Desilylative Transannular Cyclization of Nine-Membered α-Silyl (*E*)-γ-Epoxy Sulfones

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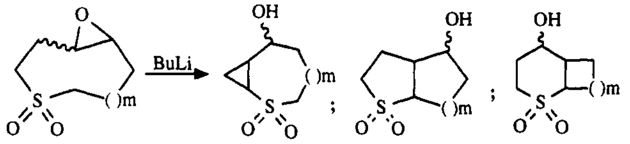
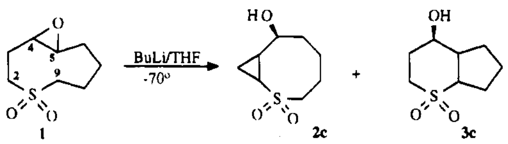
Anionic desilylation of α-silylated (*E*)-4,5-epoxythiacyclononane 1,1-dioxides results in formation of transannular cyclization products whose distribution is independent of the stereochemistry of the starting material. Unlike the species formed by direct BuLi metalation,[1] the intermediate arising from the 9-silyl regioisomer rapidly and indiscriminately attacks either epoxidic carbon forming both cis- and trans-joined bicyclic products. This lack of selectivity suggests the reactive intermediate is not a hypervalent silicon species, but is more likely a carbanion which, being associated to a large cation (K^+ or Bu_4N^+) is less discriminating than that arising from BuLi metalation. The intermediate formed by desilylation of the 2-silyl regioisomer appears to cyclize relatively slowly, such that transfer of the carbanionic functionality from C-2 to C-9 becomes competitive with cyclization. With this substrate an unexpected phenomenon has emerged, namely that t-BuOK may act as a base or a desilylating agent depending on the temperature.

In a recent paper we have reported on the butyllithium-promoted transannular cyclization occurring upon low-temperature metalation of medium size (8- and 9-membered) (*E*)- and (*Z*)-γ-epoxy sulfones.[1] The more relevant observations made in the course of that study can be summarized as follows. (i) Attack by the metalated carbon on the epoxide carbons occur stereospecifically with configurational inversion. (ii) The cyclization is stereoconvergent regarding the ring junction, cis-joined bicyclic (kinetic) products being formed irrespective of the epoxide stereochemistry. (iii) As there are two carbons α to the sulfone grouping, two regioisomeric α-lithio sulfones are formed on metalation, C_2Li and C_nLi (n = 8, 9), each of which may attack either transannular epoxidic carbon. The reaction occurs highly regioselectively, however. Thus, the C_2Li regioisomers react exclusively at C-4, giving rise to type A products independently of ring size and epoxide stereochemistry. On the other hand, the C_nLi regioisomers react specifically at C-5 in the *E* epoxides, forming type B products, while in the 9-membered *Z* epoxide attack occurs at both C-4 and C-5 giving rise to type B and C products competitively. (iv) The distribution of products arising from the two α-carbons may change drastically with the metalation mode, portionwise or at once. For example, the product ratio **2c**/**3c** from epoxy sulfone **1** changed from 7/3 to 1/4 according to whether metalation was carried out by single or, respectively, portionwise addition of BuLi. This behavior suggested that the two regioisomeric lithio derivatives were not interconverting rapidly except in the presence of unmetalated substrate. In this hypothesis, when a full equivalent of BuLi is added at once the product distribution merely reflects the relative metalation ratio at the α-carbons, while in portionwise metalation, where the excess sulfone, acting as a H^+-transfer agent, effectively mediates the interconversion of the α-metalated regioisomers, the product ratio largely reflects their relative specific cyclization rates.

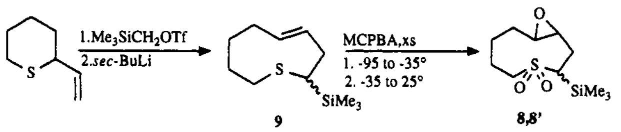


E or Z; m = 1,2 A B C



1 2c 3c

Scheme I



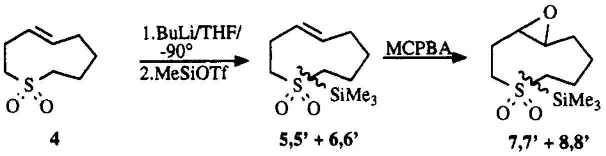
9 8,8'

In relation to these phenomena, we felt it would be of interest to examine the products of cyclization arising under conditions where the potential carbanionic sites, C-2 and C-9, would be active one at a time rather than both simultaneously.

We have achieved this goal via anionic desilylation of regiospecifically α-silylated (*E*)-γ-epoxy sulfones, and this paper reports the synthesis of the 9- and 2-trimethylsilyl derivatives, **7** and **8**, of the 9-membered (*E*)-epoxy sulfone, and the products arising therefrom by anionic desilylation.

Results

Synthesis. Epoxy sulfone **1** is not suitable for direct metalation–silylation since transannular epoxide ring opening would be much too fast to allow interception, to any significant extent, of the metalated intermediates. To circumvent this difficulty epoxidation was deferred after silylation of the alkene sulfone **4**. In order to minimize transannular cyclization of the latter,[2] we carried out metalation at very low temperature while using a reactive silylating agent to quench the lithio sulfone intermediate. The crude silylation product appeared to contain (^{13}C, NMR) the two diastereomers of both the 9- and 2-silylated regioisomers, **5**, **5′** and **6**, **6′**, along with unreacted starting material and minor unidentified side products. The presence of four silylated species giving sharp signals in the room-temperature ^{13}C NMR spectrum indicates that these 9-membered cyclic alkene sulfones do not undergo



4 5,5′ + 6,6′ 7,7′ + 8,8′

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[1] Cerè, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Org. Chem.* **1991**, *56*, 4513–4520.

[2] Cerè, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Org. Chem.* **1988**, *53*, 5689–5694 and previous papers in the series.

0022-3263/92/1957-1457$03.00/0

Table I. Product Distributions from Desilylation of 9-(Trimethylsilyl)-4,5-epoxythiacyclononane 1,1-Dioxide (7,7′) in THF

run	diastereomer ratio, 7/7′	desilylating agent, equiv %	temp, °C	time, h	3c, %	3t, %	10c, %	10t, %	1, %
1	100/0	CsF, xs	35	18	47	30	7	7	10
2	55/45				54	16	7	7	17
3	55/45				41	11	3	3	42
4	100/0	TBAF/SiO_2, 15		2.5	39	42	8	10	
5	55/45			2.5	37	45	6	12	
6	100/0	t-BuOK, 20		0.25	26	57	4	13	
7	55/45				27	55	4	14	
8	100/0	t-BuOK, 30	−70	0.25	73	15	6	6	
9				1	70	16	7	6	
10				4	71	17	6	6	

Table II. Product Distributions from Desilylation of 2-(Trimethylsilyl)-4,5-epoxythiacyclononane 1,1-Dioxide (8,8′) in THF

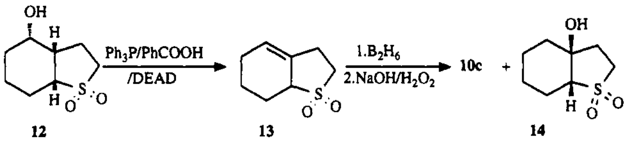
run	diastereomer ratio, 8/8′	desilylating agent, equiv %	temp, °C	time, h	2c, %	2t, %	3c, %	3t, %	11, %	1, %
1	100/0	CsF, xs	35	20	34				6	60
2	40/60				11				3	86
3	100/0	t-BuOK, 20	35	1	58	11	10	21		
4	40/60				58	10	12	21		
5	100/0	t-BuOK, 30	−10	1.5	68		12	20		
6			−40	2.5	61		27	3	5	6
7			−70	8	7				51	41
8		t-BuOK, 80		4	6				78	16
9	40/60	t-BuOK, 30		4	3				60	37

fast (in the NMR time scale) epimerization via configurational inversion of the plane of chirality associated with the trans double bond.[3] However, no significant stereo- or regioisomer separation could be achieved by either chromatography or fractional crystallization. Therefore, the crude was oxidized to a mixture of two diastereomeric pairs of regioisomeric 9- and 2-trimethylsilyl epoxy sulfones **7**, **7′** and, respectively, **8**, **8′** in ca. 4:1 ratio. The major pair could be separated by crystallization as a ca. 70:30 mixture of diastereomers, whose major component **7** was obtained pure by chromatography. The minor component **7′** could only be obtained as a ca. 50:50 mixture with **7**. The 2-silylated regioisomer **8**, **8′** could not be separated from the mother liquor, and for its synthesis the approach depicted in Scheme I was applied.

Alkylation of 2-vinylthiane with (trimethylsilyl)methyl triflate gave 1-[(trimethylsilyl)methyl]-2-vinylthianium triflate which, treated with *sec*-butyllithium, a nondesilylating base,[4] rearranged via the ylide to (*E*)-2-(trimethylsilyl)thiacyclonon-4-ene (**9**). Peracid oxidation of the latter was carried out in two stages, first at −95 °C, a temperature low enough to avoid sila-Pummerer rearrangement of the intermediate sulfoxide,[5] and then raising the temperature up to ambient to effect the epoxidation. The product was a ≈5:2 mixture of diastereomers whose major component **8** was obtained pure by crystallization. The minor isomer **8′** could not be separated and was obtained as a ca. 60:40 mixture with **8**.

Desilylation and Transannular Cyclization. The distributions of products arising from desilylation of **7** and **8** and mixtures thereof with their respective diastereomers **7′** and **8′** are collected in Tables I and II. Although solid CsF in THF has been reported to be a serviceable reagent for desilylation of C–Si bonds,[6] it has proven to be unsatisfactory in our case. In addition to being extremely slow, erratic results were observed (Table I, runs 1–3; Table II, runs 1, 2) with substantial protodesilylation product being formed along with products of transannular cyclization. Actually, with the 2-silyl derivative protodesilylation appears to be by far the major reaction course. Perhaps heterogeneity plays a role; however, tetrabutylammonium fluoride on silica (TBAF/SiO_2),[7] also a heterogeneous desilylating agent, while causing no detectable protodesilylation (Table I, runs 4, 5) gave nicely reproducible results. Potassium *tert*-butoxide was eventually chosen as desilylating agent since, confirming previous observations,[8] it was found to be the faster and more easily controllable reagent for our purposes also.

Scheme II



Products. Compounds **1**, **2c**, **2t**, **3c**, and **3t** have been described previously.[1] To establish the structure of the **10c**, **10t** pair we attempted to carry out configurational inversion of the known epimeric alcohol **12**.[1] However, when **12** was subjected to the Mitsonobu reaction conditions (Scheme II)[9] the bridgehead alkene **13** was obtained as the only product. This material could nevertheless be successfully utilized toward the synthesis of **10c** via hydroboration–oxidation[10] as shown in Scheme II. A ≈1:1 mixture of the bridgehead alcohol **14** and its regioisomer **10c** was obtained. The latter subjected to basic conditions (t-BuOK/THF) isomerized to an epimeric mixture of **10c** and **10t**.

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(3) Cerè, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A.; Lunazzi, L. *J. Org. Chem.* **1980**, *45*, 3613–3618. *trans*-Thiacyclononenes are characterized by enantiomerization barriers below 20 kcal/mol, too low to permit separation by ordinary chemical means of isomers **5** and **6** from their respective diastereomeric conformers **5′** and **6′**.

(4) Cooke, S.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1978**, 714–716.

(5) (a) Brook, A. G.; Anderson, D. G. *Can. J. Chem.* **1968**, *46*, 2115–2118. (b) Vedejs, E.; Mullins, M. *Tetrahedron Lett.* **1975**, 2017–2020.

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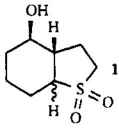
(8) (a) Efferberger, F.; Spiegler, W. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 265; (b) *Chem. Ber.* **1985**, *118*, 3872–3899.

(9) (a) Mitsonobu, O.; Eguchi, M. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3427–3434. (b) Mitsonobu, O. *Synthesis* **1981**, 61–72.

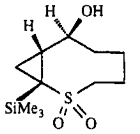
(10) Brown, H. C.; Mandal, H. K. *Synthesis* **1980**, 153–155.

Discussion

The first observation emerging from the data is that, under identical conditions, the product distributions resulting from the pure substrates **7** and **8** or from mixtures thereof with their respective diastereomers **7′** and **8′** are essentially identical (compare runs 4 and 6 with, respectively, 5 and 7 in Table I and runs 3 and 5 with, respectively, 4 and 9 in Table II). Thus, the intermediates from which cyclization occurs retain no memory of their precursors' configuration. As a consequence, for the purpose of the present work, establishing the relative configurations of the diastereomers is inconsequential. (However, from the ^{1}H NMR spectrum (Experimental Section) **8** appears to be the *RRR,SSS* diastereomer; for **7** the configurational assignment is less clear cut. (See supplementary material for a discussion of the ^{1}H NMR in relation to the geometries generated by force field computations).



10c,10t



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The desilylated intermediate from **7** appears to cyclize neither stereo- nor regiospecifically (Table I): compound **3c**, which was the only product in the BuLi cyclization, is formed here along with its epimer, **3t**, and both cis and trans epimers of the regioisomer **10** arising from the alternative regiochemical course (attachment of C-9 to C-4). That the trans epimers of either regioisomer are, at least in part, kinetic products is evident from the −70 °C experiments (Table I, runs 8–10). At this temperature, where no appreciable cis → trans isomerization was proven to occur, the trans epimers are formed to the extent of ca. 15–20% and, respectively, 50%. To these extents **3** and **10** must be kinetic in origin. Therefore, unlike those formed by direct BuLi metalation, the *reactive* species formed by desilylation are very unselective. The data (Table I, runs 4, 5 and 6–10) indicate that the reactive intermediate partitions between attack at C-5 and C-4 to give **3c**, **3t** and, respectively, **10c**, **10t**, in a ratio that, at a given temperature, is independent of the desilylating agent. This finding, and the independence of product distribution of the configuration of the silylated substrate, strongly indicate *the intermediate responsible for cyclization is likely not a hypervalent silicon species.*[11] Rather, the lack of both stereo- and regioselectivity suggests it to be a very nearly free carbanion.[16] Of course, this conclusion does not rule out the possibility that the latter may arise by cleavage of a hypervalent silicon precursor preliminarily formed by alkoxide addition to silicon. Further support for the involvement of a discrete carbanion intermediate, other than a hypervalent silicon adduct, comes from the observation that in the reaction of the 2-silyl derivative **8** about one-third of the cyclization product arises from a carbanionic species centered at C-9 (Table II, runs 3–6). This implies transfer of the carbanionic functionality, C-2 → C-9, a process which would be hard to envision for a hypervalent species where the silicon substituent was still covalently bound to the α-carbon, though quite compatible with a carbanion more or less loosely associated to a counter-ion.[16]

It is interesting to note, however, that transfer of the carbanion functionality appears not to occur appreciably in the opposite C-9 → C-2 direction. Since transfer in either direction would be likely to occur at comparable rates, this apparent discrepancy must be a consequence of transannular cyclization occurring much more rapidly from the C-9- than from the C-2-carbanion. In other words the latter cyclizes slowly enough that proton scrambling between the α positions (either intra- or intermolecularly) becomes competitive. Apparently the C-2-carbanion partitions ca. 70:30 toward cyclization and transfer, thus confirming that the latter is not a fast process.[1]

The fraction of the C-2 carbanionic species undergoing cyclization leads to **2c** as the sole *kinetic* product. The trans epimer **2t** is found in fact only in the higher temperature runs (Table II, runs 3, 4) and apparently arises from base-catalyzed isomerization of **2c**. Apparently the transition states of the alternative regio- and stereochemical courses still remain unavailable for the species involved here, just as they were for that formed by BuLi metalation.[1]

The product distribution from **8** shows further peculiarities; in particular, on decreasing temperature desilylation–cyclization becomes a progressively minor reaction course giving way to protodesilylation and deprotonation–cyclization to a *silylated* 6.1.0 bicyclic (Table II, runs 7–9). Together, compounds **1** and **11** account for more than 90% of the product at −70 °C. Since the former must arise from *tert*-butoxide attack at silicon while the latter necessarily involves the carbanionic species formed by proton removal α to silicon (and sulfur), it appears that t-BuOK may act as a base or as a desilylating agent depending on temperature. Such temperature-dependent chemoselectivity could be related to a temperature effect on the degree of aggregation of the alkoxide. However, the phenomenon is substrate-specific also, for it is observed with substrate **8** but not with **7** or other simple sulfones, such as thiane 1,1-dioxide.[17]

Experimental Section

General Data. Unless specified otherwise ^{1}H and ^{13}C NMR spectra were recorded at 200 and 20 or 50 MHz, respectively, in $CDCl_3$ solvent. Single frequency off-resonance ^{13}C spectra were obtained by irradiation at δ −4 in the proton spectrum. Ambiguities in the signal multiplicities were resolved by DEPT experiments. The ^{1}H NMR spectral assignments for **7** and **8** were secured by means of two-dimensional ^{1}H-^{13}C chemical shift correlation. Where two or more ^{13}C assignments are given in parentheses, they are interchangeable. Geometries and relative energies of diastereomers **7**, **7′** and **8**, **8′** (see supplementary material) were computed by molecular mechanics using the MMX force field.[18] Solvents and reagents were obtained dry as follows:

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(11) Although the anionic desilylation of organosilicon compounds containing a C–Si bond produces species endowed of carbanionic reactivity and forms the basis of widely used methodologies for tranferring alkyl, aryl, hydroxyalkyl, and heteroatomic groups,[12] the actual nature of such species is open to question. The fact that protonation[13] as well as hydroxyakylation[14] has been found to occur stereospecifically with configurational retention is considered suggestive evidence that the reacting intermediate is a hypervalent silicon species.[15] However, the stereochemical probe has been so far applied only to cases where the potential carbanion (α-OH[13] or α-phenylthio[14]) is much less stabilized than that (α-sulfonyl) involved in our case. Work aimed at applying the stereochemical probe to α-silyl sulfones is being undertaken in our laboratory.

(12) Review: Furin, G. G.; Vyazankina, O. A.; Gostevsky, B. A.; Vyazankin, N. S. *Tetrahedron* **1988**, *44*, 2675–2749.

(13) Nakada, M.; Urano, Y.; Kobayashi, S.; Ohno, M. *J. Am. Chem. Soc.* **1988**, *110*, 4826–4827.

(14) McDougal, P. G.; Condon, B. D. *Tetrahedron Lett.* **1989**, 789–790.

(15) Kira, M.; Sato, K.; Sakurai, H. *J. Am. Chem. Soc.* **1988**, *110*, 4599–4602.

(16) That the reactive carbanionic species formed on desilylation is very unselective is consistent with the counterion, potassium or tetrabutylammonium, allowing for much greater looseness than was the case with lithium.

(17) Cerè, V. Unpublished results.

(18) Purchased from Serena Software, P. O. Box 3076, Bloomington, IN 47404-3076.

THF was distilled from benzophenone ketyl; acetonitrile was refluxed over, and distilled, from CaH_2 and stored over molecular sieves (3 Å); before use, CsF was gently flame-heated in vacuo until evolution of water ceased and then maintained at 20 °C (0.1 mm) for 30 min; TBAF on silica gel was heated at 100 °C for 2 h and used immediately. Melting points are uncorrected. The trivial α and β notations are used to indicate the hydroxy group in bicyclic compounds to be on the opposite or, respectively, on the same side of the H atom at the nearest bridgehead.

Compounds **1**, **2c**, **2t**, **2c**, and **3t** have been described previously.[1]

(*E*)-Thiacyclonon-4-ene 1,1-Dioxide (4). To a CH_2Cl_2 solution of (*E*)-thiacyclonon-4-ene[19] (2 g, 14.3 mmol, in 90 mL) was added 85% *m*-CPBA (6.1 g, 30 equiv), and the mixture was stirred at rt for 6 h. After the mixture was cooled to 0 °C, *m*-chlorobenzoic acid was filtered off and the filtrate was washed with 10% aqueous $NaHCO_3$ and dried over $CaSO_4$. The residue after solvent evaporation was crystallized (hexane–benzene) to give **4** (2.24 g, 91%), mp 82–83 °C. ^{13}C NMR: δ 133.7 (C_5); 128.3 (C_4); 61.2 (C_9); 58.6 (C_2); 32.1 (C_6); 27.6 (C_3); 23.9 (C_7); 20.0 (C_8). ^1H NMR: δ 5.62 (m, 2 H, HC=CH); 3.28 (m, 3 H); 2.95 (m, 1 H); 2.44 (m, 3 H); 1.80 (m, 5 H). Anal. Calcd for $C_8H_{14}SO_2$: C, 55.14; H, 8.10, S, 18.40. Found: C, 54.91; H, 8.14; S, 18.26.

(*E*)-9-(Trimethylsilyl)-4,5-epoxythiacyclononane 1,1-Dioxide (7). Sulfone **4** (0.40 g, 2.3 mmol, in 23 mL THF) was metalated at −90 °C with BuLi (2.4 mmol, 1.6 M in hexane) and quenched after 5 min with trimethylsilyl trifluoromethanesulfonate (0.54 g, 2.6 mmol). After 20 min the mixture was allowed to warm to rt and the solvent was evaporated. From ^{13}C NMR analysis the residue appeared to contain, besides ≈10% unreacted **4**, four silylated products **5**, **5′**, **6**, and **6′** in a ratio ≈6:1:1:1. Since no appreciable separation could be achieved by either chromatography or crystallization, the mixture was epoxidized and worked up as described for **4**. Crystallization (hexane–benzene) of the crude oxidation product yielded a solid (0.24 g, 42%) containing only the two diastereomers of the 9-silylated regioisomer in a ratio **7**:**7′** ≈ 7:3. Flash chromatography of this material (silica gel, Et_2O/petroleum ether 80/20) gave the major component **7**; cryst hexane–benzene (84 mg, 35%), mp 152–153 °C. ^{13}C NMR: δ 59.3, 58.8 (C_4, C_5) 56.6 (C_9); 54.2 (C_2); 32.0 (C_6); 25.1, 25.0 (C_3, C_8); 22.7 (C_7); −0.6 (CH_3). ^1H NMR: δ 3.42, 3.18 (m's, 1 H each, C_2HH; low field part, AB, of an ABMX system; *J* (Hz): AB 15.1, AM 2.5, AX 10.0, BM 2.5, BX 8.4, MX, 13.0); 2.85 (ddd, *J* = 10.7, 1.2, 2.0 Hz, 1 H, C_5H); 2.73 (ddd, *J* = 9.7, 2.5, 2.3 Hz, 1 H, C_4H); 2.55 (m, 1 H, C_3H) partially superimposed to 2.48 (dd, *J* = 8.3, 1.0 Hz, 1 H, C_9H); 2.29 (m, 1 H, C_6H); 2.00 (m, 2 H, C_7HH); 1.84 (m, 1 H, C_8H); 1.65 (m, 1 H, C_3H); 1.30 (m, 1 H, C_8H); 1.07 (m, 1 H, C_6H); 0.25 (s, 9 H, Me's). Anal. Calcd for $C_{11}H_{22}O_3SSi$: C, 50.34; H, 8.45; S, 12.22. Found: C, 50.48; H, 8.51; S, 12.34.

The minor isomer, **7′**, had the following ^{13}C NMR: δ 58.6, 57.5, 56.7 (C_4, C_5, C_9); 53.5 (C_2); 27.8, 26.4 (C_3, C_6); 22.9, 22.1 (C_7, C_8); −0.9 (CH_3).

(*E*)-2-(Trimethylsilyl)thiacyclonon-4-ene (9). A MeCN solution of 2-vinylthiane[19] (1.4 g, 11 mmol, in 22 mL) was reacted with (trimethylsilyl)methyl trifluoromethanesulfonate (2.73 g, 12 mmol) added dropwise at 0 °C.[20] The mixture was allowed to warm to rt and stirred for 3 h. Solvent evaporation at reduced pressure left a solid (3.6 g, 100%) consisting of a mixture of trans and cis sulfonium salts in a ≈85:15 ratio. This crude was dissolved in 60 mL of THF and treated at −50 °C with *sec*-BuLi (9.7 mL, 1.2 M in hexane, 11.6 mmol). The temperature was raised to −15 °C stirring being continued for 1.5 h. After aqueous quenching and workup as for (*E*)-thiacyclonon-4-ene[19] the product was distilled to give 1.7 g (73%) of the title compound, bp 105–106 °C (0.6 mm). The *E* configuration of the double bond was confirmed by protodesilylation (Bu_4NF/EtOH) yielding the known sulfide (*E*)-thiacyclonon-4-ene.[19] ^{13}C NMR: δ 133.2 (C_5); 127.1 (C_4); 38.5 (C_2); 37.2 (C_3); 34.5, 32.3 (C_9, C_6); 25.5, 24.1 (C_7, C_8); −2.6 (CH_3). The ^{13}C NMR spectrum (in CD_2Cl_2) did not show any appreciable change from room temperature down to −80 °C, indicating this substituted 9-membered *trans*-thiacycloalkene essentially populates a single conformer.[3] ^1H NMR (60 MHz): δ 5.60 (m, 2 H, CH=CH); 2.55 (m, 4 H); 1.80 (m, 7 H); 0.20 (s, 9 H, Me_3). Anal. Calcd for $C_{11}H_{22}O_2SSi$: C, 50.34; H, 9.00; S, 13.01. Found: C, 50.62; H, 8.98; S, 13.06.

(*E*)-2-(Trimethylsilyl)-4,5-epoxythiacyclononane 1,1-Dioxide (8). Sulfide **9** (214 mg, 1 mmol in 20 mL CH_2Cl_2) was oxidized with 85% *m*-CPBA (0.73 g, 3.6 mmol) added portionwise at −90 °C. The temperature was slowly (6 h) raised to −35 °C and then to rt, stirring being continued for 14 more h. After workup (see **4**) the mixture, consisting (^{13}C NMR) of two diastereomers in a ≈7:3 ratio, was crystallized from hexane–benzene to give the major isomer (0.11 g, 60%) mp 168–168.5 °C. ^{13}C NMR: δ 60.9, two signals (C_4, C_5); 56.9 (C_9); 51.9 (C_2); 31.4 (C_6); 27.9 (C_3); 23.1 (C_8); 20.2 (C_7); −1.6 (CH_3). ^1H NMR: 3.11 (m, 2 H, C_9HH); 2.91 (ddd, *J* = 10.7, 2.5, 2.5 Hz, C_5H); 2.76 (dd, *J* = 11.6, 1.0 Hz, C_2H): 2.59 (ddd, *J* = 10.6, 1.6, 1.5 Hz, 1 H, C_4H); 2.35 (apparent t) superimposed to 2.32 (m) (2 H overall, C_3H and C_6H); 2.20 to 1.75 (m, 2 H, C_7HH); 1.65 to 1.30 (m's, 3 H overall, C_3H and C_8HH), 0.95 (m, 1 H, C_6H). (The couplings of the methyne proton α to both S and Si at δ 2.76, indicating it has a quasi axial setting, establish **8** is the *RRR*,*SSS* diastereomer. See supplementary material for conformational analysis based on force fields computations.) Anal. Calcd for $C_{11}H_{22}O_3SSi$: C, 50.34; H, 8.45; S, 12.22. Found: C, 50.21; H, 8.36; S, 12.34.

From the mother liquor the minor diastereomer **8′** was recovered as a ≈60:40 mixture with **8**. ^{13}C NMR: δ 61.0 (C_9); 58.2, 55.7, 53.3 (C_4, C_5, C_2); 30.2, 28.3 (C_6, C_3); 23.4 (C_8); 20.2 (C_7); −1.4 (CH_3).

Sulfide **9** was also oxidized using only 2 equiv of *m*-CPBA. The product was a ≈60:40 mixture of diastereomeric conformers, **6**, **6′**, of the alkene sulfone, identical to two of the four products obtained in the direct silylation of sulfone **4** (see text above). Further oxidation of **6**, **6′** gave **8**, **8′** in the same ratio (≈7:3) as in the one-pot oxidation. For the ^{13}C NMR spectra of **5**, **5′**, **6**, and **6′** see supplementary material.

Desilylation–Cyclization of (*E*)-9-(Trimethylsilyl)-4,5-epoxythiacyclononane 1,1-Dioxide. The silylated epoxy sulfone **7**, or 50:50 mixtures of **7**, **7′** (0.26 g, 1 mmol, in 10 mL THF), was treated with the desilylating agent (Table I). Quenching was effected by neutralization with methanolic HCl in the t-BuOK experiments by filtration followed by addition of acidic methanol in the other cases. The residue after solvent evaporation was analyzed by GLC and quantitative ^{13}C NMR. For product isolation 2.6 g (10 mmol) of crudes from several runs obtained under various conditions (see Table I) were treated so as to transform the alcohols into their *O*-silyl ethers (Me_3SiCl 1.3 g, 12 mmol; Et_3N 1.6 g, 16 mmol; 60 mL THF, rt, 4 h) and chromatographed (Florisil, ether/petroleum ether 1/1). Three fractions were obtained: the first (0.75 g, 29%) consisted solely of the known trimethylsilyl ether of **3c**.[1] The second fraction (0.5 g) was a ≈1:1 mixture of the first eluted material and a second component which could be further enriched to ca. 85% by chromatography (ether/petroleum ether 2/1). Acidic cleavage (3% HCl in MeOH) of this material gave a mixture (100 mg) of **3c** and a second component whose ^{13}C NMR coincided with that of **10c** prepared from *cis*-7-thiabicyclo[4.3.0]nonan-2α-ol 7,7-dioxide (**12**)[1] by the route outlined in Scheme II. The last fraction was a mixture **10t-TMS** and **3t-TMS**, the silyl ethers of **10t** and, respectively, **3t**. From boiling hexane **3t-TMS** crystallized out (0.85 g, 33%), mp 134–135 °C. ^{13}C NMR: δ 73.3 (C_5); 62.2 (C_1); 51.1 (C_3); 50.4 (C_6); 33.4 (C_4); 29.8 (C_7); 21.7, 20.3 (C_8, C_9); 0.1 (CH_3). ^1H NMR: δ 3.55 (m, 1 H, HCO); 3.00 (m, 2 H); 2.72 (m, 1 H); 2.10 (m, 7 H); 1.72 (m, 2 H); 1.28 (m, 1 H); 0.06 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{11}H_{22}O_3SiS$: C, 50.34; H, 8.45; S, 12.22. Found: C, 50.90; H, 8.50; S, 11.98. Acidic cleavage of **3t-TMS** gave known **3t**[1] quantitatively.

Evaporation of the mother liquor left an oily residue (0.25 g) made up of **10t-TMS** (≈80%) and **3t-TMS**: ^{13}C NMR of the major component: 74.7 (C_2); 63.2 (C_6); 51.5 (C_8); 47.4 (C_1); 35.1 (C_3); 25.7 (C_4); 23.3, 22.3 (C_5, C_9); 0.25 CH_3). The ^{13}C NMR spectrum of the alcohols obtained by acidic cleavage of this mixture showed, beside **3t**, the signals of **10t** (major product) coincident with those of the material obtained by base catalyzed epimerization of **10c** (see following text).

Desilylation–Cyclization of (*E*)-2-(Trimethylsilyl)-4,5-epoxythiacyclononane 1,1-Dioxide (8). Formation of *cis*-1β-(Trimethylsilyl)-2-thiabicyclo[7.1.0]nonan-6β-ol 2,2-Di-

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oxide (11). Above −10 °C treatment of 8 or mixtures 8, 8′ with desilylating agents gave mixtures of products of transannular cyclization (and protodesilylation) which, being all known compounds, could be identified and determined by quantitative ^{13}C NMR without separation. At lower temperatures (Table II, runs 6–9) a new product was formed, 11, which was isolated from run 7 by chromatography (silica gel, ether) as the first eluted material; cryst hexane–benzene (80 mg, 33%), mp 110–111 °C. ^{13}C NMR: δ 67.7 (C_7); 58.0 (C_3); 36.0 (C_6); 34.9 (C_1); 29.2, (C_8); 22.8 (C_4); 20.2 (C_5); 11.9 (C_9); −1.8 (CH_3). ^{1}H NMR: δ 4.12 (ddd, 1 H, *J* = 10.5, 10.5, 4.7 Hz, HCO); 3.08 m, 2 H, SCH_2); 2.30 (br s 1 H, OH); 1.98 (m, 2 H); 1.72 (m, 2 H); 1.58 (m, 2 H, it comprises 1 H of the cyclopropyl CH_2, the other appearing as a m at 1.09); 1.4 to 1.2 (m, 2 H; it comprises the bridgehead H). Anal. Calcd for $C_{11}H_{22}O_3SiS$: C, 50.34; H, 8.45; S, 12.22. Found: C, 50.86; H, 8.23; S, 12.31.

The second eluted material consisted of the protodesilylation product, 1, admixed with **2c**.

7-Thiabicyclo[4.3.0]non-1-ene 7,7-Dioxide (13). Proof of Structure of *cis*- (10c) and *trans*-7-Thiabicyclo[4.3.0]nonan-2β-ol 7,7-Dioxide (10t). For the stereochemical correlation of alcohol **10c** via Mitsonobu inversion[9] of the previously prepared α epimer 12[1] (Scheme II), a solution of the latter (0.43 g, 2.3 mmol) in THF (30 mL) was added with Ph_3P (1.19 g, 4.6 mmol) followed by benzoic acid (0.55 g, 4.6 mmol) and, after cooling to −10 °C, dropwise by DEAD (0.79 g, 4.6 mmol, in 5 mL of THF). After being stirred for 15 h at rt and concentration under reduced pressure, the residue was chromatographed (silica gel, petroleum ether/ethyl acetate 60/40). The reaction product, isolated as the second eluted material (dicarbethoxyhydrazine being eluted first) was not the expected β alcohol but the title alkene sulfone 13 (320 mg, 81%) bp 150 °C (0.3 mm (kugelrhor)). ^{13}C NMR: δ 129.2 (C_1); 126.2 (C_2); 59.3 (C_6); 50.5 (C_8); 27.7 (C_3); 23.7 (C_4); 19.7 (2 signals, C_5, C_9). ^{1}H NMR (60 MHz): δ 5.85 (br s, 1 H, HC=); 3.15 (m, 5 H); 1.75 (m, 6 H). Anal. Calcd for $C_8H_{12}O_3S$: C, 55.78; H, 7.02; S, 18.61. Found: C, 55.27; H, 7.22; S, 18.40.

A THF solution of **13** (410 mg, 2.4 mmol, in 2 mL of THF) was added dropwise at rt to a stirred solution of 305 μL of 7.8 M borane in 1,4-oxathiane[10] in 2 mL of THF. After 1 h the solution was brought to 0 °C and added dropwise with aqueous NaOH (800 μL, 3 M) followed by 30% H_2O_2 (450 μL) added at such rate that the temperature would not exceed 35 °C. After being stirred for 1 h, the mixture was extracted with THF. The residue from evaporation of the organic layer was dissolved in CH_2Cl_2, dried, and chromatographed (silica gel, ethyl acetate/ethyl ether 5/2) to give as the first eluted material a waxy solid (190 mg, 42%) whose NMR spectral properties are consistent with **7-thiabicyclo[4.3.0]nonan-1-ol (14).** Especially significant is the singlet at 75.6 ppm in the ^{13}C spectrum indicating the hydroxy group is attached to a bridgehead (C_1). The other resonances are: δ 66.7 (C_6); 50.7 (C_8); 36.7 (C_2); 32.0 (C_9); 24.8 (C_4); 23.0, 22.3 (C_3, C_5). ^{1}H NMR (60 MHZ): δ 3.25 (m, 4 H); 2.00 (m, 10 H). Anal. Calcd for $C_8H_{14}O_3S$: C, 50.50; H, 7.42; S, 16.85. Found: C, 50.31; H, 7.38; S, 17.01. If, as it appears most likely, hydroboration has occurred from the least hindered side, the hydroxy group in **14** should β and the ring fusion cis, as indicated by the structure in Scheme II.

The second eluted material (210 mg, 46%) cryst hexane–benzene, mp 59–60 °C, was *cis*-7-thiabicyclo[4.3.0]nonan-2β-ol 7,7-dioxide whose ^{13}C NMR spectrum was identical to that of **10c** from desilylation–cyclization of 7. ^{13}C NMR: δ 67.2 (C_2); 58.9 (C_6); 49.5 (C_8); 42.6 (C_1); 30.2 (C_3); 22.2, 22.1 (C_5, C_9); 18.7 (C_4). ^{1}H NMR: δ 3.40 (m, 1 H, HCO); 3.08 (m, 3 H); 2.45 (m, 2 H, inclusive of OH); 2.08 (m, 3 H); 2.0–1.2 (m, 5 H). Anal. Calcd for $C_8H_{14}O_3S$: C, 50.50; H, 7.42; S, 16.85. Found: C, 50.37; H, 7.48; S, 18.79.

A THF solution of **10c** (95 mg, 0.5 mmol in 10 mL) heated for 4 h at 70 °C in the presence of t-BuOK (0.08 g, 0.75 mmol) gave rise to a 15:85 **10c**:**10t** epimer mixture which by crystallization from acetone gave ***trans*-7-thiabicyclo[4.3.0]nonan-2β-ol 7,7-dioxide (10t)** (50 mg, 62%), mp 133–134 °C. ^{13}C NMR: δ 73.5 (C_2); 63.0 (C_6); 51.2 (C_8); 47.0 (C_1); 34.5 (C_3); 25.2 (C_5); 23.0, 22.0 (C_4, C_9). ^{1}H NMR: δ 3.29 (m, 1 H, HCO); 3.23, 3.01, 2.59, 2.46 (m's, 1 H each); 2.08 (m, 3 H); 1.9–1.2 (m, 6 H, inclusive of OH). Anal. Calcd for $C_8H_{14}O_3S$: C, 50.50; H. 7.42; S. 16.85. Found: C, 50.23; H, 7.50; S, 16.80.

Registry No. 1, 134333-89-4; **2c**, 134333-93-0; **3c**, 134451-81-3; **3c**–TMS, 134451-87-9; **3t**, 138331-46-1; **3t**–TMS, 138331-47-2; **4**, 79760-37-5; **5**, 138234-75-0; **5′**, 138331-48-3; **6**, 138234-76-1; **6′**, 138331-49-4; 7, 138234-77-2; 7′, 138331-50-7; 8, 138234-78-3; 8′, 138331-51-8; **9**, 138258-95-4; **10c**, 138331-52-9; **10t**, 138331-53-0; **10t**–TMS, 138380-78-6; 11, 138234-79-4; **12**, 134333-94-1; **13**, 138234-80-7; 14, 138234-81-8; (*E*)-thiacyclonon-4-ene, 68013-79-6; 2-vinylthiane, 66120-24-9.

Supplementary Material Available: Geometries and relative energies of diastereomers 7, 7′ and 8, 8′ (9 pages). Ordering information is given on any current masthead page.

Optically Active Quaternary Carbon Centers from the Photoaddition of Chromium–Alkoxycarbene Complexes and Optically Active Thiazolines

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The photolytic reaction of chromium–alkoxycarbene complexes with valine-derived, optically active thiazolines produced optically active β-lactam penam derivatives in fair to good yield and with high diastereoselectivity. In most cases alcoholosis of the β-lactam followed by solvolysis of the thiazolidine ring produced optically active quaternary centers having carbon substituents in four different oxidation states—alkane, alkoxy, aldehyde, and ester. The absolute configuration of the stereogenic center could be inverted by a sequence of redox manipulations of the ester and aldehyde group, making either enantiomer available from the same precursor.

Introduction

For the past several years, research in these laboratories has centered on the development of photolytic reactions of chromium–carbene complexes for use in organic synthesis. Mechanistic studies[1] indicated that photolysis of chromium–carbene complexes with visible light (metal-to-ligand charge-transfer band) promoted a reversible insertion of CO into the metal–carbon carbene double bond, producing species which had ketene-like reactivity.[2] Thus,

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