

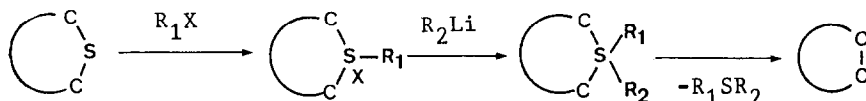
SULFIDE EXTRUSION FROM THE METHYLSULFONIUM SALTS OF 8-THIABICYCLO-
 [3.2.1]OCT-2-ENES AND THE RELATED SULFONIUM SALTS BY METHYLLITHIUM

Tadao UYEHARA,* Masayuki TAKAHASHI, and Tadahiro KATO
 Department of Chemistry, Faculty of Science,
 Tohoku University, Aramaki-Aoba, Sendai 980, Japan

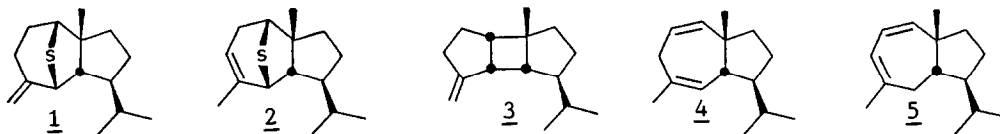
Summary: The methylsulfonium salts of 2-methylene-8-thiabicyclo[3.2.1]octane and 8-thiabicyclo[3.2.1]oct-2-enes underwent sulfide extrusion by methyllithium to give dimethyl sulfide and the hydrogen shift products (cycloheptadienes) and/or the closure products (bicycloheptenes).

Desulfurization from a cyclic sulfur compound with concomitant carbon-carbon bond formation is one of the methods which have been successfully adopted in many instances. Generally such desulfurization has been accomplished by converting a sulfide into the sulfone followed by either (i) thermolytic or photolytic extrusion of sulfur dioxide or (ii) a Ramberg-Backlund reaction.¹⁾ Among other techniques for the desulfurization, a novel one is the sulfide extrusion, organolithium-induced decomposition of a sulfonium salt into the sulfide and the desulfurized compound, as shown in Scheme 1.

Scheme 1.



For example, the reaction of thietanium salts with butyllithium gave cyclopropanes with a high degree of stereospecificity.²⁾ On the other hand, the reaction of the methylsulfonium salt of (-)-mintsulfide (1), which has the 2-methylene-8-thiabicyclo[3.2.1]octane moiety, with methyllithium afforded the closure product (3, 29%) along with the hydrogen shift product (4, 43%).³⁾ The hydrogen shift product (5) was obtained mainly (79%) from the methylsulfonium salt of (-)-isomintsulfide (2) which possesses the 8-thiabicyclo[3.2.1]oct-2-ene part.³⁾ Elucidation of chemo- and stereoselective feature of the overall process of such sulfide extrusion is interesting from synthetic

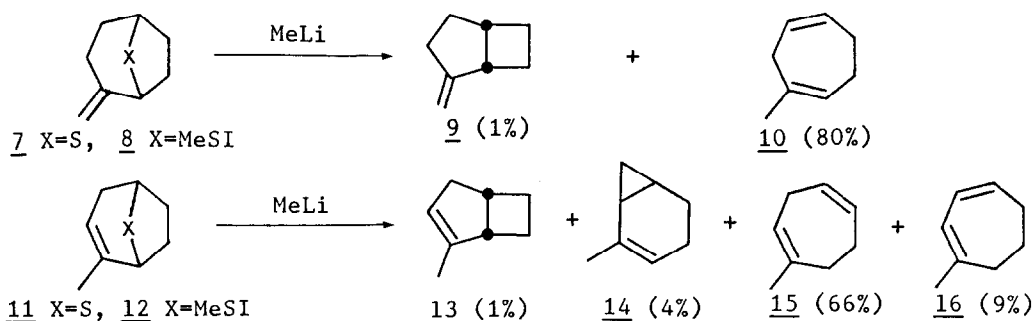


and mechanistic viewpoints. Herein we report sulfide extrusion from the methylsulfonium salts of 2-methylene-8-thiabicyclo[3.2.1]octane (7) and simple 8-thiabicyclo[3.2.1]oct-2-enes (11, 17a, b, c, and d) by methyllithium.

8-Thiabicyclo[3.2.1]octan-3-one (6)⁴⁾ was converted into 8-thiabicyclo[3.2.1]oct-2-en-2-carbaldehyde,^{5,6)} in 70% yield. From the aldehyde, 7⁷⁾ and 2-methyl-7-thiabicyclo[3.2.1]oct-2-ene (11)⁸⁾ were derived in 45% and 67% overall yields, respectively. Treatment of the sulfides with methyl iodide gave the respective sulfonium salts (8) and (12)⁹⁾ in excellent yields. Sulfide extrusion was carried out by treating a suspension of the sulfonium salt in dry THF with 1.5-2.0 eq of methyllithium in ether at -10°C for 10 min. After usual aqueous work-up, an analysis and separation of the products were performed by gas-liquid chromatography.

As shown in Scheme 2, the major course of the sulfide extrusion is hydrogen shift to give the dienes.¹⁰⁾ The reaction of 12 gave the (1,4)- and (1,3)-closure products (13 and 14, respectively) and the (1,3)- and (1,5)-hydrogen shift products (15 and 16, respectively). The conjugated diene (16), due to the second major course, corresponds to the major product obtained from the sulfonium salt of 2. This is reasonable, because 2 has no hydrogen which shifts to form the 1,4-diene similar to 15. In the case of 8, the ratio of the hydrogen shift product (10) to the closure product (9) increases in comparison with that of the sulfonium salt of 1. Thus, *cis*-fused five membered rings in 1 and 2 proved to have a little effect on the mode of the sulfide extrusion.

Scheme 2. The results of sulfide extrusion of 8 and 12 (yield).



One of the reactive intermediates of the sulfide extrusion of 12 might be 4-methyl-4-cycloheptene-1,3-diyl, a cyclic allyldiradical. The reaction mode of the cyclic diradical should be influenced considerably by a substituent at the C₃ or the C₅. Thus we prepared 8-thiabicyclo[3.2.1]oct-2-ene (17a),¹¹⁾ and its 3-methyl-, 3-phenyl-, and 3-cyano derivatives (17b, 17c, and 17d, respectively)¹²⁾ and examined sulfide extrusion of each sulfonium salt of the sulfides. The results are summarized in Table 1 and Scheme 3.¹³⁾

The ratios of the closure products (23 + 24) to the hydrogen shift products (21 + 22) follow the order: $\underline{12} < \underline{18a} < \underline{18b} < \underline{18c}$ and 18d. The outcome could not be explained only by the substituent effects on the reaction mode of the hypothetical diradical intermediate (20).¹⁴⁾ If the sulfide extrusion is a stepwise reaction, the diradical (19) would be a precursor of 20 and an intermediate to give the hydrogen shift products.¹⁵⁾ When R of 19 is a radical stabilizing substituent, it would lower the potential energies of 19, 20, and the transition state between 19 and 20. However, it would be less effective to the hydrogen shift transition state in which electronic localization is required at the allylradical part.

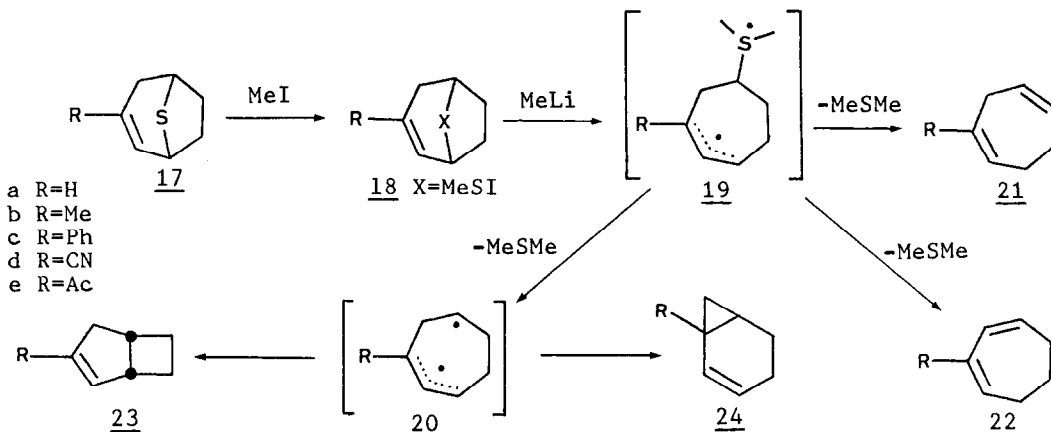
The following experimental results are in agreement with the stepwise mechanism described above. When the methylsulfonium salt of the ethylene acetal of 1-phenyl-8-thiabicyclo[3.2.1]octan-3-one¹⁶⁾ was treated with methyl-lithium, obtained were the ethylene acetals of 1-phenylbicyclo[3.2.0]heptan-2-one, 6-phenyl-2-cycloheptenone, and 6-phenyl-3-cycloheptenone in 10%, 37%, and 14% yields, respectively. However, the methylsulfonium salts of 8-thiabicyclo[3.2.1]octane¹⁷⁾ and the ethylene acetal of 8-thiabicyclo[3.2.1]octan-3-one did not undergo sulfide extrusion and gave the respective sulfides as the only isolable products.

Table 1. Sulfide extrusion from the methylsulfonium salts of 8-thiabicyclo[3.2.1]oct-2-enes by methyl lithium.

Sulfonium salt	Type of the products, Yield (%) ^{a)}			
	<u>21</u>	<u>22</u>	<u>23</u>	<u>24</u>
<u>18a</u>	45	4	2	20
<u>18b</u>	16	7	27	40
<u>18c</u>	--b)	--b)	--b)	64 ^{c)}
<u>18d</u>	--b)	--b)	--b)	70 ^{c,d)}

a) Determined by GLC unless otherwise noted. b) Determined by ¹H-NMR.
c) Isolated yield of pure product. d) Obtained as 24e.

Scheme 3. Process of the sulfide extrusion from the methylsulfonium salts of 8-thiabicyclo[3.2.1]oct-2-enes.



In conclusion, the results presented in this report are; i) at least one of the bridgehead carbons of the sulfonium salt of a 8-thiabicyclo[3.2.1]octane derivative must be allylic or benzylic for sulfide extrusion to occur; ii) thus obtained are the hydrogen shift products (cycloheptadienes) and/or the closure products (a bicyclo[3.2.0]heptane, bicyclo[3.2.0]heptenes, and/or bicyclo[4.1.0]heptenes); iii) product composition is influenced by the C₂ or C₃ substituent of a 8-thiabicyclo[3.2.1]oct-2-ene and the ratio of the closure products to the others is increased by a radical stabilizing substituent.

References and notes

- 1) a) P.D.Magnus, *Tetrahedron*, **33**, 2019 (1977); b) L.Field, *Synthesis*, **1978**, 713.
- 2) a) B.M.Trost, W.L.Schinski, F.Chen and I.B.Mantz, *J.Am.Chem.Soc.*, **93**, 676 (1971); b) B.M.Trost and R.F.Hammen, *J.Am.Chem.Soc.*, **95**, 962 (1973).
- 3) T.Uyehara, T.Ohnuma, T.Saito, T.Kato, T.Yoshida and K.Takahashi, *J.Chem.Soc., Chem.Comm.*, **1981**, 127.
- 4) a) V.Horak, J.Zavada, and A.Piskala, *Chem.Ind. (London)*, **1958**, 1113; b) V.Horak, *Collect.Czech.Chem.Comm.*, **28**, 1614 (1963); c) we prepared it by treatment of cyclohepta-2,6-dien-1-one with sodium sulfide in benzene-water two phase system, in 83% yield.
- 5) Satisfactory spectral data and elemental analyses have been obtained for all the new compounds described.
- 6) Transformation of 6 to the aldehyde: (1) HCOOEt, NaOEt; (2) *i*-PrOH, TsOH, PhH; (3) NaBH₄-CeCl₃, then dil H₂SO₄.
- 7) Preparation of 7 from the aldehyde: (1) H₂, Pd-C; (2) NaBH₄; (3) Ph₃P-CCl₄; (4) *t*-BuOK, DMSO.
- 8) Preparation of 11 from the aldehyde: (1) NaBH₄; (2) Ph₃P-CCl₄; (3) LiAlH₄.
- 9) ¹H-NMR of all the methylsulfonium salts show two S-methyl signals.
- 10) Even in low yields, we obtained the respective homologous bicyclic sulfides, formed via the [2,3]-sigmatropic rearrangement of the corresponding sulfur ylides, from the derivatives of 18a.
- 11) a) P.Y.Johnson, E.Koza, and R.E.Kohrman, *J.Org.Chem.*, **38**, 2967 (1973); b) preparation from 6: (1) LiAlH₄; (2) separation; (3) for the *exo*-alcohol: TsCl-Py, and for the *endo*-alcohol: Ph₃P-CCl₄; (4) *t*-BuOK, DMSO, in 50% overall yield.
- 12) Compounds (17b-17d) were prepared as follows; 17b: (1) PhMgBr; (2) TsOH, PhH, in 73% overall yield. 18c: (1) MeMgI; (2) TsOH, PhH, in 62% overall yield. 17d: TMSCN, ZnI₂; (2) POCl₃, Py, in 84% overall yield.
- 13) The authentic samples of following compounds, shown with the CAS registry number, were prepared: 9 [28436-00-2], 15 [34919-41-0], 16 [14947-22-9], 21a [7161-35-5], 22a [4054-38-0], 22b [14947-21-8], 23a [7095-65-0], and 24a [2566-57-6].
- 14) Thermolytic and photolytic nitrogen extrusion from 6,7-diazabicyclo[3.2.2]nona-2,6-dienes gave exclusively the closure products which would be formed, however, via the intermediate like 20; Unpublished results from this laboratory.
- 15) We can not deny strongly that 19 and 20 might be replaced by zwitterionic intermediates. However, the fact that stereochemical correlation between 1 and 3 is retention supports the diradical postulate.
- 16) The acetal was prepared from 2-cyclohepten-1-one; (1) PhLi; (2) PCC; (3) LDA, then PhSSO₂Ph; (4) MCPBA; (5) PhMe, CaCO₃; (6) Na₂S, PhH-H₂O; (7) HOCH₂CH₂OH, TsOH, PhH, in 12% overall yield.
- 17) a) S.F.Birch, R.A.Dean, N.J.Hunter, and E.V.Whitehead, *J.Org.Chem.*, **22**, 1590 (1957); b) L.A.Paquette and R.W.Houser, *J.Am.Chem.Soc.*, **91**, 3870 (1969); c) obtained from 6 by Wolff-Kishner reduction in 57% yield.
- 18) M.Oda, A.Yamamuro, and T.Watabe, *Chem.Lett.*, **1979**, 1427.

(Received in Japan 19 May 1984)