New Applications of *N*-Acyliminium Precursors: Tetracarbonyliron-Mediated Stereoselective Alkylations of 5-(*R*)-Isopropoxy-3-pyrrolin-2-ones

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Lewis acid catalyzed allylic substitutions with several nucleophiles at C-5 of the *cis*-tetracarbonyliron complexes of *N*-acetyl- and *N*-tosyl-5-(*R*)-isopropoxy-3-pyrrolin-2-ones occur highly regio- and stereoselectively. The results are interpreted as being indicative of the intermediacy of a (π-allyl)tetracarbonyliron cation, with possible preceding formation of an *N*-acyl- or an *N*-tosyliminium ion.

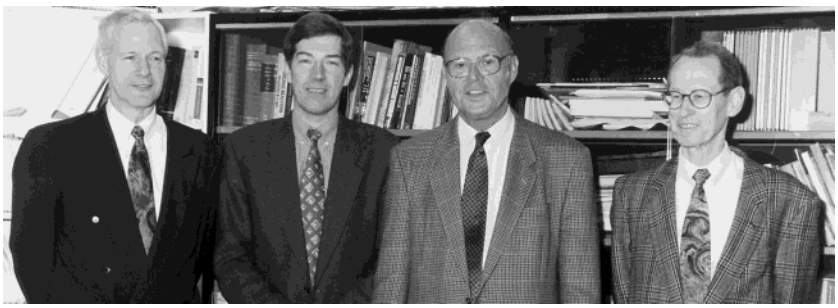
Introduction

The development of new methods of stereoselective synthesis is currently among the major objectives in organic chemistry. For stereoselective syntheses of nitrogen compounds and nitrogen-containing natural products application of *N*-acyliminium intermediates in the crucial bond formation is well established.[1] Diastereoselective addition

W. Nico Speckamp (1933) (second from right) studied chemistry at the University of Amsterdam, where he earned his Ph.D. in 1964 with Prof. H. O. Huisman. He was promoted to associate professor in 1971 and to full professor in 1980. His research interests include the development of new synthetic intermediates, the synthesis of bioactive molecules including natural products, and the study of cationic and radical reactions in heterocyclic synthesis. His work has been described in about 250 original papers and presented in over 40 plenary lectures at international meetings. Some of his more recent honours include: Guest professor at the University of Osaka (1989); Dupont Lecturer at the University of California, Berkeley (1991); ICI Americas Lecturer at the Ohio State University, Columbus (1992); First Ciba Lecturer Middle Europe (1993); Merck Swiss Lectureship (1994). In 1995 he was awarded the A. F. Holleman Prize of the Royal Dutch Academy of Sciences.

Henk Hiemstra (1952) (second from left) studied chemistry at the University of Groningen and received his Ph.D. degree in 1980 with Prof. H. Wynberg. After a postdoctoral stay at the University of Wisconsin, Madison, USA, with Prof. B. M. Trost, he joined the group of W. N. Speckamp at the University of Amsterdam in 1982, where he was strongly involved in the development of silyl-terminated cyclization reactions, adapted to the total synthesis of complex biologically active molecules such as peduncularine, biotin, and gelsemine. In 1997, he was appointed full professor in Synthetic Organic Chemistry. His present research interests include the development of new synthetic methods, transformations by transition metal catalysis and, in particular, the synthesis of bioactive natural products.

After 13 years of employment in the fragrance industry, Henk de Koning (1931) (far right) studied chemistry at the University of Amsterdam, where he obtained his Ph.D. in 1969 with Prof. H. O. Huisman. In 1983, he joined Nico Speckamp's group to work in the field of N-acyliminium chemistry until his retirement from the university in 1997.



Marinus J. Moolenaar (1945) (far left) joined the group of Professor Speckamp in 1983. The focus of his recent work includes the synthesis of natural products, such as biotin and epibatidine, utilizing N-acyliminium ion chemistry.

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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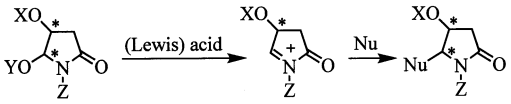
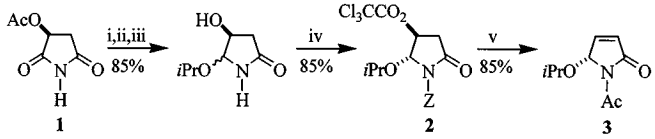
to *N*-acyliminium ions from chiral pool materials, such as hydroxyproline,[2] threonine,[3] tartaric acid,[4] and malic acid[5] are extensively studied and stereocontrol in these cases is exerted by the ring substituents of the cyclic *N*-acyliminium ions. Thus, in malic acid derived *N*-acyliminium ions the substituent OX (Scheme 1) is of major importance while also structure and nucleophilic character of the reagent have a distinct influence.[6]

Scheme 1



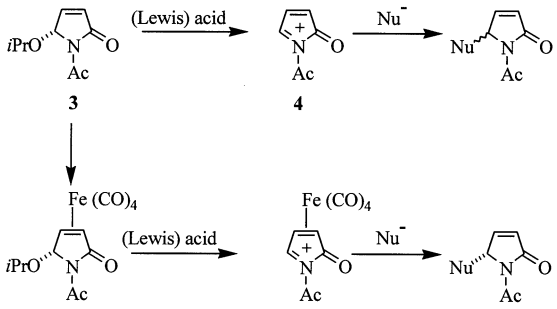
We have reported the synthesis of the multifunctional enantiopure synthon **3**[7][8][9] from the (*S*)-malic acid derived imide **1** (Scheme 2). The versatility of **3** lies in the electron-poor double bond which allows Diels-Alder reactions[7] and conjugate additions with amines,[10] thiols,[10] and carbon nucleophiles,[11] with high stereoselectivities. The 4-substituted 5-alkoxypyrrolidinones, thus obtained, can then be substituted at C-5 by *N*-acyliminium chemistry.

Scheme 2. Reagents and conditions: i: $LiBH_4$ (1.2 equiv.), THF, −20°C; ii: H_2SO_4, *i*PrOH; iii: MeOH, NaOMe (0.1 equiv.); iv: $(Cl_3CCO)_2O$ (1.05 equiv.), DMAP, (1.05 equiv.) Et_2O, −60°C → r. t.; v: Ac_2O, Py, DMAP (cat.)



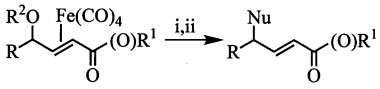
For particular applications in alkaloid total synthesis we wished to investigate the direct stereoselective substitution at C-5 of type **3** chiral enelactams. However, two major problems had to be solved. Firstly, substitution of the isopropoxy group at C-5 of enelactam **3** would proceed through the intermediacy of the achiral ion **4** (Scheme 3), thus producing racemic products. Secondly, in the presence of two electron-withdrawing groups at the nitrogen atom, formation of the cation at C-5 is very unlikely, because the nitrogen lone pair is not available for participation. Although the *N*-acyl substituent can be removed by treatment with amines, the resulting N−H enelactam is not suitable to perform the desired reactions. Due to the instability of the corresponding *N*-acyliminium ion only polymer formation occurs upon treatment with (Lewis) acid. In search of other possibilities to eliminate the influence of the second electron-withdrawing group, we considered formation of the tetracarbonyliron complex.[12] Although the metal atom is expected to draw electron density out of the double bond, the overall process could still be beneficial by backdonation of the metal atom to the ligand. Photoelectron spectra of carbonyliron complexes of alkenes with electron-withdrawing substituents indeed show a considerable net charge donation to the double bond.[13] Moreover, the metal complex would not only act as a protecting group, but also direct the approach of a nucleophile from the least hindered side, opposite to the metal atom, and the chirality would be retained.

Scheme 3



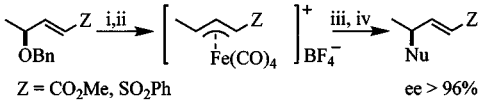
Recently, Green described regioselective allylic alkylations of γ-acetoxy-α,β-unsaturated carboxylic esters[14] and γ-benzyloxy-α,β-unsaturated ketones[15] via their respective tetracarbonyliron complexes. Upon addition of Lewis acid the (π-allyl)tetracarbonyliron cation is generated in situ and subsequently alkylated at the γ-position with silyl enol ethers to give the products after oxidative removal of the iron (Scheme 4).

Scheme 4. Reagents: i: $BF_3{\cdot}OEt_2$, Nu, CH_2Cl_2; ii: Me_3NO



Enders investigated similar reactions with enantiopure γ-benzyloxy-α,β-unsaturated carboxylic esters[16] and sulfones.[17] Upon diastereoselective complexation of the iron atom and conversion to the (η^3-allyl)tetracarbonyliron(1+) tetrafluoroborate, highly regio- and stereoselective reactions with several nucleophiles proceed in moderate to good yields with virtually complete chirality transfer and retention of the double bond geometry (Scheme 5). While only amino nucleophiles have been used for the carboxylic esters, nucleophiles for the sulfones included amines, silyl enol ethers, allylsilanes, electron-rich aromatic compounds, malonate ions, and (functionalized alkyl)zinc-copper reagents. Enders applied the reaction of enantiopure planar chiral tetracarbonyliron(1+) complexes with nucleophiles in the synthesis of various natural products.[18]

Scheme 5. Reagents: i: $Fe_2(CO)_9$, CO, Et_2O; ii: HBF_4, Et_2O; iii: Nu, CH_2Cl_2; iv: $(NH_4)_2Ce(NO_3)_6{\cdot}H_2O$



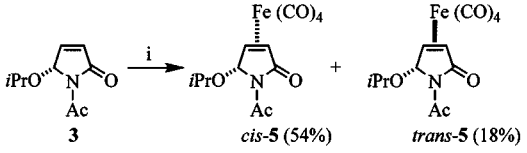
In this article we review our recent research of the iron-mediated chirality transfer in the alkylation of enantiopure 5-isopropoxy-3-pyrrolin-2-ones.

Preparation of Tetracarbonyliron Complexes of 1-Acceptor-Substituted 5-Isopropoxy-3-pyrrolin-2-ones

Stirring of the pyrrolinone **3** with nonacarbonyldiiron in diethyl ether or benzene under nitrogen in the dark at room temperature for 24 h afforded a 3:1 mixture of the moder-

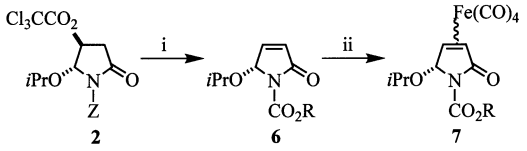
ately heat- and air-stable diastereomeric complexes *cis*-**5** and *trans*-**5**[9] in varying yields of 50−70% after flash chromatography (Scheme 6).[19][20] As after 3 h *cis*-**5** was the sole isomer present in about 30% (NMR), the eventual ratio 3:1 must be the result of a slow thermodynamic equilibration. Even after adding a larger excess of carbonyliron (> 5 equiv.) and prolonged stirring, the complexation reaction did not go to completion. An increasing amount of dodecacarbonyltriiron was formed instead. Presumably preferential formation of the *cis* complex has its origin in precoordination of tetracarbonyliron (formed by dissociation of nonacarbonyldiiron) to the C-5 oxygen substituent and subsequent delivery of the iron group to the double bond at the same side of the molecule. Preferred heteroatom-directed *cis* complexations of tetracarbonyliron are known in the literature.[21]

Scheme 6. Reagents and conditions: i: $Fe_2(CO)_9$ (2 equiv.), Et_2O, 18 h, r. t.



Two other types of *N*-protecting groups were also investigated, viz. *N*-alkoxycarbonyl and *N*-sulfonyl functions. The desired *N*-protected pyrrolinones could be easily obtained in good yields from the enantiopure trichloroacetate **2** upon treatment with base in the presence of acylating agents.[8]

Table 1. Reagents and conditions: i: A: $(tBuO_2C)_2O$ (2.2 equiv.), NEt_3 (2 equiv.), DMAP (0.1 equiv.), CH_2Cl_2, r. t.; B: $ClCO_2R$ (1.5 equiv.), DMAP (2.5 equiv.), CH_2Cl_2, r. t.; ii: $Fe_2(CO)_9$, Et_2O, r. t.



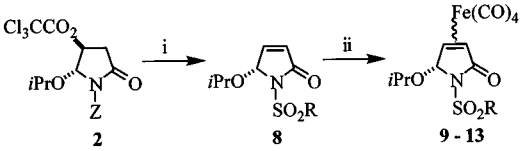
R (method)	Yield of **6** (%)[a]	Yield of **7** (%)[a]	ratio *cis*/*trans*
*t*Bu (A)	93	56	3:1
Ph (B)	73	28[b]	8:1
Cl_3CCH_2 (B)	85	17[b]	only *cis*
Allyl (B)	79	[c]	–
Et	[d]	20	3:1

[a] After column chromatography. – [b] Calculated from NMR; inseparable mixture with unreacted **6**. – [c] Complexes too unstable to be isolated. – [d] Prepared by another route (see ref.[20]).

From Table 1, it can be concluded that the iron complexes **7** of the *N*-alkoxycarbonyl compounds are not the reagents of choice. Yields are poor and the complexes are less stable than the *N*-acetyl compounds, due to insufficient electron-withdrawing properties of the alkoxycarbonyl group.

The stronger electron-withdrawing tosyl group, however, appeared to be very useful (Table 2, entry 1). The pure *cis* complex of **9** could be easily obtained in about 75% yield by column chromatography, providing a 85:15 *cis*/*trans* mixture, and subsequent recrystallization.[8][22] Likewise the 2-naphthalenesulfonyl-substituted complex **13** is obtained in reasonable yield with a high *cis*/*trans* ratio (entry 5).

Table 2. Reagents and conditions: i: A: Ts_2O (2 equiv.), LiHMDS (2−2.5 equiv.), THF, −20°C; B: as A using RSO_2Cl; ii: $Fe_2(CO)_9$, Et_2O, r. t.

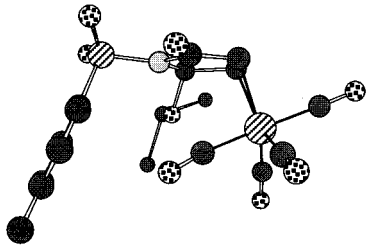


Entry	R (method)	Yield of **8** (%)[a]	Yield of complex (%)[a]	ratio *cis*/*trans*
1	*p*-Tolyl (A)	80[b]	**9** (90)	85:15
2	Mesityl (B)	43	**10** (25)[c]	only *cis*
3	2-Pyridyl (B)	43	**11** (30)[c]	5:1
4	1-Naphthyl (B)	41	**12** (32)[c]	7:2
5	2-Naphthyl (B)	49	**13** (64)[c]	15:1

[a] After column chromatography. – [b] See ref.[22]. – [c] Partly contaminated with unreacted **8**.

The complex *cis*-**9** showed the well-known[12b] upfield shifts of the double bond protons in ^1H NMR ($\delta \approx 2.5$) and of C-3 and C-4 in ^{13}C NMR ($\delta \approx 85$). The *cis* configuration was reflected by the coupling constant $J_{4,5} = 4.7$ Hz, clearly different from $J_{4,5} < 0.5$ Hz found for the *trans* complexes. An X-ray single-crystal structure determination unambiguously proved this assignment as well as the absolute configuration at C-5 (Figure 1).[23] It also revealed an elongation of the double bond from 1.32 Å in **8** to 1.40 Å. This fact, like the upfield shifts of the NMR resonances, points to a significant increase in the electron density of the double bond as a result of complexation to the iron atom.[13] One of the sulfonyl oxygen atoms, the sulfur atom, the nitrogen atom, and the ring carbonyl group are essentially in one plane, indicating electronic interactions between the sulfonyl group and the pyrrolinone ring.

Figure 1. Chem 3D™ sideview of *cis*-**9**

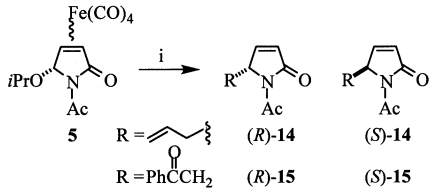


Alkylation Reactions of the Tetracarbonyliron Complexes with π-Nucleophiles

Having available the diastereoisomerically pure *cis*- and *trans*-iron complexes, the Lewis acid promoted substitution reactions with π-nucleophiles could be studied separately. Treatment of the *N*-acetyl-substituted iron complex *trans*-**5** with an excess of allyltrimethylsilane and boron trifluoride gave, after oxidative removal of the iron, in a rather fast reaction, with retention of configuration at C-5, the enan-

tiopure allylpyrrolinone (*R*)-**14** in 51% yield (Table 3, entry 1).[19][20] Quite unexpectedly, the major isomer *cis*-**5**, reacted less selectively and much more slowly under the same reaction conditions to give (*S*)-**14** in 53% yield and only 55% ee (Table 3, entry 2). In a comparison experiment uncomplexed *N*-acetylpyrrolinone **3** appeared to be completely unreactive under the same reaction conditions, thus confirming that formation of *N*-acyliminium intermediates is inhibited in the presence of a second acceptor substituent at the nitrogen atom. Likewise, reaction of *trans*-**5** with α-(trimethylsiloxy)styrene again proceeded fast and highly selectively, to afford enantiopure (*R*)-**15**, whereas *cis*-**5** reacted slowly to produce (*S*)-**15** in only 37% ee and low yield. (Table 3, entries 3, 4).

Table 3. Reagents and conditions: i: nucleophile (3 equiv.), $BF_3 \cdot OEt_2$ (3 equiv.), CH_2Cl_2, 3 or 18 h, r. t., then $Me_3NO \cdot 2\ H_2O$ (4 equiv.), 1 h, r. t.

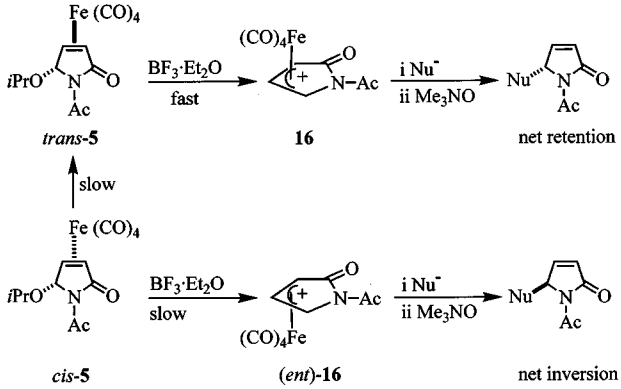


Entry	Complex	Nucleophile	Reaction time	Major product	Yield (%)[a]	(ee;%)
1	*trans*-**5**	$SiMe_3$	3 h	(*R*)-**14**	51	(>95)
2	*cis*-**5**	$SiMe_3$	18 h	(*S*)-**14**	53[b]	(55)
3	*trans*-**5**	Ph, Me_3SiO	3 h	(*R*)-**15**	48	(>95)
4	*cis*-**5**	Ph, Me_3SiO	18 h	(*S*)-**15**	18	(37)

[a] Isolated yield. – [b] Yield according to ^1H NMR; inseparable 2:1 mixture with **3**.

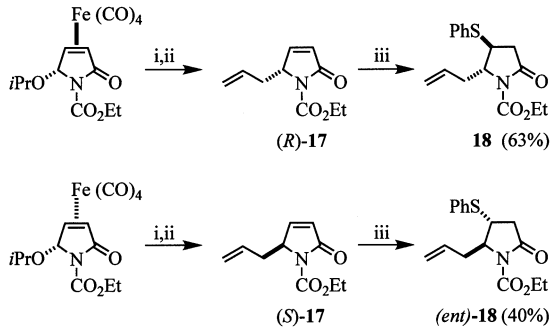
These results can be explained by presuming the cationic π-allyliron complex **16** as an intermediate in the reaction (Scheme 7). The cation **16** of *trans*-**5** is directly formed in a fast process – in which the iron atom can assist in the departure of the isopropoxide group – and then captured by the nucleophile *anti* to the iron moiety. The regioselectivity is explained by the electron-withdrawing C-2 carbonyl group, inducing most of the positive charge on C-5.[14] In the case of *cis*-**5**, direct iron-assisted formation of the cation is not possible. Two stereochemically divergent processes can occur, one leading to net inversion and one to retention. The (major) inversion pathway proceeds by slow formation of the π-allyliron cation *ent*-**16**, possibly with partial preceding isomerization of the isopropoxy function at C-5, because in one alkylation experiment partly racemized **3** was recovered. The (minor) retention route is explained by partial slow isomerization of *cis*-**5** to *trans*-**5** (the same process is already presumed in their preparation from **3**, vide supra), followed by a fast reaction with the nucleophile.

Scheme 7



Surprisingly, both the *cis* and the *trans* complex of the *N*-ethoxycarbonyl-protected compound **7** (R = Et) reacted fast in the boron trifluoride promoted reaction with allyltrimethylsilane (Scheme 8).[20] However, the ee of the product obtained from the *cis* complex was again lower than the ee of the product from the *trans* complex. The products could not be separated from the accompanying decomplexed starting material **6** (R = Et), but upon conjugate addition of thiophenol purification of the products **18** was possible. From the specific rotations it could be derived that the ee of *ent*-**18** was 76% of the ee of **18**, although the absolute ee of **18** could not be ascertained.

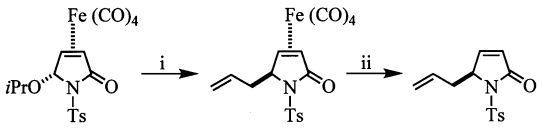
Scheme 8. Reagents and conditions: i: allyltrimethylsilane (3 equiv.), $BF_3 \cdot OEt_2$ (3 equiv.), CH_2Cl_2, 3 h, r. t.; ii: Me_3NO (4 equiv.), 1 h, r. t.; iii: PhSH (1 equiv.), NEt_3 (1 equiv.), CH_2Cl_2, 2 h, r. t.



Contrary to the results with the *N*-acetyl-substituted *cis*-iron complex, the *N*-tosyl-substituted iron complex *cis*-**9** reacted rapidly with allyltrimethylsilane to give, after oxidative removal of the iron, the enantiopure (*S*)-5-allylpyrrolinone **20** in 88% yield (Table 4, entry 1).[8][22] Upon careful, oxygen-free work-up of the reaction mixture, it was possible to isolate the *trans*-allyliron complex **19** quantitatively

(Scheme 9). Again, the uncomplexed *N*-tosylpyrrolinone **8** did not react under the same conditions.

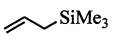
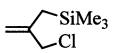
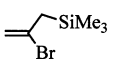
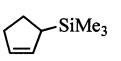
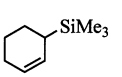
Scheme 9. Reagents and conditions: i: allyltrimethylsilane (2 equiv.), $BF_3 \cdot OEt_2$ (2 equiv.), CH_2Cl_2, 2 h, r. t.; ii: $Me_3NO \cdot 2\ H_2O$ (5 equiv.), r. t.



cis-**9** **19** **20**

The (not optimized) yields of the reactions with other allylic silanes were lower (Table 4).[8] The reactions of the cycloalkenylsilanes (entries 4, 5) proceeded with high stereoselectivity, but the configurations at the cycloalkenyl-C of the major isomers were not assigned.

Table 4. Reactions of *cis*-**9** with allylic silanes[a]

Entry	Silane	Product R=	Yield (%)[b]
1			88
2			30
3			40
4			34[c]
5			60[d]

[a] Reagents and conditions: allylic silane (2 equiv.), $BF_3 \cdot OEt_2$ (2–3 equiv.), CH_2Cl_2, 2 h, r. t., then $Me_3NO \cdot 2\ H_2O$ (5–10 equiv.), 0.5 h. – [b] After column chromatography. – [c] 2 diastereomers, ratio 83:17. – [d] 2 diastereomers, ratio 95:5.

The electronic nature and the steric bulk of the aromatic ring appear to have considerable influence on the reactivity of the other *N*-sulfonyl complexes (see Table 5).[8] The yields of the reactions with allyltrimethylsilane were moderate. Decomplexation of the starting material often occurred to some extent, giving rise to an inseparable mixture. In the case of the mesityl derivative (entry 1) partial ring opening of the N–C-5 bond was observed.

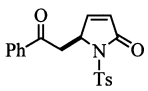
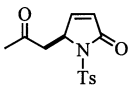
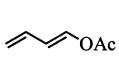
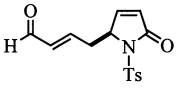
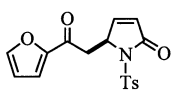
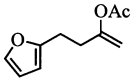
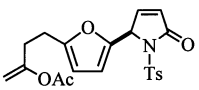
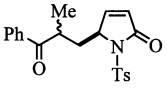
As the *N*-tosyl complex *cis*-**9** appeared to be the iron complex of choice, its reactions with enol derivatives were studied.[8][22] Unfortunately, the most obvious reagents, i.e. silyl enol ethers, could not be used, because they were destroyed by boron trifluoride–diethyl ether faster than the cation of *cis*-**9** was formed, even when freshly distilled boron trifluoride was used. So more stable enol derivatives were necessary. Alkyl enol ethers also failed to provide the desired substitution products. Enol acetates, however, gave the enantiopure ketones in moderate yields (Table 6). In some cases, formation of the reduced pyrrolinone **21** was observed (entries 1, 2, 6). The reaction of acetoxybutadiene produced a mixture of aldehydes, from which the expected aldehyde could be isolated (entry 3). The substrate in entry 5 did not react at its enol acetate moiety, but instead an electrophilic aromatic substitution at the furan ring occurred; no trace of **22**, desired as substrate for an intramolecular Diels-Alder reaction, could be detected. From entry 6 it appears that non-terminal enol acetates are reluctant to react, giving rise to large amounts of the reduction product **21** and some decomplexed starting material, besides only 5% alkylation product.

Table 5. Reactions of other *N*-sulfonyl-substituted complexes with allyltrimethylsilanes[a]

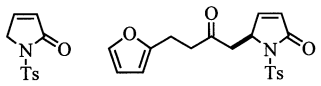
Entry	Sulfonyl complex	Product SO_2R R =	Yield (%)[b]
1	**10**	mesityl	48[c]
2	**11**	2-pyridyl	43[d]
3	**12**	1-naphthyl	51[d]
4	**13**	2-naphthyl	67[d]

[a] Reagents and conditions: allyltrimethylsilane (3 equiv.), $BF_3 \cdot OEt_2$ (2 equiv.), CH_2Cl_2, 14 h, r. t., then $Me_3NO \cdot 2\ H_2O$ (5 equiv.). – [b] After column chromatography. – [c] 13% of the ring-opened sulfonamide was also isolated. – [d] Calculated from NMR; contaminated with corresponding **8**.

Table 6. Reactions of *cis*-**9** with enol acetates[a]

Entry	Enol acetate	Product	Yield (%)[b]
1			33[c]
2			47[d]
3			33[e]
4			60
5			54
6			5[f]

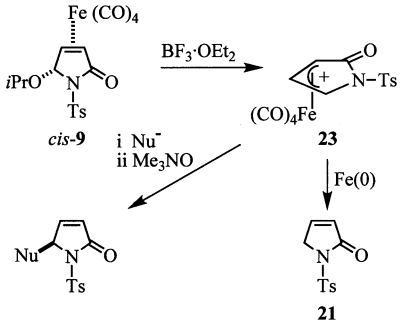
[a] Reagents and conditions: enol acetate (3 equiv.), $BF_3 \cdot OEt_2$ (2 equiv.), CH_2Cl_2, 2 h, r. t., then $Me_3NO \cdot 2\ H_2O$ (5 equiv.). – [b] After column chromatography. – [c] **21** (21%) was also isolated. – [d] Calculated from NMR; contaminated with **21** (18%). – [e] A mixture of other aldehydes (26%) was also isolated. – [f] **21** (25%) and **8** (R = *p*-tolyl; 18%) were also isolated.



21 **22**

The different behaviour (reaction rate and stereoselectivity) in the alkylation of the *N*-tosyl-substituted *cis* complex **9**, compared to the *N*-acetyl-substituted *cis* complex **5**, might be explained by the steric strain in *cis*-**9**, with three large substituents at the same side of the ring (cf. Figure 1). On account of steric relief the rate-limiting generation of the cation **23** proceeds faster than in the case of the *N*-acetyl analogue *ent*-**16**, and partial isomerization of *cis*-**9** to *trans*-**9** does not occur, thus sole formation of the inverted alkylation product is observed (Scheme 10). In the case of a slow reaction with the nucleophile, reduction of cation **23** to compound **21** is a side-reaction, with iron as the presumed reductor.

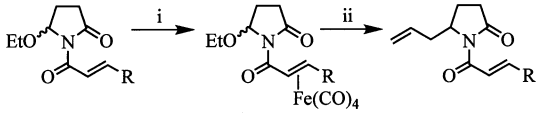
Scheme 10



The nature of the intermediary cations **16** and **23** is ambiguous. They can be described either as an iminium ion or a π-allyliron cation. Therefore we decided to study the influence of the iron complexation on the reactivity of 5-alkoxy-2-pyrrolidinones bearing an α,β-unsaturated *N*-acyl group, thus separating the effect of the iron atom on the *N*-carbonyl moiety from the direct effect on the iminium ion.[8][24] The iron complexes of the easily available pyrrolidinones were obtained in good yield as 3:2 mixtures of diastereoisomers (Scheme 11). Both iron complexes reacted rather slowly with allyltrimethylsilane in the presence of boron trifluoride (Table 7). The reaction was improved, both in time and in yield, by addition of one equivalent of acetic anhydride. This probably leads to the formation of the 5-acetoxypyrrolidinone, which is more reactive because of the better leaving group. Upon attempted allylation of the uncomplexed compounds under the same conditions, both with and without acetic anhydride, only traces of alkylation product and Michael addition product were formed, while more than 90% of the starting material was recovered.

Apparently the *N,N*-diacyliminium ion can be formed because of the complexation of iron to the alkene moiety, thus partly canceling the electron-withdrawing effect of the conjugated carbonyl function. Since in the *cis* complexes **5** and **9** the iron atom cannot assist in the departure of the isopropoxide group, the first stage in the reaction must be the relatively slow formation of the cation, in which the destabilizing effect of the C-2 carbonyl function is largely neutralized by the backdonation from the iron atom to the alkene moiety. In the case of the *trans*-iron complexes the π-allyliron cation may be formed fast by the combined influence of the iron atom and the N lone pair.

Scheme 11. Reagents and conditions: i: $Fe_2(CO)_9$ (2 equiv.), toluene, 5.5 h, r. t.; ii: allyltrimethylsilane (3 equiv.), $BF_3 \cdot OEt_2$ (3 equiv.), CH_2Cl_2, r. t., then $Me_3NO \cdot 2\,H_2O$ (10 equiv.), r. t.



24 R = Me 88% **26** R = Me
25 R = Ph 81% **27** R = Ph

Table 7. Reactions of **24** and **25** with allyltrimethylsilane[a]

Substrate	Reaction time	Yield of product (%)[b]
24	6 d	**26** (45) + **24** (17)
24[c]	8 h	**26** (66) + **24** (14)
25	4 d	**27** (27)
25[c]	16 h	**27** (54)

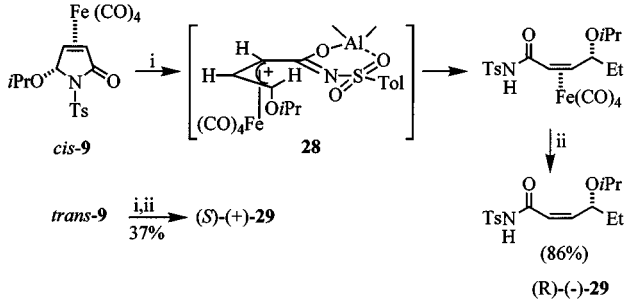
[a] Conditions: See Scheme 11. – [b] After column chromatography. – [c] In the presence of Ac_2O (1 equiv.).

Alkylation of the Iron Complex *cis*-9 with Organometallic Reagents

We also investigated organometallic reagents as nucleophiles in the allylic substitution reaction of *cis*-**9**.[8] Strongly coordinating solvents like THF appeared to compete with the substrate for the Lewis acid. So, non-coordinating solvents, such as dichloromethane or toluene, were used. Unfortunately, reactions with organomagnesium and organozinc reagents in the presence of Lewis acids were not successful. With Grignard reagents in dichloromethane in the presence of boron trifluoride–diethyl ether or ethylaluminium dichloride reduction to **21** occurred, whereas with ethylzinc iodide·DMF[25] and boron trifluoride–diethyl ether in toluene, besides reduction to **21**, *cis*/*trans* isomerization of the substrate was observed. When in the latter case ethylaluminium dichloride was used as the Lewis acid, alkylation was accompanied by ring opening at the N–C-5 bond, leading to the sulfonamide **29** (Scheme 12). The reaction gave only reproducible yields if the iron complex was added to the reactive ate complex formed from the Lewis acid and the alkylzinc reagent. In the proposed mechanism, upon bidentate coordination of aluminium and/or zinc ions, ring opening to the intermediary **28** occurs, which is then stereoselectively alkylated *trans* to the iron moiety, and upon oxidation of the iron would lead to (*R*)-**29**. The same alkylation reaction of *trans*-**9** afforded (*S*)-**29**. The enanti-

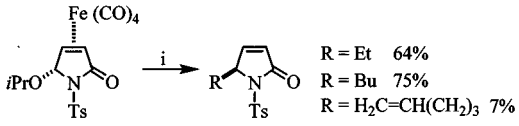
omeric purity of the products, however, has not been firmly established.

Scheme 12. Reagents and conditions: i: $EtZnI \cdot DMF$ (3 equiv.), $EtAlCl_2$ (3.6 equiv.), toluene, 10 min, r. t. then addition of *cis*-**9**, 1.5 h, r. t.; ii: Me_3NO (5 equiv.), 0.5 h, r. t.



We then tried to perform the alkylations with organolead reagents, which are known to alkylate *N*-acyliminium ions with high diastereoselectivity.[26] Upon treating *cis*-**9** with the mixed organolead reagents di(*n*-butyl)- or diethyldicyclohexyllead in the presence of boron trifluoride the primary alkyl group was smoothly transferred (Scheme 13). However, with di(4-pentenyl)dicyclohexyllead the yield dropped considerably, presumably because the radicals that are easily formed from alkyllead compounds[27] led to polymerization of the reactants. Reactions with divinyl- or diphenyldicyclohexyllead did not give the desired products. This was unexpected, because the bond between lead and an sp^2-carbon atom is weaker than the lead$-sp^3$-carbon bond.[27] So, in practice, only saturated primary alkyl groups can be transferred in the alkylation of *cis*-**9** with mixed organolead reagents.

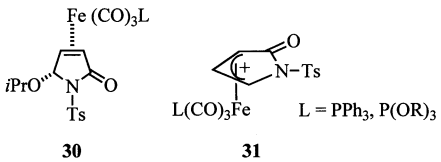
Scheme 13. Reagents and conditions: i: *c*-Hex_2PbR_2 (2 equiv.), $BF_3 \cdot OEt_2$ (2 equiv.), CH_2Cl_2, 2 h, r. t., then Me_3NO (5 equiv.), 0.5 h, r. t.



Exchange of CO for Other Ligands

Substitution of one or more carbonyl ligands in carbonyliron complexes has received much attention.[28] The substitution of a carbonyl ligand in *cis*-**9** for a worse π-acceptor, such as a phosphane or a phosphite, would render the complex **30** more electron-rich. Thus, the cation **31**, to be formed upon treatment of **30** with a Lewis acid, should be more stable and possibly would allow productive reactions with a larger variety of nucleophiles (Scheme 14).

Scheme 14



A versatile method for the exchange is the oxidative removal of a carbonyl ligand by an amine *N*-oxide in the presence of a new ligand.[29] When *cis*-**9** was treated with a slight excess of trimethylamine *N*-oxide in the presence of trimethyl phosphite, triphenyl phosphite, or triphenylphosphane (1 equiv.) in acetonitrile at 0°C, in all cases in about 4 h a new yellow-orange complex was formed, which, much to our surprise, did not contain the desired new ligand. Moreover, the same complex was obtained upon careful oxidation of *cis*-**9** with trimethylamine *N*-oxide in the absence of a new potential ligand (Scheme 15). On the basis of the spectral data (Figure 2), structure **32** was assigned to the new complex. The downfield shifts of the NMR resonances are a result of the conversion to η^3-coordination. The removal of a carbonyl ligand, a good π-acceptor, leads to increased electron density in the complex, which then reorganizes by oxidative insertion of the iron atom into the N−C-5 bond of the pyrrolinone. Apparently, the opening of the pyrrolinone ring is more favourable than insertion into the O−C-5 bond. Complex **32** did not react with allyltrimethylsilane in the presence of various Lewis acids or tetrafluoroboric acid, only starting material being isolated.

Scheme 15. Reagents and conditions: i: Me_3NO (1.1 equiv.), MeCN, 1.5 h, 0°C; ii: PPh_3 (1 equiv.), THF, 6 h, 45°C

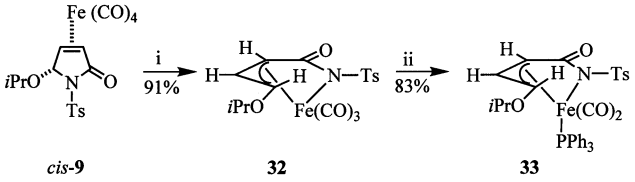
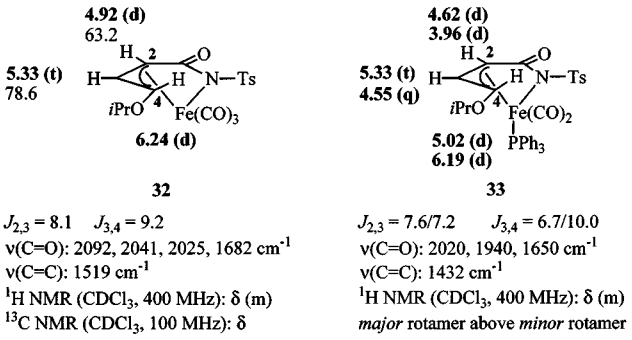


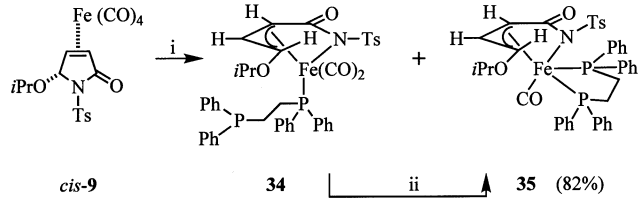
Figure 2. Spectroscopic data of **32** and **33**



When the tricarbonyliron complex **32** was treated with triphenylphosphane the yellow complex **33**, in which the phosphane ligand has thermally displaced a carbonyl ligand, was obtained as a mixture of two rotamers, in a ratio 77:23 in $CDCl_3$, as a result of Berry pseudorotation (Scheme 15). The bidentate coordination of the organic ligand via a π-allyl fragment and a σ-imide anion might (in part) be the reason for the stability of the complexes **32** and **33**. By using a bidentate phosphorus ligand the pyrrolinone ring would possibly remain intact, because then the gain of the new bidentate P−Fe−P coordination might overcome the loss of stabilization by giving up the bidentate coordination of the ring-opened pyrrolinone. Reaction of *cis*-**9**

with trimethylamine *N*-oxide in the presence of 1,2-bis(diphenylphosphanyl)ethane (dppe) gave, after column chromatographic separation, the yellow complex **34** and the red complex **35** in varying ratios, depending on the time of the reaction and the work-up. Upon standing for several hours **34** converted spontaneously into **35** by loss of a carbonyl ligand and coordination of the second P atom to the iron atom (Scheme 16). Both new complexes did not react with allyltrimethylsilane in the presence of (Lewis) acids.

Scheme 16. Reagents and conditions: i: dppe (1.5 equiv.), Me_3NO (2.2 equiv.), THF, MeCN, 1 h, 0°C, then 16 h r. t.; ii: 4−48 h



The ^{1}H-NMR data of **34** (Figure 3) are similar to those of **33**. Two rotamers are present in a ratio 3:2 in $CDCl_3$. The rotamers are also observed by ^{31}P NMR. One of the phosphorus atoms is coordinated (δ = 52.29 and 70.58) and one is free (δ = −13.05 and −11.36). IR showed bands of two CO ligands at $\tilde{\nu}$ = 2026 and 1974 cm^{-1}. The complex **35** is completely air-stable, even in solution. There is no NMR evidence for Berry pseudorotation and the ^{1}H-NMR data are still similar to those of **34**. However, ^{31}P NMR showed signals of two coordinated phosphorus atoms (δ = 75.14 and 85.75) and IR a band of only one CO ligand at $\tilde{\nu}$ = 1953 cm^{-1}. The X-ray crystal-structure determination confirmed the assigned structure of **35** (Figure 4).

Figure 3. Spectroscopic data of **34** and **35**

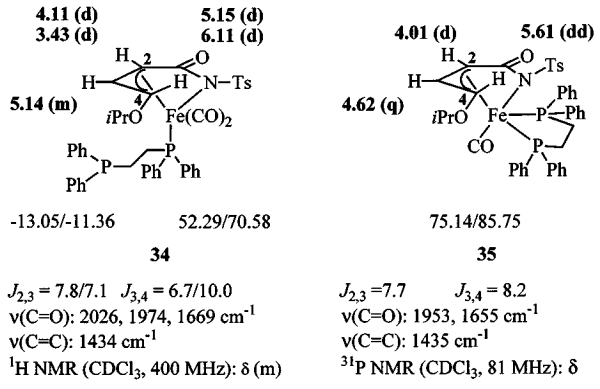
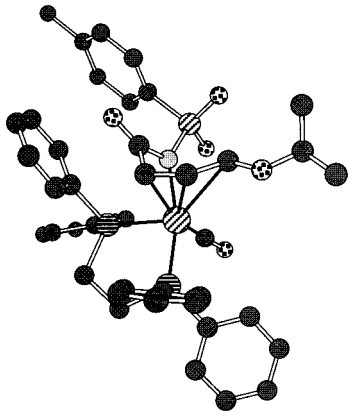


Figure 4. Chem 3D™ view of **35**



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Further details of the crystal-structure inverstigations may be obtained from the Fachinformationszentrum Karlsruhe, D-76344 Eggenstein-Leopoldshafen, Germany, on quoting the depository numbers CSD-402303 (**3**), -402949 (*rac-trans*-**5**), -402302 (**8**), -402948 (*cis*-**9**). − Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-101548 (**20**), -101549 (**35**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

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