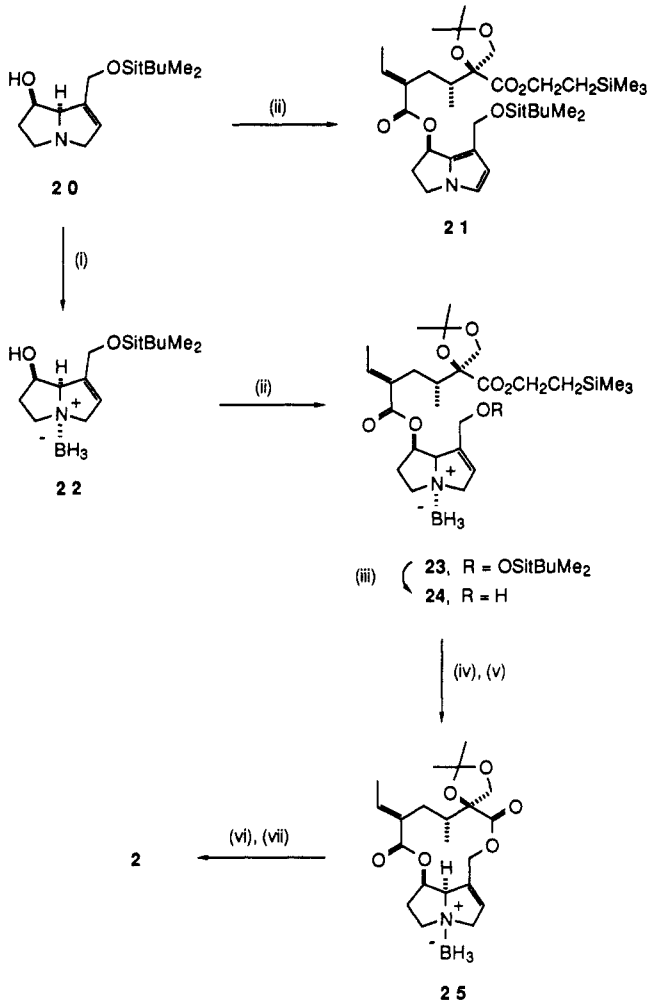
Scheme III[a]



[a] (i) BH_3·THF, THF (86%); (ii) **19**, $(EtO)_2POCl$, Et_3N, THF, 0 °C → room temperature; **20** or **22**, *n*-BuLi, DMAP (cat.), THF, 0 °C, then mix (55%); (iii) NH_4F, MeOH–H_2O, 60–65 °C (65%); (iv) MsCl, Et_3N, CH_2Cl_2; (v) *n*-Bu_4F, MeCN (75% from **24**); (vi) EtOH, 80 °C; (vii) 1 N HCl–THF (1:1) (67% from **25**).

(Scheme II). Unfortunately, condensation of this material with acetaldehyde was thwarted by a facile Dieckmann condensation, and it was necessary to convert **12** to a δ-lactone for introduction of the ethylidene group. This was accomplished by hydrolysis of the acetonide **12** and treatment of the resulting dihydroxy acid **13** with Mukaiyama's reagent.[10] After protection as its MOM ether (**15**), the lactone was condensed with acetaldehyde, and the resulting β-hydroxy lactone was acetylated. Elimination of acetic acid with 1,5-diazabicyclo[5.4.0]undec-5-ene afforded the *E* olefin **16** with only a trace of the *Z* isomer. Removal of the MOM group and hydrolysis of the lactone **17** furnished **18**, which was protected as acetonide **19** in anticipation of its coupling with **20**.[11]

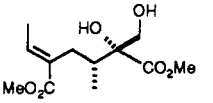
Esterification of the *tert*-butyldimethylsilyl ether **20**[3a] of retronecine[12] with **19** unexpectedly gave the unstable pyrrole **21** in addition to the desired Δ^3-pyrroline ester.[13] It was surmised that protection of **20** against pyrrole formation could be ensured via the pyrrolizidine borane,[14] and when it was found that **20** was converted to **22** in high yield by treatment with borane–THF, the latter became our focal substrate for coupling studies (Scheme III). Thus, **22** was converted to its *O*-lithio derivative and was treated with the acyl phosphate from **19** to give **23**, from which the primary silyl ether was removed to furnish **24**. Treatment of **24** with methanesulfonyl chloride,[15] deprotection of the resulting (trimethylsilyl)ethyl ester, and in situ lactonization to **25** parallels earlier precedent[3b,4a,16] and gave **25** in good yield. Ethanolysis quantitatively removed the borane from **25**, and a final acidic hydrolysis of the acetonide afforded usaramine (**2**, $[\alpha]_D^{24} = +6.8°$), identical with natural material ($[\alpha]_D^{20} + 7.1°$) by comparison of TLC behavior, IR, ^1H and ^{13}C NMR, and mass spectra. Since usaramine has been isomerized photochemically to retrorsine (**3**),[6a] this synthesis also constitutes a route to the latter alkaloid.

Acknowledgment. We are grateful to Dr. C. C. J. Culvenor, Animal Health Research Laboratory, Melbourne, Australia, for a sample of natural usaramine. Financial support was provided by the National Institute for Environmental Health Sciences (ES 03334). Funds for the purchase of a Bruker AM 300 NMR spectrometer were provided by the National Science Foundation (Grant CHE-8216190), the National Institutes of Health (Grant RR04039), and the M. J. Murdock Charitable Trust.

Supplementary Material Available: Spectral and characterization data for compounds **5–19**, **22–25**, and **2** (6 pages). Ordering information is given on any current masthead page.

(10) Mukaiyama, T. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 707.

(11) A parallel sequence from **10** led to the dimethyl ester (i) of (+)-retronecic acid, with spectroscopic properties identical with those reported for (±)-(i) [Ameer, F.; Drewes, S.; Hoole, R.; Kaye, P.; Pitchford, A. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2713].



(i)

(12) Retronecine was obtained by hydrolysis of monocrotaline [Crout, D. H. G.; Davies, N. M.; Smith, E. H.; Whitehouse, D. *J. Chem. Soc., Perkin Trans. 1* **1972**, 671].

(13) It was shown by rigorous exclusion of air that this formal dehydrogenation is not the result of aerial oxidation.

(14) Cf.: Schwartz, M. A.; Rose, B. F.; Vishnuvajjala, B. *J. Am. Chem. Soc.* **1973**, *95*, 612.

(15) The intermediate isolated at this stage was shown by mass spectrometry to be the allylic chloride rather than the mesylate [Jayasinghe, L. R. Ph.D. Thesis, Oregon State University, 1988].

(16) Vedejs, E.; Ahmad, S.; Larsen, S. D.; Westwood, S. *J. Org. Chem.* **1987**, *52*, 3938.

Stereochemical Course of Solvolytic 1,3-Deoxysilylation

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Summary: The stereochemistry of the solvolytic 1,3-deoxysilylation of 4-(trimethylsilyl)-2-butyl *p*-bromobenzenesulfonate has been determined at both reaction centers.

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Sir: We report that the title reaction of stereospecifically ^2H labeled 4-(trimethylsilyl)-2-butyl *p*-bromobenzenesulfonate proceeds predominately or exclusively with inversion at C-4 and with a slight predominance of inversion at C-2. In previously published work it was shown that the solvolysis of alkyl sulfonates with γ-silyl substituents may involve cationic intermediates stabilized by percaudal interaction with the carbon–silicon bond; these can undergo the usual carbonium ion type reactions but additionally may eliminate the silyl group to form cyclopropanes. Results for *cis*-3-(trimethylsilyl)cyclohexyl brosylate show that the reaction can proceed through a "*W*" conformation, giving substitution with retention of configuration and bicyclo[3.1.0]hexane with inversion of configuration at both centers.[1] Theoretical calculations on a model system showed that the interaction of the carbon p orbital with the back lobe of the γ-CSi bond provides for a uniquely strongly stabilized conformation.[2]

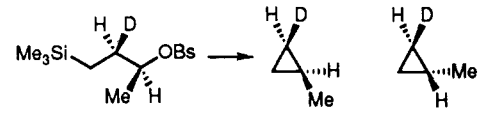
However, solvolysis of 4-(trimethylsilyl)-2-butyl brosylate gave predominately racemic substitution products, suggesting that the transition state could also be stabilized in an endo-sickle conformation as well.[3] This led us to determine the stereochemical course of the accompanying deoxysilylation reaction which produces 27% of methylcyclopropane in 97% trifluoroethanol–water (97T) and 15% in 80% ethanol–water (80E). 1,3-Deoxystannylation reactions of norbornyl mesylates[4] and of tertiary alcohols[5] generally proceed with inversion of configuration at the electrofugic center and either inversion or inversion with some retention at the nucleofugic center. A mixture of (2*S*,3*S*)- and (2*R*,3*R*)-4-(trimethylsilyl)-2-butyl-*3-d* *p*-bromobenzenesulfonate, **1**, was prepared by a reaction sequence involving deuteroboration of *cis*-2-butenyltrimethylsilane. Threo (**2**) and erythro (**3**) enriched samples of 4-(trimethylsilyl)-2-butyl-*2,3,4-d*$_3$ *p*-bromobenzenesulfonate were prepared by a route involving stereospecific diimide reduction of both *E* (95%) and *Z* (80%) enriched 3-(trimethylsilyl)-2-propenol-*2,3-d*$_2$.[6]

A 0.1 M solution of **1** in 97T was buffered with 1.1 equiv of 2,6-lutidine and allowed to react for 10 half-lives in a sealed reaction vessel. The volatile methylcyclopropane was vacuum transferred into an NMR tube containing methylene chloride and the tube sealed. The experiment was also conducted in 80E and 90E, and the results are presented in Scheme I.

In each case, the ^2H NMR showed peaks at 0.11 and 0.56 ppm. *cis*-1-Methylcyclopropane-*2-d* (**4**), formed by inversion at the α-carbon, was assigned to the upfield resonance on the basis of published assignments[7] while *trans*-1-methylcyclopropane-*2-d* (**5**), formed with retention of configuration at the α-carbon, was assigned the downfield resonance. In each solvent there is at least a slight preference for cyclopropane formation with inversion at Cα. In 97T, this preference is nearly 2:1.

Scheme II shows the three possible methylcyclopropanes which could result from the solvolysis of the threo and the erythro β,γ-labeled brosylates. For the threo isomer, inversion at Cγ would produce two cyclopropanes in equal proportions. Both would have the ring hydrogens cis to one another and the methyl group either cis (**6**) or trans (**7**) to the hydrogens. Retention of configuration (from the threo isomer) would place the ring hydrogens trans to one another with the methyl group cis to one hydrogen and trans to the other (**8**).

Scheme I

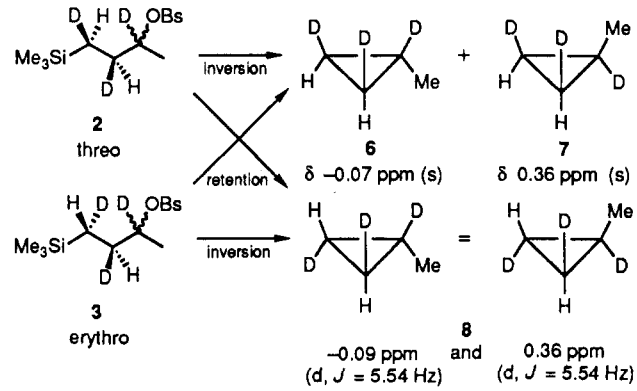


1 **4** **5**

δ*	0.11 ppm	0.56 ppm
97T	65%	35%
80E	59%	41%
90E	55% inversion	45% retention

* Chemical shift in the ^2H NMR spectrum (55.4 MHz, CH_2Cl_2).

Scheme II[a]



[a] Determined by ^1H NMR spectroscopy (^2H decoupled) in $CDCl_3$ at 360 MHz.

By use of the procedure described for methylcyclopropane isolation from **1**, both the threo- and the erythro-enriched brosylates were solvolyzed in 97T, and the volatile material was transferred to NMR tubes containing deuteriochloroform. The deuterium decoupled, ^1H NMR spectrum of the product from the threo-enriched isomer (95% **2**, 5% **3**) consisted of ring proton singlets at −0.07 and 0.36 ppm; each had a line width of 1.2 Hz and was flanked by a doublet (J = 5.6 Hz) that integrated for 10% and was presumed to be 8. The methylcyclopropanes from the erythro enriched brosylate (72% **3**, 28% **2**) likewise showed two sets of resonances for the ring protons; one set contained a doublet (J = 5.54 Hz) centered at −0.090 ppm and a singlet at −0.087 ppm in the ratio of 75:25 (±4%), while the second set showed a similar pattern centered around 0.36 ppm. Thus the stereochemistry of the 1,3-elimination at the carbon bearing silicon is predominately, if not exclusively, inversion.

These results are consistent with the observation that the solvolytic substitution products from this reaction are racemic or nearly so[8] and support the conclusion that the silicon-promoted γ-carbon participation involves both "*W*" and endo-sickle transition state conformations.

Acknowledgment. Support from the National Science Foundation, Grants No. CHE-85-06682 (project support) and No. CHE-81-05004 (NMR instrumentation), is gratefully acknowledged.

Supplementary Material Available: Schemes III and IV and information about the preparation, physical constants, and spectral data of the compounds that appear in Schemes III and IV (14 pages). Ordering information is given on any current masthead page.

(1) Shiner, V. J., Jr.; Ensinger, M. W.; Kriz, G. S. *J. Am. Chem. Soc.* **1986**, *108*, 842–844.
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(5) Fleming, I.; Urch, C. J. *J. Organomet. Chem.* **1985**, *285*, 173. Crawford, R. J.; Erickson, G. L. *J. Am. Chem. Soc.* **1967**, *89*, 3907–3908.
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(7) Yang, G. K.; Bergman, R. G. *Organometallics* **1985**, *4*, 129.
(8) See ref 3; recent, more accurate results show a slight predominance of retention.