, 799 (1981).
4. The dithiabicyclohexane (2) was synthesized in the following way. The details will be described in a full paper.



5. The endo and exo positions of 1 and 2 correspond to axial and equatorial positions of 6, respectively.
6. E. L. Eliel, A. A. Hartman, and A. G. Abatjoglou, J. Am. Chem. Soc., 1974, **96**, 1807.
7. The formation of a mixture of endo and exo products in carbon dioxide *quenching (i.e.* 5a,b *and* 9a,b*) is most probably due to formation of* exo anions (by abstraction of acidic H_{exo} in initailly formed carboxylate ions 10 corresponding to 5a and 9a), followed by partial conversion into more stable endo anions. This is supported by the following facts: 1) some starting



material was recovered even when excess BuLi was used; 2) 5a was converted into 5b with BuLi at -78 °C; 3) in a dilute solution the carboxylation (followed by methylation) of 1 gave mostly 5a at the expense of 5b.

8. The NMR spectra of 5a and 5b are as follows: 5a ($CDCl_3$, δ), 0.85 (d, J=4.5 Hz, 1H, H_S), 2.66 (d, J=4.5 Hz, 1H, H_A), 3.65 (s, 3H, CO_2CH_3), 4.74 (s, 1H, H_{exo}), 5.80-6.60 (m, 4H, olefinic); 5b ($CDCl_3$, δ), 0.62 (d, J=5.5 Hz, 1H, H_S), 2.56 (d, J=5.5 Hz, 1H, H_A), 3.77 (s, 3H, CO_2CH_3), 5.33 (s, 1H, H_{endo}), 5.85-6.50 (m, 4H, olefinic). For 1, see ref. 3. In the spectra of 1 and 5a, the doublets of H_S and H_{exo} are broad, suggesting a long-range coupling with each other.

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