X-Ray Structure Analyses of *syn*/*anti*-Conformers of *N*-Furfuroyl-, *N*-Benzoyl-, and *N*-Picolinoyl-Substituted (2*R*)-Bornane-10,2-sultam Derivatives

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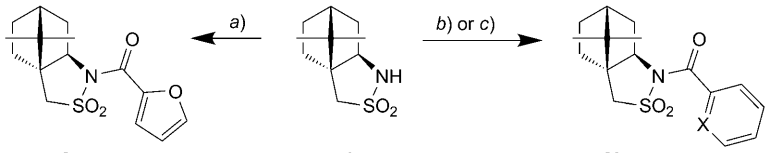
The synthesis and the X-ray structure of the three new *N*-(arylcarbonyl)-substituted derivatives **2a**–**2c** of (2*R*)-bornane-10,2-sultam are presented and discussed. Direct comparison of the solid-state analyses shows that the dipole-directed SO_2/C=O *anti*-/*syn*-conformations may be very sensitive to weak electronic/electrostatic repulsions of the heteroatom lone pairs. The optimum interactions are reached when the lone pair of the β-positioned heteroatom is oriented in the O(3)=C(11)–N(1) plane. Such rare *syn*-conformations may be observed with at least up to 1.8 kcal/mol higher energy as compared to their ground states. Additionally, these *anti*/*syn*-conformations are also very sensitive to external influences such as, for example, the crystal-packing forces.

Introduction. – Due to dipole-moment interactions [1a], *N*-acyl-substituted (2*R*)-bornane-10,2-sultam derivatives are known, in the solid state, to be mostly in the thermodynamically more stable SO_2/C=O *anti*-periplanar conformation. This fact, supported by more than twohundred X-ray-structure analyses has strongly influenced, under nonchelating conditions, the rationalizations on the origin of the diastereoselectivity for this widely used chiral auxiliary [1b]. More than a decade ago, we suggested that the *syn*-periplanar conformation could lead to a more reactive species and thus could eventually participate during the course of the reaction by displacing the *anti*/*syn* equilibrium [2][3]. We were first to report on an X-ray-structure analysis of a nonchelated SO_2/C=O *syn*-periplanar conformer for the *N*-pyruvoyl-substituted (2*R*)-bornane-10,2-sultam [2b][2]). Since this chiral sultam was earlier recognized as a disguised *pseudo*-C_2-symmetric promoter (reminiscent of a 2,5-disubstituted pyrrolidine [4]), it is particularly difficult to define which of the *anti*- or *syn*-conformers is responsible for the observed induction. Indeed, it is only recently, by studying the asymmetric 1,3-dipolar cycloadditions of chiral 2-oxoethanenitrile oxides to symmetric alkenes, that we have been able to demonstrate the higher reactivity of the nonchelated SO_2/C=O *syn*-conformers, and also to present two more examples of these rare *syn*-X-

[1]) Present address: *Firmenich SA*, Corporate R&D Division, P.O. Box 239, CH-1211 Geneva 8.
[2]) The ΔH for *syn*-s-*trans*, *anti*-s-*trans*, *syn*-s-*cis*, *anti*-s-*cis* conformers are 1.5, 0.0, 15.3, and 6.2 kcal/mol, resp. For the first example of a $TiCl_4$ chelate, see [1a].

ray-structure analyses [5][6][3]). This higher reactivity is believed to result from a better electronic delocalization on the sultam moiety through a more planar N-atom, as shown by comparison of its pyramidal height (ΔhN)[4]) between SO_2/C=O *anti*/*syn N*-acyl conformers. This latter ΔhN parameter was earlier shown to be directly correlated with the S−N−C=O dihedral angle, and to reach local and global minima near *ca.* 170° and −10°, respectively [2a]. Most of these exceptional *syn*-examples concern substrates which possess a heteroatom in the β-position, often connected to a sp^2 C(α)-atom. To study the interactions of the β-heteroatom lone pair(s) (lp) with both the SO_2 and C=O moieties, as well as its influence on the *anti*/*syn*-conformations, we decided to prepare some simple conformationally rigid new derivatives possessing these features, as shown in the *Scheme*.

Scheme



a) NaH, toluene, 2-furoyl chloride; 64%. *b*) NaH, toluene, benzoyl chloride; 96%. *c*) NaH, toluene, picolinoyl chloride; 51%.

Results. – We were aware that substituted derivatives, such as (2*R*)-*N*-(phenylglyoxyloyl)bornane-10,2-sultam [2b][5]), adopt a SO_2/C=O *anti*-conformation due to supplementary steric reasons. Consequently, we decided to acylate sultam **1** with 2-furoyl chloride (=furan-2-carbonyl chloride) in toluene, after deprotonation with NaH, to afford the unreported heterocyclic derivative **2a** in 64% yield. We were disappointed to notice that its X-ray-structure analysis exhibits an unanticipated SO_2/C=O *anti*, O=C−C−O *s-cis* disposition (*Fig. 1*). Calculations at the B3LYP/6-31G** level [10] confirmed that this conformer is indeed the most stable as compared to both the *anti*-s-*trans* and *syn*-s-*trans* conformations, although only by a small difference of *ca.* 1.1–1.6 kcal/mol (*Table 1*). This conformation may result from the fact that the furan O lp are out of the N−C=O plane and thus do not efficiently interfere with the *syn*-carbonyl lp. On the other hand, this out-of-plane disposition also disfavors an *anti*-s-*trans* disposition, due to electronic/electrostatic interactions with both S=O substituents[6]).

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[3]) A search in the past decade of the *CCDC* database (2007), allowed us to uncover two recent supplementary SO_2/C=O *syn*-structures, neither recognized nor discussed as such by their authors [7].

[4]) Defined as the orthogonal distance between the N-atom and the plane including the three N substituents. For alternative approaches to estimate the pyramidality of the N-atom, see [8].

[5]) More recently, this X-ray structure was rediscovered by Chinese authors [9].

[6]) Predictive calculations suggest that (2*R*)-*N*-(oxazole-2-carbonyl)bornane-10,2-sultam might possibly adopt a *syn*-s-*cis* conformation (1.3 kcal/mol, as compared to *syn*-s-*trans* 3.3 kcal/mol, *anti*-s-*cis* 0.0 kcal/mol, and *anti*-s-*trans* 1.5 kcal/mol) in the crystalline state.

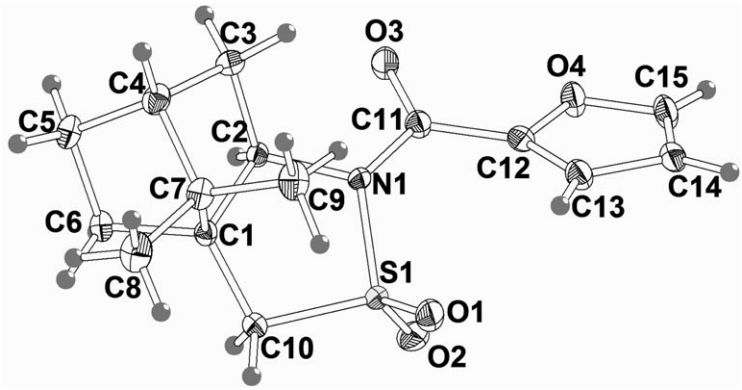

Fig. 1. *ORTEP View of (2*R*)*-N-*furoylbornane-10,2-sultam* (**2a**) (arbitrary atom numbering). Ellipsoids are represented at the 50% probability level.

Table 1. *Calculated Dihedral Angles and Energy Differences for Conformers of* **2a**, **2b**, *and* **2c**

	Conformation	S–N–C=O [°]	O=C–C–O/C/N [°]	ΔH [kcal/mol]
2a	*anti*-s-*cis*	127.3	– 20.1	0.0
	anti-s-*trans*	124.8	151.5	1.1
	syn-s-*cis*	– 20.4	– 18.1	5.1
	syn-s-*trans*	– 22.9	166.6	1.6
2b	*anti*	141.1	– 31.1	0.0
	syn	– 16.7	– 47.8	6.5
2c	*anti*-s-*cis*	148.8	– 39.3	1.0
	anti-s-*trans*	141.3	141.7	0.0[a])
	syn-s-*cis*	– 12.0	– 79.8	8.7
	syn-s-*trans*	– 16.9	140.7	1.8

[a]) Corresponds to conformer **2cA**. Conformer **2cB** is 0.1 kcal/mol higher in energy.

The *N*-benzoyl derivative **2b**[7]) was similarly prepared (NaH, toluene, PhCOCl; 96%) to measure its X-ray-structure analysis, which shows a largely favored SO_2/C=O *anti* disposition, as expected and confirmed by calculations (*Fig. 2* and *Table 1*).

We indeed synthesized derivative **2b** for conformational comparison with the also unreported *N*-picolinoyl analogue **2c** (NaH, toluene, picolinoyl chloride (= pyridine-2-carbonyl chloride) [13]; 51%). The X-ray-structure analysis of this heterocyclic analogue **2c** exhibits three conformers in the crystalline cell (*Figs. 3–5*). Two of them, (**A** in *Fig. 3* and **B** in *Fig. 4*) are very similar and express the more stable *anti*-s-*trans* conformer, as confirmed by calculations. The main difference arises from the N(2) lp, which points either above O(1) in structure **2cA**[8]) or in-between O(1) and O(2) in

7) Although erroneously mentioned in reference [11], **2b** was neither prepared nor described in [12], nor elsewhere.

8) Conformer **2cA** is reminiscent of the conformation exhibited by **2b**, as shown by comparison of their O(3)–C(11)–C(12)–C(13) dihedral angles, measured as – 32.4(3) and – 33.08(18)°, resp.

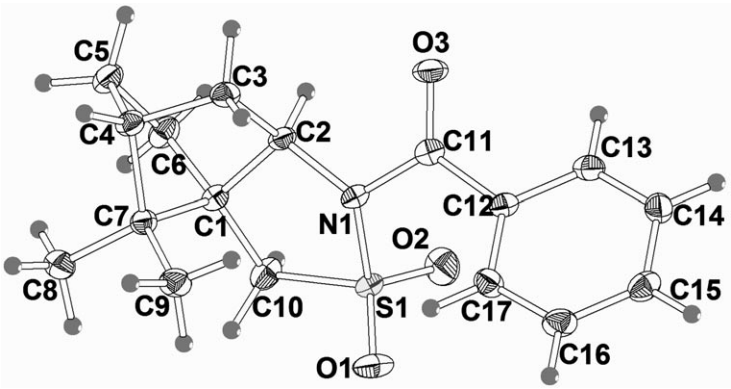

Fig. 2. *ORTEP View of (2*R*)*-N-*benzoylbornane-10,2-sultam* (**2b**) (arbitrary atom numbering). Ellipsoids are represented at the 50% probability level.

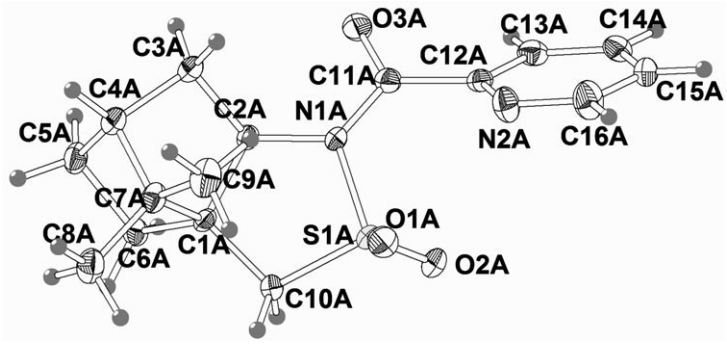

Fig. 3. *ORTEP View of (2*R*)*-N-*picolinoylbornane-10,2-sultam* (**2c**) (conformer **A**; arbitrary atom numbering). Ellipsoids are represented at the 50% probability level.

structure **2cB**, while the third one, **2cC** (*Fig. 5*), shows the expected *syn*-s-*trans* conformation, *ca.* 1.8 kcal/mol higher in energy (*Table 1*).

The *anti*-s-*trans* **2a** and *anti*-s-*cis* **2c** conformers were not detected in the solid state, although they are energetically similarly close to their ground states (*ca.* 1.0–1.1 kcal/mol higher in energy, in vacuum, *Table 1*). This shows the importance of supplementary external influences, such as the packing forces in the crystalline state[9]) or the solvent polarity in solution [15] for the control of the *syn*/*anti* and s-*cis*/*trans* ratios with respect to steric, electrostatic, electronic, and dipolar primary parameters.

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[9]) This specific influence is also expressed by structural comparison of direct crystalline analogues, such as the main (4*S*,5*S*)-stereoisomers obtained after [3 + 2] cycloadditions of the *N*-(2-oxoethanenitrile oxide) of (2*R*)-bornane-10,2-sultam to either *trans*-stilbene or *trans*-4,4′-dimethylstilbene, which surprisingly exhibit *syn*-s-*trans* (*ca.* 1.8 kcal/mol) [6] and *anti*-s-*trans* conformations (0.0 kcal/mol) [14], resp.

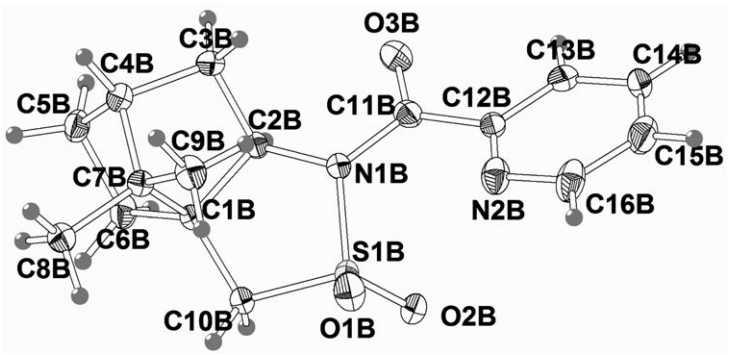

Fig. 4. *ORTEP View of (*2R*)*-N-*picolinoylbornane-10,2-sultam* (**2c**) (conformer **B**; arbitrary atom numbering). Ellipsoids are represented at the 50% probability level.

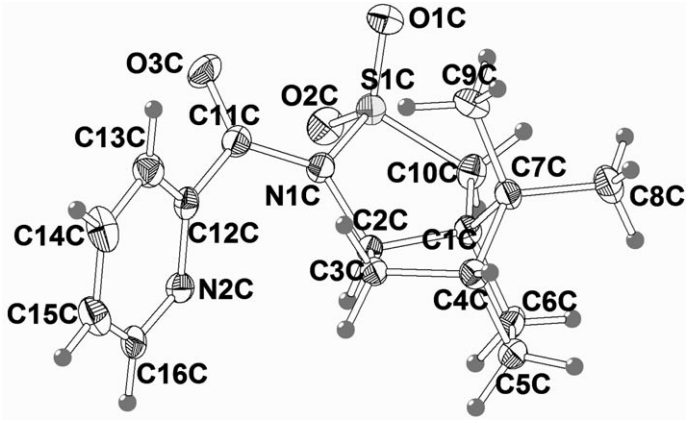

Fig. 5. *ORTEP View of (*2R*)*-N-*picolinoylbornane-10,2-sultam* (**2c**) (conformer **C**; arbitrary atom numbering). Ellipsoids are represented at the 50% probability level.

Discussion. – Examination of the *CCDC* data base of the past decade confirms that the pyramidalization in *N*-acylbornane-10,2-sultam derivatives is generally dependent on the S–N–C=O torsional angle[10]) (*Fig. 6*). This dihedral angle, statistically determined to be *ca.* 153°, ranges from *ca.* 121 to 172° with a Δ*h*N height decreasing from *ca.* 0.39 to 0.11 Å, respectively[11])[12]). A pure *anti*-periplanar conformation is nevertheless difficult to reach due to the strong steric repulsion of the *pseudo*-equatorial C(3)-atom, and the Δ*h*N height seems to reach a minimum of *ca.* 0.11 Å for angles between *ca.* 160–175° [2a].

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[10]) For the previous decade, see [2a].

[11]) An exception concerns a specific *anti*-clinal case, where a sp^2 C(α)-atom is included in a β-substituted cyclobutene ring, with Δ*h*N = 0.412 Å and S–N–C=O = 144.1° [16] (see *Fig. 6*).

[12]) Supplementary information (Δ*h*N, torsional angles, and references) of the *CCDC* examples used for *Figs. 6* and *7* can be obtained from the main authors.

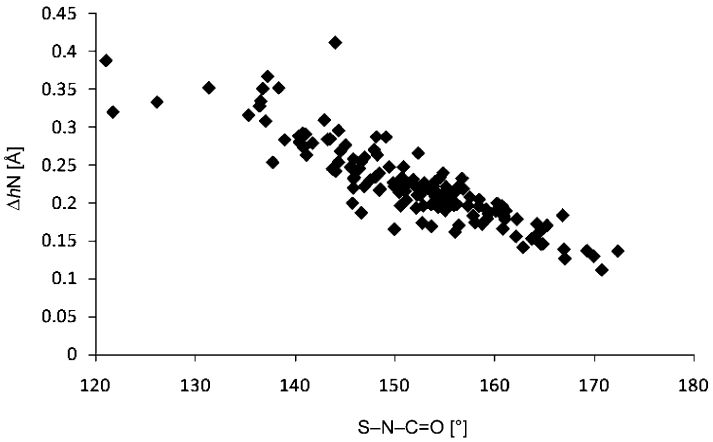

Fig. 6. *Graph of the dihedral angle S–N–C=O* [°] vs. *the pyramidal height Δ*h*N* [Å] *for* anti-*conformers*

On the other hand, *syn*-periplanarity, where the C=O is bisecting the O=S=O angle, varies from *ca.* −19 to −9° and the Δ*h*N height decreases from 0.133 to 0.066 Å, respectively[12])[13]) (*Fig. 7*).

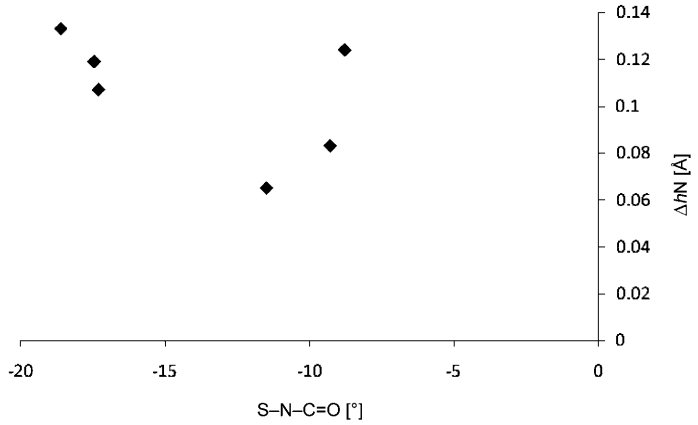

Fig. 7. *Graph of dihedral angle S–N–C=O* [°] vs. *the pyramidal height Δ*h*N* [Å] *for* syn-*conformers*

The *syn*-conformer **2cC** exhibits a very similar O(3)=C(11)–C(12)–N(2) dihedral angle (128.1(2)°, *Table* 2) when compared to the O(3)=C(13)–C(14)=O(4) torsion angle of the (2*R*)-*N*-pyruvoylbornane-10,2-sultam (121.2(5)° [2b]). Due to the bisecting disposition of the N(2B)-atom with respect to the O=S=O moiety, **2cB** possesses practically symmetrical C(2)–N–S=O(1)/O(2) torsional angles (*Table* 2).

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[13]) A structure where the C(α)-atom is included in a β-substituted cyclopropyl ring, and which does not include a heteroatom in the β-position, exhibits an exceptional Δ*h*N of 0.124 Å for S–N–C=O = −8.8° [7a] (see *Fig. 7*). Alternatively, the slope could have a positive trend for S–N–C=O dihedral angles between *ca.* either −11 and −5°, or 171 and 176°, due to strong repulsive constraints which result in a greater pyramidalization [2a].

Table 2. *Selected Bond Lengths* [Å] *and Angles* [°] *for* **2a**, **2b**, *and* **2c**

	2a	**2b**	**2cA**	**2cB**	**2cC**
S=O(1)	1.4314(10)	1.4219(9)	1.4279(13)	1.4223(14)	1.4286(13)
S=O(2)	1.4346(9)	1.4320(10)	1.4380(13)	1.4386(13)	1.4358(14)
S–N	1.7116(10)	1.7114(10)	1.7166(15)	1.7159(15)	1.7058(15)
S–C(10)	1.7875(13)	1.7873(13)	1.7907(18)	1.7953(18)	1.788(2)
N–C(2)	1.4872(14)	1.4851(15)	1.483(2)	1.487(2)	1.483(2)
N–C(11)	1.3990(17)	1.4023(16)	1.389(2)	1.401(2)	1.380(2)
C(11)–O(3)	1.2148(16)	1.2166(15)	1.220(2)	1.216(2)	1.220(2)
C(11)–C(12)	1.4737(17)	1.4970(17)	1.492(3)	1.492(3)	1.504(3)
O(1)=S=O(2)	117.27(6)	117.29(6)	118.35(8)	118.51(8)	118.44(8)
C(2)–N–S	111.51(8)	110.33(8)	112.11(11)	111.70(11)	113.25(12)
C(2)–N–C(11)	116.20(10)	115.67(9)	115.38(14)	114.82(15)	128.49(15)
C(11)–N–S	122.00(8)	119.79(8)	123.41(12)	124.30(13)	117.69(13)
C(2)–N–S=O(1)	−119.86(8)	−131.15(9)	−111.76(13)	−114.99(12)	−125.12(13)
C(2)–N–S=O(2)	110.39(8)	99.20(9)	116.69(12)	112.30(12)	102.97(13)
C(3)–C(2)–N–S	140.13(9)	144.86(9)	132.38(14)	137.39(14)	140.22(13)
S–N–C(11)=O(3)	139.00(11)	136.61(11)	152.43(15)	144.57(15)	−11.5(3)
O(3)=C(11)–C(12)–O/C/N	−17.98(19)	139.16(13)	145.24(18)	164.92(18)	128.1(2)
N–C(11)–C(12)–C(13)	−21.4(2)	151.97(12)	149.77(17)	174.26(17)	129.49(19)
ΔhN [Å]	0.284	0.335	0.266	0.269	0.066
Puckering parameter q_2	0.385	0.377	0.255	0.337	0.366
S–N–C(2)–C(1)–C(10) Φ_2	102.70	77.43	117.27	107.85	92.00

The five-membered heterocyclic sultam envelope may be characterized by the *Cremer* and *Pople* puckering parameters q_2 and Φ_2 [17] (*Table* 2)[14]), which support the fact that **2b** and **2cA** possess the most *pseudo*-equatorial and *pseudo*-axial S=O(1) substituent, respectively.

Conclusions. – We synthesized and presented the solid-structure analyses of three new *N*-(arylcarbonyl) derivatives of (2*R*)-bornane-10,2-sultam. Direct comparison of the X-ray-structure analysis of **2b** and **2c** shows that the SO_2/C=O *syn*/*anti*-conformation may be very sensitive to weak electronic/electrostatic repulsions of the heteroatom lone pairs. The optimum interactions are reached when the lp of the β-positioned heteroatom is in the O(3)=C(11)–N(1) plane. Such rare *syn*-conformations may still be observed in the solid state, when being as high in energy as 1.8 kcal/mol as compared to their ground-states[2])[6])[9])[14]). Additionally, these *anti*/*syn*-conformations are also very sensitive to external influences, such as the crystalline packing forces[9]) or the solvent polarity [15].

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[14]) We have also calculated these two parameters for both the *CCDC syn* examples [18]. The β-substituted cyclopropyl derivative shows a $q_2 = 0.341$ and $\Phi_2 = 98.40$ [7a], while the isoxazolidine derivative has $q_2 = 0.318$ and $\Phi_2 = 96.57$ (ΔhN = 0.133 Å, S–N–C=O = −18.6°) [7b]. Their corresponding *anti*-s-*trans* conformers are *ca.* 17.1 and 5.8 kcal/mol, resp., higher in energy.

Experimental Part

X-Ray-Structure Analyses (*Table 3*). All crystal measurements were performed on a *KM4CCD* κ-axis diffractometer with graphite-monochromated MoK_α radiation. The crystal was positioned at 62 mm from the *CCD* camera. Then 1050 frames were measured at 1° intervals with a counting time of 4 s for **2a**, 2111 frames were measured at 0.5° intervals with a counting time of 7 s for **2b**, and 1100 frames were measured at 1.0° intervals with a counting time of 22 s for **2c**. The data were corrected for *Lorentz* and polarization effects. Empirical correction for absorption was applied [19]. Data reduction and analysis were carried out with the *Oxford Diffraction Ltd.* programs [20]. The structure was solved by direct methods [21] and refined by using SHELXL [22]. 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 geometrically, and their positions and temperature factors were not refined. Scattering factors were taken from Tables 6.1.1.4 and 4.2.4.2 of [23]. The known configurations of the asymmetric centers were confirmed by the *Flack*-parameter refinement [24]. Crystallographic data (excluding structural factors)

Table 3. *Crystal Data and Structure Refinement of Compounds* **2a**, **2b**, *and* **2c**

	2a	**2b**	**2c**
Empirical formula	$C_{15}H_{19}NO_4S$	$C_{17}H_{21}NO_3S$	$C_{16}H_{20}N_2O_3S$
M_r [g/mol]	309.37	319.41	320.40
Temp. [K]	100(2)	110(2)	120(2)
Wavelength [Å]	0.71073	0.71073	0.71073
Crystal system	orthorhombic	monoclinic	monoclinic
Space group	$P2_12_12_1$	$P2_1$	$P2_1$
Unit-cell dimensions			
a [Å]	7.9860(6)	7.9471(3)	13.9959(8)
b [Å]	8.0079(7)	10.1004(4)	10.2183(7)
c [Å]	22.6661(17)	10.1256(4)	16.0408(11)
β [°]	90	107.826(3)	92.025(5)
V [Å^3]	1449.5(2)	773.75(5)	2291.1(3)
Z	4	2	6
D_x [Mg/m^3]	1.418	1.371	1.393
μ [mm^{-1}]	0.239	0.222	0.227
F(000) electrons	656	340	1020
Crystal size [mm]	0.55 × 0.35 × 0.20	0.45 × 0.20 × 0.15	0.35 × 0.20 × 0.15
θ Range [°]	2.70–28.64	2.69–28.61	2.74–27.50
Index ranges	$-10 \le h \le 10$	$-10 \le h \le 10$	$-18 \le h \le 18$
	$-10 \le k \le 10$	$-13 \le k \le 13$	$-13 \le k \le 13$
	$-29 \le l \le 30$	$-13 \le l \le 13$	$-20 \le l \le 20$
Reflections collected, unique	24118, 3585	12691, 3730	39259, 10489
R(int)	0.0219	0.0153	0.0274
Refinement method	Full-matrix least-squares on F^2		
Data, restraints, parameters	3585, 0, 261	3730, 1, 201	10489, 1, 601
Goodness-of-fit on F^2	1.026	1.060	0.929
$R(F)$ ($I > 2\sigma(I)$)	0.0239	0.0237	0.0307
$wR(F^2)$ (all)	0.0614	0.0650	0.0657
Abs. struct. parameter	−0.01(5)	−0.01(4)	0.01(3)
Extinction coefficient	0.0264(17)		
Largest peak and holes [Å^{-3}]	0.263, −0.289	0.258, −0.195	0.750, −0.309

for **2a**, **2b**, and **2c** were deposited as supplementary material with the *Cambridge Crystallographic Data Centre* and allocated the deposition numbers CCDC 667772, 667770, and 667771, resp. These data can be obtained free of charge *via* www.ccdc.ac.uk/data_request/cif.

*(2-Furyl)[(3a*S*,6*R*,7a*R*)-hexahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano[2,1]benzisothiazol-1-yl]methanone* (**2a**). To an ice-cold suspension of 60% NaH in mineral oil (70 mg, 1.75 mmol) in dry toluene (3 ml) under Ar, a soln. of (2*R*)-bornane-10,2-sultam (250 mg, 1.16 mmol) in toluene (3 ml) was slowly added. After 1 h, a soln. of 2-furoyl chloride (0.23 ml, 2.33 mmol) in toluene (3 ml) was added dropwise over 30 min. The resulting mixture was stirred overnight at r.t. H_2O was then added to the mixture, and the aq. phase was extracted with AcOEt. The org. phase was dried ($MgSO_4$) and concentrated and the crude material purified by column chromatography (CC) (hexane/AcOEt 9:1): **2a** (64%). M.p. 211–213°. $[\alpha]_D^{20} = -89.5$ ($c = 1.0$, $CHCl_3$). IR: 3147, 3014, 2999, 2966, 2934, 1659, 1469, 1340, 1311, 1303, 1190, 1116, 1115, 776, 757, 558, 486. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.02 (*s*, 3 H); 1.27 (*s*, 3 H); 1.36–1.49 (*m*, 2 H); 1.87–1.94 (*m*, 2 H); 1.95–2.05 (*m*, 2 H); 2.08–2.13 (*m*, 1 H); 3.49 (*d*(*AB*), $J = 13.5$, 1 H); 3.58 (*d*(*AB*), $J = 13.5$, 1 H); 4.25 (*dd*, $J = 4.5$, 7.75, 1 H); 6.53–6.54 (*m*, 1 H); 7.54 (*dd*, $J = 0.5$, 3.5, 1 H); 7.64–7.66 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 20.0 (*q*); 21.3 (*q*); 26.4 (*t*); 33.3 (*t*); 38.4 (*t*); 45.2 (*d*); 47.8 (*s*); 48.2 (*s*); 53.8 (*t*); 66.1 (*d*); 112.0 (*d*); 120.4 (*d*); 146.0 (*s*); 147.1 (*d*); 157.5 (*s*). ESI-MS: 332.1 ($[M + Na]^+$), 641.1 ($[2M + Na]^+$). HR-ESI-MS: 332.0935 ($C_{15}H_{19}NNaO_4S^+$; calc. 332.0932).

*[(3a*S*,6*R*,7a*R*)-Hexahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano[2,1]benzisothiazol-1-yl]phenylmethanone* (**2b**). As described for **2a**, with 60% NaH in mineral oil (70 mg, 1.75 mmol), (2*R*)-bornane-10,2-sultam (250 mg, 1.16 mmol), and benzoyl chloride (0.27 ml, 2.33 mmol): **2b** (96%). M.p. 148–149°. $[\alpha]_D^{20} = -170.4$ ($c = 1.0$, $CHCl_3$). IR: 3437, 2970, 2939, 2910, 2881, 1673, 1343, 1291, 1167, 1151, 1103, 1055, 728, 695, 556, 524. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.02 (*s*, 3 H); 1.34 (*s*, 3 H); 1.37–1.49 (*m*, 2 H); 1.88–2.00 (*m*, 3 H); 2.05–2.15 (*m*, 2 H); 3.42 (*d*(*AB*), $J = 13.5$, 1 H); 3.52 (*d*(*AB*), $J = 14$, 1 H); 4.19 (*dd*, $J = 4.5$, 7.25, 1 H); 7.42–7.45 (*m*, 2 H); 7.53–7.57 (*m*, 1 H); 7.76 (*m*, 2 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 19.9 (*q*); 21.3 (*q*); 26.5 (*t*); 33.2 (*t*); 38.4 (*t*); 45.1 (*d*); 47.8 (*s*); 48.1 (*s*); 53.6 (*t*); 66.0 (*d*); 128.0 (2*d*); 129.5 (2*d*); 132.7 (*d*); 133.8 (*s*); 170.1 (*s*). ESI-MS: 342.2 ($[M + Na]^+$), 661.3 ($[2M + Na]^+$). HR-ESI-MS: 342.1147 ($C_{17}H_{21}NNaO_3S^+$; calc. 342.1140).

*[(3a*S*,6*R*,7a*R*)-Hexahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano[2,1]benzisothiazol-1-yl](pyridin-2-yl)methanone* (**2c**). To picolinic acid (290 mg, 2.36 mmol), thionyl chloride (7 ml) was slowly added, and the mixture was refluxed for 2 h. After cooling, toluene (15 ml) was added, and the soln. was evaporated. The procedure was repeated two more times, to remove all the excess $SOCl_2$. The obtained picolinoyl chloride was used in the next step without further purification.

As described for **2a**, with 60% NaH in mineral oil (70 mg, 1.75 mmol), (2*R*)-bornane-10,2-sultam (250 mg, 1.16 mmol), and picolinoyl chloride [13]: **2c** (51% yield. M.p. = 87–90°. $[\alpha]_D^{20} = -184.3$ (c = 1.0, $CHCl_3$). IR: 2960, 2883, 1675, 1330, 1305, 1170, 1116, 1139, 751, 557, 490. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.02 (*s*, 3 H); 1.32 (*s*, 3 H); 1.37–1.49 (*m*, 2 H); 1.87–2.03 (*m*, 5 H); 3.43 (*d*(*AB*), $J = 13.5$, 1 H); 3.56 (*d*(*AB*), $J = 13.5$, 1 H); 4.39 (*t*, $J = 7$, 1 H); 7.45–7.48 (*m*, 1 H); 7.82–7.87 (*m*, 2 H); 8.72–8.73 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 20.0 (*q*); 21.9 (*q*); 26.3 (*t*); 33.6 (*t*); 39.2 (*t*); 45.5 (*d*); 47.7 (*s*); 48.6 (*s*); 53.4 (*t*); 66.7 (*d*); 124.6 (*d*); 126.4 (*d*); 136.8 (*d*); 148.8 (*d*); 151.1 (*s*); 167.0 (*s*). ESI-MS: 343.1 ($[M + Na]^+$), 663.2 ($[2M + Na]^+$). HR-ESI-MS: 343.1079 ($C_{16}H_{20}N_2NaO_3S^+$; calc. 343.1092).

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