

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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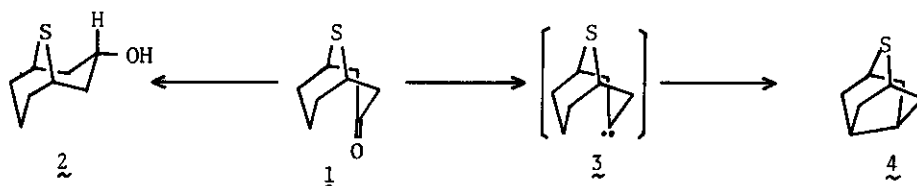
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Abstract—Treatment of cyclohepta-2,6-dienone (5) with Na₂S in H₂O-MeOH afforded 8-thiabicyclo[3.2.1]octan-3-one (6) in 38% yield. Oxidation of 6 with *m*-CPBA gave sulfone 8 and reduction of 6 with NaBH₄ gave *endo*- (9) and *exo*-alcohols (10) in 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.

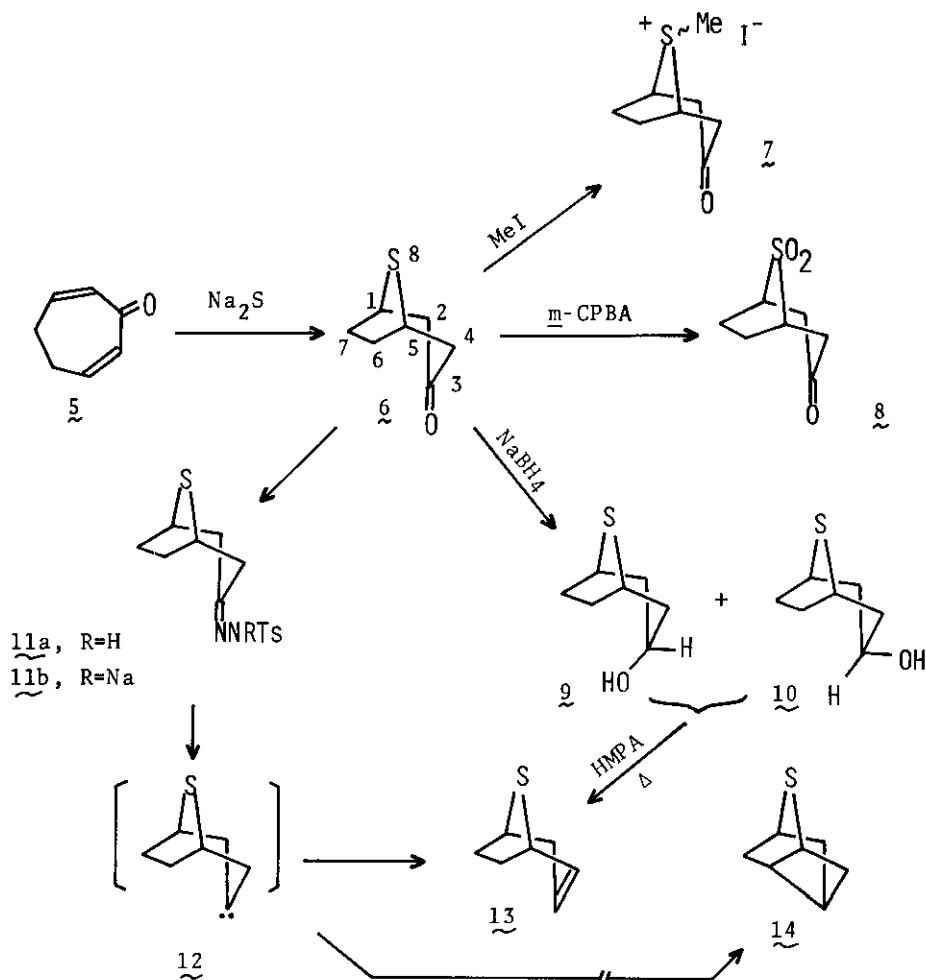
We have recently reported synthesis of 9-thiabicyclo[3.3.1]nonan-3-one (1) and some related derivatives as well as 9-thianoradamantane (4) by the transannular C-H carbene insertion reaction.² We report in this paper the synthesis of 8-thiabicyclo[3.2.1]octan-3-one (6) and the chemical behavior in comparison 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% H₂SO₄³ 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 analysis⁵ and spectral data: IR(KBr) 2950, 1700, 1405, 1350 and 1210 cm⁻¹; ¹H NMR(CDCl₃) δ 3.78 (broad s, 2H), 3.0-2.2 (m, 4H) and 2.3-1.8 (m, 4H); ¹³C NMR(CDCl₃) δ 209.0 (s, C₃), 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} ; $^1\text{H NMR}(\text{CDCl}_3)$ δ 4.50 ($\text{A}_2\text{B}_2\text{X}$ type h, $J=4.5$ and 2.5 Hz, 1H), 3.8-3.4 (m, 2H), 2.71-1.78 (m, 8H) and 1.55 (broad s, 1H, disappeared on shaking with D_2O). 10 (54.3% yield): mp 140-141°C; IR(KBr) 3200, 1450, 1250 and 1050 cm^{-1} ; $^1\text{H NMR}(\text{CDCl}_3)$ δ 3.93 ($\text{A}_2\text{B}_2\text{X}$ type h, $J=10.5$ and 4.5 Hz, 1H), 3.63 (broad s, 2H), 2.51-1.46 (m, 8H) and 1.80 (s, 1H, disappeared on shaking with D_2O). The stereochemical assignments of 9 and 10 were based on the characteristic $^1\text{H NMR}$ coupling pattern of C_3 -equatorial and -axial proton, respectively.⁶

Tosylhydrazone 11a was obtained in 71% yield on treatment of 6 with p-toluene-sulfonylhydrazine in refluxing ethanol for 15 hr: mp 193-195°C; IR(KBr) 3220, 2940, 1595, 1440, 1330, 1170, 735 and 650 cm^{-1} ; $^1\text{H NMR}(\text{CDCl}_3)$ δ 7.56 (AB-q, $J=8.3$ Hz, $J/\Delta\delta=0.265$, 4H), 4.72 (broad s, 1H, disappeared on shaking with D_2O), 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_2Cl_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} ; $^1\text{H NMR}(\text{CDCl}_3)$ 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. The 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. 2.6 Å is obviously longer than $\text{C}_7\text{-H}-\text{C}_3$ in the 9-thiabicyclo[3.3.1]nonane ring system.⁸

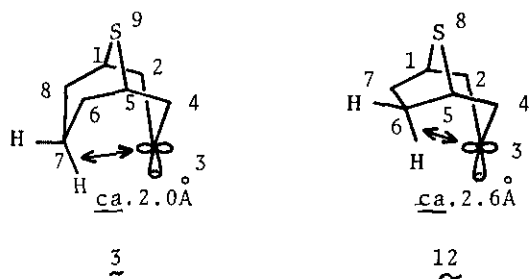


Figure 1. Interdistances between C-H bond and C_3 carbene center in 3 and 12 on the Dreiding stereomodel

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3. E. W. Garbisch, Jr., J. Org. Chem., 1965, 30, 2109.
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.
7. For a recent review, see W. J. Baron, M. R. DeCamp, M. E. Hendrick, M. Jones, Jr., R. H. Levin and M. B. Sohn, 'Carbenes', Vol. 1, eds. by M. Jones, Jr., and R. A. Moss, Wiley, New York, N. Y., 1975, pp 40-51.
8. For examples of the ring systems where the transannular C-H carbene insertion reactions are observed, see (a) A. C. Udding, J. Strating, H. Wynberg and J. L. M. A. Schlattmann, Chem. Commun., 1966, 657; (b) H. W. Geluk and Th. J. de Boër, Tetrahedron, 1972, 28, 3351; (c) T. Sasaki, S. Eguchi and T. Kiriyaama, Tetrahedron, 1971, 27, 893.

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