Asymmetric Hetero-*Diels-Alder* Addition of 1-Methoxybuta-1,3-diene to (2*R*)-*N*-Pyruvoyl- and (2*R*)-*N*-(Phenylglyoxyloyl)bornane-10,2-sultam

by **Jaroslaw Kiegiel**[a]), **Christian Chapuis**[b])[1])*, **Zofia Urbañczyk-Lipkowska**[b]), and **Janusz Jurczak**[a])[b])*

[a]) Department of Chemistry, University of Warsaw, Pasteura 1, PL-02-093 Warsaw
[b]) Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, PL-01-224 Warsaw

Cycloadditions of 1-methoxybuta-1,3-diene to (2*R*)-*N*-pyruvoyl and (2*R*)-*N*-(phenylglyoxyloyl)bornane-10,2-sultam ((−)-**1b** and (−)-**1c**, resp.) under high-pressure conditions are presented. The absolute configurations of the cycloadducts **2b,c** and of their resulting reduced alcohols **3b,c** are based on their X-ray analyses. The stereochemical course of these reactions is discussed and compared to the inverse diastereoselectivity observed for the analogous cycloaddition to (2*R*)-*N*-glyoxyloylbornane-10,2-sultam (**1a**)

Introduction. – We earlier reported the preparation of (2*R*)-*N*-glyoxyloylbornane-10,2-sultam (**1a**) [1] and its [4+2] cycloaddition to 1-methoxybuta-1,3-diene [1a][2] and 1-methoxy-3-(silyloxy)buta-1,3-diene [3] under high pressure and/or in the presence of catalytic amounts of [Eu(fod)$_3$] (fod = 6,6,7,7,8,8-heptafluoro-2,2-dimethyloctane-3,5-dionato)[2])[3]). This versatile *N*-glyoxyloyl derivative was also used for the spirocyclization of 2-substituted tryptamines [11], for *Pictet-Spengler* cyclization [12], for a formal synthesis of compactin and mevinolin [2][13], and for the preparation of purpurosaminide C [14], deoxyhexoses [15], as well as [(trimethylsilyl)oxy]furan [16] and ene additions [17]. To study in more detail the scope and limitation of this kind of hetero-*Diels-Alder* reaction, we also recently reported the synthesis and X-ray analyses of the homologous dienophiles (−)-**1b,c**, obtained by direct acylation (NaH, toluene, pyruvoyl chloride (72%) and NaH, toluene, phenylglyoxyloyl chloride (71%) [18]) of the commercially available (2*R*)-bornane-10,2-sultam [19]. Alternatively, (−)-**1b** was also obtained by ozonolysis of (2*R*)-*N*-methacryloyl- or (2*R*)-*N*-tigloylbornane-10,2-sultam (O_3, AcOEt, −78°, then Me_2S (86–90%) [20])[4]). We now wish to report on the [4+2] cycloadditions of 1-methoxybuta-1,3-diene to (−)-**1b,c**.

Results and Discussion. – Cycloaddition of 1-methoxybuta-1,3-diene to (−)-**1b,c** in CH_2Cl_2 at 20° completely failed, even in the presence of catalysts such as [Eu(hfc)$_3$] (= tris{3-[(heptafluoropropyl)hydroxymethylene](+)-camphorato}europium(III)),

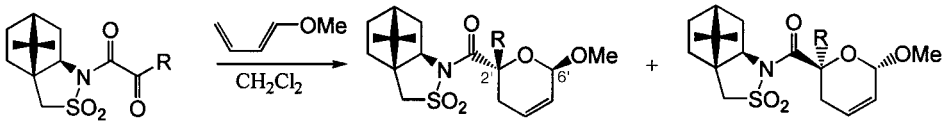
[1]) Present address: *Firmenich SA*, Corporate R&D Division, P.O. Box 239, CH-1211 Geneva 8.

[2]) For cycloadditions of glyoxylates: used as chiral dienophiles, see [4]; to chiral dienes, see [5]; catalysed by chiral catalysts, see [6]; as precursor of a chiral homo- and N-hetero-dienophile, see [7] and [8], respectively. For a recent review on asymmetric intermolecular homo- and hetero-*Diels-Alder* reactions, see [9].

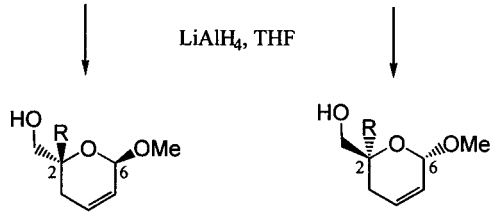
[3]) For an independent and recent synthesis of (−)-**1b**, isolated as a gum and presented without chiroptical properties, see [10].

[4]) For the diastereoselective reduction of *N*-pyruvoyl- and *N*-(phenylglyoxyloyl)amides and esters, see [21] and [22], respectively.

Scheme 1



		Pressure	*T*	Yield					
1a	R = H	12 kbar	20°	80%	(2′*R*,6′*R*)-**2a**	R = H	28% [a]	(2′*S*,6′*S*)-**2a**	R = H 72% [a]
(-)-**1b**	R = Me	14 kbar	50°	86%	(2′*R*,6′*R*)-**2b**	R = Me	66%	(2′*S*,6′*S*)-**2b**	R = Me 34%
(-)-**1c**	R = Ph	14 kbar	50°	86%	(2′*S*,6′*R*)-**2c**	R = Ph	63%	(2′*R*,6′*S*)-**2c**	R = Ph 37%



a) After acidic epimerization of the anomeric center (PPTS [1][2])

(2*R*,6*R*)-**3a**	R = H	(2*S*,6*S*)-**3a**	R = H	[2][4b]
(2*R*,6*R*)-**3b**	R = Me	(2*S*,6*S*)-**3b**	R = Me	
(2*S*,6*R*)-**3c**	R = Ph	(2*R*,6*S*)-**3c**	R = Ph	

$TiCl_4$, or $ZnCl_2$. Although very seldom reported in the literature, one example has shown that cycloaddition of menthyl pyruvate under high pressure at 20° mainly delivers the *cis* cycloadducts [23]. In the present case, no reaction took place at 8 kbar, while under 12 kbar, a conversion of *ca.* 30% was observed after 3 days at 50°. The addition of [Eu(hfc)$_3$] affected neither the conversions nor the diastereoisomer ratios. It was only at 14 kbar and 50° that complete conversion was obtained after 48 h. Cycloadducts **2b,c** were obtained in 86% yield in both cases, as 66 : 34 and 63 : 37 diastereoisomer mixtures, respectively, as shown by ^{1}H-NMR analysis of the crude product.

Diastereoisomers **2b** were inseparable by either CC or HPLC; nevertheless, crystallization from hexane/AcOEt gave the pure major diastereoisomer (2′*R*,6′*R*)-**2b** in 18% yield, as well as, in the mother liquor, a 4 : 3 diastereoisomer mixture (67%). Attempts to oxidize this mixture (MoO_3, H_2O_2 [2][13]) to the corresponding lactones failed. Similarly, this mixture remained unchanged under acidic anomeric epimerization conditions (pyridinium *p*-toluenesulfonate (PPTS), MeOH, 20° [1a][2][13]), suggesting *trans* substitution of the dihydro-2*H*-pyran ring[5]). Reduction of this mixture ($LiAlH_4$, THF; 84%) afforded, after chromatographic purification, a single alcohol **3b** by ^{1}H-NMR analysis, besides the recovered (2*R*)-bornane-10,2-sultam (88%). The same alcohol (2*R*,6*R*)-**3b** was similarly obtained in optically pure form from (2′*R*,6′*R*)-

[5]) Under more drastic conditions (PPTS, MeOH, 100°, 48%, sealed tube), we observed the diastereoselective addition of MeOH to the C=C bond, supposedly by 1,4-addition to the transient α,β-unsaturated aldehyde, prior to recyclization.

2b. X-Ray analysis of a single crystal, obtained from the major pure diastereoisomer (2′*R*,6′*R*)-**2b**, demonstrated that there are two independent, but very similar conformers of the 2,2-disubstituted dihydro-2*H*-pyran ring and confirmed the *trans* relationship of the methoxy and carbamoyl groups (see *Fig.* and *Table 1*). As already observed by NMR analyses of analogous *trans-6*-methoxy-2-methyl-3,6-dihydro-2*H*-pyran-2-carboxamides, the methoxy group adopts a pseudo-axial orientation, while the sterically more demanding sulfonamide substituent is pseudo equatorial [24a,b]. The absolute configuration could be assigned to (2′*R*,6′*R*)-**2b** by comparison with the known (2*R*) center of the chiral auxiliary.

Similarly, the diastereoisomer mixture **2c** could be separated by fractional crystallization from hexane/AcOEt, then Et_2O. Although the major diastereoisomer (2′*S*,6′*R*)-**2c** could be obtained pure according to NMR analysis, several attempts using different solvents to grow suitable crystals for X-ray analysis failed, due to high disorder in the crystal. Fortunately, X-ray analysis of the pure minor diastereoisomer (2′*R*,6′*S*)-**2c** revealed a relative *trans* substitution and an absolute (2′*R*,6′*S*)-configuration[6]). The reduction of a 1:1 diastereoisomer mixture of **2c** gave, after removal of the free sultam by crystallization (84%), a single racemic alcohol **3c** (by ^{1}H-NMR), thus allowing us to assign the relative *trans* and absolute (2′*S*,6′*R*)-configuration to the major diastereoisomer of **2c**, which was also reduced to pure (2*S*,6*R*)-**3c** in 90% yield.

The poor content and absence of *cis* diastereoisomers **2b,c** is particularly noteworthy and may be explained by a possible epimerization at the anomeric center (C(6′)) under the cycloaddition conditions[7]). The diastereoselectivity observed during the analogous cycloaddition of 1-methoxybuta-1,3-diene to **1a** was found to be time-dependent [1a][2], and a possible thermodynamic control has been suggested [20]. To test this hypothesis in the present case, both a 4:3 diastereoisomer mixture of (2′*R*,6′*R*)-**2b**/(2′*S*,6′*S*)-**2b** and pure (2′*R*,6′*S*)-**2c** were recovered unchanged after treatment with an excess of diene at 50°/14 kbar for 48 h, thus confirming kinetic control for the *trans* diastereoisomers at least. Recent PM3 calculations[8]) suggest that the preferred *endo/exo* attacks of the diene occur on the C(α)-*si* face of the SO_2/C=O-*anti*,C=O/C=O-s-*cis* conformation of **1a**, in accord with the pseudo-C_2-symmetrical simple model postulated by *Curran* and *Kim* [25]. In contrast, based on the X-ray

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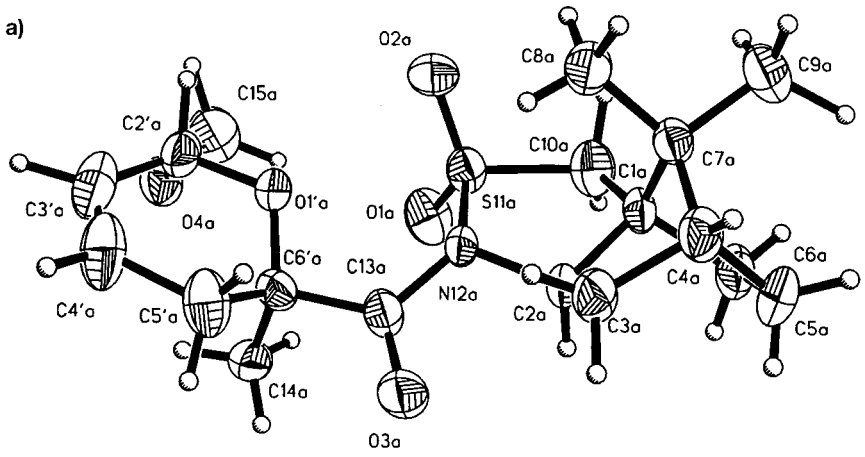
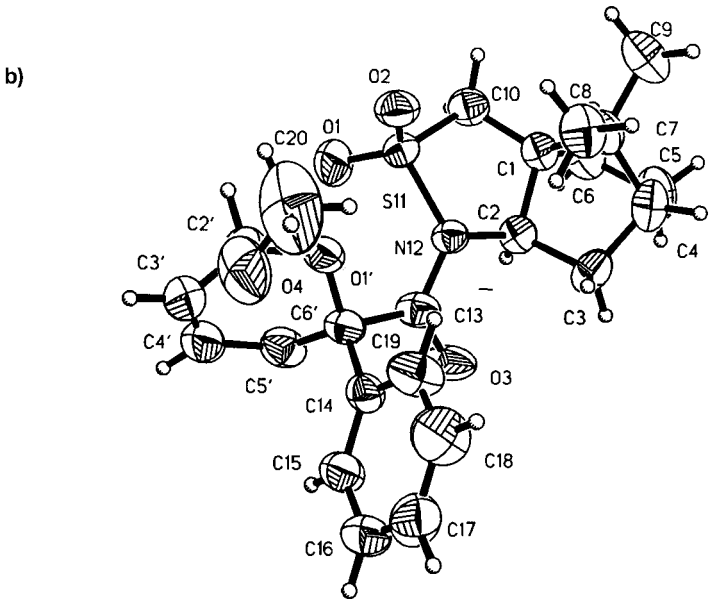
[6]) The crystallographic analyses of **2b,c** show a typical SO_2/C(O) *anti* conformation (see *Table 1*) with a resultant slight pyramidalization of the N-atom [20]; (2′*R*,6′*R*)-**2b** conformer A: $\Delta hN = 0.248(4)$ Å; conformer B: $\Delta hN = 0.247(4)$ Å; (2′*R*,6′*S*)-**2c**: $\Delta hN = 0.255(2)$ Å; a dihedral angle of 13.4(4)° was observed between C(5′)–C(6′)–C(14)–C(15) (arbitrary numbering, see *Fig.*).

[7]) Only in the case of the chromatographic purification of **2b**, a third minor crystalline diastereoisomer, unsuitable for X-ray analysis, was isolated in 3% yield. ^{13}C-NMR Analyses of this diastereoisomer suggested a relative *cis* configuration (low-field signals for MeO, C(3′), C(4′), C(5′), and C(6′); systematic numbering) [24a,b]. Further reduction afforded a levorotatory *cis*-alcohol **3b** of undefined absolute configuration. Both *cis*-**2b**, and *cis*-**3b** did not survive the acidic epimerization conditions, affording several unidentified by-products. Due to the tiny amont of material, the thermodynamic stability of *cis*-**2b** at 50°/14 kbars, in the absence and presence of diene, was unfortunately not tested. It is worthy to note that the absolute configuration of *cis*-**3a** is also unknown in the literature [24c,d].

[8]) At high pressure, glyoxylates prefer to adopt a C(O)–CHO s-*cis* conformation, as earlier reported [4c,d] and calculated for *syn*- and *anti*-**1a** [20]. The four lowest-energy transition states calculated for the cycloaddition of 1-methoxybuta-1,3-diene to **1a**, expressed in kcal/mol, are the following: C(α)-*si exo anti*-s-*cis* = – 115.4; C(α)-*si endo anti*-s-*cis* = – 115.1; C(α)-*re exo anti*-s-*cis* = – 114.6; C(α)-*re exo syn*-s-*cis* = – 114.3 [20].



2b



2c

Figure. *Molecular structures* a) *of one of the two almost identical independent conformers of (2′*R,*6′*R*)*-**2b** *and* b) *of the minor isomer (2′*R,*6′*S*)*-**2c**. Thermal ellipsoids at 50% level. Arbitrary identical numbering (disubstituted pyran atom: C(6′)); for systematic names, see *Exper. Part* (disubstituted pyran atom: C(2′)).

Table 1. *Selected Bond Lengths* [Å], *Angles* [°], *and Torsion Angles* [°] *for Two Independent Conformers of (2′*R*,6′*R*)*-**2b** *and for (2′*R*,6′*S*)*-**2c**. Arbitrary numbering, see *Figure.*

	2bA	**2bB**	**2c**
C(2)–N(12)	1.488(5)	1.494(5)	1.480(3)
C(10)–S(11)	1.784(5)	1.792(5)	1.789(2)
S(11)–O(1)	1.423(3)	1.427(3)	1.427(2)
S(11)–O(2)	1.432(3)	1.417(3)	1.422(2)
S(11)–N(12)	1.712(3)	1.704(3)	1.717(2)
N(12)–C(13)	1.403(5)	1.397(4)	1.387(3)
C(13)–O(3)	1.210(5)	1.224(4)	1.212(3)
O(1)–S(11)–O(2)	119.6(2)	119.2(2)	118.2(1)
O(1)–S(11)–N(12)	108.8(2)	108.9(2)	109.3(1)
O(2)–S(11)–N(12)	111.2(2)	111.5(2)	111.9(1)
O(1)–S(11)–C(10)	110.2(2)	109.5(2)	110.5(1)
O(2)–S(11)–C(10)	108.8(2)	109.9(2)	109.6(1)
N(12)–S(11)–C(10)	95.6(2)	95.2(2)	95.0(1)
C(13)–N(12)–C(2)	113.8(3)	113.9(3)	114.2(2)
C(13)–N(12)–S(11)	127.1(3)	126.8(2)	126.1(2)
C(2)–N(12)–S(11)	111.1(2)	111.3(2)	111.3(2)
C(3)–C(2)–N(12)–S(11)	138.9(3)	140.0(3)	138.1(2)
O(1)–S(11)–N(12)–C(13)	– 39.4(4)	– 40.2(4)	– 35.3(2)
O(2)–S(11)–N(12)–C(13)	94.4(4)	93.3(4)	97.6(2)
O(1)–S(11)–N(12)–C(2)	107.1(3)	106.5(3)	110.7(2)
O(2)–S(11)–N(12)–C(2)	– 119.1(3)	– 119.9(3)	– 116.4(2)
S(11)–N(12)–C(13)–O(3)	150.9(3)	149.5(3)	146.7(2)

analyses of C(α)-substituted transoid dienophiles [18][26], and in order to minimize the steric, dipole/dipole and electrostatic interactions [19], we propose that the major *endo/exo* attacks of the diene occur on the C(α)-*re* face of the *syn*-s-*trans* and *anti*-s-*trans* conformers for both analogues (–)-**1b,c**. This proposition rationalizes the inverted topicity of the attack observed for **1a** and (–)-**1b,c**. Thus, the thermodynamically stable *syn*-s-*transoid* conformer of (–)-**1b** [18] benefits from the cooperative steric/electronic effects[9]), as recently proposed [2][20], although the preferred orthogonality observed in the X-ray structure analysis of (–)-**1c** [18] may lead to supplementary unusual non-conjugated transition states.

Conclusion. – We have presented the asymmetric, kinetically controlled hetero-*Diels-Alder* additions of 1-methoxy-buta-1,3-diene to the chiral dienophiles (–)-**1b,c** under high-pressure conditions, and have determined the absolute configuration of the cycloadducts **2b,c** by X-ray analysis. The diastereoselectivity observed is rationalized by *endo/exo* C(α)-*re* attacks on the *syn*-s-*trans* and *anti*-s-*trans* conformers with subsequent epimerization at the anomeric center (C(6′)). Reduction, with non-destructive removal of the chiral auxiliary, delivered optically pure alcohols **3b,c** as potential building blocks for natural-products synthesis, such as, *e.g.*, (–)-frontalin, the bark beetle pheromone [27a,b], or the D ring of the marine antiviral and cytotoxic triterpenes venustriol [27c] and thyrsiferol [27d].

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[9]) X-Ray structure analysis of the free (2*R*)-bornane-10,2-sultam exhibiting *anti*-periplanar orientation of the N–H and S=O(1) bonds shall be presented and discussed in due course.

The reduction of (−)-**1b,c** under chelating and non-chelating conditions, will be presented in due course.

Financial support from the *Polish Academy of Sciences* and from the University of Warsaw (BST/592/18/98) is gratefully acknowledged.

Experimental Part

General. See [18].

*X-Ray Structure Determination of (2′*R,*6′*R*)*-**2b** and (2′*R,*6′*S*)*-**2c**. Suitable crystals were grown from Et_2O soln. The measurements were run on an *Enraf-Nonius-MACH3* diffractometer using Express software, without absorption corrections. *Table 2* shows details of the data collection and refinement. For compound **2b**, H-atom positions were found experimentally and refined. For compound **2c**, they were calculated and refined in riding mode with isotropic temperature factors 20% higher than that of the parent atoms. The known configuration of the asymmetric centres of the sultam unit was confirmed by the *Flack*-parameter refinement [28]. The structure was solved by the SHELX86 [29] and refined with the SHELXL93 [30] programs. Crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre*, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, England, as supplementary publication No. CCDC-101982 (**2b**) and 101983 (**2c**).

*(3a*S,*6*R,*7a*R*)-1-{[(2′*R,*6*R*)-3′,6′-Dihydro-6′-methoxy-2′-methyl-2′*H*-pyran-2′-yl]carbonyl}-1,4,5,6,7,7a-hexahydro-8,8-dimethyl-3*H*-3a,6-methano[2,1]benzisothiazole 2,2-Dioxide* ((2′*R*,6′*R*)-**2b**). (−)-**1b** (1.425 g, 5.0 mmol) and freshly distilled 1-methoxybuta-1,3-diene (3.04 ml, 30 mmol) were dissolved in anh. CH_2Cl_2 (15 ml) and placed in a *Teflon* reaction vessel prior to exposition to 14 kbar pressure at 50° for 48 h. The solvent was evaporated and the residue subjected to CC (SiO_2, hexane/AcOEt 6:1). *trans*-**2b** (1.587 g, 86%; 66:34

Table 2. *Crystal Data and Structure Refinement for Compounds* **2b** *and* **2c**

Identification code	(2′*R*,6′*R*)-**2b** (major)	(2′*R*,6′*S*)-**2c** (minor)
Empirical formula	$C_{18}H_{27}NO_5S$	$C_{23}H_{27}NO_5S$
Molecular mass M_r	369.47	429.52
Temperature [K]	293(2)	293(2)
Wavelength [Å]	1.54178	1.54178
Crystal system	triclinic	monoclinic
Space group	*P*1	$P2_1$(*a*-axis unique)
Unit cell dimensions [Å] [°]	$a = 7.086(1)$	$a = 8.3890(3)$
	$b = 9.844(1)$	$b = 10.8298(4)$
	$c = 13.334(2)$	$c = 12.8076(8)$
	$\alpha = 90.70(1)$	
	$\beta = 97.48(1)$	
	$\gamma = 90.15(1)$	$\gamma = 104.209(3)$
Volume [Å^3]	922.1(2)	1127.99(9)
Z	2	2
Density (calc.) [Mg/m^{-3}]	1.331	1.265
Absorption coefficient [mm^{-1}]	0.203	1.551
F(000)	396	456
Crystal size [mm]	0.14 × 0.07 × 0.35	0.07 × 0.07 × 0.42
Range for data collection	4.42 to 74.1	4.21 to 73.95
Index ranges	$0 \le h \le 9$, $-12 \le k \le 12$, $-17 \le l \le 17$	$-10 \le h \le 10$, $0 \le k \le 13$, $-15 \le l \le 15$
Reflections collected	4274	4333
Independent reflections	4274 (R(int) = 0.0000)	4130 (R(int) = 0.0352)
Refinement method	full-matrix least-squares on F^2	
Data/restraints/parameters	4274/3/665	4130/1/272
Goodness-of-fit on F^2	2.315	0.779
Final $R(I > 2\sigma(I))$	$R_1 = 0.0440$, $wR_2 = 0.0641$	$R_1 = 0.0390$, $wR_2 = 0.1148$
R indices (all data)	$R_1 = 0.0480$, $wR_2 = 0.0647$	$R_1 = 0.0399$, $wR_2 = 0.1167$
Absolute structure parameter	0.01(8)	0.01(2)
Extinction coefficient	0.0031(5)	0.0063(8)

mixture) and *cis*-**2b** (56 mg, 3%). Crystallization of *trans*-**2b** from hexane/AcOEt delivered pure (2′*R*,6′*R*)-**2b** (18%) and (2′*R*,6′*R*)-**2b**/(2′*S*,6′*S*)-**2b** 4:3 (67%).

*Data of (2′*R,*6′*R*)-***2b***: M.p. 148–150° $[\alpha]_D = +7.6$ ($c = 1.1$, $CHCl_3$). IR: 2990, 1680, 1340, 1295, 1050. ^{1}H-NMR: 0.992 (*s*, 3 H); 1.207 (*s*, 3 H); 1.30–1.41 (*m*, 2 H); 1.604 (*s*, 3 H); 1.82–1.90 (*m*, 3 H); 1.92–1.99 (*m*, 1 H); 2.01–2.07 (*m*, 1 H); 2.24–2.30 (*m*, 1 H); 2.44–2.50 (*m*, 1 H); 3.49 (*AB*, 2 H); 3.53 (*s*, 3 H); 4.07–4.11 (*m*, 1 H); 5.145 (br. *s*, 1 H); 5.76–5.80 (*m*, 1 H); 5.95–6.00 (*m*, 1 H). ^{13}C-NMR[10]): 19.96 (C(9)); 21.74 (C(8)); 23.19 (*Me*–C(6′)); 26.29 (C(5)); 33.57 (C(6)); 33.77 (C(5′)); 39.47 (C(3)); 45.32 (C(4)); 47.52 (C(1)); 47.80 (C(7)); 54.88 (C(10)); 56.075 (MeO); 67.83 (C(2)); 76.40 (C(6′)); 94.91 (C(2′)); 125.52 (C(3′)); 126.07 (C(4′)); 177.15 (C=O). MS: 369 (0, $M^{+\bullet}$), 338(45), 154(19), 127(100), 43(43). HR-MS: 338.1432 ($C_{17}H_{24}NO_4S^+$, $[M-OMe]^+$; calc. 338.1426). Anal. calc. for $C_{18}H_{27}NO_5S$: C 58.54, H 7.32, N 3.79; found: C 58.59, H 7.43, N 3.63.

*Data of (2′*S,*6′*S*)-***2b***: ^{1}H-NMR (deduced from the mixture): 0.997 (*s*, 3 H); 1.237 (*s*, 3 H); 1.31–1.41 (*m*, 1 H); 1.600 (*s*, 3 H); 1.82–1.90 (*m*, 4 H); 1.92–1.99 (*m*, 1 H); 2.01–2.07 (*m*, 1 H); 2.07–2.12 (*m*, 1 H); 2.61–2.69 (*m*, 1 H); 3.47 (*m*, 2 H); 3.472 (*s*, 3 H); 4.04–4.08 (*m*, 1 H); 5.086 (br. *s*, 1 H); 5.76–5.80 (*m*, 1 H); 5.95–6.00 (*m*, 1 H). ^{13}C-NMR (deduced from the mixture)[10]): 19.92 (C(9)); 21.56 (C(8)); 24.70 (*Me*–C(6′)); 26.22 (C(5)); 30.74 (C(6)); 33.68 (C(5′)); 39.51 (C(3)); 45.34 (C(4)); 47.46 (C(1)); 47.77 (C(7)); 54.60 (C(10)); 55.55 (MeO); 67.76 (C(2)); 75.19 (C(6′)); 94.13 (C(2′)); 124.95 (C(3′)); 125.59 (C(4′)); 176.30 (C=O).

*(3a*S,*6*R,7aR*)-1-[(3′,6′-Dihydro-*c*-6′-methoxy-2′-methyl-2′*H*-pyran-*r*-2′-yl)carbonyl]-1,4,5,6,7,7a-hexahydro-8,8-dimethyl-3*H*-3a,6-methano[2,1]benzisothiazole 2,2-Dioxide* (*cis*-**2b**). See above: isolated in 3% yield during the purification of *trans*-**2b**. M.p. 140–142° (hexane/Et_2O). $[\alpha]_D = +25.9$ ($c = 1.0$, $CHCl_3$). IR: 2990, 2960, 2930, 1660, 1140, 1050. ^{1}H-NMR: 0.987 (*s*, 3 H); 1.233 (*s*, 3 H); 1.25–1.42 (*m*, 2 H); 1.598 (*s*, 3 H); 1.82–1.99 (*m*, 4 H); 2.04–2.10 (*m*, 1 H); 2.20–2.26 (*m*, 1 H); 2.53–2.59 (*m*, 1 H); 3.481 (*m*, 2 H); 3.591 (*s*, 3 H); 4.08–4.12 (*m*, 1 H); 5.198 (br. *s*, 1 H); 5.67–5.715 (*m*, 1 H); 5.93–5.97 (*m*, 1 H). ^{13}C-NMR[10]): 20.02 (C(9)); 20.33 (C(8)); 22.14 (*Me*–C(6′)); 26.22 (C(5)); 33.89 (C(6)); 33.98 (C(5′)); 39.68 (C(3)); 45.46 (C(4)); 47.53 (C(1)); 47.91 (C(7)); 54.40 (C(10)); 56.71 (MeO); 68.00 (C(2)); 78.35 (C(6′)); 96.56 (C(2′)); 126.24 (C(3′)); 127.29 (C(4′)); 176.03 (C=O). LI-MS: 392 (100, $[M+Na]^+$), 338(26), 308(36).

*(3a*S,*6*R,7aR*)-1-{[(2′*S,*6′*R*)-3′,6′-Dihydro-6′-methoxy-2′-phenyl-2′*H*-pyran-2′-yl]carbonyl}-1,4,5,6,7,7a-hexahydro-8,8-dimethyl-3*H*-3a,6-methano[2,1]benzisothiazole 2,2-Dioxide* ((2′*S*,6′*R*)-**2c**). As described above, (2′*S*,6′*R*)-**2c**/(2′*R*,6′*S*)-**2c** 63:37 (86%) was obtained from (−)-**1c** (5.0 mmol) and 1-methoxybuta-1,3-diene (30.0 mmol), after CC (SiO_2, hexane/AcOEt 8:1). Crystallization from hexane/AcOEt afforded pure (2′*S*,6′*R*)-**2c** (48%). M.p. 184–186°. $[\alpha]_D^{25} = -202.5$ ($c = 1.0$, $CHCl_3$). IR: 2990, 1670, 1340, 1220, 1140, 1050. ^{1}H-NMR: 0.958 (*s*, 3 H); 1.162 (*s*, 3 H); 1.286 (*AB*, 2 H); 1.71–1.98 (*m*, 5 H); 2.46–2.52 (*m*, 1 H); 3.08–3.15 (*m*, 1 H); 3.368 (*AB*, 2 H); 3.597 (*s*, 3 H); 4.01–4.05 (*m*, 1 H); 5.593 (br. *s*, 1 H); 5.78–5.82 (*m*, 1 H); 6.12–6.17 (*m*, 1 H); 7.25–7.58 (3*m*, 5 H). ^{13}C-NMR[10]): 19.93 (C(9)); 21.65 (C(8)); 26.16 (C(5)); 33.83 (C(6)); 35.82 (C(5′)); 39.46 (C(3)); 45.47 (C(4)); 47.52 (C(7)); 48.01 (C(1)); 53.96 (C(10)); 55.10 (MeO); 67.90 (C(2)); 83.10 (C(6′)); 95.69 (C(2′)); 125.46 (C_o); 126.23 (C(3′)); 127.63 (C(4′)); 128.02 (C_m); 128.95 (C_p); 140.37 (C_{ipso}); 174.38 (C=O). MS: 430 (0, $M^{+\bullet}$), 400(0.5), 216(8), 189(54), 105(100), 77(12). HR-MS: 400.1582 ($C_{22}H_{26}NO_4S^+$, $[M-OMe]^+$; calc. 400.1577). Anal. calc. for $C_{23}H_{29}NO_5S$: C 64.04, H 6.73, N 3.25; found: C 63.56, H 6.53, N 3.27.

*(3a*S,*6*R,*7a*R*)-1-{[(2′*R,*6′*S*)-3′,6′-Dihydro-6′-methoxy-2′-phenyl-2′*H*-pyran-2′-yl]carbonyl}-1,4,5,6,7,7a-hexahydro-8,8-dimethyl-3*H*-3a,6-methano[2,1]benzisothiazole 2,2-Dioxide* ((2′*R*,6′*S*)-**2c**). Obtained pure (22%) by crystallization in Et_2O of the mother liquors obtained from (2′*S*,6′*R*)-**2c**. M.p. 120–122°. $[\alpha]_D^{25} = -77.9$ ($c = 1.1$, $CHCl_3$). IR: 2990, 1670, 1340, 1140, 1050. ^{1}H-NMR: 0.917 (*s*, 3 H); 0.950 (*s*, 3 H); 1.19–1.35 (*m*, 2 H); 1.67–1.92 (*m*, 5 H); 2.72–2.78 (*m*, 1 H); 2.96–3.02 (*m*, 1 H); 3.42 (*AB*, 2 H); 3.502 (*s*, 3 H); 3.93–3.97 (*m*, 1 H); 5.381 (br. *s*. 1 H); 5.76–5.80 (*m*, 1 H); 6.10–6.15 (*m*, 1 H); 7.23–7.50 (3*m*, 5 H). ^{13}C-NMR[10]): 19.95 (C(9)); 20.85 (C(8)); 26.34 (C(5)); 30.50 (C(5′)); 33.45 (C(6)); 38.86 (C(3)); 44.96 (C(4)); 47.49 (C(7)); 48.00 (C(1)); 54.58 (C(10)); 55.64 (MeO); 67.66 (C(2)); 80.50 (C(6′)); 95.58 (C(2′)); 126.06 (C_p); 126.70 (C(3′)); 127.09 (C(4′)); 127.80 (C_o); 128.00 (C_m); 140.99 (C_{ipso}); 174.04 (C=O). MS: 430 (0, $M^{+\bullet}$), 400(0.7), 216(9), 189(54), 105(100), 77(10). HR-MS: 400.1582 ($C_{22}H_{26}NO_4S^+$, $[M-OMe]^+$; calc. 400.1577). Anal. calc. for $C_{23}H_{29}NO_5S$: C 64.04, H 6.73, N 3.25, found: C 64.04, H 6.79, N 3.34.

*(2*R,*6*R*)-3,6-Dihydro-6-methoxy-2-methyl-2*H*-pyran-2-methanol* ((2*R*,6*R*)-**3b**). A soln. of (2′*R*,6′*R*)-**2b** (170.5 mg, 0.462 mmol) in THF (2.0 ml) was added at 0° to a suspension of $LiAlH_4$ (26.3 mg, 0.69 mmol) in THF (5 ml) and stirred at 10–15° for 45 min. The reaction was quenched at 0° with H_2O (10 ml) and the mixture

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[10]) Arbitrary numbering according to the *Figure*.

extracted with AcOEt (3×10 ml). The combined org. extract was dried ($MgSO_4$), then filtered through *Celite*, and evaporated and the residue purified by CC (SiO_2, CH_2Cl_2): pure free bornane-10,2-sultam (88%) and (2*R*,6*R*)-**3b** (84%). Oil. $[\alpha]_D = +2.6$ ($c = 1.4$, $CHCl_3$). IR: 3500, 2930, 1390, 1050. ^{1}H-NMR: 1.282 (*s*, 3 H); 1.75–1.81 (*m*, 1 H); 2.085–2.12 (*dd*, OH); 2.45–2.51 (*m*, 1 H); 3.35–3.40 (*m*, 1 H); 3.54–3.575 (*m*, 1 H); 3.433 (*s*, 3 H); 4.93 (br. *s*, 1 H); 5.735–5.775 (*m*, 1 H); 5.97–6.015 (*m*, 1 H). ^{13}C-NMR: 22.34 (*Me*–(2)); 30.02 (C(3)); 55.18 (MeO); 70.24 (C(2)); 72.12 (CH_2OH); 95.71 (C(6)); 124.54 (C(5)); 126.90 (C(4)). EI-MS: 158 (1, $M^{+\cdot}$), 128(10), 127 (100), 43(20).

*3,6-Dihydro-*c*-6-methoxy-2-methyl-2*H*-pyran-*r*-2-methanol* (*cis*-**3b**). Obtained in 91% yield from *cis*-**2b** as described above. Oil. $[\alpha]_D = -23.0$ ($c = 0.2$, $CHCl_3$). IR: 3450, 2960, 1395. ^{1}H-NMR: 1.240 (*s*, 3 H); 2.11–2.16 (*m*, 2 H); 3.40–3.65 (*m*, 2 H); 3.518 (*s*, 3 H); 4.93–4.97 (*m*, 1 H); 5.66–5.75 (*m*, 1 H); 5.94–6.04 (*m*, 1 H). ^{13}C-NMR: 25.06 (*Me*–C(2)); 29.71 (C(3)); 55.78 (MeO); 69.37 (CH_2OH); 70.0 (C(2)); 95.75 (C(6)); 123.86 (C(5)); 127.94 (C(4)). LI-MS: 181 (35, $[M + Na]^+$).

*(2*S*,6*R*)-3,6-Dihydro-6-methoxy-2-phenyl-2*H*-pyran-2-methanol* ((2*S*,6*R*)-**3c**). Obtained in 90% yield as described above, besides directly crystallized free sultam (84%). M.p. 70–72° (hexane/Et_2O). $[\alpha]_D = +12.6$ ($c = 0.5$, $CHCl_3$). IR: 3250, 2950, 2930, 1440, 1400, 1035. ^{1}H-NMR: 1.90–1.94 (*dd*, OH); 2.63–2.77 (*m*, 1 H); 3.446 (*s*, 3 H); 3.55–3.60 (*m*, 1 H); 3.79–3.83 (*m*, 1 H); 5.109 (br. *s*, 1 H); 5.67–5.715 (*m*, 1 H); 6.08–6.12 (*m*, 1 H); 7.24–7.28 (*m*, 1 H); 7.31–7.35 (*m*, 2 H); 7.44–7.47 (*m*, 2 H). ^{13}C-NMR: 28.09 (C(3)); 55.34 (MeO); 69.36 (CH_2OH); 76.50 (C(2)); 96.18 (C(6)); 125.92 (C(5)); 126.37 (C(4)); 127.31 (C_p); 127.47 (C_o); 127.92 (C_m); 142.06 (C_{ipso}). MS: 220 (1, $M^{+\cdot}$), 189(74), 105(100). HR-MS: 189.09243 ($C_{12}H_{13}O_2^+$, $[M - OMe]^+$; calc. 189.09155).

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Received July 3, 1998