Anal. Calcd for $C_{23}H_{18}N_2O_3$: C, 74.59; H, 4.86; N, 7.57. Found: C, 74.37; H, 4.66; N, 7.69.

Irradiation of 3e in Methanol. A methanol solution of **3e** (500 mg, 1.42 mmol in 500 mL) was irradiated for 1 h and worked up by removal of the solvent under vacuum and chromatographic separation of the residual solid on silica gel. Elution with a mixture (1:9) of benzene and petroleum ether gave 80 mg (21%) of **9**, mp 108 °C (mixture melting point), after recrystallization from methanol.

Further elution with a mixture (1:3) of benzene and petroleum ether gave 125 mg (22%) of methyl 2-(1-benzimidazolyl)-4-phenoxy-4-phenyl-3-butenoate (**11e**), mp 116 °C, after recrystallization from cyclohexane: IR ν_{max} (KBr) 3075, 3030, 2965 and 2850 (CH), 1745 (C=O), 1635 and 1595 (C=C) cm^{-1}; UV λ_{max} (methanol) 246 nm (ϵ 47 570); ^1H NMR ($CDCl_3$) δ 3.70 (3 H, s, OCH_3), 5.40 (1 H, d, J = 9 Hz, D_2O-exchangeable, methine proton), 6.30 (1 H, d, J = 9 Hz, vinylic), 7.05-7.55 (15 H, m, aromatic); mass spectrum, m/e (relative intensity) 384 (M^+, 3), 369 ($M^+ - CH_3$, 8), 354 (77), 353 ($M^+ - OCH_3$, 100), 352 ($M^+ - CH_3OH$, 33), 325 (5), 291 (7), 260 (21), 117 (89), 93 (78).

Anal. Calcd for $C_{24}H_{20}N_2O_3$: C, 75.00; H, 5.21; N, 7.29. Found: C, 75.23; H, 5.34; N, 7.18.

Continued elution of the silica gel column with benzene gave 100 mg (59%) of **1e**, mp 172 °C (mixture melting point), after recrystallization from ethanol.

Reaction of 2-(1-Benzimidazolyl)-4-phenoxy-4-phenyl-3-butenoic Acid (10e) with Diazomethane. To a stirred solution of **10e** in ether (40 mg, 0.12 mmol in 5 mL) was added an ether solution of diazomethane (1 mL, 5%) at 0 °C, and the stirring was continued for an additional hour. Removal of the solvent under vacuum and recrystallization of the product from cyclohexane gave 30 mg (72%) of **11e**, mp 116 °C (mixture melting point).

Laser Flash Photolysis. Pulse excitation was carried out at 337.1 nm (2-3 mJ, ~8 ns), employing a UV 400 Molectron nitrogen laser or at 308 and 248 nm (≤40 mJ, defocused, ~20 ns) employing a Lambda-Physik MSC 101 excimer laser. The transient phenomena were studied by using a kinetic spectrometer, described elsewhere.[29] The solvents employed were benzene and methanol, and unless oxygen effects were meant to be studied, the solutions were deoxygenated by purging with argon or nitrogen. In experiments where a large number of laser shots were necessary, e.g., for wavelength-by-wavelength measurements of transient absorption spectra, a flow system was used in which the solutions for photolysis was allowed to drain from a reservoir through a cell.

Pulse Radiolysis. The pulse radiolysis experiments were performed, employing 7-MeV electron pulses (5 ns) from the Notre Dame ARCO-LP-7 linear accelerator in the computer controlled apparatus, described elsewhere.[30]

Acknowledgment. We thank the Department of Science and Technology, Government of India, Indian Institute of Technology, Kanpur, and the Office of Basic Energy Sciences of the U.S. Department of Energy for financial support of this work.

Registry No. **1a**, 484-47-9; **1b**, 668-94-0; **1c**, 13682-20-7; **1d**, 716-79-0; **1e**, 51-17-2; **2**, 1087-09-8; **3a**, 103456-86-6; **3b**, 103456-87-7; **3c**, 103456-88-8; **3d**, 103456-89-9; **3e**, 103456-90-2; **4a**, 103456-91-3; **4b**, 103456-92-4; **4c**, 103456-93-5; **4d**, 103456-94-6; **4e**, 103456-95-7; **5a**, 103456-96-8; **5b**, 103456-99-1; **6a**, 103477-28-7; **6b**, 103457-00-7; **7a**, 103456-97-9; **7c**, 103457-01-8; **7d**, 103457-02-9; **8**, 959-28-4; **9**, 103456-98-0; **10d**, 103457-03-0; **10e**, 103457-05-2; **11d**, 103457-04-1; **11e**, 103457-06-3.

(29) (a) Das, P. K.; Encinas, M. V.; Small, R. D. Jr.; Scaiano, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 6965-6970. (b) Das, P. K.; Bobrowski, K. *J. Chem. Soc., Faraday Trans. 2* **1981**, *77*, 1009-1027. (c) Chattopadhyay, S. K.; Das, P. K.; Hug, G. *J. Am. Chem. Soc.* **1982**, *104*, 4507-4514.

(30) Patterson, L. K.; Lilie, J. *Int. J. Radiat. Phys. Chem.* **1974**, *6*, 129-141.

Synthesis and Reactions of 3-Mercaptocyclobutanol and Derivatives. Preparation of a 2,4-Dithiabicyclo[3.1.1]heptane

Eric Block,*† Jean-Alex Laffitte, and Venkatachalan Eswarakrishnan

Department of Chemistry, State University of New York at Albany, Albany, New York 12222

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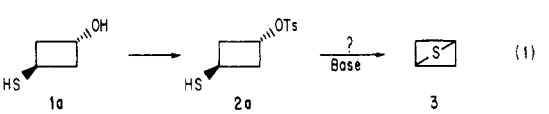
Reaction of the lithio derivative of 2-[(bis(trimethylsilyl)methyl)thio]tetrahydropyran (**4**) with epichlorohydrin gave both isomers of 3-[(2-tetrahydropyranyl)thio]-3-(trimethylsilyl)-1-(trimethylsiloxy)cyclobutane (**5**). The latter compound upon treatment with potassium carbonate in methanol gave 3-[(2-tetrahydropyranyl)thio]-3-(trimethylsilyl)cyclobutanol (**6**) while treatment with tetrabutylammonium fluoride gave *trans*- and *cis*-3-[(2-tetrahydropyranyl)thio]cyclobutanol (**7a,b**). Treatment of the latter compound with mercuric chloride in aqueous acetonitrile gave *trans*- and *cis*-3-mercaptocyclobutanol (**1a,b**), which could be oxidized to bis(3-hydroxycyclobutyl) disulfide (**11**) or could be converted by sequential acetylation and tosylation to *trans*- and *cis*-(acetylthio)cyclobutanol (**9a,b**) and *trans*- and *cis*-3-(acetylthio)cyclobutyl tosylate (**10a,b**), respectively. Compound **7a,b** could also be converted to *trans*- and *cis*-3-[(2-tetrahydropyranyl)thio]cyclobutyl tosylate (**8a,b**). X-ray crystallography of the minor isomer **8b** established the ring stereochemistry as cis, thereby establishing that the major isomers in these series of compounds have trans stereochemistry. NMR spectroscopy was also employed to determine stereochemistry of the various isomeric 1,3-disubstituted cyclobutanes. Treatment of **8a** with mercuric chloride gave *trans*-3-mercaptocyclobutyl tosylate (**2a**). This upon treatment with base gave a mixture of 3-allyl-2,4-dithiabicyclo[3.1.1]heptane (**15**) and (*Z*)-3-methyl-2,6-dithiabicyclo[5.1.1]non-4-ene (**16**). The structure of **15** was established by 2D NMR analysis as well as by hydrolysis to *cis*-1,3-cyclobutanedithiol. A mechanism is proposed for conversion of **2a** to **15** based on deuterium labeling studies.

2-Thiabicyclo[1.1.1]pentane (**3**) is a novel strained heterocycle that has thus far eluded synthesis.[1] Nucleophilic ring closure of a derivative of *trans*-3-mercaptocyclobutanol (**1a**) such as *trans*-3-mercaptocyclobutyl tosylate (**2a**) (eq 1) would represent a direct approach to **3**

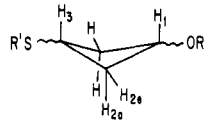


(1)

† Fellow of the John Simon Guggenheim Memorial Foundation, 1984-1985.

0022-3263/86/1951-3428$01.50/0

Table I. 300-MHz Proton NMR Spectra of 1,3-Disubstituted Cyclobutanes 1, 2, 7-10a,b[a]



1,2,7-10a,b

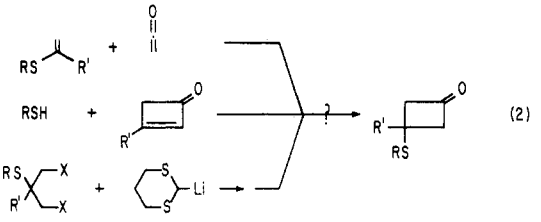
isomer	δ_{H_1} (mult)[b]	$\delta_{H_{2e}}$	$\delta_{H_{2a}}$	$\Delta\delta$ (2e − 2a)	δ_{H_3} (mult)	ratio **a**:**b** by NMR
1a	4.64 (quint)	2.45	2.30	0.15	3.59 (oct)	2.5:1
1b	4.05 (quint)	2.90	1.90	1.00	2.83–2.93 (m)	
2a	5.09 (quint)	2.66	2.25	0.41	3.59 (sept)	1.9:1
2b	4.59 (quint)	2.78	2.16	0.62	2.89 (quint)	
7a	4.58 (quint)				3.60 (quint)	2.3:1
7b	4.12 (quint)				3.05 (quint)	
8a	5.02 (quint)	2.59	2.32	0.27	3.59 (sept)	1.9:1
8b	4.64 (quint)	3.04	2.66	0.38	3.04 (quint)	
9a	4.45 (quint)	2.50	2.30	0.20	3.31 (sept)	2:1
9b	4.16 (quint)	2.85	1.99	0.86	3.51 (quint)	
10a	5.01 (quint)	2.72	2.31	0.41	3.94 (sept)	2.2:1
10b	4.70 (quint)	2.75	2.22	0.53	3.57 (m)	

[a] Chemical shifts in ppm from internal Me_4Si in $CDCl_3$. [b] Multiplicity indicated as quint (quintet), oct (octet), sept (septet), or m (multiplet).

with ample precedence in the synthesis of other sulfur-bridged carbocycles such as 7-thiabicyclo[2.2.1]heptane,[2a] 5-thiabicyclo[3.1.1]heptane,[2b,c] and 5-thiabicyclo[2.1.1]-hexane.[2d] We describe here a direct stereoselective synthesis of the new compounds **1a** and **2a** and our findings on the base-promoted reaction of **2a**.

Results and Discussion

Efforts to generate suitable precursors to **1** by 2 + 2 cycloaddition of ketene analogues with vinyl sulfides,[3-5] by nucleophilic addition of thiols to cyclobutenones[6] or by reaction of 2-(alkylthio)-1,3-dihalopropanes[7] with carbonyl anion equivalents[8,9] (eq 2) were not particularly promising.



(2)

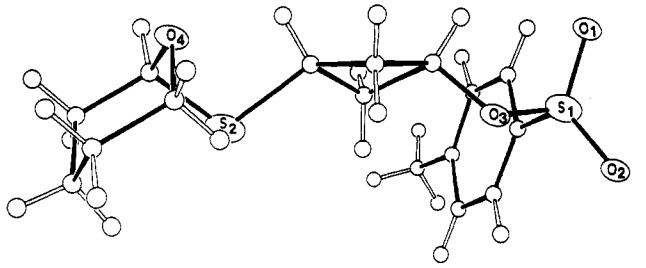
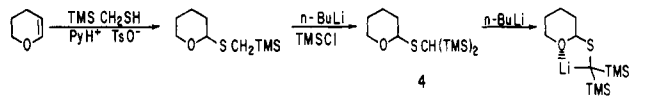


Figure 1. ORTEP view of the structure of *cis*-3-[(2-tetrahydropyranyl)thio]cyclobutyl tosylate (**8b**). Selected bond lengths (Å) and angles (deg): S1–O1, 1.43 (1); S1–O2, 1.41 (1); S1–O3, 1.59 (2); S1–C1, 1.76 (2); S2–C12, 1.84 (3); S2–C14, 1.78 (3); O3–C10, 1.40 (3); C10–C11, 1.57 (2); C10–C13, 1.55 (3); C11–C12, 1.50 (3); C12–C13, 1.49 (4); O1–S1–O2, 122.6 (10); O1–S1–O3, 106.7 (12); O1–S1–C1, 109.3 (11); O2–S1–O3, 104.8 (13); O2–S1–C1, 109.1 (13); O3–S1–C1, 102.3 (12); C12–S2–C14, 105.3 (16); S1–O3–C10, 119.3 (16); O3–C10–C11, 114.8 (20); O3–C10–C13, 113.4 (20); C10–C11–C12, 92.6 (23); S2–C12–C11, 109.9 (19); S2–C12–C13, 122.4 (22); C11–C12–C13, 90.4 (28); C10–C13–C12, 114.3 (13).

Fortunately we found that our initial objective could be simply realized through reaction of the lithio derivative of 2-[(bis(trimethylsilyl)methyl)thio]tetrahydropyran (**4**), prepared as shown in eq 3,[11] with epichlorohydrin[12] fol-



(3)

lowed by removal of the trimethylsilyl and tetrahydropyranyl groups (eq 4).[13] The first step in this sequence gave **5** in 98% yield as a 2.7:1 mixture of isomers separable by chromatography on silica gel (stereochemistry not assigned). Brief treatment of **5** with potassium carbonate in dry methanol[14] gave the stereoisomeric alcohols **6** in quantitative yield. Fluorodesilylation of **5** or **6** with tetrabutylammonium fluoride in moist tetrahydrofuran gave in 62% yield a 2.7:1 mixture of the trans and cis S-THP derivatives of **2a** and **2b**, **7a** and **7b**, respectively. Treat-

(1) For an earlier unsuccessful attempted synthesis of a derivative of **3**, see: Block, E.; Corey, E. J. *J. Org. Chem.* **1969**, *34*, 896–899.

(2) (a) Corey, E. J.; Block, E. *J. Org. Chem.* **1966**, *31*, 1663–1668. (b) Birch, S. F.; Dean, R. A.; Hunter, N. J. *J. Org. Chem.* **1958**, *23*, 1026–1030. (c) Also note recent studies on organosulfur counterparts of thromboxane A_2 (2,6-dioxabicyclo[3.1.1]heptane derivatives): Ohuchida, S.; Hamanaka, N.; Hayashi, M. *J. Am. Chem. Soc.* **1981**, *103*, 4597–4599; *Tetrahedron Lett.* **1981**, *22*, 1349–1352, 5301–5302. Ohuchida, S.; Hamanaka, N.; Hashimoto, S.; Hayashi, M. *Tetrahedron Lett.* **1982**, *23*, 2883–2886. Kale, V. N.; Clive, D. J. *J. Org. Chem.* **1984**, *49*, 1554–1563. (d) Tabushi, I.; Tamaru, Y.; Yoshida, Z. *Tetrahedron Lett.* **1970**, 2931–2934.

(3) Martin, J. C. U.S. Patent 3 345 402, 1967; *Chem. Abstr.* **1967**, *67*, 116635y.

(4) We were unable to prepare adducts of vinyl methyl sulfide with ketene, dimethyl ketene,[3] or *N,N*-dimethylketimine.[5]

(5) Falmagne, J.-B.; Escudero, J.; Taleb-Sahraoui; Ghosez, L. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 879–880.

(6) 3-Methylcyclobutenone underwent 1,4-addition with ethanethiol (but not thioacetic acid); selective cleavage of the S–Et bond could not be achieved in the resulting 3-substituted cyclobutanone or the corresponding cyclobutanol.

(7) Bland, J. M.; Stammer, C. H. *J. Org. Chem.* **1983**, *48*, 4393–4394. Anzeveno, P. B.; Matthews, D. P.; Barney, C. L.; Barbuch, R. J. *J. Org. Chem.* **1984**, *49*, 3134–3138.

(8) Ogura, K.; Yamashita, M.; Furukawa, S.; Suzuki, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1975**, 2767–2770. Seebach, D.; Beck, A. K. *Org. Synth.* **1971**, *51*, 76–81.

(9) Although 2-lithio-1,3-dithiane or the anion of methylsulfinyl methylthiomethane are known to afford cyclobutanone derivatives upon reaction with 1,3-dihalopropanes,[8] reaction with 2-(methylthio)-1,3-dibromopropane or related compounds[7] led to complex mixtures containing dehydrohalogenation products.[10]

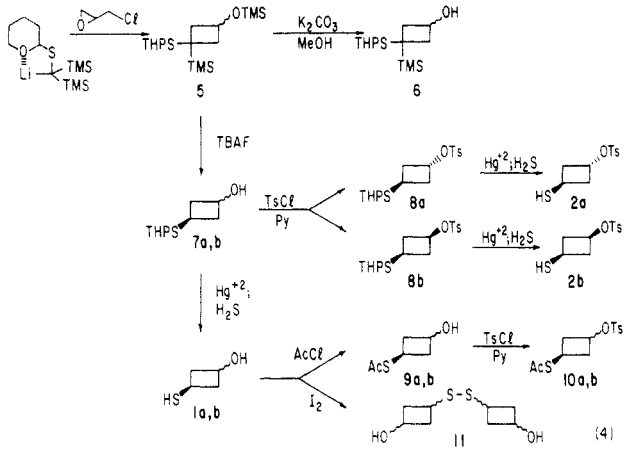
(10) Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1985**, *26*, 425–428.

(11) Block, E.; Aslam, M. *J. Am. Chem. Soc.* **1985**, *107*, 6729–6730.

(12) Takeda, T.; Naito, S.; Ando, K.; Fujiwara, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 967–968.

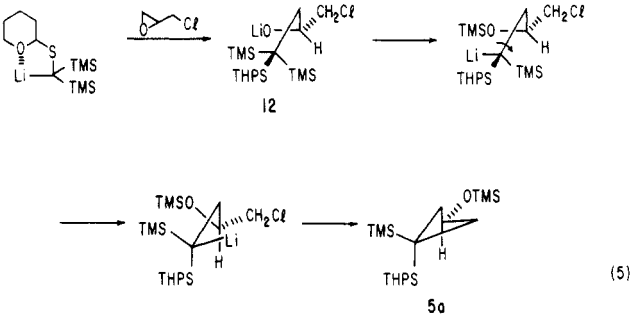
(13) Formation of *O*-trimethylsilyl **7a,b** from epichlorohydrin and the lithio derivative of 2-[((trimethylsilyl)methyl)thio]tetrahydropyran failed.

(14) Hurst, D. T.; McInnes, A. G. *Can. J. Chem.* **1965**, *43*, 2004–2011.



ment of this mixture with *p*-toluenesulfonyl chloride gave in 91% yield a 2.5:1 mixture of *trans*- and *cis*-3-[(2-tetrahydropyranyl)thio]cyclobutyl tosylate (**8a** and **8b**), respectively, which could be separated by preparative HPLC into the pure crystalline components. The stereochemistry of the cis isomer **8b** was established by X-ray crystallography; pertinent structural information is given in Figure 1. Removal of the THP group from **7a,b** using mercuric chloride in 80% aqueous acetonitrile[15] gave quantitatively a 2.5:1 mixture of *trans*- and *cis*-3-mercaptocyclobutanol (**1a** and **1b**), respectively, characterized after oxidation as a crystalline mixture of disulfides **11** or by acetylation as a 2:1 mixture of *trans*- and *cis*-3-(acetylthio)cyclobutanol (**9a** and **9b**), respectively, which could be converted to a 2.2:1 mixture of *trans*- and *cis*-3-(acetylthio)cyclobutyl tosylates (**10a** and **10b**), respectively, yellow oils separable by preparative HPLC. Removal of the THP group from tosylates **8a** and **8b** (Hg^{+2}; H_2S) gave *trans*- and *cis*-3-mercaptocyclobutyl tosylates (**2a** and **2b**), respectively. Direct acetylation of **2a** and **2b** failed, probably due to the lability of the substrate under basic conditions (see below). The stereochemistry of all of the new 1,3-disubstituted cyclobutanes prepared above was established through correlation of each compound with **8b**, assuming no inversion of stereochemistry occurs in intervening steps. Stereochemical assignments for **1**, **2**, and **7–10** are further supported by agreement of ^1H NMR data on these compounds with the following trends reported for 1,3-disubstituted cyclobutanes (see Table I): (1) the ring protons in positions 1 and 3 are more shielded in the trans isomer than in the cis isomer;[16] (2) the difference between the chemical shifts of the equatorial and axial methylene protons is larger in the cis isomer than the trans isomer;[16] (3) in the cis isomers the 1,3-protons appear as quintets since $^3J_{ax,ax}$ and $^3J_{ax,eq}$ are both equal to ca. 10 Hz (the 1,3-substituents are assumed to occupy the equatorial position so that the 1,3-ring protons are both axial); in the trans isomer the coupling pattern of the equatorial proton at position 1 or 3 is expected to be more complex since $^3J_{eq,eq}$ is much smaller (ca. 3 Hz) than $^3J_{eq,ax}$, leading to a first-order prediction of a triplet of triplets.

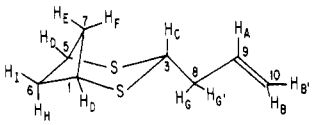
In the above work we were surprised to find that **7a** with the desired trans stereochemistry was the major product despite the fact that trans 1,3-disubstituted cyclobutanes are generally less stable than their cis isomers.[17] We found that when the isomers of **5** were separated by preparative HPLC and the major isomer was treated with TBAF, trans isomer **7a** was the exclusive product. The configuration of the major isomer of **5** is not known. However, if it is reasonably assumed that isomer **7a** is the *less* stable isomer, then fluorodesilylation would have to occur under conditions of kinetic control, most likely with *retention* of configuration at carbon from a precursor **5a** in which the 2-tetrahydropyranylthio and trimethylsiloxy groups are trans (eq 5). The formation of **5a** can be rationalized if attack by oxygen on the diastereotopic trimethylsilyl groups in intermediate **12** favors the organolithium compound with the smaller 1,3-interaction (C–H and C–Si rather than C–H and C–S, since C–Si bonds are longer than C–S bonds).[18a]



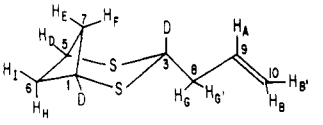
The synthesis of 2-thiabicyclo[1.1.1]pentane (**3**) was attempted by ring closure of **2a** under basic conditions. Reactions were conducted under argon in the dark, following the disappearance of **2a** by HPLC. Product analysis involved capillary GC and GC–MS at a temperature low enough to detect C_4H_6S species, assuming a retention time similar to those of thiophene and tetrahydrothiophene, which were used as internal standards. Under a variety of conditions (sodium ethoxide in ethanol or *n*-butyllithium in THF at room temperature or reflux) that led to disappearance of starting material no highly volatile products were detected. However two new volatile compounds of molecular formula $C_8H_{12}S_2$ were always seen. Isolation of pure samples of these two isomeric compounds was accomplished by preparative HPLC which gave A in 20% yield and B in 3% yield. The mass spectrum of A showed a parent ion at *m/e* 172 (6.6) with a base peak at *m/e* 131 ($P^+ - C_3H_5$) while the mass spectrum of B also showed a parent ion at *m/e* 172 (36), a small peak at *m/e* 131, and a base peak at *m/e* 85. The ^{13}C NMR spectrum of compound A showed only *seven* unique carbon atoms [δ 133.6 (CH), 117.9 (CH_2), 44.9 (CH_2), 38.7 (CH_2), 38.3 (CH), 37.4 (CH), 32.9 (CH_2)] while that of B showed eight distinct carbon atoms [δ 147.9 (CH), 120.7 (CH), 40.7 (CH), 39.6 (CH_2), 39.0 (CH), 36.1 (CH), 33.2 (CH_2), 20.7 (CH_3)]. The carbon spectrum of A requires that the molecule have a plane of symmetry. The complexity and integration pattern of the proton spectrum and the 2D proton spectrum (supplementary material) are best interpreted in terms of nine unique protons including an allyl group. The spectroscopic information points to the structure of A being 3-allyl-2,4-dithiabicyclo[3.1.1]heptane (**15**) and B being (*Z*)-3-methyl-2,6-dithiabicyclo[5.1.1]-non-4-ene (**16**) (see Table II). Under conditions giving **15** and **16** from **2a**, cis isomer **2b** gave no detectable volatile products. When **2a** was treated with base in the presence of 2,3-dimethyl-1,3-butadiene GC–MS indicated the presence of **15**, **16**, and a third volatile compound of mo-

(15) Erickson, B. W. Ph.D. Thesis, Harvard University, 1970.
(16) Gaoni, Y.; Tomazic, A. *J. Org. Chem.* **1985**, *50*, 2948–2957. Lillien, I.; Doughty, R. A. *J. Am. Chem. Soc.* **1967**, *89*, 155–156. Cistaro, C.; Fronza, C.; Mondelli, R.; Bradamante, S.; Pagani, G. A. *J. Magn. Reson.* **1975**, *17*, 219–228.
(17) Moriarty, R. M. *Top. Stereochem.* **1974**, *8*, 271–421. Lillien, I.; Doughty, R. A. *Tetrahedron* **1967**, *23*, 3321–3326.
(18) (a) Compare: Boeckman, R. K., Jr.; Chinn, R. L. *Tetrahedron Lett.* **1985**, *26*, 5005–5008. (b) Vedejs, E.; Fuchs, P. L. *J. Org. Chem.* **1971**, *36*, 366–367.

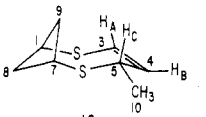
Table II. 300-MHz Proton and Carbon NMR Spectral Data for Compounds 15, 15-d_2, and 16[a]



15



15-d_2

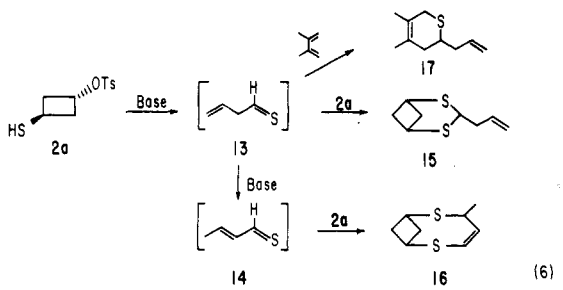


16

	15	15-d_2	16
H_A	5.84–5.72 (m, 1 H)	5.88–5.74 (m, 1 H)	6.10 (d, 1 H, J_{AB} = 9.03 Hz)
H_B	5.17–5.07 (m, 2 H)	5.23–5.07 (m, 2 H)	6.44 (t, 1 H, $J_{AB,BC}$ = 9.03 Hz)
H_C	4.93 (t, 1 H, $J_{CG,CG'}$ = 6.84 Hz)		4.0–3.85 (m, 1 H)
H_D	3.24 (t, 2 H, $J_{DE,DI}$ = 6.3 Hz)	3.26 (t, 1 H, $J_{DE,DI}$ = 6.35 Hz)	
$H_{E,I}$	2.96–2.76 (m, 2 H)	2.89–2.77 (m, 2 H)	
H_F	2.64 (dd, 1 H, J_{FH} = 7.71 Hz, J_{EF} = 12.32 Hz)	2.65 (dd, 1 H, J_{EF} = 12.29 Hz, J_{FH} = 7.68 Hz)	
$H_{G,G'}$	2.47 (t, 2 H, $J_{CG,AG}$ = 6.79 Hz)	2.49 (d, 2 H, J_{GA} = 6.84 Hz)	
H_H	2.08 (dd, 1 H, J_{HF} = 7.71 Hz, J_{HI} = 11.34 Hz)	2.10 (dd, 1 H, J_{EH} = 7.66 Hz, J_{HI} = 11.40 Hz)	
CH_3			1.40 (d, 3 H, J = 6.73 Hz)
C_1	38.27 (CH)	38.35 (CH or CD)	38.96 or 40.67 (CH)
C_3	37.43 (CH)	*c*	120.69 (CH)
C_4			147.89 (CH)
C_5	38.27 (CH)	38.35 (CH or CD)	36.14 (CH)
C_6	38.73 or 44.87 (CH_2)	38.73 or 44.82 (CH_2)	
C_7	38.73 or 44.87 (CH_2)	38.73 or 44.82 (CH_2)	38.96 or 40.67 (CH)
C_8			33.17 or 39.64 (CH_2)
C_9	133.63 (CH)	133.70 (CH)	33.17 or 39.64 (CH_2)
C_{10}	117.93 (CH_2)	118.05 (CH_2)	20.69 (CH_3)

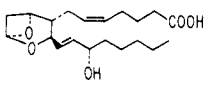
[a] Chemical shifts in ppm from internal Me_4Si in $CDCl_3$. [b] Assignment not made for protons at 3.75–3.65 (m, 1 H), 3.43–3.3 (m, 1 H), 3.0–2.85 (m, 1 H), and 2.55–2.3 (m, 2 H) ppm. [c] Too weak to measure due to attached deuterium.

lecular weight 168 with an M + 2 4.3% of the intensity of the *m/e* 168 peak, suggesting a Diels–Alder adduct $C_{10}H_{16}S$, **17**. As indicated in eq 6, we suggest that **2a** is converted into 3-butenethial **13**, which is trapped by **2a** or 2,3-dimethyl-1,3-butadiene but not by **2b** or is isomerized by base to 2-butenethial **14**. The latter compound could be trapped by **2a** but not by **2b**, giving **16**.



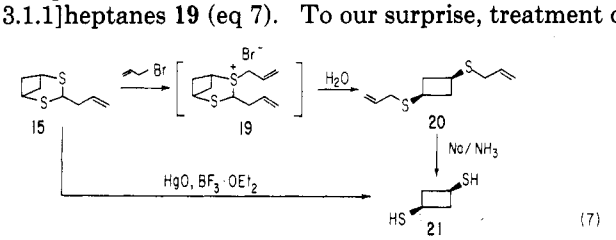
(6)

Since all previously synthesized diheterobicyclo[3.1.1]heptanes were prepared as models of the biologically potent thromboxane A_2 (**18**), which has substituents on both



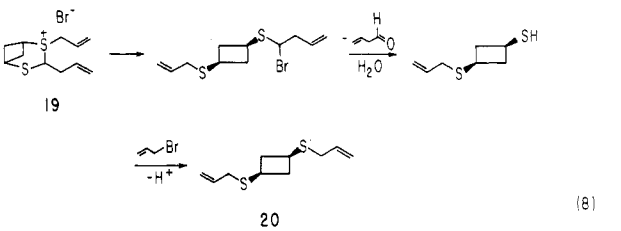
18

the 2- and 3-positions on the ring,[2c] it was of interest to alkylate **15** on sulfur to give potentially water-soluble homologues of **18**, 2,3-disubstituted 2,4-dithiabicyclo[3.1.1]heptanes **19** (eq 7). To our surprise, treatment of



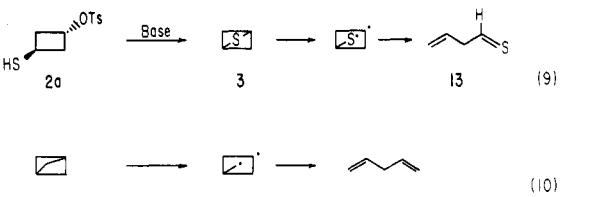
(7)

15 with allyl bromide followed by chromatography did not give sulfonium salt **19** but rather *cis*-1,3-bis(allylthio)cyclobutane (**20**). The latter compound upon sodium–liquid ammonia reduction gave *cis*-1,3-cyclobutanedithiol (**21**), also available by mercuric oxide–boron trifluoride etherate[18b] promoted hydrolysis of **15**. The formation of **20** from **15** can be rationalized as shown in eq 8.



(8)

Generation of 3-butenethial from **2a** requires additional comment. One possible mechanism involves the formation of 2-thiabicyclo[1.1.1]pentane (**3**) followed by fragmentation (eq 9), paralleling the known conversion of bicyclo[1.1.1]pentane to 1,4-pentadiene (eq 10).[19] Indeed the



(9)

(10)

strain energy in **3** would be expected to represent a substantial fraction of the energy of a carbon–sulfur bond, making **3** highly susceptible to ring opening–decomposition processes.[20] The intermediacy of **3** and the mechanism for formation of 3-butenethial could be probed with the stereoisomeric 3-deuterio-3-mercaptocyclobutyl tosylates (**2a,b**-d_1), prepared as depicted in eq 11 by using tetra-

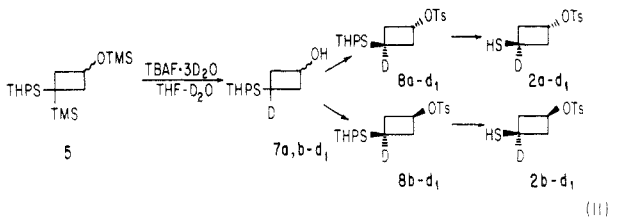
(19) Wiberg, K. B.; Barth, D. E.; Pratt, W. E. *J. Am. Chem. Soc.* **1977**, *99*, 4286–4289.

(20) The strain energies of bicyclo[1.1.1]pentane, cyclobutane, and thietane are respectively 67, 27, and 20 kcal/mol.[21] The calculated strain energy of 5-thiabicyclo[2.1.1]hexane is 32 kcal/mol, 9 kcal/mol less than that for bicyclo[2.1.1]hexane.[21] The strain energy of **3** can be estimated to be at least 50 kcal/mol. The carbon–sulfur bond energy is ca. 77 kcal/mol.[22]

(21) Allinger, N. L.; Hickey, M. J. *J. Am. Chem. Soc.* **1975**, *97*, 5167–5177. Wiberg, K. B.; Lampman, G. M.; Ciula, R. P.; Connor, D. S.; Schertler, P.; Lavanish, J. *Tetrahedron* **1965**, *21*, 2749–2769. Wiberg, K. B. *Tetrahedron Lett.* **1985**, *26*, 599–602.

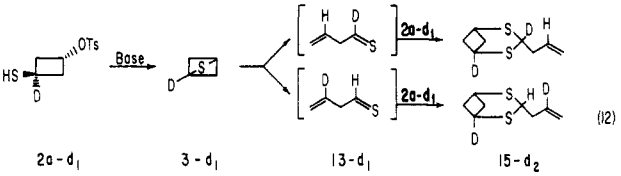
(22) Benson, S. W. *Chem. Rev.* **1978**, *78*, 23–35.

butylammonium fluoride–$3D_2O$ in the initial fluorodesilylation. The absence of deuterium scrambling during

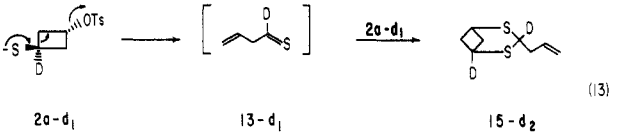


(11)

the base-promoted reaction of 3-deuterated **2a** (**2a**–d_1) rules out the involvement of symmetrical **3** (eq 12). A second mechanism for formation of 3-butenethial involves ionic fragmentation of **2a** (eq 13). Isomer **2b** should also

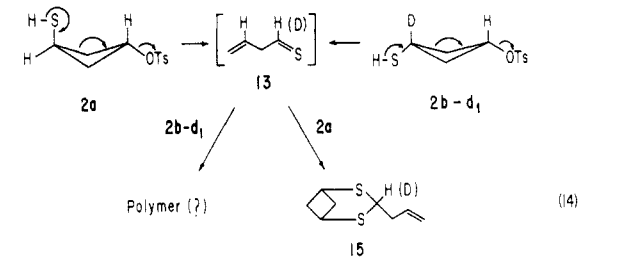


(12)



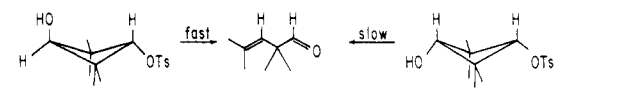
(13)

be capable of fragmenting although due to steric restraints the resultant 3-butenethial could not be captured by **2b** to give a bicyclic product. To determine if **2b** was undergoing fragmentation, a 1:1 mixture of nondeuterated **2a** and 3-deuterated **2b** was exposed to basic conditions. Analysis of the resultant **15** by GC–MS indicated the presence of ca. 18% deuterium, thus establishing that **2b** also fragments to 3-butenethial, albeit not as efficiently as **2a** (or at a slower rate) (eq 14). Our observations are



(14)

in good agreement with the earlier results of Wilcox[23] who found 2,2,4-trimethyl-3-pentenal (**23**) to be the major solvolysis product of *trans*-2,2,4,4-tetramethyl-3-hydroxycyclobutyl tosylate (**22a**) but only a minor product from solvolysis of the corresponding cis isomer **22b**.



(15)

Wilcox also found that the trans isomer **22a** underwent solvolysis 800 times faster than cis isomer **22b**, presumably a consequence of the higher energy of **22a** with an axial hydroxyl group. It is surprising that despite the facts that the C–S bond is longer than the C–O bond, that sulfur is more nucleophilic than oxygen, and that the distance of the sulfur in **2a** from the center of developing positive charge is short, anchimeric assistance by sulfur in **2a** does not occur.

(23) Wilcox, C. F., Jr.; Nealy, D. L. *J. Org. Chem.* **1963**, *28*, 3450–3454.

Experimental Section

General. NMR spectra were recorded on a Varian XL-300 or EM360A or Bruker WH-90 spectrometer using tetramethylsilane as internal standard; abbreviations used are s (singlet), d (doublet), t (triplet), and m (multiplet). Mass spectra were obtained on an AEI MS-902 mass spectrometer. Analytical gas chromatography (GC) was performed on a Perkin-Elmer Sigma 2B gas chromatograph interfaced to a Perkin-Elmer Sigma 10B data station or on a Hewlett-Packard 5890 capillary gas chromatograph with a Model 5970 mass selective detector. A 50-m OV-101 fused silica capillary column was used for all analyses. Melting points are corrected. Tetrahydrofuran and methylene chloride were dried by distillation from lithium aluminum hydride.

(Trimethylsilyl)methanethiol.[24] To a solution of 49 g (0.4 mol) of (chloromethyl)trimethylsilane in 600 mL of dry ethanol was added 61 g (0.8 mol) of thiourea. The mixture was refluxed for 48 h and was then concentrated under vacuum to give a white solid. This was dissolved in 400 mL of water and treated with 800 mL of 40% NaOH solution. The solution was then extracted twice with ethyl ether, and the ether layer was separated. The aqueous phase was acidified with concentrated HCl and extracted twice with ether. The combined ether extracts were then washed with brine, the ether was removed by distillation at atmospheric pressure, and the residue was distilled to give 30 g (62%) of the title compound as a colorless liquid, bp 119–120 °C: GC t_r 3.40 min (oven 70 °C; 99.5% pure); ^{1}H NMR ($CDCl_3$) 1.63 (d, 2 H, J = 6 Hz), 1.17–0.94 (m, 1 H, SH), 0.1 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) 8.3, –2.5 ppm; IR (neat) 2950 (s), 1245 (s), 830 (s) cm^{-1}; mass spectrum, m/e 120 (M^+), 105, 77, 73, 59.

2-Tetrahydropyranyl (Trimethylsilyl)methyl Sulfide. A solution of distilled (trimethylsilyl)methanethiol (36 g, 0.3 mol) and dihydropyran (37.8 g, 0.45 mol) in 1 L of dry dichloromethane containing pyridinium *p*-toluenesulfonate[25] (7.25 g, 0.03 mol) was stirred at room temperature for 10 h. After evaporation of the solvent, the residue was taken up in ether and washed with brine. The ether layer was dried ($MgSO_4$) and concentrated to give a colorless liquid. Distillation gave 55 g of the title compound (91%), bp 60–62 °C (0.5 mm): GC t_r 3.49 min (98% pure; oven 195 °C); ^{1}H NMR ($CDCl_3$) 4.67 (t, 1 H), 4.06–3.99 (m, 1 H), 3.49–3.42 (m, 1 H), 1.98–1.48 (m with dd inside, 8 H), 0.09 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) 84.29, 64.27, 30.89, 25.44, 21.53, 15.37, –1.93 ppm.

Bis(trimethylsilyl)methyl 2-Tetrahydropyranyl Sulfide. To a solution of 2-tetrahydropyranyl (trimethylsilyl)methyl sulfide (55.1 g, 0.27 mol) in 750 mL of THF and 75 mL of HMPA cooled to –78 °C in an argon atmosphere was added dropwise 168.7 mL of *n*-butyllithium in hexane (1.6 M, 0.27 mol). The reaction mixture was stirred for 30 min at –78 °C, then warmed to –20 °C, and then cooled to –100 °C. At –100 °C trimethylsilyl chloride (58.6 g, 0.54 mol) was added all at once. The solution was stirred for 30 min and then warmed to room temperature. Water was added, the solution was extracted twice with ether, the ether phase was washed three times with water, dried ($MgSO_4$), and concentrated to give a slightly yellow liquid, which was distilled to afford 63.8 g (86%) of the title compound as a colorless liquid, bp 90–91 °C (0.6 mm); GC t_r 5.54 min (oven 195 °C; 95% pure); ^{1}H NMR ($CDCl_3$) 4.73–4.69 (m, 1 H), 4.06–3.99 (m, 1 H), 3.45–3.35 (m, 1 H), 1.97–1.45 (m, 6 H), 0.98 (d, 1 H), 0.05 (m, 18 H) ppm; ^{13}C NMR ($CDCl_3$) 85.03, 63.20, 31.31, 25.74, 20.96, 14.54, –0.11, –0.22 ppm.

3-[(2-Tetrahydropyranyl)thio]-3-(trimethylsilyl)-1-(trimethylsiloxy)cyclobutane (5). To 63.75 g (0.23 mol) of bis(trimethylsilyl)methyl 2-tetrahydropyranyl sulfide in 750 mL of THF and 75 mL of HMPA cooled at 0 °C under argon was added dropwise 160 mL of a 1.6 M *n*-butyllithium solution in hexane, and the reaction mixture was stirred at 0 °C for 40 min. Then 25.6 g (0.28 mol) of neat epichlorohydrin was added dropwise

(24) Cooper, G. D. *J. Am. Chem. Soc.* **1954**, *76*, 2500. Decker, Q. W.; Post, H. W. *J. Org. Chem.* **1960**, 249–252.

(25) Miyashita, N.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772–3774.

maintaining the temperature below 5 °C. The reaction mixture was stirred for 2 h at 0 °C and then for 1 h at room temperature. Then water was added, the aqueous phase was extracted twice with ether, and the ether phases were combined, washed three times with water, dried over anhydrous $MgSO_4$, and concentrated under high vacuum to give 66 g (86%) of a yellow oil. The mixture was chromatographed on silica gel (eluent, 99:1 hexane–ethyl acetate) to give pure **5a** and a mixture where **5b** was the major isomer.

5a: IR (neat) 2950 (s), 2830 (m), 1250 (s), 1130 (s), 1080 (m), 1030 (m), 1000 (m), 920 (m), 840 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 4.70–4.83 (m, 2 H), 4.08–4.15 (m, 1 H), 3.46–3.53 (m, 1 H), 2.17–2.65 (m, 4 H), 1.50–1.97 (m, 6 H), 0.08 (s, 18 H) ppm [relative to the deuterochloroform signal (7.24 ppm)]; ^{13}C NMR ($CDCl_3$) 82.70, 65.68, 65.28, 42.20, 40.84, 32.36, 29.92, 25.32, 22.69, −0.05, −3.57 ppm.

5b: IR (neat) 2950 (s), 2830 (m), 1250 (s), 1190 (m), 1100 (m), 1080 (s), 1030 (m), 1000 (m), 840 (s) cm^{-1}; ^{13}C NMR ($CDCl_3$) 80.66, 66.02, 62.05, 42.93, 42.54, 32.40, 27.61, 25.30, 23.07, 0.03, −3.41 ppm.

3-[(2-Tetrahydropyranyl)thio]-3-(trimethylsilyl)cyclobutanol (6). To a solution of 0.22 g (0.7 mmol) of 3-[(2-tetrahydropyranyl)thio]-3-(trimethylsilyl)-1-(trimethylsiloxy)cyclobutane in 2 mL of dry methanol cooled at 0 °C was added a few crystals of dry potassium carbonate suspended in 0.2 mL of methanol. The reaction mixture was stirred at 0 °C for 45 min, then water and ether were added, the ether layer was separated, the aqueous layer was extracted twice with ether, and the ether phases were combined, washed twice with water, and dried over $MgSO_4$. After concentration under vacuum, 0.17 g (98%) of a yellow oil was obtained as a mixture of two isomers. Pure **6a** was obtained from hydrolysis of pure **5a** as well as **6b** from **5b**.

6a: IR (neat) 3600–3100 (s), 2840 (s), 1245 (s), 1030 (s), 1005 (s), 840 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 4.71–4.81 (m, 1 H), 4.06–4.11 (m, 1 H), 3.43–3.51 (m, 1 H), 2.14–2.64 (m, 4 H), 1.49–1.92 (m, 8 H), 0.06 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) 82.63, 65.60, 65.43, 41.80, 40.52, 32.37, 29.34, 25.31, 22.58, −3.62 ppm.

Anal. Calcd for $C_{12}H_{24}O_2SSi$: C, 55.33; H, 9.29. Found: C, 55.29; H, 9.55.

6b: IR (neat) 3600–3100 (s), 2930 (s), 2840 (s), 1245 (s), 1110 (s), 1075 (s), 1030 (s), 840 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 5.18–5.23 (m, 1 H), 4.09–4.15 (m, 1 H), 3.94–4.11 (m, 1 H), 3.51–3.59 (m, 1 H), 2.38–2.75 (m, 4 H), 1.50–2.00 (m, 6 H), 0.05 (s, 9 H) ppm; ^{13}C NMR ($CDCl_3$) 80.35, 64.47, 63.12, 43.68, 40.62, 31.65, 27.39, 25.41, 22.15, −3.92 ppm.

3-[(2-Tetrahydropyranyl)thio]cyclobutanol (7a,b). Procedure 1. To a solution of 40 g of 3-[(2-tetrahydropyranyl)-thio]-3-(trimethylsilyl)-1-(trimethylsiloxy)cyclobutane (**5**, 0.12 mol) in 500 mL of THF was added a solution of 150 g of tetrabutylammonium fluoride trihydrate (0.47 mol) in 250 mL of THF and 10 mL of water. The reaction mixture was refluxed for 24 h and then concentrated under vacuum. Water and ether were then added, the phases were separated, the aqueous phase was extracted twice with ether, and the ether phases were combined, washed three times with water, and dried over $MgSO_4$. After concentration under vacuum 20.74 g of a brown oil was isolated and purified by flash chromatography (silica gel/ether) to give 15.14 g (67%) of a yellow oil. The mixture was subjected to preparative HPLC (silica gel, 99:1 hexane–isopropyl alcohol) to give the pure cis isomer **7b** and a mixture of cis and trans isomers **7a,b**. **7b**: IR (neat) 3050–3600 (s), 2930 (s), 2850 (m), 1260 (m), 1230 (m), 1185 (m), 1100 (s), 1075 (s), 1030 (s), 1005 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 4.87–4.90 (m, 1 H), 4.04–4.17 (m, 2 H), 3.47–3.55 (m, 1 H), 2.99–3.10 (m, 1 H), 2.69–2.85 (m, 2 H), 2.59 (br s, 1 H), 1.58–2.03 (m, 8 H) ppm; ^{13}C NMR ($CDCl_3$) 81.98, 64.36, 63.38, 42.37, 42.10, 31.19, 27.58, 25.47, 21.59 ppm. **7a,b** (**7b**:**7a** ratio 1:5): IR (neat) same as **7b**; ^1H NMR ($CDCl_3$) 4.87–4.90 (m, 1 H*), 4.78–4.82 (m, 1 H), 4.54–4.63 (quint, 1 H), 4.04–4.17 (m, 1 H + 2 H*), 3.46–3.66 (m, 2 H + 1 H*), 2.99–3.10 (m, 1 H*), 2.69–2.85 (m, 2 H*), 2.45 (br s, 1 H), 2.35–2.40 (t, 4 H), 1.56–2.04 (m, 6 H + 8 H*), 1.26 (s, 1 H*) ppm; ^{13}C NMR ($CDCl_3$) 82.32, 81.98*, 66.04, 64.63, 64.36*, 63.38*, 42.37*, 42.10*, 40.23, 39.68, 31.30, 31.19*, 30.92, 27.58*, 25.47*, 25.46, 21.75, 21.59* ppm. [Note: The protons or peaks belonging to the minor isomer in the mixture are marked by *.]

Anal. Calcd for $C_9H_{16}O_2S$ mixture: C, 57.41; H, 8.56. Found: C, 57.15; H, 8.64.

Procedure 2. To a solution of 28 g of potassium fluoride dihydrate[26] (0.3 mol) in 150 mL of dimethyl sulfoxide and 25 mL of water was added 23.5 g (0.074 mol) of 3-[(2-tetrahydropyranyl)thio]-3-(trimethylsilyl)-1-(trimethylsiloxy)cyclobutane. The reaction mixture was heated and stirred at 95 °C for 48 h. Then water and dichloromethane were added, the aqueous phase was extracted twice with dichloromethane, and the dichloromethane phases were combined, washed four times with water, dried over $MgSO_4$, and concentrated under vacuum to give 12.31 g of a brown oil, which was purified by flash chromatography (silica gel/ether) to give 8.5 g of **7a,b** as a yellow oil (54%).

3-[(2-Tetrahydropyranyl)thio]cyclobutyl Tosylate (8a,b). To a solution of 14.44 g (0.077 mol) of 3-[(2-tetrahydropyranyl)thio]cyclobutanol in 50 mL of dry dichloromethane cooled at −20 °C under argon was added dropwise a solution of 17.56 g (0.092 mol) of recrystallized *p*-toluenesulfonyl chloride and 30.4 g (0.38 mol) of dry pyridine in 20 mL of dry dichloromethane. The reaction mixture was stirred at 3 °C for 32 h. Crushed ice was then added, and the reaction mixture was stirred for 30 min; after addition of 20 mL of dichloromethane, the organic phase was washed with 10% chilled HCl solution and then twice with water and dried over $MgSO_4$. Concentration under vacuum gave 23.93 g (91%) of a thick yellow oil, which became solid after 3 days at 5 °C. The mixture of isomers was separated by preparative HPLC (silica gel, 99.5:0.5 hexane–isopropyl alcohol) to give pure *cis*-3-[(2-tetrahydropyranyl)thio]cyclobutyl tosylate (**8b**) as a white solid and a mixture of trans and cis isomers **8a,b** (ratio 9:1) as a white solid as well.

8a: mp 53–54 °C; IR (CCl_4) 2940 (s), 2840 (m), 1375 (s), 1185 (s), 1170 (s), 1060 (s), 1030 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 7.77 (d, J = 8.3 Hz, 2 H), 7.34 (d, J = 7.8 Hz, 2 H), 4.98–5.06 (quint, 1 H), 4.72–4.79 (m, 1 H), 3.96–4.04 (m, 1 H), 3.55–3.63 (sept, 1 H), 3.42–3.49 (m, 1 H), 2.17–2.68 (m, 7 H, s inside at 2.45 ppm), 1.55–1.90 (m, 6 H) ppm; ^{13}C NMR ($CDCl_3$) 144.52, 133.33, 129.56, 127.43, 81.93, 73.81, 64.24, 37.57, 37.06, 31.12, 30.89, 25.17, 21.37, 21.28 ppm.

8b: mp 53–54 °C; IR (CCl_4) same as **8a**; ^1H NMR ($CDCl_3$) 7.77 (d, J = 8.3 Hz, 2 H), 7.34 (d, J = 8.3 Hz, 2 H), 4.79–4.86 (m, 1 H), 4.59–4.69 (quint, 1 H), 3.94–4.04 (m, 1 H), 3.42–3.49 (m, 1 H), 2.99–3.10 (m, 1 H), 2.14–2.68 (m, 7 H, s inside at 2.45 ppm), 1.55–1.90 (m, 6 H) ppm; ^{13}C NMR ($CDCl_3$) 144.51, 133.30, 129.49, 127.36, 81.62, 69.74, 64.02, 39.22, 39.10, 30.70, 28.15, 25.10, 21.22 ppm.

Anal. Calcd for $C_{16}H_{22}O_4S_2$: C, 56.11; H, 6.47. Found: C, 56.26; H, 6.36.

3-Mercaptocyclobutyl Tosylate (2a,b). The same procedure as for deprotection of 3-[(2-tetrahydropyranyl)thio]cyclobutanol was used. The trans and cis isomers of 3-mercaptocyclobutyl tosylate (**2a** and **2b**, respectively) were isolated as slightly yellow oils.

2a: IR (neat) 2970 (w), 2930 (w), 1597 (m), 1360 (s), 1195 (s), 1185 (s), 930 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 7.77 (d, J = 8.3 Hz, 2 H), 7.34 (d, J = 8.3 Hz, 2 H), 5.05–5.14 (m, 1 H), 3.53–3.64 (m, 1 H), 2.61–2.71 (m, 2 H), 2.45 (s, 3 H), 2.20–2.29 (m, 2 H), 1.83 (d, J = 5.8 Hz, 1 H, SH proton) ppm; ^{13}C NMR ($CDCl_3$) 144.85, 133.51, 129.82, 127.72, 73.73, 40.71, 27.14, 21.54 ppm.

2b: IR (neat) 2970 (w), 2930 (w), 1597 (m), 1360 (s), 1195 (s), 1185 (s), 940 (s), 840 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 7.77 (d, J = 8.3 Hz, 2 H), 7.34 (d, J = 7.8 Hz, 2 H), 4.59 (quint, J = 7.3 Hz, 1 H), 2.71–2.95 (2 overlapping m, 3 H), 2.45 (s, 3 H), 2.08–2.20 (m, 2 H), 1.84 (d, J = 8.3 Hz, 1 H, SH proton) ppm; ^{13}C NMR ($CDCl_3$), 144.90, 133.55, 129.81, 127.73, 69.00, 43.90, 24.36, 21.54 ppm.

Anal. Calcd for $C_{11}H_{14}O_3S_2$ (**2b**): C, 51.13; H, 5.46. Found: C, 50.88; H, 5.55.

3-Mercaptocyclobutanol (1a,b). To a solution of 0.64 g (2.4 mmol) of mercuric chloride in 80% aqueous acetonitrile (16 mL) was added at room temperature a solution of 0.2 g (1.1 mmol) of 3-[(2-tetrahydropyranyl)thio]cyclobutanol in 11 mL of the same solvent mixture. A white precipitate appeared instantaneously. The reaction mixture was stirred at room temperature for 14 h. The solution was then filtered, and the precipitate was washed with acetonitrile and suspended in dichloromethane (100 mL).

(26) Martin, M.; Sauvetre, R.; Normant, J. F. *Tetrahedron Lett.* **1983**, *24*, 5615–5618.

Hydrogen sulfide was then bubbled through it for 2 h and the solution filtered through a pad of Celite and $MgSO_4$. The filtrate was concentrated in vacuum to give 0.11 g (100%) of a slightly yellow liquid.

1b (cis): IR (neat) 3600–3050 (s), 2950 (s), 2920 (s), 2520 (w), 1415 (m), 1325 (m), 1230 (s), 1110 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 4.01–4.11 (m, 1 H), 2.81–2.94 (m, 3 H), 2.34 (s, 1 H), 1.81–2.00 (m, 3 H) ppm; ^{13}C NMR ($CDCl_3$) 62.54, 45.88, 23.58 ppm.

1b (cis):**1a** (trans) (1:2.5 ratio): IR (neat) same as **1b**; ^1H NMR ($CDCl_3$) 4.64 (quint, J = 6.4 Hz, 1 H), 4.01–4.11 nm, 1 H*), 3.53–3.64 (m, 1 H), 3.02 (s, 1 H + 1 H*), 2.81–2.94 (m, 3 H*), 2.40–2.49 (m, 2 H), 2.24–2.32 (m, 2 H), 1.83–2.00 (m, 1 H + 3 H*) ppm; ^{13}C NMR ($CDCl_3$) 65.68, 62.54*, 45.88*, 43.39, 27.08, 23.58* ppm. [Note: The protons or peaks belonging to the minor isomer in the mixture are marked by *.]

3-(Acetylthio)cyclobutanol (9). To a solution of 123 mg (3 mmol) of sodium hydroxide in 4 mL of water was added 320 mg (3 mmol) of 3-mercaptocyclobutanol mixture. The reaction mixture was then cooled at 0 °C, and 290 μL (3 mmol) of distilled acetic anhydride was added dropwise; the mixture was stirred for 15 min at room temperature and then saturated with solid sodium chloride. The reaction mixture was then extracted twice with dichloromethane, dried over $MgSO_4$, and concentrated under vacuum to give 360 mg (80%) of a colorless liquid.

9b (cis): IR (neat) 3600–3050 (s), 2950 (s), 2920 (s), 1690 (s), 1410 (m), 1350 (m), 1230 (m), 1100 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 4.11–4.21 (m, 1 H), 3.42–3.54 (m, 1 H), 2.92 (br s, 1 H), 2.74–2.85 (m, 2 H), 2.28 (s, 3 H), 1.89–2.02 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$) 196.36, 63.62, 40.99, 30.32, 26.87 ppm.

9b (cis):**9a** (trans) (ratio 1:2): IR (neat) same as **9b**; ^1H NMR ($CDCl_3$) 5.14 (br s, 1 H + 1 H*), 4.41–4.50 (m, 1 H), 4.11–4.21 (m, 1 H*), 3.86–3.95 (m, 1 H), 3.42–3.54 (m, 1 H*), 2.74–2.85 (m, 2 H*), 2.43–2.53 (m, 2 H), 2.22–2.36 (m, 5 H + 3 H*, 2 singlets inside at 2.28 and 2.30 ppm), 1.89–2.02 (m, 2 H*) ppm; ^{13}C NMR ($CDCl_3$) 196.27*, 196.06, 64.63*, 62.63, 40.30*, 38.87, 30.57*, 29.94, 26.36* ppm. [Note: The protons or peaks belonging to the minor isomer in the mixture are marked by *.]

3-(Acetylthio)cyclobutyl Tosylate (10a,b). The same procedure as for 3-[(2-tetrahydropyranyl)thio]cyclobutyl tosylate was used. An isomeric mixture of 3-(acetylthio)cyclobutyl tosylate was isolated (65%) and subjected to preparative HPLC (silica gel 99.8:0.2 hexane–isopropyl alcohol) to give pure trans and pure cis isomers **10a** and **10b**, respectively.

10a: IR (neat) 2940 (m), 1690 (s), 1600 (m), 1360 (s), 1190 (s), 1170 (s), 1060 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 7.77 (d, J = 8.8 Hz, 2 H), 7.36 (d, J = 7.8 Hz, 2 H), 4.96–5.05 (m, 1 H), 3.89–3.98 (m, 1 H), 2.66–2.76 (m, 2 H), 2.45 (s, 3 H), 2.25–2.34 (m, 5 H, s inside at 2.28 ppm) ppm; ^{13}C NMR ($CDCl_3$) 195.39, 144.98, 133.65, 129.92, 127.81, 73.19, 37.22, 31.46, 30.50, 21.66 ppm.

10b: IR (neat) 2950 (m), 1690 (s), 1600 (m), 1360 (s), 1190 (s), 1170 (s), 1050 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 7.78 (d, J = 8.8 Hz, 2 H), 7.35 (d, J = 7.8 Hz, 2 H), 4.70 (quint, J = 7.3 Hz, 1 H), 3.40–3.68 (m, 1 H), 2.69–2.80 (m, 2 H), 2.46 (s, 3 H), 2.15–2.29 (m, 5 H, s inside at 2.27 ppm) ppm; ^{13}C NMR ($CDCl_3$) 195.19, 145.02, 133.46, 129.87, 127.83, 70.12, 38.43, 30.28, 27.58, 21.68 ppm.

Anal. Calcd for $C_{13}H_{16}O_4S_2$ mixture: C, 51.97; H, 5.37. Found: C, 52.31; H, 5.40.

Bis(3-hydroxycyclobutyl) Disulfide (11). To a solution of a mixture of isomers of 3-mercaptocyclobutanol (180 mg, 1.7 mmol) in 10 mL of dry ethanol was added a solution of iodine (220 mg, 0.86 mmol) in 5 mL of dry ethanol. The reaction mixture was stirred for 30 min, and an aqueous sodium bisulfite solution was added followed by water. The aqueous phase was extracted twice with ether. The ether layer was then washed with water, dried over $MgSO_4$, and concentrated under vacuum to give 130 mg (73%) of a white solid, which was recrystallized in chloroform: mp 114–115 °C; IR (CH_2Cl_2) 3500 (m), 2830 (w), 1062 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 4.54–4.62 (m), 4.09–4.17 (m), 3.52–3.63 (m), 2.93–3.03 (m), 2.65–2.75 (m), 2.28–2.44 (m), 1.98–2.08 (m) ppm; ^{13}C NMR ($CDCl_3$) 65.86, 65.81, 62.76, 41.28, 39.42, 39.29, 38.03, 37.59, 34.41 ppm.

Anal. Calcd for $C_8H_{14}O_2S_2$: C, 46.57; H, 6.84. Found: C, 46.29; H, 6.62.

Note: For the proton NMR spectrum, the ratios for the integration of the multiplet at 4.54–4.62 ppm vs. the one at 4.09–4.17 ppm and of the multiplet at 3.52–3.63 ppm vs. the one at 2.93–3.03 are both 2.5:1. The ratio of the sum of the integration of multiplets at 2.65–2.75 and at 1.98–2.08 ppm vs. the integration of the multiplet at 2.28–2.44 ppm is also 2.5:1.

Tetrabutylammonium Fluoride–Deuterium Oxide (TBAF–3D_2O). Deuterium oxide (4 mL) was added to TBAF–3H_2O (6.11 g, from concentration of an Aldrich THF solution), and the solution was heated in a round-bottomed flask with magnetic stirring at 45 °C under vacuum (0.1 mm) for 9 h. More deuterium oxide (4 mL) was added to the flask, and the process was repeated, after which time the waxy solid (5.87 g) showed the absence of a water signal seen in the material before exposure to deterium oxide. The waxy solid was assumed to be TBAF–3D_2O and was used as such.

3-Deuterio-3-[(2-tetrahydropyranyl)thio]cyclobutyl Tosylate (8a,b-d_1). To a solution of 3-[(2-tetrahydropyranyl)-thio]-3-(trimethylsilyl)-1-(trimethylsiloxy)cyclobutane (**5**) (1.6 g, 4.8 mmol) in THF (20 mL) was added a solution of TBAF–3D_2O (5.87 g, 18 mmol) in THF (9.9 mL) and D_2O (0.4 mL). The reaction mixture was heated under reflux for 24 h and then concentrated under vacuum. Water and ether were then added, the aqueous phase was extracted twice with ether, and the ether layers were combined, washed three times with water, and dried ($MgSO_4$). Concentration gave the 3-[(2-tetrahydropyranyl)-thio]-3-deuterio-1-(deuteriooxy)cyclobutane (**7a,b**-d_2) as an oil (0.83 g, 4.4 mmol, 91%). Without further purification this oil was dissolved in dry methylene chloride (3 mL), and the solution was cooled to −20 °C under argon and treated with *p*-toluenesulfonyl chloride (1 g, 5.2 mmol) and dry pyridine (1.75 g, 22 mmol). The reaction mixture was stirred at 3 °C for 40 h and worked up as in the case of **8a,b**. The resultant oil (1.1 g, 73%) was subjected to preparative HPLC (silica gel, 99.5:0.5 hexane–isopropyl alcohol) to give pure *trans*- and *cis*-3-deuterio-3-[(2-tetrahydropyranyl)-thio]cyclobutyl tosylate (**8a**-d_1 and **8b**-d_1, respectively).

8a-d_1 (trans): ^1H NMR ($CDCl_3$) 7.75 (d, J = 8.3 Hz, 2 H), 7.32 (d, J = 8 Hz, 2 H), 5.04–4.95 (quint, 1 H), 4.74–4.71 (m, 1 H), 4.02–3.95 (m, 1 H), 3.47–3.40 (m, 1 H), 2.60–2.54 (m, 2 H), 2.42 (s, 3 H), 2.34–2.24 (m, 2 H), 1.90–1.52 (m, 6 H) ppm; ^{13}C NMR ($CDCl_3$) 144.74, 133.54, 129.76, 127.72, 82.15, 74.08, 64.57, 37.70, 37.14, 31.12, 31.02 (t, J = 24.4 Hz), 25.38, 21.64, 21.56.

8b-d_1 (cis): ^1H NMR ($CDCl_3$) 7.70 (d, J = 8.5 Hz, 2 H), 7.26 (d, J = 8.1 Hz, 2 H), 4.77–4.74 (m, 1 H), 4.62–4.52 (quint, 1 H), 3.96–3.90 (m, 1 H), 3.42–3.35 (m, 1 H), 2.64–2.52 (m, 2 H), 2.37 (s, 3 H), 2.15–2.08 (m, 2 H), 1.85–1.48 (m, 6 H); ^{13}C NMR ($CDCl_3$) 144.78, 133.66, 129.76, 127.72, 81.91, 70.00, 64.37, 39.36, 39.29, 31.02, 28.13 (t, J = 23.5 Hz), 25.40, 21.60, 21.52.

3-Deuterio-3-mercaptocyclobutyl Tosylate (2a,b-d_1). The same procedure as for **2a,b** was used to afford **2a,b**-d_1 as slightly yellow oils.

2a-d_1 (trans): ^1H NMR ($CDCl_3$) 7.70 (d, J = 8.4 Hz, 2 H), 5.06–4.97 (quint, 1 H), 2.64–2.52 (m, 2 H), 2.37 (s, 3 H), 2.23–2.10 (m, 2 H), 1.75 (s, 1 H, SH); ^{13}C NMR ($CDCl_3$) 144.90, 133.48, 129.83, 127.73, 73.74, 40.57, 26.86 (t, J = 24.6 Hz), 21.58.

2b-d_1 (cis): 7.74 (d, J = 8.3 Hz, 2 H), 7.32 (d, J = 8.9 Hz, 2 H), 4.60–4.51 (quint, 1 H), 2.78–2.68 (m, 2 H), 2.42 (s, 3 H), 2.15–2.05 (m, 2 H), 1.79 (s, 1 H, SH); ^{13}C NMR ($CDCl_3$) 144.93, 133.59, 129.83, 127.78, 69.03, 42.77, 24.08 (t, J = 23 Hz), 21.64.

3-Allyl-2,4-dithiabicyclo[3.1.1]heptane (15) and (*Z*)-3-Methyl-2,6-dithiabicyclo[5.1.1]non-4-ene (16). A solution of *trans*-3-mercaptocyclobutyl tosylate (1.22 g, 4.7 mmol) in 80 mL of THF was cooled to 0 °C under argon and treated with *n*-butyllithium (1.6 M, 3.3 mL, 5.3 mmol) in hexane. The reaction mixture was stirred at 0 °C for 15 min, warmed to 25 °C, and stirred for 30 min. Water was added, the solution was extracted twice with ether, and the ether extract was washed three times with water, dried ($MgSO_4$), and concentrated, giving a pale yellow oil. Preparative HPLC (hexane) gave two components, 3-allyl-2,4-dithiabicyclo[3.1.1]heptane (**15**) (80 mg, 20%) and (*Z*)-3-methyl-2,6-dithiabicyclo[5.1.1]non-4-ene (**16**) (13 mg, 3%). 3-Allyl-2,4-dithiabicyclo[3.1.1]heptane (**15**) had a GC t_r of 5.19 min (oven 168 °C): ^1H NMR 5.84–5.72 (m, 1 H), 5.17–5.07 (m, 2 H), 4.93 (t, 1 H), 3.24 (t, 2 H), 2.96–2.76 (m, 2 H), 2.64 (dd, 1 H), 2.47 (t, 2 H), 2.08 (dd, 1 H) ppm; ^{13}C NMR ($CDCl_3$) 133.6, 117.9, 44.9, 38.7, 38.3, 37.4, 32.9 ppm; mass spectrum, m/e (relative intensity) 174 (M + 2, 0.5), 173 (M + 1, 0.7), 172 (M^+, 6.6), 133 (9), 132 (7.2), 131 (M − C_3H_5, 100), 97 (11), 87 (11), 86 (15), 85 (86), 79 (9), 59 (16), 58 (18), 53 (17), 51 (7). (*Z*)-3-Methyl-2,6-dithiabicyclo-

[5.1.1]non-4-ene (16) had a GC t_r of 5.81 min (oven 168 °C): ^{1}H NMR ($CDCl_3$) 6.44 (t, 1 H) ppm.

3-Allyl-1,3-dideuterio-2,4-dithiabicyclo[3.1.1]heptane (15-d_2). A solution of *trans*-3-deuterio-3-mercaptocyclobutyl tosylate **2a**-d_1 (60 mg, 0.23 mmol) in 4 mL of THF was cooled to 0 °C under argon and treated with *n*-butyllithium (1.6 M, 0.19 mL, 0.3 mmol) in hexane. The reaction mixture was stirred at 0 °C for 15 min, warmed to 25 °C, and stirred for 30 min. Workup as for **15** followed by preparative HPLC gave the title compound (6 mg, 30%): GC t_r 5.23 min (oven 168 °C); ^{1}H NMR ($CDCl_3$) 5.88–5.74 (m, 1 H), 5.23–5.07 (m, 2 H), 3.26 (t, J = 6.35 Hz, 1 H), 2.89–2.77 (m, 2 H), 2.65 (dd, 1 H), 2.49 (d, J = 6.84 Hz, 2 H), 2.10 (dd, 1 H) ppm; ^{13}C NMR ($CDCl_3$) 133.70, 118.05, 44.82, 38.73, 38.35, 32.93 ppm; mass spectrum (GC–MS), *m/e* (relative intensity) 176 (M + 2, 0.3), 175 (M + 1, 1.1), 174 (M^+, 16.5), 135 (8), 134 (7), 133 (M – C_3H_5, 100), 89 (5), 88 (5), 87 (18), 86 (74), 85 (18).

Reaction of 1:1 *cis*-3-Deuterio-3-mercaptocyclobutyl Tosylate (2b-d_1) and *trans*-3-Mercaptocyclobutyl Tosylate (2a) with Base. A 1:1 mixture of **2b**-d_1 and **2a** (120 mg total, 0.46 mmol) in 7 mL of THF was treated with *n*-butyllithium (1.6 M, 0.32 mL, 0.51 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 15 min, warmed to room temperature, and stirred for an additional 30 min. Workup and preparative HPLC as in the case of **15** gave **15** with ca. 18% deuterium incorporation as determined by integration of the ^{1}H NMR spectrum. In another experiment a 3.3:1 mixture of **2a** and **2b**-d_1 was treated with *n*-butyllithium. Workup as above followed by HPLC analysis showed ca. 13% deuterium incorporation into **15**.

***cis*-1,3-Bis(allylthio)cyclobutane (20).** A mixture of **15** (35 mg, 0.2 mmol) and excess allyl bromide (0.25 g, 2 mmol) was heated under reflux for 20 h. Excess allyl bromide was removed, and the residue was subjected to preparative TLC (1:1 hexane–methylene chloride) to give the title compound as an oil (25 mg, 63%): GC t_r 7.44 min (oven 168 °C); ^{1}H NMR ($CDCl_3$) 5.84–5.70 (m, 2 H), 5.04 (t, 4 H), 3.23 (q, 2 H), 3.09 (d, 4 H), 2.72–2.62 (m, 2 H), 2.04–1.94 (m, 2 H) ppm; ^{13}C NMR ($CDCl_3$) 134.86, 116.54, 39.36, 34.58, 33.96 ppm; mass spectrum (GC–MS), *m/e* (relative intensity) 202 (M^+ + 2, 0.1), 201 (M^+ + 1, 0.5), 200 (M^+, 8.1), 161 (8), 160 (8), 159 (91), 87 (10), 86 (7), 85 (100), 75 (2), 74 (2), 73 (41).

***cis*-1,3-Cyclobutanedithiol (21). (a) From 20.** Ammonia (10 mL) was condensed in a three-necked flask fitted with a dry ice condenser and a gas inlet tube. *cis*-1,3-Bis(allylthio)cyclobutane (**20**) (20 mg, 0.1 mmol) in ether (2 mL) was added, the solution was cooled to –78 °C, and sodium (10 mg, 0.43 mmol) was added. The mixture was stirred at –78 °C for 30 min, then the flask was warmed to room temperature, and the ammonia was evaporated. Methanol and solid ammonium chloride were added. Evaporation of the solvent gave the title compound (10 mg, 83%) as an oil: GC t_r 3.31 min (oven 130 °C); ^{1}H NMR ($CDCl_3$) 3.23–3.15 (m, 2 H), 3.0–2.96 (m, 2 H), 2.04–1.96 (m, 2 H), 1.83 (d, 2 H) ppm; ^{13}C NMR 47.80, 28.55 ppm; mass spectrum (GC–MS), *m/e* (relative intensity) 122 (M^+ + 2, 2.5), 121 (M^+ + 1, 1.8), 120 (M^+, 30), 89 (2), 88 (2), 87 (33), 85 (20), 61 (13), 60 (100), 59 (52), 55 (23), 53 (19).

(b) From 15. A solution of **15** (42 mg, 0.244 mmol) in 1 mL of THF was added to a slurry of red mercuric oxide (106 mg, 0.5 mmol) and boron trifluoride etherate (70 mg, 0.5 mmol) in 15% aqueous THF (0.42 mL). The red mercuric oxide gradually dissolved and a white precipitate appeared. The mixture was stirred for 30 min, ethyl ether was added, and hydrogen sulfide was bubbled into the solution for 15 min. Precipitated salts were removed by filtration through a pad of Celite and $MgSO_4$. Removal of the solvent left an oil, which was found by GC and GC–MS analysis to be a 1:1 mixture of **21** and **15**.

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Registry No. **1a**, 103562-47-6; **1b**, 103562-48-7; **2a**, 103562-49-8; **2a**-d_1, 103562-51-2; **2b**, 103562-50-1; **2b**-d_1, 103562-52-3; **4**, 103562-53-4; **5a**, 103562-54-5; **5b**, 103562-55-6; **6a**, 103562-56-7; **6b**, 103562-57-8; **7a**, 103562-58-9; **7a**-d_1, 103562-60-3; **7b**, 103562-59-0; **7b**-d_1, 103562-61-4; **8a**, 103562-62-5; **8a**-d_1, 103562-64-7; **8b**, 103562-63-6; **8b**-d_1, 103562-65-8; **9a**, 103562-66-9; **9b**, 103562-67-0; **10a**, 103562-68-1; **10b**, 103562-69-2; **11**, 103562-70-5; **15**, 103562-71-6; **15**-d_2, 103562-72-7; **15** (D-labeled), 103562-73-8; **16**, 103562-74-9; **20**, 103562-75-0; **21**, 103562-76-1; TsCl, 98-59-9; TBAF·3H_2O, 87749-50-6; TBAF·3D_2O, 103562-77-2; Me_3SiCH_2Cl, 2344-80-1; Me_3SiCH_2SH, 18165-76-9; Me_3SiCl, 75-77-4; 3,4-dihydro-2*H*-pyran, 110-87-2; 2-tetrahydropyranyl (trimethylsilyl)methyl sulfide, 98194-90-2; epichlorohydrin, 106-89-8; allyl bromide, 106-95-6.

Supplementary Material Available: Tables of crystal data, atomic coordinates, bond lengths, bond angles, anisotropic temperature factors, and hydrogen coordinates for **8b** and 2D proton NMR spectra of **15** and **16** (11 pages). Ordering information is given on any current masthead page.

Tandem Pd-Catalyzed Elimination–Cyclization

Barry M. Trost* and Serge Mignani

McElvain Laboratories of Organic Chemistry, Department of Chemistry, University of Wisconsin—Madison, Madison, Wisconsin 53706

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Attempted generation of 2-(trimethylsilyl)buta-1,3-diene by palladium-catalyzed elimination of 3-acetoxy-2-(trimethylsilyl)-1,3-butadiene led instead to 3-(trimethylsilyl)-1,3,7-octatriene, a potentially useful building block. Such a product presumably arises by a palladium-catalyzed dimerization of the desired diene. Indeed, the intermediate diene can be smoothly intercepted by the presence of an equivalent amount of a dienophile during the elimination reaction to give good yields of the desired Diels–Alder adducts. The effect of the choice of metal on this reaction is explored. The mechanistic implications of these observations are discussed.

The potential utility of 2-silylated-1,3-butadienes in Diels–Alder reactions has led to a number of routes based upon the chemistry of 1,4-disubstituted-2-butenes.[1] These routes do not easily lend themselves for the preparation

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