Diastereoselective Alkyl *Grignard* 1,4-Additions to *para*-Substituted (2*R*)-*N*-Cinnamoylbornane-10,2-sultam Derivatives: Influence of N-Atom Pyramidalization

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Dedicated to Dr. *Charles Fehr*, on the occasion of his 65th birthday

Several typical ^{13}C-NMR displacements (of C=O, C(α), C(β), and C_{ipso}), as well as conformational or energy properties (S–N–C=O dihedral angle, ΔE *syn*/*anti*; HOMO/LUMO) could be correlated with the electronic parameters of *p*-substituted *N*-cinnamoylbornane-10,2-sultams **2**. Even under nonchelating conditions, the pyramidalization of the sultam N-atom decreases for electron-attracting *p*-substituents, inducing a modification of the sultam-ring puckering. Detailed comparison of the X-ray structure analyses of **2b**, **2d**, and **2m** showed that the orientation of the sterically directing pseudo-axial S=O(2) and H–C(2) is modified and precludes any conclusion about the π-facial stereoelectronic influence of the N lone pair on the alkyl *Grignard* 1,4-addition. We also showed that the aggregating alkyl *Grignard* reagent may be used in equimolar fashion, demonstrating that the sultam moiety is chelated with a *Lewis* acid such as $MgBr_2$. The *Schlenk* equilibrium may also be used to generate the appropriate conditions of effective 1,4-diastereoselectivity. Although the *anti*-s-*cis*/*syn*-s-*cis* difference of conformational energies for *N*-cinnamoyl derivatives **2** is higher than for the simple *N*-crotonoyl analogue, an X-ray structure analysis of the SO_2/C=O *syn* derivative **10** confirms the predictive validity of our conformational calculations for $\Delta E \leq 1.8$ kcal/mol.

Introduction. – The (2*R*)-bornane-10,2-sultam auxiliary **1** [1] generally exerts a decisive steric influence on the C(α) atom of its *N*-alkenoyl derivatives, and has been judiciously recognized as a disguised pseudo-C_2-symmetric promoter [2]. In contrast, its steric influence on the remote C(β) atom is almost inexistent[3]). Since we have tried, for years, to show the stereoelectronic influence of the N lone pair (lp) on the *N*-alkenoyl moiety [5], we became particularly interested in chemical reactions exclusively restrained to the C(β) atom. Although they are quite rare, several 1,4-

[1]) Master Thesis No. 236362 University of Warsaw (30th June 2010), presented at the 'Multiple Faces of Chemistry: from Marie Curie to Nowadays' in Paris, France (31st Jan.–1st Feb. 2011).

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[3]) Thus, for example, the conjugate addition of an organozirconocene proceeds with only 9% d.e. on the *N*-crotonoylbornane-10,2-sultam [3a], while, in absence of electronic conjugation with the carbonyl group, *syn*-dihydroxylation involving the C(β) atom proceeds with only 0 – 20% d.e., even in the cooperative presence of two conformationally rigidifying and directing prosthetic groups [4]. In this latter case, it is noteworthy that the weak purely steric influence of the sultam moiety on C(β) directs the approach on the same face as for a C(α) steric attack.

additions to *N*-alkenoylbornane-10,2-sultams have been reported[4]). In 2004, we suggested that this hypothetic stereoelectronic effect[5]) could be potentially demonstrated by simple *Grignard* addition to appropriately *para* (= *p*)-substituted cinnamoyl derivatives. In the meantime, a Chinese group reported this transformation [20], but unfortunately their experimental protocol is unsuitable for our mechanistic postulate. Indeed, primarily interested in complete chemical conversions, *Liu* and co-workers initiated the conjugated addition at $-78°$, and then increased the temperature to $-40°$, until completion of the reaction. They rationalized their results on the basis of *Oppolzer*'s initial model [9a] but did not discuss the poorer diastereoselectivities observed for sterically more demanding, hence less reactive, *Grignard* reagents, and, moreover, did not find any electronic correlation. Since we recently demonstrated that the unchelated minor SO_2/C=O *syn*-conformer may, in some instances, be more reactive than its thermodynamically more stable *anti*-conformer [21][6]), the conformational rigidity of the *N*-alkenoyl side chain is primordial to the N-lp stereoelectronic control, in opposition to the C_2-symmetrical steric influence, exerted by either the S=O(2) or C(3) substituents, on the C(α) atom [2], hence, apparently to a much lesser extent, on the C(β) atom. We thus decided to reinvestigate, in more detail, the 1,4-addition of the simple ethyl *Grignard* reagent to *p*-substituted cinnamoyl derivatives of type **2**[7]), at a conformationally rigidifying and constant low temperature, since such a

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[4]) Indeed, whereas chemical reactions involving either the C(α) or both C(α) and C(β) atoms are legion (> 300 reports), specific reactions at the C(β) atom are limited, *e.g.*, to either $MeNO_2$/DBU/THF/DMPU [6] (DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, DMPU = tetrahydro-1,3-dimethylpyrimidin-2(1*H*)-one), or electrochemical CO_2 [7], or RS^- [8] *Michael* additions, as well as the 1,4-additions of simple *Grignard* reagents [9], Mg-cuprates [10], Li-cuprates [11], ^{t}BuHgCl- or In–Cu^I-generated alkyl radical [12], Rh^I or Cu^I/zirconocenes [3], $EtAlCl_2$ or Cu^I/zincates [13], $TiCl_4$/allylSiMe$_3$ [14], $TiCl_4$/Cl_3CLi [15], or Li-enolates [16]. Method [6] apparently does not involve any chelate and gave *ca.* 50% d.e. in favor of the same face as for a C(α) steric attack, *anti* to the N lp, in case of the more reactive SO_2–C=O *syn* s-*cis* conformer. The same π-facial selectivity was also obtained in almost all the other examples of chelation [3b][8–16] (see the discussion for exceptions). The absolute configuration of the 1,4-adducts was not determined in [3a][7][11f][12][13b][14]. We are indebted to Prof. *M. J. Wu* for providing confirmation. In accord with the senior author, whom we thank for his answer (25th Oct. 2010), we must establish that the absolute configurations as depicted for compounds **18** and **19** in [13a] do not correspond to those expected from *Oppolzer*'s original reports (Table 1, Entry 11 in [11a]) [11e]. The case of [9e] is noteworthy, since the C(β) atom is under the direct C(α)-*re* steric influence of the second bornane-10,2-sultam chirophor. The case of [7] is also noteworthy (50% (*R*) configuration at the newly created stereogenic β-center, as suggested by the respective ^{1}H-NMR analyses [11e][15] and this work) since it is not a nucleophilic addition to **2d**, but rather a radical anion coupling to CO_2 as electrophilic agent. In our case, radical addition of ^{i}PrI or cHexI (In, $InCl_3$, H_2O) to **2d** according to [12] afforded **7d** (87% yield, 25% d.e.) and **8d** (75% yield, 13% d.e.) as minor diastereoisomers. The fact that for nonchelated *N*-alkenoylsultams, the sense of induction is both reversed and contra-steric, is consistent with a stereoelectronic control [11a][17]. Similarly, the stereoelectronic influence may also be invoked for the contra-steric trapping of the corresponding enolates [9a]. No information concerning the ambiguous absolute configuration of the starting material used in [11g] was forthcoming (28th Oct. 2010).

[5]) See the conclusions in [18] and [19a].

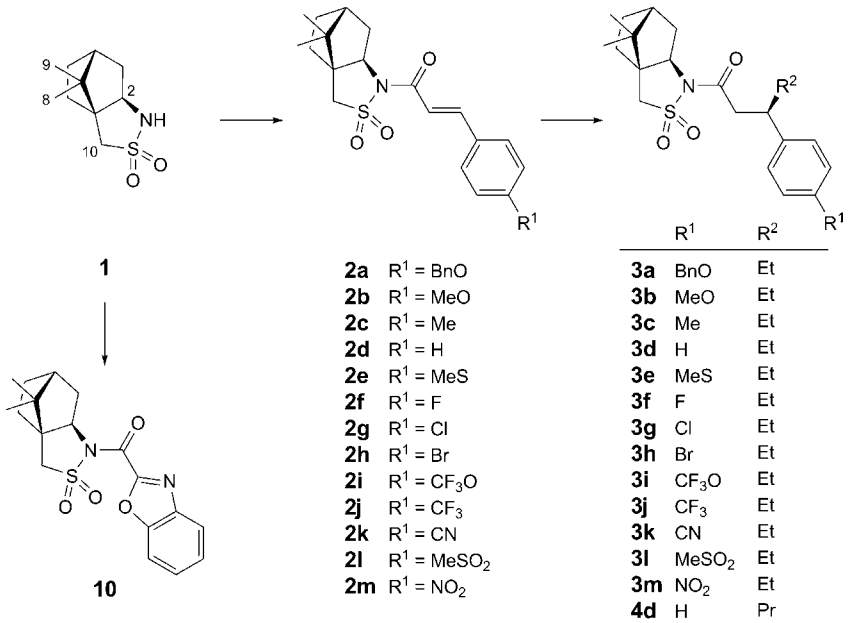
[6]) Thus following the *Acree–Curtin–Hammett* principle [22].

[7]) Harder nucleophiles such as MeMgCl or PhMgCl are known to react principally in a 1,2-fashion [9][20].

substitution should electronically influence the C(β) reactive center, without any substantial drastic direct perturbations.

Results. – First of all, we synthesized an electronically and statistically relevant series of adequately *p*-substituted (2*R*)-*N*-cinnamoylbornane-10,2-sultams (*Scheme*), comprising the reported fully characterized derivatives **2b** [20b][19][23][24], **2d**[8]) [6][8][11a][14][19][20][23][25]–[27], **2k**[9]) [25d][26], **2l**[10]) [28], **2m** [19b][19d][28], and their un- or very partially characterized analogues **2a** [23], **2c** [20a][19a][17c][26] [27], **2e** [28], **2f** [20][29], **2g** [20][19a][19d][26][28], **2h** [26][27a], and **2i** [29], as well as the unreported substrate **2j**. The conjugate addition of 2.2 mol-equiv. of EtMgBr (THF, $-78°$, 4 h; see *General Procedure B* as well as *Footnote 37* in the *Exper. Part*) to

Scheme



[8]) ESI-MS: 368.3 ($[M+Na]^+$). HR-ESI-MS: 368.1296 ($C_{19}H_{23}NNaO_5S^+$; calc. 368.1327).

[9]) IR (KBr): 2995, 2943, 2881, 2231, 1675, 1631, 1344, 1319, 1289, 1237, 1221, 1164, 1133, 1117, 1067, 1039, 989, 883, 827, 760, 535, 494, 424 cm^{-1}. ESI-MS: 393.1 ($[M+Na]^+$). HR-ESI-MS: 393.1249 ($C_{20}H_{22}N_2NaO_3S^+$, calc. 393.1210).

[10]) ESI-MS: 446.1 ($[M+Na]^+$). HR-ESI-MS: 446.1072 ($C_{20}H_{25}NNaO_5S^+$, calc. 446.1065).

2a afforded **3a** with 80% d.e. after complete conversion (*Table 1*). This ratio (±2%) was obtained by direct integration of the Me(8) signal in the ^{1}H-NMR spectrum, as earlier reported in a similar case [11e][15]. Indeed, the Me(8) signal of the corresponding minor diastereoisomer systematically resonated at higher field by *ca.* 0.26–0.28 ppm for all the analogues **3a**–**3m**. This ratio was also confirmed by comparison of the C(2) signal in the ^{13}C-NMR spectrum, since a similar shift of *ca.* 0.15–0.17 ppm to higher field was observed for the minor stereoisomers of **3a**–**3m**[11]). For the corresponding *p*-MeO and *p*-MeS derivatives **2b** and **2e**, the diastereoselectivities reached 76 and 77% d.e., respectively (*Table 1*). The entropically less chaotic *p*-Me derivative **2c** gave a π-facial selectivity of 79% d.e., similar to **2a**, while the unsubstituted *N*-cinnamoyl substrate **2d** [20] exhibited 73% d.e. In the halogen series, the diastereoselectivity decreased from 78 to 67 and 64% d.e. for the *p*-F adduct **3f** [20], *p*-Cl adduct **3g** [20], and *p*-Br adducts **3h**, respectively. The *p*-CF_3O derivative **2i** is sterically comparable to **2b** but was slightly less selective, with 73% d.e. This trend was even more pronounced for the *p*-CF_3 analogue **2j** (62% d.e.), as compared to **2c**[12]). The absolute configuration of this series was based on the X-ray structure analysis of **3f**[13]) [32], associated with its correlation with the major stereoisomers in both the ^{1}H- and ^{13}C-NMR analyses of **3a**–**3m**. The loss of selectivity was even more pronounced for the adducts with electron-demanding substituents such as *p*-cyano adduct **3k** (49%

Table 1. *Diastereoselectivities and* Hammett, *IR, and NMR Parameters for* **2a**–**2m**

	d.e. [%]	log(d.r.)	Conv. [%][a])	σ_{para}	$\sigma_{Inductive}$	$\sigma_{Resonance}$	$\tilde{\nu}$(C=O) [cm^{-1}]	$\tilde{\nu}$(C(α)=C(β)) [cm^{-1}]	$\tilde{\nu}$(C=C$_{arom}$) [cm^{-1}]	δ(H–C(α)) [ppm]	δ(H–C(β)) [ppm]
2a	80	0.954	100	−0.41	0.29	−0.46	1669	1614	1596	7.04	7.75
2b	76	0.865	100	−0.27	0.27	−0.45	1671	1616	1599	7.07	7.79
2c	79	0.931	100	−0.14	−0.04	−0.11	1676	1623	1606	7.12	7.77
2d	73	0.807	100	0.00	0.00	0.00	1678	1624	1600	7.17	7.79
2e	77	0.886	100	0.06	0.23	−0.20	1671	1614	1589	7.11	7.74
2f	78	0.908	100	0.15	0.50	−0.34	1678	1626	1598	7.07	7.75
2g	67	0.704	100	0.24	0.46	−0.23	1676	1628	1587	7.14	7.73
2h	64	0.659	100	0.26	0.44	−0.19	1676	1628	1593	7.15	7.71
2i	73	0.807	100	0.35	0.55	−0.19	1682	1634	1604	7.14	7.75
2j	62	0.630	100	0.53	0.45	0.08	1683	1632	1617	7.23	7.78
2k	49	0.466	100	0.70	0.56	0.13	1675	1631	1607	7.24	7.75
2l	45	0.421	74	0.73	0.59	0.12	1676	1629	1600	7.28	7.81
2m	46	0.432	15	0.78	0.65	0.15	1672	1628	1599	7.29	7.79

[a]) For chemical yields, see the *Exper. Part.*

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11) Alternatively, the same kind of shifts were observed for either the C(3) (*ca.* 0.15–0.22 ppm), or the C(9) signals (*ca.* 0.33–0.51 ppm). In the ^{1}H-NMR analyses, the Me(8) and Me(9) signals resonated in the region δ(H) 0.90–1.03 and 1.09–1.31 ppm, respectively (see also *Table 6* for ^{13}C-NMR attributions).

12) Thus contrasting with the almost isosteric couple **2d**/**2f** since the electronically more demanding F-atom is sterically considered as slightly larger than a H-atom [30a]. The steric demand of a CF_3 group is thus in between that of a Me and a ^{i}Pr substituent [30b]. ^{19}F-NMR Analysis was also used earlier for the determination of the d.e. [21][31] in specific cases such as **3f**, **3i**, and **3j**.

13) Dihedral angle S–N–C=O = 153.2° and ΔhN = 0.226 Å.

d.e.), *p*-methylsulfonyl derivative **3l** (45% d.e.), and *p*-nitro analogue **3m** (46% d.e.)[14]). In both the latter cases, the conversion was incomplete, thus demonstrating the negative influence of the strongly electron-withdrawing groups on both the kinetics and diastereoselectivities, as presented in both *Table 1* and *Fig. 1*. The general trend thus expressed may be resumed by *Eqn. 1*. The electronic parameter σ_{para} may also be decomposed into its $\sigma_{\text{Inductive}}$ and $\sigma_{\text{Resonnance}}$ component[15]), as earlier determined and systematically indexed [33]. In this manner, a better bi-linear regression was found:

$$\log(\text{d.r.}) = -0.459\sigma_{para} + 0.834 \quad (n = 13,\ R^2 = 0.83,\ \text{standard deviation (s.d.)} = 0.834) \qquad (1)$$

$$\log(\text{d.r.}) = -0.433\sigma_{\text{Inductive}} - 0.603\sigma_{\text{Resonance}} + 0.815\ (n = 13,\ R^2 = 0.87,\ \text{s.d.} = 0.075) \qquad (2)$$

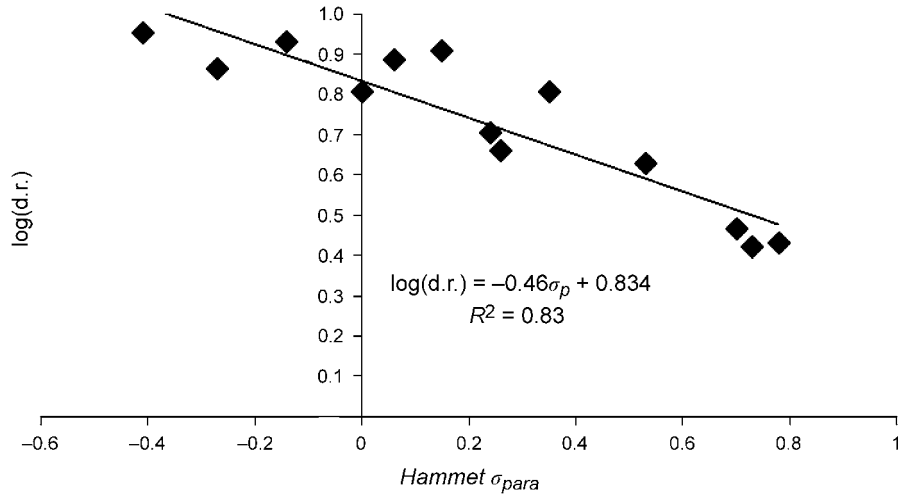

Fig. 1. *Diastereoselectivity* (log(d.r.)) *of the 1,4-addition of EtMgBr to* **2a**–**2m** *at* $-78°$ *in THF as a function of the* Hammett *constant* σ_{para}

In contrast to previous studies correlating the barrier of rotation around the N-atom in the IR analyses of simple *p*-substituted cinnamamides [34], we were unable to find any significant correlations between either the $\tilde{\nu}$(C=O) ($1676 \pm 7\ \text{cm}^{-1}$), the $\tilde{\nu}$(C(α)=C(β)) ($1624 \pm 10\ \text{cm}^{-1}$), or the $\tilde{\nu}$(C=C$_{\text{arom}}$), ($1602 \pm 15\ \text{cm}^{-1}$) and the electronic parameters ($R^2 \leq 0.75$). Similarly, the ^{1}H-NMR data showed that the δ(H) of H–C(β) of **2a**–**2m** is strongly influenced by the direct steric and anisotropic effect of the proximate aromatic ring, and no valid correlation was found, in contrast to the δ(H) of H–C(α) which may well be expressed by *Eqn. 3*. A similar observation was earlier already reported for

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14) This trend is opposite to the increased diastereoselectivities partially observed in the case of the sterically demanding silyl monocuprate 1,4-addition to *p*-substituted *N*-cinnamoyl derivatives of type **2** [11e].

15) We found that $\sigma_{para} = 0.981\sigma_{\text{Inductive}} + 1.205\sigma_{\text{Resonance}} + 0.012$ ($n = 13$, $R^2 = 0.98$, s.d. = 0.063).

simple cinnamic acid esters, cinnamamides, and similar compounds [35]. The predictabilities were even more impressive in the ^{13}C-NMR spectra of **2a**–**2m** (see *Table 6*, *Exper. Part*), where the δ(C) of all the main C-atoms of the *N*-cinnamoyl side chains were particularly well correlated with the electronic parameters, as expressed by *Eqns. 4–7.*

$$\delta(H\text{–}C(\alpha)) = 0.089\sigma_{\text{Inductive}} + 0.334\sigma_{\text{Resonance}} + 7.167\ (n = 13,\ R^2 = 0.96,\ \text{s.d.} = 0.018) \quad (3)$$

$$\delta(C{=}O) = -1.092\sigma_{\text{Inductive}} - 1.436\sigma_{\text{Resonance}} + 164.383\ (n = 13,\ R^2 = 0.97,\ \text{s.d.} = 0.078) \quad (4)$$

$$\delta(C(\alpha)) = 4.553\sigma_{\text{Inductive}} + 8.204\sigma_{\text{Resonance}} + 117.502\ (n = 13,\ R^2 = 0.99,\ \text{s.d.} = 0.287) \quad (5)$$

$$\delta(C(\beta)) = -3.996\sigma_{\text{Inductive}} - 2.435\sigma_{\text{Resonance}} + 145.536\ (n = 13,\ R^2 = 0.99,\ \text{s.d.} = 0.128) \quad (6)$$

$$\delta(C_{ipso}) = 5.534\sigma_{\text{Inductive}} + 17.785\sigma_{\text{Resonance}} + 133.951\ (n = 13,\ R^2 = 0.99,\ \text{s.d.} = 0.434) \quad (7)$$

At this point, to demonstrate the crucial role of the temperature on the conformational equilibrium, hence the diastereoselectivities of such reactions, we briefly determined the *Eyring* plot of **2d**, by performing the quantitative conjugate addition of EtMgBr in THF at $-63°$ (72% d.e.), $-42°$ (68% d.e.), $-18°$ (66% d.e.), and $0°$ (60% d.e.). These results are shown in *Fig. 2*, which allowed us to determine the corresponding enthalpic ($\Delta\Delta H^{\ddagger} = 0.59$ kcal/mol), and entropic ($\Delta\Delta S^{\ddagger} = 0.73$ cal/(K mol)) factors, obtained from both the slope, and the intercept, respectively. These values are close to those already reported for the transition states of *Diels–Alder* reactions, for similar dienophiles [36].

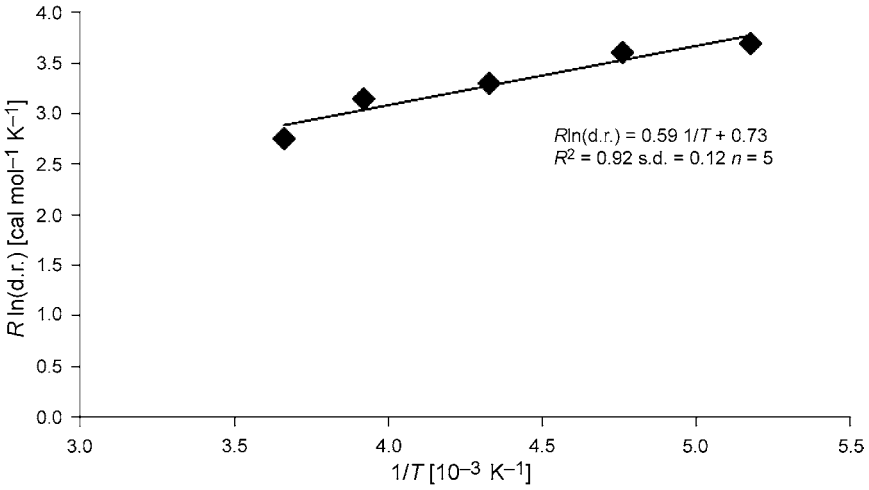

Fig. 2. Eyring *plot for the temperature dependence of the EtMgBr 1,4-addition to* **2d** *in THF*

Finally, we also studied the steric contribution of the nucleophile by adding, at $-78°$ in THF, 2.2 mol-equiv. of the more reactive alkyl MgCl reagents of increasing bulkiness to **2d**. Thus, after 4 h and full conversion, the already reported adducts **4d**–**8d**

could be isolated [20][16]). Their diastereoisomer ratios were also determined and confirmed by ^{1}H-[17]) and ^{13}C-NMR[18]) analyses, respectively, and their absolute configurations were analogously determined, as in the case of **2d**, with the help of the reported X-ray structure analyses of **5g** (R^1 = Cl, R^2 = Bu) [37], **6g** (R^1 = Cl, R^2 = Bn) [38], and **7f** [39] (R^1 = F, R^2 = ^{i}Pr)[19]). The corresponding observed diastereoselectivities, as well as the steric parameters of the nucleophile alkyl MgCl, are reported in *Table 2* as well as in *Fig 3*. The *Taft* steric parameter $-E_s$ was earlier obtained from kinetic data, by acid- and base-catalyzed hydrolysis of esters in aqueous acetone [40], and approximately follows the size of the group. It is independent from polar effects [41] but may be sensitive to solvation, field, or resonance effects [42], and its correlation with the observed diastereoselectivity for adducts **3d**–**8d** is not perfect, as shown by *Eqn. 8*.

Charton's ν values, which are independent of kinetic data and are derived from the *van der Waals* radii [43], gave a more interesting correlation (*Eqn. 9*).

The best linear regression was obtained from *Meyer*'s steric parameter V^a (*Eqn. 10*), obtained by MM2 calculations, and which corresponds to the volume of the portion of the substituent that is within 3 Å of the reaction center [44][20]). In all three cases (*Eqn. 8–10*), the diastereoselectivity diminished with respect to the increasing size of the nucleophile, meaning that the transition-state energy differences decrease for the transfer of bulky substituents. A similar trend was earlier observed for

Table 2. *Diastereoselectivities for the Adducts* **3d**–**8d**, *Steric Factors, and HOMO and LUMO Levels of the Nucleophiles Alkyl MgR*

	d.e. [%]	log(d.r.)	Yield[a]) [%]	*Taft* $-E_s$	*Charton* υ	*Meyer* $V^a \cdot 10^2$	HOMO [eV]	LUMO [eV]
EtMgCl	78 (**3d**)	0.908	96	0.07	0.56	4.31	– 0.246	– 0.044
PrMgCl	76 (**4d**)	0.865	95	0.36	0.68	4.78	– 0.247	– 0.044
BuMgCl	72 (**5d**)	0.788	95	0.39	0.68	4.79	– 0.245	– 0.044
BnMgCl	58 (**6d**)	0.575	79[b])	0.38	0.70	5.09	– 0.242	– 0.042
^{i}PrMgCl	46 (**7d**)	0.432	94	0.47	0.76	5.74	– 0.234	– 0.045
cHexMgCl	24 (**8d**)	0.213	91	0.79	0.87	6.25	– 0.228	– 0.045

[a]) Isolated by CC (SiO_2). [b]) Besides the 1,2-adduct (8%).

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16) IR (KBr; in cm^{-1}): **4d**: 2957, 2931, 2882, 1693, 1453, 1418, 1383, 1322, 1272, 1237, 1214, 1205, 1164, 1131, 1114, 1065, 1032, 989, 772, 699, 611; **5d**: 2956, 2928, 1693, 1454, 1412, 1375, 1327, 1274, 1235, 1211, 1164, 1132, 1111, 1065, 1039, 987, 761. 700, 610; **6d**: 3027, 2959, 1693, 1495, 1453, 1412, 1375, 1326, 1273, 1235, 1213, 1164, 1132, 1114, 1067, 1039, 987, 759, 697, 613; **7d**: 2959, 1696, 1494, 1454, 1413, 1385, 1327, 1269, 1212, 1164, 1133, 1111, 1065, 1039, 987, 757, 700, 612; **8d**: 2923, 2852, 1695, 1450, 1413, 1375, 1327, 1269, 1235, 1213, 1164, 1132, 1112, 1066, 1039, 987, 782, 757, 699, 610.

17) Me(8) of minor diastereoisomer, at higher field by *ca.* 0.16–0.29 ppm.

18) C(2), and C(9) of minor diastereoisomer, at higher field by *ca.* 0.16–0.19 and *ca.* 0.23–0.36 ppm, resp.

19) Dihedral angle S–N–C=O and ΔhN; for **5g**, 160.3° and 0.200 Å; for **6g**, 150.2° and 0.217 Å; for **7f**, 158.1° and 0.175 Å.

20) As shown earlier, the E_s, ν, and V^a values, as well as the *van der Waals* radii are linearly intercorrelated [45].

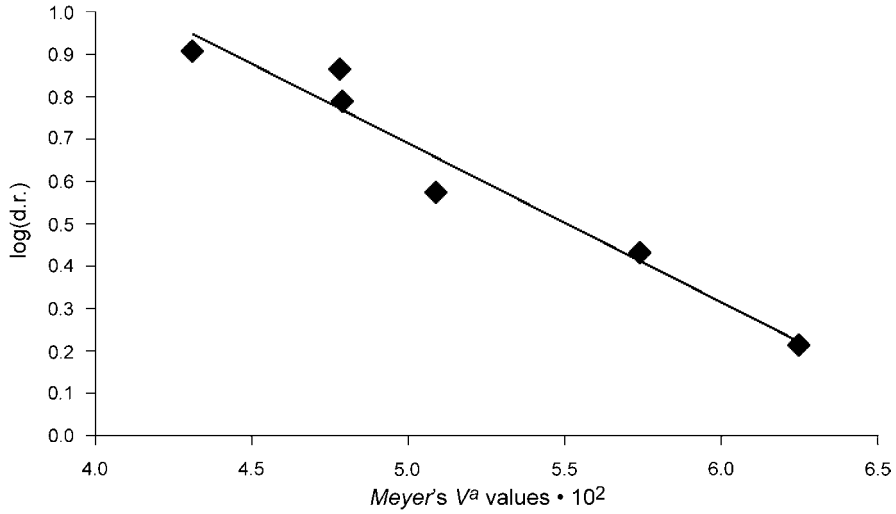

Fig. 3. *Diastereoselectivity* vs. Meyer*'s steric values for* Grignard-*nucleophile 1,4-addition to* **2d**

the *N*-crotonoyl- [9a][46] and *N*-cinnamoylbornane-10,2-sultams [20], although with apparently higher diastereoselectivities, on addition of bromo *Grignard* reagents[21])! The fact that a linear correlation was obtained for all three steric parameters suggests that the influence of the nucleophile is essentially steric in nature.

$$\log(\text{d.r.}) = -1.040(-E_s) + 1.057 \ (n = 6,\ R^2 = 0.77,\ \text{s.d.} = 0.145) \tag{8}$$

$$\log(\text{d.r.}) = -2.469\nu + 2.379 \ (n = 6,\ R^2 = 0.86,\ \text{s.d.} = 0.116) \tag{9}$$

$$\log(\text{d.r.}) = -37.485\ V^{\text{a}} + 2.564 \ (n = 6,\ R^2 = 0.95,\ \text{s.d.} = 0.066) \tag{10}$$

Discussion. – The stereoelectronic influence of a N lp was initially suggested by *Eschenmoser* and co-workers [47], and both *Oppolzer et al.* [9a][48] and *Curran et al.* [49] invoked this possibility, before discarding it[22]) in favor of a purely steric rationalization [2]. We earlier suggested that both steric and stereoelectronic influences may match or mismatch, depending on the SO_2/C=O *syn* or *anti* conformation, respectively [50]. Furthermore, we also suggested that the minor *syn*-s-*cis* conformer is more reactive than its more stable concurrent *anti*-s-*cis* partner, and may thus eventually participate to the global stereochemical course of the reaction [5] (*Fig. 4*).

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21) In that latter case, the d.e. determinations by HPLC analyses were not performed directly with the crude 1,4-adducts but after derivatization.

22) In view of the poor correlation of the diastereoselectivity and the electronic nature of the attacking reagent, as well as the fact that the reactive sites are not directly connected to the N-atom. See page 311 and ref. 48a in [2]. This may be due to the fact that essentially C(α) or C(α) and C(β) attacks were considered, and that the steric influence on C(α) is apparently much stronger than the stereoelectronic effect.

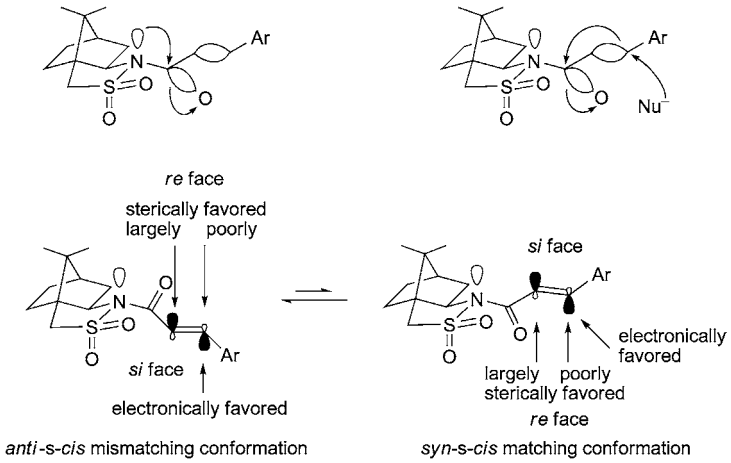

Fig. 4. *Hypothetical stereoelectronic influence of the N lone pair*

To illustrate the stereoelectronic role of the N lp, we shall pedagogically use the 'banana'-bond description of an unsaturation, as proposed in the 1930's by *Pauling* [51], in contrast to the *Hückel* representation, resulting from a combination of both a σ- and π-bond [52]. Despite the fact that some theoretical chemists consider both models to be practically equivalent [53], the latter one is much better known, better accepted, and, therefore, found in most modern textbooks. In the first representation, the N lp tends to distinguish between both equivalent adjacent bonds, by delocalization to the carbonyl O-atom of the *anti*-periplanar bent bond, rendering this one more labile. Consequently, a nucleophilic attack on the SO_2/C=O *syn*-s-*cis* C(β) atom should stereoelectronically preferentially occur from the 'bottom' C(α)-*re* face[23]), since the *anti*-periplanar broken C(α)–C(β) 'banana' bond would preferentially delocalize on the carbonyl by assisting the opening of the weakest *anti*-periplanar C=O bent bond. If this memory-aid rule of thumb is correct, we should retrieve a similar trend in the *Hückel* description, and, therefore, we calculated the corresponding HOMO, LUMO, and conformational energies of substrates **2a**–**2m**, as expressed in *Table 3*, at the B3LYP/6-31G** level [54]. These calculations, performed on both *anti*-s-*cis* and *syn*-s-*cis* conformers **2a**–**2m** show several general trends. First of all, for both of them, the pyramidality of the N-atom globally decreases for electron-withdrawing substituents and is crudely correlated with the electronic parameters according to *Eqn. 11*. Systematically, the N-atom is more planar in the *syn*-s-*cis*, as compared to the *anti*-s-*cis* conformation (*ca.* 0.16–0.17 Å *vs.* 0.24–0.25 Å). As earlier remarked by comparison of X-ray analyses, this pyramidality

[23]) Although the reacting center is the C(β) C-atom, we prefer throughout this report to distinguish both π-faces with respect to the C(α) atom. This has the advantage of being directly comparable with the plethora of previous discussions/rationalizations concerning chemical reactions involving either the C(α) or both C(α) and C(β) atoms, as well as to avoid any inversion of priority on the C(β) atom when the *Michael* acceptor is branched to other than aryl substituents. *Oppolzer* and co-workers reported that the reverse contra-steric *si*-face 1,4-addition is observed in the case of the unchelated SO_2/C=O *anti*-s-*cis* conformation [11a].

Table 3. *Structure and LUMO Parameters of the* anti-*s*-cis *and* syn-*s*-cis *Conformers of* **2a** – **2m**

	Δ*h*N [Å]	S–N–C=O [°]	O=C–C(α)=C(β) [°]	C(α)=C(β)–C_{ipso}–C_o [°]	HOMO [eV]	LUMO [eV]	C(α)-*re*	C(α)-*si*	C(β)-*re*	C(β)-*si*	Δ*E* [kcal/mol]
anti-s-*cis:*											
2a	0.253	149.4	– 8.2	– 1.0	– 0.212	– 0.058	0.148	0.142	0.192	**0.193**	
2b	0.252	149.8	– 8.2	0.1	– 0.211	– 0.058	0.146	0.140	0.198	0.190	
2c	0.245	150.4	– 8.1	– 0.2	– 0.224	– 0.063	0.157	0.144	0.188	**0.195**	
2d	0.240	150.8	– 8.0	0.2	– 0.230	– 0.065	0.153	0.149	0.196	**0.197**	
2e	0.251	150.2	– 8.2	– 0.1	– 0.208	– 0.064	0.148	0.144	0.185	0.183	
2f	0.241	150.6	– 8.2	– 0.1	– 0.230	– 0.067	0.151	0.149	0.199	**0.200**	
2g	0.242	151.0	– 8.3	0.2	– 0.233	– 0.072	0.155	0.152	0.190	**0.191**	
2h	0.245	150.7	– 8.3	– 0.1	– 0.230	– 0.073	0.155	0.150	0.187	**0.190**	
2i	0.248	151.1	– 8.4	0.0	– 0.232	– 0.070	0.156	0.147	0.184	**0.188**	
2j	0.238	151.3	– 8.4	0.2	– 0.245	– 0.079	0.160	0.158	0.181	**0.182**	
2k	0.239	151.7	– 8.2	0.8	– 0.247	– 0.090	0.151	0.154	0.156	0.154	
2l	0.240	151.6	– 8.8	0.3	– 0.250	– 0.085	0.159	0.162	0.167	0.166	
2m	0.242	151.8	– 9.2	0.3	– 0.255	– 0.104	0.200	0.192	0.136	0.132	
syn-s-*cis:*											
2a	0.171	– 20.4	– 4.9	– 4.0	– 0.219	– 0.063	0.146	0.150	**0.202**	0.200	6.16
2b	0.177	– 19.8	– 2.8	– 0.7	– 0.218	– 0.062	0.148	0.147	0.188	0.190	6.10
2c	0.170	– 19.7	– 5.2	– 3.2	– 0.230	– 0.068	0.149	0.155	**0.188**	0.179	6.16
2d	0.175	– 19.8	– 4.5	– 1.3	– 0.238	– 0.071	0.151	0.156	0.190	0.197	6.23
2e	0.172	– 19.1	– 4.0	– 1.6	– 0.214	– 0.068	0.150	0.148	**0.189**	0.187	6.12
2f	0.171	– 19.7	– 4.6	– 1.6	– 0.237	– 0.072	0.158	0.160	**0.191**	0.190	6.37
2g	0.169	– 19.2	– 5.1	– 2.0	– 0.240	– 0.078	0.153	0.154	**0.179**	0.172	6.43
2h	0.169	– 19.4	– 4.5	– 1.5	– 0.237	– 0.077	0.155	0.156	**0.177**	0.176	6.39
2i	0.170	– 19.8	– 3.5	– 1.6	– 0.239	– 0.075	0.159	0.159	**0.191**	0.185	6.50
2j	0.169	– 19.8	– 4.7	– 4.1	– 0.252	– 0.085	0.157	0.159	0.160	0.164	6.48
2k	0.159	– 18.1	– 5.2	– 2.9	– 0.254	– 0.095	0.155	0.155	**0.156**	0.152	6.66
2l	0.162	– 17.9	– 4.1	– 2.5	– 0.257	– 0.091	0.153	0.160	0.165	0.168	6.71
2m	0.161	– 18.4	– 4.9	– 2.3	– 0.262	– 0.110	0.130	0.128	0.097	0.102	6.68

is related to the S–N–C=O dihedral angle [5][55], itself correlated with the electronic parameters according to *Eqn. 12*.

$$\Delta h\mathrm{N}_{syn} = -0.012\sigma_{\mathrm{Inductive}} - 0.014\sigma_{\mathrm{Resonance}} + 0.172 \ (n = 13,\ R^2 = 0.75,\ \mathrm{s.d.} = 0.003) \quad (11)$$

$$\mathrm{S{-}N{-}C{=}O}_{anti} = 1.306\sigma_{\mathrm{Inductive}} + 2.623\sigma_{\mathrm{Resonance}} + 150.644 \ (n = 13,\ R^2 = 0.92,\ \mathrm{s.d.} = 0.229) \quad (12)$$

Prediction of the MO energies is also possible, in view of the relationships shown in *Eqns. 13–16*. Both the HOMO and the LUMO of the *anti*-s-*cis* conformers are slightly higher in energy as compared to those of their corresponding *syn*-s-*cis* conformers. Nevertheless, the reactivity of the *Michael* acceptor is mostly dependent on the LUMO C(β) coefficients, as their square values are relevant, according to the *Schrödinger* reactivity equation [5], hence from the donating properties of the aromatic moiety, in either a push–pull or pull–pull combination with the sultam moiety. Depending on the considered π-face, the C(β) LUMO coefficients are slightly different, due to the N lp desymmetrization, but not as systematically as would be expected from the 'banana' bond theory. Indeed, in both reactive conformations, the preferred stereoelectronic attack is favored on the expected π-face in eight cases out of thirteen (bold numbers), and is systematically 'opposite' for electron-attracting substituents. Finally, to reach an SO_2/C=O *syn* conformation, the calculated conformational energy increases for electron withdrawing groups, according to *Eqn. 17*. This also contributes to a lower reactivity of the electronically poor *Michael* acceptors, since they are statistically more inclined to adopt the *anti*-s-*cis* mismatching conformation.

$$\mathrm{HOMO}_{anti} = -0.030\sigma_{\mathrm{Inductive}} - 0.051\sigma_{\mathrm{Resonance}} - 0.227 \ (n = 13,\ R^2 = 0.88,\ \mathrm{s.d.} = 0.006) \quad (13)$$

$$\mathrm{HOMO}_{syn} = -0.030\sigma_{\mathrm{Inductive}} - 0.051\sigma_{\mathrm{Resonance}} - 0.233 \ (n = 13,\ R^2 = 0.87,\ \mathrm{s.d.} = 0.006) \quad (14)$$

$$\mathrm{LUMO}_{anti} = -0.031\sigma_{\mathrm{Inductive}} - 0.042\sigma_{\mathrm{Resonance}} - 0.066 \ (n = 13,\ R^2 = 0.90,\ \mathrm{s.d.} = 0.005) \quad (15)$$

$$\mathrm{LUMO}_{syn} = -0.031\sigma_{\mathrm{Inductive}} - 0.044\sigma_{\mathrm{Resonance}} - 0.072 \ (n = 13,\ R^2 = 0.90,\ \mathrm{s.d.} = 0.005) \quad (16)$$

$$\Delta E = 0.671\sigma_{\mathrm{Inductive}} + 0.546\sigma_{\mathrm{Resonance}} + 6.199 \ (n = 13,\ R^2 = 0.94,\ \mathrm{s.d.} = 0.057) \quad (17)$$

Oppolzer et al. [9a] and *Liu* and co-workers [20] underlined the necessity to use an excess of at least 2.0 mol.-equiv. of *Grignard* reagent for a complete conversion. This observation suggests, as proposed by *Oppolzer*, a chelated intermediate aggregated with a second equivalent of metallic nucleophile[24]). This chelation usually involves the

[24]) Such an aggregate was also invoked to explain the absence of 1,6-addition in case of a *N*-(2,4-dienoyl) substrate [9a]; furthermore, >3.0 mol-equiv. were necessary for bis-chelated *N*-fumaroyl derivatives [9e].

pseudo-equatorial S=O(1) substituent [56]. In a later work, the enolate generated after 1,4 -addition was trapped *in situ* by an electrophile, and the observed final diastereoselectivity could only be explained by chelation with the pseudo-axial S=O(2) group[25]). Unsatisfied by this lack of chelating unity, we also wondered whether the *Grignard* reagent was involved in a *Schlenk* equilibrium [57] (*Eqn. 18*).

$$2\ RMgX \rightleftharpoons MgX_2 + R_2Mg \tag{18}$$

Since iodo *Grignard* reagents are known for rarely forming aggregates [58], we first tested the addition of 2.2 mol-equiv. of BuMgI to **2d**, at $-78°$ in Et_2O[26]). The conversion was very poor, and the diastereoselectivity reached only 29% d.e. A firm conclusion is nevertheless difficult to reach, since substrate **2d** is extremely insoluble in Et_2O, particularly at $-78°$, so that the heterogeneity of the reaction could also be at the origin of this ambivalent result[27]). In a second control experiment, we added 1.1 mol-equiv. of anh. $MgBr_2$ (generated *in situ* by addition of $BrCH_2CH_2Br$ to Mg/THF) to a THF solution of **2d**, before adding, at $-78°$, 1.1 mol-equiv. of commercially available Bu_2Mg[28]). This experiment worked perfectly well, and after complete conversion, **5d** was isolated in 83% yield and 72% d.e. This $MgBr_2$ chelating experiment was repeated, but with 1.1 mol-equiv. of BuMgCl as nucleophile, thus affording **5d** in 96% yield and 72% d.e. We also treated **2d** with 1.1 mol-equiv. of anh. $ZnBr_2$ in THF, prior to the addition of 1.1 mol-equiv. of BuMgCl at $-78°$. In this case, the partial, *ca.* 50% conversion allowed the isolation of **5d** in 22% yield and 41% d.e. [59]. Finally, we also added 2.2 mol-equiv. of Bu_2Mg to a THF solution of **2d** at $-78°$ and obtained, after 4 h, **5d** in 85% yield and 59% d.e. It is noteworthy that the addition of EtMgCl (2.5 mol-equiv., THF, $-78°$) in the presence of 2.5 mol-equiv. of either LiCl or [18]crown-6 ether [60] did not influence significantly the aggregation since **2d** was isolated in 55 or 59% yield and 74 or 67% d.e., respectively. A different coordinating solvent such as chiral tetrahydro-2-methylfuran seems to be more influent as **5d** was obtained in 69% yield but only 40% d.e. during the addition of 2.5 mol-equiv of BuMgCl at $-78°$. *Oppolzer* and *Kingma* reported that the sense of induction was inverted when the alkyl *Grignard* reagent was additionally complexed with Cu^I [10a]. Curiously, he only reported C(α) substituted *Michael* acceptors and rationalized this reverse selectivity by Cu aggregation involving the easily interconverted s-*trans* conformer [10a]. It was only ten years later that *Huang et al.* reported, in an obscure journal [10b], a similar

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[25]) Furthermore, in a later article, only 1.25 mol-equiv. of *Grignard* reagent were employed, according to the Exper. Part (*vs.* 1.4 mol-equiv. according to the discussion) published in [9c]. This inversion of chelation is questionable since compounds 266 and 268 in [46a] possess an identical configuration, and epimerization was not excluded.

[26]) Due to the *Schlenk* equilibrium, the catalytic presence of MgI_2 is known to catalyze the attack and opening of THF during the preparation of the *Grignard* reagent.

[27]) When the *Grignard* reagent was prepared in Et_2O and added to a clear THF soln. of **2d** at $-78°$, a d.e. of 24% was observed. Similarly, addition of 2.2 mol-equiv. of BuMgBr to **2d** in Et_2O at $-78°$ afforded **5d** in 20% yield and 50% d.e. after 4 h. Alternatively, addition of 2.2 mol.-equiv. of EtMgI to **2d** in Et_2O at $-78°$ afforded **3d** in 25% yield and 31% d.e.

[28]) In heptane soln. containing 1% of Et_3Al as a viscosity reducer. The supplier is unable to either infirm or confirm the presence of any traces of either MgX_2 or HgX_2.

comparative inversion between alkyl MgBr and alkyl MgBr/CuI 1,4-additions to *N*-crotonoylbornane-10,2-sultam, thus suggesting that, in some instances, and certainly depending on either the C(β) or metal coordinating substituents, even C(α)-unsubstituted *Michael* acceptors may eventually also adopt a s-*trans* reactive conformation[29]). At this point, it is also noteworthy that we need to take into account two further exceptions, namely the allyl MgCl/CuBr·DMS/LiCl/Me_3SiCl conditions [10c–10f], as well as the Me_2CuLi/PBu_3 1,4-addition to *N*-crotonoylbornane-10,2-sultam [11i][11j][30]), which both favor the particularly rare C(α)-*si* face attack[31]). We thus became convinced that our arguments, based on alkyl *Grignard* 1,4-additions, could be biased due to a possible transfer of steric chiral information from the bornane skeleton to the C(β) position through a conformationally rigid bimetallic aggregate, directing its coordinating ligands in thermodynamically preferred directions. It was thus necessary to focus our attention on nonchelating/nonaggregating conditions, such as those employed for the addition of $MeNO_2$ to *N*-crotonoylbornane-10,2-sultam [6]. We similarly treated the *N*-(*p*-methoxycinnamoyl) substrate **2b** with $MeNO_2$/DBU, to afford **9b** in 65% yield and 59% d.e. Under the same conditions, the π-facial selectivity diminished for both the *N*-cinnamoyl acceptor **2d** (→ **9d**; 58%, 52% d.e.), **2g** (→ **9g**; 48%, 51% d.e.), as well as the electronically deficient and planar *N*-*p*-nitrocinnamoyl) derivative **2m** (→ **9m**; 18%, 24% d.e.). The extent of induction was measured and confirmed by ^{1}H- and ^{13}C-NMR analyses, respectively[32]), while the absolute configuration was based on both mechanistic considerations, with respect to X-ray analyses reported for analogous substrates [6][61], as well as on ^{1}H- and ^{13}C-NMR comparisons with an authentic sample of **9d**[33]), obtained independently.

Although the four adducts **9** obtained under nonchelating conditions are in full agreement with our initial hypothesis, we considered it would be useless to apply these conditions to all the series of electronically modified acceptors **2**, due to the following considerations. Indeed, paralleling the experimental approach, we also wondered about the reliability of our calculations. We thus decided to compare them with the known X-

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[29]) In our case, addition of 2.5 mol-equiv. of EtMgCl/CuI to **2d** at $-78°$ afforded **3d** in 54% yield and 70% d.e. It is noteworthy that the *anti*-s-*trans* and *syn*-s-*trans* conformations are 3.39 and 6.21 kcal/mol higher in energy as compared to the ground state, respectively. This is a substantial difference as compared to the *N*-crotonoyl analogue [5].

[30]) We are indebted to Prof. *C. L. Willis* for scrupulous control and confirmation of the absolute configuration of her adduct (9th Nov. 2010). In our case, addition of $Bu_2CuLi \cdot Bu_3P$ to **2d** in THF at $-78°$ afforded **5d** in 23% yield and 44% d.e.

[31]) In the first case, the sense of induction was based on an optical rotation of -1.6 [10c] and confirmed, after removal of the auxiliary, by the asymmetric *Flack* indexes of three intermediate X-ray analyses [10d][10e].

[32]) Here again, the minor diastereoisomer **9** exhibits its Me(8) signal by *ca.* 0.03 ppm at higher field in the ^{1}H-NMR spectrum, while in the ^{13}C-NMR spectrum C(2) and C(9) also resonate by *ca.* 0.26–0.37 ppm at higher field. We found $\log(\text{d.r.}) = 0.354\sigma_{para} + 0.514$ ($n = 4$, $R^2 = 0.94$, s.d. = 0.044), or $\log(\text{d.r.}) = -0.314\sigma_{\text{Inductive}} - 0.44\sigma_{\text{Resonance}} + 0.498$ ($n = 4$, $R^2 = 0.98$, s.d. = 0.044).

[33]) Because we were unable to obtain the original ^{1}H- and ^{13}C-NMR analyses of **9d** from the main author of [61] (10th Nov. 2010), we scrupulously repeated the addition of (2*R*)-*N*-acetylbornane-10,2-sultam to *trans*-β-nitrostyrene ($TiCl_4$, Et_3N, THF, $-78°$) and could isolate **9d** in 83% yield and 83% d.e. after purification by CC (SiO_2), in slight contrast with the original report in which the adduct was purified by crystallization [61].

ray structure analysis of the pyramidalized electron-donating *p*-MeO substrate **2b** [24] and of the unreported analogue **2d** (*Fig. 5*), as well as the electron-poor *p*-nitrocinnamoyl derivative **2m** (*Fig. 6*). First of all, comparison of the crystal structures of **2b** and **2m** confirmed that, for electron-withdrawing substituents, the N-atom tends to become more planar. Interestingly, and we can even say surprisingly for us, the case of the unsubstituted *N*-cinnamoyl derivative **2d** is noteworthy since it is even more pyramidalized than expected. The S–N–C=O dihedral angle is well correlated with ΔhN or, alternatively, with the sum of all three *N*-substituent angles (C(2)–N–S + C(2)–N–C(11) + C(11)–N–S [62]). Furthermore, to demonstrate the qualitative predictive properties of our calculations[34]), we also prepared the unreported *N*-(benzoxazolylcarbonyl) derivative **10** (NaH, toluene, benzoxazole-2-carbonyl chloride [63]; yield 79%). As we anticipated, it co-adopts both an *anti*-s-*syn*-clinal and *syn*-s-*anti*-clinal disposition as shown in *Fig. 7* and *Table 4*.

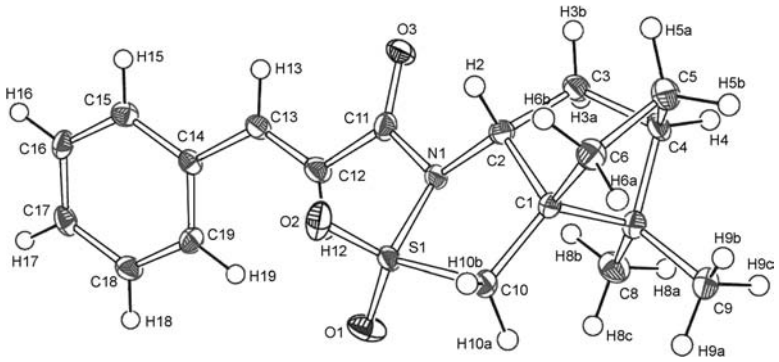

Fig. 5. *ORTEP Diagram of* **2d**. Arbitrary atom numbering. Ellipsoids are represented at the 50% probability level.

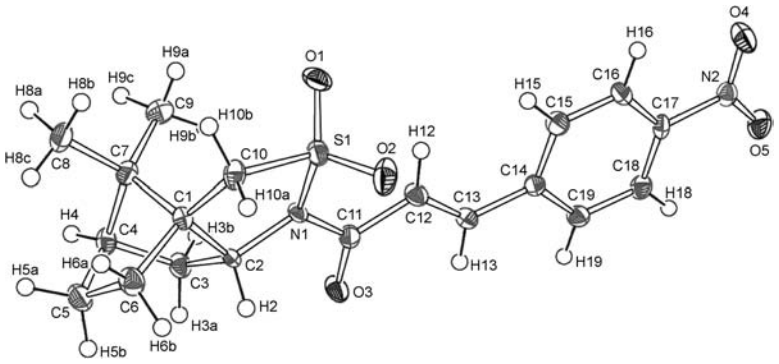

Fig. 6. *ORTEP Diagram of* **2m**. Arbitrary atom numbering. Ellipsoids are represented at the 50% probability level.

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[34]) See footenote 6 in [55] for solid-state SO_2/C=O *syn* conformations not exceeding 1.8 kcal/mol. The conformational analysis of **10** suggests the following energies in kcal/mol: *anti*-s-*syn*-clinal 0.00; *anti*-s-*anti*-clinal 0.77; *syn*-s-*syn*-clinal 1.63; *syn*-s-*anti*-clinal 4.58.

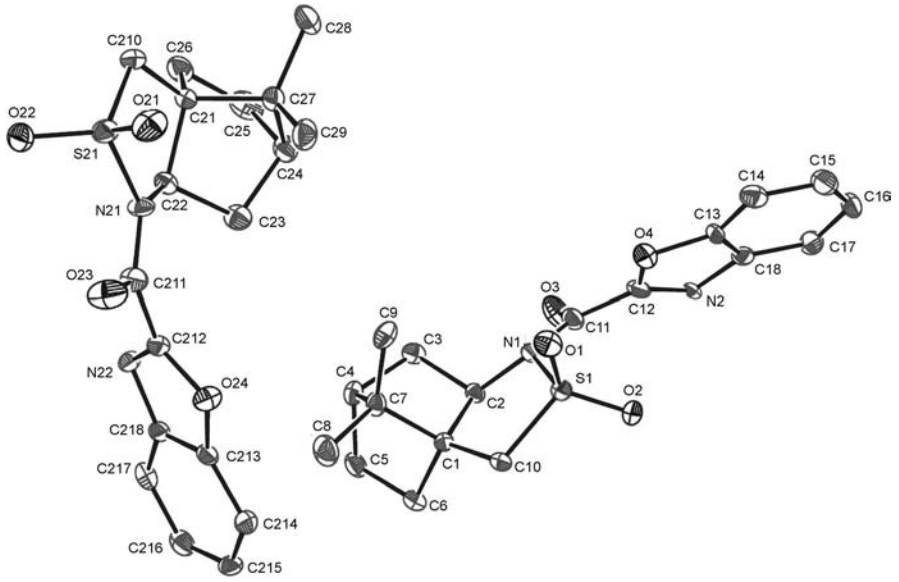

Fig. 7. *ORTEP Diagram of* syn-/anti-**10**. Arbitrary atom numbering. Ellipsoids are represented at the 50% probability level.

Table 4. *Selected Bond Lengths* [Å] *and Angles* [°] *of* **2b**, **2d**, **2m**, *and* **10**

	2d	**2b** [24]	**2m**	**10**$_{anti}$	**10**$_{syn}$
S=O(1)	1.4307(15)	1.408	1.4283(12)	1.4239(13)	1.4250(13)
S=O(2)	1.4359(15)	1.421	1.4302(12)	1.4289(13)	1.4310(13)
S–N	1.7051(17)	1.677	1.7022(13)	1.7170(14)	1.7136(14)
S–C(10)	1.783(2)	1.771	1.7835(16)	1.7782(17)	1.7797(18)
N–C(2)	1.476(2)	1.458	1.4820(17)	1.485(2)	1.488(2)
N–C(11)	1.403(2)	1.393	1.3927(19)	1.385(2)	1.356(2)
C(11)–O(3)	1.213(2)	1.206	1.2154(18)	1.218(2)	1.213(2)
C(11)–C(12)	1.485(3)	1.460	1.481(2)	1.486(2)	1.496(2)
C(12)=C(13)	1.323(3)	1.323	1.320(2)	1.302(2)[a])	1.292(2)[a])
O(1)=S=O(2)	117.66(9)	117.0	116.56(7)	118.35(8)	119.58(8)
C(2)–N–S	107.78(13)	110.3	112.82(9)	112.63(11)	113.67(11)
C(2)–N–C(11)	117.55(16)	118.4	119.33(12)	115.46(13)	129.57(14)
C(11)–N–S	119.71(13)	120.4	123.09(11)	122.52(12)	116.34(12)
C(2)–N–S=O(1)	– 147.74(13)	– 140.8	– 121.08(11)	– 116.49(12)	– 123.32(13)
C(2)–N–S=O(2)	82.24(14)	89.8	109.42(11)	113.19(12)	105.01(13)
C(3)-C(2)–N–S	153.89(15)	149.6	136.58(12)	135.54(13)	139.20(14)
S–N–C(11)=O(3)	142.37(18)	148.2	160.58(13)	158.16(15)	– 4.2(2)
O(3)=C(11)–C(12)=C(13)	– 18.6(3)	– 18.8	– 6.7(3)	– 38.8(3)[b])	118.4(2)[b])
C(12)=C(13)–C(14)=C_o	– 14.8(3)	– 14.4	2.6(3)		
C(12)=C(13)–C(14)=$C_{o'}$	164.4(2)	165.0	– 178.27(17)		
Δ*h*N [Å]	0.341	0.285	0.191	0.271	0.056
Puckering parameter q_2	0.417	0.390	0.321	0.299	0.363
S–N–C(2)–C(1)–C(10) Φ_2	43.95	57.28	101.91	107.83	96.78

[a]) C(12)=N(2). [b]) O(3)=C(11)–C(12)=N(2).

Comparison of both $\mathbf{10}_{anti}$ and $\mathbf{10}_{syn}$ also confirmed that the *syn* conformers are more planar, as calculated in *Table 3*. Both ΔhN and the S–N–C=O torsional angle of $\mathbf{10}_{syn}$ constitute new extreme values, as compared to the previous records for such a conformation (0.066 Å [55], and $-8.8°$ [64]). Another salient structural characteristic is the pseudo-axial orientation of the S=O(2) substituent, particularly marked for the electron-donating analogues **2b** and **2d**, or the conformer $\mathbf{10}_{syn}$ as compared to $\mathbf{10}_{anti}$, as expressed by the small dihedral C(2)–N–S=O(2) angles. This pseudo-axial orientation is also evident from the Φ_2 puckering parameter which, for both **2b** and **2d**, are the smallest ever reported for an SO_2/C=O *anti* disposition (usually comprised inbetween 77° [55] and 140° [65]). We thus can be confident in our gas-phase calculations and can envisage three possible rationalizations. In the first one, a conformational equilibrium implicates both the most-stable less-reactive mismatching *anti*-s-*cis* and the minor more reactive steric/stereoelectronic matching *syn*-s-*cis* conformers. In that option, the more planar N, resulting from electron-withdrawing *p*-substituents, induces more difficulties to reach a *syn*-s-*cis* cooperative disposition, and thus results in lower d.e. This intuitively postulated dependence of the diastereoselectivity on the conformational energy was opposed by a multilinear correlation of log(d.r.) with respect to $\sigma_{\text{Inductive}}$, $\sigma_{\text{Resonance}}$, and ΔE, which increased insignificantly the square of the correlation coefficient R^2 from 0.87 to 0.88 only, thus rendering this hypothesis less attractive as the main origin for substrates of type **2**. In the second option, the stereoelectronic influence is stronger for pyramidalized electron-rich conformers, thus explaining that, for electron-poor, more planar substrates, the π-facial discrimination diminishes. Finally, we can also imagine the absence of any stereoelectronic effect. The *p*-substituent would electronically modify the tilting of the N-atom, and thus, the puckering of the sultam ring. As a result, for a strongly pyramidalized N-atom, both S=O(2) and H–C(2) substituents would adopt a pseudo-axial orientation, while for electron-attracting *p*-substituted cinnamoyl derivatives, the more planar N-atom would rather direct these two substituents in a less pseudo-axial direction, thus diminishing their π-facial directing abilities. The steric directing influence of the sultam substituents would thus be indirectly a colateral consequence of the electronic effect of the *p*-substituent at the cinnamoyl moiety. One could argue that this geometry optimizes the steric influence on C(α), and to a lesser extent on C(β), thus explaining their higher diastereoselectivities in the SO_2/C=O *anti*-s-*cis* disposition. In both stereoelectronic or S=O(2)/C(2)–(C3) steric differential interactions, one would expect a better diastereoselectivity for **2d** as compared to **2b**. This argument is nevertheless moderated by the fact that the conformation in solution may be quite different from that in the solid state. A cumulative interaction between two or three of these hypotheses is also not excluded.

The steric influence of the chiral promoter is significantly more important on the proximate C(α) atom, as compared to the stereoelectronic effect. The situation could be inverted for the C(β) atom, especially for sterically nondemanding nucleophiles. When the bulkiness of the incoming *Grignard* reagent increases, the steric directing influence gains in importance and, consequently, the diastereoselectivity decreases due to the poor steric differentiation of the chiral auxiliary on the remote C(β) atom. This logical explanation does not constitute a proof of the stereoelectronic influence on

small nucleophiles but at least does not constitute a disproof of our postulate[35]). Finally, by fixing the C(3)–C(2)–N–C(11) torsional angle, we calculated both the stereoelectronic and geometric influence of the S–N–C=O conformation at *ca.* $\pm 1.5°$, and $\pm 3°$ around the minimum *syn*-s-*cis* and *anti*-s-*cis* conformers, respectively. We thus found that the most-reactive conformations in terms of LUMO and atomic coefficient levels are not necessarily those in the thermodynamically most-favored orientation. A very slight conformational change may even invert the stereoelectronic π-facial preference.

Conclusions. – For electron-rich pyramidalized substrates of type **2**, the 'banana' bond rationalization is statistically well corroborated by the *Hückel* representation. We showed that the alkyl *Grignard* reagent may be used in an equimolar amount, provided that the sultam moiety is chelated with a *Lewis* acid such as $MgBr_2$. The *Schlenk* equilibrium (*Eqn. 18*) may also be used to generate the appropriate conditions for effective 1,4-addition. Further developments to determine the scope, the limitations, and the effects of the nature of the *Lewis* acid are actually under study and shall be disclosed in due course. Addition of poorly aggregating iodo *Grignard* alkyl reagents resulted in both poor conversions and diastereoselectivities, thus allowing, as rationalization, a possible transmission of the chiral information of the bornane skeleton to the C(β) reactive center through a rigidified bimetallic chelated-(mixed Mg or Cu)-aggregated species, as earlier suggested by *Oppolzer* and co-workers. Even under nonchelating $MeNO_2$ 1,4-addition conditions, the concomitant electronic influence on both the N-pyramidalization and the ring puckering modifies the orientation of both the sterically directing S=O(2) and H–C(2) substituents, thus precluding any evident demonstration of a pure and dissociated stereoelectronic effect on the diastereoselectivity. These calculated geometries are consistent with the new X-ray structure analyses of **2d** and **2m**. It is noteworthy that when S=O(1) becomes more pseudo-axial, the pseudo-C_2 symmetry of the chiral auxiliary is lost [2][67]. Furthermore, theoretical calculations (*Table* 5) suggest that the LUMO atomic coefficients on both C(α) and C(β) strongly depend on very slight modifications of the reactive conformation, so that the effective stereoelectronic effect should be calculated and compared with the transition state, rather than on extreme SO_2/C=O *anti* or *syn* reactive conformations. Several typical NMR displacements (of C=O, C(α), C(β), and C_{ipso}), as well as conformational or energy properties (S–N–C=O dihedral angle, ΔE *syn*/*anti*; HOMO/LUMO) could nevertheless be very well correlated with the electronic parameters. Finally, from the synthetic point of view, this methodology may also be extended to give access to natural products and medicinal intermediates [68]. Amazingly, neither uncatalyzed nor *Lewis* acid mediated [4 + 2] cycloadditions of 1,3-dienes to dienophiles of type **2** have been reported. Their study could bring some interesting insights, as the C(α) and C(β) LUMO coefficients are strongly dependent on the electronic nature of

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[35]) The increasing mismatching steric influence was also observed for the counter anions or substituents of the *Grignard* reagent at $-78°$; for example: EtMgCl/THF (78% d.e.), EtMgBr/THF (73% d.e.), EtMgI/Et_2O (31% d.e.), BuMgCl/THF (72% d.e.), BuMgBr/THF (57% d.e.), and BuMgI/Et_2O (29% d.e.). For an inverse trend in the Mg cuprate addition to *Michael* acceptors connected to *Evans*' chiral auxiliaries, see [66].

the aryl substituent, and hence may cooperatively influence the same face in some instances[36]), thus leading to subtle predictable differences. The knowledge acquired during this study could eventually help us in redesigning a modified set of experiments, to bring to the fore this hypothetical stereoelectronic effect. Indeed, if 1,4-additions are ideal in minimizing the steric influence of the sultam skeleton on the C(α) position, the *Michael* acceptor should also maintain constant its sultam ring puckering, thus minimizing the S=O(2) and C(2)–C(3) steric influence on the remote C(β) position. Moreover, the electronically tunable nucleophiles chosen should have the same steric impact. All these requirements suggest the use of conjugated additions, at a constant temperature, of adequately *p*-substituted thiophenols or methyl thiosalicylates [8] to strongly pyramidalized sultam acceptors of type **2b**, **2c**, or **2d**, and comparison of the general trend with more planar counterparts of type **2k** or **2m**, or alternatively with the more isosteric **2i**, **2j**, or **2f** analogues, respectively.

Table 5. *Calculated Influences of the N-Pyramidalization on the Geometry and the MO Parameters of* **2d**

	SO_2/C=O *anti*-periplanar			SO_2/C=O *syn*-periplanar		
C(3)–C(2)–N–C(11) [°]	– 69.4	– 64.4	– 59.4	– 67.8	– 64.8	– 61.8
ΔE [kcal/mol]	0.07	0.00	0.33	6.30	6.23	6.25
ΔhN [Å]	0.278	0.240	0.202	0.199	0.175	0.148
S–N–C=O [°]	147.7	150.8	153.5	– 21.3	– 19.8	– 18.7
C(2)–N–S=O(1) [°]	– 129.5	– 129.5	– 130.0	– 120.8	– 120.2	– 119.1
C(2)–N–S=O(2) [°]	98.2	98.1	97.5	103.8	104.5	105.5
lp–N–S=O(2) [°]	– 156.2	– 158.5	– 161.2	– 154.8	– 155.7	– 156.0
O=C–C(α)=C(β) [°]	– 7.8	– 8.0	– 7.9	– 4.0	– 4.5	– 6.4
C(α)=C(β)–C_{ipso}=C_o [°]	0.4	0.2	0.3	– 3.1	– 1.3	– 4.2
HOMO [eV]	– 0.2304	– 0.2304	– 0.2302	– 0.2376	– 0.2375	– 0.2374
LUMO [eV]	– 0.0656	– 0.0652	– 0.0648	– 0.0708	– 0.0705	– 0.0703
C(11) up	0.155	0.155	0.150	0.126	0.128	0.131
C(11) down	0.143	0.137	0.144	0.136	0.133	0.135
C(α) up	**0.151**	**0.153**	0.153	**0.156**	**0.158**	**0.162**
C(α) down	0.146	0.149	**0.155**	0.153	0.154	0.158
C(β) up	0.196	0.196	**0.195**	**0.196**	**0.196**	**0.196**
C(β) down	**0.198**	**0.197**	0.193	0.191	0.190	0.191

The X-Ray measurements were performed in the Structural Research Laboratory at the Chemistry Department of the University of Warsaw. We are indebted to Prof. *A. Eschenmoser* for stimulating discussions after the presentation of our matching/mismatching stereoelectronic concept at the IXth Eur. Symp. Org. Chem. in Warsaw, 18–23 June 1995.

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36) For example, the C(α)-*re* face is electronically favored for both *anti*-s-*cis* and *syn*-s-*cis* **2e**, as well as *anti*-s-*cis* **2m** and *syn*-s-*cis* **2j**, in contrast to *syn*-s-*cis* **2l**, suggesting a C(α)-*si* face stereoelectronic preference in the latter case (see *Table 3*). Recently, double diastereoselection was used for determining the reactive conformation of *Evans*' *N*-enoyloxazolidin-2-ones in case of conjugate additions [69]. For 1,4-additions with *Evans*' derivatives, see ref. cited in [70].

Experimental Part

1. *General*. See [19a]. For ^{13}C-NMR attributions, see *Table 6*. All crystal measurements were performed with a *KM4CCD* κ-axis diffractometer and graphite-monochromated MoK_α radiation, see *Table 7*. The crystal was positioned at 61.2 mm from the CCD camera; 2224 frames were measured at 1° intervals with a counting time of 10 s for **2d**, 1392 frames were measured at 1° intervals with a counting time of 20 s for **2m**, and 2221 frames were measured at 1° intervals with a counting time of 3 s for **10**. The data were corrected for *Lorentz* and polarization effects. Empirical correction for absorption was applied [71]. Data reduction and analysis were carried out with the Oxford Diffraction programs [72]. The structure was solved by direct methods [73] and refined with SHELXL [74]. The refinement was based on F^2 for all reflections, except for 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 in [75]. The known configurations of the asymmetric centers were confirmed by the *Flack*-parameter refinement [76]. CCDC-779696, -779697, and -793873 contain the supplementary crystallographic data (excluding structural factors) for **2d**, **2m**, and **10**, resp. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif.

Table 6. *^{13}C-NMR Assignments of* **2a**–**2m**

	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**	**2j**	**2k**	**2l**	**2m**
C(1)	48.7	48.7	48.7	48.6	48.7	48.7	48.7	48.8	48.8	48.8	48.9	48.9	48.7
C(2)	65.4	65.4	65.4	65.3	65.4	65.4	65.4	65.4	65.4	65.4	65.5	65.4	65.3
C(3)	38.8	38.7	38.7	38.6	38.7	38.7	38.6	38.7	38.7	38.6	38.6	38.6	38.4
C(4)	44.9	44.9	44.9	44.8	44.9	44.9	44.9	44.9	44.9	44.9	44.8	44.8	44.7
C(5)	26.7	26.7	26.7	26.6	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.5
C(6)	33.0	33.0	33.0	32.9	33.0	33.0	33.0	33.0	33.0	33.0	33.0	33.0	32.9
C(7)	48.0	48.0	48.0	47.9	48.0	48.0	48.0	48.0	48.0	48.1	48.1	48.0	47.9
C(8)	20.1	20.1	20.1	20.0	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	19.9
C(9)	21.1	21.1	21.1	20.9	21.1	21.0	21.0	21.0	21.0	21.0	21.0	21.0	20.8
C(10)	53.4	53.4	53.4	53.2	53.4	53.4	53.3	53.4	53.3	53.3	53.4	53.3	53.2
C=O	164.7	164.7	164.6	164.3	164.5	164.3	164.2	164.2	164.1	163.9	163.6	163.6	163.3
C(α)	115.2	115.1	116.5	117.5	116.5	116.4	118.1	118.2	118.6	120.1	121.1	121.3	121.6
C(β)	145.5	145.5	145.8	145.6	145.2	144.4	144.2	144.3	143.8	143.7	143.1	142.9	142.3
C_{ipso}	127.5	127.3	131.7	134.3	131.0	130.8	132.9	133.4	133.1	137.9	138.7	139.7	140.4
C_o	130.6	130.6	128.9	128.7	129.2	130.7[a])	129.3	130.2	130.2	128.9	129.1	129.3	129.2
C_m	115.4	114.5	129.8	128.9	126.0	116.2[a])	130.0	132.3	121.3	126.0	132.8	128.1	124.1
C_p	161.1	161.9	141.4	130.7	142.7	117.4	136.7	125.2	158.8	131.3	113.8	141.8	148.6
R[1]	70.3[b])	55.6	21.7		15.3				150.8	123.9[c])	118.6	44.6	

[a]) C_o (*d*, J = 34.8 Hz); C_m (J = 86.8 Hz). [b]) 127.7 (2*d*), 128.4 (*d*), 128.9 (2*d*), and 136.6 (*s*). [c]) *q*, J = 270 Hz.

2. *Acylation of* **1**: *General Procedure A*. To a suspension of 60% NaH in mineral oil (1.2 equiv.) in dry toluene (10 ml) under Ar was added at 0° a soln. of **1** (1.1 equiv.) in dry toluene (20 ml). After 30 min. at 20°, the suspension was cooled to 0° and a soln. of the appropriate acyl chloride (2.2 mmol) in toluene (20 ml) was added dropwise. The mixture was stirred at 20° for 18 h. Then H_2O (10 ml) was added, and the aq. phase was extracted with CH_2Cl_2. The org. layer was dried ($MgSO_4$) and concentrated. The crude material was purified by CC (SiO_2, toluene/AcOEt 95:5) to afford products **2a**–**2j** or **10**.

Table 7. *Crystal Data and Structure Refinement of Compounds* **2d**, **2m**, *and* **10**

	2d	**2m**	**10**
Empirical formula	$C_{19}H_{23}NO_3S$	$C_{19}H_{22}N_2O_5S$	$C_{18}H_{20}N_2O_4S$
M_r	345.44	390.45	360.42
Temp. [K]	100(2)	100(2)	100(2)
Wavelength [Å]	0.71073	0.71073	0.71073
Crystal system	triclinic	monoclinic	monoclinic
Space group	P_1	$P2_1$	$P2_1$
Unit-cell dimensions			
a [Å]	7.3497(3)	7.8294(3)	7.07460(10)
b [Å]	7.6149(2)	7.1339(3)	13.1149(2)
c [Å]	8.6919(3)	16.9557(7)	18.1568(4)
α [°]	101.544(3)		
β [°]	111.169(3)	99.398(4)	93.239(2)
γ [°]	96.679(3)		
V [Å^3]	434.89(3)	934.33(7)	1681.95(5)
Z	1	2	4
Density [Mg/m^3]	1.319	1.388	1.423
Absorpt. coeff. [mm^{-1}]	0.203	0.207	0.219
$F(000)$ electrons	184	412	760
Crystal size [mm]	$0.35 \times 0.13 \times 0.08$	$0.44 \times 0.08 \times 0.06$	$0.28 \times 0.20 \times 0.16$
θ Range for data [°]	2.79 to 26.37	3.08 to 26.36	2.73 to 26.36
Index ranges	$-9 \le h \le 9$	$-9 \le h \le 9$	$-8 \le h \le 8$
	$-9 \le k \le 9$	$-8 \le k \le 8$	$-16 \le k \le 16$
	$-10 \le l \le 10$	$-21 \le l \le 21$	$-22 \le l \le 22$
Reflections collected, unique	14163/3549	20835/3816	55240/6854
R(int)	0.0283	0.0339	0.0433
Refinement method	full-matrix least-squares on F^2		
Criterion for observed	$R(F)$ $(I > 2\sigma(I))$		
Data, restraints, parameters	3549, 3, 259	3816, 1, 285	6854, 1, 455
Goodness-of-fit on F^2	1.065	0.914	0.928
R_1 (GT)	0.0280	0.0263	0.0363
wR_2 (all)	0.0735	0.0497	0.0527
Abs. struct. parameter	−0.04(6)	−0.04(5)	0.02(4)
Largest peak and holes [Å^{-3}]	0.233, −0.178	0.237, −0.259	0.216, −0.259

*(−)-(2*R*)-*N*-[4-(Benzyloxy)cinnamoyl]bornane-10,2-sultam* (*=(−)-(2*E*)-3-[4-(Benzyloxy)phenyl]-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]-prop-2-en-1-one*; **2a**); Yield 83%. M.p. 115–120°. $[\alpha]_D^{20} = -60.9$ ($c = 1.0$, $CHCl_3$). IR: 3030, 2984, 2966, 2874, 1669, 1614, 1596, 1510, 1468, 1455, 1422, 1388, 1375, 1328, 1303, 1262, 1248, 1235, 1209, 1174, 1131, 1110, 1081, 1062, 1042, 1004, 984, 885, 828, 776, 758, 748, 698, 612, 548, 529, 497. ^{1}H-NMR: 0.98 (*s*, 2 H); 1.20 (*s*, 3 H); 1.40–1.49 (*m*, 2 H); 1.89–1.91 (*m*, 3 H); 2.08–2.20 (*m*, 2 H); 3.45, 3.54 (*AB*, $J = 13.8$, 2 H); 3.98 (*t*, $J = 6.8$, 1 H); 5.08 (*s*, 2 H); 7.04 (*d*, $J = 15.4$, 1 H); 6.94–7.40 (*m*, 7 H); 7.53 (*d*, $J = 8.8$, 2 H); 7.75 (*d*, $J = 15.4$, 1 H). ESI-MS: 474.2 ($[M + Na]^+$). HR-ESI-MS: 474.1715 ($C_{26}H_{29}NNaO_4S^+$; calc. 474.1690).

*(−)-(2*R*)-*N*-(4-Methylcinnamoyl)bornane-10,2-sultam* (*=(−)-(2*E*)-3-(4-Methylphenyl)-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]prop-2-en-1-one*; **2c**): Yield 95%. M.p. 204–210°. $[\alpha]_D^{20} = -95.9$ ($c = 1.0$, $CHCl_3$). IR: 3009, 2991, 2968, 2941, 2908, 2879, 1676, 1623, 1606, 1570, 1514, 1480, 1457, 1417, 1393, 1369, 1331, 1316, 1285, 1267, 1233, 1209, 1184, 1165, 1132, 1113, 1062, 989, 882, 815, 772, 717, 618, 548, 523, 497, 436. ^{1}H-NMR: 0.99 (*s*, 3 H); 1.21 (*s*, 3 H); 1.38–1.45 (*m*, 2 H); 1.91–1.94 (*m*, 3 H); 2.14–2.17 (*m*, 2 H); 2.37 (*s*, 3 H); 3.46, 3.55 (*AB*, $J = 13.7$,

2 H); 3.99 (t, J = 6.8, 1 H); 7.12 (d, J = 15.4, 1 H); 7.16–7.24 (m, 2 H); 7.46–7.50 (m, 2 H); 7.77 (d, J = 15.4, 1 H). ESI-MS: 382.1 ($[M + Na]^+$). HR-ESI-MS: 382.1453 ($C_{20}H_{25}NNaO_3S^+$; calc. 382.1450).

*(−)-(2*R*)-*N*-[4-(Methylthio)cinnamoyl]bornane-10,2-sultam* (= *(−)-(2*E*)-3-[4-(Methylthio)phenyl]-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]-prop-2-en-1-one*; **2e**): Yield 87%. M.p. 153–158°. $[\alpha]_D^{20} = -86.6$ (c = 1.0, $CHCl_3$). IR: 3006, 2986, 2963, 2940, 2878, 1671, 1614, 1589, 1550, 1494, 1456, 1407, 1368, 1336, 1315, 1275, 1230, 1206, 1187, 1164, 1132, 1112, 1093, 1062, 1042, 988, 882, 815, 762, 615, 546, 537, 500, 480, 463, 404. ^{1}H-NMR: 0.99 (s, 3 H); 1.20 (s, 3 H); 1.38–1.50 (m, 2 H); 1.85–1.95 (m, 3 H); 2.13–2.18 (m, 2 H); 2.50 (s, 3 H); 3.47, 3.56 (AB, J = 14, 2 H); 3.99 (t, J = 5,4, 1 H); 7.11 (d, J = 15.4, 1 H); 7.18–7.27 (m, 2 H); 7.47–7.51 (m, 2 H); 7.74 (d, J = 15.4, 1 H). ESI-MS: 414,1 ($[M + Na]^+$). HR-ESI-MS: 414.1174 ($C_{11}H_{16}NaO_3^+$; calc. 414.1187).

*(−)-(2*R*)-*N*-(4-Fluorocinnamoyl)bornane-10,2-sultam* (= *(−)-(2*E*)-3-(4-Fluorophenyl)-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]prop-2-en-1-one*; **2f**): Yield 89%. M.p. 178–186°. $[\alpha]_D^{20} = -90.2$ (c = 1.0, $CHCl_3$). IR: 3008, 2993, 2946, 2904, 1678, 1626, 1598, 1509, 1459, 1416, 1394, 1366, 1332, 1283, 1265, 1232, 1206, 1159, 1130, 1112, 1063, 1042, 987, 940, 883, 830, 777, 548, 526, 499, 455, 439. ^{1}H-NMR: 0.99 (s, 3 H); 1.21 (s, 3 H); 1.39–1.50 (m, 2 H); 1.91–1.96 (m, 3 H); 2.14–2.18 (m, 2 H); 3.46, 3.57 (AB, J = 14, 2 H); 4.0 (t, J = 7.2, 1 H); 7.07 (d, J = 15.4, 1 H); 7.03–7.13 (m, 2 H); 7.54–7.61 (m, 2 H); 7.75 (d, J = 15.4, 1 H). ESI-MS: 386.1 ($[M + Na]^+$). HR-ESI-MS: 386.1202 ($C_{19}H_{22}FNNaO_3S^+$; calc. 386.1216).

*(−)-(2*R*)-*N*-(4-Chlorocinnamoyl)bornane-10,2-sultam* (= *(−)-(2*E*)-3-(4-Chlorophenyl)-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]prop-2-en-1-one*; **2g**): Yield 79%. M.p. 207–212°. $[\alpha]_D^{20} = -98.8$ (c = 1.0, $CHCl_3$). IR: 3007, 2991, 2941, 2880, 1676, 1628, 1593, 1494, 1410, 1373, 1343, 1325, 1311, 1296, 1281, 1236, 1219, 1165, 1132, 1116, 1092, 1064, 1013, 992, 885, 829, 819, 782, 762, 730, 547, 536, 499, 491, 405. ^{1}H-NMR: 0.99 (s, 3 H); 1.20 (s, 3 H); 1.34–1.51 (m, 2 H); 1.85–1.98 (m, 3 H); 2.14–2.18 (m, 2 H); 3.47, 3.54 (AB, J = 13.8, 2 H); 3.99 (t, J = 6.8, 1 H); 7.14 (d, J = 15.5, 1 H); 7.10–7.37 (m, 2 H); 7.49–7.54 (m, 2 H); 7.73 (d, J = 15.5, 1 H). ESI-MS: 402.1 ($[M + Na]^+$). HR-ESI-MS: 402.0907 ($C_{19}H_{22}ClNNaO_3S^+$; calc. 402.0924).

*(−)-(2*R*)-*N*-(4-Bromocinnamoyl)bornane-10,2-sultam* (= *(−)-(2*E*)-3-(4-Bromophenyl)-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]prop-2-en-1-one*; **2h**): Yield 76%. M.p. 208–210°. $[\alpha]_D^{20} = -79.8$ (c = 1.0, $CHCl_3$). IR: 3006, 2989, 2939, 2879, 1676, 1628, 1587, 1565, 1490, 1459, 1417, 1405, 1392, 1374, 1343, 1325, 1296, 1275, 1236, 1219, 1165, 1132, 1115, 1064, 1039, 1009, 991, 884, 826, 817, 781, 760, 727, 546, 535, 497, 445. ^{1}H-NMR: 0.99 (s, 3 H); 1.20 (s, 3 H); 1.38–1.51 (m, 2 H); 1.92–1.98 (m, 3 H); 2.14–2.18 (m, 2 H); 3.47, 3.57 (AB, J = 13.7, 2 H); 3.99 (t, J = 5.8, 1 H); 7.15 (d, J = 15.4, 1 H); 7.11–7.50 (m, 4 H); 7.71 (d, J = 15.4). ESI-MS: 446.0 ($[M + Na]^+$). HR-ESI-MS: 446.0412 ($C_{19}H_{19}BrN_4NaO_3S^+$; calc. 446.0424).

*(−)-(2*R*)-*N*-[4-(Trifluoromethoxy)cinnamoyl]bornane-10,2-sultam* (= *(−)-(2*E*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]-3-[4-(trifluoromethoxy)phenyl]prop-2-en-1-one*; **2i**): Yield 91%. M.p. 120–125°. $[\alpha]_D^{20} = -81.3$ (c = 1.0, $CHCl_3$). IR: 3000, 2963, 2883, 1682, 1634, 1508, 1457, 1418, 1408, 1374, 1337, 1288, 1272, 1259, 1214, 1147, 1135, 1112, 1069, 995, 982, 880, 833, 796, 776, 757, 546, 536, 498. ^{1}H-NMR: 0.99 (s, 3 H); 1.20 (s, 3 H); 1.39–1.51 (m, 2 H); 1.91–1.96 (m, 3 H); 2.14–2.19 (m, 2 H); 3.48, 3.57 (AB, J = 13.8, 2 H); 4.00 (t, J = 5.6, 1 H); 7.14 (d, J = 15.5, 1 H); 7.10–7.27 (m, 2 H); 7.58–7.64 (m, 2 H); 7.75 (d, J = 15.5, 1 H). ESI-MS: 452.1 ($[M + Na]^+$). HR-ESI-MS: 452.1119 ($C_{20}H_{22}F_3NNaO_4S^+$; calc. 452.1139).

*(−)-(2*R*)-*N*-[4-(Trifluoromethyl)cinnamoyl]bornane-10,2-sultam* (= *(−)-(2*E*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]-3-[4-(trifluoromethyl)phenyl]prop-2-en-1-one*; **2j**): Yield 75%. M.p. 164–168°. $[\alpha]_D^{20} = -76.5$ (c = 0.26, $CHCl_3$). IR: 2992, 2966, 2939, 2904, 1683, 1632, 1418, 1335, 1321, 1285, 1233, 1214, 1169, 1127, 1113, 1070, 1060, 1045, 1015, 987, 883, 833, 769, 545, 486, 457. ^{1}H-NMR: 1.00 (s, 3 H); 1.21 (s, 3 H); 1.34–1.60 (m, 2 H); 1.93–2.05 (m, 3 H); 2.15–2.19 (m, 2 H); 3.48, 3.58 (AB, J = 13.9, 2 H); 4.00 (t, J = 7, 1 H); 7.23 (d, J = 15.4, 1 H); 7.28–7.71 (m, 4 H); 7.78 (d, J = 15.4, 1 H). ESI-MS: 436.1 ($[M + Na]^+$). HR-ESI-MS: 436.1170 ($C_{20}H_{22}F_3NNaO_3S^+$; calc. 436.1129).

3. *EtMgBr Addition to* **2**: *General Procedure B.* A soln. of substrate **2a**–**2m** (1 mmol) in anh. THF (5 ml) under Ar was cooled to −78°. Then alkylmagnesium halide (1M or 2M soln. in THF, 2.2 equiv.) was

added dropwise along the cold wall of a long reaction flask[37]). The wall of the flask was then rinsed by dropwise addition of THF (0.5 ml). The mixture was stirred at $-78°$ for 4h and then quenched with aq. sat. NH_4Cl soln. The aq. phase was extracted with Et_2O (2×10 ml) and the combined org. layer washed with brine (10 ml), dried ($MgSO_4$), and concentrated. Both the conversion and d.e. [%] were measured by ^{1}H-NMR integration. Pure material **3** was obtained after purification by CC (SiO_2, hexane/AcOEt 9:1).

*(2*R*)*-N-*{(3*R*)-3-[4-(Benzyloxy)phenyl]pentanoyl}bornane-10,2-sultam* (=*(3*R*)-3-[4-(Benzyloxy)-phenyl]-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]pentan-1-one*; **3a**): IR: 3088, 3065, 3030, 3006, 2960, 2947, 2926, 2886, 2869, 2081, 1986, 1966, 1923, 1886, 1822, 1681, 1608, 1583, 1512, 1498, 1486, 1456, 1415, 1378, 1357, 1332, 1310, 1271, 1255, 1234, 1208, 1180, 1164, 1132, 1114, 1083, 1065, 1041, 1026, 990, 962, 945, 911, 878, 865, 848, 834, 817, 796, 775, 743, 698, 649, 639, 625, 602, 564, 549, 532, 496, 466, 447, 420. ^{1}H-NMR: 0.81 (*t*, *J* = 7, 3 H); 0.96 (*s*, 3 H); 1.15 (*s*, 3 H); 1.28–1.33 (*m*, 2 H); 1.56–1.61 (*m*, 3 H); 1.82–1.88 (*m*, 3 H); 2.01–2.03 (*m*, 2 H); 3.00–3.10 (*m*, 2 H); 3.39, 3.49 (*AB*, *J* = 13.8, 2 H); 3.80 (*t*, *J* = 6.2, 1 H); 5.02 (*s*, 2 H); 6.85–6.95 (*m*, 2 H); 7.10–7.14 (*m*, 2 H); 7.35–7.45 (*m*, 5 H). ^{13}C-NMR: 12.1 (*q*); 20.1 (*q*); 21.1 (*q*); 26.6 (*t*); 29.6 (*t*); 33.0 (*t*); 38.7 (*t*); 42.4 (*t*); 42.7 (*d*); 44.8 (*d*); 47.9 (*s*); 48.5 (*s*); 53.2 (*t*); 65.4 (*d*); 70.2 (*t*); 114.8 (2*d*); 127.7 (2*d*); 128.1 (*d*); 128.7 (2*d*); 128.8 (2*d*); 136.3 (*s*); 137.4 (*s*); 157.5 (*s*); 170.9 (*s*). ESI-MS: 504.2 ([*M* + Na]$^+$). HR-ESI-MS: 504.2185 ($C_{28}H_{35}NNaO_4S^+$; calc. 504.2189).

*(2*R*)*-N-*{(3*R*)-3-[4-(Methylthio)phenyl]pentanoyl}bornane-10,2-sultam* (=*(3*R*)-3-[4-(Methylthio)-phenyl]-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]pentan-1-one*; **3e**): IR: 3075, 3023, 2962, 2922, 2885, 1898, 1692, 1598, 1494, 1458, 1444, 1426, 1409, 1388, 1377, 1327, 1287, 1267, 1251, 1242, 1213, 1164, 1133, 1111, 1099, 1085, 1068, 1040, 989, 954, 926, 907, 878, 828, 806, 781, 762, 751, 723, 675, 609, 566, 552, 537, 494, 438. ^{1}H-NMR: 0.79 (*t*, *J* = 7, 3 H); 0.95 (*s*, 3 H); 1.15 (*s*, 3 H); 1.30–1.34 (*m*, 3 H); 1.62–1.68 (*m*, 2 H); 1.83–1.89 (*m*, 3 H); 2.15–2.19 (*m*, 2 H); 2.44 (*s*, 3 H); 3.05–3.11 (*m*, 2 H); 3.39, 3.49 (*AB*, *J* = 13.8, 2 H); 3.79 (*t*, *J* = 6.4, 1 H); 7.12–7.20 (*m*, 4 H). ^{13}C-NMR: 12.1 (*q*); 15.3 (*q*); 20.1 (*q*); 21.0 (*q*); 26.6 (*t*); 29.4 (*t*); 32.9 (*t*); 38.6 (*t*); 41.9 (*t*); 42.9 (*d*); 44.8 (*d*); 47.9 (*s*); 48.5 (*s*); 53.1 (*t*); 65.3 (*d*); 127.0 (2*d*); 128.4 (*d*); 128.6 (*d*); 136.0 (*s*); 141.0 (*s*); 170.6 (*s*). ESI-MS: 444.2 ([*M* + Na]$^+$). HR-ESI-MS: 444.1643 ($C_{22}H_{31}NNaO_3S_2^+$; calc. 444.1608).

*(2*R*)*-N-*[(3*R*)-3-(4-Bromophenyl)pentanoyl]bornane-10,2-sultam* (=*(3*R*)-3-(4-Bromophenyl)-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]pentan-1-one*; **3h**): IR: 3005, 2992, 2973, 2930, 2887, 1908, 1689, 1589, 1485, 1459, 1412, 1406, 1384, 1328, 1287, 1253, 1242, 1211, 1180, 1165, 1134, 1120, 1108, 1072, 1041, 1008, 990, 927, 909, 878, 832, 820, 807, 781, 759, 727, 716, 675, 613, 603, 566, 549, 535, 498, 452, 425. ^{1}H-NMR: 0.79 (*t*, *J* = 7, 3 H); 0.96 (*s*, 3 H); 1.15 (*s*, 3 H); 1.30–1.34 (*m*, 2 H); 1.57–1.70 (*m*, 3 H); 1.84–1.89 (*m*, 3 H); 2.01 (*d*, *J* = 6.4, 2 H); 2.99–3.13 (*m*, 2 H); 3.40 3.50 (*AB*, *J* = 13.9, 2 H); 3.79 (*t*, *J* = 6.2, 1 H); 7.07–7.41 (*m*, 4 H). ^{13}C-NMR: 12.0 (*q*); 20.1 (*q*); 21.0 (*q*); 26.6 (*t*); 29.4 (*t*); 33.0 (*t*); 38.6 (*t*); 41.9 (*t*); 42.8 (*d*); 44.8 (*d*); 47.9 (*s*); 48.5 (*s*); 53.2 (*t*); 65.4 (*d*); 120.2 (*s*); 129.7 (2*d*); 131.6 (2*d*); 143.0 (*s*); 170.5 (*s*). ESI-MS: 478.1 ([*M* + Na]$^+$). HR-ESI-MS: 476.0871 ($C_{21}H_{28}BrN_4NaO_3S^+$; calc. 476.0851).

*(2*R*)*-N-*{(3*R*)-3-[4-Trifluoromethoxy)phenyl]pentanoyl}bornane-10,2-sultam* (=*(3*R*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]-3-[4-(trifluoromethoxy)phenyl]pentan-1-one*; **3i**): IR: 3047, 3016, 3000, 2966, 2936, 2879, 2463, 1897, 1692, 1610, 1595, 1511, 1481, 1418, 1392, 1331, 1299, 1285, 1259, 1223, 1212, 1164, 1133, 1109, 1069, 1039, 1017, 988, 944, 928, 878, 839, 821, 808, 781, 754, 720, 694, 665, 611, 594, 555, 538, 509, 490, 452, 423. ^{1}H-NMR: 0.78 (*t*, *J* = 7.6, 3 H); 0.96 (*s*, 3 H); 1.15 (*s*, 3 H); 1.30–1.36 (*m*, 2 H); 1.61–1.67 (*m*, 3 H); 1.82–1.90 (*m*, 3 H); 2.01 (*d*, *J* = 6.2, 2 H); 3.01–3.07 (*m*, 2 H); 3.40, 3.51 (*AB*, *J* = 14, 2 H); 3.80 (*t*, *J* = 6.4, 1 H); 7.09–7.15 (*m*, 2 H); 7.21–7.27 (*m*, 2 H). ^{13}C-NMR: 12.0 (*q*); 20.0 (*q*); 21.0 (*q*); 26.6 (*t*); 29.5 (*t*); 33.0 (*t*); 38.6 (*t*); 41.9

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[37]) In view of both the high reactivity of *N*-alkenoylbornane-10,2-sultam derivatives, and their high conformational dependence on temperature, this experimental detail is primordial for the good reproducibility of the results, as earlier already emphasized in the experimental part of [77]. Thus, for example, differences of up to 29% d.e. were reported by the Chinese authors between both enantiomers of bornane-10,2-sultam derivatives **2**, after 1,4-addition of alkyl *Grignard* reagents [20b]!

(*t*); 42.7 (*d*); 44.8 (*d*); 47.9 (*s*); 48.5 (*s*); 53.1 (*t*); 65.4 (*d*); 119.0 (*s*); 121.0 (2*d*); 129.2 (2*d*); 142.7 (*s*); 147.8 (*s*); 170.5 (*s*). ESI-MS: 482.2 ([*M* + Na]$^+$). HR-ESI-MS: 482.1589 ($C_{22}H_{28}F_3NNaO_4S^+$; calc. 482.1577).

*(2*R*)-*N*-{(3*R*)-3-[4-(Trifluoromethyl)phenyl]pentanoyl}bornane-10,2-sultam* (=*(3*R*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]-3-[4-(trifluoromethyl)phenyl]pentan-1-one*; **3j**): IR: 3018, 3005, 2971, 2938, 2904, 1924, 1692, 1617, 1585, 1482, 1418, 1392, 1324, 1287, 1267, 1243, 1213, 1166, 1124, 1111, 1068, 1041, 1015, 989, 954, 879, 845, 821, 807, 781, 755, 715, 665, 613, 604, 550, 536, 506, 490, 454. ^{1}H-NMR: 0.72 (*t*, *J* = 7, 3 H); 0.90 (*s*, 3 H); 1.09 (*s*, 3 H); 1.23 – 1.30 (*m*, 2 H); 1.57 – 1.64 (*m*, 2 H); 1.78 – 1.85 (*m*, 3 H); 1.97 (*d*, *J* = 6.4, 2 H); 3.02, 3.39 (*AB*, *J* = 13.9, 2 H); 3.05 – 3.34 (*m*, 2 H); 3.73 (*t*, *J* = 5.6, 1 H); 7.23 – 7.30 (*m*, 2 H); 7.43 – 7.50 (*m*, 2 H). ^{13}C-NMR: 12.0 (*q*); 20.0 (*q*); 21.0 (*q*); 26.6 (*t*); 29.4 (*t*); 32.9 (*t*); 38.6 (*t*); 41.6 (*t*); 43.1 (*d*); 44.8 (*d*); 47.9 (*s*); 48.5 (*s*); 53.1 (*t*); 65.4 (*d*); 124.4 (*q*, *J* = 1500); 125.4 (*d*); 125.5 (*d*); 128.1 (*d*); 128.2 (*d*); 129.0 (*s*); 148.2 (*s*); 170.2 (*s*). ESI-MS: 466.2 ([*M* + Na]$^+$). HR-ESI-MS: 466.1640 ($C_{22}H_{28}F_3NNaO_3S^+$; calc. 466.1653).

*(2*R*)-*N*-[(3*R*)-3-(4-Cyanophenyl)pentanoyl]bornane-10,2-sultam* (=*4-{(1*R*)-1-Ethyl-3-oxo-3-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]propyl}benzonitrile*; **3k**): IR: 3003, 2967, 2935, 2888, 2875, 2227, 1920, 1687, 1607, 1504, 1481, 1460, 1417, 1384, 1328, 1285, 1268, 1244, 1227, 1213, 1166, 1136, 1113, 1087, 1071, 1042, 991, 954, 928, 909, 879, 837, 808, 782, 755, 732, 683, 642, 611, 571, 540, 495, 437. ^{1}H-NMR: 0.79 (*t*, *J* = 7.6, 3 H); 0.96 (*s*, 3 H); 1.17 (*s*, 3 H); 1.39 – 1.45 (*m*, 2 H); 1.72 – 1.85 (*m*, 3 H); 1.97 – 2.04 (*m*, 3 H); 2.13 (*d*, *J* = 6.4, 2 H); 3.18 – 3.32 (*m*, 2 H); 3.39, 3.49 (*AB*, *J* = 13.9, 2 H); 3.90 (*t*, *J* = 6.2, 1 H); 7.40 – 7.47 (*m*, 2 H); 7.67 – 7.73 (*m*, 2 H). ^{13}C-NMR: 12.0 (*q*); 20.0 (*q*); 21.0 (*q*); 26.6 (*t*); 29.3 (*t*); 33.0 (*t*); 38.6 (*t*); 41.4 (*t*); 43.4 (*d*); 44.8 (*d*); 47.9 (*s*); 48.6 (*s*); 53.1 (*t*); 65.4 (*d*); 110.4 (*s*); 119.3 (*s*); 128.8 (2*d*); 132.4 (2*d*); 149.8 (*s*); 170.1 (*s*). ESI-MS: 423.2 ([*M* + Na]$^+$). HR-ESI-MS: 423.1685 ($C_{22}H_{31}NNaO_3S_2^+$; calc. 423.1598).

*(2*R*)-*N*-{(3*R*)-3-[4-Methylthio)phenyl]pentanoyl}bornane-10,2-sultam* (=*(3*R*)-3-[4-(Methylthio)-phenyl]-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]pentan-1-one*; **3l**): IR: 2961, 2926, 2878, 2855, 1923, 1695, 1637, 1598, 1575, 1459, 1414, 1384, 1328, 1313, 1250, 1214, 1150, 1134, 1113, 1089, 1064, 1039, 989, 955, 909, 876, 836, 807, 778, 724, 686, 649, 617, 565, 536, 511, 496, 456, 419. ^{1}H-NMR: 0.79 (*t*, *J* = 7, 3 H); 0.97 (*s*, 3 H); 1.15 (*s*, 3 H); 1.26 – 1.43 (*m*, 2 H); 1.61 – 1.78 (*m*, 3 H); 1.86 – 1.93 (*m*, 3 H); 2.01 (*d*, *J* = 6.5, 2 H); 3.05 (*s*, 3 H); 3.12 – 3.50 (*m*, 2 H); 3.40, 3.51 (*AB*, *J* = 14, 2 H); 3.78 (*t*, *J* = 6, 1 H); 7.42 (*d*, *J* = 8.4, 2 H); 7.86 (*d*, *J* = 8.4, 2 H). ^{13}C-NMR: 12.0 (*q*); 20.0 (*q*); 21.1 (*q*); 26.6 (*t*); 29.3 (*t*); 33.0 (*t*); 38.6 (*t*); 41.5 (*t*); 43.2 (*d*); 44.8 (*d*); 45.0 (*q*); 47.6 (*s*); 48.6 (*s*); 53.2 (*t*); 65.4 (*d*); 121.0 (2*d*); 127.7 (*d*); 128.9 (*d*); 138.3 (*s*); 152.2 (*s*); 170.1 (*s*). ESI-MS: 444.2 ([*M* + Na]$^+$). HR-ESI-MS: 444.1608 ($C_{22}H_{31}NNaO_3S_2^+$; calc. 444.1643).

*(2*R*)-*N*-[(3*R*)-3-(4-Nitrophenyl)pentanoyl]bornane-10,2-sultam* (=*(3*R*)-3-(4-Nitrophenyl)-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]pentan-1-one*; **3m**): IR: 3079, 2960, 2881, 2850, 1676, 1626, 1597, 1520, 1482, 1458, 1413, 1393, 1374, 1341, 1288, 1265, 1235, 1215, 1176, 1165, 1134, 1113, 1083, 1065, 1038, 982, 940, 910, 882, 856, 838, 754, 712, 615, 547, 536, 500, 451. ^{1}H-NMR: 0.88 (*t*, *J* = 7.5, 3 H); 0.97 (*s*, 3 H); 1.15 (*s*, 3 H); 1.26 – 1.43 (*m*, 2 H); 1.82 – 1.92 (*m*, 6 H); 2.05 – 2.20 (*m*, 2 H); 2.70 – 3.25 (*m*, 2 H); 3.39 – 3.59 (*m*, 2 H); 3.84 (*t*, *J* = 6, 1 H); 7.24 – 8.15 (*m*, 4 H). ^{13}C-NMR: 12.2 (*q*); 20.1 (*q*); 21.0 (*q*); 26.6 (*t*); 29.3 (*t*); 33.0 (*t*); 38.6 (*t*); 41.4 (*t*); 43.2 (d); 44.8 (*d*); 47.8 (*s*); 48.6 (*s*); 53.2 (*t*); 65.4 (*d*); 123.7 (2*d*); 130.4 (2*d*); 145.8 (*s*); 146.3 (s); 170.1 (*s*). ESI-MS: 443.2 ([*M* + Na]$^+$). HR-ESI-MS: 443.1624 ($C_{21}H_{28}N_2NaO_5S^+$; calc. 443.1617).

4. *(3*R*)-3-(4-Methoxyphenyl)-4-nitro-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]butan-1-one* (**9b**). A soln. of **2b** (375 mg, 1.00 mmol), DBU (914 mg, 6.0 mmol), and $MeNO_2$ (366 mg, 6.0 mmol) in THF (17 ml) and DMPU (3.45 ml) was stirred under N_2 for 24 h at 20°. The mixture was then diluted with Et_2O and extracted with H_2O. The org. phase was dried ($MgSO_4$) and concentrated and the residue purified by CC (SiO_2, cyclohexane/AcOEt 95 : 5 → 8 : 2): **9b** (65%); 59% d.e. IR: 2959, 1691, 1551, 1514, 1457, 1413, 1376, 1327, 1249, 1213, 1178, 1165, 1133, 1113, 1064, 1034, 989, 909, 830, 761, 728. ^{1}H-NMR: 0.95 (*s*, 3 H); 1.11 (*s*, 3 H); 1.26 – 1.42 (*m*, 3 H); 1.70 – 1.90 (*m*, 3 H); 2.02 (br. *d*, *J* = 6.6, 1 H); 3.15 (*dd*, *J* = 4.2, 7.6, 2 H); 3.46 (*dd*, *J* = 13.8, 19.8, 2 H); 3.76 (*t*, *J* = 7.5, 1 H); 3.76 (*s*, 3 H); 4.07 (*quint.*, *J* = 7.4, 1 H); 4.64 (*dq*, *J* = 5.2, 12.4, 2 H); 6.83 (*d*, *J* = 8.6, 2 H); 7.17 (*d*, *J* = 8.6, 2 H). ^{13}C-NMR: 20.0 (*q*); 20.6 (*q*); 26.6 (*t*); 32.9 (*t*); 38.5 (*t*); 38.8 (*t*); 39.0 (*d*); 44.8 (*d*);

47.9 (*s*); 48.7 (*s*); 53.0 (*t*); 55.4 (*q*); 65.4 (*d*); 79.9 (*t*); 114.5 (2*d*); 128.8 (2*d*); 130.4 (*s*); 159.3 (*s*); 168.9 (*s*). HR-ESI-MS: 437.1717 ($[M+H]^+$, $C_{21}H_{29}N_2O_6S^+$; calc. 437.1741).

*(3*R*)-4-Nitro-3-phenyl-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]butan-1-one* (**9d**). As described for **9b**, with **2d** (100 mg, 0.29 mmol), DBU (265 mg, 1.74 mmol), $MeNO_2$ (106 mg, 1.74 mmol), THF (5 ml), and DMPU (1 ml): **9d** (58%); 52% d.e. IR: 2975, 2925, 2851, 1689, 1551, 1455, 1376, 1326, 1279, 1237, 1215, 1164, 1133, 1066, 1039, 989, 867, 765, 699. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.12 (*s*, 3 H); 1.25–1.41 (*m*, 3 H); 1.97–1.99 (*m*, 3 H); 3.03 (br. *d*, *J* = 6.8, 1 H); 3.20 (*dd*, *J* = 4.2, 7.2, 2 H); 3.45 (*q*, *J* = 6.8, 2 H); 3.80 (*t*, *J* = 6.2, 1 H); 4.13 (*quint.*, *J* = 7.5, 1 H); 4.67 (*dq*, *J* = 3.4, 7.5, 2 H); 7.2–7.4 (*m*, 5 H). ^{13}C-NMR: 20.0 (*q*); 21.0 (*q*); 26.6 (*t*); 33.0 (*t*); 38.5 (*t*); 38.6 (*t*); 39.7 (*d*); 44.8 (*d*); 48.0 (*s*); 48.7 (*s*); 53.1 (*t*); 65.4 (*d*); 79.7 (*t*); 127.7 (2*d*); 128.1 (*d*); 129.2 (2*d*); 138.5 (*s*); 168.8 (*s*). HR-ESI-MS: 407.1661 ($[M+H]^+$, $C_{20}H_{27}N_2O_5S^+$; calc. 407.1635).

*(3*R*)-3-(4-Chlorophenyl)-4-nitro-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]butan-1-one* (**9g**). As described for **9b**, with **2g**: **9g** (48%); 51% d.e. IR: 2961, 2886, 1693, 1553, 1494, 1414, 1377, 1328, 1278, 1238, 1215, 1165, 1135, 1119, 1094, 1063, 1040, 1014, 990, 830, 775, 736, 537. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.11 (*s*, 3 H); 1.24–1.45 (*m*, 3 H); 1.8–2.04 (*m*, 3 H); 2.04 (br. *s*, 1 H); 3.17 (*dd*, *J* = 4.2, 7.4, 2 H); 3.45 (*dd*, *J* = 13.8, 20.2, 2 H); 3.79 (*t*, *J* = 6.2, 1 H); 4.04–4.19 (*m*, 1 H); 4.69 (*dq*, *J* = 7, 7.8, 2 H); 7.20–7.34 (*m*, 4 H). ^{13}C-NMR: 20.0 (*q*); 21.0 (*q*); 26.6 (*t*); 32.9 (*t*); 38.4 (2*t*); 39.1 (*d*); 44.8 (*d*); 48.0 (*s*); 48.8 (*s*); 53.0 (*t*); 65.4 (*d*); 79.4 (*t*); 129.2 (2*d*); 129.4 (2*d*); 134.0 (*s*); 137.0 (*s*); 168.5 (*s*). HR-ESI-MS: 463.1069 ($C_{20}H_{25}ClN_2NaO_5S^+$; calc. 463.1070).

*(3*R*)-4-Nitro-3-(4-nitrophenyl)-1-[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]butan-1-one* (**9m**). As described for **9b**, with **2m** (390 mg, 1.00 mmol), DBU (914 mg, 6.0 mmol), $MeNO_2$ (366 mg, 6.0 mmol), THF (17 ml), and DMPU (3.45 ml): **9m** (18%); 24% d.e. IR: 2959, 1674, 1622, 1595, 1518, 1342, 1325, 1279, 1233, 1209, 1164, 1132, 1113, 1069, 1046, 1040, 998, 849, 770, 753, 693, 613. ^{1}H-NMR: 0.95 (*s*, 3 H); 1.09 (*s*, 3 H); 1.29–2.0 (*m*, 7 H); 3.09–3.15 (*m*, 2 H); 3.30–3.36 (*m*, 1 H); 3.46 (*q*, *J* = 7, 2 H); 3.75 (*t*, *J* = 7, 1 H); 5.01 (*dq*, *J* = 4, 12.4, 2 H); 7.50 (*d*, *J* = 4, 2 H); 8.16 (*d*, *J* = 4, 2 H). ^{13}C-NMR: 19.8 (*q*); 20.6 (*q*); 26.3 (*t*); 29.7 (*t*); 32.7 (*t*); 38.3 (*t*); 41.8 (*d*); 44.5 (*d*); 47.7 (*s*); 48.4 (*s*); 52.9 (*t*); 65.2 (*d*); 83.2 (*t*); 123.8 (2*d*); 127.0 (2*d*); 146.9 (*s*); 149.6 (*s*); 168.0 (*s*). HR-ESI-MS: 436.5042 ($[M+H]^+$, $C_{20}H_{26}N_3O_6S^+$; calc. 436.5019).

5. *(2*R*)-N-(Benzoxazol-2-ylcarbonyl)bornane-10,2-sultam* (= *Benzoxazol-2-yl[(3a*S*,6*R*,7a*R*)-tetrahydro-8,8-dimethyl-2,2-dioxido-3*H*-3a,6-methano-2,1-benzisothiazol-1(4*H*)-yl]methanone*; **10**). Obtained in 79% yield according to *Procedure A*. M.p. 163–166°. $[\alpha]_D^{20} = -113.8$ (*c* = 0.69, $CHCl_3$). IR: 3097, 2993, 2958, 2939, 2881, 2850, 1936, 1819, 1680, 1606, 1560, 1478, 1453, 1407, 1391, 1374, 1352, 1328, 1317, 1261, 1251, 1237, 1220, 1197, 1167, 1141, 1120, 1107, 1085, 1062, 1038, 1027, 1004, 975, 938, 917, 908, 892, 859, 829, 806, 783, 755, 695, 665, 634, 617, 578, 568, 543, 531, 509, 490, 452, 445, 430. ^{1}H-NMR: 1.03 (*s*, 3 H); 1.31 (*s*, 3 H); 1.50 (*t*, *J* = 7, 2 H); 1.90–2.15 (*m*, 5 H); 3.57 (*q*, *J* = 13.6, 2 H); 4.44 (*dd*, *J* = 7, 5, 1 H); 7.18–7.27 (*m*, 1 H); 7.41–7.56 (*m*, 1 H); 7.68 (*d*, *J* = 7, 1 H); 7.95 (*d*, *J* = 7, 1 H). ^{13}C-NMR: 20.2 (*q*); 22.0 (*q*); 26.4 (*t*); 33.7 (*t*); 39.5 (*t*); 45.7 (*d*); 48.1 (*s*); 49.2 (*s*); 53.7 (*t*); 66.8 (*d*); 111.9 (*d*); 122.5 (*d*); 125.9 (*d*); 128.3 (*d*); 129.2 (*s*); 140.4 (*s*); 150.7 (*s*); 156.7 (*s*). ESI-MS: 383.1 ($[M+Na]^+$). HR-ESI-MS: 383.0995 ($C_{18}H_{20}N_2NaO_4S^+$; calc. 383.1041).

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Received May 10, 2011