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Grignard 1,4-Additions to *para*-Substituted (2*R*)-*N*-Cinnamoylbornane-10,2-sultam Derivatives: Revised Configuration for the N,OAc-Keteneacetal Formation in the Presence of Cu^{I}

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Dedicated to the memory of *Joseph Challande* (1906-1965)[2]).

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[2]) Active member of the French resistance (cie FTPF 93.03), arrested after denunciation on 9th Dec. 1943 in Ambilly by the Feldgendarmes of the 9th Kp, he was interrogated at the Hôtel Pax (#303), seat of the GeStaPo in Annemasse. In absence of a confession, he was transferred to Fort de Montluc in Lyon (20th Dec.), then to Compiègne, from where he was deported on 22nd Jan. 1944 by railway convoy I.172 to Buchenwald. Assigned to the Kdo Weimar, in Block 17/56, with the official number 43062 (24th Jan.), he was liberated by the 3rd US army forces on 11th Apr. 1945 [1]. After a convalescence period in a Red Cross camp, he was repatriated *via* the hotel *Lutetia* in Paris, before he finally met again with his wife and elder daughter, the late grandmother and mother of *C. C.*, respectively.

By using an ^{19}F-NMR analytical method, we have corrected and improved the linear correlation initially found between the diastereoselectivity observed during the EtMgBr conjugated addition to *Michael* acceptors of type **1**, as a function of their σ_{para} *Hammett* electronic parameters. Based on ^{1}H-NMR analyses, we have also discovered that the original configuration of the acetylated intermediate, obtained by either hydride, *Grignard*, or cuprate conjugate additions to α-substituted *N*-enoyl bornane-10,2-sultams was, from the initial report, erroneously attributed by *Oppolzer et al*. A new, much simpler rationalization for these 1,4-additions is proposed.

Keywords: Grignard 1,4-addition, Conjugated, *Michael* additions, Cinnamoyl, Sultam.

Introduction. - Four years ago, we presented a series of alkyl 1,4-additions to electronically modified *para*-substituted (2*R*)-*N*-cinnamoylbornane-10,2-sultam derivatives **1** [2][3]). At that time, we found a clear predictable electronic influence, as

[3]) For reviews on the general use of (2*R*)-bornane-10,2-sultam as chiral auxiliary, see [3]. In the last review, the authors suggest that, from both possible stereoisomers obtainable by reduction of the camphor sulfonimine, the *exo* is exclusively isolated, as a result of the steric shielding of the Me(8) substituent

expressed by a linear correlation between the level of asymmetric induction and the *Hammett* σ_{para} parameter (log (d.r.) = $-0.459\sigma_{para} + 0.834$, $n = 13$, $R^2 = 0.83$, s.d. = 0.083) using EtMgBr in THF at -78°. Both the reactivity and selectivity were decreasing for electron demanding *para*-substituents on the cinnamoyl moiety of the *Michael* acceptors. We were intrigued by the fact that the two largest deviations, were both obtained for F containing substrates, namely *p*-F-**2a** (78% de measured, calculated 71% de) and *p*-CF_3O-**2b** (73% de measured, calculated 65% de). We wondered whether this situation originated from either the regular standard experimental error, or an eventual analytical problem, or if any electronic factors resulting from this specific F atom could be responsible for these deviations, and thus decided to study in more detail this class of *Michael* acceptors.

Results. - We concentrated our attention on both anomalous results considered in the introduction, in addition to their *p*-CF_3 analog **2c** (62% de measured, calculated 59% de) [2]. The initial analytical method was based on the integration of the Me(8)

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exerted on the approach of the reducing agent [3e]. In fact, the *endo*-stereoisomer would possess two *trans*-fused five member rings, which is geometrically and thermodynamically impossible, except for some very specific strained situations [4]. For bicyclo[2.2.1]heptane derived sultam analogs devoid of Me(8), and consequently of disguised C_2 symmetry, see [5]. For selected reviews on asymmetric 1,4-additions, see [3f][3g].

singlet in the ^{1}H-NMR analysis of the crude reaction products, as earlier reported in a similar case [6]. Although the sensitivity and precision (+/- 2%), hence experimental error, of the high field NMR method is not fundamentally modified, we now opted for a simple and direct ^{19}F-NMR analysis, as earlier reported for this kind of substrates [7][8]. Indeed, with $CFCl_3$ as reference, compound *p*-F-**2a** exhibits two distinct diastereotopic signals at -117.39 (major) and -117.50 ppm (minor), while the *p*-CF_3O-**2b** and *p*-CF_3-**2c** analogs exhibit displacements at -58.18/-58.23, and -62.68/-62.73 ppm, respectively. The signals of the major (3*R*)-diastereoisomers appear systematically at higher field.

Oppolzer et al. [9], as well as *Liu* and co-workers [10], earlier, judiciously noticed that a two-fold excess of *Grignard* reagent was necessary for an efficient 1,4-addition (see *Table*, *Entries 1-3*)[4]). When we repeated our initial conditions (2.2 mol.-equiv. of EtMgBr, THF, -78°, 4 h), the observed diastereoisomeric excess for **2a**-**c** slightly decreased from 78 to 74%, and from 73 to 68% for **2a**,**b** and remained practically unchanged for **2c** (from 62 to 60% de), in accord with the expected calculated behavior. When these new values were incorporated into the linear correlation, an improved equation model was found (log (d.r.) = $-0.466\sigma_{para} + 0.82$, n =

[4]) For an example where only 1.2-1.4 mol.-equiv. of EtMgBr was used, resulting in a chemical yield of 55-61%, see [11a][11b]. For ulterior ameliorated conditions using 2.5 mol.-equiv., see [11c]. The stoichiometry is not indicated in [11d].

13, $R^2 = 0.91$, s.d. = 0.059). It is noteworthy that the usual picture in the 500 MHz ^{1}H-NMR shows two major *singlet*s for the gem-dimethyl groups, accompanied by two minor signals for the minor (*S*)-diastereoisomer [2]. Based on the thirteen examples earlier studied, it appears that the worse separation between the major Me(8) and the minor Me(9) of the (*S*)-diastereoisomer is observed for **2a** and **2b**, thus slightly corrupting the measured ratio between major and minor Me(8) signals by integration, although we still remain within the deviation of the standard error (*ca.* 4% on de) with respect to the initial results. This point being settled and corrected, we also studied these *Michael* additions under different conditions as summarized in the *Table*, more specifically either in different solvents, or in the presence of both a *Lewis* acid and a single equivalent of EtMgX, in analogy to the *Schlenk* equilibrium [2][12][13]. The diastereoselectivity is slightly higher in toluene as compared to THF (*Entries 4*, *10 vs. 6*, *12*), while the reaction is eventually sluggish in CH_2Cl_2 (*Entry 10 vs. 11*), although the π-facial selectivity is not drastically influenced (*Entries 4*, *10 vs. 5*, *11*). With $TiCl_4$, the reaction was even slower and only 31% of conversion was obtained after 24h in THF (*Entry 13*). The situation was even worse with $ZnBr_2$, although the diastereoselectivity remained around *ca.* 75% de (*Entry 14*). When the temperature was increased, the conversion logically increased, albeit at the expense of the diastereoselectivity (*Entries 14-16*). Since the situation was not optimal at 20° (*Entry 17*), we finally chose to perform the reactions at 4° using an ice bath. The conversion increased by using ZnI_2,

but the π-facial selectivity dropped (*Entry 18 vs. 16*). When a non-chelating *Lewis* acid such as $BF_3 \cdot Et_2O$ was used, the diastereoselectivity increased, but now to the expense of the conversion (*Entry 19 vs. 16*), suggesting either that the SO_2/C=O *syn*-chelated conformation is important for the activation of the *Michael* acceptor, or that the chelating bimetallic complex is formed, but reacts with modest conversion, due to the low excess of *Grignard* reagent, as suggested by the sense of induction. The most encouraging results were obtained under pseudo *Schlenk* conditions by using $MgCl_2$ (*Entry 20 vs. 18*, or *16*). It is noteworthy that $MgBr_2$ was less efficient either in terms of conversion or diastereoselectivity (*Entry 23 vs. 20*). This trend was also observed for the analogous adducts **2b** (*Entry 24 vs. 21*) and **2c** (*Entry 25 vs. 22*). With $MgCl_2$, the decrease of diastereoselectivity follows the same electronic trend as earlier observed in the presence of a double amount of EtMgBr (*Entries 20*, *21*, *22 vs. 1*, *2*, *3*). MgI_2, known to catalyze the attack and opening of THF at such a temperature, was not tested, since we earlier also showed that the diastereoselectivity of these *Grignard* additions to **1d** was diminishing when EtMgCl (78% de, *Entry 6*) was changed for EtMgBr (73% de, *Entry 7*), and more spectacularly for the non-aggregating EtMgI in Et_2O (31% de, *Entry 8*). It is worthy of note that in toluene, addition of 2.2 mol.-equiv. of EtMgI/Et_2O to **1d** at -78°, failed to afford **2d** (*Entry 9*). Similar negative results were obtained by addition of 1.1 mol.-equiv. of either EtMgI, or Et_2Mg in the presence of 1.1 mol.-equiv. of MgI_2 (generated from Mg and I_2) to **1d** in toluene.

Oppolzer et al. [9][14], as well as *Huang et al.* and *Chen et al.* [15], earlier also noticed that the sense of induction could be reversed by using a cuprous salt/*Grignard* reagent complex. They invoked a s-*trans*, rather than a s-*cis* conformation of the C_α=C_β double bond to rationalize their results. Our substrates are energetically less prone to such a s-*trans* conformation, as compared to either their *N*-crotonoyl, or C_α-substituted *Michael* acceptors [2]. Due to the lower reactivity of **1a** (*Entry 26*), we again were forced to work at 4° (*Entry 27*). At this temperature the conversion was much improved and obviously, the sense of induction also depends on the halide used to generate the organo-copper reagent (*Entry 27 vs. 28* and *29*). We thus strengthened our earlier conviction that the alkyl *Grignard* 1,4-additions, with or without Cu^I, could be biased due to a possible transfer of steric chiral information from the bornane skeleton to the remote C_β position, through a conformationally rigid multi-metallic aggregate, directing its 'coordinating' ligands in thermodynamically and geometrically preferred directions, more specifically in the case of Br^- and Cl^-, in contrast to the non-aggregating softer I^- [2]. In the latter case, the free nucleophile could eventually attack, as usual, the opposite face. This could also explain the reverse selectivity observed in the presence of an excess of either LiCl [16], or Cu^I non-aggregating *Lewis* acids [17].

Discussion. – We initially decided to study the 1,4-additions because the remote reactive β-center was believed to be poorly sterically influenced by the prosthetic group, and thus we hoped to put in evidence the stereoelectronic effect of the pyramidalized N lone pair (lp) [2][5]). Indeed, in 1986 *Oppolzer* and *Poli* rationalized the hydride conjugated addition to *N*-2-methyl-pent-2-enoyl sultam **4c** by a bottom C_β-*re* face attack on the SO_2/C=O *anti* and C=O/C=C s-*cis* conformation, followed, after rotation and chelation of the resulting (*Z*)-**5b** to the pseudo equatorial S=O, by addition of the electrophile on the bottom C_α-*re* face [22], sterically directed by the masked C_2 chirophor[6]) (*Scheme* 2). Two years later, in the light of the transoid form exhibited by

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[5]) For a 1,4-vinyl cuprate additions systematically opposite to the N lp, whatever the adopted SO_2/C=O *syn* or *anti*, C=O/C=C s-*cis* disposition, see [17]. For similar 1,4-additions of alkenylzirconocene chloride, see [18]. For X-ray analyses of SO_2/C=O *syn* conformers of type **3**, see [19] and references cited therein. For thiol 1,4-conjugated additions on *N*-methacryloyl sultam **4a** with C_α-*re* protonation, see [20]. For radical conjugated additions with similar π-facial $H^\cdot$ insertion, see [21]. For specific references related to 1,4-additions using this prosthetic group, see [2].

[6]) In the *anti*-s-*cis* orientation, the C_β is slightly closer to C(2), as compared to SO_2. In fact the C_α electrophilic addition, due to the pseudo C_2 symmetry of the chirophor, may equally be performed in the *anti*-s-*cis* conformation. At that time this rotation seemed necessary since the pseudo equatorial Li-chelated S=O/C=O

this kind of α-substituted *Michael* acceptors in the crystalline state [23][7]), *Oppolzer et al*., succeeding in trapping the corresponding (*E*)-ketene N,OAc acetal, consequently modified their initial rationalization in the specific case of α-substituted *Michael* acceptors, now suggesting that they should react in a s-*trans* conformation to afford **6** [23] (*Scheme* 2). These authors did not mention the fact that (*E*)-**5b** should be protonated in a contra-steric fashion in order to respect the final configuration at the C_α center. In fact this problem was already discussed and resolved in the meantime, by proposing chelation of the intermediate (*E*)-**5b** with the bottom pseudo axial S=O

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syn s-*cis* conformer, as initial reactive conformation, would not be as selective as for the sterically C(2) influenced proximate C_α, as wisely later recognized by *Kim* and *Curran* [3d]. Indeed, in this conformation the C_β is practically equidistant to both the SO_2 and C(2) centers. For 1,4-additions, we have in the past rather privileged a stereoelectronic control of the N lp, although we could not prove it up to now, and it would only apply to the *anti*-s-*cis* conformer in the present case [2]. This reactive conformation was nevertheless correctly recognized by *Oppolzer* and *Poli* in their initial study [22].

[7]) For ulterior examples, see [24]. In the crystalline state the SO_2/C=O *anti*-conformations exhibit the following O=C-C_α=C_β transoid dihedral angles: **4b** 134° [23]; **4a** 137° [24a]; 131° [24b]; 141° [24c].

moiety, thus offering the apparently less hindered front face to the electrophile trajectory [3b][3c][9][8]).

We earlier demonstrated that the non-chelated minor SO_2/C=O *syn*-conformer may, in some instances, be more reactive than its thermodynamically more stable *anti*-conformer [7], thus following the *Acree-Curtin-Hammett* principle [28]. Furthermore, the sense of induction may strongly depend on the chelating properties of the reagent and additives, as well as on the conformationally rigidifying low temperature of the reaction[9]). The necessity, for an efficient *Grignard* addition, to use at least two equivalents of EtMgBr, suggests, as proposed by *Oppolzer et al.*, a chelated

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[8]) When a dienophile possessing a modified chiral sulfonamide auxiliary lacking the pseudo-equatorial S=O was used for a *Diels-Alder* cycloaddition, $TiCl_4$ chelation with the pseudo axial S=O resulted in total inversion of the π-facial selectivity [25]. It is noteworthy that RMgX/Cu^I and *Gilman* reagents ($R_2CuLi{\cdot}PBu_3$) both induce the same π-facial selectivities in both C_β and concomitant electrophilic C_α additions for very similar *Michael* acceptors [14][26][27]. For a stereochemical error in [6b], see footnote 4 in [2].

[9]) Although we are working with pure (*E*)-stereoisomers, *Feringa* et *al*. earlier showed that the sense of induction may depend not only on the configuration of the *Michael* acceptor, but also on the kinetics of both its conjugated addition and (*Z*) to (*E*) isomerization [13].

intermediate aggregated with a second equivalent of metallic nucleophile[10]). This chelation usually involves the pseudo-equatorial S=O substituent, as seen by an X-ray structure analysis [30]. It is noteworthy that amongst the multiple diastereoselective chemical reactions using bornane-10,2-sultam as chiral auxiliary, the conjugate additions would belong to the very rare examples necessitating involvement of the pseudo axial S=O for chelation [3c]. We already expressed our doubts for this specific chelation [2], especially in the case of α-substituted substrates, since the R_3 substituent should exhibit severe steric repulsion with both the C(3) and Me(8) backbone (*Scheme* 3), as compared to the pseudo equatorial S=O/C=O *syn*-conformation[11]).

The rationalization proposed by *Oppolzer et al.* seems sound for the simple *Grignard* additions through a chelating bi-metallic complex as presented in *Scheme* 3 [3c][9], where the O=C-C=C dihedral angle is obviously deflected from 0° by the steric influence of the C(3) sultam backbone, and the proximity of the Mg-R^2, thus offering its bottom C_β face to the *Grignard* reagent. On the other hand, we have strong doubts

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[10]) Such an aggregate was also invoked to explain the absence of 1,6-addition in case of a *N*-(2,4-dienoyl)camphorsultam [9]; furthermore, >3.0 mol.-equiv. were necessary for *bis*-chelated *N*-fumaroyl derivatives [29].

[11]) Based on B3LYP/6-31G-d,p calculations, we estimated this pseudo axial complexation to be *ca*. 5 kcal/mol higher in energy, as compared to the pseudo equatorial S=O$^{\cdots}$Li$^+$O$^-$-C=C$_\alpha$ coordination.

concerning the transition state of the corresponding cuprous catalyzed, or cuprate additions as represented in references [3b][14][26a]. Indeed, in their drawings, *Oppolzer et al.* do not specify which of the S=O bonds is involved for chelation, furthermore coordination with the pseudo axial S=O would reduce the reactivity of the chelate, since the N lp would be in the nodal plane and thus unavailable for the activating delocalization of the π-system. Additionally to the fact that the s-*trans* conformation is thermodynamically higher in energy as compared to the s-*cis* disposition for the C_{α}-unsubstituted substrates, we also think that the distance between the C_{β} position and the Mg atom is inappropriate to allow this bimetallic complex to operate as depicted in [14]. Indeed, the distance decreases by *ca*. 20% in the s-*cis* conformation and thus would minimize the steric interaction of either the Me(8), or the C(3) with the Cu^{I} π-complex, and then Cu-C_{β} σ-bond [31]. Furthermore, they omitted to take into account the fact that they used an excess of alkyl-*Grignard* (2.5 mol.-equiv.). Their rationalization perfectly accounts for the observed final configuration. However in our laboratory, for more than a decade, we use another simpler rule of thumb, which avoids this conformational complication, by considering only the *syn*-s-*cis* conformation. We rather suggest, in the light of *Feringa*'s observations and rationalization, as expressed in a catalytic context, that we could eventually have a tri-metallic complex, where one equivalent of Mg would be responsible for chelation, while the second Mg atom would complex with both

the first Mg atom and the cuprous salt in an apical mode [13]. In such an arrangement we need to explain why either the Cu···C=C π-complex, or the Cu-C$_\beta$ σ-bond, prior to alkyl transfer, occurs on the top face rather than on the usual sterically more accessible bottom face. We suggest either that the bottom Cu^I aggregation is destabilized by a steric interaction with the pseudo axial S=O moiety, or that the Cu^I top coordination is additionally stabilized by the N lp. The first proposal is very certainly geometrically more appropriate. In this case, the O=C-C=C dihedral angle is maintained close to 0° and leads to a (*Z*)-enolate (R^3 < CHR^1R^2), while under non-aggregating condition this angle is greater and the opposite enolate is obtained by nucleophilic approach on the opposite face. Our hypothesis also accounts perfectly for both the C$_\beta$ conjugated additions, as well as for the C$_\alpha$ electrophilic trapping of the intermediate enolate, whose stereochemical final outcomes were earlier reported [3a][3b][9][11][14][15][26a][32].

Although this monolithic explanation is tempting by its logic and simplicity, our rationalization was never published, because we were faced by several contradictions concerning the acetylating trapping of the transient (*E*)- and (*Z*)-enolates, as published by *Oppolzer et al.* [3b][12])[23][26a]. During the preparation of the present manuscript, hindered by the reported low chemical yield of an isolated ketene N,OAc acetal (<20%,

[12]) It is noteworthy that on page 42, Scheme 10, structure **14** should have an Et instead of a Me substituent in β-position.

based on **4a** [26a]), as well as the fact that, for instance, toluene instead of THF was used to stereoselectively generate another ketene N,OAc acetal from **4c** [23], with sometimes, as we shall see, the addition of HMPA (hexamethylphosphoric triamide) [32], we decided to have a much closer look at their experimental data. Although announced as imminent in their preliminary communications[13]), these primordial experimental results were never confirmed in a full paper, and we had to read and check several Ph. D. theses to find them, and to have access to their NMR analyses [32]. We attributed their ^{13}C-NMR signals to each C atoms of both (*E*)- and (*Z*)-ketene N,OAc acetals **7a** and **7b**, but this exercise was inconclusive since the respective displacements are very similar. To our upmost surprise, their stereochemical attributions were in contrast to our own expectations based on ^{1}H-NMR analyses of the vinyl-Me displacements[14]). We confirmed our own attributions after synthesis of **7b** (**4a**, 2.3 mol.-equiv. EtMgCl, THF, -78°, then AcCl, -78° to 20°, 90% yield). Indeed, although the NOESY was non-instructive for the vinyl-Me, a full analysis allowed to determine that the bornane C(2)-H was correlating with the CH_2-Et, thus allowing us to attribute the

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[13]) See reference 7 in [14], and reference 23 in [26a].

[14]) For ^{1}H-NMR comparison with (*E*)- and (*Z*)-O-silyl ketene N,O-acetals attributed on the basis of NOE experiments, with expected shifts, see [33]. We attributed the signals at 1.79/1.56, and 1.80/1.54 ppm to the (*E*)-/(*Z*)-**7a**, -**7b** stereomers, respectively.

(*E*) configuration to **7b** issued from this experiment (*Scheme* 4). We finally consolidated our work by preparing (*Z*)-**7a** (**4b**, L-Selectride®, THF, -78° to -42°, then AcCl, -78° to -42°, 90% yield), whose configuration was confirmed by the full NOESY analysis: correlations between the C(2)-H and the CH_3-vinyl, as well as between the OAc and both signals of the vinyl-CH_2CH_3 were evident. The analytical data and corrected stereochemical assignments, partially extracted from the original Ph. D. thesis are now presented as *addendum* in the present *Exp. Part* for the sake of completeness and comparison, corrected with our own attributions. Bedazzled by a single crystal X-ray structure analysis as origin of their stereochemical determination, supplementary NMR experiments were initially obviously either neglected, or ignored[15]). We concluded that, working in parallel in both (*E*)- and (*Z*)-series, the analytical samples were eventually inadvertently inverted at some point, either in one of the synthetic, NMR, or X-ray laboratories[16])! Alternatively, the probability that the crystallographer picked up a single crystal of the minor stereomer for his X-ray analysis is negligible, but cannot be totally excluded[17]).

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[15]) This solid piece of experimental evidence also hindered and confused our own analytical and critical mind for years!

[16]) For another example of *E*/*Z* inversion, see footnote 41 in [34].

[17]) For an example where we corrected a conformational equilibrium initially biased on the basis of a single crystal X-ray structure analysis, see [35]. We are

Conclusions. – By using an alternative ^{19}F-NMR analytical method, we cosmetically corrected and improved the linear correlation between the diastereoselectivity observed during the EtMgBr conjugated addition to *Michael* acceptors of type **1**, as a function of their σ_{para} *Hammett* electronic parameters. We also discovered that the initial configuration of the trapped intermediate enolates derived from α-substituted *N*-enoyl bornane-10,2-sultams was erroneously attributed by *Oppolzer et al.*. Consequently, the rationalizations for these kinds of substrates, as reported during the last thirty years, should be revised at the light of the following proposals referring to *Scheme* 3: In these cases the (2*R*)-*N*-enoyl-bornane-10,2-sultam reacts in a O=C-C$_\alpha$=C$_\beta$ s-*cisoid* conformation. The SO_2/C=O orientation is thermodynamically more stable in the *anti*-disposition under non chelating conditions, but may react in the *syn* conformation either under chelating control, or when the substitutions render this minor conformer more reactive, thus following the *Acree-Curtin-Hammett* principle. For *Grignard*, or non-aggregating *Grignard*/Cu^I conditions, the nucleophile attacks from the bottom face, opposite to the N lp, whatever is the small or larger O=C-C$_\alpha$=C$_\beta$ torsion angle. In case of unsubstituted C$_\alpha$, this angle, close to 0°, leads to a transient (*Z*)-enolate, while the larger angle resulting from α-substitution

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particularly indebted to both Prof. *H.-R. Hagemann* and Dr. *D. Jeannerat* (University of Geneva) for their help in the stereochemical analysis of (*E*)-**7b**.

leads to either a (*E*)-enolate (for $R^3 < CHR^1R^2$), or (*Z*)-enolate (for $R^3 > CHR^1R^2$)[18]). Consequently, the α-electrophilic addition depends on the transient enolate, and results from the classical steric control exerted by the masked C_2 symmetry of the bornane-10,2-sultam [3d]. For aggregating Cu^I/*Grignard* conditions, we suggest a trimetallic complex, were the Cu^I is connected, *via* one of its substituents, to the apical position of the non-chelated Mg atom, opposite to the pseudo axial S=O, thus adding the R^2 nucleophile on the top of the s-*cis* conformer[19]). This situation enforces the O=C-C_α=C_β

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[18]) The configuration of the resulting C_α-substituted enolate is inverted for a small nucleophile like H^-. In the *anti*-s-*cis* complex with L-Selectride®, the O=C-C=C dihedral angle is obviously closer to 0° than in the *Grignard syn*-s-*cisoid* bimetallic chelate, eventually due to the size of the nucleophile, and/or the geometry of the complex in the TS.

[19]) It is noteworthy that in the case of *Gilman* reagents a large excess is always used (2.6 to 10.0 mol.-equiv.), so that a multi-metallic square planar π-complex would also approach from the top face [36], for the reasons exposed here above, or alternatively from the bottom face in the *anti*-s-*cis* conformation for either steric or stereoelectronic reasons. For *Gilman* reagents exhibiting the same π-facial selectivity as RMgX/Cu^I, see footnote 8, for *Gilman* reagents reacting similarly to simple RMgX, see [6a][16a][16c][37]. In the case of [38] a thermodynamically more stable s-*trans* reactive conformation cannot be excluded; furthermore, similar addition to a β-*t*Am analog would help in

torsion angle to be smaller, and thus leads to either a transient (*Z*)-enolate (for $R^3 < CHR^1R^2$), or (*E*)-enolate ($R^3 > CHR^1R^2$). The consecutive C_α electrophilic attack being similarly mainly sterically directed by the bornane-10,2-sultam skeleton. The chiral auxiliary overrides the influence of the newly formed C_β-stereocenter, which only modulates the final result. As the stereoelectronic influence of the N lp remains to be clarified[20]), and in view of the multiple conformational and chelating freedoms envisaged, further theoretical $TS^{\#}$ calculations are obviously necessary to support a firm conclusion concerning our aggregated tri-metallic hypothesis[21]). In this case, copper salts, such as CuCN, CuSCN, $Cu(OTf)_{n=1,2}$, as well as the more complex *Gilman*

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understanding the influence of the terminal unsaturation on the Cu^I π-facial complex formation.

[20]) Based on electrostatic and dipolar interactions, we anticipated that the X-ray analysis of (2*R*)-*N*-2'-carbonylpyrimidine **3a** would exhibit a rare SO_2/C=O *syn* conformation, in analogy to (2*R*)-*N*-picolinoylbornane-10,2-sultam **3b** [19], but in the solid state, we rather observed an usual *anti* conformation (S-N-C=O = 153.38(13)°), very similar to (2*R*)-*N*-benzoylbornane-10,2-sultam **3c** [19]. The syntheses and structural analyses of *N*-carbonyl-2-pyrazine, -4-pyrimidine, and -3-piridazine are under investigations.

[21]) According to the model suggested by *Feringa et al*. [13], aggregation of the cuprous salt on the chelating Mg atom may also be envisaged, although we privilege our option, due to the steric influence of either the Me(8), or C(3), or pseudo axial S=O, depending on the considered chelation [14].

reagents, will also be included in this experimental study, with trapping of the intermediate ketene N,OAc acetals[22]). These results, with supplementary hydride 1,4-additions in the presence of chelating *Lewis* acids, shall be presented in due course.

Experimental Part

General, see [40]. Crystallographic data of **3a** were deposited as supplementary material with the *Cambridge Crystallographic Data Centre* and allocated the deposition number CCDC-1428062. These data can be obtained free of charge *via* www.ccdc.ac.uk/data_request/cif.

The preparation of **1a**, **1b**, **1c**, **1d**, and **1e** are described in the Exper. Part reported in [2], as well as in the literature cited therein. The conjugate additions of EtMgX, as well as analytical data of **2a**, **2b**, **2c**, **2d**, and **2e** are also described in [2].

(Pyrimidin-2-yl)[(3a*S*,6*R*,7a*R*)-(tetrahydro-8,8-dimethyl-2,2-dioxido-3a,6-methano-2,1-benzothiazol-1(3*H*,4*H*)-yl)]methanone (**3a**). A soln. of (+)-(1*R*)-bornane-10,2-sultam (190 mg, 0.89 mmol,) in dry toluene (5 ml) was slowly added to the suspension of NaH (60% in mineral oil, 38 mg, 0.97 mmol) in dry toluene (5 ml) at 0° under Ar. After 30 min at 20°, the mixture was cooled to 0° and a freshly prepared soln. of pyrimidine-2-carbonyl chloride (0.81 mmol, [41]) in toluene (5 ml) was slowly

[22]) The role of the solvent, as well as of coordinating or disaggregating additives, such as TMSCl and LiCl, shall also be explored [39].

added. The mixture was stirred overnight at 20°. H_2O (5 ml) was added and the aq. phase was extracted with CH_2Cl_2. The org. phase was dried ($MgSO_4$), filtered, and concentrated under vacuum. The residue was purified on CC (SiO_2, hexane/AcOEt 8:2) to afford **3** in 79% yield. M.p. 68 – 72° (EtOH). $[\alpha]_D^{20}$ = –137.2 (*c* = 1.0, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 200 MHz): 0.93 (*s*, 3 H); 1.21 (*s*, 3 H); 1.24 – 1.44 (*m*, 2 H); 1.73 – 2.10 (*m*, 3 H); 3.48 (*q*, *J* = 13.6, 20.4, 2 H); 4.22 – 4.26 (*m*, 1 H); 7.46 (*t*, *J* = 4.9, 1 H); 8.89 (*d*, *J* = 4.9, 2 H). ^{13}C-NMR ($CDCl_3$, 200MHz): 20.1 (*q*), 21.8 (*q*), 26.4 (*t*), 33.5 (*t*), 38.6 (*t*), 45.5 (*d*), 48.0 (*s*), 49.1 (*s*), 53.3 (*t*), 66.2 (*d*), 122.7 (*d*), 157.6 (2*d*), 159.6 (*s*), 164.3 (*s*) HR-MS: 344.1044 ($[M + Na]^+$, $C_{15}H_{19}N_3NaO_3S^+$; calc. 344.1045).

(1*Z*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-dimethyl-2,2-dioxido-3a,6-methano-2,1-benzothiazol-1(3*H*,4*H*)-yl]-2-methylbut-1-en-1-yl Acetate ((*Z*)-**7a**). L-Selectride® (1.0M/THF, 0.34 mmol, 0.34 ml) was added dropwise at -78° to a soln. of *N*-tigloyl sultam **4b** (83 mg, 0.28 mmol) in THF (5 ml). After stirring for 2 h at -42° (MeCN/CO_2), the mixture was treated with AcCl (0.105 ml, 1.47 mmol) at -78°. After 1 h at -42°, the reaction was quenched with an aq. sat. NH_4Cl soln. Workup and CC (SiO_2, cyclohexane/AcOEt 9:1) to afforded pure (*Z*)-**7a** (90% yield) *Z*/*E* ratio 96:4 by ^{1}H-NMR. R_f (cyclohexane/AcOEt 9:1) = 0.10. $[\alpha]_D^{20}$ = –53.5 (*c* = 3.4, $CHCl_3$). For analyses: *vide infra*.

(1*E*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-Dimethyl-2,2-dioxido-3a,6-methano-2,1-benzothiazol-1(3*H*,4*H*)-yl]-2-methylpent-1-en-1-yl Acetate ((*E*)-**7b**). EtMgCl

(2M/THF, 0.25 ml, 0.5 mmol) was added dropwise at -78° to a soln. of *N*-methacryloylsultam **4a** (63 mg, 0.22 mmol) in THF (2 ml) and the mixture was allowed to warm to 20° in 15 min. After cooling to -78°, AcCl (0.035 ml, 0.5 mmol) was added in one portion and the mixture was slowly warmed to 20°. After 4 h, the reaction was quenched with an aq. sat. NH_4Cl soln. Workup, then purification by CC (SiO_2, cyclohexane/AcOEt 9:1) afforded pure (*E*)-**7b** (90% yield). R_f (cyclohexane/AcOEt 9:1) = 0.11. $[\alpha]_D^{20}$ = +44.1 (*c* = 0.9, $CHCl_3$). For analyses: *vide infra*. After four weeks in $CDCl_3$, the *E*/*Z* ratio was 94:6 by ^{13}C-NMR analysis, since the *E*/*Z*-stereoisomers were not resolved on our apolar HP-1 GC capillary column (6.5 psi H_2; 30 m/0.32 mm/0.25 µm; 220° iso, 4.65 min, 99% pure).

Addendum

The following section corresponds to the experimental data reported in [32][23]), corrected for some details with the help of the original hand-written reports, as well as with our own stereochemical inverted (*E*)- and (*Z*)-attributions[24]).

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[23]) It is noteworthy that on Page 31 of this thesis, in Table 10, Entries 6 and 7, the *E*/*Z* ratios of ketene N,OAc acetals should be inverted! (irrespectively of the error of attribution).

[24]) We are indebted to Prof. *G. Poli* (University *Pierre* et *Marie Curie*, Paris) for providing us with his hand-written archives, as well as for his comments on this manuscript. We thank Drs. *J.-M. Gaudin* and *C. Starkenmann* (*Firmenich* SA)

(1*Z*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-dimethyl-2,2-dioxido-3a,6-methano-2,1-benzothiazol-1(3*H*,4*H*)-yl]-2-methylbut-1-en-1-yl Acetate (*Z*)-**7a**: MeLi (0.85 ml, 1.37 mmol) was added dropwise at -40° to a soln. of CuI·PBu$_3$ (268 mg, 0.68 mmol) in THF (4 ml). Then, the suspension was cooled to -80° and the methacryloylsultam **4a** (97 mg, 0.34 mmol) in THF (2 ml) was added. After 1 h stirring at -80°, AcCl (0.242 ml, 3.4 mmol) was added and the mixture was warmed slowly to 20°. After 1 h, the reaction was quenched with an aq. sat. NH_4Cl soln. Workup and FC (SiO_2, hexane/AcOEt 3:1) without altering the stereoisomer ratio furnished the title compound (*Z*)-**7a** (81 mg, 73% yield. *Z*/*E* ratio 88:12 by ^{1}H-NMR. GC (10 psi H_2, OV-1, 12m, 0.2 mm; 150°, 10 min, then 10°/min to 250°: 15.61 min, not separated, 96% pure).

Alternatively, L-Selectride® (1.0M/THF, 0.46 mmol, 0.46 ml) was added dropwise at -80° to a soln. of tigloylsultam **4b** (114 mg, 0.38 mmol) in toluene (7 ml). After stirring for 1 h at -60°, the mixture was treated with AcCl (0.143 ml, 2 mmol) at -80°. After a slow warming to -60° during 1 h, the reaction was quenched with an aq. sat. NH_4Cl soln. Workup and FC (SiO_2, hexane/AcOEt 3:1) then crystallization (hexane) afforded pure (*Z*)-**7a** (101 mg, 81% yield) *Z*/*E* ratio 99:1 by ^{1}H-NMR. M.p.: 104 – 105°.

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for providing us with the e-mail address, and the Ph. D. thesis of Dr. *A. J. Kingma* (*BASF GmbH*, Ludwigshafen), respectively. Finally, we are particularly indebted to this latter for allowing us to incorporate the *corrigendum* of his Ph. D. thesis in the present report [32].

GC (10 psi H_2, OV-1, 12 m, 0.2 mm; 150°, 10 min, then 10°/min to 250°: 15.60 min, 99% pure). IR: 2970, 2920, 1760, 1680, 1460, 1360, 1330, 1250. ^{1}H-NMR: 0.84 (*s*, 3 H); 0.99 (*t*, *J* = 7.5, 3 H); 1.13 (*s*, 3 H); 1.23 – 1.29 (*m*, 1 H); 1.40 – 1.46 (*m*, 1 H); 1.53 – 1.61 (*m*, 1 H); 1.56 (*s*, 3 H); 1.80 – 2.00 (*m*, 4 H); 2.13 – 2.24 (*m*, 1 H); 2.16 (*s*, 3 H); 2.32 – 2.43 (*m*, 1 H); 3.18 (*s*, 2 H); 3.34 (*dd*, *J* = 8, 4.5, 1 H). ^{13}C-NMR: 167.9 (*s*); 133.7 (*s*); 127.9 (*s*); 63.9 (*d*); 49.6 (*t*); 49.5 (*s*); 47.5 (*s*); 44.4 (*d*); 35.6 (*t*); 32.5 (*t*); 26.9 (*t*); 25.1 (*t*); 20.3 (*q*); 20.1 (2*q*); 15.5 (*q*); 12.9 (*q*). MS: 341 (1, M^+), 299 (17), 152 (6), 135 (100), 107 (30), 93 (28), 84 (35), 69 (43), 55 (32). HR-MS: 341.1670 (M^+, $C_{17}H_{27}NO_4S^+$; calc. 341.1661).

(1*E*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-dimethyl-2,2-dioxido-3a,6-methano-2,1-benzothiazol-1(3*H*,4*H*)-yl]-2-methylbut-1-en-1-yl Acetate ((*E*)-**7a**). MeMgCl (0.35 ml, 1.04 mmol) was added at -80° dropwise to a soln. of *N*-methacryloylsultam **4a** (118 mg, 0.42 mmol) in THF (5 ml) and the mixture was allowed to reach 20° in 15 min. After cooling to -80°, HMPA (0.5 ml) and AcCl (0.30 ml, 4.16 mmol) were added in one portion and the reaction was slowly warmed to 20°. After 2 h stirring, the reaction was quenched with an aq. sat. NH_4Cl soln. Workup and FC (SiO_2, hexane/AcOEt 3:1) without altering the stereoisomer ratio furnished the title compound (*E*)-**7a** (26 mg, 20% yield) *E*/*Z* ratio 87:13 by ^{1}H-NMR. GC (10 psi H_2, OV-1, 12 m, 0.2 mm; 150°, 10 min, then 10°/min to 250°: 15.61 min, 82% pure). IR: 2970, 2920, 1760,

1680, 1460, 1360, 1330, 1250. ^{1}H-NMR: 0.84 (*s*, 3 H); 0.90 (*t*, *J* = 7.5, 3 H); 1.121 (*s*, 3 H); 1.17 – 1.23 (*m*, 1 H); 1.37 (*t*, *J* = 9, 1 H); 1.46 – 1.52 (*m*, 2 H); 1.74 – 1.86 (*m*, 2 H); 1.79 (*s*, 3 H); 1.88 – 1.98 (*m*, 3 H); 2.13 (*s*, 3 H); 3.12 (*d*, *J* = 13.5, 1 H); 3.18 (*d*, *J* = 13.5, 1 H); 3.29 (*dd*, *J* = 8, 4.5, 1 H); ^{13}C-NMR: 168.5 (*s*); 133.4 (*s*); 127.9 (*s*); 63.9 (*d*); 49.6 (*t*); 49.5 (*s*); 47.5 (*s*); 44.3 (*d*); 35.6 (*t*); 32.5 (*t*); 26.9 (*t*); 25.3 (*t*); 20.5 (*q*); 20.3 (*q*); 20.1 (*q*); 16.2 (*q*); 11.3 (*q*). MS: 341 (2, M^+), 299 (38), 152 (10), 135 (100), 107 (30), 93 (30), 84 (30), 69 (28), 57 (28). HR-MS: 341.1661 (M^+, $C_{17}H_{27}NO_4S^+$, calc. 341.1661).

(1*Z*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-Dimethyl-2,2-dioxido-3a,6-methano-2,1-benzothiazol-1(3*H*,4*H*)-yl]-2-methylpent-1-en-1-yl Acetate ((*Z*)-**7b**). L-Selectride® (1.0M/THF, 0.8 ml, 0.8 mmol) was added at -80° dropwise to a soln. of *N*-[(*E*)-2-methylpent-2-enoyl]bornane-10,2-sultam **4c** (200 mg, 0.643 mmol) in THF (6ml). Then after 5 min, the mixture was warmed to -30° over 30 min and stirring was continued for further 2 h. The mixture was cooled to -80° and AcCl (0.1 ml, 1.415 mmol) was added. The mixture was slowly warmed up to -60° in 1 h. Addition of NH_4Cl, then workup and FC (hexane/AcOEt 3:1) afforded pure (*Z*)-**7b** (191 mg, 84% yield) which was crystallized (MeOH) (134 mg, 59% yield[25]).

[25]) This experiment conducted to the controversial single crystal X-ray structure determination showing the (*E*)-configuration [3b][23].

Alternatively, EtMgCl (0,59 ml, 1.2 mmol) was added dropwise at -80° to a slurry of CuCl (9.3 mg, 0.09 mmol) in THF (3 ml). Then, a soln. of methacryloylsultam **4a** (134 mg, 0.47 mmol) in THF (2 ml) was slowly added. The mixture was stirred for 15 min, then AcCl (0.167 ml, 2.35 mmol) was added in one portion, and the mixtue was warmed to 20° over 2 h. Workup then FC (hexane/AcOEt 4:1) afforded (*Z*)-**7b** (155 mg, 93% yield), further crystallized (hexane) to afford pure (*Z*)-**7b** (137 mg, 82% yield). M.p.: 125°. GC (10 psi H_2, OV-1, 12 m, 0.2 mm; 150°, 10 min, then 7.5°/min to 250°: 16.73 min, 100% pure). IR: 2960, 2880, 1760, 1690, 1330. ^{1}H-NMR: 0.82 (*t*, *J* = 7.0, 3 H); 0.87 (*s*, 3 H); 1.12 (*s*, 3 H); 1.18 – 1.60 (*m*, 5 H); 1.54 (*s*, 3 H); 1.76 – 1.98 (*m*, 4 H); 2.03 – 2.09 (*m*, 1 H); 2.15 (*s*, 3 H); 2.36 – 2.40 (*m*, 1 H); 3.14 (*d*, *J* = 13.5, 1 H); 3.18 (*d*, *J* = 13.5, 1 H); 3.33 (*dd*, *J* = 7.5, 4.5, 1 H). ^{13}C-NMR: 168.0 (*s*); 132.4 (*s*); 128.5 (*s*); 64.0 (*d*), 49.7 (*t*); 49.6 (*s*); 47.6 (*s*); 44.5 (*d*); 35.7 (*t*); 34.3 (*t*); 32.6 (*t*); 26.9 (*t*); 21.5 (*t*); 20.4 (*q*); 20.3 (*q*); 20.1 (*q*); 15.9 (*q*); 13.8 (*q*). MS: 355 (0.9, M^+), 313 (40), 284 (34), 220 (13), 152 (19), 135 (100), 107 (89), 98 (64), 93 (84), 69 (80). HR-MS: 313.1716 (M^+, $C_{18}H_{29}NSO_4^+$-C_2H_2O, calc. 313.1711).

(1*E*)-1-[(3a*S*,6*R*,7a*R*)-Tetrahydro-8,8-Dimethyl-2,2-dioxido-3a,6-methano-2,1-benzothiazol-1(3*H*,4*H*)-yl]-2-methylpent-1-en-1-yl Acetate ((*E*)-**7b**). Starting from *N*-[2-methylidene-pentanoyl]bornane-10,2-sultam **4d** [22] (61 mg, 0.196 mmol)

the same procedure described for the preparation of (*Z*)-**7b**, by using L-Selectride® was followed. FC (SiO_2, hexane/AcOEt 3:1) afforded pure (*E*)-**7b** (58 mg, 84% yield).

Alternatively[26]), EtMgCl (2M/THF, 83 µl, 0.17 mmol) was added at -80° dropwise to a soln. of methacryloylsultam **4a** (31.4 mg, 0.11 mmol) in THF (1 ml), and the mixture was allowed to warm to 20° over 15 min. After cooling to -80°, AcCl (17.4 µl, 0.25 mmol) was added in one portion and the mixture was slowly warmed to 20°. After 2 h stirring, the reaction was quenched with an aq. sat. NH_4Cl soln. Workup, FC (SiO_2, hexane/AcOEt 7:1) afforded (30 mg, 77% yield) pure (*E*)-**7b** (24 mg, 61% yield) after crystallization. M.p.: 100 – 101°. GC (10 psi H_2, OV-1, 12 m, 0.2 mm; 150°, 10 min, then 10°/min to 250°: 15.65 min, 100% pure). IR: 2960, 2880, 1765, 1685, 1460, 1370, 1330, ^{1}H-NMR: 0.81 (*t*, *J* = 7.5, 3 H); 0.86 (*s*, 3 H); 1.13 (*s*, 3 H); 1.20 – 1.24 (*m*, 1 H); 1.32 – 1.46 (*m*, 3 H); 1.52 (*dd*, *J* = 13.5, 8.0, 1 H); 1.80 (*s*, 3 H); 1.80 – 2.00 (*m*, 6 H); 2.15 (*s*, 3 H); 3.14 (*d*, *J* = 13.5, 1 H); 3.18 (*d*, *J* = 13.5, 1 H); 3.31 (*dd*, *J* = 8.0, 4.5, 1 H). ^{13}C-NMR: 168.6 (*s*); 132.2 (*s*); 128.5 (*s*); 64.0 (*d*); 49.7 (*s*); 49.7 (*t*); 47.6 (*s*); 44.4 (*d*); 35.7 (*t*); 34.3 (*t*); 32.6 (*t*); 26.9 (*t*); 20.6 (*q*); 20.4 (*q*); 20.2 (*q*); 20.1 (*t*); 16.8 (*q*);

[26]) It is noteworthy that for this example, only 1.5 equiv. of *Grignard* reagent, instead of the recommended 2.0 – 2.5 fold excess was used! This may eventually account for the lower chemical yield. It may also indicate that this experiment was eventually performed at the beginning of the project, although references [11a][11b] refer to later examples.

13.9 (*q*). MS 355 (0.7, M^+), 313 (30), 284 (25), 135 (100), 107 (61), 98 (42), 93 (61), 69 (80). HR-MS: 313.1697 (M^+, $C_{18}H_{29}NSO_4^+$-C_2H_2O; calc. 313.1711).

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Table. 1,4-Addition of 1.1 mol.-equiv. of EtMgX to **1** with 1.1-mol.-equiv. of additive in THF.

Entry	**1** *p*X	Additive	T [°]	Time [h]	Conversion [%]	de of **2**
1	**1a** F	EtMgBr	–78	4	100	74
2	**1b** CF_3O	EtMgBr	–78	4	100	68
3	**1c** CF_3	EtMgBr	–78	4	100	60
4	**1d** H	EtMgCl	–78	4[a])	100	82
5	**1d** H	EtMgCl	–78	4[b])	100	83
6	**1d** H	EtMgCl	–78	4	100	78 [2]
7	**1d** H	EtMgBr	–78	4	100	73 [2]
8	**1d** H	EtMgI	–78	4[c])	100	31 [2]

9	**1d** H	EtMgI	–78	4[a])	2	–
10	**1b** MeO	EtMgCl	–78	4[a])	100	86
11	**1b** MeO	EtMgCl	–78	4[b])	78	84
12	**1b** MeO	EtMgCl	–78	4	33	82
13	**1a** F	$TiCl_4$	–78	24	31	54
14	**1a** F	$ZnBr_2$	–78	96	7	76
15	**1a** F	$ZnBr_2$	–20	96	18	44
16	**1a** F	$ZnBr_2$	4	96	34	26
17	**1a** F	$ZnBr_2$	20	24	25	33
18	**1a** F	ZnI_2	4	72	68	21
19	**1a** F	$BF_3 \cdot Et_2O$	4	96	26	50
20	**1a** F	$MgCl_2$	4	72	55	61
21	**1b** CF_3O	$MgCl_2$	4	72	100	58
22	**1c** CF_3	$MgCl_2$	4	72	26	53
23	**1a** F	$MgBr_2$	4	72	15	54
24	**1b** CF_3O	$MgBr_2$	4	72	33	58
25	**1c** CF_3	$MgBr_2$	4	72	38	51
26	**1a** F	EtMgBr/CuCl	–78	24	0	–
27	**1a** F	EtMgBr/CuCl	4	24	69	26

28	**1a** F	EtMgBr/CuBr	4	72	100	–37
29	**1a** F	EtMgBr/CuI	4	72	100	–17

[a]) Toluene. [b]) CH_2Cl_2. [c]) Et_2O.

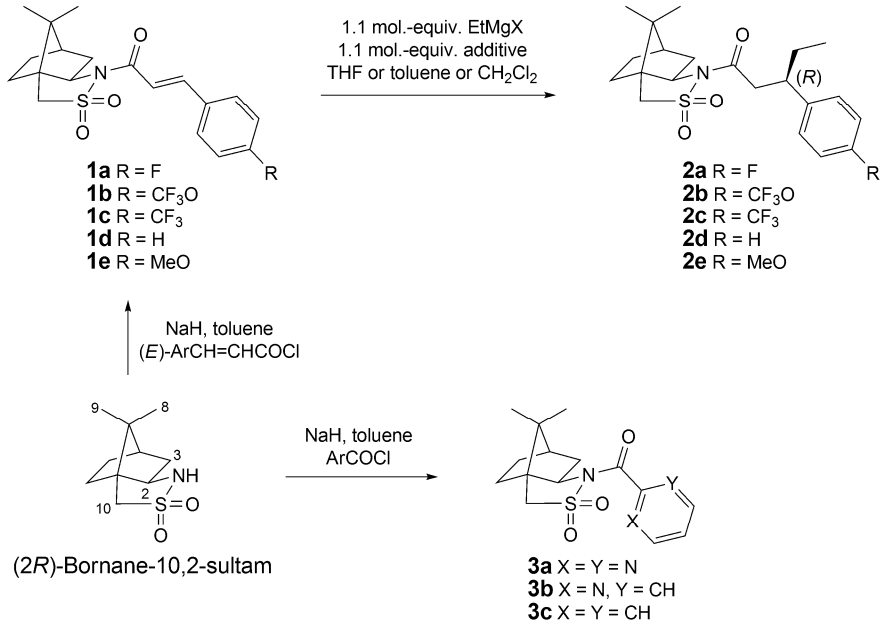
Captions:

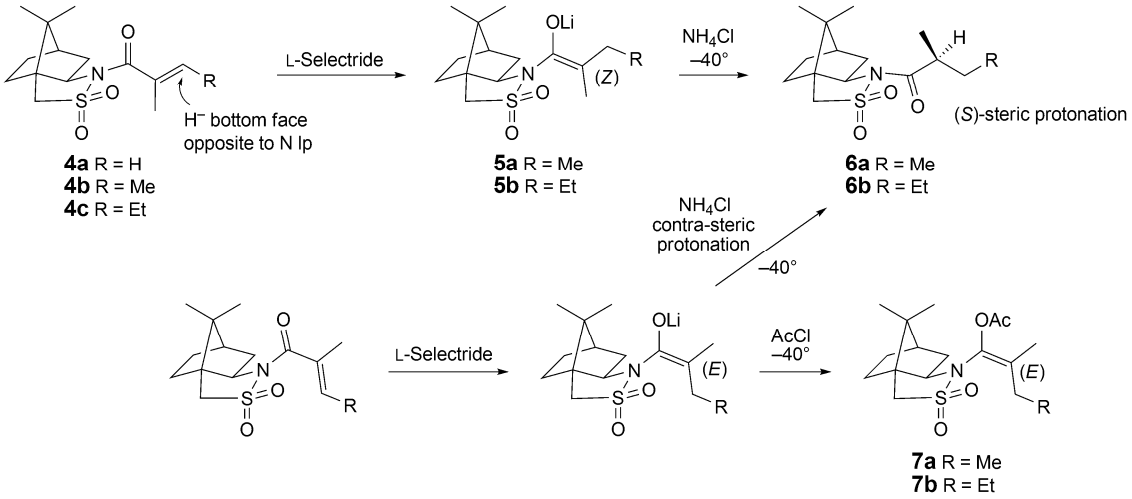
Scheme 2[a])

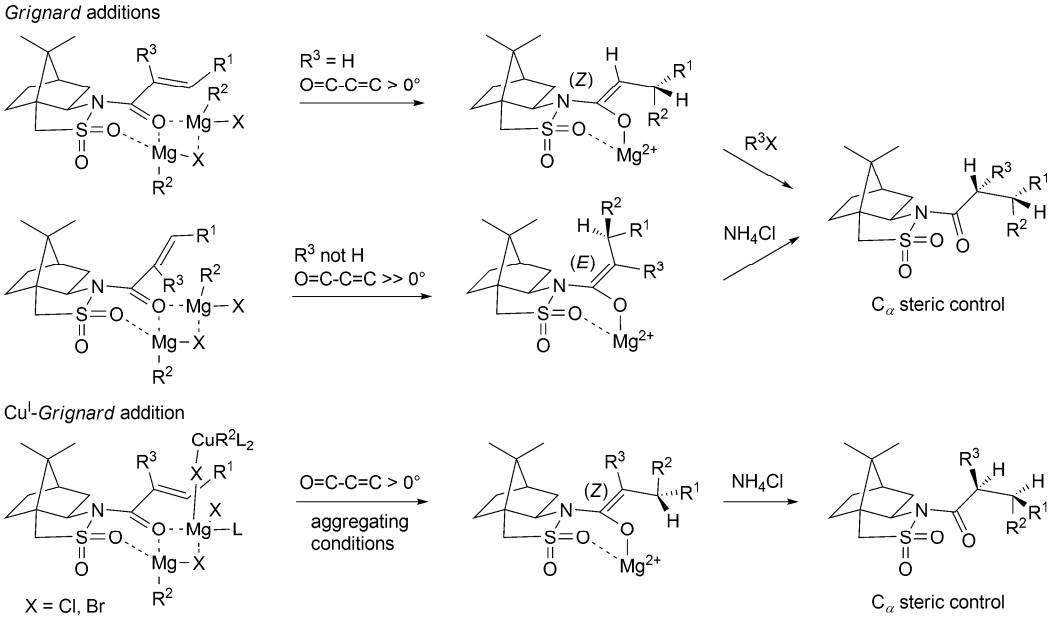
[a]) Initial *anti*-s-*cis* reactive conformation for eventually either stereoelectronically, or sterically controlled 1,4-hydride addition to **4**, followed by C_α steric protonation of the hypothetical (*Z*)-enolate **5** in either the *anti*-, or *syn*-conformation in analogy to [22], for rationalization of the observed configuration of **6**; *versus* later modified sterically controlled top face 1,4-hydride addition on the *anti*-s-*trans* reactive conformation of **4**, followed by either C_α contra-steric protonation in either the *anti*-, or *syn*-conformation, or suggested front face protonation of the (*E*)-enolate **5** in the pseudo axial S=O chelated conformation, as a consequence of the X-ray structure analysis of initially attributed (*E*)-**7b** [3b][23].

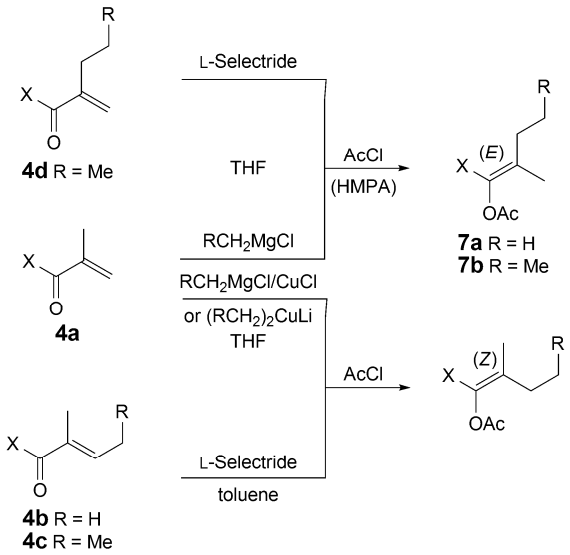
Scheme 3[a])

[a]) Under chelating control, the O=C-C=C torsion angle is close to 0° for either small R^3 = H, or when the apical aggregated X-Cu^I enforces the s-*cis* conformation, thus leading to the (*Z*)-enolate. This cisoid angle, estimated to *ca.* 50 – 70°, depending on R^2, R^3, even increases during the TS of the simple *Grignard* addition, when R^3 is bigger than H, up to afford the (*E*)-enolate. Then, the electrophilic C_α attack is sterically controlled by the sultam in all cases.









X = (2*R*)-Bornane-10,2-sultam