Synthesis of a Six-Membered-Ring (2*R*)-10a-Homobornane-10a,2-sultam and Structural Comparison with *Oppolzer*'s, *Lang*'s, and *King*'s Sultams

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The new six-membered-ring (2*R*)-10a-homobornane-10a,2-sultam (−)-**3a** was synthesized and its X-ray structural analysis was compared with that of the novel structure of the five-membered-ring (2*R*)-bornane-10,2-sultam analogues (−)-**1a**,**b** as well as with that already published for the six-membered-ring *trans*-decalin-like sultam **4a**. Based on DN** density-function calculations and X-ray crystallographic studies of the *N*-methylated analogues (−)-**1e** and **4b** and by comparing with the conformation of the *N*-fluoro derivatives (−)-**1c** and (+)-**1d**, the anomeric stabilization was estimated to be smaller than the 2.0–2.5 kcal/mol earlier suggested. The direction of pyramidalization is rationalized in terms of H-bond and steric and electronic interactions and extended to the known toluenesultam derivatives **10a**–**c**.

Introduction. – Owing to its ready availability in both antipodal forms as well as to the crystallinity imparted to its derivatives, the tricyclic five-membered-ring (2*R*)-bornane-10,2-sultam (−)-**1a** [1] has found wide application in various asymmetric methodologies and syntheses [2]. Its ability to generally induce high diastereoselectivity at the C(α)-atom of *N*-(α,β-unsaturated acyloyl) derivatives was rationalized by *Kim* and *Curran* on the basis of a steric argument, in which the approach is directed by the C(3) substituent in the chelated *syn*-s-*cis* conformation or by the pseudo-axial O(1)=S substituent for the nonchelated *anti*-s-*cis* conformer [3]. Thus, this prosthetic group was compared to a masked C_2-symmetrical form of (2*R*,5*R*)-2,5-dimethylpyrrolidine. Based on results from [4+2] cycloadditions [4][5] or *syn*-dihydroxylations [6], we later completed this steric model by hypothesizing the concurrent high reactivity of the *syn*-s-*cis* conformer under uncatalyzed conditions [4]. In this same work, we also introduced the matching or mismatching stereoelectronic influence of the N lone pair (lp) on the LUMO π-facial atomic coefficients of the C(α)/C(β) reacting centers. In addition, by comparing structurally analogous dienophiles derived from (−)-**1a** and (−)-**2a** [7], we also demonstrated that the *anti*-s-*cis vs. anti*-s-*trans* equilibrium, hence the global diastereoselectivity, were strongly influenced by the pseudo-equatorial O(2)=S substituent. We invoked the generalized anomeric effect [8] to rationalize the orientation of the N lp as well as its stereoelectronic influence on both the C(α)/Cβ) π-system and *syn*/*anti* conformational stabilization of the dienophiles [9][2]).

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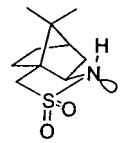
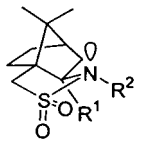
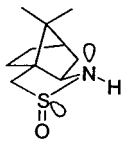
[2]) For N lp through-bond and through-space directing interactions, initially suggested by *Müller* and *Eschenmoser*, see [10a]. For nonexhaustive more recent examples, see [10b–g]. *Cieplak* also proposed a hyperconjugative influence of the N lp on the incipient bond-formation through the intermediacy of a sp^2 atom, see Schemes 85 and 86 as well as reference 105 in [11].



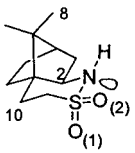
(–)-**1a**



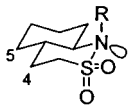
(–)-**1b** R^1=Me, R^2=H
(–)-**1c** R^1=H, R^2=F
(+)-**1d** R^1=Me, R^2=F
(–)-**1e** R^1=H, R^2=Me



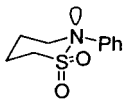
(–)-**2a**



(–)-**3a**



4a R=H
b R=Me



4c

More recently, *King et al.* also suggested an anomeric stabilization [12a]. We now wish to report the synthesis of the tricyclic six-membered-ring sultam (–)-**3a** as well as its X-ray-structural analysis for comparison with those of (–)-**1a**,**b**,**e** and the racemic six-membered-ring *trans*-decalin-like sultams **4a**,**b** [12a].

Results. – The commercially available (+)-camphorsulfonyl chloride **5** was treated with CH_2N_2 in Et_2O to afford, after thermal treatment, the known unsaturated C_{11} ketone (+)-**6** in 84% yield according to a previously reported procedure [13]. Further protection of the carbonyl moiety (ethylene glycol, TsOH, THF; 79% yield) followed by hydroboration (9-BBN, THF, 20°, then NaOH, H_2O_2; 90% yield) furnished the known primary alcohol (–)-**7a** [14][3]). This intermediate was then converted to the corresponding crude unreported mesylate (–)-**7b** (MsCl, CH_2Cl_2, Et_3N, 0°; 95% yield [16]) prior to an S_N2 displacement (AcSK, DMSO, 45°; 96% yield [17]) to afford the thioacetate (–)-**7c**. Oxidation (30% H_2O_2 solution, 85%, AcOH solution [18]), with concomitant deprotection, delivered the new sulfonic acid (+)-**8a** in 92% isolated yield. A route similar to that earlier published by *Oppolzer et al.* [1] was then followed for the preparation of (–)-**3a**.

Thus, treatment with $SOCl_2$ at 100° [19] furnished the sulfonyl chloride (–)-**8b** in 63% yield[4]). Rather than addition of gaseous NH_3 under anhydrous conditions [21], we preferred, for technical reasons, the NH_4OH procedure initially reported by *Sutherland* and co-workers [22] and recently re-actualized by *Davis et al.* [19] and *Capet et al.* [23]. The new sulfonamide (+)-**8c**, thus obtained in 69% yield, was then cyclized under basic conditions (NaOMe, MeOH [1]) to furnish the sulfonimine (–)-**9** in 75% yield[5]).

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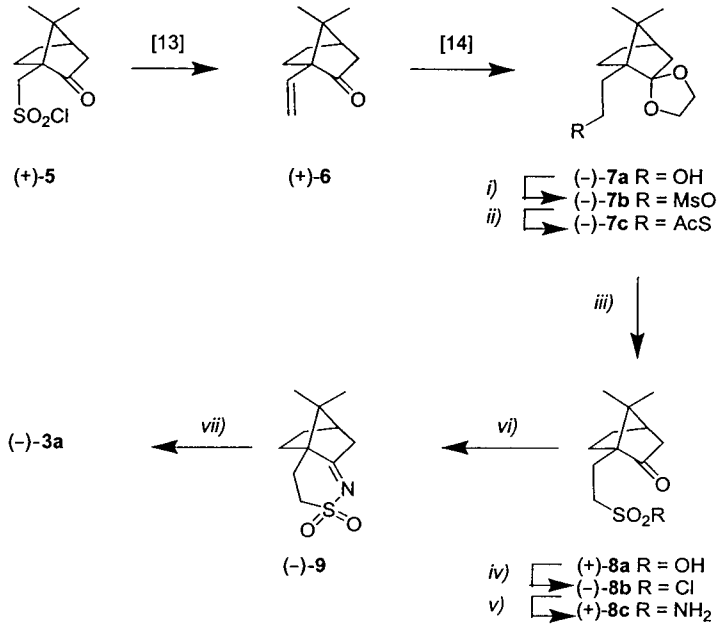
[3]) According to [15], a lower chemical yield was obtained by direct hydroboration of the unprotected ketone (+)-**6**.

[4]) For the use of PCl_5, see [20].

[5]) For cyclization under acidic conditions, see [19]. For a bornanesulfonimide possessing a six-membered ring connected to C(2) and C(3), see [24].

Scheme



i) MsCl, CH_2Cl_2, Et_3N, 20°; 95%. *ii*) AcSK, DMSO, 45°; 96%. *iii*) 30% H_2O_2 soln., AcOH, 60°; 92%. *iv*) $SOCl_2$, 100°; 63%. *v*) NH_4OH, dioxane, 20°; 69%. *vi*) NaOMe, MeOH, 65°; 75%. *vii*) $NaBH_4$, MeOH, H_2O, 20°; 90%.

Finally, reduction with $NaBH_4$ in H_2O afforded the desired (2*R*)-10a-homobornane-10a,2-sultam (–)-**3a** in 90% yield after recrystallization from hexane/AcOEt[6]).

To determine the orientation of the N-pyramidalization, (–)-**3a** was subjected to an X-ray crystallographic study, and its structure is depicted in *Fig. 1*. For comparison, the X-ray structural analysis of (–)-**1a** that we performed some years ago[7]) is now also presented in *Fig. 2*. This latter shows, in contrast to the saccharine-derived sultam **10a** [26], a single crystallographic conformation in which the H–N bond is practically *anti*-periplanar to the pseudo-axial O(1)=S substituent[8]).

Discussion. – The X-ray analysis of *King*'s sultam **4a** shows a N lp bisecting the O(1)=S=O(2) angle [12a] and an H–N bond fully *anti*-periplanar to the O(1)=S substituent (H–N–S=O(1) 176.9°) with an effective H-bond to the O(1)=S moiety of

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[6]) For alternative methods of reduction with $LiAlH_4$ or H_2/*Raney*-Ni, see [1] and [22], respectively. For a detailed synthesis of (–)-**1a**, see [20] and page 2836 in [25].

[7]) See footnote 9 in [5].

[8]) An intermolecular H-bond between the H–N and O(1)=S moiety of (–)-**1a** may be responsible for this conformations. DN** Calculations [27] on an isolated structure rather suggest a difference of 0.4 kcal/mol in favor of the pseudo-equatorial conformer. In the case of (–)-**2a**, the H–N bond adopts a pseudo-equatorial orientation due to the diminished steric *gauche* interaction of the missing O(2)=S substituent. This conformation also avoids a stereoelectronic destabilizing *syn*-periplanar orientation of both N/S lp [7]. Finally, an intermolecular H-bond may also be invoked: H–N 0.79(4), H···O(1) 2.071(4), and N···O(1) 2.832(5) Å; N–H···O(1) 160.00(53)°.

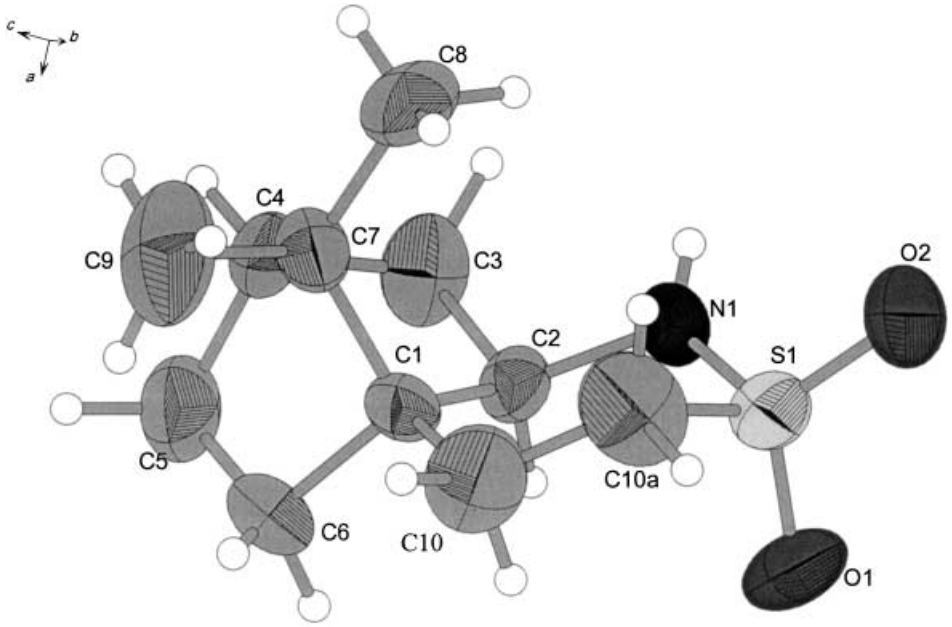

Fig. 1. *ORTEP Diagram of (–)-***3a** *with arbitrary atom numbering*. Ellipsoids are represented at the 50% probability level.

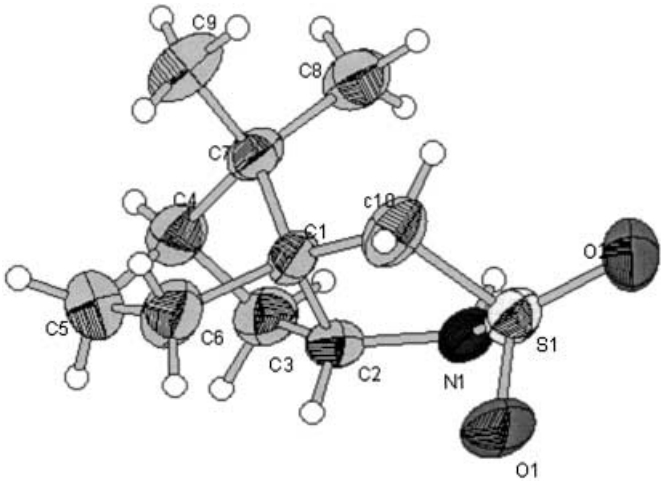

Fig. 2. *ORTEP Diagram of (–)-***1a** *with arbitrary atom numbering*. Ellipsoids are represented at the 50% probability level.

another molecule[9]). *King et al.* [12a] attributed the pyramidalization observed in their X-ray analysis partially to a generalized anomeric stabilization[10]). This latter may result either from π-delocalization of the N lp into the vacant d orbital of the S-atom [28] or from a negative hyperconjugation of the N lp with the electron-deficient C–S bond (n N to σ^* C–S) [29]. On our side, we earlier postulated a possible anomeric stabilization of the N lp, with the pseudo-axial O(1)=S substituent in the specific case of the N-substituted derivatives of (–)-**1a** [4b][9b]. We had also questioned the possible cumulative hyperconjugative influence of the H–C(2) bond[11]). For this reason and for comparison, we also performed the X-ray structural analysis of the known free sultam (–)-**1b**, prepared in 1988 by *Differding* and *Lang* [30][12]) (see *Fig. 3*). An intermolecular H-bond is also observed between the pseudo-equatorial H–N group and a pseudo-axial O(1)=S moiety[13]), the latter being sterically slightly deviated from its usual pseudo-axial position by the supplementary Me–C(2) substituent. Due to a smaller S–N–C(2)–C(3) dihedral angle and in contrast to its demethyl analogue, the Me(8) substituent of (–)-**1b** disfavors a pseudo-axial orientation of the H–N bond[14]). In contrast to (–)-**1a**, the N-atom is flatter and the O(1)=S bond is longer as compared to O(2)=S, while the S–N bond is shorter. Density function DN** calculations again indicate that the structure of (–)-**1b** without H-bonding interactions prefers to orientate the H–N bond in the pseudo-equatorial direction. This conformation, which places the N lp *anti*-periplanar to the O(1)=S bond, is 0.32 kcal/mol lower in energy. The pyramidalization observed in the X-ray structure analysis of (–)-**1b** could thus be the result of either both an intermolecular H-bonding and a steric interaction or a stereoelectronic stabilization of the N lp with the O(1)=S.

In addition, *King et al.* [12] prepared the *N*-Me-substituted sultam **4b** and showed by X-ray structure analysis that the observed conformer in the crystalline state orientates the Me substituent in the axial direction[15]), thus increasing the dipole

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[9]) In the absence of H-bonding interaction, DN** calculations performed on a single structure rather suggest that the equatorial conformer **4a** is 0.26 kcal/mol more stable than the axial H–N conformer.

[10]) Indeed, they conclude that it would seem imprudent to ascribe the axial orientation of the H–N exclusively to the anomeric effect due to the presence of the H-bond.

[11]) See bottom of page 160 in [4b] and footnote 11 in [9b].

[12]) Sultam (–)-**1b** shows the following IR (KBr): 3268, 2966, 2879, 1500, 1459, 1417, 1377, 1314, 1291, 1218, 1173, 1118, 1081, 992, 755 and ^{13}C-NMR resonances: 21.2 (*Me*–C(7)); 22.1 (*Me*–C(7)); 26.4 (C(5)); 27.4 (*Me*–C(2)); 27.5 (C(6)); 45.2 (C(3)); 45.7 (C4)); 49.9 (C(7)); 50.2 (C(10)); 58.2 (C(1)); 66.1 (C(2)). For the ^{13}C-NMR analysis of (–)-**1a**, see [19a]. The IR analysis of solid (–)-**1a**: **3286**, 2959, 2880, 1477, 1459, 1404, 1377, 1328, 1293, 1213, 1183, *1161*, *1133*, 1065, 859, 839, 790, 762, shows bathochromic displacements in the $\tilde{\nu}$(N–H) and in both *asym.* and *sym.* $\nu(SO_2)$ stretching regions when compared to a 2.5% $CHCl_3$ soln.: **3341**, 2964, 2885, 1457, 1394, 1341, 1316, 1213, *1165, 1137*, 1067, 863, 775 or to a GC-FTIR: **3380**, 2966, 2895, 1398, 1356, *1173*, *1144*, 1078 analysis of the monomer [1].

[13]) The geometry of this H-bond is the following: H···O(1) 2.291(4) Å, N···O(1) 2.981(7) Å, N–H···O(1) 144.45(25)°.

[14]) The distances separating the N-atom and C-atom of the Me(8) substituent are the following: (–)-**1a**, 3.103(5) Å; (–)-**1a**′, 3.104(5) Å; (–)-**1b**, 2.971(3) Å; (–)-**3a**, 3.152(6) Å. Rather than a hyperconjugative influence of the H–C(2) bond, a modification of the crystal packing caused by steric intermolecular interactions of the supplementary Me–C(2) group is not excluded to explain this H-bonded preferential H–N orientation.

[15]) In contrast to our expectations based on a N lp anomeric stabilization by the axial O=S bond.

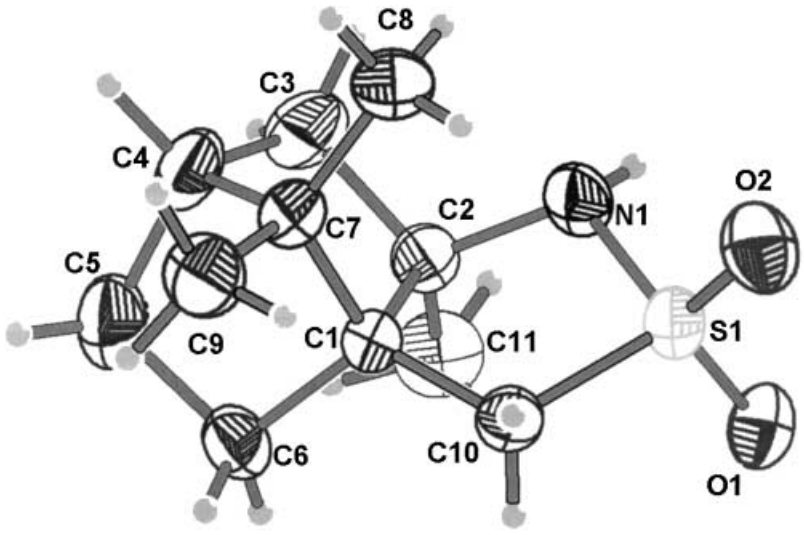

Fig. 3. *ORTEP Diagram of (−)-***1b** *with arbitrary atom numbering*. Ellipsoids are represented at the 50% probability level.

moment of this molecule to 5.7 D as opposed to 5.0 D for the equatorial conformer. By simple analogy to a monomethyl-substituted cyclohexane, the anomeric stabilization was estimated to be between 2.0 and 2.5 kcal/mol[16]).

The X-ray crystallographic study of the *N*-methylsultam (−)-**1e** (see *Fig. 4*), initially synthesized by *Sutherland* and co-workers, but, except for melting and chiroptical properties, never characterized since 1938 [22], exhibits an expected pseudo-equatorial orientation of the Me−N substituent, resulting from the steric repulsion of the Me(8) group. Like (−)-**1b**, it also shows typical features of an anomeric stabilization of the N lp with the O(1)=S, resulting in a shortening of the S−N bond and elongation of the O(1)=S bond [8g] (see *Table 1*).

Interestingly, the N-atom is particularly flat for the six-membered ring sultam (−)-**3a** as compared to (−)-**1a**,**b** (see *Table 1*) or **4a** (ΔhN = 0.393(3) Å), probably for the same reasons. Indeed, similarly to the pseudo-axial five-membered ring analogue (−)-**1b**[17]), the chair-like six-membered-ring sultam (−)-**3a** imposes a Me(8) steric pressure on the axial substituent at the N-atom. Consequently, the deviated pseudo-axial[18])

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[16]) This estimation is based on the knowledge that the Ph substituent in sultam **4c** adopts an equatorial orientation according to X-ray structural analysis [31] and that the *K* value for Ph in a cyclohexane ring is 209, corresponding to a difference of 3.0 kcal/mol [32].

[17]) The bornane skeleton as compared to a *trans*-decalin-like skeleton as in **4a** also imparts a small deformation of the chair-like conformation. The C(1)−C(2)−N angle is 103.9(3)° for (−)-**1a** as compared to 115.1(3)° for (−)-**3a**. Similarly, the dihedral angles C(7)−C(1)−C(2)−N are 102.4(3)° and 92.4(4)°, respectively. Thus, a purely axial H−N-bond would be closer to the Me(8) substituent for the six-membered-ring analogue.

[18]) DN** Calculations suggest that the equatorial H−N conformer (−)-**3a** is 1.28 kcal/mol lower in energy as compared to the purely axial conformer in the absence of H-bonding.

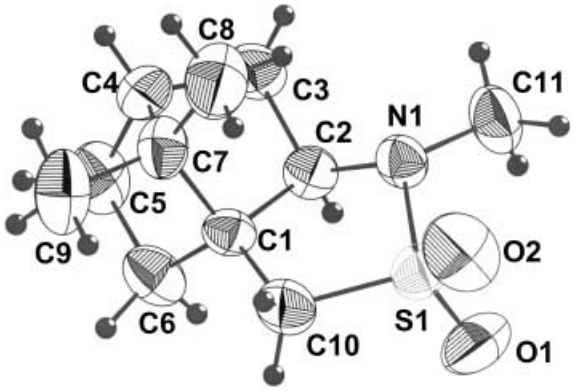

Fig. 4. *ORTEP Diagram of (−)-***1e** *with arbitrary atom numbering*. Ellipsoids are represented at the 50% probability level.

Table 1. *Selected Bond Lengths* [Å] *and Angles* [°] *for (−)-***1a,b,e** *and (−)-***3a**

	(−)-**1a** R^2=H	(−)-**1b** R^2=H	(−)-**1e** R^2=H	(−)-**3a** R^2=H
S=O(1)	1.401(3)	1.4460(16)	1.436(3)	1.412(4)
S=O(2)	1.453(3)	1.4267(17)	1.421(2)	1.430(4)
S−N	1.750(3)	1.6228(18)	1.646(2)	1.594(4)
S−C	1.688(4)	1.7863(19)	1.770(4)	1.776(6)
N−C(2)	1.443(5)	1.482(3)	1.463(4)	1.471(6)
N−R^2	0.84(3)	0.80(3)	1.467(4)	0.72(4)
O(1)=S=O(2)	118.51(18)	115.14(10)	115.84(18)	118.7(2)
C(2)−N−S	108.4(3)	111.91(13)	107.80(19)	118.7(3)
C(2)−N−R^2	113(2)	118.1(19)	116.1(3)	120(4)
S−N−R^2	111(2)	108.5(19)	114.7(3)	115(4)
C(2)−N−S=O(1)	73.4(3)	87.44(15)	83.4(2)	59.4(4)
C(2)−N−S=O(2)	−153.8(3)	−142.59(14)	−147.5(2)	−169.8(4)
C(3)−C(2)−N−S	159.7(3)	150.55(16)	155.7(3)	168.6(4)
R^2−N−S=O(1)	−161.4(3)	−44.7(3)	−47.7(3)	−148.2(3)
Δ*h*N	0.368(5)	0.318(4)	0.412(4)	0.162(4)

H−N bond directs the N lp close to the O(1)=S[19]). Additionally, the short H−N bond of (−)-**3a** also forms an intermolecular H-bond with the O(1)=S of another molecule[20]), and its S−N bond is also very short as compared to (−)-**1a**,**b** (see *Table 1*) and **4a** (1.633(2) Å). Both structures (−)-**1a** and (−)-**3a** exhibit shorter axial O(1)=S bonds as compared to the equatorial O(2)=S bonds, in contrast to the six-membered-ring sultam **4a** (axial O(1)=S 1.4384(14) Å; equatorial O(2)=S 1.428(2) Å), although **4a** also involves its O(1)=S substituent in an H-bond[21]).

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[19]) The dihedral angle O(1)=S−N-lp is −45.0(3)° as compared to −59.4(3)° for an ideal bisection of the O(1)=S=O(2) angle. For efficient *syn*-periplanar anomeric stabilizations, see [8d,e].

[20]) The H···O(1) and N···O(1) distances are 2.43(4) and 3.099(6) Å, respectively, while the N−H···O(1) angle is 159(5)°.

[21]) For (−)-**1a**, the H···O(1) distance is 2.45(3) Å, and the N···O(1) distance is 3.240(4) Å, while the N−H···O(1) angle is 158(3)°. For comparison, the H-bond in **4a** seems more effective, with the H−N and H···O(1) distances of 0.90 and 2.10 Å, respectively, and an N−H···O(1) angle of 174°.

Rather than the *N*–Me analogues of (–)-**1b** and (–)-**3a**, we preferred to turn our attention towards the sterically less-demanding *N*-fluoro derivatives, to decrease and determine more precisely the differences in conformational energy[22]). Indeed, the F-atom is sterically slightly more voluminous than the H-atom (1.35 *vs* 1.20 Å) as compared to 2.0 Å for the *Van der Waals* radius of a Me group [32][23]). *Davis et al.* recently showed by ^{19}F-NMR analysis that the *N*-fluorosultam (–)-**1c** is a mixture of conformers at 20° [33]. He also found that at –66° this mixture consists of a 3 : 97 ratio of the pseudo-axial/equatorial conformers[24]). This corresponds to a difference of energy of *ca.* 1.5 kcal/mol, which is in good agreement with the 1.85 kcal/mol found in favor of the pseudo-equatorial *N*-fluoro derivative (–)-**1c** by DN** calculations. We thus suggest that the anomeric stabilization, whatever its origin, is lower than the 2.0–2.5 kcal/mol proposed by *King et al.* [12a]. This discrepancy probably comes from their having underestimated the *gauche* interactions exerted by the SO_2 moiety. Indeed, in their anomerically stabilized conformation, the axial Me–N substituent of **4b** additionally interacts with both *syn*-clinal CH(8a)–CH(4a) and S–CH_2(3). In contrast, in the equatorial orientation, the Me–N substituent additionally interacts with the *syn*-clinal axial O(1)=S moiety. If we hypothesize that the *syn*-clinal interactions of the Me–N with a S–CH_2 or a O=S moiety are of similar amplitude[25]), then the axial anomerically stabilized conformer of **4b** is sterically destabilized by a single *syn*-clinal Me–N/CH(8a)–CH(4a) 1,4-interaction representing *ca.* 0.85 kcal/mol when the *Newman* strains are neglected and not 2.0–2.5 kcal/mol as suggested. Furthermore, more precise DN** calculations suggest that axial and equatorial conformers of **4b** are practically of similar energy, since this latter is thermodynamically more stable by 0.08 kcal/mol. As the density-function method takes into account both steric and electronic factors, we wondered whether the axial orientations observed in the X-ray structure analyses of **4a**,**b** could find their origin in external effects such as intermolecular H-bonding, dipole-dipole, hydrophobic, or solid-solid packing interactions. Since the data reported for **4a**,**b** did not mention any ^{13}C-NMR multiplicities or ^{1}H-NMR *Overhauser* experiments [12a], we had some difficulty to assign the signals and thus performed these supplementary analyses to determine the conformation of **4b** in solution[26]). The ^{13}C-NMR analysis of **4b** allowed us to tentatively attribute the

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[22]) We are indebted to Drs. *E. Differding* for his preliminary authorization and *G. Rihs* for providing us with the X-ray structure analysis of (+)-**1d**, mentioned in [30]. This structure shows a pseudo-equatorial F–N bond (F–N–C(2)–C(1) 162.9(3)°; F–N 1.421(3) Å, S–N 1.723(3) Å, N–C 1.493(5) Å, O(1)=S 1.442(3) Å, O(2)=5 1.432(3) Å, S–C 1.776(3) Å).

[23]) The *K* values for F and Me are 1.31 and 20.5, respectively; this corresponds to a difference of energy of 0.15 and 1.70 kcal/mol, respectively, between the equatorial *vs.* axial conformers in a cyclohexane ring.

[24]) The conformational attribution is based on ^{19}F-NMR coupling constant analysis by comparison with the purely pseudo-equatorial *N*-fluoro-3,3-dichloro analogue of (–)-**1c** as exhibited by its X-ray-structural analysis [33].

[25]) The sterically more demanding *Van der Waals* radius of a CH_2 group (1.9 Å) as compared to an O-atom (1.4 Å) is relative to the difference of the bond lengths for **4b**: S–CH_2 (1.764(2) Å); O(1)=S (1.439(2) Å).

[26]) We are particularly indebted to Prof. *King* for a sample of **4b** as well as for pertinent comments on the manuscript.

signals reported for **4a**[27]) and shows an upfield γ-shift of all three *gauche* C(3), C(4a), and C(8) atoms in accord with an axial Me–N substituent. Furthermore, a NOESY experiment shows correlations with the axial H–C(3) (2.95 ppm), H–C(4a) (1.45 ppm), and H–C(8) (1.36 ppm) as well as equatorial H–C(8) (1.88 ppm), in agreement with the conformation exhibited by the X-ray structural analysis or at least by an equilibrium[28]). We, nevertheless, think that this conformation does not exclusively result from a stereoelectronic effect. We base our argument on the fact that DN** calculations on *trans*-decahydro-1,2,2-trimethylquinoline suggest that, for purely steric reasons, the Me–N axial conformer is thermodynamically slightly privileged by 0.03 kcal/mol. These theoretical results espouse well the substantial number of Me–N axial conformers observed by *Eliel* and co-workers in the case of protonated *trans*-decahydro-1,2-dimethylquinolines according to ^{13}C-NMR analyses [34][29]).

Besides the slightly greater steric influence of the F-atom, the electronegative nature of this substituent is also electronically different from the more electropositive H-atom. According to *Bent*'s rule [35], an electron-withdrawing substituent at the N-atom increases its s character, thus the sum of the substituent–N angles tends to ideally reach 270° for a purely s-like N, as compared to 360° for a purely sp^2-planar N [36]. This is well-reflected by the greater pyramidalization of the cyclic *N*-fluorosultams as expressed by the X-ray analyses of (+)-**1d** (F–N–C(2) = 111.6(3)°, F–N–S = 106.2(2)°, C(2)–N–S = 109.2(2)°, ΔhN = 0.521(4) Å) as compared to (–)-**1a** or (–)-**1b** (see *Table 1*). This increased pyramidalization is also consistent with the supplementary anomeric stabilization of the F and N lone electron pairs [36][30]). Thus, in the case of (–)-**1c** or (+)-**1d**, a more pseudo-axial F–N substituent would be sterically more demanding with respect to the Me(8), due to both its size and the N-hybridization [37]. As a result, this steric effect would certainly exceed the 0.15 kcal/mol observed for a cyclohexane skeleton[23]). Similar N-hybridizations are also observable in the X-ray structural analyses reported by *Kakuda et al.* for **10b**,**c** [38].

Earlier, we have similarly explained the sense of the N-pyramidalization in the case of saccharine-derived sultams [4b][39]. These toluenesultams differ remarkably from the camphorsultams by the substitution at the α-position of the S-atom. Consequently

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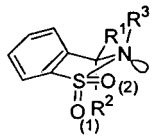
[27]) The ^{13}C-NMR attributions are the following, consistant with analogous skeletons [34]: **4b**: 25.0 (C(7)); 25.3 (C(6)); 29.4 (Me–N); 30.5 (C(8)); 30.6 (C(4)); 31.8 (C(5)); 34.0 (C(4a)); 45.5 (C(3)); 63.0 (C(8a)); **4a**: 24.7 (C(7)); 25.4 (C(6)); 30.4 (C(4)); 30.9 (C(5)); 32.5 (C(8)); 41.1 (C(4a)); 50.3 (C(3)); 59.6 (C(8a)).

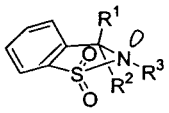
[28]) Besides broadening of the peaks, no additional signals were noticed between 20° and –90° [12a]. This suggests a possible rapid inversion of the N-atom with a barrier estimated to 1.7 kcal/mol based on DN** calculations. Investigations to determine this value by NMR techniques are under way and shall be reported in due course. For comparison, the barrier of N-inversion for 1,2,2,6-tetramethylpiperidine is 9.1 – 11.0 kcal/mol according to NMR analysis [34d].

[29]) According to the authors, solvation of the decahydroquinolinium ion only partially rationalizes these observations. They additionally invoke puckering of the heterocycle in the region of the N-atom to explain the greater *gauche* repulsion of the Me–N group by the more proximate 2,8a equatorial substituents.

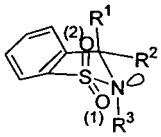
[30]) The amplitude of a stereoelectronic stabilization may be altered by the greater electronegativity and anomeric involvement of the F-atom, making the N lp less available for delocalization into the SO_2 moiety as suggested by the longer S–N bond of (+)-**1d** as compared to (–)-**1b** (see *Footnote 22* and *Table 1*). Nevertheless, a simple steric effect of the halogen atom is not excluded to rationalize this bond length. Similarly, a more sp^2 planar N-atom results in a shorter S–N bond as observed for (–)-**3a**.



10a R^1=Me, R^2=H, R^3=H



10b R^1=cHex, R^2=Me, R^3=H



10c R^1=cHex, R^2=Me, R^3=F

the aromatic ring tends to bisect the O(1)=S=O(2) angle. Small substituents at the stereogenic center such as a Me group prefer a pseudo-equatorial orientation, whereas large substituents like cyclohexyl or *tert*-butyl [39] are obliged to adopt a pseudo-axial orientation to avoid steric interaction with the aromatic ring[31]). As a consequence, this inverts the five-membered-ring envelope and brings the O(2)=S into the pseudo-axial orientation. This is probably why *Kakuda et al.* could not explain why the pyramidalization of their sultam **10b** was inverted with respect to *Oppolzer*'s analogue **10a**[32]). In fact, the H–N bond is consistently *anti*-periplanar to the pseudo-axial O=S bond, hypothetically due to an H-bond[33]). Similarly, the more pyramidalized *N*-fluoro analogue **10c**[34]) obliges the larger substituent to adopt an even more pseudo-axial orientation due to both the N-hybridization and the slightly more bulky F-atom, which exerts both a steric repulsion with the Me substituent and an electrostatic repulsion with the O(1)=S.

Conclusions. – Density-function DN** calculations for (–)-**1a**, (–)-**3a**, and **4a**,**b** systematically privilege the *anti*-periplanar orientation of the N lp with respect to the pseudo-axial O(1)=S substituent in contrast to their X-ray-structure analyses. We postulate that the intermolecular H-bond observed in the crystalline structures of (–)-**1a**, (–)-**3a**, and **4a** is mainly responsible for the orientation of the H–N bond. Thus, according to X-ray structure and NMR analysis, the N lp is practically bisecting the SO_2 angle in (–)-**1a** and **4a**,**b**[35]), while it adopts a preferential *anti*-periplanar disposition with the O(1)=S substituent in (–)-**1b**,**c**,**e** and (+)-**1d**. In the six-membered-ring sultam analogue (–)-**3a**, due to the steric repulsion of the Me(8) group and the intermolecular H-bond with the O(1)=S, the N-atom is very flat and, thus, suggests that the anomeric

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[31]) The case of **10b** is particular because the stereogenic center bears both a Me and a cyclohexyl substituent; thus, in the absence of a sterically influential directing substituent at the N-atom, the aromatic ring also bisects the Me–C-cyclohexyl angle, and the intermolecular H-bond involves the sterically more accessible O(1). As a result, the N lp does not bisect the O(1)=S=O(2) angle.

[32]) We are indebted to Dr. *G. Bernardinelli* for confirming an intermolecular H-bond between the A···A and B···B conformers of **10a**. The geometries of these H-bonds are the following: H–N 1.114(5) and 1.063(5), H···O(1) 1.997(4) and 2.081(4) Å; N···O(1) 3.040(7) and 3.012(6) Å, and N–H···O(1) 158.37(24) and 144.71(25)°, respectively. The unfortunate omission of this crucial detail in the original report [26] did not help us to rationalize the N-pyramidalization.

[33]) An intermolecular H-bond was also reported for **10b**: N···O 2.955(3) Å [38].

[34]) The following angles were reported: for **10b**, S–N–C 155.6(2), S–N–H 108(2), and C–N–H 113(2)°; for **10c**, S–N–C 107.0(2), S–N–F 102.3(2), and C–N–F 105.7(2)° [38].

[35]) Sultam (–)-**1a** exhibits the longest S–N and the shortest S–C bond lengths a compared to (–)-**1b**,**e**, (+)-**1d**, or (–)-**3a** (see *Table 1* and *Footnote 22*). We think that this unusual deformation results from the C(2)–H···O(2) intercalary crystal packing associated with the H-bond as well as to the H–N–S=O(2) *gauche* interaction.

stabilization estimated to be 2.0–2.5 kcal/mol by *King et al.* [12] is certainly smaller and is probably less than 1.5 kcal/mol. This value follows from the conformational equilibrium of the pseudo-equatorial *N*-fluoro derivative (−)-**1c**[36]). Furthermore, the origin and preference of this anomeric stabilization, orientating the N lp either *anti*-periplanar to the O(1)=S or inbetween the O(1)=S=O(2) angle, remains to be precised. The very specific stereoelectronic nature of the N-atom allows it to adapt its hybridization to the subtlest steric, stereoelectronic, and H-bonding interactions of its environment. The chameleon-like nature of this atom imposes the greatest caution for conformational prognostics. If the *a posteriori* rationalization of the N-pyramidalization in $R^1-SO_2-N-R^2_2$ systems seems reasonable, the *a priori* estimation of the expected conformation and sense of tilting often requires the greatest prudence, as shown by the X-ray crystallographic studies of acyclic sulfonamides recently published by *Ohwada et al.* [40][37]). Indeed, in some instances, the σ N through-space interaction with a spatially more-extended π^* orbital may sometimes be more stabilizing than the usual N σ-σ^* or n-σ^* hyperconjugation. There is no doubt that the additional possible pyramidal nature of the N-atom in acyclic/cyclic sulfonamides renders this class of molecules more attractive than simpler planar amides and will motivate further experimental, theoretical, and computational studies[38]), especially in the context of enantioselective chiral-relay amplification [43].

To determine the most relevant orbital interactions of the N lp with the $C-SO_2$ moiety for (−)-**1a**–**c**,**e** and (−)-**3a** as well as to ascertain the origin of the unexpected conformation of **4b**, we have recently undertaken a *Gaussian*-NBO analysis [44] to clarify whether the N lp interacts with the vacant S d, the σ^* S–C, or the σ^* O(1)=S orbitals. These results, associated with the diastereoselectivity dependence observed in the [4 + 2] cycloaddition of the bis-*N*,*N*′-fumaroyl dienophile derived from (−)-**3a** to cyclopentadiene, as a function of the solvent polarity [7][9c][45], shall be presented in due course.

The X-ray analyses of (−)-**1a**,**b**,**e** and (−)-**3a** were recorded by the crystallographic department of the University of Warsaw. Financial support from the *National Committee for Scientific Research* (PBZ 6.05/T09/99) is gratefully acknowledged. We are also indebted to Prof. *A. S. Cieplak* for stimulating discussions.

Experimental Part

General. See [6].

X-Ray Crystal-Structure Analyses. Crystal data regarding structures (−)-**1a**,**b**,**e** and (−)-**3a** are given in *Table 2*. All measurements of crystals were performed on a *Kuma-KM4CCD k*-axis diffractometer with

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36) This value allows fitting both possibilities: $\Delta G^\circ_{observed} = \Delta G^\circ_{stereoelectronic} +/- \Delta G^\circ_{conformational}$ according to our matching or *King*'s mismatching hypotheses, respectively.

37) This prudence should also be extended to our DN** method of calculation since the tiny difference of Me–N axial/equatorial conformational energies found for **4b** and *trans*-decahydro-1,2,2-trimethylquinoline may well be below its standard error for unusual sulfonamide functionalities. We, thus, may only conclude that these energies are very close.

38) For recent syntheses of new sultams by direct *Diels–Alder* additions, see [41]. For a rationalization of the N-pyramidalization in such structures, see footnote 9 in [6a]. For a recent stereochemical rationalization in opposition to *Curran*'s sterically based arguments, see [42]. The diastereoselectivity increases while the chemical yield decreases, and polymerization of a less-stable major stereoisomer is not excluded in this latter case. For such recognized alterations of the diastereoisomer ratio, see [4b][6b].

graphite-monochromated MoK_α radiation. The crystal was positioned at 65 mm from the *KM4CCD* camera. A 1.6° intervals with a counting time of 10s, 288 frames were measured for (−)-**1a** and (−)-**3a**. A 1.0° intervals with a counting time of 15 s, 1050 frames were measured for (−)-**1b**. A 1.3° intervals with a counting time of 25 s, 576 frames were measured for (−)-**1e**. The data were corrected for *Lorentz* and polarization effects. No absorption correction was applied. Data reduction and analysis were carried out with the *Kuma* diffraction (Wroclaw) programs.

The structure was solved by direct methods [46] and refined by means of SHELXL [47]. The refinement was based on F^2 for all reflections, except those with very negative F^2. Weighted R factors wR and all goodness-of-fit S values are based on F^2. Conventional R factors are based on F with F set to zero for negative F^2. The $F_o^2 > 2\sigma(F_o^2)$ criterion was used only for calculating R factors and is not relevant to the choice of reflections for the refinement. The R factors based on F^2 are about twice as large as those based on F. All H-atoms were located from a differential map and refined isotropically. Scattering factors were taken from Tables 6.1.1.4 and 4.2.4.2 in [48]. The known configurations of the asymmetric centers of the sultam unit was confirmed by the *Flack*-parameter refinement [49].

Crystallographic data (excluding structural factors) for the structures of (−)-**1a**,**b**,**e** and (−)-**3a** have been deposited as supplementary material with the *Cambridge Crystallographic Data Centre* and allocated the deposition number CCDC 175470, 178139, 175471, and 175472, resp. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EW, UK (Fax: int. code + (1223)336-033; e-mail: deposit@ccdc.cam.ac.uk).

*(−)-(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-1,8,8-trimethyl-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide* (−)-**1e**). A soln. of (−)-**1a** (1.0 g, 4.64 mmol) in toluene (15 ml) was added to a suspension of NaH (60% in mineral oil; 470 mg, 11.6 mmol, 2.5 mol-equiv.) in toluene (30 ml). After 0.5 h at 20°, a soln. of MeI (0.329 ml, 5.2 mmol, 1.1 mol-equiv.) in toluene (5 ml) was added, and the mixture was stirred for further 22 h, prior to addition of H_2O (15 ml). The mixture was extracted with CH_2Cl_2, the org. phase was washed with brine, dried ($MgSO_4$), and evaporated, and the residue was purified by crystallization: 98% of pure (−)-**1e**. R_f 0.43 (hexane/AcOEt 7:3). M.p. 77–78° (Et_2O). $[\alpha]_D^{20} = -51.6$ ($c = 1.0$, $CHCl_3$) ([19]: $[\alpha]_D = -59.6$ ($c = 5.0$, $CHCl_3$)). IR: 2933, 1460, 1304, 1256, 1203, 1168, 1133. ^{1}H-NMR: 0.92 (*s*, 3 H); 1.10 (*s*, 3 H); 1.30 (*m*, 1 H); 1.45 (*m*, 1 H); 1.68 (*m*, 1 H); 1.86 (*m*, 2 H); 1.91 (*m*, 2 H); 2.53 (*s*, 3 H); 2.91 (*d*, $J = 6$, 1 H); 3.12 (*s*, 2 H). ^{13}C-NMR: 19.95 (*Me*−C(7)); 20.2 (*Me*−C(7)); 27.0 (C(5)); 27.4 (N−*Me*); 31.95 (C(6)); 34.6 (C(3)); 44.3 (C(4)); 47.55 (C(7)); 48.9 (C(10)); 49.9 (C(1)); 68.1 (C(2)). ESI-MS: 230.1 ($[M+H]^+$), 252.1 ($[M+Na]^+$), 481.2 ($[2M+Na]^+$). HR-MS: 230.1209 ($C_{11}H_{20}NO_2S^+$; calc. 230.1227).

*(−)-(4a*S*,8a*R*)-Octahydro-9,9-dimethyl-4a,7-methano-4a*H*-2,1-benzothiazine 2,2-Dioxide* ((−)-**3a**). $NaBH_4$ (1.75 g, 46.0 mmol) was added to a soln. of sulfonimide (−)-**9** (900 mg, 3.9 mmol) in MeOH (70 ml) and H_2O (21 ml). After 1 h at 20°, 1M aq. H_2SO_4 (59 ml, 59.0 mmol) was added, and the mixture was extracted with CH_2Cl_2 (3 × 50 ml). The org. phase was dried ($MgSO_4$) and evaporated and the residue purified by CC (SiO_2, hexane/AcOEt 7:3): 90% of pure (−)-**3a**. R_f 0.36 (hexane/AcOEt 6:4). M.p. 147–150° (hexane/AcOEt). $[\alpha]_D^{20} = -47.7$ ($c = 1.0$, $CHCl_3$). IR: 3331, 2949, 1315, 1143, 944. ^{1}H-NMR: 0.93 (*s*, 3 H); 1.11 (*d*, $J = 8.0$, 2 H); 1.24 (*s*, 3 H); 1.77 (*m*, 5 H); 2.20 (*m*, 2 H); 3.03 (*m*, 2 H); 3.63 (*m*, 1 H); 4.08 (*m*, 1 H). ^{13}C-NMR: 20.5 (*Me*−C(7)); 22.1 (*Me*−C(7)); 24.7 (C(10)); 26.8 (C(5)); 35.2 (C(6)); 37.1 (C(3)); 43.9 (C(7)); 45.7 (C(4)); 46.3 (C(10a)); 47.3 (C(1)); 62.2 (C(2)). HR-MS: 252.1036 ($C_{11}H_{19}NO_2NaS^+$; calc. 252.1029). Anal. calc. for C57.61, H 8.35, N 6.11, S 13.98; found: C 57.40, H 8.49, N 5.88, S 13.87.

*(−)-2-{(1*S*,4*R*)-7,7-Dimethylspiro[bicyclo[2.2.1]heptane-2,2′-[1,3]dioxolan]-1-yl}ethyl Methanesulfonate* ((−)-**7b**). A soln. of MsCl (0.98 ml, 12.6 mmol) in CH_2Cl_2 (27 ml) was added dropwise to a soln. of (−)-**7a** (2.8 g, 12.6 mmol) and Et_3N (2.28 ml, 16.4 mmol) in CH_2Cl_2 (40 ml) at 0°. After 18 h at 20°, the mixture was evaporated and the residue extracted with AcOEt (3 × 25 ml) after addition of H_2O (20 ml). The org. phase was washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by CC (SiO_2, hexane/AcOEt 7:3): 95% of pure (−)-**7b**. Light yellow oil. R_f 0.41 (hexane/AcOEt 6:4). $[\alpha]_D^{20} = -12.9$ ($c = 1.0$, $CHCl_3$). IR: 2960, 1316, 1145. ^{1}H-NMR: 0.78 (*s*, 3 H); 0.95 (*s*, 3 H); 1.13 (*m*, 2 H); 1.26 (*d*, $J = 12.6$, 1 H); 1.43 (*m*, 1 H); 1.66 (*m*, 2 H); 1.93 (*m*, 3 H); 2.91 (*s*, 3 H); 3.65 (*m*, 2 H); 3.83 (*m*, 2 H); 4.19 (*m*, 3 H). ^{13}C-NMR: 20.6 (*Me*−C(7)); 20.6 (*Me*−C(7)); 26.6 (C(1)); 26.8 (C(5)); 27.1 (C(6)); 37.6 (*Me*−SO_3); 44.4 (C(3)); 44.9 (C(4)); 49.2 (C(7)); 52.8 (C(1)); 62.5 (CH_2O); 64.5 (CH_2O); 69.0 (C(10a)); 116.6 (C(2)). ESI-MS: 305.3 ($[M+H]^+$), 327.2 ($[M+Na]^+$), 631.3 ($[2M+Na]^+$).

*(−)-2-{(1*A*,4*R*)-7,7-Dimethylspiro[bicyclo[2.2.1]heptane-2,2′-[1,3]dioxolan]-1-yl}ethyl Ethanethioate* ((−)-**7c**). A soln. of (−)-**7b** (3.8 g, 12.5 mmol) and AcSK (4.3 g, 38 mmol) in dry DMSO (10 ml) was heated at 45° for 4 h. After addition of H_2O (20 ml) to the cold mixture, extraction was performed with $CHCl_3$ (3 × 25 ml). The org. phase was washed with H_2O, dried ($MgSO_4$), and evaporated. Purification by CC (SiO_2, toluene) afforded 96% of (−)-**7c**. R_f 0.55 (hexane/AcOEt 6:4. $[\alpha]_D^{20} = -1.8$ ($c = 1.0$, $CHCl_3$). IR: 3364, 2950, 2881, 1693, 1476,

Table 2. *Crystal Data and Structure Refinement of Compounds (−)-***1a**,**b**,**e**, *and (−)-***3a**

	(−)-**1a**	(−)-**1b**	(−)-**1e**	(−)-**3a**
Empirical formula	$C_{10}H_{17}NO_2S$	$C_{11}H_{19}NO_2S$	$C_{11}H_{19}NO_2S$	$C_{11}H_{19}NO_2S$
Formula weight	215.31	229.33	229.33	229.33
Temp [°K]	293(2)	293(2)	293(2)	293(2)
Wavelength [Å]	0.71073	0.71073	0.71073	0.71073
Crystal system	orthorhombic	orthorhombic	orthorhombic	orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Unit-cell dim.				
a [Å]	9.2620(19)	7.6819(15)	8.8242(18)	9.5434(19)
b [Å]	10.412(2)	10.689(2)	11.426(2)	10.910(2)
c [Å]	11.181(2)	13.991(3)	11.733(2)	11.507(2)
Volume [Å^3]	1078.3(4)	1148.8(4)	1183.0(4)	1198.0(4)
Z	4	4	4	4
Density [Mg/m^3]	1.326	1.326	1.288	1.471
Absorpt. coeff. [mm^{-1}]	0.275	0.263	0.255	0.264
$F(000)$ Electrons	464	496	496	568
Crystal size [mm]	$0.5\times0.5\times0.3$	$0.44\times0.4\times0.4$	$0.35\times0.35\times0.35$	$0.4\times0.4\times0.4$
θ Range for data [°]	4.14 to 19.99	3.58 to 26.50	3.39 to 22.49	4.00 to 19.99
Index ranges	$-8\le h\le6$	$-9\le h\le9$	$-9\le h\le9$	$-4\le h\le9$
	$-10\le k\le9$	$-13\le k\le13$	$-12\le k\le12$	$-10\le k\le10$
	$-10\le l\le10$	$-17\le l\le17$	$-12\le l\le12$	$-11\le l\le11$
Reflections collected	3731/996	16424/2375	8529/1537	4204/1111
R(int)	0.0393	0.0469	0.0782	0.0225
Refinement method	Full-matrix least-squares on F^2 in all cases			
Data/restraints/parameters	996/0/196	2375/0/213	1537/0/213	1111/0/225
Goodness-of-fit on F^2	1.203	1.090	1.000	1.114
Final R indices [$I>2\sigma(I)$]	$R_1=0.0331$	0.0346	0.0351	0.0390
	$wR_2=0.0800$	0.0868	0.0672	0.0943
R indices (all data)	$R_1=0.0348$	0.0375	0.0450	0.0408
	$wR_2=0.0835$	0.0891	0.0714	0.0964
Abs. struct. parameter	−0.10(14)	−0.08(8)	−0.02(10)	0.09(18)
Extinction coefficient	0.224(14)	0.028(4)	0.023(3)	0.062(7)
Largest peak and holes [eÅ^{-3}]	0.144, −0.231	0.218, −0.269	0.130, −0.146	0.123, −0.216

1444, 1390, 1354, 1300, 1209, 1135, 1113, 1043, 1026, 953. ^{1}H-NMR: 0.85 (*s*, 3 H); 1.0 (*s*, 3 H); 1.26 (*m*, 2 H); 1.35 (*d*, $J=12.6$, 1 H); 1.50 (*m*, 1 H); 1.71 (*m*, 2 H); 2.05 (*m*, 3 H); 2.31 (*s*, 3 H); 2.88 (*m*, 2 H); 3.75 (*m*, 1 H); 3.95 (*m*, 3 H). ^{13}C-NMR: 20.5 (*Me*−C(7)); 20.7 (*Me*−C(7)); 26.1 (C(10a)); 26.4 (C(10)); 26.9 (C(5)); 27.3 (*Me*−C(O)S); 30.6 (C(6)); 44.8 (C(3)); 45.0 (C(4)); 49.0 (C(7)); 54.3 (C(1)); 62.6 (CH_2O); 64.6 (CH_2O); 116.9 (C(2)); 125.3 (C(O)S). HR-MS: 307.1349 ($C_{15}H_{24}O_3NaS^+$; calc. 307.1338). ESI-MS: 307.1349 ($[M+Na]^+$), 285.1557 ($[M+H]^+$).

*(+)-(1*S*,4*R*)-7,7-Dimethyl-2-oxobicyclo[2.2.1]heptane-1-ethanesulfonic Acid* ((+)-**8a**). A soln. of 30% aq. H_2O_2 soln. (3 ml, 264 mmol) was added dropwise to a soln. of (−)-**7c** (1.5 g, 52.8 mmol) in AcOH (10 ml) at 60°. After 18 h at 60°, the excess H_2O_2 was destroyed by addition of 5% Pd/C (32 mg). After an additional hour, the cold mixture was filtered over *Celite*, the column washed with MeOH, and the filtrate evaporated. Toluene (30 ml) was added and evaporated to eliminate the remaining traces of H_2O. The residue was purified by CC (SiO_2, hexane/AcOEt 1:1): 92% of pure (+)-**8a**. R_f 0.43 (hexane/AcOEt 6:4). M.p. 128–130° (toluene). $[\alpha]_D^{20}=+11.7$ ($c=1.0$, $CHCl_3$). IR: 3382, 2970, 2895, 2276, 1704, 1446, 1419, 1379, 1245, 1189, 1125, 1040, 813, 774. ^{1}H-NMR: 0.91 (*s*, 3 H); 1.0 (*s*, 3 H); 1.40 (*m*, 2 H); 1.79 (*m*, 2 H); 2.18 (*d*, $J=4.8$, 2 H); 2.40 (*m*, 1 H); 3.02 (*m*, 1 H); 3.65 (*m*, 1 H); 3.90 (*m*, 1 H); 4.25 (*m*, 1 H). HR-MS: 245.0835 ($C_{11}H_{19}So_4^+$; calc. 245.0842).

*(−)-(1*S*,4*R*)-7,7-Dimethyl-2-oxobicyclo[2.2.1]heptane-1-ethanesulfonyl Chloride* ((−)-**8b**). A mixture of (+)-**8a** (1.0 g, 4.1 mmol) and freshly distilled $SOCl_2$ (0.8 ml, 10.1 mmol) was heated at 100° for 4.5 h. Toluene (30 ml) was added and distilled to eliminate the excess of $SOCl_2$. The residue was purified by CC (SiO_2, hexane/

AcOEt 8:2): 63% of pure (−)-**8b**. R_f 0.45 (hexane/AcOEt 6:4). M.p. 106–110° (hexane/AcOEt). $[\alpha]_D^{20} = -1.03$ ($c = 1.0$, $CHCl_3$). IR: 3439, 2960, 1732, 1445, 1369, 1167, 1054, 764. ^{1}H-NMR: 0.94 (*s*, 3 H); 1.01 (*s*, 3 H); 1.47 (*m*, 2 H); 1.76 (*m*, 2 H); 1.86 (*d*, $J = 18.2$, 1 H); 2.10 (*m*, 1 H); 2.25 (*m*, 2 H); 2.40 (*m*, 1 H); 3.53 (*dd*, $J = 4$, 14, 1 H); 4.42 (*dd*, $J = 4.6$, 13.8, 1 H). ^{13}C-NMR: 19.2 (*Me*−C(7)); 20.2 (*Me*−C(7)); 21.5 (C(10)); 26.9 (C(5)); 27.8 (C(6)); 43.2 (C(3)); 43.2 (C(4)); 47.8 (C(7)); 58.8 (C(1)); 61.7 (C(10a)); 217.5 (C(2)). MS: 287.3 ($[M + Na]^+$), 551.3 ($[2M + Na]^+$).

(+)-(1S,4R)-7,7-Dimethyl-2-oxobicyclo[2.2.1]heptane-1-ethanesulfonamide ((+)-**8c**). A soln. of (−)-**8b** (470 mg, 1.7 mmol) in 1,4-dioxane (1 ml) was added dropwise to NH_4OH (12.8 ml) at 7°. After 2 h at 20°, the mixture was extracted with CH_2Cl_2 (3 × 25 ml), the org. phase dried ($MgSO_4$) and evaporated, and the residue purified by CC (SiO_2, hexane/AcOEt 6:4): 69% of (+)-**8c**. R_f 0.17 (hexane/AcOEt 6:4). M.p. 150–153° (hexane/AcOEt). $[\alpha]_D^{20} = +1.1$ ($c = 1.0$, $CHCl_3$). IR: 3334, 2963, 1737, 1566, 1319, 1151, 1051, 944, 912. ^{1}H-NMR: 0.89 (*s*, 3 H); 0.97 (*s*, 3 H); 1.42 (*m*, 2 H); 1.72 (*m*, 2 H); 1.95 (*d*, $J = 18.4$, 1 H); 2.03 (*m*, 3 H); 2.35 (*dt*, $J = 4.6$, 18.4, 1 H); 3.36 (*td*, $J = 4.4$, 12.6, 1 H); 3.70 (*td*, $J = 4.2$, 13.6, 1 H); 5.14 (br. *s*, 2 H). ^{13}C-NMR: 19.3 (*Me*−C(7)); 20.0 (*Me*−C(7)); 20.5 (C(10)); 26.8 (C(5)); 26.8 (C(6)); 43.2 (C(3)); 43.2 (C(4)); 47.6 (C(7)); 51.1 (C(10a)); 58.8 (C(1)); 219.0 (C(2)). HR-MS: 268.0970 ($C_{11}H_{19}NO_3NaS^+$; calc. 268.0978).

*(−)-(4aS)-3,4,5,6,7,8-Hexahydro-9,9-dimethyl-4a,7-methano-4a*H*-2,1-benzothiazine 2,2-Dioxide* ((−)-**9**). A soln. of 1% (*w*/*v*) MeONa/MeOH (1.4 ml, 0.26 mmol) was added to a soln. of (+)-**8c** (200 mg, 0.9 mmol) in MeOH (14.5 ml). After 2 h at 20°, an additional amount of 1% MeONa/MeOH (1.0 ml, 0.185 mmol) was added, and the mixture was refluxed for 18 h. The solvent was evaporated, H_2O (15 ml) added, the mixture extracted with CH_2Cl_2 (3 × 30 ml), the extract dried ($MgSO_4$) and concentrated, and the residue purified by CC (SiO_2, hexane/AcOEt 8:2): 75% of pure (−)-**9**. R_f 0.34, (hexane/AcOEt 6:4). M.p. 144–148° (hexane/AcOEt). $[\alpha]_D^{20} = -95.0$ ($c = 1.0$, $CHCl_3$). IR: 3448, 2968, 1649, 1428, 1329, 1157, 812. ^{1}H-NMR: 0.90 (*s*, 3 H); 0.96 (*s*, 3 H); 1.38 (*m*, 1 H); 1.77 (*m*, 2 H); 1.98 (*m*, 3 H); 2.12 (*d*, $J = 19.4$, 1 H); 2.26 (*m*, 1 H); 2.64 (*dt*, $J = 4.4$, 19.2, 1 H); 3.01 (*td*, $J = 3.8$, 3.6, 1 H); 3.29 (*dt*, $J = 4.8$, 13.8, 1 H). ^{13}C-NMR: 18.1 (*Me*−C(7)); 19.6 (*Me*−C(7)); 21.3 (C(10)); 26.4 (C(5)); 28.9 (C(6)); 40.8 (C(3)); 42.5 (C(4)); 42.5 (C(10a)); 48.6 (C(7)); 52.5 (C(1)); 196.2 (C(2)). HR-MS: 250.0869 ($C_{11}H_{17}NO_2NaS^+$; calc. 250.0872).

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