Configuration and Conformational Equilibria of Methyl-Substituted *trans*- and *cis*-1-Thiadecalins

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^{13}C and ^{1}H NMR spectra of a number of methyl-substituted *trans*- and *cis*-1-thiadecalins have been recorded. Assignment of signals was made by off-resonance decoupling, parametrization of substituent effects, and comparison with carbon and nitrogen analogues; at the same time, the configuration of the compounds was established. The conformational equilibria of the conformationally heterogeneous parent, 3β-methyl-, 8β-methyl-, and 10-methyl-*cis*-1-thiadecalins were determined by low-temperature ^{13}C NMR.

In the last few years the chemistry of saturated sulfur-containing heterocycles and their S-substituted derivatives have been the subject of a fair amount of interest.[1] In order to further our investigations of the conformational and configurational preferences and the rearrangement reactions of thiane- and 1,3-dithiane-1-imides[2] a conformationally rigid system offering the possibility of biasing the conformational preferences of substituents on sulfur and on the adjacent carbon atoms was needed. *trans*-1-Thiadecalin (**1**) provides such a system: ring inversion is prohibited for reasons of strain, and substitution at certain positions will bias the site of a new substituent on S-1 or C-2 through syn–axial interactions. Suitable substitution of *cis*-1-thiadecalin (**11**) also leads to conformationally homogeneous compounds with similar properties. Finally, the conformational preferences of mobile *cis*-1-thiadecalins of the sulfimides derived from them promised to be interesting.

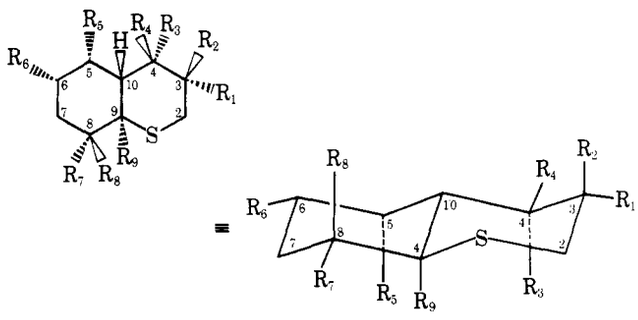
A number of methyl-substituted *trans*- and *cis*-1-thiadecalins (Schemes I and II) were accordingly prepared,[3] and their ^{13}C and ^{1}H NMR spectra were recorded at room temperature (Tables I and IV). When compounds proved to be conformationally heterogeneous at room temperature (**11, 12, 14,** and **17**), the low temperature ^{13}C NMR spectra were recorded and the proportion of conformers determined by integration of appropriate signals. In the sequel, the spectral assignments and, at the same time, the configuration and conformation of the 17 compounds investigated are discussed, and the conformational equilibria of the four mobile compounds are rationalized.

^{13}C NMR Spectra. The noise-decoupled room temperature ^{13}C spectrum of *trans*-1-thiadecalin (**1**) shows the expected nine sharp lines. The most downfield signals appear as doublets in the off resonance decoupled spectrum and are thus identified as C-9 and C-10. Comparison of the spectra of thiane[5a,6] and cyclohexane[4,7] shows that carbon atoms α and β to sulfur experience downfield shifts of 2.9 and 0.6 ppm, respectively. The most downfield doublet is accordingly assigned to C-9, the more upfield one to C-10.

The three signals at next higher field belong to carbon atoms 4, 5, and 8, which have two α and three β substituents.[4] Replacement of CH_2 by sulfur has nearly no influence at the exocyclic γ position (compare the CH_3 shifts of *cis*-3,5-dimethylthiane[5a] with the CH_3 shifts in *cis*-1,3-dimethylcyclohexane[7]) and the most downfield signal of the three is therefore assigned to C-5 (the corresponding shift in *trans*-decalin is 34.48[5c]). C-4 is "doubly γ" to the sulfur atom, which in thiane leads to an upfield shift of 0.7 ppm compared to cyclohexane; the signal at 34.40 consequently must be C-4. C-8 is in a position analogous to that of the CH_3(2) group in *cis*-2,4-dimethylthiane[5a] which is shifted upfield by 1.2 ppm compared to *cis*-3,5-dimethylcyclohexane; the signal at 32.58 ppm comes closest to the value computed from the shift in *trans*-decalin (34.48 − 1.2 = 33.28).

The four most upfield signals belong to C-2, C-3, C-6 and C-7, which have only two α and two β substituents.[4] C-2 is shifted downfield (similar to C-9) from the corresponding

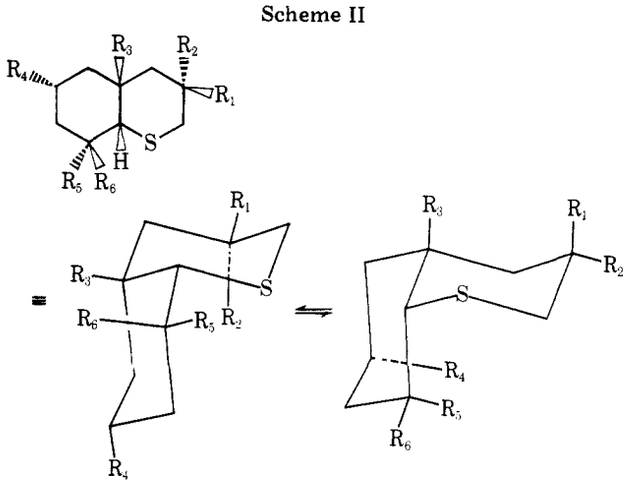
Scheme I



R = H unless indicated

1, all R's = H
2, R_1 = CH_3 (3α-CH_3)
3, R_2 = CH_3 (3β-CH_3)
4, R_3 = CH_3 (4α-CH_3)
5, R_4 = CH_3 (4β-CH_3)
6, R_5 = CH_3 (5α-CH_3)
7, R_6 = CH_3 (6α-CH_3)
8, R_7 = CH_3 (8α-CH_3)
9, R_8 = CH_3 (8β-CH_3)
10, R_9 = CH_3 (9-CH_3)

Scheme II



R = H unless indicated

11, all R's = H
12, R_1 = CH_3 (3β-CH_3)
13, R_2 = CH_3 (3α-CH_3)
14, R_3 = CH_3 (10-CH_3)
15, R_4 = CH_3 (6α-CH_3)
16, R_5 = CH_3 (8α-CH_3)
17, R_6 = CH_3 (8β-CH_3)

Table I. ^{13}C Chemical Shifts[a] of *trans*- and *cis*-1-Thiadecalins

Compd[b]	Registry no.	Temp[c]	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	CH_3
						trans-1-Thiadecalin						
Parent, 1	54340-73-7	+30	30.0_4	28.2_3	34.4_0	34.5_6	26.3_4	26.7_6	32.5_8	47.0_1	44.2_7	—
3α-CH_3, 2	63702-90-9	+30	36.7_6	34.2_2	43.2_6	34.5_1	26.2_3	26.7_8	32.0_6	46.3_8	44.5_4	22.7_8
3β-CH_3, 3	63730-12-1	+30	36.2_1	28.1_0	40.2_7	34.7_6	26.4_5	26.8_3	32.3_4	47.6_5	37.7_2	17.3_7
4α-CH_3, 4	63730-13-2	+30	23.1_0	35.3_0	32.4_4	31.9_9	26.7_3	26.7_3	33.2_3	38.5_0	47.2_0	12.3_2
4β-CH_3, 5	63730-14-3	+30	29.2_8	37.3_8	37.7_2	30.2_1	26.5_7	26.5_7	32.7_5	46.4_4	50.3_9	20.1_0
5α-CH_3, 6	63730-91-0	+30	29.8_3	28.6_9	31.7_3	34.1_4	33.7_7	20.5_4	33.1_2	40.5_7	46.8_1	13.0_7
6α-CH_3, 7	63702-92-1	+30	30.0_3	28.1_4	34.3_4	43.2_9	(32.5_8)	35.2_2	(32.5_0)	46.6_5	43.9_3	22.5_1
8α-CH_3, 8	63702-93-2	+30	29.9_6	28.1_0	34.6_6	34.8_7	25.7_0	36.1_9	37.2_3	54.6_4	44.0_3	20.3_6
8β-CH_3, 9	63730-15-4	+30	30.0_9	28.1_9	35.2_5	35.1_6	20.1_4	33.7_7	32.4_3	51.4_1	36.7_1	13.8_1
9-CH_3, 10	63702-94-3	+30	26.4_6	28.8_5	29.1_3	30.6_7	26.8_8	22.1_5	40.4_6	43.9_6	47.3_7	18.1_9
						cis-1-Thiadecalin						
Parent, 11	57259-80-0	+30	27.4_5	*d*	*d*	*d*	*d*	*d*	30.6_9	42.1_5	36.7_5	
		+60	27.6_2	24.5_9	30.0_4	29.0_0	23.8_7	24.2_3	30.9_4	42.4_6	37.1_0	
Parent, 11A[e]		−70	29.9_2	21.1_0	32.5_0	24.4_0	26.6_9	20.8_8	31.8_6	43.1_1	36.0_1	
Parent, 11B[e]		−70	23.5_9	28.2_8	24.9_2	34.2_2	19.6_1	28.2_8	27.3_4	40.4_1	36.7_5	
3β-CH_3, 12	63730-16-5	+30	36.6_3	27.0_7	41.4_5	26.0_1	26.7_4	21.4_0	31.4_5	42.7_8	37.4_2	22.5_0
3β-CH_3, 12		+55	36.7_1	27.2_4	41.5_2	26.3_3	26.7_7	21.6_2	31.5_7	42.9_3	37.5_9	22.3_8
3β-CH_3, 12A[f]		−68	36.6_0	26.7_2	41.4_0	25.1_4	26.7_2	20.8_3	31.2_4	42.6_7	37.1_5	22.8_5
3α-CH_3, 13(B)	63730-17-6	+30	30.7_0	34.8_5	(34.2_8)	(34.4_6)	19.9_3	28.5_6	27.5_0	40.0_1	37.8_1	23.1_0
10-CH_3, 14	63702-95-4	+30	*d*	23.5_9	*d*	*d*	21.7_9	*d*	29.1_4	47.0_9	32.8_5	28.2_0
10-CH_3, 14		+55	26.1_5	23.7_4	34.5_9	37.8_3	21.9_5	25.1_9	29.2_6	47.3_3	32.9_8	28.2_5
10-CH_3, 14A[g]		−68	30.0_3	23.3_4	41.3_5	28.2_8	21.8_7	20.5_5	27.0_1	47.0_5	32.7_0	27.3_2
10-CH_3, 14B[g]		−68	23.3_8	23.3_4	29.8_2	42.5_5	21.3_3	27.5_3	29.3_0	46.5_3	32.7_0	28.3_9
6α-CH_3, 15 (A)	63730-18-7	+30	30.0_7	21.4_2	32.7_6	(33.6_1)	(33.5_6)	29.6_8	32.0_9	42.6_1	36.5_3	22.6_8
8α-CH_3, 16 (A)	63730-19-8	+30	29.5_3	22.2_8	33.0_3	24.3_2	26.7_9	29.0_9	38.1_4	50.7_5	37.5_0	20.0_3
8β-CH_3, 17	63730-20-1	+30	24.9_5	27.8_6	27.3_1	32.9_0	21.1_9	*d*	30.6_7	49.0_5	36.7_7	21.0_2
8β-CH_3, 17		+55	25.1_7	28.1_5	27.2_9	32.8_4	21.3_1	34.4_3	30.9_1	49.2_2	36.8_4	20.9_5
8β-CH_3, 17A[h]		−68	29.7_9	*i*	32.1_2	24.6_3	*i*	26.3_8	33.3_6	47.8_2	30.2_1	18.3_9
8β-CH_3, 17B[h]		−68	23.2_3	28.2_7	25.8_9	34.5_1	20.7_7	35.8_8	29.3_1	48.6_4	37.7_6	21.7_4

[a] In $CDCl_3$, from internal Me_4Si. Parentheses indicate that assignments are not unambiguous. [b] *trans*- or *cis*-1-Thiadecalin. C-9 and C-10 are used instead of C-8a and C-4a to allow unambiguous use of "a" for axial. "α" means the substituent is on the opposite ring side as the hydrogen at C-10; "β" means on the same side of the ring as this hydrogen. For conformations A and B, see formula schemes in text. [c] °C. Only when compounds were found to be conformationally inhomogeneous at room temperature, low and high temperature ^{13}C NMR spectra were recorded. [d] Signals were broad to very broad due to slow ring inversion at this temperature and could not be measured accurately. [e] 58% A, 42% B. We are grateful to Professor W. v. Philipsborn, Universität Zürich, for measuring spectra of this compound at a number of temperatures. [f] >95% A; no signals of B could be detected. [g] 33% A, 67% B. [h] 17% A, 83% B. [i] Not observed because either overlaid by a signal of the major component or too small to be discerned.

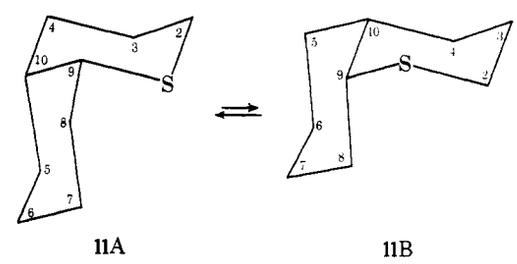
signal (26.99 ppm) in *trans*-decalin,[5c] and is found at 30.04. C-3, like C-10, is also shifted slightly downfield, and the remaining, most upfield two signals are carbon atoms 6 and 7. Comparison of the spectra of ethylcyclohexane[5c] and methyl cyclohexyl sulfide[5b] shows that the C-atom "doubly δ" to the sulfur (C-4) is shifted slightly more upfield than the one γ to it (C-3,5). The most upfield signal in *trans*-1-thiadecalin is consequently assigned to C-6.

The positions of methyl substitution in compounds **2–10** follow from the synthetic procedures;[3] the ^{13}C spectra (and to a lesser extent, the proton spectra) indicate the configuration (α or β; see footnote *b*, Table I) of the methyl groups and the trans character of the ring fusion. The signals of axial methyl groups (in **3**, **4**, and **9**) are invariably at higher field than the corresponding equatorial signals (**2**, **5**, and **8**); when only one isomer was isolated, the position of the methyl group was still evident by comparison with signals of analogously orientated methyl groups (**6** with **4**; **7** with **2**). Shift changes in carbon atoms near the methyl substituent (α, β, and γ) were in agreement with values calculated using the parameters developed for methylcyclohexanes[4,7] and methyldecahydroquinolines.[8,9] Chemical shifts of carbon atoms remote (>γ) from the site of methyl substitution were generally close to corresponding shifts in the parent compound **1**, which allowed unambiguous assignment of trans ring fusion in **2–10**. To facilitate assignments in **10**, where most of the signals were substantially shifted compared to **1**, 9-methyl-*trans*-1-thiadecalin-2,2-d_2 (**10**-d_2) was prepared,[3] in which the signal due to C-2 disappears through loss of NOE and by coupling with the deuterium C-3 is shifted palpably upfield (−0.18 ppm), and C-4 is noticeably broadened.

The noise-decoupled room temperature ^{13}C spectrum of *cis*-1-thiadecalin (**11**) shows only four sharp signals; the remaining five signals are broad to very broad depending on the chemical shifts of the corresponding carbon atoms in conformation A and B. Ring inversion therefore is already slow at +30 °C. Elevation of the probe temperature to +60 °C results in sharpening of all nine signals due to fast inversion between A and B. Lowering the temperature stepwise to −70 °C leads through coalescence (ca. −20 °C) to two sets of sharp signals which can be assigned to conformers A and B because of their unequal proportion (ratio 58% A, 42% B).

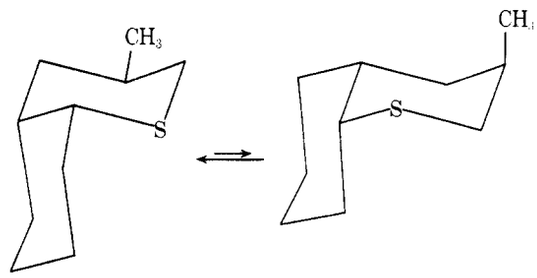
Assignment of the signals of each conformer to the various ring atoms is based on a combination of off resonance decoupling, comparison with chemical shifts in the low-temperature spectrum of *cis*-decalin[4c] corrected for the replacement of C-1

Scheme III



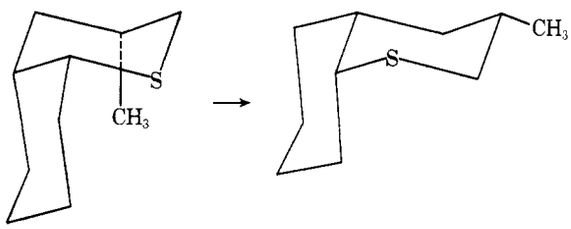
11A 11B

Scheme IV



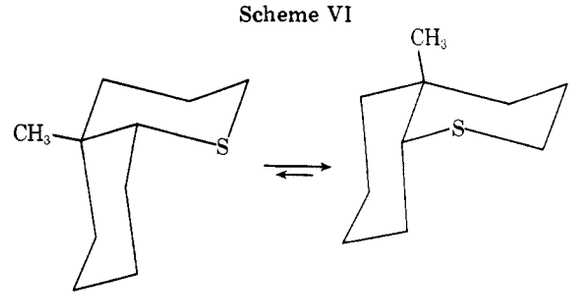
12A 12B

Scheme V



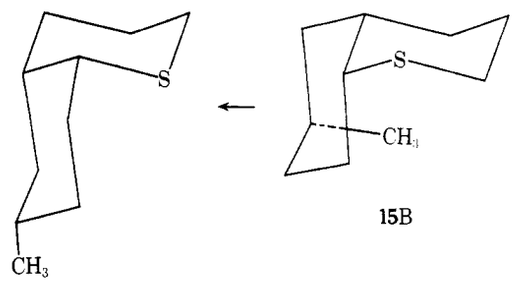
13A 13B

Scheme VI



14A 14B

Scheme VII



15A 15B

by S, effects of methyl substitution (in compounds **12–17**), and shift changes of corresponding signals in A and B upon raising the temperature. The two most downfield signals in **11A** and **11B** are clearly C-9 and C-10; the remaining signals can be split into four groups for each conformer depending on the number of α, β, and γ effects[4] they encounter. Thus, **11A** has C-4 and C-8 (two α, three β, no γ_a) next to C-9 and C-10; C-8, in an analogous position relative to S-1 as in **1**, must resonate at higher field. Next come C-2 and C-6 (two α, two β, no γ_a), with C-2, adjacent to the sulfur atom, shifted more downfield. C-5 (two α, three β, one γ_a) is at next higher field. The two most upfield signals belong to C-3 and C-7 (two α, two β, one γ_a) with C-3, β to the sulfur atom, the more downfield signal. The signals of **11B** can be assigned in an entirely analogous way. C-5 (two α, three β, no γ_a) and C-3 and C-7 (two α, two β, no γ_a) are the three most downfield signals next to C-9 and C-10. C-8 and C-4 are analogously substituted (two α, three β, one γ_a), but here C-8 is more *downfield* shifted by the sulfur β to it. The two most upfield signals are C-2 and C-6. Assignment of the spectrum of **11** at +60 °C follows from the spectra of the two frozen conformers, taking into account a downfield shifting of the signals of ~0.8 ppm upon raising the temperature by ~100 °C.

A number of signals in the room-temperature ^{13}C spectrum of 3β-methyl-*cis*-1-thiadecalin (**12**) are slightly broadened, the biasing influence of the methyl group being insufficient to make **12A** the exclusive conformation. At +55 °C the signals are sharp, as at −68 °C; only the signals due to **12A** can be detected at low temperature, indicating that this conformer predominates to >95%. Chemical shifts of C atoms close to the site of the methyl substituent show the expected α_e, β_e and γ_e effects compared with **11A**, whereas C-6, C-7, and C-8 show only very minor changes. The configuration and conformation of **12**(A) are thus established.

All signals in the room-temperature spectrum of 3α-methyl-*cis*-1-thiadecalin (**13**), on the other hand, are sharp, and no changes except the usual temperature dependence of ^{13}C shifts are observed upon variation of the probe temperature. **13** must be conformationally homogeneous (**13B**), since a severe syn–axial interaction exists between CH_3 and C-5 in conformation A. As in the case of **12**(A), the signals next to the methyl substituent show the expected shift changes (α_e, β_e), while C-6, C-7, and C-8 are in good agreement with their values in **11B**.

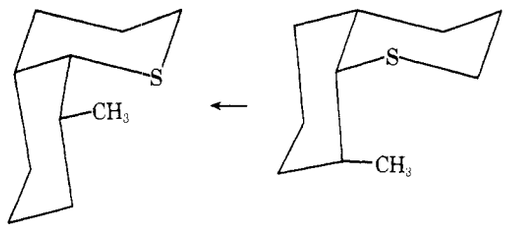
Compound **14**, 10-methyl-*cis*-1-thiadecalin (see footnote *b*, Table I), like the parent compound **11**, is conformationally heterogeneous, as indicated by the broad signals for C-2, C-4, C-5, and C-7 in the rt ^{13}C spectrum. Once more the signals become sharp at +55 °C, and two sets of signals (ratio 33% A, 67% B) are observed at −68 °C.

Replacement of H by CH_3 on C-10 is known in *cis*-decalin[4c] and *cis*-decahydroquinoline[9] to bring about considerable shift changes in most of the carbon atoms compared to the parent compound. Only C-2 and C-7 in both **14A** and **14B** are expected to be shifted by less than 1 ppm, relative to **11A** and **11B**. However, assignment was complicated since 8 signals (four of each conformer) appear between 30 and 27 ppm. To aid the decision which of the two conformers was the minor and which the major one, the room- and low-temperature spectra of **14**-2,2-d_2 were therefore recorded. Here the signals due to C-2 disappear through loss of the NOE and through being split into quintets. This makes possible the assignment of C-2 at 30.03 (minor) and 23.38 ppm (major) in the undeuterated analogues at low temperature. Since C-2 in conformation B (one γ_a) resonates at much higher field than in A (no γ_a), the major set of signals can be assigned unambiguously to **14B** and the minor one to **14A**. The rest of the signals are matched to the carbon atoms by the same criteria as listed for **11**.

The signals of **15** (6α-methyl-*cis*-1-thiadecalin) are sharp at room temperature, since conformation **15B** is prohibited because of the syn–axial CH_3/C-4 interaction. The signals in the thiane ring (C-2, C-3, C-4) are in excellent agreement with **11A**, which confirms the configurational and conformational assignment. Signals of C-6, C-5, and C-7 show the expected downfield shifts due to α_e and β_e effects.

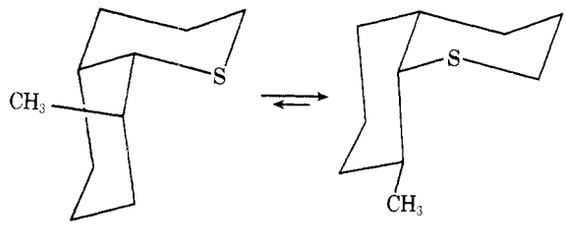
In **16**, conformation B is excluded because of the two syn–axial interactions of the methyl group with C-2 and C-4, opposed by only one additional gauche interaction between CH_3 and S in **16A**. This consideration is verified by the sharpness of the signals of **16A** at room temperature, which does not change upon lowering the temperature. The strain imposed upon the molecule by the CH_3/S interaction manifests itself in less good agreement of signals remote from the site of substitution (C-3, C-4) compared to **11A** or **15A**. The carbon

Scheme VIII



16A 16B

Scheme IX



17A 17B

atoms close to the methyl group show shift effects similar to the ones observed in the corresponding 8α-methyl-*cis*-decahydroquinoline.[9]

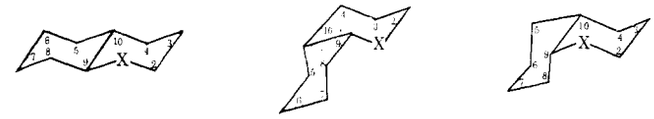
In compound **17**, finally, the effect of two syn-axial CH_3/H interactions in **17A** is set against one gauche CH_3/S in **17B**. The compound is conformationally heterogeneous, as indicated by the broadened signals of the rt spectrum. At −69 °C the two conformers appear in a ratio of 17:83, with conformation **17B** predominating. Assignment of the signals is straightforward for the major conformer, using the criteria listed for **11**; it is less easy for **17A**, since two of the signals (C-3 and C-6) are not observed and off-resonance decoupling could not be performed on the rest. Comparison with the shift effects reported for the corresponding conformers of 8β-methyl-*cis*-decahydroquinoline,[9] however, leaves no doubt as to the correctness of the conformational assignments.

Comparison with Carbocyclic Analogues and Shift Effects Produced by Methyl Substitution. Comparison with carbocyclic analogues for which ^{13}C data have been reported allows calculation of a set of increments for replacement of CH_2 by S. These data have been compiled in Table II for *trans*-1-thiadecalin and for the two conformers of *cis*-1-thiadecalin, A and B.

As in the case of the corresponding parameters for replacement of CH_2 with NH,[8] the standard deviations of the values are relatively large, indicating differences in geometry between individual pairs of methyl-substituted decalins and 1-thiadecalins. This reduces the worth of such averaged parameters and makes the calculation of chemical shifts with two parameters (one multiplicative and one additive), which has been suggested in other heterocyclic systems[14] fruitless, since deviations between values calculated and found are far larger than between values calculated with or without the multiplicative parameter which is always close to unity. For this reason, **10** and its matching decalin have not been used for the calculation of the values in Table II, since geometrical differences to the other compounds in the corresponding series seem very pronounced. Generally the effects of replacing CH_2 by S are small with the exception of the α carbons, but they are still noticeable on positions four bonds removed (C-6; "double δ").

Comparison of the chemical shifts of the three parent compounds **1**, **11A**, and **11B** with the methyl-substituted thiadecalins allows the calculation of effects of methyl substitution. The results are similar to the values found for

Table II. Shift Differences $\Delta\delta^a$ between 1-Thiadecalins (X = S) and Decalins[b] (X = CH_2)



C atom	Effect	Shift differences: Trans[c]	Cis A[d]	Cis B[e]
C-2	α	+2.4 ± 0.8	+2.2 ± 0.2	+1.3 ± 0.8
C-3	β	+0.9 ± 0.4	+0.1 ± 0.5	+0.5 ± 0.1
C-4	dγ	−0.3 ± 0.4	−0.7 ± 0.2	−1.2 ± 0.6
C-5	γ	+0.2 ± 0.5	−1.9 ± 0.3	+0.8 ± 0.5
C-6	dδ	−0.8 ± 0.2	−0.8 ± 0.3	−1.7 ± 0.4
C-7	γ	−0.5 ± 0.3	−0.8 ± 0.3	+0.3 ± 0.6
C-8	β	−1.9 ± 0.5	−1.1 ± 0.4	+1.1 ± 0.3
C-9	α	+3.2 ± 0.6	+6.4 ± 1.0	+3.9 ± 0.3
C-10	β	+0.3 ± 0.5	−0.3 ± 0.5	+0.1 ± 0.6

[a] In parts per million. A plus sign indicates that the signal in the S compound is downfield from the signal in the CH_2 analogue. The differences reported are averages for the pairs of compounds considered (see footnotes *c*, *d*, and *e*) with their standard deviations. [b] ^{13}C chemical shifts of *trans*-decalin in $CDCl_3$ are reported in this paper; the other decalin values are from ref 4c, but values of C-1 and C-10 of *cis-syn*-1-methyldecalin and of C-3 and C-7 of *trans-anti*-1-methyldecalin have been reversed. [c] Compounds **1**, **2**, **5**, **7**, and **8** and the corresponding decalins were used for the calculation. [d] Compounds **11A** (−68 °C), **14A** (−68 °C), **15A**, and **16A** and the corresponding decalins were used for the calculation. [e] Compounds **11B** (−68 °C), **14B** (−68 °C), and **13B** and the corresponding decalins were used for the calculation.

Table III. Conformational Equilibria in Mobile *cis*-1-Thiadecalins[a]

Compd	A, %	B, %	K	$\Delta G°$ (kcal/mol)
Parent, **11**	58	42	1.4	+0.14
3β-CH_3, **12**	>95	<5	>19	>+1.2
10-CH_3, **14**	33	67	0.49	−0.29
8β-CH_3, **17**	17	83	0.20	−0.65

[a] In $CDCl_3$ at −68 °C (205 K). For enumeration of signals used in integration, see Experimental Section.

methyldecalins[4] and methyldecahydroquinolines,[8,9] and for methylthianes.[5,6] Individual α, β, etc. values, however, once more differ quite strongly, especially for carbon atoms close to sulfur. The worth of averaged methyl-substitution parameters with (large) standard deviations, therefore, is rather low; as in similar cases it seems more opportune to calculate individual parameters from the shift data as needed.

Conformation of *cis*-1-Thiadecalins. The room-temperature ^{13}C NMR spectra of **11**, **12**, **14**, and **17** showed the presence of the two conformers in these compounds. Inversion was frozen out at −70 °C and the signal areas of corresponding carbon atoms (see Experimental Section) could then be integrated. Nuclear Overhauser enhancement and T-1's of such carbon atoms have been reported to be nearly equal in other heterocyclic systems.[10] The resulting equilibrium constants and conformational free-energy differences are summarized in Table III.

Conformation A in *cis*-1-thiadecalin (**11**) is preferred by 0.14 kcal/mol. This is in reasonable, if not complete, agreement with the value calculated by a force-field method[11] (0.32 kcal/mol); a comparison of the experimental with the calculated $\Delta G°$ values in the methylthiane series,[5a] however, leads

Table IV. Pertinent ^{1}H Chemical Shifts[a] of *trans*- and *cis*-1-Thiadecalins[b]

Compd	H_{2e}	H_{2a}	H_9	CH_3
		Trans		
Parent, **1**	2.48–2.89, not resolved		~2.40 (br m)	
3α-CH_3, **2**	2.15–2.55, not resolved		~2.43 (br m)	0.92 (d, 6)
3β-CH_3, **3**	2.21 (d, 13, of d, 3)	3.03 (d, 13, of d, 3)	overlap H_{2e}, H_{2a}	1.19 (d, 7.5)
4α-CH_3, **4**	2.21 (d, 13, of t, 4)	2.97 (d, 13, of d, 10.5 of d, 2.5)	~2.97 (br)	0.86 (d, 7)
4β-CH_3, **5**	2.47 (d, 13, of t, 4)	2.97 (d, 13, of d, 11, of d, 3)	~2.45 (br)	0.92 (d, 5)
5α-CH_3, **6**		2.30–2.93, not resolved		0.89 (d, 7)
6α-CH_3, **7**	2.48–2.89, not resolved		2.34 (br m)	0.87 (d, 6.5)
8α-CH_3, **8**	~2.64, not resolved		2.16 (t, 10)	0.99 (d, 6)
8β-CH_3, **9**		2.43–2.87, not resolved		1.01 (d, 7)
9-CH_3, **10**	2.39 (d, 14, of t, 3.5)	2.89 (d, 14, of d, 12, of d, 3.5)		1.36 (s)
		Cis		
Parent, **11** (A ⇌ B)	~2.55, not resolved		2.97 (half-width 13)	
3α-CH_3, **12B**	2.18–2.44, not resolved		2.57 (d, 12, of t, 4)	0.95 (d, 6)
3β-CH_3, **13A**	2.08–2.62, overlap w H_{3a}		3.15 (half-width 9)	0.84 (d, 6)
10-CH_3, **14** (A ⇌ B)	2.24–2.82, overlap w H_9		2.46[c] (d, 6 of d, 3)	1.16 (s)
6α-CH_3, **15A**	~2.63, not resolved		3.25 (half-width 8)	0.94 (d, 5.5)
8α-CH_3, **16A**	~2.57, not resolved		3.20 (half-width 7)	0.97 (d, 7)
8β-CH_3, **17** (A ⇌ B)		2.26 − 2.78, not resolved		1.11 (d, 6)

[a] In ppm, from Me_4Si; the reported shift values are centers of groups of signals in the spectra. The parenthesized data are multiplicity and coupling constants in Hz. [b] For preferred conformations of *cis*-1-thiadecalins, see Schemes III–IX. [c] From **14**-2,2-d_2.

to the conclusion that this agreement may be coincidental. Assuming additivity of conformational free energies and using the values from the methylthianes,[5a] one would predict conformation A to be the more favored, as indeed it is. In *cis*-2,3-dimethylthiane, the 2-CH_3-*e*-3-CH_3-*a* conformer is favored by 0.16 kcal/mol compared to 0.02 kcal/mol calculated with the values from the monomethylthianes.[5a] If the experimental value of *cis*-2,3-dimethylthiane is used as a basis for calculation, conformation **11B** differs from the 2-CH_3-*a*-3-CH_3-*e* form of this molecule by a gauche interaction between C-4 and C-6, and conformation **11A** from 2-CH_3-*e*-3-CH_3-*a* by a gauche interaction between S-1 and C-7. With a C–C–C–C gauche interaction from methylcyclohexane[12] (0.87 kcal/mol) and a C–C–C–S interaction similar to the one between CH_3 and S in **17B** (see below; 0.95 kcal/mol) one obtains a calculated preference of 0.08 kcal/mol for conformation A, reasonably close to the experimental value.

Introduction of a methyl group instead of a proton at C-10 in **11** (compound **14**) leads to a marked preference of conformer B (67%). In addition to the situation in **11**, one has to offset the $\Delta G°$ in methylcyclohexane (−1.74 kcal/mol[12b]) against 3-methylthiane (−1.40 kcal/mol[5a]), giving a preference of **11B** of 0.14 − 1.74 − (−1.40) = −0.20 kcal/mol, in good agreement with the experimental result of −0.29 kcal/mol. Closer agreement can hardly be expected, since the second ring obviously changes the opportunities of the axial methyl group in both conformations for reducing sterical strain by bending outward, and the change is not likely to be identical for the two conformers.

The sizeable changes in chemical shift upon cooling of **12** indicate a nonnegligible proportion of conformation B at room temperature. However, at −68 °C there is less than 5% of this conformation, since no signals of the minor conformer are detected. The slight preference for A in **11** is enhanced in **12** by 1.40 kcal/mol (the preference of the methyl group in 3-methylthiane for the equatorial position) to 0.14 + 1.40 = 1.54 kcal/mol. This corresponds to 2% of B at −68 °C, which is too little to be detected by ^{13}C NMR.

Compound **17**, finally, exists predominantly ($\Delta G°_{205}$ = 0.65 kcal/mol) in conformation B. Here the preference of a methyl group in methylcyclohexane for the equatorial position is opposed by the CH_3/S gauche interaction, which can thus be estimated as −0.65 = 0.14 − 1.74 + *x*; *x* = −0.65 + −0.14 + 1.74 = 0.95 kcal/mol. This value is slightly larger than the gauche–butane interaction found in methylcyclohexane, and rather larger than the value deduced for a CH_3–C–C–S interaction from the experimental data of 3-methylthiane, 5-methyl-1,3-dithiane, and cyclohexyl methyl sulfide[5a] (~0.6 kcal/mol). Obviously, the deviation of the bond angles from tetrahedral geometry due to the sulfur atoms are such that CH_3 in **17** (and C-7 in the A conformation of *cis*-1-thiadecalins, generally; see above) are closer to the sulfur than axial CH_3 in 3-methylthiane, and a different C/S gauche interaction must be used. Similar reasoning may apply in the case of *cis*-decahydroquinolines, where a similar difference between C/N gauche interactions was observed.[9]

The remaining compounds are conformationally homogeneous either because trans ring fusion forbids inversion, or because of severe C/C syn-axial interections in the alternative conformations.

^{1}H NMR Spectra. Since only the protons on the C atoms adjacent to sulfur are resolved, and since the shift difference is less pronounced than in other heterocyclic systems (e.g., the decahydroquinolines[9]), even 100-MHz ^{1}H NMR spectra offer only limited information regarding the configurational and conformational properties of the *trans*- and *cis*-1-thiadecalins. The apparent chemical shifts and coupling constants of the protons at C-2 (H_{2e}, H_{2a}) and C-9 (H_9) and of the methyl groups, if any, of the compounds **1**–**17** are collected in Table IV.

The most telling ^{1}H signal is the one due to H_9: in *cis*-1-thiadecalins preferentially in conformation A this proton is coupled to three protons which are all gauche positioned, and the signal appears as a broad singlet with a half-width of ~8 Hz (**13, 15**). If conformation B is preferred, a large anti coupling with H_{8a} occurs and the signal appears as a doublet ($J \approx 12$ Hz) of triplets. If the conformational equilibrium allows for comparable amounts of conformations A and B, the half-width of the signal is intermediate (**11, 14**). Another aid in structural assignment is the apparent coupling constant of the methyl groups in the *trans*-1-thiadecalin series which is larger (~7 Hz) for axial CH_3 (**3, 4, 6, 9**) than for equatorial (~6 Hz; **5, 7, 8**). Thus, the limited information that could be extracted from the ^{1}H spectra of **1**–**17** confirms the conclusions from the

^{13}C spectra which proved considerably more valuable in the structural analysis of 1-thiadecalins.

Experimental Section

Synthesis and analytical data of the compounds investigated are described in detail elsewhere.[3]

NMR spectra were recorded on a Varian XL-100 pulsed Fourier transform nuclear magnetic resonance spectrometer. ^1H NMR spectra were recorded in the CW mode, in 5-mm o.d. tubes. ^{13}C spectra were measured at 25.16 MHz, in the pulsed mode, in 10-mm o.d. tubes. Solvent in both cases was $CDCl_3$, with 2–5% Me_4Si admixed as internal reference; the deuterium of the solvent provided the internal lock signal. Integration of corresponding signals in the low-temperature spectra was effected by counting squares of the signal areas, and by multiplication of signal height with half-width, after expanding electronically as much as resolution and noise level permitted. The following signals (numbers refer to position of carbon atoms) were integrated and gave the following (parenthesized) percentages (only one conformer of each pair is reported): **11A** 2 (60), 4 (58), 5 (58), 6 (59), 9 (58), 10 (58); **14A** 4 (32), 6 (34), 9 (33); **17A** 5 (14), 9 (17), CH_3 (19). Error limits are estimated to be of the same size as reported in ref 13, that is, ±2% (in favorable cases of $K \approx 1$) to ±10% (in unfavorable cases of $K \approx 20$). The resulting errors for the $\Delta G°$ values in Table II are ±0.06 kcal/mol or better.

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Stereochemistry of α Halogenation of Sulfoxides. 1. A Proton Nuclear Magnetic Resonance Study of the Bromination of *trans*-2-Thiahydrindan 2-Oxide

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The stereochemistry of bromination of the title compound with bromine in the presence of pyridine to give the α-bromo sulfoxide has been studied by ^1H NMR and stereospecific deuterium labeling methods. The reaction appears to be completely regio- and stereospecific and involves inversion of configuration at both sulfur and α carbon. This result is discussed on the basis of various possible halogenation mechanisms. However, no clear-cut mechanistic choice appears to be possible.

The stereochemistry of α halogenation of sulfoxides by halogens or halogen sources (X_2) in the presence of base (B:)[1] has been extensively investigated in recent years.

$$RS(O)CHR_1R_2 \xrightarrow[B:]{X_2} RS(O)CXR_1R_2$$

The reaction is normally found to be stereospecific, and occasionally highly so, at both sulfur and α carbon.[7] The results, however, are puzzling, as the actual steric course appears to depend rather unpredictably both on sulfoxide structure (open chain[7] or cyclic,[8-11] type and nature of the substituent at C_α[7,12]) and reaction conditions (halogenating agent, presence or absence of an electrophile such as $AgNO_3$).[7] Thus, if it is reasonable to suppose that a single fundamental mechanism is operating in every case, it has been nevertheless impossible to fit all the results in a coherent framework. Apparently, the factors which ultimately control the stereochemistry are incompletely understood.

It has been suggested that the conformational flexibility of the substrate and/or reactive intermediates formed along the reaction path may play a key role in determining the steric course,[11,12] yet no comprehensive study has been reported on the halogenation of conformationally rigid sulfoxides.[13] In this paper we report on the stereochemistry of bromination of *trans*-2-thiahydrindan 2-oxide (**1a**), a system which, by virtue of the trans ring fusion, cannot undergo appreciable skeletal deformation at the reaction centers.[14] This system is particularly advantageous, since the four α protons are all stereochemically different, either because of their relation to the S–O bond or the ring fusion, and can be readily identified in