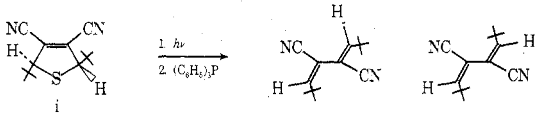
(19) (a) For a review of thiyl radicals, see R. M. Kellogg, "Methods in Free Radical Chemistry," Marcel Dekker, New York, N. Y., 1969, pp 1-120. (b) W. C. Lumma, Jr., and G. A. Berchtold, *J. Amer. Chem. Soc.*, **89**, 2761 (1967); *J. Org. Chem.*, **34**, 1566 (1969); P. Y. Johnson and G. A. Berchtold, *ibid.*, **35**, 584 (1970); K. K. Maheshwari and G. A. Berchtold, *Chem. Commun.*, 13 (1969); A. Padwa and A. Battisti, *J. Amer. Chem. Soc.*, **93**, 1304 (1971); P. Y. Johnson, *Tetrahedron Lett.*, 1991 (1972); J. Kooi, H. Wynberg, and R. M. Kellogg, *Tetrahedron*, **29**, 2135 (1973).

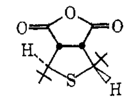
(20) See, for example, P. J. Kropp, E. J. Reardon, Jr., Z. L. F. Gaibel, K. F. Williard, and H. H. Hattaway, Jr., *J. Amer. Chem. Soc.*, **95**, 7058 (1973), and references cited therein. This applies to π-π^* excited states of olefins; in **4** we do not know if the lowest excited state (presumably a triplet) is n-π^* or π-π^*. The ready cis-trans isomerization of virtually all olefinic systems on excitation certainly suggests that twisting about the double bond is a very important process.

(21) An alternative is that the barriers to isomerization in the allylic portions of the biradical are low. The barrier in the allyl radical itself is calculated to be 12 kcal/mol: S. W. Benson, "Thermochemical Kinetics," Wiley, New York, N. Y., 1968. Whether this fairly high barrier is applicable here in unknown.

(22) (a) Carboalkoxy groups are not essential chromophores. Compound i, formed from addition of the appropriate thiocarbonyl ylide to dicyanoacetylene, is transformed rapidly on irradiation to unstable products that on treatment with triphenyl phosphine yield ii and iii. (b) After much effort compound iv was prepared in abominable yield by addition of the thiocarbonyl ylide to acetylenedicarboxylic acid followed by dehydration with dicyclohexylcarbodiimide. All other routes attempted failed utterly. It could not be obtained, however, in sufficient quantity or purity to allow investigation of the effect of geometrical constriction.



i ii (major) iii (minor)



iv

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Rearrangement of the Tricyclic Orthothio Esters Derived from Mercaptoacetic Acid and Alkanedithiols. Crystal Structure of a Rearrangement Product

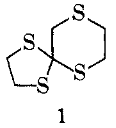
John F. Blount, David L. Coffen,* and Frederick Wong

Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

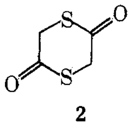
Received April 10, 1974

Equimolar amounts of mercaptoacetic acid and ethanedithiol undergo acid-catalyzed condensation to produce a tricyclic ortho ester, 1,4-dithiane-2,5-dione bis(ethylene thioketal). Dissolving this substance in concentrated sulfuric acid followed by quenching with water results in formation of a highly rearranged tricyclic disulfide. By X-ray crystallography the structure of this rearrangement–oxidation product was determined to be 1-[2-(1,3-dithiolanylidene)]-2,3,6,9-tetrathiaspiro[4.4]nonane. Similar condensation and rearrangement reactions were observed when 1,3-propanedithiol was used instead of ethanedithiol. A reaction mechanism involving acid-catalyzed dissociation and recombination is formulated to account for these rearrangements.

Orthothio esters of several simple carboxylic acids have been prepared,[1] generally by straightforward methods involving the direct condensation of the acid, an ester, or its chloride with 3 equiv of the RSH component. The ortho ester **1** of mercaptoacetic acid was described by Backer and Wiggerink[2] as the product resulting from the condensation of chloroacetyl chloride with ethanedithiol. Schöberl and Wiehler[3] prepared symmetrical ortho esters of type **3** by treating dithioglycolide (**2**) with various mercaptans. Boron trifluoride catalyzed self-condensation of mercaptoacetic acid produced the orthothio ester **3b**. Schöberl and Wiehler also described an unusual reaction of their compounds of type **3**, namely their nitration in nitric acid which produced the 1,4-dithiin derivatives **4**.



1



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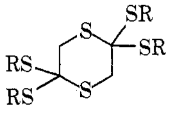
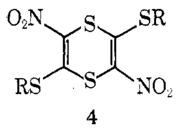
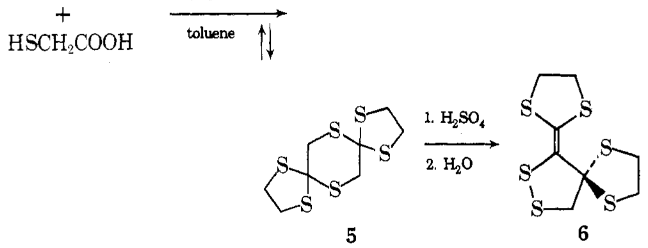


3a, R = phenyl, benzyl
b, R = CH$_2$COOH



4

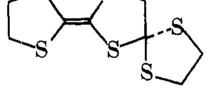
The possibility of utilizing compounds of type **4** as progenitors of protected α-mercaptoamino acids evoked our interest in the orthothio esters of mercaptoacetic acid. During the course of our work with compounds of this type, we had occasion to prepare the tricyclic ortho ester **5**, which is easily done, albeit in modest yield, by the direct, acid-catalyzed condensation of equimolar quantities of ethanedithiol and mercaptoacetic acid. The structure of



5 6

this high-melting, poorly soluble, colorless substance is evident from its nmr and mass spectra. The former consists of two signals, an AB quartet at 3.49 ppm (J = 6 Hz) and a singlet at 3.61 ppm in 2:1 ratio; and the latter contains a weak M$^+$ peak at m/e 300 and an intense peak (100%) at m/e 150.

One of the few liquids in which compound **5** is appreciably soluble is concentrated sulfuric acid. When the resulting yellow solution of **5** is kept overnight at room temperature and then quenched by pouring over crushed ice, a bright yellow product is obtained in high yield. Following the acquisition of routine spectroscopic and analytical data, **7** and **8** appeared to be tenable structures for this rearrangement product. The nmr spectrum consists of a multiplet (>20 lines) and a singlet in a 4:1 ratio in which the former can easily be construed as two overlapping AA′BB′ multiplets. A strong infrared band at 1540 cm^{-1} and a weak (ϵ 550) uv absorption at 370 mμ encouraged the contemplation of tetrathioethylene derivatives as candidate structures,[4] as did also the observation that compound **1** can be rearranged to the tetrathioethylene **9** under similar reaction conditions.



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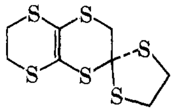

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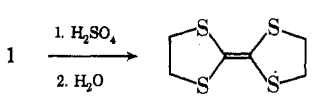
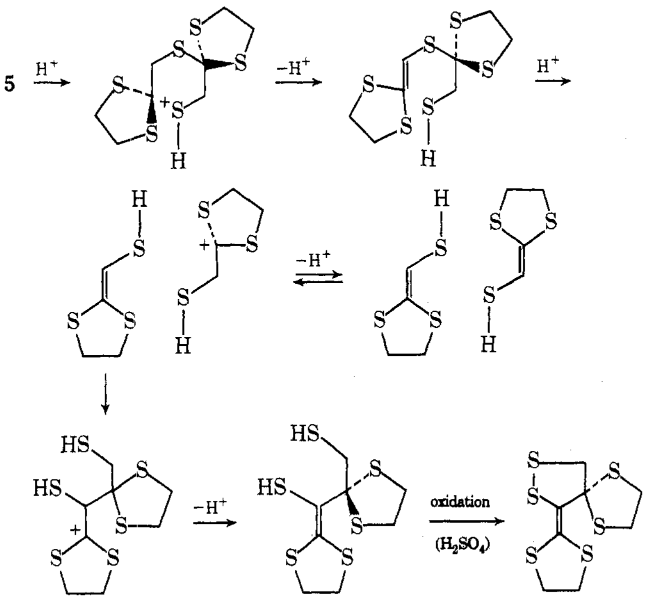


9

An X-ray crystallographic structure determination was undertaken to distinguish between structures **7** and **8**. In this way it evolved that neither structure is correct, as the rearrangement product actually has structure **6**.

The genesis of compound **6** posed an intriguing mechanism problem. While several pathways may perhaps be contrived, we find that shown in Scheme I, which entails the symmetrical scission and unsymmetrical recombination of the starting orthothio ester, to be quite reasonable. The oxidation of a dimercaptan to a cyclic disulfide by sulfuric acid is not wholly without precedent,[5] although somewhat surprising in the case of a presumably strained 1,2-dithiolane.[6]

Scheme I



6

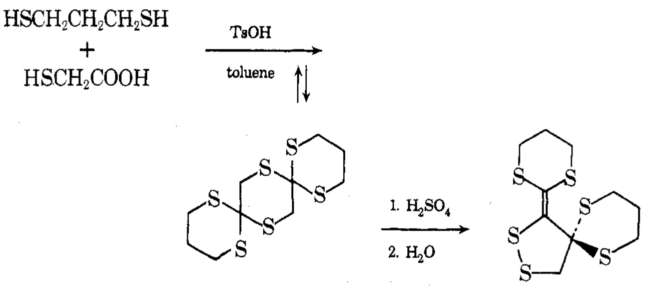
Table I
Crystal Data for Compound 6

Crystal system	Monoclinic	Orthorhombic
Space group	$P2_1$	$Fdd2$
a, Å	9.035 (8)	16.197 (8)
b, Å	7.981 (6)	37.91 (2)
c, Å	8.988 (6)	8.037 (6)
β, deg	107.93 (4)	
Z	2	16
d_{calcd}, g cm^{-3}	1.607	1.607
μ (Mo Kα), cm^{-1}	10.2	10.2

Table II
"Distances" and "Angles" Involving the Half-Atoms of the Two Conformers

Bond	Distance, Å	Bond	Angle, deg
C7A–C7B	0.81	S5–C7A–C8B	116
C7A–C8B	1.16	S5–C7B–C8A	111
C7B–C8A	1.53	S6–C8A–C7B	115
C8A–C8B	0.71	S6–C8B–C7A	118
S4A–S4B	2.00		

This rearrangement appeared to be sufficiently novel as to merit the existence of at least two examples. Accordingly 1,3-propanedithiol and mercaptoacetic acid were condensed to give the orthothio ester **10**. The rearrangement of this material proceeded more slowly but again cleanly to provide in good yield the product **11**. Structures **10** and **11** were assigned by analogy but nicely corroborated by their spectroscopic properties as iterated in the Experimental Section.



10 **11**

Crystallography. Crystals of compound **6** were found to exist in both monoclinic and orthorhombic forms, but it was not established that both are obtained in a single crystal crop. Efforts to solve the structure by both direct methods and Patterson methods using an orthorhombic crystal were fruitless. However, a complete crystal structure analysis of the monoclinic form was successfully carried out using a multiple solution procedure.[7]

The intensity data were collected on a Hilger-Watts diffractometer using Zr filtered Mo Kα radiation and crystals of approximate size 0.1 × 0.2 × 0.4 mm (monoclinic) and 0.2 × 0.2 × 0.25 mm (orthorhombic). The crystal data are presented in Table I.

Early in the refinement of the structure it became apparent that the crystal contained at least two conformers. A disordered model involving two conformers was adopted in which it was possible to resolve S(4), C(7), and C(8) each into two half-atoms. All half-atoms were assigned occupancy factors of 0.5. Toward the conclusion of the refinement, hydrogen atoms were introduced at their calculated positions. Two pairs of protons (H5Aa, H5Ab and H5Ba, H5Bb) were introduced at C(5) to correspond to the two different conformations (A and B). The final refinement was carried out by full-matrix least squares. Anisotropic thermal parameters were used for all atoms except the hydrogen and the four half-carbons, C7A, C7B, C8A, and C8B, which had isotropic temperature factors. The hydrogen atom parameters were not refined. The

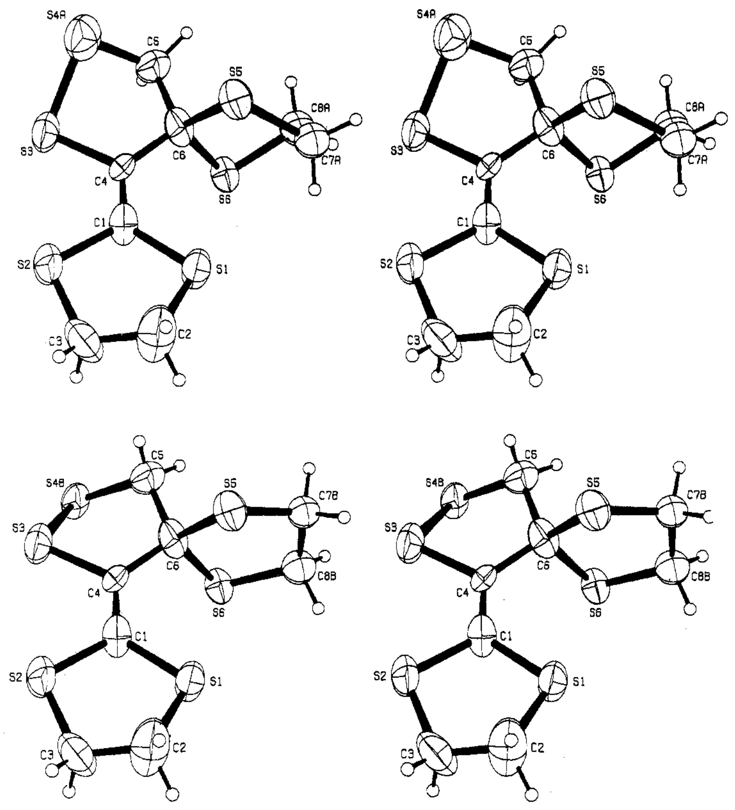


Figure 1. Stereodrawings of **6** showing the two most probable conformations.

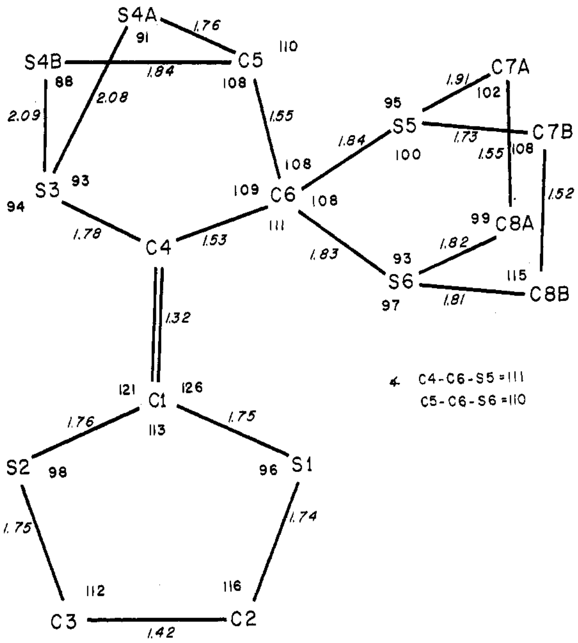


Figure 2.

final discrepancy index is $R = 5.2\%$ for 1251 observed data.[8]

The two most probable conformational arrangements involving the six half-atoms are shown in the stereodrawing in Figure 1. The bond distance and angles are given in Figure 2 and Table II. The conformer involving S4B, C7A, and C8A was ruled out because of the close intramolecular contact of 2.34 Å (H5Bb-H8Ab). Other atoms, particularly S(2), C(2), and C(3), probably occupy slightly different positions in the two conformers, but these differences were too small to resolve as separate half-atoms. The standard deviations of the bond distances and angles are larger than desired, owing in part to the disorder involving the different conformers. One of the more reliable distances is that of the ethylenic C(1)-C(4) bond, which is 1.32 (1) Å.

Experimental Section[9]

1,4-Dithiane-2,5-dione Bis(ethylene Thioketal) (5). A solution of mercaptoacetic acid (27.6 g, 0.3 mol), ethanedithiol (28.3 g, 0.3 mol), and *p*-toluenesulfonic acid (1.5 g) in toluene (500 ml) was heated under reflux for 2.5 days while collecting water in a Dean-Stark trap. The solution was cooled, diluted with ether (400 ml), and set aside while the product crystallized. The product was collected and washed with ether to give 9.45 g (21%) of colorless crystals, mp 268-270°. An analytical sample was prepared by high-vacuum sublimation. The infrared spectrum (Nujol) shows no bands above 1500 cm^{-1}. The nmr spectrum (recorded in DMSO-d_6) and mass spectrum are described in the text.

Anal. Calcd for $C_8H_{12}S_6$: C, 31.97; H, 4.02; S, 64.01. Found: C, 31.72; H, 4.08; S, 64.23.

1-[2-(1,3-Dithiolanylidene)]-2,3,6,9-tetrathiaspiro[4.4]nonane (6). Compound **5** (500 mg) was added gradually to concentrated sulfuric acid (5 ml) with swirling to give a clear solution. This was kept overnight and then poured over crushed ice. After the ice had melted, the product was collected, washed with water, and air dried to give 500 mg of a yellow solid showing a single, yellow spot on tlc. A recrystallization from benzene gave 410 mg (82%) of bright yellow crystals, mp 135-137°, in two crops. The product had an ir (Nujol) band at 1540 cm^{-1} and uv (CH_2Cl_2) bands at 232 mμ (ϵ 8090), 298 (7200), and 370 (550). The nmr spectrum ($CDCl_3$) consisted of a complex multiplet centered at 3.43 ppm (8 H) and a singlet at 3.71 ppm (2 H), mass spectrum *m/e* 298 (100%, M$^+$).

Anal. Calcd for $C_8H_{10}S_6$: C, 32.18; H, 3.38; S, 64.44. Found: C, 32.14; H, 3.25; S, 64.04.

Rearrangement of Compound 1 to Compound 9. A solution of compound **1**[2] (500 mg) in concentrated sulfuric acid (10 ml) was kept for 5 min and then quenched by rapid dilution with water. The resulting mixture was extracted three times with methylene chloride. The extract was dried, treated with charcoal, and evaporated. The residue was vacuum sublimed and the solid sublimate was triturated with ether, collected, and washed with ether to give 180 mg (36%) of compound **9** as a light yellow solid, mp 196-197° (lit.[10] mp 202-204°). The compound was identified by comparison of its ir and nmr spectra and of its tlc behavior with those of an authentic sample.[10]

1,4-Dithiane-2,5-dione Bis(trimethylene Thioketal) (10). A solution of mercaptoacetic acid (27.6 g, 0.3 mol), 1,3-propanedithiol (32.5 g, 0.3 mol), and *p*-toluenesulfonic acid (1.0 g) in toluene (500 ml) was heated under reflux for 4 days while collecting water in a Dean-Stark trap. The resulting orange solution was cooled and diluted with ether (500 ml). The product was collected, washed with ether, and air dried to give 32.4 g (66%) of colorless crystals. A sample for analysis was recrystallized from chlorobenzene and had mp 253-258°. The ir (Nujol) spectrum shows no bands above 1500 cm^{-1}. An nmr spectrum was not recorded because of the poor solubility. The mass spectrum had peaks at *m/e* 132 (100%), 165, 196, and 328 (M$^+$).

Anal. Calcd for $C_{10}H_{16}S_6$: C, 36.55; H, 4.91; S, 58.54. Found: C, 36.70; H, 4.91; S, 58.47.

1-[2-(1,3-Dithianylidene)]-2,3,6,10-tetrathiaspiro[4.5]decane (11). Compound **10** (8 g) was added gradually to concentrated sulfuric acid and the resulting solution was stirred for 3 days at room temperature. The solution was poured over ice and the precipitate was extracted into methylene chloride. After drying with sodium sulfate, the solvent was boiled off with gradual addition of benzene. The product crystallized from the resulting benzene solution to give, in three crops, 6.4 g (80%) of compound **11** as yellow crystals: mp 202-205°; ir (Nujol) 1500 cm^{-1}; uv (CH_2Cl_2) 238 mμ (ϵ 8100), 300 (7300), and 355 (1300, shoulder); nmr ($CDCl_3$) 2.10 (m, 4 H), 3.00 (m, 8 H), and 4.06 ppm (s, 2 H); mass spectrum *m/e* 156 (100%), 220, and 326 (M$^+$).

Anal. Calcd for $C_{10}H_{14}S_6$: C, 36.78; H, 4.32; S, 58.91. Found: C, 36.88; H, 4.40; S, 57.97.

Registry No.—**1**, 177-29-7; **5**, 51795-67-6; **6**, 51795-68-7; **9**, 24719-68-4; **10**, 51795-69-8; **11**, 51795-70-1; mercaptoacetic acid, 68-11-1; ethanedithiol, 540-63-6; 1,3-propanedithiol, 109-80-8.

Supplementary Material Available. Listings of atomic coordinates and thermal parameters for **6** will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24 × reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JOC-74-2374.

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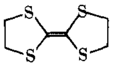
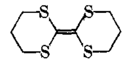
(4) Compound i exhibits uv absorption at 358 mμ (ε 470). Symmetrical tetrathioethylenes exhibit no infrared C═C bands, but we have examined the laser Raman spectra of several and find that these bands appear at exceptionally low frequencies as listed below (recorded with solid samples). We are greatly indebted to Mrs. Fie Chang for recording these data.



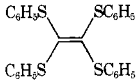
i

1550 cm^{-1}



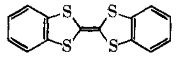
ii

1460 cm^{-1}



iii

1450 cm^{-1}



iv

1530 cm^{-1}

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(8) See paragraph at end of paper regarding supplementary material.

(9) Melting points are uncorrected. Nmr spectra were recorded on Varian T-60 and HA-100 instruments and are reported in parts per million from internal tetramethylsilane. Infrared and mass spectra were recorded on Perkin-Elmer 137 and CEC-110B instruments, respectively. Elemental analyses were conducted under the supervision of Dr. F. Scheidl of our microanalytical laboratory.

(10) D. L. Coffen, J. Q. Chambers, D. R. Williams, P. E. Garrett, and N. D. Canfield, *J. Amer. Chem. Soc.*, **93**, 2258 (1971).

Stereospecific Synthesis of 3,7-Disubstituted Bicyclo[3.3.0]octanes[1]

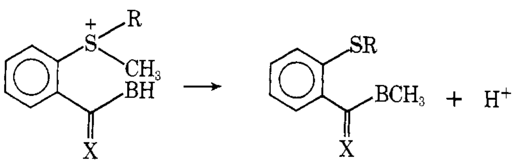
Roger Lok[2] and James K. Coward*

Department of Pharmacology, Yale University School of Medicine, New Haven, Connecticut 06510

Received March 18, 1974

The synthesis of several 3,7-disubstituted bicyclo[3.3.0]octanes has been accomplished by a series of stereospecific reactions, starting with the monoethylene ketal of 3,7-bicyclo[3.3.0]octanedione. The configurations at carbons 3 and 7 were established by the use of pmr spectroscopy.

As part of a project aimed at understanding biochemical one-carbon transfer, we have been studying several types of molecules in order to elucidate the stereochemistry and the nature of catalysis involved in nonenzymic transalkylation reactions.[3] Specifically, we are interested in providing a chemical model for enzyme-catalyzed methylations involving *S*-adenosylmethionine (SAM).[4] In a previous paper[5] we noted the stability of **1** under conditions where one might observe intramolecular transmethylations (eq 1). Independently, Eschenmoser and his coworkers[6] were unable to observe any intramolecular transmethylation in the reaction shown in eq 2. In both reactions, a six-membered cyclic intermediate can conceivably be formed, but no product resulting from intramolecular nucleophilic attack at the sp[3] carbon was obtained. Failure of these reactions may be ascribed to the inability of the atoms involved to achieve the required linear geometry in the transition state. This is in marked contrast to the numerous intramolecular reactions involving six-membered cyclic intermediates occurring at sp[2] carbons.[7] We have continued to examine models[8] of compounds in which the nucleophile, the leaving group, and the electrophilic center can be aligned in the collinear array required for a nucleophilic displacement. A molecule which can achieve such a conformation is the methylsulfonium salt **2** of a 3,7-disubstituted bicyclo[3.3.0]octane.



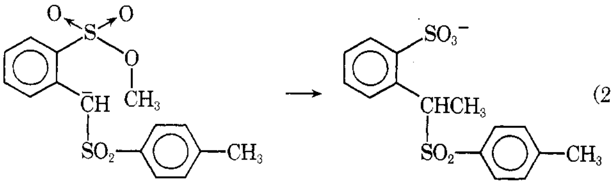
(1)

1

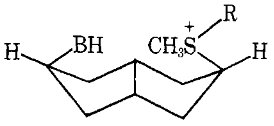
$\mathbf{a}, R = CH_3; X = H_2; BH = NH_2 \longrightarrow \mathbf{a}, R = CH_3; X = H_2; B = NH$

$\mathbf{b}, R = CH_3; X = O; BH = OH \longrightarrow \mathbf{b}, R = CH_3; X = O; B = O$

$\left.\begin{matrix}\mathbf{c}, R = CN; X = O; BH = OH \\ \mathbf{d}, R = CN; X = O; BH = NH_2\end{matrix}\right\} \longrightarrow \mathbf{c,d}, R = CN; X = O; B = O$



(2)



2

Tabushi and his coworkers[9] have shown that 3-substituted bicyclo[3.3.0]octanes prefer a "W" conformation. Models of **2** indicate that the rigid backbone of this bicyclic ring system allows an endo nucleophilic base (BH) at C-7 and the methyl of an endo sulfonium moiety at C-3 to come in close proximity to one another. Only a small deviation from the fully extended "W" conformation brings the nucleophilic and electrophilic centers within bond-making distance for a possible intramolecular transmethylation reaction. The compound in which RS of **2** is homocysteine appears to be a plausible model for enzymic methylations involving SAM. There are very little data on the 3,7-disubstituted bicyclooctanes in the literature.[10a] We have carried out the synthesis of some stereospecifically substituted bicyclooctane derivatives, **3**–**6**, and the results of these efforts are the subject of this paper.