# Chapter III: Michael addition of achiral sulfonamides

## 1 Introduction

This chapter will deal with the addition of achiral sulfonamides to Michael acceptors. We will first present the general procedure and the analytical methods used throughout this study. The discussion will include previous results obtained in our laboratory. The discussion will focus on the regio- and diastereoselectivities of the addition reactions.

## 2 Addition of achiral sulfonamides to cyclohexenone

### 2.1 General procedure[67]

Unless otherwise stated the general procedure was as follows: A few drops of *n*-BuLi were added to a mixture of THF, HMPA (8 equivalents) and a few crystals of *o*-phenantroline until the persistence of a red color. After dissolution of 1 equivalent of sulfonamide in the THF solution, the mixture was cooled to -78°C (concentration: *ca.* 0.1M). After addition of 1.05 equivalents of *n*-BuLi (freshly titrated by 2,5-dimethoxybenzylic alcohol or diphenylacetic acid) and stirring for 1 hour, 1.1 equivalents of the Michael acceptor were added. After stirring for 1 hour at -78°C the resulting reaction mixture was quenched by addition of an excess of triethylamine and trimethylsilyl chloride and warmed up to room temperature. Hydrolysis by addition of a few ml of a dilute HCl solution completed the reaction. The resulting mixture was diluted with diethyl ether and washed five times with a saturated solution of NaCl to remove HMPA. The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure.

### 2.2 Analysis

Analyses of the mixture were performed at this step. We wanted indeed to prevent any changes in the product distribution that could occur during the purification step.

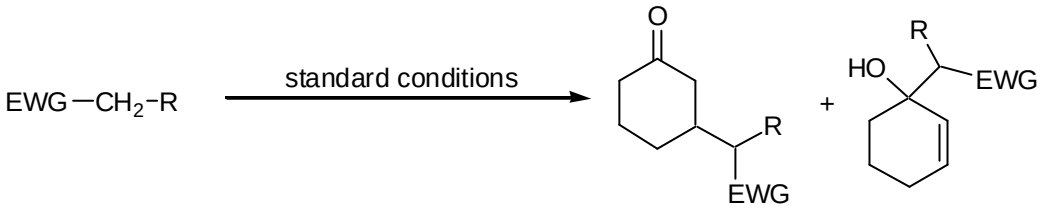
Regioselectivity could be determined by quantitative $^{13}C$ NMR. These analyses were realized by taking the spectrum overnight with a relaxation time of 30 seconds between two irradiations. After this delay all the nuclei should have come back to the ground state. The intensity of the signal is thus proportional to the quantity of compound present. The chemical shift of the carbon atom α to the sulfonamide was different in the 1,2-adduct than in the 1,4-adduct and could thus be used for the estimation of the product ratio. The assignments had been done on the purified products and further confirmed by $^{1}H,^{13}C$-HETCOR. $^{1}H$ NMR was not useful in this study as none of the protons in the 1,4-adduct gave a signal that could be used unambiguously. The 1,2-adduct could however be clearly identified by the signals of the olefinic protons.

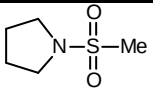
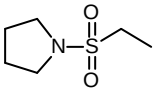
Diastereoslectivity could be measured by both $^{13}C$ NMR and GC. The carbon atom α to the sulfonamide had a slightly different chemical shift in the different diastereomers. Moreover the diastereomers of the 1,4-adduct could be separated by GC. In cases where both analyses were performed, the measures were consistent within the range of experimental error.

## 2.3 Results

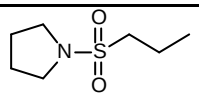
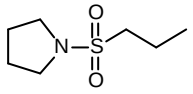
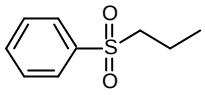
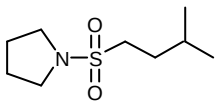
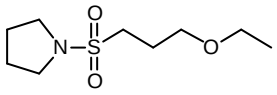
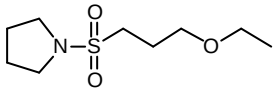
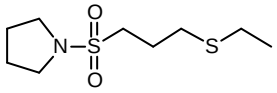
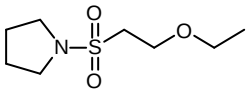
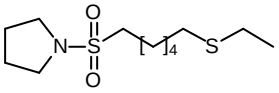
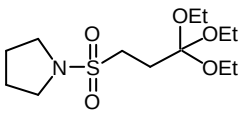
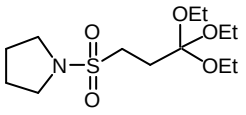
The results are summarized in table 17.

**Table 17:** *Addition of sulfur-stabilized carbanions to cyclohexenone.*

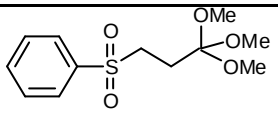
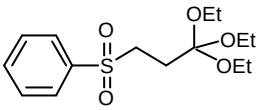
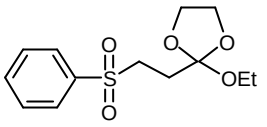



| Entry | Starting compound | 1,4 : 1,2 | dr (1,4)[a] | dr (1,2)[b] | Remarks | Ref |
|---|---|---|---|---|---|---|
| 1 |  **11** | < 1 : 20 **84** | | | | this work |
| 2 |  **38** | 1.9 : 1 **85 86** | 4.9 : 1[c] | | | this work |

[a] diastereomeric ratio of the 1,4-adduct
[b] diastereomeric ratio of the 1,2-adduct
[c] Measured by $^{13}C$ NMR

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 |  **87** | 4 : 1<br>**88 89** | | | 12 eq. HMPA | ref [67] |
| 4 |  **87** | 1 : 1<br>**90 91** | 4 : 1[c] | 1 : 1[c] | 6 eq. HMPA | ref [67] |
| 5 |  **92** | 4 : 1<br>**93 94** | 4 : 1[d] | | 6 eq. HMPA | ref [64] |
| 6 |  **39** | 3.8 : 1<br>**95 96** | 6.1 : 1[c] | 1.2 : 1[c] | | this work |
| 7 |  **59** | 4.9 : 1<br>**97 98** | 6.7 : 1[c,e] | 1.3 : 1[e] | | this work |
| 8 |  **59** | < 1 : 20<br>**98** | | | 0 eq. HMPA | this work |
| 9 |  **63** | > 20 : 1<br>**99** | 9 : 1[c,d] | | | this work |
| 10 |  **69** | | | | degradation | this work |
| 11 |  **64** | | | | no reaction | this work |
| 12 |  **52** | > 20 : 1<br>**100** | 6.1 : 1[c] | | | this work, ref [67] |
| 13 |  **52** | < 1 : 20<br>**101** | | | 0 eq. HMPA | ref [67] |

[d] Measured by $^1$H NMR on the silylated enol ether
[e] Measured by GC

| | | | | | |
|---|---|---|---|---|---|
| 14 |  **3** | 9 : 1 **102** **103** | 3.2 : 1[d] | 5.7 eq. HMPA | ref [63] |
| 15 |  **104** | 49 : 1 **105** | 10 : 1[d] | 5.7 eq. HMPA | ref [63] |
| 16 |  **106** | 19 : 1 **107** | 6.7 : 1[d] | 5.7 eq. HMPA | ref [63] |

### *2.3.1 Regioselectivity*

Despite the presence of HMPA only 1,2-addition was observed with **11** (entry 1). The amount of 1,4-adduct increases with the length and the steric hindrance of the alkyl chain on the sulfonamide (entries 2-6).

For a same alkyl chain and same quantity of HMPA, the sulfone gave higher 1,4-selectivity than the corresponding sulfonamide (entries 4 and 5).

Sulfonamides having one or more heteroatoms at the $\gamma$ carbon reacted with high regioselectivity in favor of the 1,4-adduct (entries 7, 9, 12, 14-16). With the exception of ether **59** no or only traces of the 1,2-adduct were observed.

When the heteroatom was at the $\beta$ position, the sulfonamide was not stable under the reaction conditions (entry 10). $\beta$-elimination could indeed take place in the strong basic conditions. No reaction occurred with sulfonamide **64** which had a heteroatom at 6 carbon atoms from the sulfonamide (entry 11).

Regioselectivities were excellent with all orthoesters (entries 12-16). Less HMPA was necessary to obtain the same result with a sulfone than with a sulfonamide (entries 12 and 15). It can be seen that the nature of the rather remote orthoester function slightly influenced the regioselectivity (entries 14-16).

### *2.3.2 Diastereoslectivity*

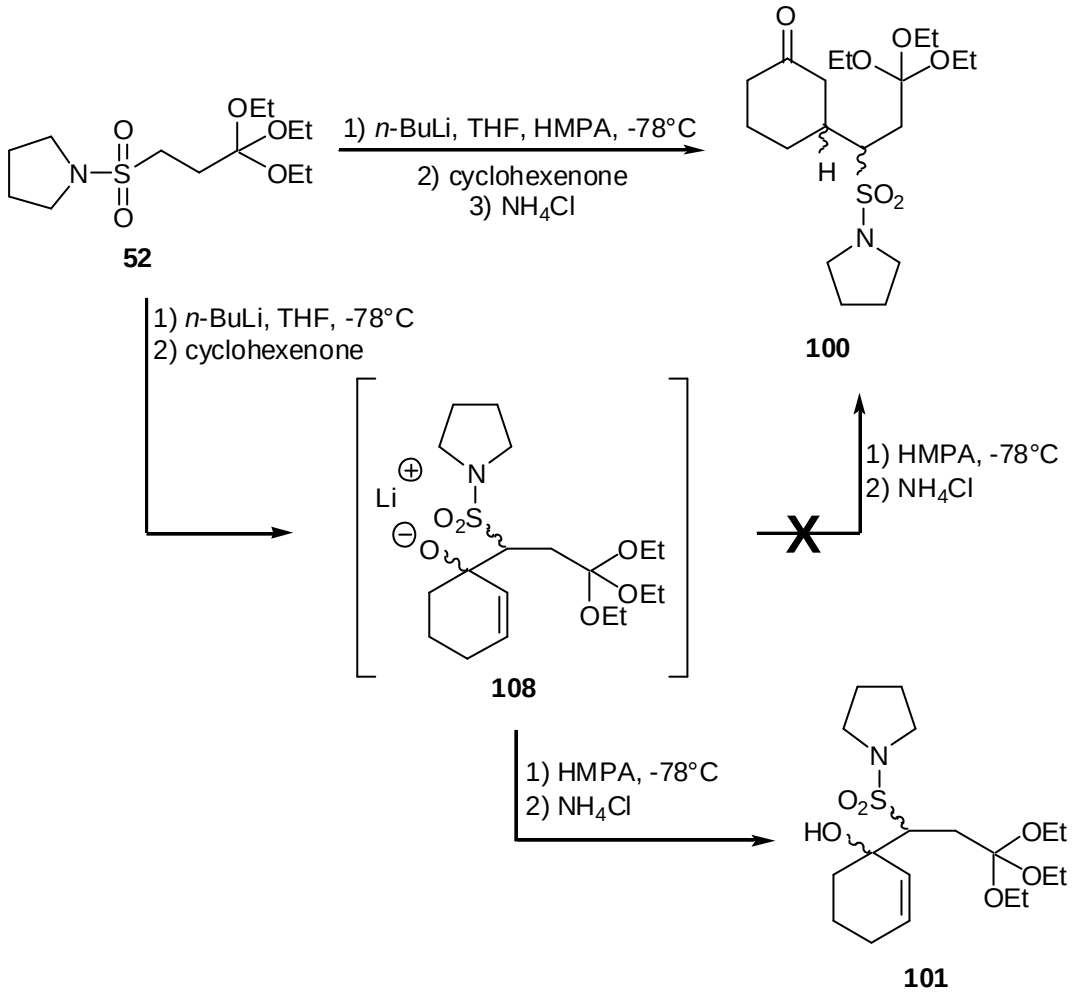
No significant difference in the diastereoselectivity could be measured. For all the sulfones or sulfonamides used it varied from 80 : 20 to 90 : 10 in the 1,4-adduct.

Again slight differences were observed when the remote orthoester function was changed (entries 14-16)

## 2.4 Discussion

### *2.4.1 Kinetic or thermodynamic control?*

The question had been already answered by C. Huart (scheme 79).[67]




Scheme 79

Orthoester **52** added to cyclohexenone in a conjugate way in the presence of HMPA and in a 1,2-addition in the absence of HMPA. To know if any equilibration occurred in the presence of HMPA, the anion was formed and was added to cyclohexenone in absence of HMPA. Once the alkoxide **108** resulting from a 1,2-addition formed, HMPA was added and the mixture was stirred for 30 minutes then quenched. Only 1,2-adduct **101** was isolated and no equilibration towards 1,4 adduct **100** had happened. It could be concluded that the 1,4-addition in the presence of HMPA was under kinetic control.

### *2.4.2 Organolithium compounds: literature*

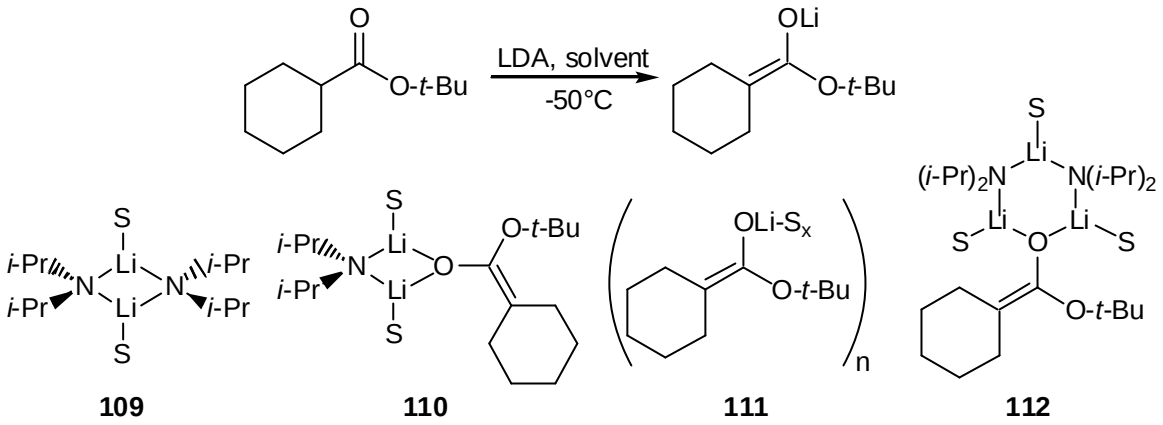
All the reactions have been realized with lithiated carbanions. We have already shown that the cation influences the outcome of the addition reaction.[104] Its role is essentially based on complexation and coordination phenomena. We will thus present a brief review of literature results.

The coordinations that occur are tetrahedral and octahedral, thus the coordination number is either four or six.[135] In organic compounds however the coordination number four seems to be predominant. Popov has shown that lithium cation had four molecules of 1-methyl-2-pyrrolidinone in its primary solvation sphere.[136] 1-methyl-2-pyrrolidinone was replaced by dioxane in the solvation sphere of lithium when less than 4 equivalents were used. Yeager came to the same conclusions in his spectroscopic studies of ionic solvation in propylene carbonate.[137] More precise studies have recently been conducted by Matsubara.[138] They revealed the same result: the lithium cation was complexed by four ester molecules. In all three studies the coordination occurred through the oxygen atom of a carbonyl function.

We have already seen that in α-sulfamoylated carbanions the lithium cation is complexed by the two oxygen atoms of the sulfonamide. There remain thus two free sites that will be occupied by the solvent or any other ligand and that could be of importance for the outcome of the reaction.

Another major point in organolithium chemistry is the aggregation. Seebach has alerted chemists on the possible consequences of aggregation and mixed aggregation in organolithium compounds.[139] An interesting study has been realized by Collum, who investigated solvent-dependent mixed aggregation effects in lithium diisopropylamide-mediated ester enolization reactions.[140] Lithium diisopropylamide (LDA) was shown to be a dimer **109** solvated by two molecules of solvent. In the course of the reaction it formed mixed dimers **110** with the resulting enolate. On completion of the enolization, enolates **111** appeared at the expense of these mixed dimers (scheme 80). In *tert*-butyl methyl ether a mixed trimer **112** was also observed.

[135] Donnay, G.; Gryder, J. W. *J. Chem. Educ.*, **1965**, *42*, 223.
[136] Wuepper, J. L.; Popov, A. I. *J. Am. Chem. Soc.*, **1969**, *91*, 4352-4356.
[137] Yeager, H. L.; Fedyk, J. D.; Parker, R. J. *J. Phys. Chem.*, **1973**, *77*, 2407-2410.
[138] Matsubara, K.; Kaneuchi, R.; Maekita, N. *J. Chem. Soc., Faraday Trans.*, **1998**, *94*, 3601-3605.
[139] Seebach, D. *Angew. Chem. Int. Ed. Engl.*, **1988**, *27*, 1624-1654.
[140] Sun, X.; Collum, D. B. *J. Am. Chem. Soc.*, **2000**, *122*, 2459-2463.




Scheme 80

A comparative study in THF and *tert*-butyl methyl ether revealed that in both cases LDA dimer was rapidly consumed and mixed aggregates appeared. In THF, enolate **111** was formed rapidly (figure 19 (B)). In *tert*-butyl methyl ether however, nearly no enolate was formed. Even after a prolonged reaction time the major species was the mixed dimer **110** (figure 19 (A)).

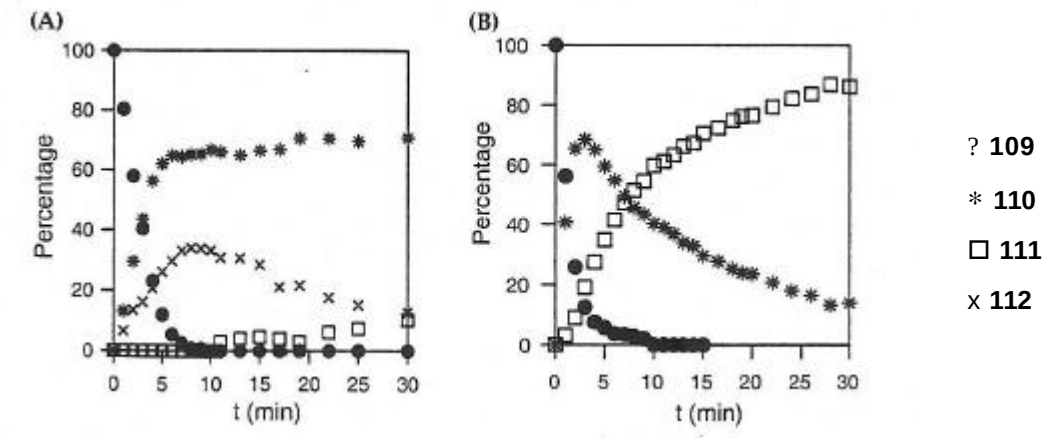



Figure 19

The relative stabilization of the different species by the solvent could explain these differences. The mixed aggregates were especially stabilized in *tert*-butyl methyl ether, hence inhibiting the reaction. The solvent is thus of extreme importance.

### *2.4.3 HMPA: literature*

All the reactions were realized in the presence of HMPA.[141] This polar and dissociating solvent is extensively used in organolithium chemistry and is well known

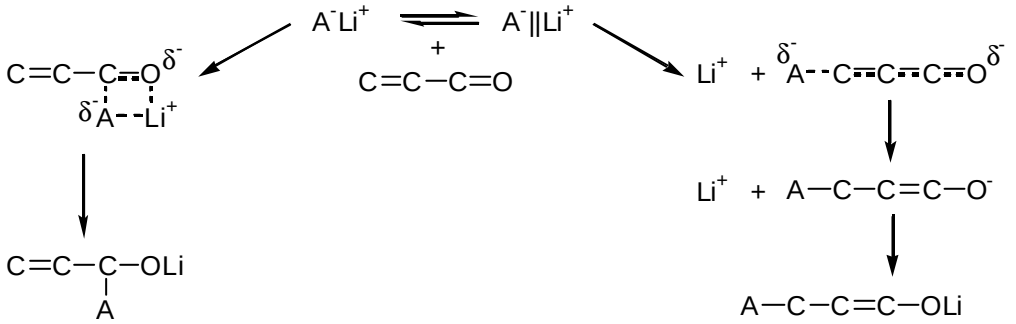
[141] Normant, J. F. *Bull. Soc. Chim. Fr.*, **1968**, 761.

to alter the regiochemistry of these reagents.[142] First examples for the addition to enones were described by Seyden-Penne[143,144] and Krief.[99] The evidence that such reactions could occur under kinetic control was published by these two groups.[145] Different explanations were given for the mode of action of HMPA.

A very first explanation could be that the higher polarity of the reaction mixture favors the decomposition of the initial alkoxide resulting from a 1,2-addition. An equilibration towards the 1,4-adduct would occur. In other words the reaction would be under thermodynamic control. This could certainly apply in certain cases, such as that shown in scheme 51.[99]

Another explanation is based on the high affinity of HMPA to coordinate lithium cation. Reich has shown in his titration studies that HMPA completely solvated the lithium cation resulting in the formation of $[Li(HMPA)_4]^+$.[146] In the case of 2-lithio-1,3-dithianes 4 equivalents of HMPA were sufficient to replace completely the solvent in the primary solvation sphere of the lithium cation. When applied to the theory of Lefour and Loupy,[104] these results show that in the presence of HMPA the enone will not be complexed by the cation and hence 1,4-addition should be the major reaction.

Another possible theory was developed by Cohen.[147] He based his discussion on the ion-pairing in the reagent. According to this theory, contact ion pairs (CIP) will undergo 1,2-addition, whereas solvent-separated ion pairs (SSIP) result in 1,4-addition (scheme 81).

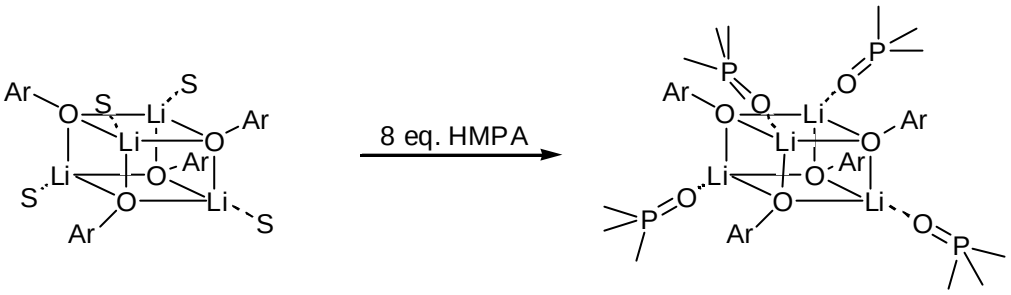


Scheme 81

[142] House, H. O., *Modern Synthetic Reactions*; 2nd ed; W.A. Benjamin, Inc.: Menlo Park, CA, 1972 527-530.
[143] Sauvetre, R.; Seyden-Penne, J. *Tetrahedron Lett.*, **1976**, *44*, 3949-3952.
[144] Sauvetre, R.; Roux-Schmitt, M. C.; Seyden-Penne, J. *Tetrahedron*, **1978**, *34*, 2135-2140.
[145] Wartski, L.; El Bouz, M.; Seyden-Penne, J.; Dumont, W.; Krief, A. *Tetrahedron Lett.*, **1979**, *17*, 1543-1546.
[146] Reich, H. J.; Borst, J. P.; Dykstra, R. R. *Tetrahedron*, **1994**, *50*, 5869-5880. and references cited therein
[147] Cohen, T.; Abraham, W. D.; Myers, M. *J. Am. Chem. Soc.*, **1987**, *109*, 7923-7924.

Addition of CIP is supposed to involve a four-center transition state with a very low activation energy. A conjugate addition to a cyclic enone, that cannot adopt a cisoid configuration, would require breaking the carbon-lithium bond without compensation from the simultaneous formation of an oxygen-lithium bond. 1,4-addition is therefore disfavored. SSIP on the other hand would attack on the position with the highest value of the LUMO coefficient. Based on this considerations, the presence of HMPA would lead to conjugate addition because it generates SSIP. Evidence has been furnished by the fact that low temperatures, addition of HMPA or increased size of the nucleophile, which all strongly favor SSIP, promoted 1,4-addition.

There are however some limitations to this theory. HMPA does not necessarily provoke deaggregation. Jackman has shown that the tetrasolvated tetramer of 3,5-dimethylphenolate remained tetrameric after addition of 8 equivalents of HMPA; only a replacement of the solvent took place (scheme 82).[148]




Scheme 82

A similar observation has been made by Collum in the study described above (scheme80).[140] Besides *tert*-butyl methyl ether, a mixture of HMPA in THF also favored the stabilization of the mixed dimer **110** and resulted in inhibition of the enolization reaction.

Another objection had been made by Reich.[146] It is based on the Curtin-Hammett principle, that states that conclusions on the reactive species can be made only if the reaction rates are faster than the interconversion rates. His study showed that 2-lithio-1,3-dithiane gave conjugate addition even at HMPA concentrations where CIP was the major species present. But no data on the interconversion of CIP into SSIP could be obtained. Thus either this interconversion was faster than the reaction or other effects of HMPA played a role. So conclusions based on the presence of CIP or SSIP should be taken carefully.

[148] Jackman, L. M.; Chen, X. *J. Am. Chem. Soc.*, **1992**, *114*, 403-411.

### *2.4.4 Regioselectivity*

With sulfonamide **11** the addition occurred only in the 1,2-position (entry 1). The same behavior has already been observed by C. Huart[67] and Mladenova.[106] It has indeed been shown that the size of the nucleophile could influence the regioselectivity.[98] The approach to form a quaternary center would indeed be much more sterically demanding for a secondary anion than for the primary anion derived from **11**. The steric factor could thus explain the evolution going from ethyl- to propyl- and 3-methylbutyl substituted sulfonamide (entries 2-6).

The difference between the sulfone and the sulfonamide could be explained by the general perturbation theory. The stabilization of the anion by a sulfone is better than by a sulfonamide (table 4). Thus the addition of a sulfamoylated anion could be charge-controlled whereas frontier control could be possible for a sulfonylated anion.

With a heteroatom at the γ-position regioselectivity became good to excellent. Whereas the ether **59** gave still a certain amount of 1,2-addition, the thioether **63** and the orthoesters **52**, **3**, **104** and **106** allowed to obtain nearly complete regioselectivity. A complexation by the internal ligand could be imagined in these cases, and an effect similar to that of HMPA could be possible.

The difference between an ether and a thioether could easily be rationalized. Diethyl ether, in contrast to THF, is only a poor ligand for lithium.[149] On the other side it has been shown that sulfides have excellent solvating properties for lithium compounds.[150]

The presence of three oxygen atoms should enhance the donating-ability, thus stronger complexation should occur with an orthoester. A higher regioselectivity was observed compared to the ether (entries 12-16 compared to 7).

To show that this complexation actually played a role we have used ether **69** and thioether **64**. In these compounds complexation would lead to a four- or an eight-membered ring respectively; hence be unfavored. Unfortunately sulfonamide **69** underwent an elimination reaction under the reaction conditions. The more

[149] Reich, H. J.; Borst, J. P.; Dykstra, R. R.; Green, D. P. *J. Am. Chem. Soc.*, **1993**, *115*, 8728-8741.
[150] Olmstead, M. M.; Power, P. P. *J. Am. Chem. Soc.*, **1990**, *112*, 8008-8014.

interesting **64** did not react under the standard conditions. Starting materiel was recovered unchanged. We were thus not able to prove our hypothesis.

Even if this internal complexation really occurred, it was not sufficient to control the regiochemistry of the reaction. The addition of **59** and **52** in absence of HMPA resulted in complete 1,2-addition.

### *2.4.5 Diastereoselectivity*

Two stereocenters were created upon the addition to the enone; thus 4 stereoisomers could be formed. The 2 diastereomers are the *anti*-adduct and the *syn*-adduct according to Masamune's nomenclature[151] (figure 20).

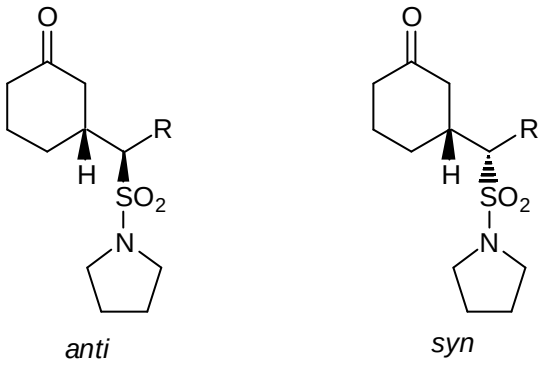
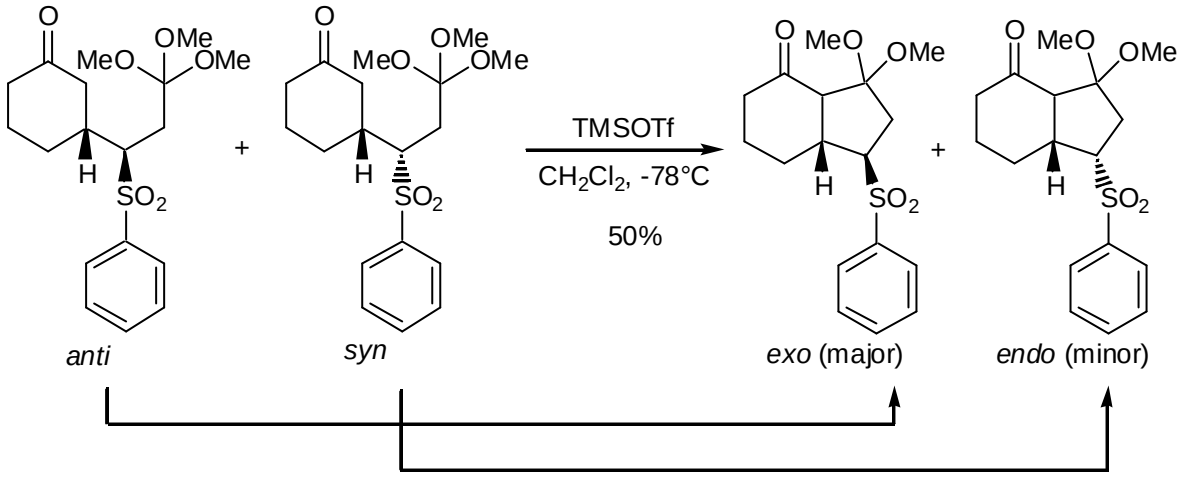



Figure 20

In the 1,4-addition one diastereomer was formed in large excess. The influence of the substituent on the diastereoselectivity seemed to be negligible.

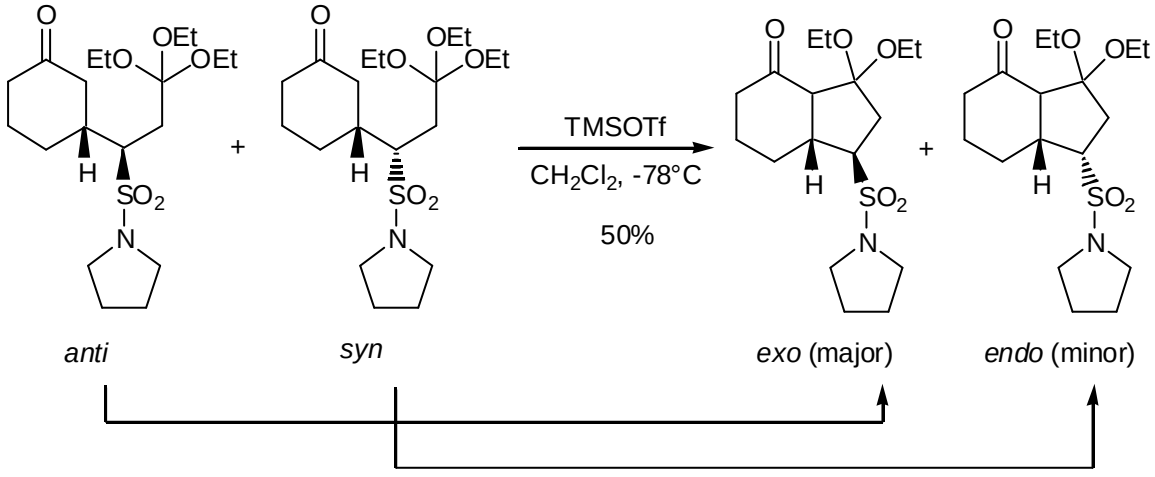
It has been shown that the major diastereomer formed in the addition of α-sulfonylated anions was the *anti*-adduct.[63] Indeed two diastereomeric bicyclic compounds were formed in the cyclization step. As the ring closure always occurred *cis*, these isomers only differed by the relative chemistry of the sulfonamide. In the cyclization product the relative stereochemistry of the major isomer had been established and the phenylsulfonyl group was shown to be *exo* which could result only from the *anti*-adduct (scheme 83).[152]

[151] Masamune, S.; Ali, S. K.; Snitman, D. L.; Garvey, D. S. *Angew. Chem. Int. Ed. Engl.*, **1980**, *19*, 557-558.
[152] Nemery, I. *Master Degree UCL-ORSY*, **1986**




Scheme 83

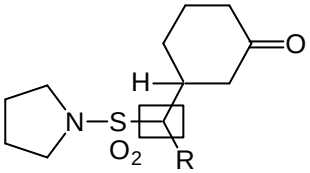
The same observation was made by C. Huart for the addition of α-sulfamoylated anions.[67] In this case the *exo*-compound was also the major one (scheme 84). One can thus conclude that the *anti*-adduct was the major isomer in the addition reaction.

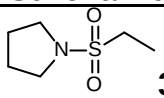
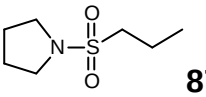
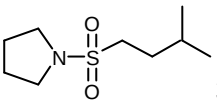
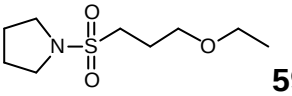
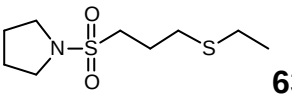



Scheme 84

It can be assumed that the other addition reactions took place with the same stereochemistry. We also compared the values of the chemical shifts corresponding to the carbon atom α to the sulfonamide in both isomers (table 18).

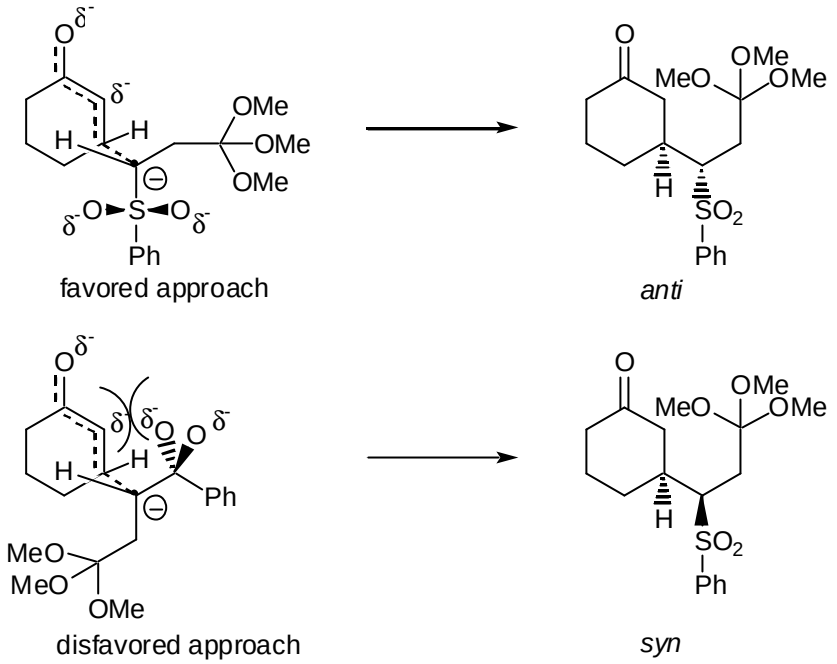
**Table 18:** *Chemical shifts of the carbon atom α to the sulfonamide.*



| Entry | Sulfonamide | $\delta_{major}$ (ppm) | $\delta_{minor}$ (ppm) |
|---|---|---|---|
| 1 |  **38** | 60.8 | 59.3 |
| 2 |  **87** | 67.2 | 67.1 |
| 3 |  **39** | 63.5 | 63.4 |
| 4 |  **59** | 62.1 | 62.0 |
| 5 |  **63** | 63.7 | 63.5 |

In all cases the major isomer has a slightly higher chemical shift than the minor isomer. We are very well aware that this was not a definite proof of stereochemistry but at least it was consistent with our hypothesis.

In the case of the addition of α-sulfonylated carbanions a model had been proposed that could account for the observed stereochemistry.[63] Electrostatic repulsions between the partial negative charges on the oxygen atoms of the sulfone and on the α-carbon of the enone would disfavor one of the two possible approaches. The disfavored approach is the one leading to the *syn*-adduct (scheme 85).




Scheme 85

The situation should be nearly the same for the sulfonamides and a similar model could be applied.[67]

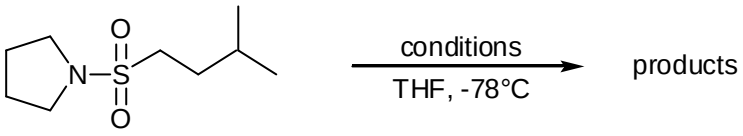
We have seen that the remote functions in the carbanion could induce minor changes in the stereochemistry. They were however small compared to the total diastereoselectivity. The above model seems thus to remain valid to explain the general outcome of the reaction.

For the 1,2-adduct the evaluation of the diastereoselectivity was not always possible. When the measure was possible, nearly no selectivity was observed. These results were consistent with the observations made earlier for the addition of α-sulfonylated[64] or α-sulfamoylated[67] anions.

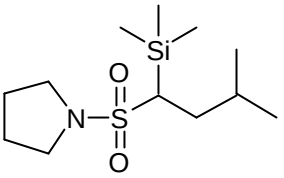
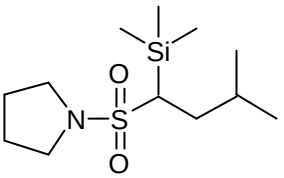
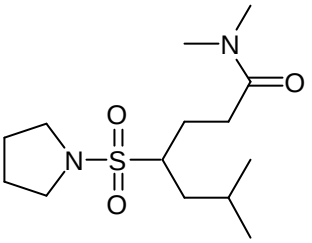
# 3 Addition of achiral sulfonamides to other Michael acceptors

As pointed out in the introduction, the scope and limitations of the cyclopentannulation sequence had not been studied. Only cyclic enones have been used as substrates. We have chosen *N,N*-dimethylacrylamide as another possible Michael acceptor (table 19).

**Table 19:** *Addition of **39** to N,N-dimethylacrylamide.*




**39**

| Entry | Conditions | Products |
|---|---|---|
| 1 | 1) *n*-BuLi; 2) *N,N*-dimethylacrylamide; 3) $HCl_{dil}$ | No reaction |
| 2 | 1) *n*-BuLi; 2) *N,N*-dimethylacrylamide; 3) $Et_3N$, TMSCl; 4) $HCl_{dil}$ |  **113** 30% |
| 3 | 1) *n*-BuLi; 2) *N,N*-dimethylacrylamide, TMSOTf, THF; 3) $HCl_{dil}$ |  **113** 15% |
| 4 | 1) *n*-BuLi; 2) *N,N*-dimethylacrylamide, TIPSOTf, THF; 3) $HCl_{dil}$ |  **114** 31% |
| 5 | 1) *n*-BuLi; 2) *N,N*-dimethylacrylamide, $AlMe_3$, $(TMS)_2SO_4$,[153] THF; 3) $HCl_{dil}$ | No reaction |

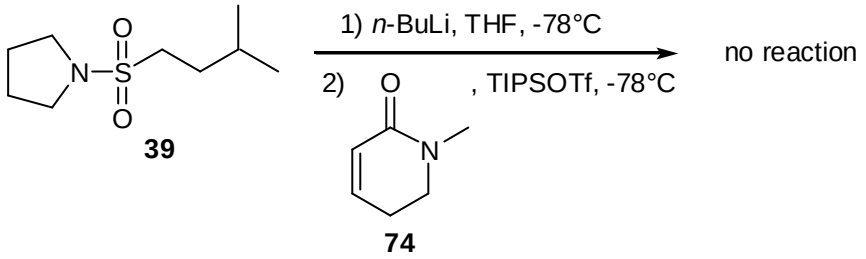
When the reaction was run in the standard conditions, α-silylated sulfonamide **113** was the only compound isolated (entry 2). Without silylating agent no reaction occurred (entry 1).

An amide being less reactive than an enone it could be activated by pre-complexation with a Lewis acid. When a mixture of *N,N*-dimethylacrylamide and trimethylsilyl trifluoromethanesulfonate was added to the anion of **39**, silylated sulfonamide **113** was isolated in poor yield (entry 3). With triisopropylsilyl trifluoromethanesulfonate 31% of the desired adduct **114** could be obtained, whereas 28% of the starting material was recovered (entry 4). Unfortunately the yields could not be optimized.

[153] Hanawa, H.; Maekawara, N.; Maruoka, K. *Tetrahedron Lett.*, **1999**, *40*, 8379-8382.

The use of bis(dimethylaluminum) sulfate as Lewis acid[153] did not promote the reaction (entry 5).

We then applied conditions of entry 4 to add sulfonamide **39** to unsaturated lactam **74**. No reaction was observed (scheme 86).



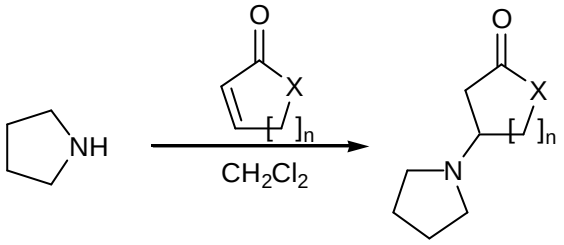

Scheme 86

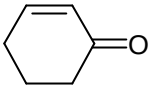
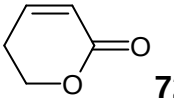
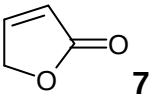
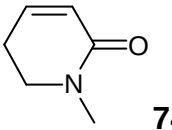
In any case, the necessity to use a Lewis acid to promote the reaction is incompatible with an orthoester function.[154] Unsaturated lactams seem to be unsuitable as reagents in our cyclopentannulation reaction.

To quantify the reactivity of the Michael acceptors, we added pyrrolidine to cyclohexenone, the unsaturated lactones **71** and **72**, and the unsaturated lactam **74** (table 20).

[154] Pindur, U., *Preparation and chemistry of ortho acids, ortho esters and ortho amides*, in *Supplement B: The Chemistry of Acids Derivatives*, Patai, S., Editor. John Wiley & Sons, Inc.: New York. 1992, p. 967-1005.

**Table 20:** *Addition of pyrrolidine to Michael acceptors.*




| Entry | Michael acceptor | Time | Yield |
|---|---|---|---|
| 1 |  | <1h | quant. |
| 2 |  **72** | 72h | 67% |
| 3 |  **71** | 24h | 70% |
| 4 |  **74** | 30h | 0% |
| 5 | **74** + $K_2CO_3$ | 72h | 40% |

The difference in reactivity was quite important. Whereas pyrrolidine reacted readily with the other Michael acceptors (entries 1-3), we did not observe any adduct with lactam **74** (entry 4). Only after addition of potassium carbonate we observed a reaction, but it remained slow. Only 40% of the desired product could be obtained after 3 days (entry 5).

# 4 Conclusion

We have shown in this chapter that the Michael addition of sulfonamides gave results similar to the addition of sulfones. Steric hindrance and, above all, the presence of a heteroatom $\gamma$ to the sulfonamide favored the 1,4-addition. No significant variations in diastereoselectivity were observed.

Attempts to extend the Michael addition to unsaturated lactams failed.