CHEMISTRY
AN ASIAN JOURNAL

DOI: 10.1002/asia.200800071

Asymmetric Friedel–Crafts Alkylation of Electron-Rich N-Heterocycles with Nitroalkenes Catalyzed by Diphenylamine-Tethered Bis(oxazoline) and Bis(thiazoline) Zn^{II} Complexes

Han Liu, Shao-Feng Lu, Jiaxi Xu, and Da-Ming Du*[a]

Abstract: The asymmetric Friedel–Crafts alkylation of electron-rich N-containing heterocycles with nitroalkenes under catalysis of diphenylamine-tethered bis(oxazoline) and bis(thiazoline)-Zn^{II} complexes was investigated. In the reaction of indole derivatives, the complex of ligand **4f** with *trans*-diphenyl substitutions afforded better results than previously published ligand **4e** with *cis*-diphenyl substitutions. Excellent yields (up to greater than 99%) and enantioselectivities (up to 97%) were achieved in most cases. The complex of ligand **4d** bearing *tert*-butyl groups gave the best results in the reactions of pyrrole. Moderate to good yields (up to 91%) and enantioselectivities (up to 91%) were achieved in most cases. The origin of the enantioselectivity was attributed to the NH–π interaction between the catalyst and the incoming aromatic system in the transition state. Such an interaction was confirmed through comparison of the enantioselectivity and the absolute configuration of the products in the reactions catalyzed by designed ligands.

Keywords: asymmetric catalysis · Friedel–Crafts reaction · indoles · nitroalkenes · pyrroles

Introduction

Asymmetric Friedel–Crafts reactions are an efficient way to construct stereogenic centers on the α or β position of different kinds of aromatic systems.[1] During the past decade, indole and its derivatives have been demonstrated to be good substrates for the asymmetric Friedel–Crafts reaction with unsaturated aldehydes,[2] unsaturated ketones,[3] unsaturated 2-acyl imidazoles, or unsaturated ketophosphonates,[4] epoxides,[5] ketoesters,[6] glyoxylate,[6a,b] imines,[7] enamines,[8] and electron-deficient olefins, such as nitroalkenes,[9] alkylidene malonates,[10] and ethenetricarboxylates.[11] Recently, the aromatic systems have been expanded successfully to electron-rich benzenes,[4b,6e,12] substituted pyrroles,[3d,4a,6e,13] and 2-methoxyfurans.[4a,14] Among these kinds of electron-deficient acceptors, we were interested in nitroalkenes[15] for their high electrophilicity and potential transformation of nitro group.[16]

Guiry et al.[17] and our group[18a] developed independently the diphenylamine-tethered bis(oxazoline) ligands. We developed the diphenylamine-tethered bis(thiazoline) ligands to further tune their coordination ability (Figure 1). The ligands mentioned above have been applied successfully in the asymmetric Henry reaction of α-ketoesters,[18] asymmetric Nozaki–Hiyama–Kishi reactions,[19] asymmetric Micheal additions of nitroalkanes to nitroalkenes,[20] and asymmetric Friedel–Crafts reactions of nitroalkenes with indoles

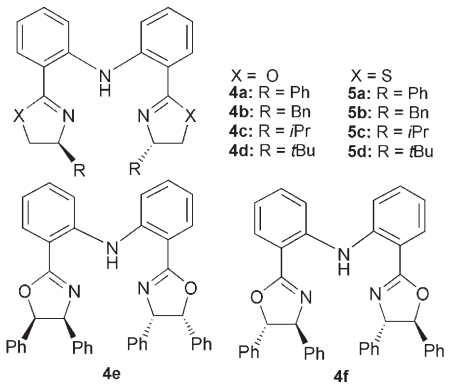


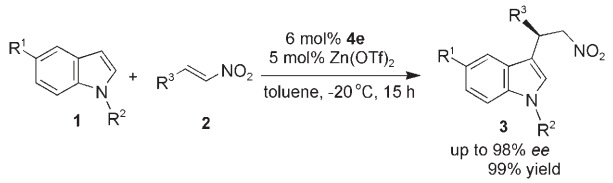
Figure 1. Diphenylamine-tethered bis(oxazoline) and bis(thiazoline) ligands.

[a] H. Liu, Dr. S.-F. Lu, Prof. Dr. J. Xu, Prof. Dr. D.-M. Du
Beijing National Laboratory for Molecular Sciences (BNLMS)
Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education
College of Chemistry and Molecular Engineering
Peking University
Beijing 100871 (China)
Fax: (+86) 10-62751708
E-mail: dudm@pku.edu.cn

Supporting information for this article is available on the WWW under http://www.chemasianj.org or from the author.

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(Scheme 1)[9e] and 2-methoxyfuran.[14b] Herein, we document our detailed investigation on the asymmetric Friedel–Crafts alkylation of indole derivatives and pyrrole[21] with nitroalkenes as part of our project to expand the application of the diphenylamine-tethered bis(oxazoline) and bis(thiazoline) ligands.



Scheme 1. Asymmetric Friedel–Crafts alkylation of indole derivatives with nitroalkenes.

Results and Discussion

Asymmetric Friedel–Crafts Alkylation of Indole Derivatives with Nitroalkenes

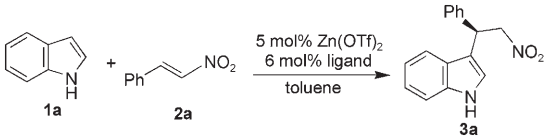
In a preliminary communication, we reported the application of the diphenylamine-tethered bis(oxazoline) and bis(thiazoline) ligands in the asymmetric Friedel–Crafts reaction of indole derivatives **1** with nitroalkenes **2** (Scheme 1).[9e] Through the fine screening of Lewis acids, solvents, ligands, and reaction temperature, 5 mol% complex of ligand **4e** and $Zn(OTf)_2$ in toluene at −20 °C was found to give the best results, and products **3** were obtained with high enantioselectivities. One year later, we reported the asymmetric Friedel–Crafts alkylation of 2-methoxyfuran with nitroalkenes.[14b] Novel ligand **4f** was synthesized and the complex of this ligand and $Zn(OTf)_2$ in xylene at room temperature was found to be efficient. Considering that the ligand **4f** is easier to prepare than **4e** owing to the commercial availability of (1*R*,2*S*)-2-amino-1,2-diphenylethanol, we rescreened the catalytic activity of the ligands in toluene at 10 °C (Table 1). The novel ligand **4f** gave enantioselectivities comparable to ligand **4e** at 10 °C. When the reaction was conducted at −20 °C, **4f** gave slightly better *ee* values.

Encouraged by this result, we tested the scope of the asymmetric Friedel–Crafts alkylation through catalysis with **4f**–$Zn(OTf)_2$ (Table 2). Compared with the results we published previously, better enantioselectivities were achieved in most cases. For *para*- and *meta*-substituted aromatic nitroalkenes, the *ee* values are higher than 90%. The aromatic ni-

Abstract in Chinese:

本文研究了二苯胺骨架双噁唑啉和双噻唑啉配体–$Zn(OTf)_2$ 配合物催化的两类富电子含氮杂环化合物与硝基烯烃的不对称 Friedel–Crafts 烷基化反应。在吲哚衍生物与硝基烯烃的反应中，具有反式二苯基取代的配体 **4f** 的 $Zn(OTf)_2$ 配合物催化获得很好的产率(up to >99%)和对映选择性(up to 97%ee)。在吡咯的烷基化反应中，叔丁基取代的配体 **4d** 的 $Zn(OTf)_2$ 配合物给出最高 91%产率和 91%ee。通过配体结构的修饰和催化活性的比较研究，为提出的过渡态及其中的 NH-π 相互作用提供了证据。

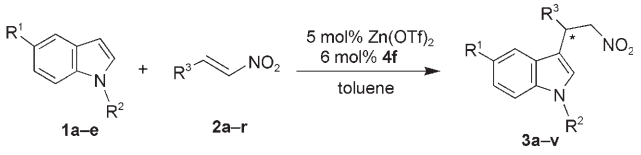
Table 1. Effects of ligands and temperature on the asymmetric Friedel–Crafts alkylation of indole and nitrostyrene.[a]



Entry	Ligand	T [°C]	Yield [%][b]	*ee* [%][c]
1	**4a**	10	99	83
2	**4b**	10	99	66
3	**4c**	10	94	30
4	**4d**	10	95	68
5	**4e**	10	99	90
6	**4f**	10	99	87
7	**5a**	10	99	78
8	**5b**	10	99	59
9	**5c**	10	93	11
10	**5d**	10	87	2
11	**4e**	−20	99	94
12	**4f**	−20	99	96

[a] All reactions were conducted on a 0.5-mmol scale in 3 mL toluene with 5 mol% ligand–$Zn(OTf)_2$. [b] Yield of isolated product. [c] Determined by HPLC using a Chiracel OD-H column with 70:30 hexane/2-propanol as eluent.

Table 2. Asymmetric Friedel–Crafts alkylation of indoles with nitroalkenes catalyzed by **4f**–$Zn(OTf)_2$.[a]



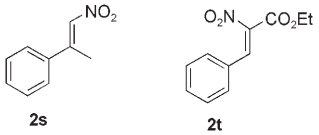
Entry	R^1	R^2	R^3	Product	Yield [%][b]	*ee* [%][c]
1	H	H	Ph	**3a**	>99	96 (*R*)
2	H	H	4-Me-C_6H_4	**3b**	99	93
3	H	H	4-MeO-C_6H_4	**3c**	88	90
4	H	H	4-F-C_6H_4	**3d**	99	95
5	H	H	4-Cl-C_6H_4	**3e**	>99	95
6	H	H	3-Br-C_6H_4	**3f**	99	95
7	H	H	4-Br-C_6H_4	**3g**	93	95
8	H	H	3-NO_2-C_6H_4	**3h**	>99	94
9	H	H	4-NO_2-C_6H_4	**3i**	93	97
10	H	H	3,4-$(MeO)_2$-C_6H_3	**3j**	89	90
11	H	H	2-MeO-C_6H_4	**3k**	93	87
12	H	H	2-Cl-C_6H_4	**3L**	94	72
13	H	H	2-thienyl	**3m**	>99	87
14	H	H	2-furyl	**3n**	88	80
15	H	H	2-naphthyl	**3o**	90	90
16	H	H	$PhCH_2CH_2$	**3p**	80	91
17	H	H	Cy	**3q**	79	94
18	H	H	*t*Bu	**3r**	54[d]	97[d]
19	Cl	H	Ph	**3s**	85	88
20	Me	H	Ph	**3t**	94	97
21	MeO	H	Ph	**3u**	99	97
22	H	Me	Ph	**3v**	86	97 (*R*)

[a] All reactions were conducted on a 0.5-mmol scale in 3 mL toluene with 5 mol% **4f**–$Zn(OTf)_2$ at −20 °C for 24 h . [b] Yield of isolated product. [c] Determined by HPLC using a Chiracel OD-H or Chiracel AD column. For details, see Experimental Section. [d] The reaction was conducted at 30 °C for 130 h.

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

CHEMISTRY
AN ASIAN JOURNAL

troalkenes with electron-withdrawing substitutions give higher *ee* values than those with electron-donating substituents. However, owing to the high *ee* values in both cases, this electronic effect is negligible. On the contrary, the aromatic nitroalkenes with *ortho* substituents give significantly lower enantioselectivities (Table 2, entries 11 and 12). Such a phenomenon can be attributed to the unfavored interaction between the *ortho*-substituted group and the ligand. The nitroalkenes containing thiophene and furan give 87% and 80% *ee*, respectively (Table 2, entries 13 and 14), while the 2-naphthyl substrate gives 90% *ee* (entry 15). To our delight, good enantioselectivities can be achieved in the cases of α-monosubstituted, α,α-disubstituted, and α,α,α-trisubstituted aliphatic nitroalkenes, though the yields are lower (Table 2, entries 16–18). In the case of sterically hindered *tert*-butyl-substituted nitroalkene **2r** (Table 2, entry 18), elevated temperature and prolonged reaction time must be used for obtaining acceptable conversion. Other indole derivatives were also tested in the reaction. The enantioselectivities are not affected significantly by the substitutions on the indole. Notably, the *ee* value of **3v** (Table 2, entry 22) with *N*-methyl substitution is much higher than we published previously. The absolute configuration of products was identified as *R* through comparison of the optical rotation with literature data.[9c] We also tried to expand the scope of the type of acceptor to acetophenone-derived nitroalkene **2s** and ester-containing nitroalkene **2t** (Figure 2), but no conversion could be observed by catalysis with our complexes.



2s **2t**

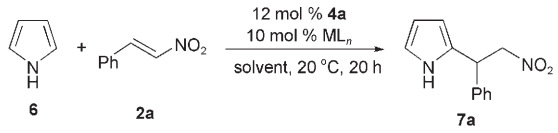
Figure 2. Inactive nitroalkenes in the asymmetric Friedel–Crafts alkylation of indole.

Asymmetric Friedel–Crafts Alkylation of Pyrrole with Nitroalkenes

As a rational and reasonable expansion of our methodology, we investigated the asymmetric Friedel–Crafts alkylation of pyrrole. Substituted pyrroles have been widely used, not only as important building blocks for natural alkaloids and substructures of pharmaceutical molecules,[22] but also as chemical materials,[23] for their significant bioactivities and photoelectronic properties. Thus, the development of efficient methods to construct pyrroles with chiral side chains is still demanding. Compared with the asymmetric Friedel–Crafts alkylation of indole derivatives, the asymmetric Friedel–Crafts alkylation of pyrrole has not been fully developed, owing to its relatively low reactivity, weak steric interactions with chiral ligands caused by its small molecular size, and instability toward acids. In 2001, MacMillan et al. reported the successful application of their organocatalyst derived from (*S*)-phenylalanine in the asymmetric Friedel–Crafts alkylation of pyrrole with unsaturated aldehydes.[13a] In 2005, Palomo et al. reported the asymmetric reaction of pyrrole with unsaturated α-hydroxyketones by catalysis with bis(oxazoline)–Cu^{II} complexes.[13b] In 2006, Evans and coworkers reported the asymmetric reaction of pyrrole and tetrahydroindole with unsaturated 2-acyl imidazoles by catalysis with pybox–Sc^{III} complexes.[4a,13c] Recently, Antilla et al. reported the asymmetric reaction of substituted pyrroles with acyl imines by catalysis with chiral phosphoric acid.[13d] Pedro et al. also reported the asymmetric reaction of pyrrole with enones by catalysis with a 3,3′-dibromobinol–Zr^{IV} complex.[3d] Both excellent yields and excellent enantioselectivities have been achieved. Other authors have also attempted the reaction of pyrrole with ethenetricarboxylates,[11] but with unsatisfactory yield and enantioselectivity. To the best of our knowledge, the asymmetric Friedel–Crafts reaction of pyrrole and nitroalkenes has not been developed,[24] though the racemic form has been developed recently by several groups[25]

Considering that the reaction conditions optimized for indoles may not be appropriate for the reaction of pyrrole, we evaluted the effect of Lewis acids, solvents, temperature, and chiral ligands. As listed in Table 3, when AgOTf and $Mg(OTf)_2$ were used, no conversion of nitrostyrene was observed, which indicates that no reactive complex could be formed. When $Pd(OAc)_2$ was used, the red complex was formed and it was reactive, but the product exhibits no enantioselectivity. Sc^{III} and In^{III} triflates, which have been successfully used in the asymmetric Friedel–Crafts reaction by Evans et al.[4,13] and the racemic form by Yadav et al.,[25a]

Table 3. Effects of Lewis acids and solvents on the asymmetric Friedel–Crafts alkylation of pyrrole with nitrostyrene.[a]



6 **2a** **7a**

Entry	Lewis acid	Solvent	Yield [%][b]	*ee* [%][c]
1	AgOTf	toluene	0	n.d.
2	$Mg(OTf)_2$	toluene	0	n.d.
3	$Sc(OTf)_3$	toluene	0	n.d.
4	$In(OTf)_3$	toluene	2	−26
5	$Yb(OTf)_3$	toluene	18	0
6	$La(OTf)_3$	toluene	35	−2
7	$Pd(OAc)_2$	toluene	76	0
8	$Cu(OTf)_2$	toluene	37	−48
9	CuOTf	toluene	81	−45
10	$Zn(OTf)_2$	toluene	51	60
11	$Zn(OTf)_2$	xylene	68	58
12	$Zn(OTf)_2$	benzene	33	58
13	$Zn(OTf)_2$	THF	0	n.d.
14	$Zn(OTf)_2$	CH_3CN	0	n.d.
15	$Zn(OTf)_2$	DCM	31	7
16	$Zn(OTf)_2$	DCE	6	−2
17	$Zn(OTf)_2$	hexane	39	−2

[a] All reactions were conducted on a 0.25-mmol scale in 3 mL solvent with 10 mol% **4a**–ML_n at 20°C for 20 h. [b] Yield of isolated product. [c] Determined by HPLC using a Chiracel OD-H column with 70:30 hexane/2-propanol as eluent. n.d. = not determined.

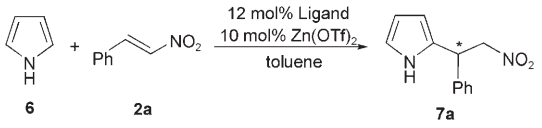
 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

respectively, gave only disappointing results. A black residue was formed, without any conversion of nitrostyrene. This could be attributed to the strong Lewis acidity of the metal cations and the special structure of ligand **4a**. When the Sc^{III} or In^{III} coordinates to the NH-bridged ligand **4a**, the proton on the NH bridge would be activated and may catalyze the polymerization of pyrrole as a Brønsted acid. Compared to $Zn(OTf)_2$, $Cu(OTf)_2$ and CuOTf gave reversed but lower enantioselectivities, which can be attributed to the different coordination geometry of Cu^{I} and Cu^{II} complexes. After the screening, $Zn(OTf)_2$ was found to be the best choice of the Lewis acid.

In the screening of solvent, toluene gave the best results. Benzene and xylene were abandoned because of toxicity or difficulty of removing, respectively, though they gave similar results to toluene. Coordinating solvents such as THF and acetonitrile can coordinate to the metal cation and inhibit the reaction. Polar solvents such as dichloromenhane (DCM) and 1,2-dichloroethane (DCE) gave lower yields and enantioselectivities. Hexane gave poor result owing to the poor solubility of the complex and nitroalkene.

In the screening of ligands, ligand **4d** with *tert*-butyl substitution on the oxazoline ring gave the best result at room temperature. The reaction can be completed within 24 h with 79% *ee*. (Table 4)When the reaction was conducted at

Table 4. Effects of ligands and temperature on the asymmetric Friedel–Crafts alkylation of pyrrole and nitrostyrene.[a]



6 2a 7a

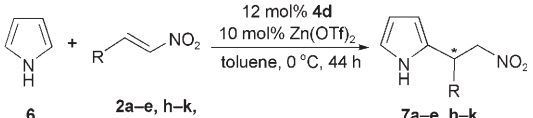
Entry	Ligand	T [°C]	t [h]	Yield [%][b]	*ee* [%][c]
1	**4a**	20	20	58	57
2	**4b**	20	20	76	63
3	**4c**	20	20	53	41
4	**4d**	20	20	54	79
5	**4e**	20	20	86	66
6	**4f**	20	20	85	70
7	**5a**	20	20	73	45
8	**5b**	20	20	71	73
9	**5c**	20	20	76	27
10	**5d**	20	20	40	1
11	**4d**	0	44	81	78
12	**4d**	−20	120	48	82

[a] All reactions were conducted on 0.25-mmol scale in 3 mL solvent with 10 mol% ligand–$Zn(OTf)_2$. [b] Yield of isolated product. [c] Determined by HPLC using a Chiracel OD-H column with 70:30 hexane/2-propanol as eluent.

0 °C for 44 h, the yield was improved by reducing the possible dialkylation reaction without loss of enantioselectivity. At −20 °C, full conversion could not be achieved even after 120 h, indicating the much lower reactivity of pyrrole than that of indole. The bis(oxazoline)s **4a** and **4b** gave lower enantioselectivities than **4d**. Ligands **4e** and **4f** with double phenyl substitutions in the oxazoline rings did not further enhance the enantioselectivity. Meanwhile, bis(thiazoline) ligands **5a** and **5b** with the same configuration gave enantioselectivities comparable with their corresponding bis(oxazoline) ligands **4a** and **4b**, but it is very strange that the bis(thiazoline) **5d** gave a much lower enantioselectivity than the corresponding bis(oxazoline) **4d**. The configuration of products is the same from both type of ligands **4** and **5**.

With the optimized conditions in hand, we investigated the scope of the reaction (Table 5). In the cases of *para*- and *meta*-substituted aromatic nitroalkenes (Table 5, entries 1–8), moderate to good yields and enantioselectivities can be

Table 5. Asymmetric Friedel–Crafts alkylation of pyrrole with nitroalkenes catalyzed by **4d**–$Zn(OTf)_2$.[a]



6 2a–e, h–k, m, n, p 7a–e, h–k, m, n, p

Entry	R	Product	Yield [%][b]	*ee* [%][c]
1	Ph	**7a**	81	78
2	4-Me-C_6H_4	**7b**	58	78
3	4-MeO-C_6H_4	**7c**	61	68
4	4-F-C_6H_4	**7d**	76	81
5	4-Cl-C_6H_4	**7e**	84	81 (*S*)
6	3-NO_2-C_6H_4	**7h**	88	80
7	4-NO_2-C_6H_4	**7i**	59	91
8	3,4-$(MeO)_2$-C_6H_3	**7j**	59	70
9	2-MeO-C_6H_4	**7k**	42	38
10	2-thienyl	**7m**	91	80
11	2-furyl	**7n**	83	79
12	$PhCH_2CH_2$	**7p**	64	11

[a] All reactions were conducted on a 0.25-mmol scale in 3 mL solvent with10 mol% ligand–$Zn(OTf)_2$. [b] Yield of isolated product. [c] Determined by HPLC using a Chiracel OD-H or Chiracel OF column. For details, see Experimental Section.

obtained. Similar to the phenomenon we observed in the asymmetric Friedel–Crafts alkylation of indole derivatives, aromatic nitroalkenes with electron-donating groups give lower enantioselectivities than those with electron-withdrawing groups; *ortho* substitutions are still unfavored in this reaction (Table 5, entry 9). Other aromatic nitroalkenes derived from thiophene and furan give similar results (Table 5, entries 10 and 11). Compared with the reaction of indole derivatives, an aliphatic nitroalkene gives a much lower *ee* value in the reaction with pyrrole (Table 5, entry 12). The absolute configuration of the product **7e** was determined to be *S* through XRD analysis of its single crystal (Figure 3). Other pyrrole derivatives such as *N*-methylpyrrole and *N*-benzylpyrrole are inactive in our reaction even at room temperature for 48 h, indicating the much lower reactivity of pyrrole derivatives than that of indole derivatives.

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

CHEMISTRY
AN ASIAN JOURNAL

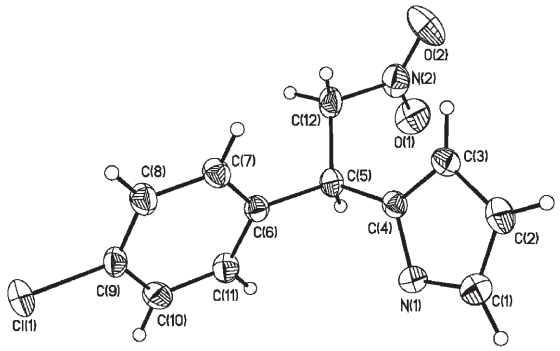


Figure 3. ORTEP drawing of product **7e**; thermal ellipsoids are shown at 50% probability.

Mechanistic Aspects of the Asymmetric Friedel–Crafts Alkylation

Having developed the asymmetric Friedel–Crafts alkylation of indole derivatives and pyrrole with nitroalkenes by catalysis with diphenylamine-tethered bis(oxazoline) and bis(thiazoline) Zn^{II} complexes, we turned our attention to the origin of the enantioselectivity. The absolute configurations of the products of the asymmetric Friedel–Crafts alkylation of indoles and pyrrole were determined to be *R* and *S*, respectively (compounds **3** and **7** have same stereogenic center, but compounds **3** are *R* configured and compounds **7** are *S* configured owing to the group-order rule). In our recent publication,[14b] the absolute configuration of the products of the asymmetric alkylation of 2-methoxyfuran was also determined to be *S*. These results indicate that the electron-rich aromatic systems attack the β-carbon atom of nitroalkenes from the *Si* face, which is opposite to the reaction of indole with nitroalkenes catalyzed by 2,2-dimethylmalonate-derived bis(oxazoline)–$Zn(OTf)_2$ complexes. On the basis of the configurations of the products and the XRD structure of the ligand we have published before,[18a] we postulate the proposed transition state of the reaction as illustrated in Figure 4.

Compared to the 2,2-dimethylmalonate-derived bis(oxazoline)–$Zn(OTf)_2$ complexes,[9c] our catalysts work in a bifuntional form. The NH–π interaction[26] directs the indole attack from the back side. The nitrostyrene molecule coordinates to the metal cation through the two oxygen atoms, while the hydrogen atom on the α-carbon atom is directed to the back side to eliminate the steric repulsion between the phenyl group and incoming indole.

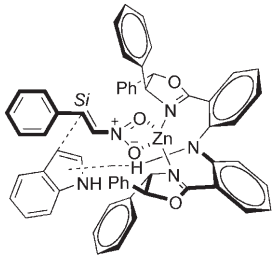


Figure 4. Proposed transition state of the asymmetric Friedel–Crafts alkylation catalyzed by **4f**–$Zn(OTf)_2$ complex.

To confirm the role of the NH–π interaction in the origin of the enantioselectivity, we prepared ligands **8** and **9**, which have similar skeletons to ligands **4**[9e] and **5**, but without the NH fragment. In the reaction of indole with nitrostyrene, the ligands **8** and **9** gave much lower *ee* values (Figure 5). On the basis of these results, we deduced that if

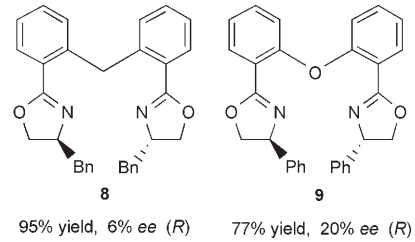


Figure 5. Ligands without a central NH fragment and their performance in the asymmetric Friedel–Crafts alkylation of indole with nitrostyrene.

we use a large substituent in place of the H atom of the NH fragment (e.g., an *N*-phenyl substituent), the attack from the back side may be shielded (Figure 6), and the absolute

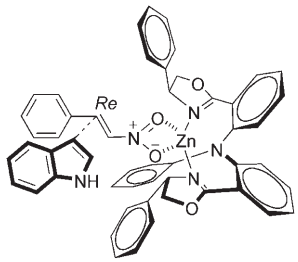
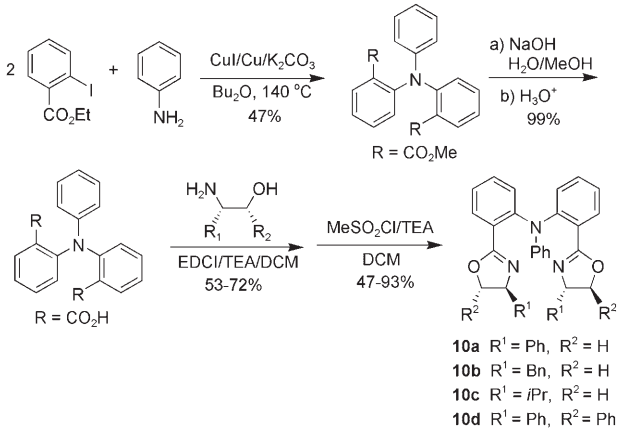


Figure 6. Proposed transition state of the asymmetric Friedel–Crafts alkylation catalyzed by **10a**–$Zn(OTf)_2$ complex.

configuration of the products may be reversed. To check our postulation, we synthesized triphenylamine-tethered bis(oxazoline) ligands **10a–d** in four steps from 2-iodobenzoate and aniline (Scheme 2). In the reaction of indole with nitrostyrene by catalysis with 5 mol% **10**–$Zn(OTf)_2$ complexes in



Scheme 2. Synthesis of triphenylamine-tethered bis(oxazoline) ligands **10a–d**.

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

3 mL toluene at 10 °C, ligands **10a–c** gave the *S* configuration with very low enantioselectivity, in accord with our prediction. Ligand **10d** gave the *R* product with 20 % *ee* , which may be attributed to the phenyl group on the 5-position of the oxazoline ring (Table 6). Such a result can be further evidence of our proposed transition state.

Table 6. Effects of ligands **10a–d** on the asymmetric Friedel–Crafts alkylation of indole and nitrostyrene.[a]

Entry	Ligand	Yield [%][b]	*ee* [%][c]
1	**10a**	86	31 (*S*)
2	**10b**	53	17 (*S*)
3	**10c**	47	9 (*S*)
4	**10d**	82	20 (*R*)

[a] All reactions were conducted on a 0.5-mmol scale in 3 mL toluene with 5 mol % ligand–$Zn(OTf)_2$ at 10 °C. [b] Yield of isolated product. [c] Determined by HPLC using a Chiracel OD-H column with 70:30 hexane/2-propanol as eluent.

Conclusions

We have demonstrated that the **4f**–$Zn(OTf)_2$ complex efficiently catalyzes the asymmetric Friedel–Crafts alkylation of indole derivatives with nitroalkenes. Compared with the previously published **4e**–$Zn(OTf)_2$ complex, better enantioselectivities and comparable yields were obtained in most cases. We have also demonstrated that the **4d**–$Zn(OTf)_2$ complex catalyzes the asymmetric Friedel–Crafts alkylation of pyrrole with nitroalkenes. Moderate to good yields and enantioselectivities were obtained in most cases. The origin of the enantioselectivity was attributed to the NH–π interactions between the catalysts and the incoming N-containing heterocycles in the transition state. This interaction was confirmed through comparison of the enantioselectivity and absolute configurations of the products in the reactions catalyzed by designed ligands. Further application of this methodology to the synthesis of functional chiral molecules is currently underway in our laboratory.

Experimental Section

General

Commercially available compounds were used without further purification. Solvents were dried according to standard procedures. Column chromatography was carried out using silica gel (200–300 mesh). Melting points were measured on a Yanaco melting point apparatus and are uncorrected. The ^{1}H NMR spectra were recorded on Mercury 300 MHz spectrometers, while the ^{13}C NMR spectra were recorded at 75 MHz. Infrared spectra were obtained on a Nicolet AVATAR 330 FTIR spectrometer. Mass spectra were obtained on a VG-ZAB-HS (EI) mass spectrometer. The ESI-MS spectra were obtained on Thermo Firrnigan LCQ Deca XP Plus mass spectrometer. Optical rotations were measured on a Perkin–Elmer 341 LC spectrometer. The enatiomeric excesses (*ee values*) of the products were determined by chiral HPLC analysis using an Aglient HP 1100 instrument (*n*-hexane/2-propanol as eluent). Elemental analyses were carried out on an Elementar Vario EL instrument. The nitroalkenes were prepared according to a literature procedure.[27]

Synthesis

Typical procedure for the asymmetric Friedel–Crafts alkylation of indole derivatives with nitroalkenes: To a flame-dried Schlenk tube were added $Zn(OTf)_2$ (9.3 mg, 0.025 mmol) and ligand **4f** (18.3 mg, 0.03 mmol) under nitrogen, followed by addition of toluene (3 mL). The mixture was stirred at room temperature for 2 h and the nitroalkene (0.5 mmol) was added. Then the mixture was further stirred for 10 min and cooled to −20 °C. The indole derivative (0.5 mmol) was added at −20 °C and the mixture was stirred at this temperature for 24 h. The mixture was separated directly by silica gel column chromatography with petroleum ether/ethyl acetate (10:1 to 5:1) as eluent, and the product was obtained in pure form.

3a: Compound **3a** was prepared according to the typical procedure. The product was obtained (134 mg, >99 % yield) as a white solid. M.p. 113–115 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 23.7 min, t_{minor} = 19.2 min); $[\alpha]_D^{20} = -23.0$ (*c* 1.0, CH_2Cl_2, 96 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (s, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.15–7.31 (m, 7H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 2.4 Hz, 1H), 5.16 (t, *J* = 8.1 Hz, 1H), 5.02 (dd, J_1 = 12.4 Hz, J_2 = 7.6 Hz, 1H), 4.90 ppm (dd, J_1 = 12.4 Hz, J_2 = 8.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.1, 136.4, 128.9, 127.7, 127.5, 126.0, 122.6, 121.6, 119.9, 118.8, 114.2, 111.4, 79.5, 41.5 ppm. Ref. [9c]: $[\alpha]_D^{20} = +25.3$ (*c* 0.9, CH_2Cl_2, 84 % *ee*) for *S* configuration.

3b: Prepared according to the typical procedure. The product was obtained (139 mg, 99 % yield) as a colorless solid. M. p. 121–123 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 18.8 min, t_{mino} = 15.6 min); $[\alpha]_D^{20} = -13.3$ (*c* 0.8, CH_2Cl_2, 93 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01 (s, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.19–7.22 (m, 3H), 7.04–7.15 (m, 3H), 6.96 (d, *J* = 2.1 Hz, 1H), 5.13 (t, *J* = 7.8 Hz, 1H), 5.02 (dd, J_1 = 12.3 Hz, J_2 = 7.5 Hz, 1H), 4.89 (dd, J_1 = 12.3 Hz, J_2 = 8.4 Hz, 1H), 2.33 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.2, 136.4, 136.1, 129.5, 127.6, 126.0, 122.6, 121.5, 119.8, 118.9, 114.5, 111.3, 79.6, 41.1, 21.0 ppm.

3c: Prepared according to the typical procedure. The product was obtained (130 mg, 88 % yield) as a colorless solid. M.p. 141–143 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 24.7 min, t_{minor} = 20.8 min); $[\alpha]_D^{20} = -27.0$ (*c* 0.7, CH_2Cl_2, 90 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (s, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.00 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 5.13 (t, *J* = 7.8 Hz, 1H), 5.04 (dd, J_1 = 12.0 Hz, J_2 = 7.5 Hz, 1H), 4.88 (dd, J_1 = 12.0 Hz, J_2 = 8.4 Hz, 1H), 3.76 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8, 136.4, 131.1, 128.8, 126.0, 122.6, 121.4, 119.9, 118.9, 114.7, 114.2, 111.3, 79.7, 55.2, 40.8 ppm.

3d: Prepared according to the typical procedure. The product was obtained (141 mg, 99 % yield) as a colorless oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 25.1 min, t_{minor} = 19.5 min); $[\alpha]_D^{20} = -35.0$ (*c* 0.5, CH_2Cl_2, 95 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (s, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.23–7.37 (m, 4H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 8.7 Hz, 2H), 6.97 (s, 1H), 5.20 (t, *J* = 7.8 Hz, 1H), 5.06 (dd, J_1 = 12.3 Hz, J_2 = 7.5 Hz, 1H), 4.90 ppm (dd, J_1 = 12.3 Hz, J_2 = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.9 (d, *J* = 244.5 Hz), 136.3, 134.8 (d, *J* = 3.2 Hz), 129.3 (d, *J* = 8.0 Hz), 125.8, 122.6, 121.4, 119.9, 118.7, 115.7 (d, *J* = 21.4 Hz), 113.9, 111.4, 79.4, 40.7 ppm.

3e: Prepared according to the typical procedure. The product was obtained (150 mg, >99 % yield) as a colorless solid. M.p. 132–134 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 28.5 min, t_{minor} = 22.2 min); $[\alpha]_D^{20} = -7.1$ (*c* 1.0, CH_2Cl_2, 95 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (s, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.20–7.32 (m, 5H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.00 (s, 1H), 5.17 (t, *J* = 7.8 Hz, 1H), 5.05 (dd, J_1 = 12.3 Hz, J_2 = 7.5 Hz, 1H), 4.90 ppm (dd, J_1 = 12.3 Hz, J_2 = 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.6,

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

136.4, 133.3, 129.1, 129.0, 125.8, 122.8, 121.5, 120.0, 118.7, 113.8, 111.4, 79.2, 40.9 ppm.

3f: Prepared according to the typical procedure. The product was obtained (170 mg, 99% yield) as a colorless oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 30.3 min, t_{minor} = 21.4 min); $[\alpha]_D^{20} = -16.0$ (*c* 0.5, CH_2Cl_2, 95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13 (s, 1H), 7.52 (s, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.34 (t, J = 8.4 Hz, 1H), 7.27 (d, J = 6.6 Hz, 1H), 7.12–7.23 (m, 3H), 6.96 (s, 1H), 5.18 (t, J = 7.8 Hz, 1H), 5.02 (dd, J_1 = 12.6 Hz, J_2 = 7.5 Hz, 1H), 4.89 ppm (dd, J_1 = 12.6 Hz, J_2 = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.5, 136.2, 130.7, 130.6, 130.4, 126.3, 125.7, 122.8, 122.7, 121.5, 119.9, 118.5, 113.2, 111.4, 79.0, 40.9 ppm.

3g: Prepared according to the typical procedure. The product was obtained (160 mg, 93% yield) as a colorless solid. M.p. 147–149 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 30.5 min, t_{minor} = 23.3 min); $[\alpha]_D^{20} = +1.8$ (*c* 0.5, CH_2Cl_2, 95% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (s, 1H), 7.45 (d, J = 8.1 Hz, 2H), 7.39 (t, J = 9 Hz, 2H), 7.26 (s, 1H), 7.21 (d, J = 8.4 Hz, 2H), 7.09 (t, J = 7.5 Hz, 1H), 7.02 (s, 1H), 5.15 (t, J = 8.1 Hz, 1H), 5.05 (dd, J_1 = 12.3 Hz, J_2 = 7.5 Hz, 1H), 4.90 ppm (dd, J_1 = 12.3 Hz, J_2 = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.3, 138.2, 136.4, 132.0, 129.5, 125.8, 122.9, 121.5, 120.1, 118.8, 113.8, 111.4, 79.1, 41.0 ppm.

3h: Prepared according to the typical procedure. The product was obtained (155 mg, > 99% yield) as a yellowish oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 50.1 min, t_{minor} = 36.3 min); $[\alpha]_D^{20} = -14.8$ (*c* 0.8, CH_2Cl_2, 94% *ee*); IR (neat): $\tilde{\nu}$ = 3424, 1551, 1527, 1458, 1421, 1377, 1349, 1101, 737 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.26 (s, 1H), 8.22 (s, 1H), 8.15 (d, J = 8.1 Hz, 1H), 7.73 (d, J = 7.5 Hz, 1H), 7.52 (t, J = 7.9 Hz, 1H), 7.41 (d, J = 8.4 Hz, 2H), 7.25 (t, J = 8.4 Hz, 1H), 7.09–7.14 (m, 2H), 5.32 (t, J = 7.9 Hz, 1H), 5.13 (dd, J_1 = 12.7 Hz, J_2 = 7.0 Hz, 1H), 5.01 ppm (dd, J_1 = 12.6 Hz, J_2 = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.5, 141.5, 136.4, 134.1, 129.9, 125.6, 123.0, 122.7, 122.6, 121.5, 120.2, 118.4, 112.9, 111.6, 78.8, 41.0; MS (70 eV, EI): *m*/*z* (%) 311 $[M]^+$ (40), 264 (85), 251 (30), 217 (28), 43 ppm (100); HRMS (EI) calcd for $C_{16}H_{13}N_3O_4$: 311.09061; found: 311.09110.

3i: Prepared according to the typical procedure. The product was obtained (144 mg, 93% yield) as a colorless solid. M.p. 149–150 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 59.7 min, t_{minor} = 46.5 min); $[\alpha]_D^{20} = +14.7$ (*c* 0.6, CH_2Cl_2, 97% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.24 (s, 1H), 8.18 (d, J = 8.7 Hz, 2H), 7.52 (d, J = 8.7 Hz, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.24 (t, J = 7.8 Hz, 1H), 7.10 (t, J = 7.6 Hz, 1H), 7.06 (d, J = 2.1 Hz, 1H), 5.30 (t, J = 7.8 Hz, 1H), 5.11 (dd, J_1 = 12.6 Hz, J_2 = 7.1 Hz, 1H), 4.99 ppm (dd, J_1 = 12.6 Hz, J_2 = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.2, 146.7, 136.4, 128.7, 125.6, 124.1, 123.1, 121.6, 120.3, 118.5, 112.9, 111.6, 78.7, 41.2 ppm.

3j: Prepared according to the typical procedure. The product was obtained (145 mg, 89% yield) as a yellowish oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 27.1 min, t_{minor} = 22.1 min); $[\alpha]_D^{20} = -24.9$ (*c* 0.8, CH_2Cl_2, 90% *ee*); IR (neat): $\tilde{\nu}$ = 3367, 1593, 1550, 1515, 1459, 1421, 1377, 1262, 1236, 1142, 1025, 909, 809, 730 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.31 (s, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.34 (d, J = 8.1 Hz, 1H), 7.22 (t, J = 7.5 Hz, 1H), 7.12 (t, J = 7.4 Hz, 1H), 6.99 (br, 1H), 6.89–6.92 (m, 2H), 6.82 (d, J = 8.1 Hz, 1H), 5.17 (t, J = 7.9 Hz, 1H), 5.07 (dd, J_1 = 12.1 Hz, J_2 = 7.6 Hz, 1H), 4.93 (dd, J_1 = 12.1 Hz, J_2 = 8.5 Hz, 1H), 3.85 (s, 3H), 3.82 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.9, 148.1, 136.3, 131.6, 125.9, 122.4, 121.5, 119.7, 119.6, 118.7, 114.1, 111.3, 111.1, 111.0, 79.5, 55.70, 55.67, 41.1 ppm; MS (70 eV, EI): *m*/*z* (%) 326 $[M]^+$ (64), 279 (90), 266 (100), 84 (20); HRMS (EI) calcd for $C_{18}H_{18}N_2O_4$: 326.12666; found: 326.12706.

3k: Prepared according to the typical procedure. The product was obtained (137 mg, 93% yield) as a colorless solid. M.p. 93–95 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{minor} = 11.6 min, t_{major} = 12.9 min); $[\alpha]_D^{20} = -46.8$ (*c* 0.6, CH_2Cl_2, 87% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96 (s, 1H), 7.45 (d, J = 7.8 Hz, 1H), 6.99–7.26 (m, 6H), 6.86 (d, J = 7.8 Hz, 1H), 6.79 (t, J = 7.2 Hz, 1H), 5.58 (dd, J_1 = 8.6 Hz, J_2 = 7.0 Hz, 1H), 4.89–5.03 (m, 2H), 3.85 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.8, 136.3, 128.8, 128.6, 127.1, 126.4, 122.3, 121.9, 120.7, 119.6, 119.0, 113.7, 111.2, 110.7, 78.0, 55.4, 35.4 ppm; Ref. [9c]: $[\alpha]_D^{20} = +49.6$ (*c* 0.75, CH_2Cl_2, 61% *ee*) for the *S* configuration.

3l: Prepared according to the typical procedure. The product was obtained (141 mg, 94% yield) as a colorless oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 14.3 min, t_{minor} = 22.7 min); $[\alpha]_D^{20} = -50.0$ (*c* 0.7, CH_2Cl_2, 72% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (s, 1H), 7.42 (m, 2H), 7.33 (d, J = 8.1 Hz, 1H), 7.04–7.24 (m, 6H), 5.73 (t, J = 8.0 Hz, 1H), 4.91–5.03 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.4, 133.8, 130.1, 128.9, 128.8, 127.2, 126.1, 122.7, 121.9, 120.5, 119.9, 118.8, 113.1, 111.4, 77.6, 37.9 ppm.

3m: Prepared according to the typical procedure. The product was obtained (136 mg, > 99% yield) as a yellowish oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 19.6 min, t_{minor} = 21.7 min); $[\alpha]_D^{20} = -21.5$ (*c* 0.6, CH_2Cl_2, 87% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (s, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.28 (d, J = 8.1 Hz, 1H), 7.14–7.21 (m, 2H), 7.09 (t, J = 7.5 Hz, 1H), 6.94–6.98 (m, 2H), 6.90 (t, J = 4.3 Hz, 1H), 5.42 (t, J = 7.8 Hz, 1H), 4.89–5.02 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.8, 136.2, 126.9, 125.6, 125.2, 124.8, 122.6, 121.9, 119.9, 118.7, 113.7, 111.5, 79.9, 36.8 ppm.

3n: Prepared according to the typical procedure. The product was obtained (113 mg, 88% yield) as a colorless solid. M.p. 85–87 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 13.0 min, t_{minor} = 17.9 min); $[\alpha]_D^{20} = +40.6$ (*c* 0.9, CH_2Cl_2, 80% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (s, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.04–7.34 (m, 4H), 6.99 (d, J = 1.5 Hz, 1H), 6.27 (dd, J_1 = 3.0 Hz, J_2 = 1.8 Hz, 1H), 6.12 (d, J = 3.3 Hz, 1H), 5.21 (t, J = 7.6 Hz, 1H), 5.01 (dd, J_1 = 12.4 Hz, J_2 = 8.2 Hz, 1H), 4.86 ppm (dd, J_1 = 12.4 Hz, J_2 = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.1, 142.2, 136.2, 125.5, 122.7, 122.5, 119.9, 118.6, 111.5, 111.3, 110.4, 107.3, 77.8, 35.6 ppm.

3o: Prepared according to the typical procedure. The product was obtained (142 mg, 90% yield) as a colorless solid. M.p. 128–130 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 1.0 mL min^{-1}, 254 nm, t_{major} = 20.7 min, t_{minor} = 25.4 min); $[\alpha]_D^{20} = -26.2$ (*c* 0.6, CH_2Cl_2, 90% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.24 (d, J = 7.8 Hz, 1H), 7.90 (s, 1H), 7.85 (m, 1H), 7.74 (t, J = 4.6 Hz, 1H), 7.11–7.52 (m, 7H), 7.01 (t, J = 7.4 Hz, 1H), 6.84 (s, 1H), 6.03 (t, J = 7.8 Hz, 1H), 4.98–5.05 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.4, 134.5, 134.1, 131.0, 129.1, 128.2, 126.8, 126.0, 125.9, 125.3, 124.6, 122.60, 122.56, 119.9, 118.7, 114.0, 111.4, 78.4, 36.9 ppm.

3p: Prepared according to the typical procedure. The product was obtained (117 mg, 80% yield) as a colorless oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 85:15, 1.0 mL min^{-1}, 254 nm, t_{major} = 35.1 min, t_{minor} = 41.3 min); $[\alpha]_D^{20} = +24.3$ (*c* 1.1, CH_2Cl_2, 91% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05 (s, 1H), 7.59 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.11–7.29 (m, 5H), 7.07 (d, J = 6.9 Hz, 2H), 7.00 (d, J = 2.1 Hz, 1H), 4.57–4.69 (m, 2H), 3.74–3.84 (m, 1H), 2.48–2.67 (m, 2H), 2.06–2.24 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.2, 136.5, 128.4, 128.3, 126.00, 125.96, 122.4, 122.2, 119.8, 118.7, 113.3, 111.6, 80.4, 35.9, 33.9, 33.2 ppm.

3q: Prepared according to the typical procedure. The product was obtained (108 mg, 79% yield) as a colorless oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel AD column (hexane/2-propanol 90:10, 1.0 mL min^{-1}, 254 nm, t_{major} = 13.0 min, t_{minor} = 16.7 min); $[\alpha]_D^{20} = +44.4$ (*c* 0.5, CH_2Cl_2, 94% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (s, 1H), 7.57–7.60 (m, 1H), 7.28–7.31 (m, 1H), 7.08–7.21 (m, 2H), 6.89 (d, J = 2.4 Hz, 1H), 4.79 (dd, J_1 = 12.0 Hz, J_2 = 6.3 Hz, 1H), 4.69 (dd, J_1 = 12.0 Hz, J_2 = 9.4 Hz, 1H), 3.61–3.69 (m, 1H), 1.61–1.83 (m, 6H), 0.88–1.29 ppm (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.1, 126.7,

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

122.2, 122.1, 119.5, 119.0, 113.0, 111.4, 78.4, 41.8, 40.4, 31.1, 30.3, 26.2, 26.1, 26.0 ppm.

3r: Prepared according to the typical procedure, though the reaction was conducted at 30 °C for 130 h. The product was obtained (66 mg, 54 % yield) as a colorless solid. M.p. 131–133 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 90:10, 1.0 mL min^{-1}, 254 nm, t_{major} = 17.1 min, t_{minor} = 27.6 min); $[\alpha]_D^{20}$ = −19.6 (*c* 0.7, CH_2Cl_2, 97 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (s, 1H), 7.61 (d, J = 7.5 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 7.09–7.19 (m, 2H), 6.98 (d, J = 2.4 Hz, 1H), 4.71–4.87 (m, 2H), 3.77 (dd, J_1 = 11.1 Hz, J_2 = 4.8 Hz, 1H), 0.99 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.7, 128.2, 122.1, 121.9, 119.6, 119.3, 112.9, 111.1, 78.0, 45.5, 34.4, 28.0 ppm.

3s: Prepared according to the typical procedure. The product was obtained (128 mg, 85 % yield) as a colorless solid. M.p. 132–134 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 85:15, 0.9 mL min^{-1}, 254 nm, t_{major} = 28.3 min, t_{minor} = 36.0 min); $[\alpha]_D^{20}$ = +30.4 (*c* 0.5, CH_2Cl_2, 88 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.12 (s, 1H), 7.37 (d, J = 2.1 Hz, 1H), 7.21–7.35 (m, 6H), 7.12 (dd, J_1 = 8.6 Hz, J_2 = 2.0 Hz, 1H), 7.05 (d, J = 2.4 Hz, 1H), 5.11 (t, J = 8.0 Hz, 1H), 5.01 (dd, J_1 = 12.3 Hz, J_2 = 8.1 Hz, 1H), 4.90 ppm (dd, J_1 = 12.3 Hz, J_2 = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.7, 134.7, 129.0, 127.7, 127.6, 127.1, 125.6, 123.0, 122.8, 118.3, 114.0, 112.4, 79.3, 41.3 ppm.

3t: Prepared according to the typical procedure. The product was obtained (132 mg, 94 % yield) as a colorless solid. M.p. 138–139 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 85:15, 1.0 mL min^{-1}, 254 nm, t_{major} = 34.0 min, t_{minor} = 41.3 min); $[\alpha]_D^{20}$ = +10.1 (*c* 1.0, CH_2Cl_2, 97 % *ee*); IR (neat): $\tilde{\nu}$ = 3423, 3413, 1560, 1536, 1482, 1456, 1432, 1377, 1210, 1099, 949, 916, 804, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (s, 1H), 7.24–7.36 (m, 7H), 7.05 (d, J = 8.4 Hz, 1H), 6.96 (d, J = 2.4 Hz, 1H), 5.18 (t, J = 7.8 Hz, 1H), 5.06 (dd, J_1 = 12.3 Hz, J_2 = 7.2 Hz, 1H), 4.94 (dd, J_1 = 12.3 Hz, J_2 = 8.4 Hz, 1H), 2.42 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.2, 134.7, 129.2, 128.9, 127.7, 127.5, 126.3, 124.3, 121.8, 118.4, 113.8, 111.0, 79.5, 41.5, 21.5 ppm; MS (70 eV, EI): *m*/*z* (%) 280 $[M]^+$(70), 233 (100), 220 (90), 146 (17); HRMS (EI) calcd for $C_{17}H_{16}N_2O_2$: 280.12118; found: 280.12179.

3u: Prepared according to the typical procedure. The product was obtained (147 mg, 99 % yield) as a colorless solid. M.p. 134–136 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 85:15, 1.0 mL min^{-1}, 254 nm, t_{major} = 30.1 min, t_{minor} = 35.2 min); $[\alpha]_D^{20}$ = +31.8 (*c* 1.0, CH_2Cl_2, 97 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99 (s, 1H), 7.19–7.34 (m, 6H), 6.96 (d, J = 2.4 Hz, 1H), 6.86 (d, J = 2.4 Hz, 1H), 6.83 (d, J = 1.5 Hz, 1H), 5.12 (t, J = 8.0 Hz, 1H), 5.02 (dd, J_1 = 12.3 Hz, J_2 = 7.5 Hz, 1H), 4.91 (dd, J_1 = 12.3 Hz, J_2 = 8.1 Hz, 1H), 3.76 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.1, 139.1, 131.5, 128.9, 127.7, 127.5, 126.5, 122.2, 114.0, 112.6, 112.1, 100.7, 79.4, 55.8, 41.5 ppm.

3v: Prepared according to the typical procedure, though the reaction was conducted for 48 h. The product was obtained (120 mg, 86 % yield) as a colorless oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 85:15, 1.0 mL min^{-1}, 254 nm, t_{major} = 50.7 min, t_{minor} = 53.7 min); $[\alpha]_D^{20}$ = −25.4 (*c* 0.7, CH_2Cl_2, 97 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.45 (m, 1H), 7.18–7.33 (m, 7H), 7.02–7.08 (m, 1H), 6.82 (s, 1H), 5.15 (t, J = 8.0 Hz, 1H), 5.00 (dd, J_1 = 12.3 Hz, J_2 = 7.6 Hz, 1H), 4.89 (dd, J_1 = 12.3 Hz, J_2 = 8.4 Hz, 1H), 3.67 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.3, 137.1, 128.8, 127.7, 127.4, 126.4, 126.3, 122.1, 119.4, 118.9, 112.6, 109.5, 79.4, 41.4, 32.7 ppm.

Typical procedure for the asymmetric Friedel–Crafts alkylation of pyrrole with nitroalkenes: To a flame-dried Schlenk tube were added $Zn(OTf)_2$ (9.3 mg, 0.025 mmol) and ligand **4d** (12.6 mg, 0.03 mmol) under nitrogen, followed by addition of toluene (3 mL). The mixture was stirred at room temperature for 2 h and the nitroalkene (0.5 mmol) was added. Then the mixture was stirred further for 10 min and cooled to 0 °C. Pyrrole (17.0 mg, 0.25 mmol) was added at 0 °C and the mixture was stirred at this temperature for 44 h. The mixture was separated directly by silica gel column chromatography with petroleum ether/ethyl acetate (15:1) as eluent, and the product was obtained in pure form.

7a: Prepared according to the typical procedure. The product was obtained (44 mg, 81 % yield) as an oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 19.9 min, t_{minor} = 17.6 min); $[\alpha]_D^{20}$ = −57.2 (*c* 0.8, MeOH, 78 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85 (s, 1H), 7.19–7.36 (m, 5H), 6.63–6.65 (m, 1H), 6.13–6.16 (m, 1H), 6.05–6.07 (m, 1H), 4.93 (dd, J_1 = 11.1 Hz, J_2 = 6.9 Hz. 1H), 4.85 (t, J = 7.0 Hz, 1H), 4.76 ppm (dd, J_1 = 11.1 Hz, J_2 = 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.9, 129.1, 128.8, 128.0, 127.8, 118.1, 108.5, 105.7, 79.1, 42.8 ppm.

7b: Prepared according to the typical procedure. The product was obtained (40 mg, 69 % yield) as a white solid. M.p. : 97–100 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 16.4 min, t_{minor} = 14.4 min); $[\alpha]_D^{20}$ = −51.1 (*c* 1.7, MeOH, 78 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.82 (s, 1H), 7.10–7.18 (m, 4H), 6.67–6.69 (m, 1H), 6.15–6.18 (m, 1H), 6.07 (s, 1H), 4.97 (dd, J_1 = 11.1 Hz, J_2 = 6.6 Hz. 1H), 4.86 (t, J = 6.6 Hz, 1H), 4.78 (dd, J_1 = 11.1 Hz, J_2 = 7.5 Hz, 1H), 2.33 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.9, 134.8, 129.9, 129.1, 127.8, 118.0, 108.6, 105.6, 79.3, 42.5, 21.0 ppm.

7c: Prepared according to the typical procedure. The product was obtained (37 mg, 61 % yield) as a yellowish oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 24.8 min, t_{minor} = 20.3 min); $[\alpha]_D^{20}$ = −53.0 (*c* 0.5, MeOH, 68 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88 (s, 1H), 7.13 (d, J = 14.7 Hz, 2H), 6.86 (d, J = 14.7 Hz, 2H), 6.53–6.68 (m, 1H), 6.14–6.17 (m, 1H), 6.05–6.07 (m, 1H), 4.94 (dd, J_1 = 11.1 Hz, J_2 = 6.4 Hz. 1H), 4.71–4.85 (m, 2H), 3.77 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2, 129.8, 129.2, 129.0, 118.0, 114.5, 108.5, 105.5, 79.3, 55.2, 42.1 ppm.

7d: Prepared according to the typical procedure. The product was obtained (44 mg, 76 % yield) as a white solid. M.p. 94–97 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 15.3 min, t_{minor} = 14.6 min); $[\alpha]_D^{20}$ = −61.0 (*c* 1.6, MeOH, 81 % *ee*); IR (neat): $\tilde{\nu}$ = 3385, 1606, 1550, 1509, 1430, 1380, 1227, 161, 1124, 1100, 1037, 841, 808, 742, 726 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98 (s, 1H), 7.19–7.23 (m, 2H), 7.02–7.08 (m, 2H), 6.70 (s, 1H), 6.20 (s, 1H), 6.10 (s, 1H), 4.97 (dd, J_1 = 11.1 Hz, J_2 = 6.9 Hz, 1H), 4.88 (t, J = 7.2 Hz, 1H), 4.77 ppm (dd, J_1 = 11.1 Hz, J_2 = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.2 (d, J = 245.6), 133.7 (d, J = 3.2 Hz), 129.4 (d, J = 8.2 Hz), 128.5, 118.3, 115.9 (d, J = 21.5 Hz), 108.5, 105.7, 79.0, 42.0 ppm; MS (70 eV, EI): *m*/*z* (%) 234 $[M]^+$ (18), 187 (100), 174 (52); HRMS (EI) calcd for $C_{12}H_{11}N_2O_2F$: 234.08046; found: 234.08077.

7e: Prepared according to the typical procedure. The product was obtained (53 mg, 84 % yield) as a white solid. M.p. 102–104 °C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 18.1 min, t_{minor} = 16.9 min); $[\alpha]_D^{20}$ = −49.0 (*c* 1.3, MeOH, 81 % *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87 (s, 1H), 7.33 (d, J = 11.1 Hz, 2H), 7.17 (d, J = 11.1 Hz, 2H), 6.70–6.72 (m, 1H), 6.16–6.19 (m, 1H), 6.06–6.09 (m, 1H), 4.97 (dd, J_1 = 11.7 Hz, J_2 = 6.9 Hz, 1H), 4.88 (t, J = 7.5 Hz, 1H), 4.77 ppm (dd, J_1 = 11.7 Hz, J_2 = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.5, 133.8, 129.2, 129.1, 128.2, 118.4, 108.6, 105.8, 78.8, 42.2 ppm.

7h: Prepared according to the typical procedure. The product was obtained (58 mg, 88 % yield) as an oil. The ee value was determined by chiral HPLC on a Daicel Chiracel OF column (hexane/2-propanol 75:25, 1.0 mL min−1, 235 nm, tmajor = 91.5 min, tminor = 81.2 min); $[\alpha]_D^{20}$ = −43.8 (c 1.1, MeOH, 80 % ee); IR (neat): $\tilde{\nu}$ = 3425, 2978, 2363, 1553, 1529, 1432, 1378, 1351, 1124, 1099, 802, 729 cm−1; 1H NMR (300 MHz, CDCl3): δ = 8.17 (s, 1H), 8.14 (s, 2H), 7.52–7.62 (m, 2H), 6.76 (s, 1H), 6.18–6.21 (m, 1H), 6.12 (s, 1H), 5.01–5.08 (m, 2H), 4.89 ppm (dd, J1 = 15.1 Hz, J2 = 11.0 Hz, 1H); 13C NMR (75 MHz, CDCl3): δ = 148.4, 140.4, 134.0, 130.1, 127.3, 123.0, 122.8, 118.9, 108.8, 106.3, 78.4, 42.4 ppm; MS (70 eV, EI): m/z (%) 261 [M]+ (5), 214 (44), 167 (46), 149 (100); HRMS (EI) calcd for C12H11N3O4: 261.07496; found: 261.07518.

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

7i: Prepared according to the typical procedure. The product was obtained (39 mg, 59% yield) as a white solid. M.p. 126–129°C. The ee value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 80:20, 0.9 mL min−1, 254 nm, tmajor = 58.8 min, tminor = 56.0 min); $[\alpha]_D^{20} = -43.6$ (c 0.8, MeOH, 91% ee); IR (neat): $\tilde{\nu}$ = 3410, 2926, 1553, 1518, 1378, 1349, 113, 1098, 1035, 858, 729 cm−1; 1H NMR (300 MHz, CDCl3): δ = 8.20 (d, J = 7.8 Hz, 2H), 8.06 (s, 1H), 7.43 (d, J = 8.1 Hz, 2H), 6.75–6.77 (m, 1H), 6.19–6.21 (m, 1H), 6.11 (s, 1H), 5.00–5.08 (m, 2H), 4.86 ppm (dd, J1 = 15.3 Hz, J2 = 11.7 Hz, 1H); 13C NMR (75 MHz, CDCl3): δ = 145.4, 129.0, 127.1, 124.3, 119.1, 119.0, 109.0, 106.5, 78.5, 42.6 ppm; MS (70 eV, EI): m/z (%) 261 [M]+ (14), 214 (100), 201 (17), 168 (29); HRMS (EI) calcd for C12H11N3O4: 261.07496; found: 261.07526.

7j: Prepared according to the typical procedure. The product was obtained (41 mg, 59% yield) as a white solid. M.p. 126–129°C. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 28.5 min, t_{minor} = 21.0 min); $[\alpha]_D^{20} = -53.3$ (*c* 0.8, MeOH, 70% *ee*); IR (neat): $\tilde{\nu}$ = 3373, 2936, 2838, 1551, 1516, 1465, 1378, 1262, 1236, 1142, 1025, 912, 805, 734 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89 (s, 1H), 6.78–6.86 (m, 2H), 6.71 (s, 2H), 6.17–6.19 (m, 1H), 6.09 (s, 1H), 4.98 (dd, J_1 = 10.8 Hz, J_2 = 6.0 Hz, 1H), 4.76–4.88 (m, 2H), 3.87 (s, 3H), 3.83 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.4, 148.7, 130.2, 129.1, 120.0, 118.1, 111.4, 110.9, 108.6, 105.5, 79.3, 55.9, 42.6 ppm; MS (70 eV, EI): *m*/*z* (%) 276 $[M]^+$ (40), 229 (100), 216 (84); HRMS (EI) calcd for $C_{14}H_{16}N_2O_4$: 276.11101; found: 276.11078.

7k: Prepared according to the typical procedure. The product was obtained (26 mg, 42% yield) as an oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 13.7 min, t_{minor} = 15.2 min); $[\alpha]_D^{20} = -21.6$ (*c* 1.3, MeOH, 38% *ee*); IR (neat): $\tilde{\nu}$ = 3431, 2924, 1551, 1492, 1463, 1438, 1378, 1245, 1122, 1027, 799, 757, 725 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.29 (s, 1H), 7.24–7.30 (m, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 6.89–6.95 (m, 2H), 6.68 (s, 1H), 6.12–6.14 (m, 1H), 6.10 (s, 1H), 5.22 (t, *J* = 7.8 Hz, 1H), 4.87–4.99 (m, 2H), 3.91 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.5, 129.2, 129.1, 129.0, 126.3, 121.3, 117.8, 111.2, 108.3, 106.0, 77.6, 55.6, 38.2 ppm; MS (70 eV, EI): *m*/*z* (%) 246 $[M]^+$ (31), 199 (74), 184 (100), 80 (46); HRMS (EI) calcd for $C_{13}H_{14}N_2O_3$: 246.10044; found: 246.10067.

7m: Prepared according to the typical procedure. The product was obtained (51 mg, 91% yield) as an oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 15.5 min, t_{minor} = 17.4 min); $[\alpha]_D^{20} = -44.3$ (*c* 1.9, MeOH, 80% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (s, 1H), 7.25 (d, *J* = 4.8 Hz, 1H), 6.96 (d, *J* = 4.8 Hz, 1H), 6.94 (s, 1H), 6.70 (s, 1H), 6.15–6.18 (m, 1H), 6.10 (s, 1H), 5.19 (t, *J* = 7.8 Hz, 1H), 4.93 (dd, J_1 = 12.9 Hz, J_2 = 7.5 Hz, 1H), 4.82 ppm (dd, J_1 = 13.2 Hz, J_2 = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.9, 128.2, 127.2, 125.8, 125.5, 118.2, 108.7, 105.8, 79.6, 38.1 ppm.

7n: Prepared according to the typical procedure. The product was obtained (43 mg, 83% yield) as an oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 11.1 min, t_{minor} = 12.3 min); $[\alpha]_D^{20} = +13.1$ (*c* 0.7, MeOH, 79% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.28 (s, 1H), 7.40 (s, 1H), 6.71–6.73 (m, 1H), 6.32–6.34 (m, 1H), 6.14–6.19 (m, 2H), 6.09 (s, 1H), 5.01 (t, *J* = 7.6 Hz, 1H), 4.89 (dd, J_1 = 12.9 Hz, J_2 = 7.8 Hz, 1H), 4.80 ppm (dd, J_1 = 12.9 Hz, J_2 = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.6, 142.7, 126.1, 118.3, 110.6, 108.8, 107.8, 106.6, 77.7, 36.9 ppm.

7p: Prepared according to the typical procedure. The product was obtained (39 mg, 64% yield) as an oil. The *ee* value was determined by chiral HPLC on a Daicel Chiracel OD-H column (hexane/2-propanol 70:30, 0.8 mL min^{-1}, 235 nm, t_{major} = 30.2 min, t_{minor} = 26.5 min); $[\alpha]_D^{20} = +0.53$ (*c* 1.9, MeOH, 11% *ee*); IR (neat): $\tilde{\nu}$ = 3427, 2926, 1549, 1496, 1454, 1430, 1379, 1031, 795, 723, 701 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (s, 1H), 7.19–7.32 (m, 3H), 7.12 (d, *J* = 7.2 Hz, 2H), 6.72 (s, 1H), 6.19–6.21 (m, 1H), 6.06 (s, 1H), 4.50–4.53 (m, 2H), 3.45–3.55 (m, 1H), 2.63–2.72 (m, 1H), 2.49–2.59 (m, 1H), 2.00 ppm (q, *J* = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.7, 129.2, 128.5, 128.3, 126.2, 117.5, 108.8, 105.6, 80.3, 36.7, 33.7, 32.9 ppm; MS (70 eV, EI): *m*/*z* (%) 244 ($[M]^+$, 39), 197 (53), 93 (100), 80 (42); HRMS (EI) calcd for $C_{14}H_{16}N_2O_2$: 244.12118; found: 244.12150.

2,2′-Bis[*N*-(1*S*)-(1-phenyl-2-hydroxyethyl)carbamoyl]diphenyl ether: A solution of 2,2′-dicarboxyl diphenylether[28] (516 mg, 2 mmol) in thionyl chloride (5 mL) was heated at reflux for 3 h. The excess thionyl chloride was removed under reduced pressure to afford the diacyl dichloride. The above diacyl dichloride in CH_2Cl_2 (20 mL) was added dropwise to a solution of (*S*)-phenylglycinol (548 mg, 4 mmol) and Et_3N (1.4 mL, 10 mmol) in CH_2Cl_2 (10 mL) at 0°C and stirred at room temperature for 48 h. The reaction mixture was successively washed with saturated NH_4Cl (aq), saturated $NaHCO_3$ (aq), and brine. The organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified by silica gel column chromatography using CH_2Cl_2/MeOH (50:1) as eluent to afford the bis(hydroxyamide) 832 mg (84% yield) as a colorless solid. M.p. 93–95°C; $[\alpha]_D^{20} = -88.8$ (*c* 0.6, CH_2Cl_2); IR (neat): $\tilde{\nu}$ = 3305, 3062, 1635, 1604, 1533, 1477, 1445, 1304, 1232, 1105, 1069, 1031, 895, 753, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 7.2 Hz, 4H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.22–7.23 (m, 6H), 7.14–7.16 (m, 4H), 6.92 (d, *J* = 8.1 Hz, 2H), 5.17–5.24 (m, 2H), 3.70–3.83 (m, 4H), 3.26 ppm (br, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.2, 153.5, 139.1, 132.8, 131.5, 128.5, 127.4, 126.4, 125.7, 124.6, 118.8, 65.7, 55.9 ppm; ESI-MS: *m*/*z* 497.1 $[M+H]^+$; elemental analysis (%) calcd for $C_{30}H_{28}N_2O_5 \cdot 1/2H_2O$: C 71.27, H 5.78, N 5.54; found: C 71.52, H 5.84, N 5.54.

9: To an ice-cooled solution of the bis(hydroxyamide) (496 mg, 1 mmol) and Et_3N (0.62 mL, 4.4 mmol) in CH_2Cl_2 (5 mL) was added dropwise methanesulfonyl chloride (0.17 mL, 2.2 mmol) by syringe. The reaction mixture was allowed to warm to room temperature and stirred further for 4 h. Then saturated NH_4Cl (aq) was poured into the reaction mixture and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The solvent was removed in vacuo to afford the crude bismesylate. The crude bismesylate was dissolved in methanol (3 mL) and a solution of NaOH (80 mg, 2 mmol) in water (3 mL) was added. After heating at reflux for 4 h, the mixture was cooled to room temperature and the solvent was removed in vacuo. The residue was extracted with CH_2Cl_2 (3 × 10 mL). The combined extracts were washed with brine and dried over anhydrous Na_2SO_4, and concentrated in vacuo to afford the crude ligand **9**. The crude product was purified by silica gel column chromatography using petroleum ether/ethyl acetate (2:1) as eluent to afford **9** (276 mg, 60% yield) as a colorless oil. $[\alpha]_D^{20} = -84.9$ (*c* 0.5, CH_2Cl_2); IR (neat): $\tilde{\nu}$ = 3058, 1645, 1601, 1485, 1450, 1356, 1233, 1160, 1118, 1057, 1032, 973, 761, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.99 (m, 2H), 7.42–7.47 (m, 2H), 7.17–7.28 (m, 12H), 7.00 (d, *J* = 8.1 Hz, 2H), 5.27 (dd, J_1 = 9.9 Hz, J_2 = 8.4 Hz, 2H), 4.65 (dd, J_1 = 9.9 Hz, J_2 = 8.4 Hz, 2H), 4.12 ppm (t, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.6, 155.8, 142.4, 132.4, 131.8, 128.5, 127.4, 126.7, 123.3, 120.0, 119.7, 74.9, 69.7 ppm; MS (70 eV, EI): *m*/*z* (%) 460 $[M]^+$ (75), 339 (15), 236 (100), 222 (42), 91 (34); HRMS (EI) calcd for $C_{30}H_{24}N_2O_3$: 460.17869; found: 460.17952.

General procedure for the preparation of bis(hydroxyamide)s of triphenylamine-tethered ligands: To a 100-mL flask were added 2,2′-dicarboxyltriphenylamine[29] (666 mg, 2 mmol), EDCI-HCl (900 mg, 4.5 mmol), DMAP (25 mg, 0.2 mmol), and CH_2Cl_2 (35 mL). Then *N*-methylmorpholine (0.72 mL, 6.5 mmol) was added, and the mixture became clear. The chiral amino alcohol (4.5 mmol) was added, and the solution was stirred at room temperature for 48 h. The reaction was quenched by addition of 30 mL of saturated NH_4Cl (aq). The phase was separated, and the organic phase was washed with saturated $NaHCO_3$ (aq) and brine. After drying over anhydrous Na_2SO_4, the solvent was removed in vacuo and the crude product was purified by silica gel column chromatography using CH_2Cl_2/CH_3OH (50:1) as eluent. In the case of the bis(hydroxyamide) of ligand **10c**, the TBS-protected (*S*)-valinol was used instead of (*S*)-valinol to eliminate side reactions. The TBS group was removed with TBAF in THF before purification.

2,2′-Bis[*N*-(1*S*)-(1-phenyl-2-hydroxyethyl)carbamoyl]triphenylamine: Prepared according to the general procedure. The product was obtained

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

(795 mg, 69% yield) as a colorless solid. M.p. 129–131 °C; $[\alpha]_D^{20} = +51.7$ (*c* 0.6, CH_2Cl_2); IR (neat): $\tilde{\nu} = 3267, 3063, 1629, 1597, 1544, 1482, 1444, 1307, 1263, 1069, 1030, 755, 734, 698\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.85$ (s, 2H), 7.50 (d, $J = 7.2$ Hz, 2H), 7.27–7.33 (m, 2H), 7.19–7.21 (m, 2H), 7.08–7.15 (m, 10H), 6.90–7.00 (m, 7H), 6.83 (d, $J = 7.8$ Hz, 2H), 4.69–4.71 (m, 2H), 3.53 (s, 4H), 3.26 ppm (br, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.4, 147.9, 145.4, 138.8, 131.5, 130.4, 129.2, 128.4, 127.2, 126.5, 124.3, 123.3, 122.8, 66.0, 56.6$ ppm; ESI-MS: *m/z* 572.2 $[M+H]^+$; elemental analysis calcd (%) for $C_{36}H_{33}N_3O_4 \cdot 1/2H_2O$: C 74.46, H 5.90, N 7.24; found: C 74.98, H 5.70, N 7.30.

2,2′-Bis[*N*-(1*S*)-(1-benzyl-2-hydroxyethyl)carbamoyl]triphenylamine: Prepared according to the general procedure. The product was obtained (634 mg, 53% yield) as a white solid. M.p. 191–193 °C; $[\alpha]_D^{20} = -48.6$ (*c* 0.5, CH_2Cl_2); IR (neat): $\tilde{\nu} = 3521, 3397, 3304, 3062, 2865, 1628, 1596, 1557, 1518, 1490, 1440, 1299, 1247, 1078, 1044, 759, 746, 699\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.09$–7.43 (m, 20H), 6.91–7.00 (m, 5H), 3.89 (s, 2H), 3.23–3.28 (m, 4H), 2.89 (br, 2H), 2.55–2.64 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.0, 147.9, 145.2, 138.1, 131.9, 131.5, 130.0, 129.3, 129.2, 128.4, 126.7, 126.4, 124.4, 123.3, 122.4, 62.8, 53.5, 36.3$ ppm; ESI-MS: *m/z* 600.2 $[M+H]^+$; elemental analysis calcd (%) for $C_{38}H_{37}N_3O_4$: C 76.10, H 6.22, N 7.01; found: C 76.04, H 6.42, N 7.01.

2,2′-Bis[*N*-(1*S*)-(1-(1-methylethyl)-2-hydroxyethyl)carbamoyl]triphenylamine: Prepared according to the general procedure. The product was obtained (722 mg, 72% yield) as a colorless solid. M.p. 112–114 °C; $[\alpha]_D^{20} = -55.8$ (*c* 0.9, CH_2Cl_2); IR (neat): $\tilde{\nu} = 3264, 3067, 2959, 2874, 1626, 1597, 1546, 1483, 1443, 1306, 1251, 1158, 1078, 787, 755, 736, 696\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.62$ (d, $J = 7.2$ Hz, 2H), 7.44 (br, 2H), 7.34 (dt, $J_1 = 7.8$ Hz, $J_2 = 1.5$ Hz, 2H), 7.13–7.28 (m, 4H), 6.92–7.03 (m, 5H), 3.40–3.47 (m, 4H), 3.23 (d, $J = 9.0$ Hz, 2H), 3.01 (br, 2H), 1.71–1.82 (m, 2H), 0.84 (d, $J = 6.6$ Hz, 6H), 0.71 ppm (d, $J = 6.9$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.5, 148.0, 145.3, 131.9, 131.4, 130.2, 129.3, 126.8, 124.4, 123.3, 122.4, 62.8, 57.9, 29.1, 19.25, 19.17$ ppm; ESI-MS: *m/z* 504.2 $[M+H]^+$; elemental analysis calcd (%) for $C_{30}H_{37}N_3O_4 \cdot 1/2H_2O$: C 70.29, H 7.47, N 8.20; found: C 70.87, H 7.41, N 8.21.

2,2′-Bis[*N*-(1*S*,2*R*)-(1,2-diphenyl-2-hydroxyethyl)carbamoyl]triphenylamine: Prepared according to the general procedure. The product was obtained (1.045 g, 72% yield) as a colorless solid. M.p. 108–110 °C; $[\alpha]_D^{20} = +5.0$ (*c* 0.6, CH_2Cl_2); IR (neat): $\tilde{\nu} = 3282, 3262, 1629, 1597, 1483, 1445, 1318, 1255, 1192, 1094, 1062, 755, 699\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.06$ (br, 2H), 7.40 (d, $J = 6.9$ Hz, 2H), 7.28 (t, $J = 7.5$ Hz, 2H), 7.17–7.20 (m, 7H), 7.03–7.15 (m, 9H), 6.92–6.96 (m, 7H), 6.81 (d, $J = 6.6$ Hz, 4H), 6.69 (br, 2H), 4.89–4.91 (m, 2H), 4.73 (s, 1H), 3.62 ppm (br, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.0, 147.4, 145.1, 140.0, 136.4, 131.3, 130.1, 129.0, 128.2, 127.7, 127.6, 127.3, 127.1, 126.4, 126.1, 124.1, 123.0, 122.8, 76.2, 60.2$ ppm; ESI-MS: *m/z* 724.2 $[M+H]^+$; elemental analysis calcd (%) for $C_{48}H_{41}N_3O_4 \cdot 1/2H_2O$: C 78.67, H 5,78, N 5.73; found: C 78.49, H 5.62, N 5.64.

General procedure for the preparation of triphenylamine-tethered ligands: To an ice-cooled solution of the bis(hydroxyamide) (1 equiv) in CH_2Cl_2 (1 mmol/10 mL) was added Et_3N (4.4 equiv). Then methanesulfonyl chloride (2.2 equiv) was added dropwise at 0 °C. The temperature was allowed to rise to room temperature and the solution was stirred for 48 h. The full conversion of bis(hydroxyamide) to the corresponding bis(oxazoline) ligand was indicated by TLC analysis. The reaction was quenched by addition of 20 mL of saturated NH_4Cl (aq). The phase was separated, and the organic phase was washed with saturated $NaHCO_3$ (aq) and brine. After being dried over anhydrous Na_2SO_4, the solvent was removed in vacuo and the crude product was purified by silica gel column chromatography using petroleum ether/ethyl acetate (5:1) as eluent.

10a: Prepared according to the general procedure from 545 mg (0.95 mmol) of corresponding bis(hydroxyamide). The product was obtained (345 mg, 68% yield) as a white solid. M.p. 153–154 °C; $[\alpha]_D^{20} = -355.4$ (*c* 0.5, CH_2Cl_2); IR (neat): $\tilde{\nu} = 3063, 1642, 1592, 1485, 1449, 1323, 1263, 1118, 1073, 1031, 952, 749, 699\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.88$ (dd, $J_1 = 7.5$ Hz, $J_2 = 1.5$ Hz, 2H), 7.42–7.48 (m, 2H), 7.14–7.32 (m, 12H), 6.87–6.89 (m, 5H), 6.75 (d, $J = 7.8$ Hz, 2H), 4.96 (t, $J = 9.9$ Hz, 2H), 4.35 (dd, $J_1 = 9.9$ Hz, $J_2 = 8.7$ Hz, 2H), 3.58 ppm (t, $J = 8.7$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.1, 147.9, 146.2, 141.6, 132.3, 132.1, 129.6, 128.8, 128.3, 127.3, 127.0, 124.8, 124.3, 120.6, 119.9, 74.7, 69.3$ ppm; MS (70 eV, EI): *m/z* (%) 535 $[M]^+$ (100), 298 (30), 236 (12), 195 (39), 77 (16); elemental analysis calcd (%) for $C_{36}H_{29}N_3O_2$: C 80.72, H 5.46, N 7.84; found: C 80.79, H 5.56, N 7.84.

10b: Prepared according to the general procedure from 530 mg (0.89 mmol) of the corresponding bis(hydroxyamide). The product was obtained (465 mg, 93% yield) as a yellowish oil. $[\alpha]_D^{20} = -92.1$ (*c* 0.7, CH_2Cl_2); IR (neat): $\tilde{\nu} = 3061, 3027, 2894, 1650, 1592, 1486, 1449, 1356, 1323, 1288, 1265, 1076, 1031, 965, 748, 697\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.73$ (d, $J = 7.8$ Hz, 2H), 7.39 (t, $J = 7.6$ Hz, 2H), 7.14–7.27 (m, 12H), 7.07 (d, $J = 7.5$ Hz, 4H), 6.92 (t $J = 7.2$ Hz, 1H), 6.76 (d, $J = 7.8$ Hz, 2H), 4.11–4.22 (m, 2H), 3.87 (t, $J = 8.7$ Hz, 2H), 3.47 (t, $J = 7.9$ Hz, 2H), 2.87 (dd, $J_1 = 13.6$ Hz, $J_2 = 4.6$ Hz, 2H), 1.90 ppm (dd, $J_1 = 12.9$ Hz, $J_2 = 10.2$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 164.2, 147.5, 145.7, 138.1, 131.9, 131.3, 129.1, 128.9, 128.7, 128.3, 126.2, 125.0, 124.1, 120.5, 120.1, 71.8, 66.9, 41.1$; MS (70 eV, EI): *m/z* (%) 563 $[M]^+$ (100), 472 (25), 338 (32), 117 (22), 91 ppm (42); HRMS (EI) calcd for $C_{38}H_{33}N_3O_2$: 563.25728; found: 563.25783.

10c: Prepared according to the general procedure from 338 mg (0.67 mmol) of the corresponding bis(hydroxyamide). The product was obtained (176 mg, 56% yield) as a yellowish oil. $[\alpha]_D^{20} = -90.5$ (*c* 0.4, CH_2Cl_2); IR (neat): $\tilde{\nu} = 3063, 2957, 2871, 1646, 1593, 1486, 1449, 1352, 1323, 1263, 1118, 1035, 966, 765, 748, 693\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.74$ (d, $J = 6.6$ Hz, 2H), 7.38 (t, $J = 7.0$ Hz, 2H), 7.13–7.21 (m, 4H), 7.07 (t, $J = 7.8$ Hz, 2H), 6.76 (t, $J = 7.4$ Hz, 1H), 6.66 (d, $J = 7.8$ Hz, 2H), 3.70–3.80 (m, 2H), 3.51–3.58 (m, 4H), 1.37–1.40 (m, 2H), 0.86 (d, $J = 6.6$ Hz, 6H), 0.71 ppm (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 163.8, 147.2, 145.9, 131.8, 131.6, 129.1, 128.4, 125.2, 124.0, 120.4, 119.9, 71.7, 70.3, 32.5, 19.1, 18.3$ ppm; MS (70 eV, EI): *m/z* (%) 467 $[M]^+$ (100), 424 (20), 338 (24), 297 (20), 196 ppm (15); HRMS (EI) calcd for $C_{30}H_{33}N_3O_2$: 467.25728; found: 467.25663.

10d: Prepared according to the general procedure from 1.044 g (1.44 mmol) of the corresponding bis(hydroxyamide). The product was obtained (468 mg, 47% yield) as a white solid. M.p. 190–191 °C; $[\alpha]_D^{20} = -204.8$ (*c* 0.5, CH_2Cl_2); IR (neat): $\tilde{\nu} = 3062, 1645, 1591, 1489, 1451, 1323, 1158, 1032, 967, 749, 758, 696\ cm^{-1}$; H NMR (300 MHz, $CDCl_3$): $\delta = 7.96$ (d, $J = 7.5$ Hz, 2H), 7.38–7.45 (m, 4H), 7.29–7.34 (m, 6H), 7.17–7.24 (m, 10H), 7.11 (t, $J = 3.6$ Hz, 4H), 6.99 (t, $J = 7.2$ Hz, 1H), 6.76–6.81 (m, 6H), 4.85 (d, $J = 9.9$ Hz, 2H), 4.71 ppm (d, $J = 9.9$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 164.2, 148.8, 146.5, 140.9, 139.7, 132.5, 132.2, 130.0, 129.1, 128.6, 128.3, 128.0, 127.4, 127.2, 125.7, 125.0, 124.5, 120.7, 120.0, 89.1, 78.1$ ppm; MS (70 eV, EI): *m/z* (%) 687 $[M]^+$ (100), 524 (13), 357 (25), 298 (30), 195 (32); elemental analysis calcd (%)for $C_{48}H_{37}N_3O_2$: C 83.82, H 5.42, N 6.11; found: C 83.81, H 5.58, N 6.09.

X-ray analysis of **7e**: The crystal was measured on a Rigaku RAXIS RAPID IP diffractometer at 293 K by using graphite-monochromated $Mo_{K\alpha}$ radiation with $\lambda = 0.71073$ Å. The Rapid-AUTO site was used for data collection and cell refinement. Computing data reduction was performed using CrystalStructure (Rigaku/MSC, 2000). The structure was solved by direct methods using SHELXS-97 (G. M. Sheldrick, 1997). Full-matrix least-squares refinement on F^2 was performed with SHELXL-97 (G. M. Sheldrick, 1997). Refinement of F^2 against all reflections was performed. The weighted *R* factor *wR* and goodness of fit *S* are based on F^2, conventional *R* factors are based on *F*, with *F* set to zero for negative F^2. CCDC 631421 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgements

This project was supported by the National Natural Science Foundation of China (Grant nos. 20772006, 20572003, and 20521202), the Program for New Century Excellent Talents in University (NCET-07–0011).

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

[1] For recent reviews, see: a) M. Bandini, A. Melloni, A. Umani-Ronchi, *Angew. Chem.* **2004**, *116*, 560; *Angew. Chem. Int. Ed.* **2004**, *43*, 550; b) M. Bandini, A. Melloni, S. Tommasi, A. Umani-Ronchi, *Synlett* **2005**, 1199; c) Y. Wang, K.- L. Ding, *Chin. J. Org. Chem.* **2001**, *21*, 763; d) K. A. Jørgensen, *Synthesis* **2003**, 1117.

[2] For some recent examples, see: a) J. F. Austin, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2002**, *124*, 1172; b) C.-F. Li, H. Liu, J. Liao, Y.- J. Cao, X.-P. Liu, W.- J. Xiao, *Org. Lett.* **2007**, *9*, 1847.

[3] For some recent examples, see: a) H. D. King, Z. Meng, D. Denhart, R. Mattson, R. Kimura, D. Wu, Q. Gao, J. E. Macor, *Org. Lett.* **2005**, *7*, 3437; b) M Bandini, M. Fagioli, P. Melchiorre, A. Melloni, A. Umani-Ronchi, *Tetrahedron Lett.* **2003**, *44*, 5843; c) G. Bartoli, M. Bosco, A. Carione, F. Pesciaioli, L. Sambri, P. Melchiorre, *Org. Lett.* **2007**, *9*, 1403; d) G. Blay, I. Fernandez, J. R. Pedro, C. Vila, *Org. Lett.* **2007**, *9*, 2601; e) H. Yang, Y.-T. Hong, S. Kim, *Org. Lett.* **2007**, *9*, 2281.

[4] a) D. A. Evans, K. R. Fandrick, H.- J. Song, *J. Am. Chem. Soc.* **2005**, *127*, 8942; b) D. A. Evans, K. A. Scheidt, K. R. Fandrick, H. W. Lam, J. Wu, *J. Am. Chem. Soc.* **2003**, *125*, 10780; c) D. A. Evans, K. R. Fandrick, H.- J. Song, K. A. Scheidt, R. Xu, *J. Am. Chem. Soc.* **2007**, *129*, 10029; d) W. Zhou, L.-W. Xu, L. Li, L. Yang, C.-G. Xia, *Eur. J. Org. Chem.* **2006**, 5225.

[5] a) A. Bandini, P. G. Cozzi, P. Melchiorre, A. Umani-Ronchi, *Angew. Chem.* **2004**, *116*, 86; *Angew Chem. Int. Ed.* **2004**, *43*, 84.

[6] For some recent examples, see: a) H. Li, Y.-Q. Wang, L. Deng, *Org. Lett.* **2006**, *8*, 4063; b) W. Zhuang, T. B. Poulsen, K. A. Jørgensen, *Org. Biomol. Chem.* **2005**, *3*, 3284; c) B. Török, M. Abid, G. London, J. Esquibel, M. Torok, S. C. Mhadgut, P. Yan, G. K. S. Prakash, *Angew. Chem.* **2005**, *117*, 3146; *Angew. Chem. Int. Ed.* **2005**, *44*, 3086; d) M. P. A. Lyle, N. D. Draper, P. D. Wilson, *Org. Lett.* **2005**, *7*, 901; e) W. Zhuang, N. Gathergood, R. G. Hazell, K. A. Jørgensen, *J. Org. Chem.* **2001**, *66*, 1009; f) H.- M. Dong, H.-H. Lu, L.- Q. Lu, C.-B. Chen, W.- J. Xiao, *Adv. Synth. Catal.* **2007**, *349*, 1597; g) M. Rueping, B. J. Nachtsheim, S. A. Moreth, M. Bolte, *Angew. Chem.* **2008**, *120*, 603; *Angew. Chem. Int. Ed.* **2008**, *47*, 593.

[7] For some recent examples, see: a) Y.-Q. Wang, J. Song, R. Hong, H. Li, L. Deng, *J. Am. Chem. Soc.* **2006**, *128*, 8156; b) Y.-X. Jia, J.-H. Xie, H.-F. Duan, L.-X. Wang, Q.- L. Zhou, *Org. Lett.* **2006**, *8*, 1621; c) Q. Kang, Z.- A. Zhao, S.- L. You, *J. Am. Chem. Soc.* **2007**, *129*, 1484; d) M. Terada, S. Yokoyama, K. Sorimachi, D. Uraguchi, *Adv. Synth. Catal.* **2007**, *349*, 1863; e) G. B. Rowland, E. B. Rowland, Y. Liang, J. A. Perman, J. C. Antilla, *Org. Lett.* **2007**, *9*, 2609; f) M. J. Wanner, P. Hauwert, H. E. Schoemaker, R. de Gelder, J. H. van Maarseveen, H. Hiemstra, *Eur. J. Org. Chem.* **2008**, 180.

[8] a) M. Terada, K. Sorimachi, *J. Am. Chem. Soc.* **2007**, *129*, 292; b) Y.- X. Jia, J. Zhong, S.-F. Zhu, C.- M. Zhang, Q.- L. Zhou, *Angew. Chem.* **2007**, *119*, 5661; *Angew. Chem. Int. Ed.* **2007**, *46*, 5565.

[9] For some recent examples, see: a) R. P. Herrera, V. Sgarzani, L. Bernardi, A. Ricci, *Angew. Chem.* **2005**, *117*, 6734; *Angew. Chem. Int. Ed.* **2005**, *44*, 6576; b) W. Zhuang, R. G. Hazell, K. A. Jørgensen, *Org. Biomol. Chem.* **2005**, *3*, 2566; c) Y.-X. Jia, S.-F. Zhu, Y. Yang, Q.- L. Zhou, *J. Org. Chem.* **2006**, *71*, 75; d) M. Bandini, A. Garelli, M. Rovinetti, M. Tommasi, A. Umani-Ronchi, *Chirality* **2005**, *17*, 522; e) S.-F. Lu, D.- M. Du, J. Xu, *Org. Lett.* **2006**, *8*, 2115; f) E. M. Fleming, T. McCabe, S. J. Connon, *Tetrahedron Lett.* **2006**, *47*, 7037; g) P. K. Singh, A. Bisai, V. K. Singh, *Tetrahedron Lett.* **2007**, *48*, 1127; h) Y. Sui, L. Liu, J.- L. Zhao, D. Wang, Y.- J. Chen, *Tetrahedron* **2007**, *63*, 5173.

[10] a) W. Zhuang, T. Hansen, K. A. Jørgensen, *Chem. Commun.* **2001**, 347; b) J. Zhou, Y. Tang, *J. Am. Chem. Soc.* **2002**, *124*, 9030; c) J. Zhou, M.-C. Ye, Y. Tang, *J. Comb. Chem.* **2004**, *6*, 301; d) J. Zhou, Y. Tang, *Chem. Commun.* **2004**, 432.

[11] S. Yamazaki, Y. Iwata, *J. Org. Chem.* **2006**, *71*, 739.

[12] For some recent examples, see: a) A. Ishii, V. A. Soloshonok, K. Mikami, *J. Org. Chem.* **2000**, *65*, 1597; b) Y. Yuan, X. Wang, X. Li, K. Ding *J. Org. Chem.* **2004**, *69*, 146; c) J.- L. Zhao, L. Liu, Y. Sui, Y.- L. Liu, D. Wang, Y.- J. Chen, *Org. Lett.* **2006**, *8*, 6127.

[13] a) N. A. Paras, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2001**, *123*, 4370; b) C. Palomo, M. Oiarbide, B. G. Kardak, J. M. Garcia, A. Linden, *J. Am. Chem. Soc.* **2005**, *127*, 4154; c) D. A. Evans, K. R. Fandrick, *Org. Lett.* **2006**, *8*, 2249; d) G. Li, G. B. Rowland, E. B. Rowland, J. C. Antilla, *Org. Lett.* **2007**, *9*, 4065.

[14] a) D. Uraguchi, K. Sorimachi, M. Terada, *J. Am. Chem. Soc.* **2004**, *126*, 11804; b) H. Liu, J. Xu, D.- M. Du, *Org. Lett.* **2007**, *9*, 4725.

[15] For a recent review, see: O. M. Berner, L. Tedeschi, D. Enders, *Eur. J. Org. Chem.* **2002**, 1877.

[16] N. Ono, *The Nitro Group in Organic Synthesis*; Wiley-VCH, New York, **2001**.

[17] H. A. McManus, P. J. Guiry, *J. Org. Chem.* **2002**, *67*, 8566.

[18] a) S.-F. Lu, D.- M. Du, S.-W. Zhang, J. Xu, *Tetrahedron: Asymmetry* **2004**, *15*, 3433; b) D.- M. Du, S.-F. Lu, T. Fang, J. Xu, *J. Org. Chem.* **2005**, *70*, 3712.

[19] H. A. McManus, P. G. Cozzi, P. J. Guiry, *Adv. Synth. Catal.* **2006**, *348*, 551.

[20] S.-F. Lu, D.- M. Du, J. Xu, S.-W. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 7418.

[21] Our research on asymmetric Friedel–Crafts reactions of pyrrole with nitroalkenes was communicated at the 4th Sino–Australia Organic Chemistry Symposium, Beijing, China, September 26–28, 2006. We have applied a Chinese patent: D. M. Du, H. Liu, J. Xu, Chiral five-member ring heterocycles and their enantioselective synthetic methods. Patent application NO.200710003416.9, application date: 2007.02.06.

[22] For recent reviews, see: a) A. Fürstner, *Angew. Chem.* **2003**, *115*, 3706; *Angew. Chem. Int. Ed.* **2003**, *42*, 3582; b) H. Hoffmann, T. Lindel, *Synthesis* **2003**, 1753; c) G. Balme, *Angew. Chem.* **2004**, *116*, 6396; *Angew. Chem. Int. Ed.* **2004**, *43*, 6238.

[23] For recent reviews, see: a) S. Yamaguchi, K. Tamao, *J. Organomet. Chem.* **2002**, *653*, 223; b) N. J. Guemione, W. Hayes, *Curr. Org. Chem.* **2004**, *8*, 637.

[24] During the preparation of the manuscript, Trost and co-worker reported the asymmetric Friedel–Crafts reaction of pyrroles with nitroalkenes: B. M. Trost, C. Müller, *J. Am. Chem. Soc.* **2008**, *130*, 2438.

[25] a) J. S. Yadav, S. Abraham, B. V. S. Reddy, G. Sabitha, *Tetrahedron Lett.* **2001**, *42*, 8063; b) Z.-P. Zhan, W.-Z. Yang, R.-F. Yang, *Synlett* **2005**, 2425; c) C. Lin, J. Hsu, M. N. V. Sastry, H. Fang, Z. Tu, J.-T. Liu, C.-F. Yao, *Tetrahedron* **2005**, *61*, 11751; d) L.-T. An, J.-P. Zhou, L.- L. Zhang, Y. Zhang, *Tetrahedron Lett.* **2007**, *48*, 4297; e) H. Firouzabadi, N. Iranpoor, F. Nowrouzi, *Chem. Commun.* **2005**, 789; f) N. Azizi, F. Arynasab, M. R. Saidi, *Org. Biomol. Chem.* **2006**, *4*, 4275.

[26] For previous studies on indole–NH interactions, see, for example: a) P. Emseis, T. W. Failes, D. E. Hibbs, P. Leverett, P. A. Williams, *Polyhedron* **2004**, *23*, 1749; b) M. A. Muñoz, R. Ferrero, C. Carmona, M. Balón, *Spectrochim. Acta Part A* **2004**, *60*, 193; c) H. Adams, K. D. M. Harris, G. A. Hembury, C. A. Hunter, D. Livingstone, J. F. McCabe, *Chem. Commun.* **1996**, 2531; d) R. Mahalakshmi, A. Sengupta, S. Raghothama, N. Shamala, P. Balaram, *J. Pept. Res.* **2005**, *66*, 277; e) M. A. Muñoz, O. Sama, M. Galán, P. Guardado, C. Carmona, M. Balón, *J. Phys. Chem. B* **1999**, *103*, 8794.

[27] a) D. Lucet, S. Sabelle, O. Kostelitz, T. L. Gall, C. Mioskowski, *Eur. J. Org. Chem.* **1999**, 2583; b) S. E. Denmark, L. Marcin, *J. Org. Chem.* **1995**, *60*, 3221; c) S. E. Denmark, L. Marcin, *J. Org. Chem.* **1993**, *58*, 3850.

[28] M. Gomez, S. Jansat, G. Muller, M. A. Maestro, J. Mahia, *Organometallics* **2002**, *21*, 1077.

[29] J. E. Field, D. Venkataraman, *Chem. Mater.* **2002**, *14*, 962.

Received: March 5, 2008
Published online: May 21, 2008

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim