STUDIES ON HETERO-CAGE COMPOUNDS. 9.[1] SYNTHESIS AND CHEMICAL REACTIVITY OF 8-THIABICYCLO[3.2.1]OCTAN-3-ONE SYSTEM IN COMPARISON WITH 9-THIABICYCLO[3.3.1]NONAN-3-ONE SYSTEM

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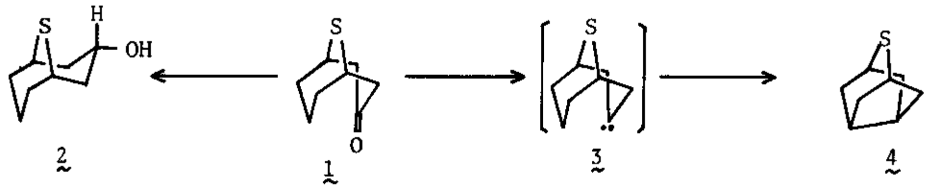
Abstract——Treatment of cyclohepta-2,6-dienone (5) with Na_2S in H_2O-MeOH afforded 8-thiabicyclo[3.2.1]octan-3-one (6) in 38% yield. Oxidation of 6 with m-CPBA gave sulfone 8 and reduction of 6 with $NaBH_4$ gave endo- (9) and exo-alcohols (10) in 33:67 ratio. The carbene 12 generated via Na salt of tosylhydrazone 11a yielded only 8-thiabicyclo[3.2.1]oct-2-ene (13), a H migration product.

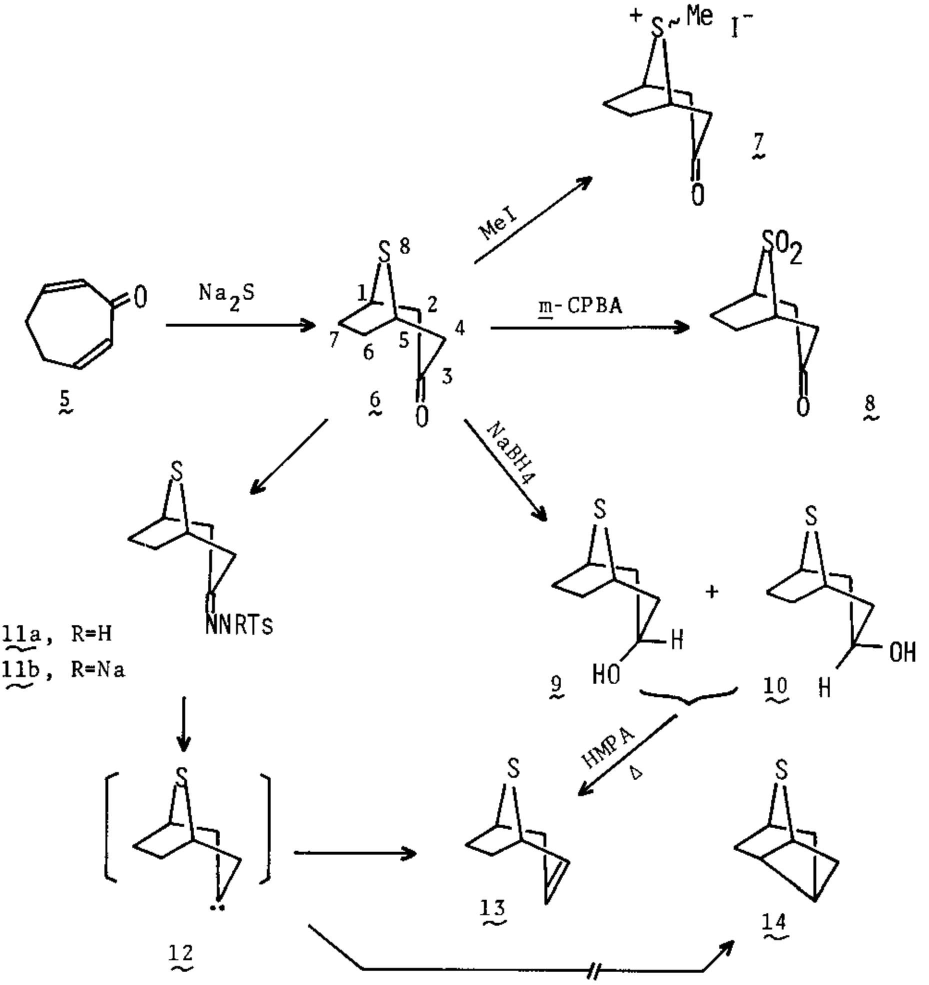
We have recently reported synthesis of 9-thiabicyclo[3.3.1]nonan-3-one (1) and some related derivatives as well as 9-thianoradamantane (4) by the transannular C-H carbene insertion reaction.[2] We report in this paper the synthesis of 8-thiabicyclo[3.2.1]octan-3-one (6) and the chemical behavior in comparison with 9-thiabicyclo[3.3.1]nonan-3-one (1) system (Scheme I and II).

Treatment of cyclohepta-2,6-dienone (5) generated from the corresponding ethyleneketal and 3% H_2SO_4[3] with a 1.44-fold excess amount of sodium sulfide in 80% aqueous methanol for 2 days at room temperature (ca. 20°C) afforded an adduct 6 as a sublimable solid, mp 150-153°C,[4] in 38% yield. The structure of 6 was determined as 8-thiabicyclo[3.2.1]octan-3-one based on analysis[5] and spectral data: IR(KBr) 2950, 1700, 1405, 1350 and 1210 cm^{-1}; ^1H NMR($CDCl_3$) δ 3.78 (broad s, 2H), 3.0-2.2 (m, 4H) and 2.3-1.8 (m, 4H); ^{13}C NMR($CDCl_3$) δ 209.0 (s, C_3), 52.9 (t, $C_{2,4}$), 45.5 (d, $C_{1,5}$) and 34.3 (t, $C_{6,7}$) (Scheme II). Heating 6 with methyl iodide (10-fold excess) in chloroform under reflux for 3 days gave the corresponding sulfonium methiodide 7, mp 170-171°C(dec), in 5.7% yield. Oxidation of 6 with m-chloroperbenzoic acid (m-CPBA) (2.5-fold excess) in

CH_2Cl_2 at room temperature for 12 hr gave the corresponding sulfone 8 in 96% yield: mp 251-254°C(dec); IR(KBr) 2980, 1710, 1405, 1290 and 1110 cm^{-1}; ^1H NMR($CDCl_3$) δ 3.7-3.1 (m, 2H), 3.28 (broad s, 2H) and 3.0-1.7 (m, 6H). These reactivities of 6 were very similar to those of 9-thiabicyclo[3.3.1]nonan-3-one (1).[2] On the other hand, $NaBH_4$ reduction of 1 gave exclusively *endo*-3-alcohol



Scheme I

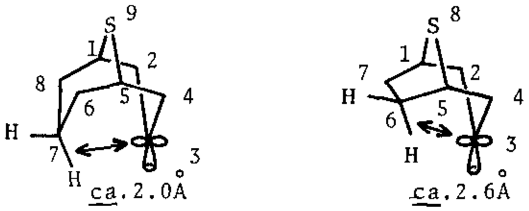


Scheme II

2 (Scheme I),[2] while the reduction of 6 under the same conditions gave a mixture of endo- (9) and exo-3-alcohols (10) in 33:67 ratio (glc analysis) (Scheme II). These isomers could be separated by chromatography on a silica gel column (Mallinckrodt, 100 mesh, CHCl$_3$). 9 (27.7% yield): mp 240-241°C; IR(KBr) 3300, 2920, 1420, 1305, 1250 and 1035 cm^{-1}; ^{1}H NMR(CDCl$_3$) δ 4.50 (A$_2$B$_2$X type h, J=4.5 and 2.5Hz, 1H), 3.8-3.4 (m, 2H), 2.71-1.78 (m, 8H) and 1.55 (broad s, 1H, disappeared on shaking with D$_2$O). 10 (54.3% yield): mp 140-141°C; IR(KBr) 3200, 1450, 1250 and 1050 cm^{-1}; ^{1}H NMR(CDCl$_3$) δ 3.93 (A$_2$B$_2$X type h, J=10.5 and 4.5Hz, 1H), 3.63 (broad s, 2H), 2.51-1.46 (m, 8H) and 1.80 (s, 1H, disappeared on shaking with D$_2$O). The stereochemical assignments of 9 and 10 were based on the characteristic ^{1}H NMR coupling pattern of C$_3$-equatorial and -axial proton, respectively.[6]

Tosylhydrazone 11a was obtained in 71% yield on treatment of 6 with p-toluenesulfonylhydrazine in refluxing ethanol for 15 hr: mp 193-195°C; IR(KBr) 3220, 2940, 1595, 1440, 1330, 1170, 735 and 650 cm^{-1}; ^{1}H NMR(CDCl$_3$) δ 7.56 (AB-q, J=8.3Hz, J/Δδ=0.265, 4H), 4.72 (broad s, 1H, disappeared on shaking with D$_2$O), 3.64 (broad s, 2H), 3.1-2.4 (m, 4H), 2.42 (s, 3H) and 2.2-1.6 (m, 4H). The sodium salt 11b was prepared by treatment of 11a with sodium methoxide in methanol, which was dried under reduced pressure (0.15 mmHg) at 50° and decomposed in refluxing diglyme for 2 hr. The usual work-up and purification on a silica gel column eluting with CH$_2$Cl$_2$ afforded ketone 6 (14%) and olefin 13, a H migration product, as a semisolid (36%): IR(KBr) 3040, 2960, 1630, 1450, 1185 and 805 cm^{-1}; ^{1}H NMR(CDCl$_3$) δ 6.5-6.0 (m, 1H), 5.7-5.1 (m, 1H), 3.71-3.37 (m, 2H) and 2.7-1.4 (m, 6H). The structure of olefin 13 was confirmed also by an alternative synthesis from alcohols 9 and 10. Th olefin 13 was obtained in 57% yield on heating of a mixture of 9 and 10 in hexamethylphosphoric triamide (HMPA) under reflux for 1 hr (Scheme II).

The absence of the C$_6$-H carbene insertion product 14 may be due to the somewhat longer distance between the C$_6$-H bond and the C$_3$ carbenic center and also to the unfavorable C-H bond alignment for the insertion reaction as depicted in Figure I.[7] The distance measured on a Dreiding stereomodel, ca. 2.6Å is obviously longer than C$_7$-H—C$_3$: in the 9-thiabicyclo[3.3.1]nonane ring system.[8]



3 **12**

Figure I. Interdistances between C-H bond and C_3 carbene center in **3** and **12** on the Dreiding stereomodel

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4. All melting points were measured in a sealed tube and are uncorrected.
5. All new compounds described here had CHN microanalytical properties in agreement with the assigned structures.
6. For conformational and NMR studies on endo- and exo-bicyclo[3.3.1]nonan-3-ols, see (a) J. P. Schaefer, J. C. Lark, C. A. Flegal and L. M. Honig, J. Org. Chem., 1967, **32**, 1372; (b) M. Fisch, S. Smallcombe, J. C. Gramain, M. A. McKervey and J. E. Anderson, J. Org. Chem., 1970, **35**, 1886; (c) Ref 2.
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