A Novel Approach to Dihydropyrrolones from Iron-Substituted α,β-Unsaturated Imines and Organolithium and Grignard Reagents: Developments, Mechanisms and Stereoselective Syntheses

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Dedicated to Prof. Horst Kunz on the occasion of his 60th birthday

Keywords: Carbonylations / Grignard reactions / Iron / Lactams / Lithium / Schiff bases / *N*-sulfinylimines

Reactions of *N*-sulfonylimines, derived from $Cp(CO)_2Fe$-substituted (*Z*)-enals and benzenesulfonamide, with Grignard or organolithium reagents furnish *N*-sulfonyldihydropyrrolones. When *N*-sulfinylimines and organometallic reagents are used, unprotected α,β-unsaturated γ-lactams are formed exclusively. Recent mechanistic studies and diastereoselective variations for the synthesis of chiral 5-substituted dihydropyrrolones from iron-substituted azadienes are discussed here.

Introduction

α,β-Unsaturated γ-lactams, α,β-butenolides, and γ-lactones constitute important classes of natural products with broad biological activity. These skeletons can be obtained by the cyclization of appropriate acyclic precursor molecules. Many synthetic methods mediated by transition metals have been developed for the construction of lactone and lactam frameworks, and new reactions are still being discovered.[1,2] This holds true for catalytic as well as stoichiometric carbonylation routes. The latter are of particular interest if the synthesis of molecules can be approached by sequential transformations. In a series of papers, Liu and co-workers reported on the chemistry and application of alkynyl-, allyl- and propargyltungsten compounds for the synthesis of heterocyclic compounds.[3−6] For instance, propargyltungsten compounds were reported to undergo facile proton-catalyzed alkoxycarbonylation to yield (η^3-γ-, -δ-, and -ε-lactonyl)tungsten compounds, which subsequently were cleaved to furnish α-methylenebutyrolactones.[7]

Recently, we reported on novel reaction cascades of β-[dicarbonyl(cyclopentadienyl)iron]-substituted (*Z*)-enals **1** with electron-rich primary amines,[8,9] metal hydrides,[10] and C-nucleophiles (Grignard reagents, organolithium compounds),[11] opening up a flexible approach to either five-membered lactam or lactone skeletons.[12] Thus, metal alkoxides are formed by the initial attack of nucleophiles at the aldehyde functionality of these iron compounds, and because of their close proximity to the iron moiety, reaction cascades are initialized by a subsequent carbonylation reaction. Particularly notable are those reaction cascades including unprecedented reduction steps involving (π-alkene)-hydridoiron intermediates. For example, saturated γ-lactones **3** were obtained from **1** and K-Selectride upon hydrolysis.[10] Our attempts to synthesize β-[dicarbonyl(cyclopentadienyl)iron]-substituted azadienes from **1** and electron-rich primary amines by the Weingarten procedure[13,14] resulted in the formation of dihydropyrrolones **4**.[8,9] These are formed in a titanium-mediated intra-

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MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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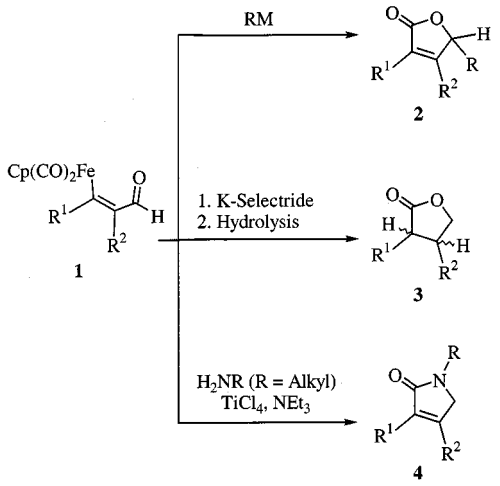
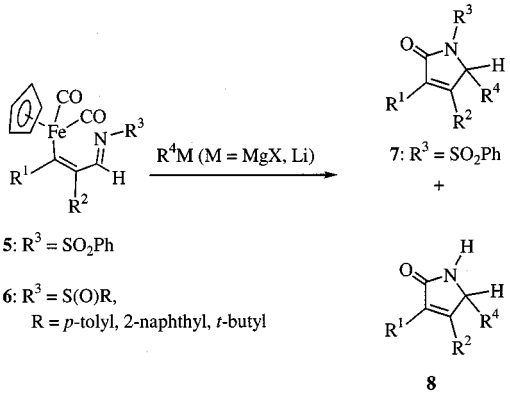
molecular cyclocarbonylation, followed by reduction − involving (π-alkene)hydridoiron intermediates − of the hemiaminal functionality. Scheme 1 outlines the synthetic strategies that seem to be especially suitable for ring-annulated target compounds.[12]



Scheme 1

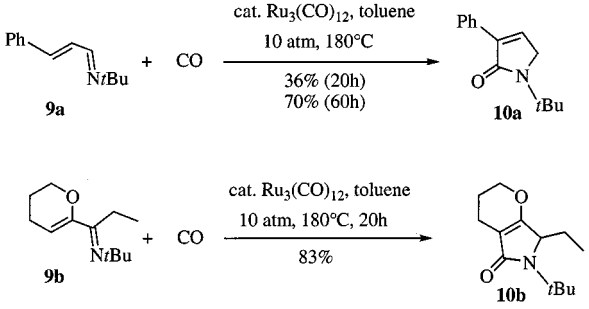
In experiments conducted with acceptor-substituted amino compounds such as aniline or benzenesulfonamide, the initially formed titanium hemiaminals proved to be less activated toward intramolecular carbonylation, and the corresponding azadienes were obtained exclusively.[8,9] In this paper, our results on the development of reaction cascades leading to 5-substituted α,β-unsaturated γ-lactams **7** and **8** from β-[dicarbonyl(cyclopentadienyl)iron]-substituted α,β-unsaturated *N*-sulfonyl- and *N*-sulfinylimines **5** and **6** are summarized (Scheme 2).[15]



Scheme 2

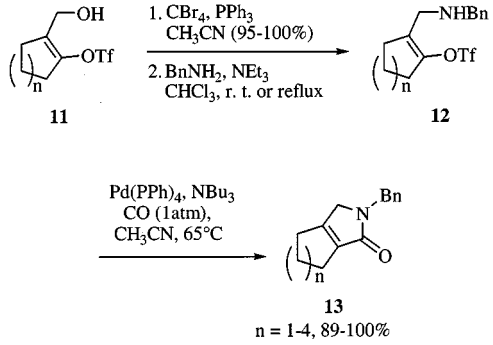
γ-Lactam units are important nitrogen-heterocyclic moieties for pharmaceutical applications.[16] Reactions mediated by transition metals open up many different routes for the construction of lactam skeletons.[2,17] For example, Ley et al. extensively studied the reactions of (π-allyl)iron complexes derived from vinyl epoxide for the synthesis of β-lactone and β-lactam derivatives by demetallation with ceric ammonium nitrate.[18] Alternatively, a carbonylation procedure was developed for the construction of δ-lactones. These strategies have been applied to a number of natural product syntheses. Synthetic approaches to (π-allyl)tricarbonyl(lactam)iron complexes for the synthesis of γ-lactams and of δ-lactams were also explored.[18] Besides such more broadly applicable methods, numerous other, more specific or restricted methodologies were developed. For instance, Rudler et al. reported the synthesis of substituted 2- and 3-pyrrolinones from [(*N*-benzyl-*N*-methylamino)carbene]- or [*N*-allyl-*N*-methylamino)carbene]chromium complexes and alkynes by a rearrangement involving the migration of the benzyl or the allyl group from the nitrogen to the carbon atom.[19]

Recently, Murai et al. reported an $Ru_3(CO)_{12}$-catalyzed carbonylation of α,β-unsaturated *N*-(*tert*-butyl)imines **9** at 180 °C in toluene, leading to α,β-unsaturated γ-lactams **10** (Scheme 3).[20] When imines with an *i*Pr, *n*Bu, or *p*-Me-OC_6H_4 residue on the imino nitrogen atom were employed, no γ-lactam formation was observed.



Scheme 3

Also, annulated dihydropyrrolones **13** have been prepared by the palladium-catalyzed reaction of γ-amino-functionalized vinyl triflates **12** with carbon monoxide (Scheme 4).[21] The aminovinyl triflates were prepared from the corresponding alcohols by treatment with carbon tetrabromide and triphenylphosphane in acetonitrile (95−100%), followed by nucleophilic substitution with benzylamine (37−70%).



Scheme 4

Synthesis of 5-Substituted *N*-Sulfonyl-γ-lactams

Since electrophilic *N*-(arylsulfonyl)imines undergo clean reactions with various Grignard and organolithium compounds,[22,23] we investigated the synthesis of 5-substituted dihydropyrrolones from β-[dicarbonyl(cyclopentadienyl)iron]-substituted α,β-unsaturated *N*-sulfonylimines.[15] Major limitations are, however, the harsh reaction conditions

that have to be employed to remove the *N*-(arylsulfonyl) group.[24] The *N*-sulfonylimines **5** are accessible in moderate to good yields (66% to quant.) from benzenesulfonamide, an acceptor-substituted amino compound, and iron-substituted (*Z*)-enals **1** by the use of titanium tetrachloride and triethylamine (Scheme 5).[8,9,15a] Purification was effected by recrystallization, as decomposition was observed during silica gel chromatography.[25] The X-ray crystal structure analyses for **5a** and **5b** are shown in Figure 1 and Figure 2.[26,27] The *N*-sulfonylimines exist as the (*E*)-imine isomers and adopt an *s-trans* conformation around the (C=C)−(C=N) single bond. For the cyclopentene derivative **5a**, shorter Fe−C, C=C and (C=C)−(CH=N) bond lengths and a longer C=N bond length are observed in the solid state compared to **5b**. Thus, it is concluded that the resonance of the azadiene unit observed in **5a** is weaker. Therefore, **5a** would be expected to be the more rigid and less flexible of the two *N*-sulfonylimines.

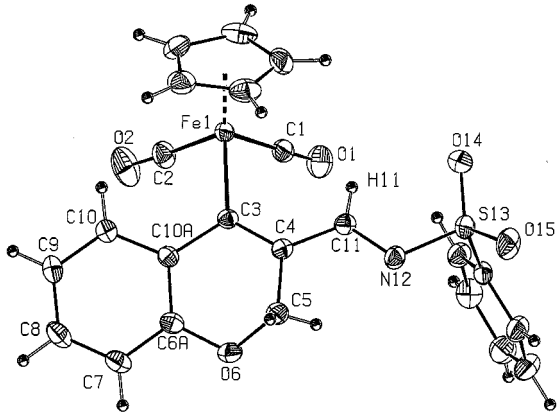
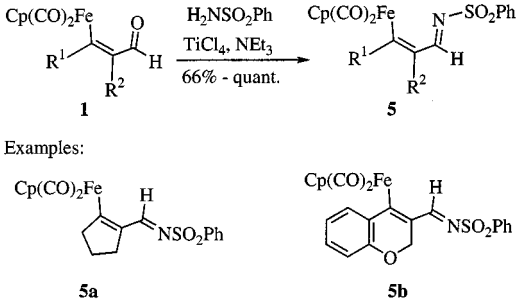


Figure 2. Crystal structure of *N*-sulfonylimine **5b**; selected bond lengths [Å] and angles [°]: Fe−C3 2.021(2), C3−C4 1.369(3), C4−C11 1.431(3), C11−N12 1.289(3), C11−H11 0.885(3), N12−S13 1.658(2), Fe−C2 1.766(3), C2−O2 1.141(4), Fe−C1 1.761(3), C1−O1 1.135(4); Fe−C3−C4 125.3(2), C3−C4−C11 124.8(2), Fe−C3−C4−C11 −1.9(2), C3−C4−C11−H11 −0.7(2)



Scheme 5

We found that the imines **5c−e** (see Scheme 2, Table 1) gave the corresponding 5-substituted γ-lactams **7** on treatment with organolithium reagents (method A: MeLi, *n*BuLi) or RMgCl (method B: R = allyl, *n*Pr) upon prolonged stirring at room temperature.[15a] Also, the allylation of the *N*-sulfonylimine **14** (derived from bornane-10-sulfonamide) was investigated, γ-lactam **15** being obtained in 39% yield (Table 1, Entry 4).

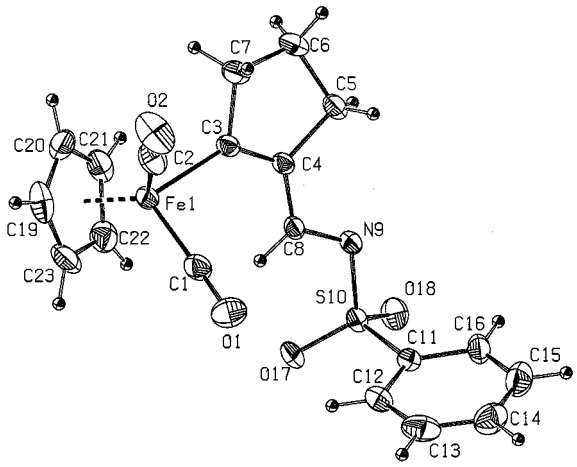


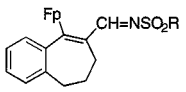
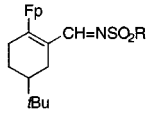
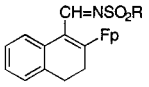
Figure 1. Crystal structure of *N*-sulfonylimine **5a**; selected bond lengths [Å] and angles [°]: Fe−C3 1.981(3), C3−C4 1.358(4), C4−C8 1.416(4), C8−N9 1.303(4), C8−H8 0.930(4), N9−S10 1.645(3), Fe−C2 1.762(5), C2−O2 1.146(6), Fe−C1 1.757(4), C1−O1 1.132(5); Fe−C3−C4−C8 3.4(4), C3−C4−C8−H8 4.6(4)

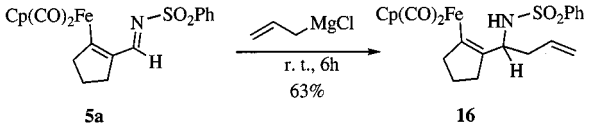
From the cyclopentene derivative **5a** and allylmagnesium chloride, the 1,2-adduct **16** was isolated exclusively, in 63% yield (Scheme 6). Similarly, for reactions of the β-[dicarbonyl(cyclopentadienyl)iron]-substituted cyclopentene-1-carbaldehyde with metal hydrides, the 1,2-addition reaction was the sole one observed; no further transformations starting with a carbonylation process took place.[10] Allyl addition to **5d** at room temperature in CH_2Cl_2 afforded the γ-lactam **7e** in only 19% yield (Table 1, Entry 6, method B). For this example, the influence of higher temperatures on the course of the reaction cascade was studied (Table 1, Entry 7, method C). By raising the temperature to 50 °C in 1,2-dichloroethane, the γ-lactam **7e** was obtained in good yield (75%). Presumably, the purely aliphatic substitution patterns of **5a** and **5d**, in addition to the rigidity of **5a** as concluded from the X-ray structure, are responsible for the reactivities observed at ambient temperature.

Surprisingly, treatment of **5e** (Table 1, Entries 8−10) with organometallic reagents gave the deprotected γ-lactams **8a−c** (ca. 1690 cm^{-1}), together with **7f−h** (1720−1730 cm^{-1}), in good overall yield. Furthermore, addition of an allylic Grignard compound to the chromene derivative **5b** gave the allyliron complex **17a**, resulting from ring-opening of the chromene framework, in 84% yield (Scheme 7). However, for reactions with *n*PrMgCl or *n*BuMgCl, even after a prolonged reaction time (3 d), incomplete turnover was observed and the corresponding allyliron complexes **17b** and **c** were isolated in low yield (18−24%). The structure of **17a** was elucidated by X-ray analysis.[15a]

In summary, yields around 40−55% of *N*-sulfonyl-γ-lactams **7** were generally obtained in these iron-mediated processes, even though these intramolecular reaction cascades are rather complex, and sterically demanding annulated *N*-sulfonylimines had been employed.[15a] Higher temperature was successfully applied to achieve better turnover in the intramolecular cyclocarbonylation of the metal alkoxide de-

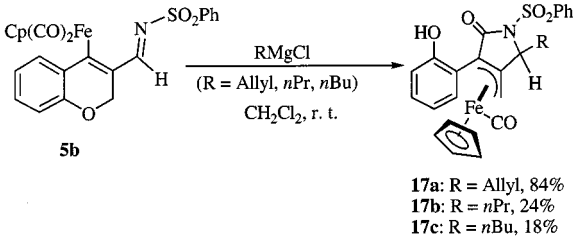
Table 1. Synthesis of 5-substituted dihydropyrrolones **7** from iron-substituted *N*-sulfonylazadienes **5** and organometallic reagents

Entry	Reactant	R	No.	Method	R'M	Products / Yields 7	[%]	8	[%]
1		Ph	**5c**	A	*n*BuLi	**7a**	43%	–	–
2		Ph	**5c**	A	MeLi	**7b**	54%	–	–
3		Ph	**5c**	B	AllylMgCl	**7c**	42%	–	–
4		**14**	B	AllylMgCl	**15**	39%	–	–	
5		Ph	**5d**	A	*n*BuLi	**7d**	36%	–	traces
6		Ph	**5d**	B	AllylMgCl	**7e**	19%	–	–
7		Ph	**5d**	C	AllylMgCl	**7e**	76%	–	–
8		Ph	**5e**	B	AllylMgCl	**7f**	37%	**8a**	41%
9		Ph	**5e**	B	*n*PrMgCl	**7g**	25%	**8b**	25%
10		Ph	**5e**	A	MeLi	**7h**	44%	**8c**	56%



5a **16**

Scheme 6



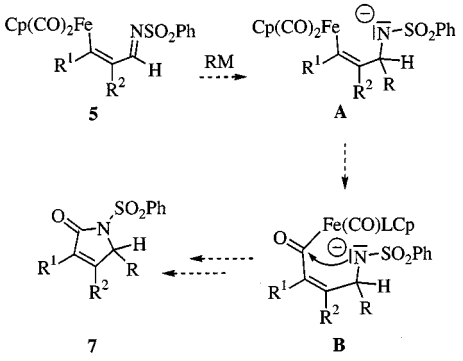
5b

17a: R = Allyl, 84%
17b: R = *n*Pr, 24%
17c: R = *n*Bu, 18%

Scheme 7

rived from **5d** and allylmagnesium chloride (Table 1). The generality of this result, however, has yet to be explored.

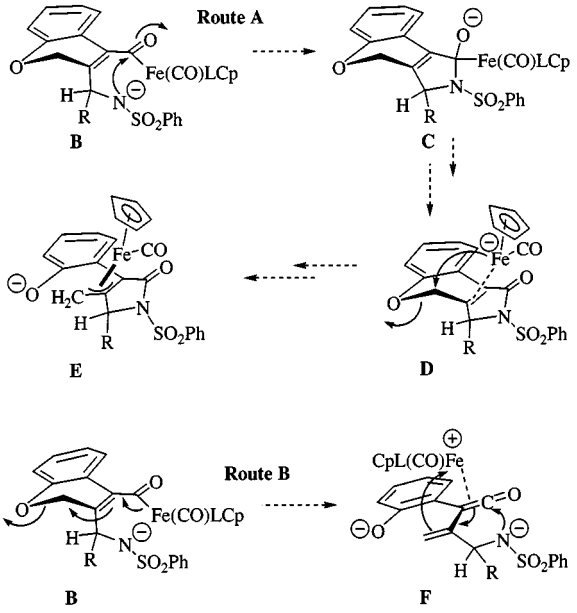
The experiments described are in agreement with the mechanistic discussion shown in Scheme 8 and Scheme 9. Either CO insertion, followed by aminolysis of the acyliron intermediate, or attack of the metallated amide at a coordinated molecule of carbon monoxide has to be considered as the carbonylation step.[9,10] Only for the reaction of **5d** with *n*BuLi was the appearance and disappearance of a new absorption at 1853 cm^{-1} observed in the IR monitoring. For an anionic ferrilactam intermediate, one might expect an absorption for the carbonyl ligand in this region. In all the other examples examined, new absorptions appeared at 1950−1990 cm^{-1} and at 1640−1660 cm^{-1}, attributed to intermediate acyliron complexes. Therefore, the carbonylation step in Scheme 8 and Scheme 9 is shown to proceed via the acyliron species **B**. No major differences were observed between the reactions of Grignard and organolithium compounds. The absorptions around 1720−1730 cm^{-1} of the *N*-sulfonyl-γ-lactams **7** were always determined by IR monitoring prior to aqueous workup.[15]



5 **A** **7** **B**

Scheme 8

Of importance for the mechanistic studies is the formation of the allyliron complex **17a** from the chromene-derived *N*-sulfonylimine **5b** (Scheme 7).[15a] To date, it was postulated that anionic (π-alkene)iron intermediates, such as **D** (Scheme 9, Route A), were formed after reductive elimination in the reaction cascades of iron-substituted (*Z*)-enals **1** with nucleophiles, providing the best explanation for the experimental results (e.g. the observed reduction steps involving hydridoiron intermediates).[8−10] The origin of **17** could be explained mechanistically by an intramolecular nucleophilic substitution reaction resulting from the attack of the anionic iron moiety at the neighboring methylene group (see **D** in Scheme 9).[15a] A similar opening of the chromene ring, resulting from an internal S_N2 process by a



Scheme 9

(π-alkene)hydridoiron intermediate and furnishing a demetallated α,β-butenolide, was proposed in previous studies.[10]

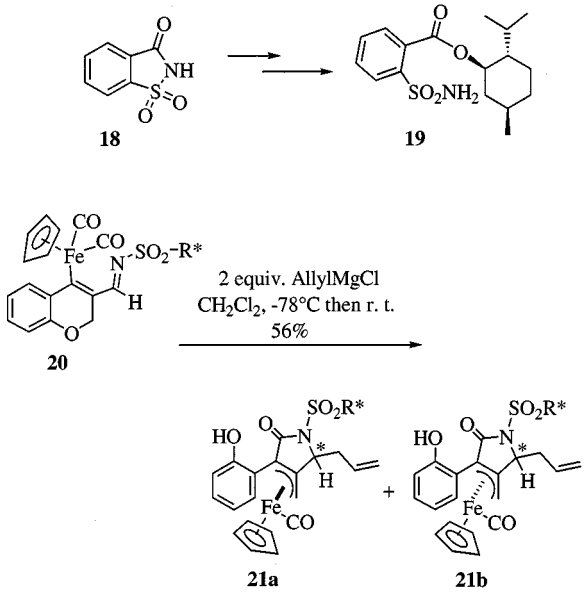
Alternatively, a keteneiron complex **F** (Scheme 9, Route B) could be formed from **B**. Subsequent attack of the metallated amide on the complexed ketene would lead to **E** and to the allyl complex observed after hydrolysis.[15a]

The formation of *N*-unsubstituted γ-lactams **8a−c** in the reaction of the highly reactive iron compound **5e** with organometallic reagents (Table 1, Entries 8−10) could be attributed to the removal of the phenylsulfonyl group by an iron-mediated redox process during hydrolysis, involving the electron-rich iron fragment remaining after the ring closure, hence furnishing the γ-lactam moiety.[15a] This observation led us to investigate reactions with *N*-sulfinylimines, since one advantage of this class of compound is the smooth cleavage of the N−S bond in sulfinamides.[15b] The extension of these reaction cascades to the asymmetric synthesis of 5-substituted γ-lactams seemed appealing, too. However, preliminary experiments led to the synthesis of chiral γ-lactams from chiral *N*-sulfonylimines.

Synthesis of Chiral 5-Substituted γ-Lactams

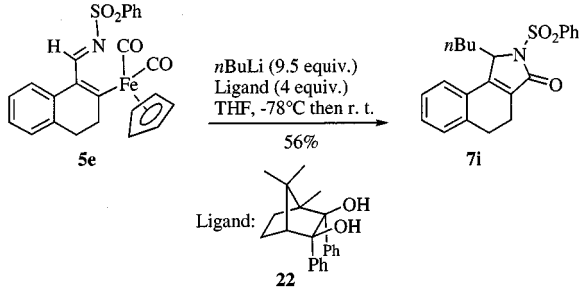
The development of stereoselective syntheses of optically active amines from imines has in the past been a major challenge for organic chemists.[28,29] Generally, the chirality is incorporated via the residue on the imino nitrogen atom, and thus a number of enantiopure amines have been employed in the 1,2-addition of nucleophiles to C=N double bonds.[28] Restricted to the application of electron-poor amino compounds for the synthesis of β-[dicarbonyl(cyclopentadienyl)iron]-substituted azadienes, we decided to investigate a chiral sulfonamide as a chiral auxiliary.[8,9][15a]

The chiral benzenesulfonamide **19** was derived from saccharin **18** and (−)-menthol in two steps. The imine **20** was synthesized in 53% yield.[15a] Addition of an allylic Grignard compound gave a 1:1 mixture of the two diastereomeric ring-opened allyliron complexes **21** (Scheme 10), in 56% overall yield. A diastereomeric ratio of 76:24 was determined for the newly formed chiral centers in **21a** and **21b** by ^{1}H NMR spectroscopy.[15a]



Scheme 10

An addition, mediated by a chiral ligand, of *n*BuLi to **5e** was investigated too. According to the work of Itsuno et al., the alkylation of *N*-(trimethylsilyl)benzaldimine with a modified chiral organometallic reagent derived from 2 equiv. of alcohol **22** and *n*BuLi provided a direct route to the optically active primary amine product, in 76% yield and with an enantiomeric excess of 62%.[29] When applying this protocol to the *N*-sulfonylimine **5e** (Scheme 11), the reaction cascade yielded the γ-lactam **7i** in 56% yield. However, a racemic mixture was obtained.



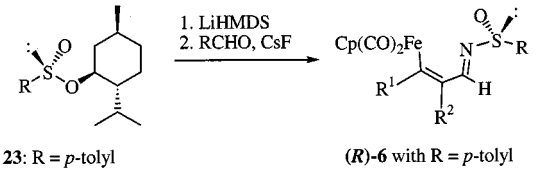
Scheme 11

Application of *N*-Sulfinylimines

Studies by Davis and others have demonstrated that enantiopure sulfinylimines are versatile chiral building blocks for organic synthesis.[30,31] Addition of organometallic reagents to the C=N bond provides sulfinamides diastereoselectively, and hydrolysis of these gives primary amines.[32−36] Addition reactions of allylmagnesium bromide to (*p*-tolylsulfinyl)imines in ether at 0 °C were reported by Hua et al.

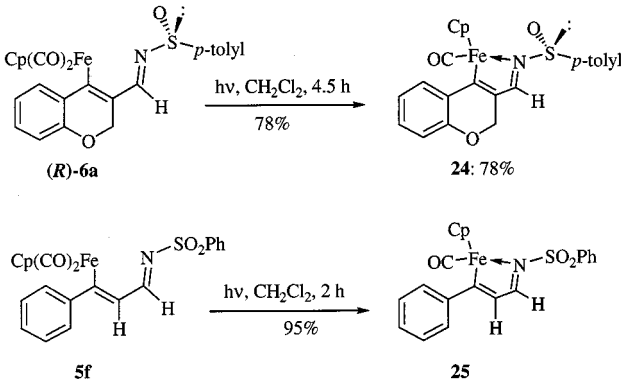
to proceed with high diastereoselectivities (82−98% *de*).[32] Yang et al. employed sulfinylimines bearing a camphor-derived mercapto auxiliary to prepare enantiopure amines with high diastereofacial selectivity (82−96% *de*).[33] The *N*-sulfinyl group activates the C=N double bond and in addition is a powerful stereodirecting group. A chair-like transition state, involving chelation of the oxygen atom at the sulfinyl group, has been proposed for the allylation procedure.[30−36] Moreau et al. investigated the reaction of alkyl Grignard reagents (R = Me, Bn) with (*p*-tolylsulfinyl)-imines.[34] Moderate diastereoselectivities (60−74% *de*) were achieved with BnMgCl, whereas MeMgCl furnished the methyl *p*-tolyl sulfoxide, due to reaction at the sulfur atom. A loss of selectivity is reported for reactions in polar solvents, as well as at higher temperatures, and an influence of the order of addition has also been observed.[34] Recently, the highly diastereoselective addition of Grignard reagents to (*tert*-butylsulfinyl)imines and the trimethylaluminium-mediated 1,2-addition of organolithium reagents to *N*-(*tert*-butylsulfinyl) ketimines has been reported by Ellman et al.[35,36]

Following the one-pot procedure of Davis et al.,[31] the commercially available Andersen reagent (i.e. **23**, Scheme 12), was treated first with 1.5 equiv. of lithium bis-(trimethylsilyl)amide at −65 °C, and then with the iron-substituted (*Z*)-enals **1** (1 equiv.) in the presence of cesium fluoride to yield the optically active (*p*-tolylsulfinyl)imines **6** in 48−62% yield after chromatography.[15b] IR spectroscopy showed characteristic absorptions of the *N*-sulfinylimines at about 2020, 1970 (CO ligands), and 1540−1565 (C=N) cm^{-1}. For the sulfinyl aldimine **6b** (Table 2), a mixture of (*E*)- and (*Z*)-imine isomers was observed by ^1H and ^{13}C NMR spectroscopy in $CDCl_3$ (ratio = 55:45). For *tert*-butylsulfinyl ketimines, formation of (*E*)-/(*Z*)-imine isomers and rapid (*E*)/(*Z*) interconversion has been reported.[35] However, because of the rapid (*E*)/(*Z*) interconversion, diastereoselective addition reactions with product ratios exceeding the initial (*E*)/(*Z*) ratios have still been possible.



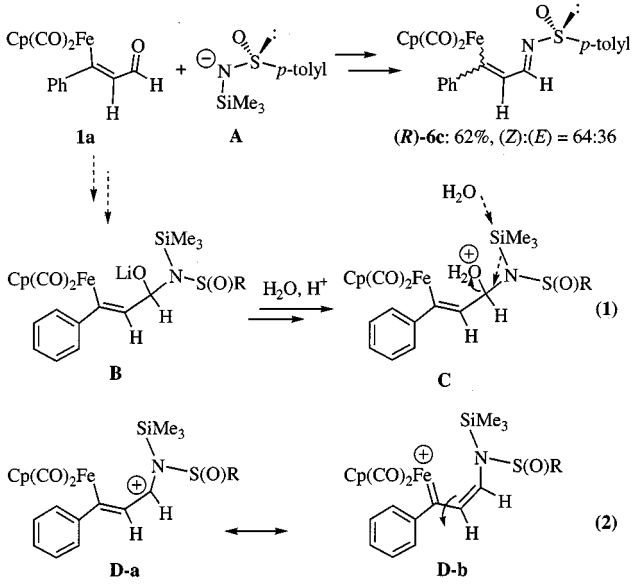
Scheme 12

The (*p*-tolylsulfinyl)imines **6** are amorphous solids, that can be handled in air and stored at −22 °C without any sign of decomposition. However, it should be noted that all procedures have to be carried out in the dark, since the compounds proved to be light-sensitive.[37] To obtain analytically pure material, the (*p*-tolylsulfinyl)imines had to be chromatographed quickly. Exposure of solutions of **6** to sunlight led to a gradual change in color, from yellow-orange to dark brown, and at the same time, a new spot of higher R_f value was observed by TLC monitoring. For several compounds, these newly formed species were identified as the metallacycles formed by release of carbon monoxide. The metallacycle **24** (54:46 diastereomeric ratio) was obtained in 78% yield from (*R*)-**6a** by irradiation of a solution of the compound in dichloromethane with a medium-pressure mercury lamp at room temperature (Scheme 13).[15b] Since the formation of metallacycles proceeds easily and smoothly, the participation of the sulfinyl group in the course of the reaction is expected. In contrast, *N*-sulfonylimines are less sensitive to sunlight and the formation of metallacycle **25** is observed only upon irradiation with a medium-pressure mercury lamp, as shown for **5f** in Scheme 13.[37]



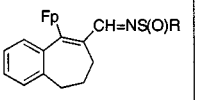
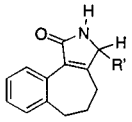
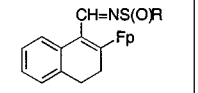
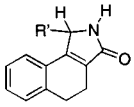
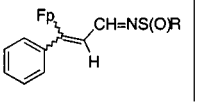
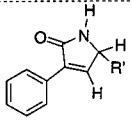
Scheme 13

During the conversion of the acyclic β-[$Cp(CO)_2Fe$]-substituted (*Z*)-enal **1a** into the sulfinylimine (*R*)-**6c**, (*Z*)/(*E*) isomerization about the C=C double bond was observed, leading to an inseparable 64:36 mixture of (*Z*) and (*E*) isomers in 62% yield. Davis et al. proposed that the sulfinylimines are formed by a Peterson-type olefination reaction initialized by the reaction of silylsulfinamide anion **A** with the aldehydes (see Scheme 14, Equation 1).[31] The formation of the (*Z*)/(*E*)-isomeric mixture from (*Z*)-**1a** can be explained by a carbocation intermediate **D** being involved in a stepwise, acid-catalyzed elimination process during hydrolysis with aqueous ammonium chloride solution. For the carbo-



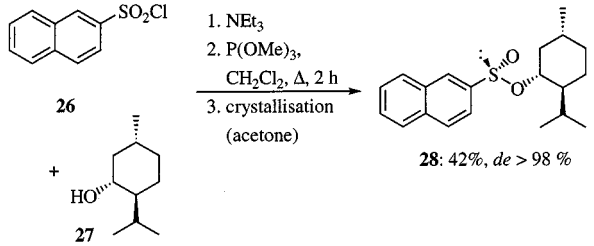
Scheme 14

Table 2. Synthesis of 5-substituted dihydropyrrolones **8** from *N*-sulfinylazadienes **6** and organolithium or Grignard reagents

Entry	Reactant	R	No.	R'M	Product	No.	Yield [%]	*ee* [%]
1		*p*-tolyl	(*R*)-**6b**	AllylMgCl		**8d**	64%	40%
2		*p*-tolyl	(*S*)-**6b**	AllylMgCl		**8d**	63%	42%
3		2-naphthyl	(*R*)-**6d**	AllylMgCl		**8d**	63%	40%
4		*p*-tolyl	(*R*)-**6b**	BnMgCl		**8e**	27%	62%
5		*p*-tolyl	(*R*)-**6e**	AllylMgCl		**8a**	66%	52%
6		*tert*-butyl	(*R*)-**6f**	AllylMgCl		**8a**	55%	38%
7		*tert*-butyl	(*R*)-**6f**	MeLi		**8c**	91%	10%
8		*p*-tolyl	(*R*)-**6c**	AllylMgCl		**8f**	55%	66%

cation intermediate **D**, resonance stabilization involving the iron fragment is expected, leading to a cationic ironcarbene intermediate (resonance structure **D-b**) and thus to free rotation around the former C=C double bond (Scheme 14, Equation 2).

Similarly to the (*p*-tolylsulfinyl)imines, the (*R*)-configured (2-naphthylsulfinyl)imine (*R*)-**6d** [Table 2, (*E*)-/(*Z*)-imine isomeric mixture; ratio = 55:45] was obtained in 46% yield starting from (1*R*,2*S*,5*R*)-(−)-menthyl (*R*)-2-naphthalenesulfinate **28** (Scheme 15).[38,39] For **28**, the absolute configuration at the sulfur atom was established by X-ray analysis (Figure 3).[39] This sulfinate has been synthesized previously by Sharpless et al., but the sulfur configuration was not determined.[38]



Scheme 15

The β-[Cp(CO)$_2$Fe]-substituted *N*-(*tert*-butylsulfinyl)imine (*R*)-**6f** (Table 2) was available, analytically pure and in 65% yield, from [Cp(CO)$_2$Fe]Na and the β-bromo-substituted precursor imine.[15b] The latter was prepared from (*R*)-*tert*-butylsulfinamide and the corresponding β-bromo-substituted (*Z*)-enal in the presence of Ti(OEt)$_4$ in quantitative yield.

Since the (*p*-tolylsulfinyl)imines derived from iron-substituted (*Z*)-enals **1** are insoluble in diethyl ether, the reactions with allylmagnesium chloride were carried out in CH_2Cl_2. When performing the allyl additions, the corresponding *N*-

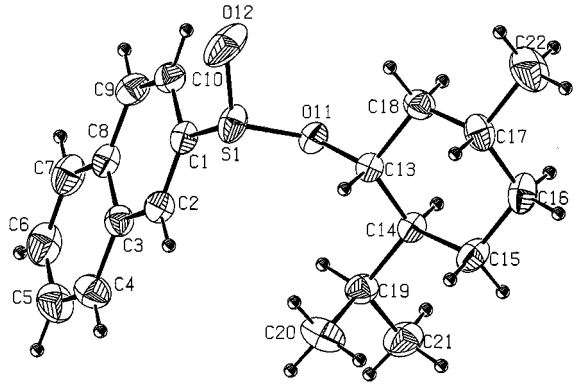


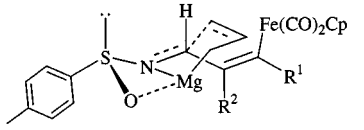
Figure 3. Crystal structure of **28**; selected bond lengths [Å] and angles [°]: S−C1 1.793(3) S−O12 1.458(3) S−O11 1.6126(18) O11−C13 1.473(3); O12−S−O11 108.8(2), O11−S−C1 94.4(1), O12−S−C1 106.3(2)

unsubstituted γ-lactams **8** in Table 2 were formed exclusively in 55−66% yield.[15] The reactions with (*p*-tolylsulfinyl)-imines, summarized in Table 2, proceeded smoothly and with a high degree of regioselectivity, as the nucleophile attacks solely the imine carbon atom (1,4-addition) and not the sulfur or iron carbon atom (1,2- and 1,6-addition). As expected, the reaction of **6b** with *n*PrMgCl furnished *n*-propyl *p*-tolyl sulfoxide in 95% yield, due to the exclusive attack of the Grignard reagent at the sulfur atom.

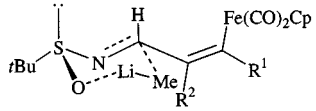
For the reactions summarized in Table 2, the enantiomeric excesses were determined by ^{1}H NMR shift experiments with Eu(hfc)$_3$ to be 40−66%. The stereoselectivity varied, depending upon the substitution pattern of the *N*-(*p*-tolylsulfinyl)imines **6**. The best results were obtained with the acyclic compound **6c** (Table 2, Entry 8). It turned out that a larger substituent at the sulfur atom, such as the 2-naphthyl residue in (*R*)-**6d** or the *tert*-butyl group in (*R*)-**6f**, did not improve the stereoselectivity. The addition of

BnMgCl to (*R*)-**6b** in toluene was carried out according to the procedure of Moreau et al.,[34] to yield **8e** in only 27% yield and 62% *ee* (Table 2, Entry 4), because of radical side reactions.[41] The methyl-substituted γ-lactam **8c** could be prepared in 91% yield but with low enantioselectivity (10% *ee*) using MeLi in THF, following a protocol published recently by Ellman et al.[35,36] (Table 2, Entry 7).

Generally, the 1,2-asymmetric induction observed in allyl additions to (*p*-tolylsulfinyl)imines and in addition reactions of organometallic reagents to *N*-(*tert*-butylsulfinyl)imines is explained by six-membered, chair-like transition states.[32,35,36] For the addition of BnMgCl to *N*-sulfinylimines, acyclic transition states have been proposed.[34,41] Possibly because of the steric demand of the annulated frameworks with the iron moiety in the β-position in, for example, **6b** or **6f**, the transition states **A** and **B** depicted in Scheme 16 are destabilized, resulting in lower stereoselectivities. For compound **8c** (Table 2, Entry 7), the absolute configuration of the major enantiomer was confirmed as (*S*) by comparison of the optical rotation value with data obtained from optically pure material synthesized by a palladium-catalyzed cyclocarbonylation route.[15b]



A



B

Scheme 16

Similarly to the mechanisms proposed for *N*-sulfonylimines, the reaction cascades starting from *N*-sulfinylimines presumably proceed via an acyliron intermediate (Scheme 8). After ring closure, the remaining electron-rich or even negatively charged iron fragment is postulated during hydrolysis to mediate the cleavage of the N−S bond by redox processes, leading to the exclusive formation of the deprotected γ-lactams **8**. A hydridoiron species could also be involved in these processes.[9,10] The cleavage is in accordance with the expected reactivity of *N*-acyl-*p*-toluenesulfinamides toward nucleophilic attack at the sulfur atom.[42] As a by-product, ferrocene was obtained. The structure of sulfur-containing by-products could be elucidated by comparison of the NMR spectroscopic data for crude product mixtures with literature data for sulfenic acids and their decomposition products.[15b,43−45] Hence, the thiosulfonate *p*-tolyl−SO_2−S−*p*-tolyl,[44] the thiosulfinate *t*Bu−S(O)S−*t*Bu, and the sulfinic acid *t*BuSO_2H were identified.[45]

Conclusion

We were able to show that *N*-sulfonylimines **5**, which are available from β-[Cp(CO)$_2$Fe]-substituted (*Z*)-enals **1** and benzenesulfonamide, open up an access to 5-substituted dihydropyrrolones **7** upon treatment with Grignard and organolithium reagents. The formation of the allyliron complexes **17** and **21** can be explained by nucleophilic ring-opening of the chromene framework, involving the participation of anionic (π-alkene)iron complex intermediates or of keteneiron complexes in the reaction cascades. Non-*N*-protected γ-lactams **8** are formed exclusively from chiral *N*-sulfinylimines. So far, in reactions with *p*-tolyl-, 2-naphthyl-, and *tert*-butyl-substituted sulfinylimines, only moderate stereoselectivities have been observed, possibly because of the bulky annulated compounds employed.

Acknowledgments

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[26] Crystallographic data for **5a**: $C_{19}H_{17}FeNO_4$; M_r = 411.25; μ = 7.693 mm^{-1} (corrections with ψ scans); $F(000)$ = 848, d_x = 1.456 gcm^{-3}, monoclinic, $P2_1/n$, a = 11.5788(4), b = 12.5046(2), c = 13.1860(2) Å, β = 100.733(4)°, V = 1875.78(8) Å^3 from 50 reflections (63° < θ < 73°), yellow-brown square, 0.26 × 0.45 × 0.77 mm. Cell dimensions and intensities were measured at 298 K with a CAD4 (Enraf−Nonius) diffractometer with graphite-monochromated Cu-K_α radiation (scan type: ω/2θ). 1.5° ≤ θ ≤ 75.0°; 0 ≤ h ≤ 14; 0 ≤ k ≤ 15; −16 ≤ l ≤ 16. Of 3852 measured reflections (with Friedel pairs), 3852 were unique and 3226 observed [$|F|/\sigma(F) > 4.0$]; R_σ for 3852 equivalent reflections is 0.0277. Data were corrected for Lorentz and polarization effects. The structure was solved by direct methods (SIR 92). Full-matrix, least-squares refinements (SHELX-93) based on F^2 using weight of $1/[\sigma^2(F_o^2) + (0.0998{\cdot}P)^2 + (0.717{\cdot}P)]$ with $P = [\mathrm{Max}(F_o^2,0) + 2{\cdot}F_c^2]/3$ gave final values $wR2$ = 0.1532 ($R1$ = 0.0548 for obsd. rflns.). All nonhydrogen atoms were refined anisotropically. A riding model starting from the calculated positions for the hydrogen atoms was employed. The final difference electron density map showed a minimum of −0.539 and a maximum of 0.71 eÅ^{-3}. Crystallographic data for **5a** have been deposited with the Cambridge Crystallographic Data Base (deposition no. CCDC-137180). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

[27] Crystallographic data for **5b**: $C_{23}H_{17}FeNO_5S$; M_r = 475.29; μ = 0.877 mm^{-1}; $F(000)$ = 976, d_x = 1.546 gcm^{-3}, monoclinic, $P2_1/c$, a = 14.5301(9), b = 11.7811(5), c = 12.185(1) Å, β = 101.752(6)°, V = 2042.1(2) Å^3 from 75 reflections (25° < θ < 27°), yellow plate, 0.1 × 0.5 × 0.6 mm. Cell dimensions and intensities were measured at 298 K on a CAD4 (Enraf−Nonius) diffractometer with graphite-monochromated Mo-K_α radiation (scan type: ω/2θ). 1.4° ≤ θ ≤ 30.0°; 0 ≤ h ≤ 20; 0 ≤ k ≤ 16; −17 ≤ l ≤ 16. Of 6025 measured reflections, 5902 were unique and 4201 observed [$|F|/\sigma(F) > 4.0$]; R_{int} for 5902 equivalent reflections is 0.0143. Data were corrected for Lorentz and polarization effects. The structure was solved by direct methods (SIR 92). Full-matrix, least-squares refinements (SHELX-93) based on F^2 using weight of $1/[\sigma^2(F_o^2) + (0.0665{\cdot}P)^2 + (0.720{\cdot}P)]$ with $P = [\mathrm{Max}(F_o^2,0) + 2{\cdot}F_c^2]/3$ gave final values $wR2$ = 0.1320 ($R1$ = 0.0478 for obsd. rflns.). All nonhydrogen atoms were refined anisotropically. A riding model starting from the calculated positions for the hydrogen atoms was employed. The final difference electron density map showed a minimum of −0.47 and a maximum of 0.68 eÅ^{-3}. Crystallographic data for **5b** have been deposited with the Cambridge Crystallographic Data Base (deposition no. CCDC-137181). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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[39] Crystallographic data for **28**: $C_{20}H_{26}O_2S$; M_r = 330.47; μ = 1.59 mm^{-1} (corrections with ψ scans); $F(000)$ = 356, d_x = 1.178 gcm^{-3}, monoclinic, $P2_1$, a = 9.2482(12), b = 10.1268(6), c = 10.2258(15) Å, β = 103.454(6)°, V = 931.4(2) Å^3 from 25 reflections (41° < θ < 43°), colorless plate, 0.032 × 0.384 × 0.448 mm. Cell dimensions and intensities were measured at 298 K with a CAD4 (Enraf−Nonius) diffractometer with graphite-monochromated Cu-K_α radiation (scan type: ω/2θ). 1.5° ≤ θ ≤ 75.0°; 0 ≤ h ≤ 11; 0 ≤ k ≤ 12; −12 ≤ l ≤ 12. Of 4154 measured reflections, 3693 were unique (with Friedel pairs) and 3340 observed [$|F|/\sigma(F) > 4.0$]; R_{int} for 3693 equivalent reflections is 0.0606. Data were corrected for Lorentz and polarization effects. The structure was solved by direct methods (SIR 92). Full-matrix, least-squares refinements (SHELXL-97) based on F^2 using weight of $1/[\sigma^2(F_o^2)+(0.0871{\cdot}P)^2 + (0.09{\cdot}P)]$ with $P = [\mathrm{Max}(F_o^2,0) + 2{\cdot}F_c^2]/3$ gave final values $wR2$ = 0.1415 ($R1$ = 0.0499 for obsd. rflns.). All nonhydrogen atoms were refined anisotropically. A riding model starting from the calculated positions for the hydrogen atoms was employed. The final difference electron density map showed a minimum of −0.19 and a maximum of 0.32 eÅ^{-3}. Crystallographic data for **28** have been deposited with the Cambridge Crystallographic Data Base (deposition no. CCDC-137182). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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