Conjugate Addition of Organozinc Compounds to Nitroolefins

Audrius Rimkus,[1] Norbert Sewald*

University of Bielefeld, Department of Chemistry, PO Box 10 01 31, 33501 Bielefeld, Germany
Fax +49(521)1068094; E-mail: norbert.sewald@uni-bielefeld.de

Received 22 September 2003

Dedicated Prof. Dr. Klaus Burger on the occasion of his 65th birthday.

Abstract: Symmetrical (R_2Zn) or mixed diorganozinc compounds (R^1ZnR^2) smoothly react with a series of nitroolefins in the presence of catalytic amounts of copper(I) salts and provide synthetically versatile nitro compounds in moderate to good yields. Simple alkyl groups, functionalized residues, or mixed trimethylsilylmethyl organozinc compounds (TMSM)ZnR may be employed for conjugate addition, while the TMSM group is not being transferred. *ipso*-Substitution is observed in absence of the copper(I) salt.

Enantiomerically pure copper(I) complexes with BINOL based chiral phosphoramidite ligands efficiently catalyze the addition of dialkylzinc compounds to nitroalkenes. For instance, diethylzinc addition occurs with high yields and excellent enantioselectivity. Nitrostyrene, 3-nitroacrolein dimethylacetal, and 3-nitroacrylates have been used as substrates. The nitroolefin moiety predominates over the acrylate moiety and acts as the more powerful Michael acceptor. 2-Alkyl-3-nitropropanoates are exclusively obtained with excellent yield and enantioselectivity. The products can easily be transformed into β^2-homoamino acids, compounds of high relevance for different areas of preparative organic chemistry.

Key words: asymmetric catalysis, Michael additions, ligands, organometallic reagents, amino acids

1 Introduction

The conjugate addition of nucleophiles to α,β-unsaturated compounds is one of the most powerful bond forming strategies and has been widely utilized in organic synthesis.[2] This is mainly due to the broad spectrum of donors (organometallic reagents, heteroatom Michael donors, other carbanions) and acceptors (α,β-unsaturated reagents) that can be employed in this type of reaction.[3]

Nitroolefins are one of the strongest Michael acceptors providing a common pathway to nitroalkanes, which are particularly versatile intermediates in organic synthesis since the nitro group may be easily transformed into a wide variety of functionalities.[4,5]

Our ongoing interest is directed toward conjugate addition of functionalized and unfunctionalized organozinc reagents to aromatic and aliphatic nitroolefins,[6–8] which has also been investigated by other groups.[9,10]

Organometallics bearing functional groups are versatile intermediates for the synthesis of a wide range of more complex organic compounds.[11,12] The use of organozinc compounds is particularly favored due to their reactivity, lower basicity, and remarkable functional group tolerance. [11,13]

It has been shown earlier that mixed organozinc reagents (TMSM)ZnR can be efficiently added to a range of Michael acceptors.[14] Since the TMSM[15,16] group is a non-transferable ligand, this type of organometallics is particularly useful when a highly functionalized or/and chiral residue R is to be transferred.

Significant progress in asymmetric conjugate addition has been reported over the past few years. Especially, phosphoramidite-type chiral ligands provided a major breakthrough in this field.

Hence, both chemoselectivity and stereoselectivity are important issues to be addressed in this context. In this feature article, we provide an overview on the subject and summarize recent results of our own work on conjugate addition of symmetrical and mixed diorganozinc compounds as well as functionalized organozinc cuprates to aliphatic and aromatic nitroolefins. Enantioselective conjugate addition of dialkylzinc compounds catalyzed by enantiomerically pure phosphoramidite/copper complexes will also be discussed.

2 Synthesis of Nitroolefins

The aliphatic nitroolefins **1b**–**e** (Figure 1) were synthesized according to literature procedures[17] by dehydrating nitroalcohols obtained by base-catalyzed nitroaldol reaction of the corresponding nitroalkane and an aldehyde.[5,18] Water elimination proceeds by either basic elimination of trifluoroacetic acid (**1b**, **1d**,**e**)[19a] or with *N*,*N*′-dicyclohex-

SYNTHESIS 2004, No. 1, pp 0135–0146
Advanced online publication: 25.11.2003
DOI: 10.1055/s-2003-44355; Art ID: Z14103SS

ylcarbodiimide (DCC) in the presence of copper(I) chloride (**1c**).[19b] Nitrostyrene (**1a**) has been prepared by conventional nitroaldol condensation.[20]

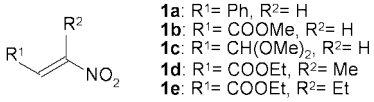


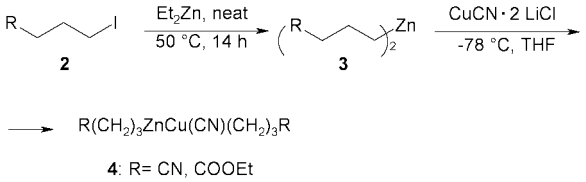
Figure 1 Nitroolefins

3 Conjugate Addition of Organozinc Compounds

Recent years have witnessed a remarkable revival of the use of organozinc reagents in synthetic chemistry.[11] In particular, conjugate addition reactions, key steps in the synthesis of numerous biologically active compounds including steroids, prostaglandins, terpenes, and others,[12] have been examined. Most favorably, these reactions are catalyzed by copper(I) salts. Notably, the source of the cuprous ion and even the counterion have been found to influence the reaction result.[21] Often copper(II) triflate is used as the copper(I) source, because it is easier to purify and handle and is reduced in situ to copper(I) by the organozinc compounds. Nitroolefins are highly efficient electrophilic species with a C–C–N atom pattern. They can be considered as appropriate starting materials for a broad spectrum of interesting compounds. We have developed an approach towards the synthesis of β^2-homoamino acids via conjugate addition of organozinc reagents to the nitroalkenes **1b**–**e**. Nitrostyrene **1a** initially was used as a model substrate.

3.1 Conjugate Addition of Functionalized Organozinc Cuprates and Diorganozinc Compounds

Diorganozinc reagents R_2Zn are less readily available compared to organozinc halides RZnX. However, diorganozinc reagents R_2Zn and their transmetallated correlates RZnCu(CN)R display a significantly higher reactivity and efficiency towards electrophiles compared to the copper-zinc halides RZnCu(CN)X.[22] When nitroolefins are used, useful nitro intermediates can be prepared following this methodology. The functionalized diorganozinc compounds are easily prepared by an iodine-zinc exchange reaction (Scheme 1).[22]



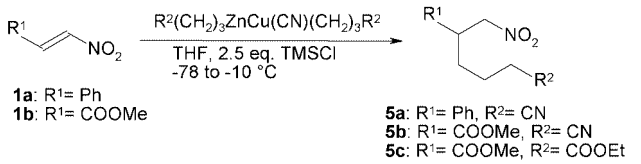
Scheme 1 Synthesis of the functionalized diorganozinc compounds

Biographical Sketches

Audrius Rimkus was born in 1974 in Klaipeda (Lithuania). After graduating with a BSc degree in Chemistry from the University of Vilnius, he studied for a PhD in Germany under the supervision of Prof. N. Sewald at the Universities of Leipzig and Bielefeld. He is now working as postdoctoral fellow in the group of Prof. S. Niwayama at the Oklahoma State University (Stillwater, USA).

Norbert Sewald was born in 1961 in Munich (Germany). He obtained his Diploma degree in Chemistry and his PhD in Organic Chemistry at the Technical University of Munich. After a postdoctoral fellowship with Prof. J. E. Baldwin at the Dyson Perrins Laboratory, University of Oxford, he started independent research at the Technical University of Munich and later at the University of Leipzig. In 1998 he finished his habilitation and was appointed to full Professor of Organic and Bioorganic Chemistry at the University of Bielefeld in 1999. His research interests in general comprise organic chemistry at the interface of biology and medical sciences. Special focus is placed on the development of synthetic methods, the isolation, structure elucidation, and total synthesis of bioactive natural products, studies regarding the interaction of peptides with proteins or DNA, analysis of the solution structure of peptides using NMR, and the development of novel molecular tools for biochemical research.

The organozinc cuprates **4**[23] were applied in conjugate additions to nitroolefins **1** to give functionalized nitro compounds **5** (Scheme 2) in moderate to good yields (Table 1).

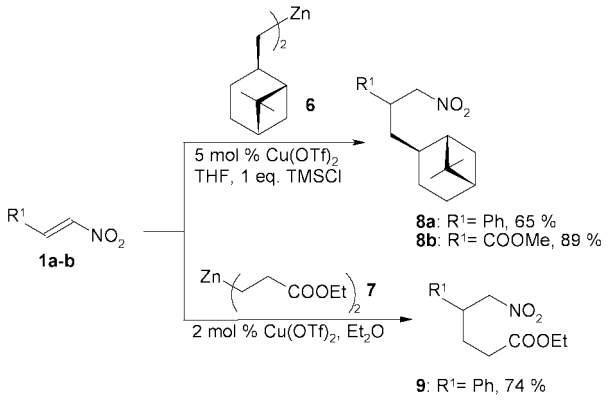


Scheme 2 Addition of functionalized diorganozinc cuprates to nitroolefins

Table 1 Addition of Functionalized Diorganozinc Cuprates to Nitroolefins **1a**,**b**

Entry	R^1	R^2	Yield (%)	Product
1	Ph	CN	67	**5a**
2	COOMe	CN	66	**5b**
3	COOMe	COOEt	53	**5c**

A wide variety of functionalized diorganozinc compounds can be easily prepared via boron-zinc transmetallation.[11,12a] Diorganozinc compounds like dimyrtanylzinc **6** or bis[2-(ethoxycarbonyl)ethyl]zinc **7**[24] can efficiently be added to nitroolefins in a copper-catalyzed conjugate addition reaction, providing access to more complex molecules **8** and **9** (Scheme 3). Although **6** was employed in an enantiomerically pure form, no diastereoselectivity was observed (dr 1:1).

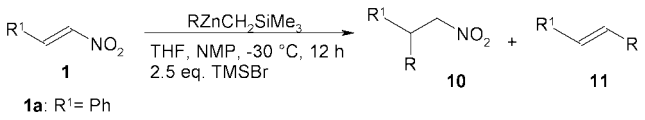


Scheme 3 Conjugate addition of diorganozinc compounds to nitroolefins

3.2 Conjugate Addition of Alkyl Trimethylsilylmethylzinc Compounds

The trimethylsilylmethyl (TMSM) group is known as a non-transferable ligand in organocopper and -zinc chemistry.[16] It can be advantageously employed as a 'dummy' ligand (TMSM)ZnR when the transferable moiety R is expensive or laborious to obtain.

There is a series of reports that under certain circumstances the nitro group may act as a leaving group in nucleophilic substitutions at nitroalkenes. This *ipso*-type substitution (vinylic substitution) usually takes place, when nitroolefins bearing an acceptor group are used together with 'soft' nucleophiles.[25,26] In contrast, dialkylzinc compounds or mixed diorganozinc compounds (TMSM)ZnR have been found to smoothly add to nitroolefins and other Michael acceptors in a mixture of THF and the polar co-solvent *N*-methylpyrrolidone (NMP) in the absence of any copper or transition metal catalyst.[14] Formation of the *ipso*-product of type **11** (Scheme 4) has not been observed under these conditions. However, we found that in the absence of copper(I) salts the addition of alkyl(trimethylsilylmethyl)zinc reagents[27] to nitrostyrene **1a** in a THF/NMP mixture leads to predominant formation of the *ipso*-substituted products **11** (Scheme 4; Table 2, entries 1 and 2). This side reaction can be suppressed upon addition of a catalytic amount of copper(I) salt or copper(II) triflate (ca. 2–4 mol%). Exclusive formation of the 1,4-adduct is then observed in moderate to good yields. Longer reaction times usually are connected with decreasing yields (Table 2, entry 5).



Scheme 4 Addition of (TMSM)ZnR compounds to nitrostyrene

Table 2 Addition of (TMSM)ZnR Compounds to Nitrostyrene **1a**. Effect of the Copper Salt

entry	R	Cu-Salt	Yield (%)	
1	*c*-Hexyl	–	**10a**: 5	**11a**: 28
2	*n*-Heptyl	–	**10b**: 15	**11b**: 43
3	*c*-Hexyl	CuCl	**10a**: 70	–
4	*n*-Heptyl	$Cu(OTf)_2$	**10b**: 83	–
5[a]	*n*-Heptyl	$Cu(OTf)_2$	**10b**: 64	–

[a] Longer reaction time (24 h).

Further aliphatic residues could be successfully added to nitroolefins **1a**–**c** under analogous reaction conditions affording the corresponding nitro compounds **10** in moderate to good yields (Scheme 5, Table 3). The addition results show, that alkyl(trimethylsilylmethyl)zinc reagents are suitable for the addition to functionalized nitroolefins.

Noteworthy, the 3-nitroacrylates **1b** are dissonant, ambidentate electrophiles (nitroolefin *vs.* acrylate moiety). However, the nitroolefin moiety acts as the exclusive Michael acceptor, giving rise to the exclusive formation of 2-alkyl-3-nitroacrylates **10d**–**f**.

Scheme 5 Copper catalyzed addition of alkyl trimethylsilylmethyl zinc compounds to nitroolefins

Table 3 Copper Catalyzed Conjugate Addition of Trimethylsilylmethylzinc Compounds to Nitroolefins **1a–c**

Entry	Nitroolefin	R^2	Yield (%)	Product
1	**1a**	*n*-Butyl	72	**10c**
2	**1b**	*n*-Heptyl	46	**10d**
3	**1b**	*c*-Hexyl	69	**10e**
4	**1b**	*n*-Hexyl	56	**10f**
5[a]	**1c**	*c*-Hexyl	45	**10g**
6[a]	**1c**	*n*-Heptyl	72	**10h**

[a] TMSCl was used instead of TMSBr.

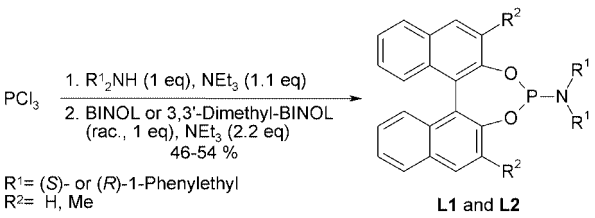
3.3 Enantioselective Catalytic Conjugate Addition of Dialkylzinc Compounds

Seebach et al. reported that the enantioselective addition of primary dialkylzinc reagents to aryl substituted nitroolefins is achieved using an excess of titanium TADDOLates.[28] The catalytic, ligand accelerated addition of diethylzinc to nitrostyrene was first described by Alexakis et al.[29] In recent years there has been considerable effort towards catalytic asymmetric conjugate additions of organozinc compounds to both acyclic and cyclic nitroolefins.[6–10] Promising results from our previous investigations[6,7] encouraged us to study stereoselective conjugate additions to 3-nitroacrylates, which are valuable substrates en route to the synthesis of β^2-homoamino acids.[6,9,10a]

3.3.1 Chiral Catalysts

Numerous reports are dedicated to the utilization of chiral ligands in the catalytic enantioselective conjugate addition of diorganozinc compounds to nitroolefins.[6–10] Syntheses of BINOL-based enantiomerically pure copper(I)/phosphoramidite complexes and their applications in conjugate additions of dialkylzinc compounds to cyclic and acyclic enones were first reported by Feringa et al.[30]

In our investigation, the original procedure described by Feringa et al.[30,31] for the synthesis of phosphoramidites **L1** and **L2** was modified (Scheme 6, Figure 2). Starting from phosphorus trichloride, at first enantiomerically pure



Scheme 6 Synthesis of phosphoramidites

bis(phenylethyl)amine and then racemic BINOL or its 3,3′-dimethyl derivative are reacted subsequently, followed by chromatographic resolution of the diastereomeric phosphoramidites. Alternatively, enantiomerically pure BINOL may be employed which is easily obtained by enzymatic resolution with bovine pancreas cholesterol esterase.[32] The 3,3′-dimethyl derivative of BINOL was synthesized according to Woodward's method.[33] The ligands **L1** and **L2** have been isolated in moderate to good yield (46–54%). Noteworthy, we determined the specific optical rotation value $[\alpha]_D$ of the ligand (*P*,*S*,*S*)-**L1** as +15.5 (*c* = 0.8, $CHCl_3$), which substantially differs from the data reported by Feringa et al.[31] ($[\alpha]_D$ +202.1, *c* = 0.79, $CHCl_3$). However, our value has been confirmed by two other groups.[34]

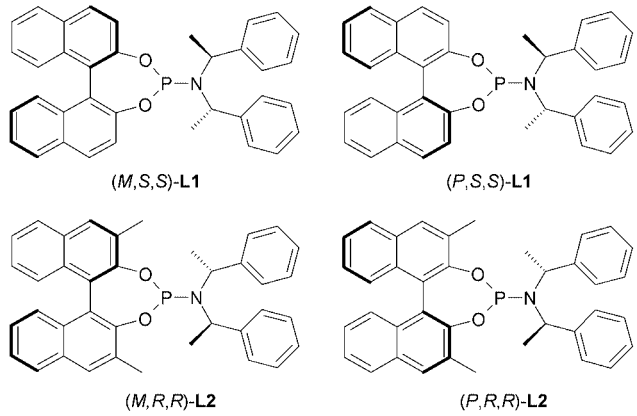
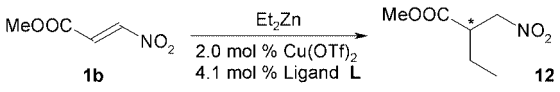


Figure 2 Chiral phosphoramidite ligands

3.3.2 Addition to 3-Nitroacrylates

Feringa et al. argued that low ee values are observed upon copper(I) catalyzed conjugate addition to nitroacrylates, because the high reactivity of these derivatives would lead to a strongly competing blank reaction.[9] However, ourselves[6] and others[10a] found that excellent ee values can be obtained (Scheme 7), depending on ligand, solvent, and reaction conditions employed.



Scheme 7 Enantioselective copper(I) catalyzed conjugate addition to methyl 3-nitroacrylate

Table 4 Enantioselective Copper(I) Catalyzed Conjugate Addition of Diethylzinc to Methyl 3-Nitroacrylate **1b**[a]

Entry	Ligand	Solvent	T (°C)	ee,%[d]	Isomer
1	(*M*,*S*,*S*)-**L1**	Toluene	−50	10	(+)-**12**
2	(*M*,*S*,*S*)-**L1**	Toluene	−30	28	(+)-**12**
3	(*P*,*S*,*S*)-**L1**	Toluene	−30	12	(−)-**12**
4	(*M*,*S*,*S*)-**L1**	Et_2O	−30	68	(+)-**12**
5	(*M*,*S*,*S*)-**L1**	Et_2O	−78	77	(+)-**12**
6	(*M*,*S*,*S*)-**L1**	THF	−30	16	(−)-**12**
7	(*P*,*R*,*R*)-**L2**	Toluene	−30	67	(+)-**12**
8	(*M*,*R*,*R*)-**L2**	Toluene	−30	52	(+)-**12**
9	(*P*,*R*,*R*)-**L2**	Et_2O	−30	73	(+)-**12**
10	(*M*,*R*,*R*)-**L2**	Et_2O	−30	12	(−)-**12**
11[b]	(*P*,*R*,*R*)-**L2**	Et_2O	−78	92	(+)-**12**
12[b]	(*M*,*R*,*R*)-**L2**	Et_2O	−78	15	(+)-**12**
13[c]	(*M*,*S*)-**L3**	Toluene	−30	36	(+)-**12**

[a] Isolated yields of **12** range from 70–94%.
[b] 0.5 mol% $Cu(OTf)_2$ and 1.0 mol% ligand.
[c] 3 mol% $Cu(OTf)_2$ and 6 mol% ligand.
[d] Determined by chiral GC on a FS-Lipodex E column.

Substrate and catalyst as well as the nature of the copper salt influence the enantioselectivity of conjugate additions to enolates, as recently investigated by us and Alexakis et al.[21] Even the concentration was found to be a parameter influencing the ee value.[10d] The best addition results for **1b** were obtained with ligand (*P*,*R*,*R*)–**L2** in diethyl ether at –78 °C, which provides **12** in 94% yield and 92% ee (Table 4, entry 11). Enantioselectivity drops to 15% ee when the diastereomeric ligand (*M*,*R*,*R*)-**L2** is used under these reaction conditions (Table 1, entry 12). Even less than 0.5 mol% of copper(II) and 1.0 mol% of chiral phosphoramidite are sufficient for very fast and clean reactions at –78 °C.

In comparison, Pfaltz's oxazoline-phosphite ligand (*M*,*S*)-**L3** (Figure 3) provides **12** with 36% ee in toluene at –78 °C, which is comparable to the result obtained with phosphoramidite (*M*,*S*,*S*)-**L1** under the same reaction conditions (entries 2 and 13).

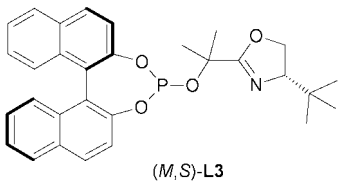
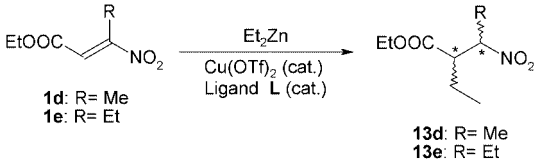


Figure 3 Pfaltz's oxazoline-phosphite

3.3.3 Addition to 3-Alkyl Substituted 3-Nitroacrylates

Hoveyda et al. examined the enantioselective conjugate addition to cyclic nitroalkenes and reported high ee values (93–95%) and acceptable diastereomeric ratios (81:19→83:17).[10b] We performed analogous additions to branched, acyclic nitroolefins. Diethylzinc was added to 3-alkyl-substituted 3-nitroacrylates **1d**,**e** catalyzed by enantiomerically pure copper(I)/phosphoramidite complexes leading to 2,3-disubstituted nitroesters **13** (Scheme 8).



Scheme 8 Addition to 3-alkyl substituted 3-nitroacrylates

Compared to nitroacrylate **1b**, the reactivity of 3-alkyl substituted nitroolefins **1d** and **1e** seems to be increased leading to a complete conversion of starting material within 20 minutes or less even at –78 °C. The solvent, reaction temperature as well as the catalyst amount have been varied (Table 5). Decreasing the amount of catalyst to 0.5 mol% does not have any significant influence on the diastereoselectivity of the addition (Table 5, entries 1 and 6). Unfortunately, the enantiomers could not be separated on the chiral GC and HPLC columns tested so far. Therefore, no ee values can be given yet. The dr values of **13** are moderate to good, with the best case being 89:11 when the ligand **L1** is employed in toluene at –30 °C (Table 5, entry 8). Products of the Nef reaction, which can be even predominantly formed under similar reaction/work-up conditions,[10b,35] were not observed.

3.3.4 Addition to Nitrostyrene and 3-Nitroacrolein Dimethylacetal

Conjugate additions of diethylzinc to nitrostyrene **1a** and 3-nitroacrolein dimethylacetal **1c** catalyzed by copper(I)/phosphoramidite ligands show varying enantioselectivities (Scheme 9, Table 6). Only low enantioselectivities have been induced when the 3,3′-dimethylated ligand **L2** was used in the additions to nitrostyrene **1a** (entries 1 and 2). In contrast to the substrate **1b** (Table 4, entry 11), diethyl ether is obviously not a solvent of choice for additions to nitrostyrene. The absolute configuration of the resulting nitro compound **14a** has been assigned by comparing the retention behavior in chiral GC according to data reported by Seebach et al.[28]

The use of dimethylacetal **1c** leads to a high enantioselectivity of 86% ee, when the ligand (*P*,*R*,*R*)-**L2** is employed (Table 6, entry 3). This enantioselectivity is comparable in its absolute value to the result recently obtained by us using the ligand (*M*,*S*,*S*)-**L1** (entry 4), albeit the addition product has the opposite configuration.

Table 5 Addition to 3-Alkyl Substituted 3-Nitroacrylates **1d**,**e**

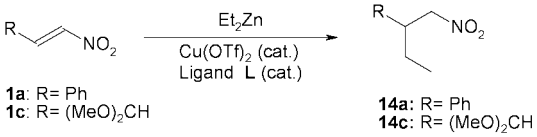
Entry	R	Ligand[a]	$Cu(OTf)_2$ (mol%)	Solvent	T (°C)	dr (%)	Conversion (%)
1	Me	(*P*,*R*,*R*)-**L2**	1.0	Et_2O	−78	63: 37	57[c]
2	Me	(*M*,*R*,*R*)-**L2**	1.0	Et_2O	−78	65: 35	99
3	Me	(*P*,*R*,*R*)-**L2**	1.0	Toluene	−78	57: 43	99
4	Me	(*M*,*R*,*R*)-**L2**	1.0	Toluene	−78	60: 40	99
5	Me	(*M*,*S*,*S*)-**L1**	1.0	Et_2O	−30	45: 55	99
6	Me	(*P*,*R*,*R*)-**L2**	0.5	Et_2O	−78	70: 30	99
7	Me	(*M*,*R*,*R*)-**L2**[b]	2.0	THF	−20	63: 37	99
8	Me	(*M*,*S*,*S*)-**L1**	1.0	Toluene	−30	89: 11	99
9	Et	(*P*,*R*,*R*)-**L2**	2.0	Et_2O	−78	64: 36	74[c]
10	Et	(*M*,*R*,*R*)-**L2**	2.0	Et_2O	−78	49: 51	99
11	Et	(*P*,*R*,*R*)-**L2**[b]	2.0	Toluene	−30	57: 43	88[c]

[a] Ligand to copper salt ratio is 2:1.
[b] 4.1 mol% of ligand has been used.
[c] Isolated yield, %.

Table 6 Addition to Nitrostyrene **1a** and 3-Nitroacrolein Dimethylacetal **1c**

Entry	R	Ligand	Solvent	T (°C)	ee (%)[a]	Isomer	Yield (%)
1	Ph	(*P*,*R*,*R*)-**L2**	Et_2O	−78	16	(*R*)[28]	99[b]
2	Ph	(*M*,*R*,*R*)-**L2**	Et_2O	−78	6	(*R*)[28]	79
3	$(MeO)_2CH$	(*P*,*R*,*R*)-**L2**	Toluene	−30	87	(+)	73
4[7]	$(MeO)_2CH$	(*M*,*S*,*S*)-**L1**	Toluene	−30	86	(-)	84

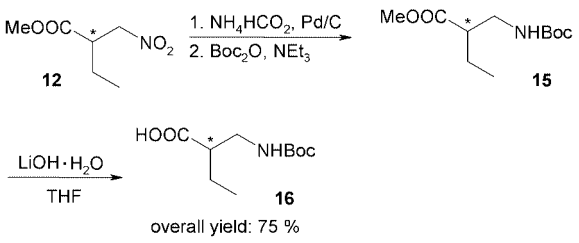
[a] Ee was determined by chiral GC on the FS-Lipodex E (Macherey-Nagel) column.
[b] Conversion, %.



Scheme 9 Addition to nitrostyrene and 3-nitroacrolein dimethylacetal

4 Synthesis of β²-Homoaminoacids

Enantioselective conjugate addition to 3-nitroacrylates provides an efficient route to β²-homoamino acids (sidechain at C^{α}, amino group at C^{β}),[6,9,10a] which are found as components in several biologically active compounds.[36,37] Moreover, the corresponding β-peptides adopt novel and unique folding patterns.[38] 3-Nitroacrylates are ideally suited as direct precursors of β²-homoamino acids as the side chain R may be introduced by conjugate addition of diorganozinc compounds R_2Zn. The β-nitroester **12** can be reduced and the resulting amino group protected e.g. by the Boc group. The ester is subsequently saponified to give the β²-homoamino acid **16** in an overall yield of 75% (Scheme 10).



Scheme 10 Synthesis of the Boc-protected β²-homoamino acid **16**

5 Conclusions

In summary, we have shown that conjugate addition of organozinc compounds to functionalized nitroalkenes is a powerful method providing access to a broad variety of functionalized nitro derivatives. The transferable residue R of alkyl(trimethylsilyl)zinc compounds [(TMSM)ZnR] can also be successfully added to aliphatic and aromatic nitroolefins affording the corresponding nitro compounds in moderate to good yields. A catalytic amount of copper(I) salt in the reaction medium prevents the formation of *ipso*-substituted product.

Diethylzinc can be efficiently added to nitrostyrene, 3-nitroacrylates and 3-nitroacrolein dimethylacetal. The addition to 3-nitroacrylates or 3-nitroacrolein dimethylacetal, respectively, provides nitro precursors of β^2-homoamino acids. Enantioselectivities up to 92% ee and chemical yields up to 94% are obtained in the presence of copper(I) salts and BINOL-type ligands in the frame of ligand-accelerated asymmetric catalysis. The nitroolefin moiety present in the 3-nitroacrylates, which are ambidentate electrophiles, acts as the predominant Michael acceptor, giving rise to the unambiguous formation of 2-alkyl-3-nitroacrylates. Consequently, 3-nitroacrylates are ideally suited as valuable precursors in the catalytic asymmetric synthesis of β^2-homoamino acids.

All moisture and air sensitive reactions were performed in flame-dried glassware under argon or nitrogen. THF and Et_2O were distilled from sodium benzophenone ketyl immediately prior to use. Toluene was distilled first over CaH_2 and then over sodium, Et_3N was distilled over CaH_2. Petroleum ether (PE, bp 30–60 °C) and EtOAc were used for flash chromatography and were distilled over CaH_2. All other reagents were used as received.

Analytical TLC was performed on silica gel plates 60 F_{254} on aluminum foil (Merck). The compounds were visualized by illumination with UV light, staining with iodine or cerium sulfate/ammonium molybdate solution. Flash column chromatography was carried out with silica gel 60 (40–63 μm) from Merck.

Melting points were determined using a melting point apparatus B-540 (Büchi) and are uncorrected. IR spectra were collected on a FT/IR-410 (Jasco) spectrometer from the neat oil film (NaCl plates) or from a solid in a KBr pellet. Peaks are reported in cm^{-1} with the following abbreviations for signal intensity: s, strong; m, medium; w, weak; br, broad.

^1H NMR spectra were recorded in $CDCl_3$ at 200 MHz, 250 MHz, or 500 MHz; ^{13}C NMR spectra were recorded at 50 MHz, 63 MHz, or 126 MHz; ^{31}P NMR spectra were recorded at 81 MHz or 202 MHz. TMS was used as an internal standard (^1H, ^{13}C) and 85% phosphoric acid (H_3PO_4) as an external standard (^{31}P). Shift values are reported in parts per million (ppm). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet.

Capillary gas chromatography was performed on a GC-17A (Shimadzu) gas chromatograph using a HP-5MS (25 m, 0.25 mm ID, 0.33 μm, Hewlett Packard) column. Enantiomer separations were performed on FS-Lipodex E (50 m, 0.25 mm ID, Macherey-Nagel) column.

EI mass spectra (70 eV) were recorded using GC-MS on a HP 5890 gas chromatograph (Hewlett Packard) with an HP 5972 A integrated mass detector unit (Hewlett Packard) or a GCMS-QP5050A (Shimadzu) on HP-5MS (30 m, 0.25 mm ID, 0.25 μm, Hewlett Packard) columns. MALDI-ToF mass spectra were recorded on Voyager-DE™ (PerSeptive Biosystems) using 2,5-dihydroxybenzoic acid (DHB) as matrix.

Microanalyses were performed on CHNS-932 (Leco), CHN-O-Rapid (Heraeus) and Vario EL (Heraeus) apparatus.

Conjugate Addition of Transmetallated Functionalized Diorganozinc Compounds to Nitroolefins; General Procedure

A mixture of an iodo derivative **2** (4.7 mmol) and neat Et_2Zn (2.95 g, 23.9 mmol) was stirred at 50 °C for 14 h (reaction monitoring by GC of hydrolyzed reaction aliquots). The ethyl iodide formed, and excess Et_2Zn were removed in vacuo (35 °C, 1 h, ca. 0.01 mbar). The resulting oil was dissolved in anhyd THF (4 mL) and added to a THF solution (5 mL) of CuCN (211 mg, 2.4 mmol) and LiCl (199 mg, 4.7 mmol) at –20 °C. The resulting light-green solution was cooled to –78 °C, and TMSCl (598 mg, 5.5 mmol) was added, followed by a solution of nitroolefin (2.3 mmol) in THF (1.5 mL) dropwise. The reaction mixture was slowly allowed to warm up –10 °C overnight. Then Et_2O was added (20 mL) and the mixture was quenched with a solution of sat. NH_4Cl (10 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), and filtered. The solvent was evaporated, and the residual oil was purified by flash chromatography to afford the product.

6-Nitro-5-phenylhexanenitrile (5a)

Colorless oil; yield: 67% (196 mg).

IR (neat): 2937 (w), 2246 (w), 1550 (s), 1454 (w), 1430 (w), 1380 (m), 1043 (w), 763 (w), 701 (w) cm^{-1}.

^1H NMR (250 MHz): δ = 1.38–1.71 (2 H, m), 1.72–1.98 (2 H, m), 2.29 (2 H, t, *J* = 7.0 Hz), 3.48 (1 H, m), 4.57 (2 H, d, *J* = 7.6 Hz), 7.07–7.52 (5 H, m).

^{13}C NMR (63 MHz): δ = 17.0, 23.0, 31.9, 43.8, 80.6, 119.3, 127.5, 128.2, 129.3, 138.1.

MS (EI): *m*/*z* (%) = 184 (19), 158 (10), 132 (30), 130 (42), 118 (44), 117 (54), 116 (91), 115 (24), 104 (31), 103 (36), 91 (100), 90 (21), 89 (49), 78 (28), 77 (39), 65 (24), 51 (24), 41 (22), 39 (27).

Anal. Calcd for $C_{12}H_{14}N_2O_2$ (218.25): C, 66.04; H, 6.47; N, 12.84. Found: C, 66.12; H, 6.23; N, 12.79.

Methyl 5-Cyano-2-(nitromethyl)pentanoate (5b)

Colorless oil; yield: 66% (310 mg).

IR (neat): 2956 (s), 2246 (m), 1735 (s), 1560 (s), 1436 (s), 1380 (s), 1207 (s), 1058 (m), 970 (m), 736 (w) cm^{-1}.

^1H NMR (250 MHz): δ = 1.56–1.94 (4 H, m), 2.41 (2 H, t, *J* = 6.6 Hz), 3.23 (1 H, m), 3.78 (3 H, s), 4.46 (1 H, dd, *J* = 14.3, 5.2 Hz), 4.76 (1 H, dd, *J* = 14.3, 8.6 Hz).

^{13}C NMR (63 MHz): δ = 17.0, 22.9, 28.2, 42.3, 52.7, 75.1, 118.6, 171.7.

MS (CI): *m*/*z* (%) = 202 (10), 201 (100), 169 (41), 154 (11), 122 (27).

Anal. Calcd for $C_8H_{12}N_2O_4$ (200.19): C, 48.00; H, 6.04; N, 14.00. Found: C, 48.17; H, 5.98; N, 13.88.

1-Methyl 6-Ethyl 2-(Nitromethyl)-hexanedioate (5c)

Colorless oil; yield: 53% (150 mg).

IR (neat): 2958 (m), 1735 (s), 1558 (s), 1438 (w), 1378 (m), 1203 (m), 1180 (m), 1031 (m) cm^{-1}.

^1H NMR (250 MHz): δ = 1.26 (3 H, t, *J* = 7.1 Hz), 1.56–1.80 (4 H, m), 2.34 (2 H, t, *J* = 6.9 Hz), 3.23 (1 H, m), 3.76 (3 H, s), 4.13 (2 H, q, *J* = 7.1 Hz), 4.46 (1 H, dd, *J* = 14.3, 4.9 Hz), 4.76 (1 H, dd, *J* = 14.3, 9.2 Hz).

^{13}C NMR (63 MHz): δ = 14.2, 22.0, 28.6, 33.6, 42.7, 52.5, 60.6, 75.0, 172.4, 172.8.

MS (CI): *m*/*z* (%) = 249 (15), 248 (100), 214 (8), 203 (6), 202 (9), 201 (37), 169 (6), 155 (8).

Anal. Calcd for $C_{10}H_{17}NO_6$ (247.25): C, 48.58; H, 6.93; N, 5.67. Found: C, 48.56; H, 6.84; N, 5.67.

Conjugate Addition of Dimyrtanylzinc (6) to Nitroolefins; General Procedure

TMSCl (0.19 mL, 1.53 mmol) was added dropwise at –30 °C to a solution of nitroolefin (1.53 mmol) and $Cu(OTf)_2$ (29 mg, 0.08 mmol, 5 mol% referring to nitroolefin) in THF (5 mL). The mixture was stirred for 10 min, and a solution of dimyrtanylzinc[12a,39] **6** (ca. 3.5 mmol, ca. 1 M solution in THF) was added dropwise. The mixture was stirred for 4 h at –30 °C and diluted with THF (10 mL). Aqueous HCl solution (10%, 5 mL) was added and stirring was continued for 15 min. The mixture was poured into a mixture containing Et_2O (100 mL) and sat. aq NH_4Cl (50 mL), stirred for 20 min and filtered over Celite®. The layers were separated. The aqueous layer was washed with Et_2O (2 × 30 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), and filtered. The solvent was evaporated, and the residual oil was purified by flash chromatography to afford the product.

(1*S*,2*S*,5*S*)-6,6-Dimethyl-2-(3′-nitro-2′-phenyl-1′-propyl)bicyclo[3.1.1]heptane (8a)

Colorless oil (mixture of diastereomers 1:1); yield: 74% (325 mg).

IR (neat): 2910 (s), 1552 (s), 1495 (w), 1468 (w), 1454 (w), 1378 (m), 762 (m), 700 (m) cm^{-1}

^{1}H NMR (500 MHz): δ = 0.98 (6 H, s), 1.13 (3 H, s), 1.20 (3 H, s), 1.36 (1 H, m), 1.53 (1 H, m), 1.64–1.98 (18 H, m), 2.22 (1 H, m), 2.29 (1 H, m), 3.47–3.57 (2 H, m), 4.45–4.57 (4 H, m), 7.15–7.21 (4 H, m), 7.23–7.29 (2 H, m), 7.30–7.36 (4 H, m).

^{13}C NMR (126 MHz): δ = 21.3, 22.8; 23.2, 23.4; 26.2, 26.3; 28.0, 28.1; 33.3, 33.6; 37.6, 38.0; 38.6, 38.7; 40.4, 40.7; 41.2, 41.3; 42.3, 42.4; 44.7, 47.3; 81.1, 81.4; 127.5, 127.7, 128.9, 139.2, 139.7.

MS (CI): *m*/*z* (%) = 309 (18), 255 (18), 254 (20), 253 (100), 131 (10), 110 (11).

Anal. Calcd for $C_{18}H_{25}NO_2$ (287.40): C, 75.22; H, 8.77; N, 4.84. Found: C, 75.32; H, 9.19; N, 4.84.

Ethyl 3-{(1′*S*,2′*S*,5′*S*)-6′,6′-Dimethylbicyclo[3.3.1]hept-2′-yl}-2-(nitromethyl)propanoate (8b)

Colorless oil (mixture of diastereomers 1:1); yield: 89% (368 mg).

IR (neat): 2912 (s, br), 1736 (s), 1558 (s), 1439 (m), 1379 (m), 1248 (m), 1203 (m), 1174 (m) cm^{-1}.

^{1}H NMR (250 MHz): δ = 0.99 (6 H, 2 s), 1.19 (6 H, s), 1.39–1.50 (2 H, m), 1.54–1.63 (2 H, m), 1.63–2.09 (16 H, m), 2.30–2.41 (2 H, m), 3.18–3.29 (2 H, m), 3.74 (3 H, s), 3.75 (3 H, s), 4.40 (1 H, dd, *J* = 14.3, 10.4 Hz), 4.41 (1 H, dd, *J* = 14.3, 10.1 Hz), 4.70 (1 H, dd, *J* = 14.4, 2.5 Hz), (1 H, dd, *J* = 14.4, 2.5 Hz).

^{13}C NMR (126 MHz): δ = 22.0, 22.1; 23.2; 26.2; 28.0; 33.4, 33.5; 36.8, 37.1; 38.5, 38.5; 38.6, 38.6; 41.2, 41.2; 41.4, 41.5; 45.8, 46.2; 52.4, 52.5; 75.2, 75.7; 173.1, 173.2.

MS (EI): *m*/*z* (%) = 234 (4), 82 (34), 81 (33), 79 (32), 69 (100), 67 (87), 55 (91), 41 (94), 18 (61), 15 (37).

Anal. Calcd for $C_{14}H_{23}NO_4$ (269.34): C, 62.43; H, 8.61; N, 5.20. Found: C, 62.47; H, 8.70; N, 5.34.

Ethyl 4-Phenyl-5-nitropentanoate (9); Conjugate Addition of Bis[2-(ethoxycarbonyl)ethyl]zinc (7) to Nitrostyrene (1a)

Anhyd $ZnCl_2$ (305 mg, ca. 2.24 mmol) was heated to its melting point in vacuo (ca. 0.01 mbar). The residue was weighed (285 mg, 2.09 mmol), Et_2O (9 mL) was added, and the mixture was sonicated until the salt dissolved. 1-Ethoxy-1-(trimethylsilyloxy)cyclopropane[24] (0.91 g, 5.22 mmol) was added, and the mixture was stirred for 4 h at r.t. Et_2O (ca. 6–7 mL) was removed under reduced pressure, and the residual solution was diluted with hexane (8 mL). The supernatant liquid was separated, and the solvent was removed in vacuo to give **7** as an oil. Et_2O (3 mL) was added, and the mixture was added dropwise at –40 °C to a solution of **1a** (155 mg, 1.04 mmol) and $Cu(OTf)_2$ (8 mg, 0.02 mmol, 2 mol% referring to nitroolefin) in Et_2O (5 mL). The reaction mixture was allowed to warm up to 0 °C overnight. It was diluted with Et_2O (20 mL) and quenched by addition of a solution of sat. aq NH_4Cl (20 mL). The aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), and filtered. The solvent was evaporated, and the residual oil was purified by flash chromatography (PE) to afford the product.

Colorless oil; yield: 65% (170 mg).

IR (neat): 2981 (w), 1731 (s), 1552 (s), 1454 (m), 1378 (m), 1182 (m), 1159 (m), 1037 (m), 765 (w), 701 (m) cm^{-1}.

^{1}H NMR (250 MHz): δ = 1.21 (3 H, t, *J* = 7.2 Hz), 1.88–2.24 (4 H, m), 3.49 (1 H, m), 4.08 (2 H, q, *J* = 7.2 Hz), 4.51–4.64 (2 H, m), 7.12–7.43 (5 H, m).

^{13}C NMR (63 MHz): δ = 14.2, 28.1, 31.7, 43.7, 60.6, 80.6, 127.6, 128.0, 129.1, 138.3, 172.5.

MS (CI): *m*/*z* (%) = 252 (10), 219 (14), 218 (100), 172 (11).

Anal. Calcd for $C_{13}H_{17}NO_4$ (251.28): C, 62.14; H, 6.82; N, 5.57. Found: C, 62.19; H, 6.89; N, 5.60.

Conjugate Addition of Alkyl(trimethylsilylmethyl)zinc Compounds to Nitroolefins; General Procedure

1,2-Dibromoethane (0.07 mL, 0.8 mmol) was added dropwise to a stirred mixture of Zn dust (0.52 g, 8.0 mmol) in THF (2.5 mL) at r.t. under argon, whilst heating with a heat gun to boil the solvent gently. After ca. 1 min the reaction mixture foams and the heating is interrupted. After 1–3 min, this heating-cooling procedure is repeated twice more. Upon complete addition the mixture was cooled to r.t. and then TMSCl (0.07 mL, 0.55 mmol) was added dropwise over 5 min, again with gentle heating. After complete addition, the mixture was stirred at r.t. for further 5 min. THF solutions (1.5 mL) of the appropriate iodo derivative (2.0 mmol) and of dodecane (ca. 0.4 mL) as internal standard for GC analysis were added dropwise over 5 min, and then the reaction was stirred at 50 °C for 2–4 h. The zinc insertion reaction was monitored by GC analysis. When the reaction was complete, the reaction mixture was cooled to r.t. and the excess zinc dust allowed to settle for 15 min. The pale gray solution was transferred to a flame dried flask that contained a solution of copper salt (0.05 mmol, 5 mol% referring to nitroolefin) in THF (2.0 mL) cooled to –40 °C. A solution of trimethylsilylmethyllithium (1 M in pentane, 2.0 mL, 2.0 mmol) was added dropwise to the alkyl zinc iodide solution, which was then stirred at –40 °C for 1 h. NMP (0.33 mL, 3.4 mmol), TMSBr (0.35 mL, 2.7 mmol) and then nitroolefin (1.1 mmol) in THF (1.5 mL) were subsequently added dropwise at –40 °C. The reaction was allowed to warm up to –30 °C, stirred at this temperature for 3 h and finally allowed to warm up slowly to r.t. overnight. The reaction mixture was poured into sat. NH_4Cl solution (10 mL) and stirred at r.t. for 10 min. The resulting solution was extracted with Et_2O (3 × 30 mL). The combined extracts were washed with brine (30 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude residue was purified by column chromatography.

1-Cyclohexyl-2-nitro-1-phenylethane (10a)
White crystals; yield: 70% (174 mg); mp 64–65 °C.

IR (KBr): 2915 (s), 2852 (s), 1548 (s), 1442 (s), 1380 (s), 755 (s), 700 (s) cm^{-1}.

^1H NMR (200 MHz): δ = 0.77–1.88 (11 H, m), 3.27 (1 H, ddd, *J* = 9.9, 8.0, 5.9 Hz), 4.62 (1 H, dd, *J* = 12.3, 9.9 Hz), 4.80 (1 H, dd, *J* = 12.3, 5.9 Hz), 7.06–7.43 (5 H, m).

^{13}C NMR (50 MHz): δ = 26.5, 31.0, 31.4, 41.3, 50.7, 79.3, 127.9, 128.7, 129.1, 139.3.

MS (EI): *m*/*z* (%) = 186 (24), 105 (17), 104 (100), 91 (23), 83 (20), 55 (50), 41 (24).

Anal. Calcd for $C_{14}H_{19}NO_2$ (233.31): C, 72.07; H, 8.21; N, 6.0. Found: C, 72.32; H, 7.91; N, 5.98.

(*E*)-1-Cyclohexyl-2-phenylethene (11a)
Colorless oil; yield: 28% (50 mg).

IR (neat): 3025 (s), 2924 (s), 2850 (s), 1492 (m), 1446 (s), 963 (s), 742 (s), 692 (s) cm^{-1}.

^1H NMR (200 MHz): δ = 1.08–1.95 (10 H, m), 2.18 (1 H, m), 6.22 (1 H, dd, *J* = 6.6, 16.1 Hz), 6.40 (1 H, d, *J* = 16.1 Hz), 7.14–7.47 (5 H, m).

^{13}C NMR (50 MHz): δ = 26.6, 26.7, 33.5, 41.7, 126.5, 127.2, 127.8, 129.0, 137.3, 138.6.

MS (EI): *m*/*z* (%) = 186 (24), 129 (27), 128 (23), 117 (10), 115 (23), 105 (11), 104 (100), 91 (20).

1-Nitro-2-phenylnonane (10b)
Light yellow oil; yield: 64% (106 mg).

IR (neat): 2927 (s), 2856 (m), 1554 (s), 1454 (w), 1376 (m), 1056 (w), 763 (w), 701 (m) cm^{-1}.

^1H NMR (250 MHz): δ = 0.86 (3 H, m), 1.11–1.35 (10 H, m), 1.60–1.73 (2 H, m), 3.44 (1 H, m), 4.47–4.61 (2 H, m), 7.13–7.41 (5 H, m).

^{13}C NMR (63 MHz): δ = 14.0, 22.6, 26.9, 29.0, 29.3, 31.7, 33.1, 44.4, 81.1, 127.5, 127.6, 128.8, 128.9, 129.0, 139.6.

MS (CI): *m*/*z* (%) = 273 (13), 272 (69), 219 (11), 218 (16), 217 (21), 216 (100), 214 (35), 203 (16), 189 (28).

(*E*)-1-Phenyl-1-nonene (11b)
Colorless oil; yield: 43% (176 mg).

^1H NMR (250 MHz): δ = 0.89 (3 H, t, *J* = 7.0 Hz), 1.17–1.36 (8 H, m), 1.32–1.57 (2 H, m), 2.21–2.27 (2 H, m), 6.22 (1 H, dt, *J* = 15.8 Hz, 6.6 Hz), 6.38 (1 H, d, *J* = 15.8 Hz), 7.12–7.40 (5 H, m).

^{13}C NMR (63 MHz): δ = 14.1, 22.7, 29.2, 29.4, 29.7, 31.9, 33.1, 125.9, 126.7, 128.5, 129.7, 131.3, 138.0.

MS (CI): *m*/*z* (%) = 246 (2), 245 (14), 204 (15), 203 (100), 202 (43), 201 (19), 190 (12), 189 (81), 175 (7), 141 (9), 133 (13), 119 (14), 117 (19), 105 (26).

Anal. Calcd (%) for $C_{15}H_{22}$ (202.34): C, 89.04; H, 10.96; found: C, 88.97; H, 11.15.

2-Phenyl-1-nitrohexane (10c)
Light yellow oil; yield: 72% (180 mg).

IR (neat): 2960 (m), 2931 (m), 2859 (m), 1552 (s), 1454 (m), 1378 (m), 763 (m), 700 (s) cm^{-1}.

^1H NMR (200 MHz): δ = 0.84 (3 H, t, *J* = 6.6 Hz), 1.05–1.41 (4 H, m), 1.60–1.79 (2 H, m), 3.44 (1 H, m), 4.55 (2 H, m), 7.13–7.41 (5 H, m).

^{13}C NMR (50 MHz): δ = 14.2, 22.8, 29.4, 33.1, 44.8, 81.5, 128.0, 128.0, 129.4, 140.1.

MS (EI): *m*/*z* (%) = 160 (17), 119 (10), 118 (100), 117 (14), 105 (11), 104 (23), 91 (55).

Anal. Calcd for $C_{12}H_{17}NO_2$ (207.27): C, 69.54; H, 8.27; N, 6.76. Found: C, 69.59; H, 8.17; N, 6.79.

Methyl 2-(Nitromethyl)nonanoate (10d)
Colorless oil; yield: 46% (80 mg).

IR (neat,): 2959 (w), 2926 (m), 2856 (m), 1739 (s), 1559 (s), 1438 (m), 1379 (s), 1251 (w), 1203 (w), 1174 (w) cm^{-1}.

^1H NMR (250 MHz): δ = 0.88 (3 H, t, *J* = 6.9 Hz), 1.14–1.48 (9 H, m), 1.46–1.78 (3 H, m), 3.20 (1 H, m), 3.75 (3 H, s), 4.41 (1 H, dd, *J* = 14.2, 4.9 Hz), 4.73 (1 H, dd, *J* = 14.2, 9.2 Hz).

^{13}C NMR (63 MHz): δ = 14.0, 22.6, 26.6, 28.9, 29.2, 29.3, 31.7, 43.0, 52.3, 75.2, 172.8.

MS (CI): *m*/*z* (%) = 255 (5), 254 (34), 233 (4), 232 (29), 200 (65), 198 (59), 196 (16), 186 (16), 185 (100), 173 (28), 142 (82), 141 (11), 140 (34).

Anal. Calcd for $C_{11}H_{21}NO_4$ (231.29): C, 57.12; H, 9.15; N, 6.06. Found: C, 57.82; H, 9.09; N, 5.72.

Methyl 2-Cyclohexyl-3-nitropropanoate (10e)
Colorless oil; yield: 69% (453 mg).

IR (neat): 2931 (s), 2854 (m), 1735 (s), 1558 (s), 1438 (m), 1376 (m), 1253 (w), 1203 (m), 1172 (w), 1041 (w) cm^{-1}.

^1H NMR (250 MHz): δ = 0.97–1.36 (5 H, m), 1.59–1.84 (6 H, m), 3.11 (1 H, m), 3.74 (3 H, s), 4.44 (1 H, dd, *J* = 14.6, 4.0 Hz), 4.79 (1 H, dd, *J* = 14.6, 10.5 Hz).

^{13}C NMR (63 MHz): δ = 25.9, 26.1, 26.2, 30.4, 30.5, 38.5, 48.7, 52.2, 73.9, 172.4.

MS (CI): *m*/*z* (%) = 215 (19), 183 (53), 181 (55), 179 (19), 168 (79), 156 (69), 125 (100), 123 (68), 121 (39), 111 (17), 109 (17).

Methyl 2-(Nitromethyl)octanoate (10f)
Colorless oil; yield: 56% (131 mg).

IR (neat): 2954 (m), 2931 (m), 2858 (m), 1739 (s), 1558 (s), 1438 (m), 1380 (m), 1253 (w), 1203 (m), 1176 (m), 1049 (w) cm^{-1}.

^1H NMR (250 MHz): δ = 0.88 (3 H, t, *J* = 6.9 Hz), 1.17–1.42 (8 H, m), 1.46–1.79 (2 H, m), 3.19 (1 H, m), 3.75 (3 H, s), 4.42 (1 H, dd, *J* = 14.3, 4.9 Hz), 4.74 (1 H, dd, *J* = 14.3, 9.5 Hz).

^{13}C NMR (50 MHz): δ = 14.0, 22.5, 26.6, 28.9, 29.3, 31.5, 42.9, 52.4, 75.2, 172.8.

MS (CI): *m*/*z* (%) = 241 (1), 240 (13), 219 (13), 218 (100), 186 (23), 184 (14), 173 (11), 172 (10), 171 (36), 139 (7), 128 (5).

Anal. Calcd for $C_{10}H_{19}NO_4$ (217.26): C, 55.28; H, 8.81; N, 6.45. Found: C, 55.07; H, 8.95; N, 6.76.

2-Cyclohexyl-1,1-dimethoxy-3-nitropropane (10g)
Light yellow oil; yield: 45% (64 mg).

IR (neat): 2927 (s), 2852 (s), 1554 (s), 1448 (m), 1380 (m), 1205 (m), 1130 (m), 1068 (s), 966 (m), 732 (m) cm^{-1}.

^1H NMR (200 MHz): δ = 0.82–1.84 (11 H, m), 2.53 (1 H, m), 3.34 (3 H, s), 3.36 (3 H, s), 4.29 (1 H, dd, *J* = 13.5, 5.6 Hz), 4.35 (1 H, d, *J* = 4.8 Hz), 4.51 (1 H, dd, *J* = 13.5, 6.4 Hz).

^{13}C NMR (50 MHz): δ = 26.7, 26.8, 26.9, 30.0, 31.1, 37.6, 45.8, 54.8, 56.0, 74.3, 105.4.

MS (EI): *m*/*z* (%) = 153 (5), 75 (100), 71 (10), 55 (9), 47 (11), 41 (13).

Anal. Calcd for $C_{11}H_{21}NO_4$ (231.29): C, 57.12; H, 9.15; N, 6.06. Found: C, 57.18; H, 9.04; N, 6.03.

1,1-Dimethoxy-2-(nitromethyl)nonane (10h)
Colorless oil; yield: 72% (120 mg).

IR (neat):2929 (s), 2858 (s), 1554 (s), 1466 (m), 1381 (s), 1190 (m), 1117 (s), 1072 (s), 970 (w), 723 (w) cm^{-1}.

^1H NMR (250 MHz): δ = 0.88 (3 H, t, *J* = 6.6 Hz), 1.19–1.41 (10 H, m), 1.57 (2 H, m), 2.53 (1 H, m), 3.39 (3 H, s), 3.40 (3 H, s), 4.28 (1 H, d, *J* = 4.9 Hz), 4.29 (1 H, dd, *J* = 12.9, 6.6 Hz), 4.54 (1 H, dd, *J* = 12.8, 5.8 Hz).

^{13}C NMR (63 MHz): δ = 14.1, 22.6, 26.7, 27.7, 29.1, 29.6, 31.8, 40.9, 54.9, 56.1, 75.6, 105.8.

MS (CI): *m*/*z* (%) = 216 (32), 214 (54), 182 (26), 170 (11), 169 (100).

Anal. Calcd for $C_{12}H_{25}NO_4$ (247.34): C, 58.27; H, 10.19; N, 5.66. Found: C, 58.54; H, 10.28; N, 5.61.

Synthesis of Phosphoramidites; General Procedure
A solution of bis(1-phenylethyl)amine (2.06 g, 9.16 mmol) and Et_3N (1.05 g, 10.38 mmol) in toluene (8 mL) was added dropwise under argon to the solution of PCl_3 (1.25 g, 9.16 mmol) in toluene (120 mL). The mixture was stirred at 70 °C for 6 h and allowed to cool to r.t. Et_3N (2.10 g, 20.76 mmol) was added dropwise under argon. The reation mixture was cooled to –78 °C and a solution of BINOL (9.17 mmol) or its 3,3′-dimethyl derivative, resp., in a mixture of toluene (24 mL) and THF (4 mL) was added dropwise. The mixture was allowed to warm up slowly to r.t. and was stirred for an additional 12 h. The mixture was filtered and the solvents were removed under reduced pressure. The diastereomers were purified and separated by column chromatography.

***O,O′*-(*M*)-1,1′-Binaphthyl-2,2′-diyl)-*N*,*N*-(*S*,*S*)-bis(1-phenylethyl)phosphoramidite [(*M*,*S*,*S*)-L1]**
Colorless crystals; yield: 46% (1.15 g); mp 102–104 °C; $[\alpha]_D^{29}$ –485.7 (*c* = 0.7, $CHCl_3$).

IR (KBr): 3057 (w), 2970 (w), 2927 (w), 1590 (m), 1460 (m), 1327 (m), 1231 (s), 1204 (m), 947 (s) cm^{-1}.

^1H NMR (200 MHz): δ = 1.76 (6 H, d, *J* = 7.2 Hz), 4.55 (2 H, dq, *J* = 11.5, 7.2 Hz), 7.03–7.71 (18 H, m), 7.85–8.07 (4 H, m).

^{13}C NMR (50 MHz): δ = 22.6 (d, *J* = 8.2 Hz), 52.7 (d, *J* = 12.2 Hz), 122.3, 122.4, 123.0, 124.6, 122.7, 125.1, 125.3, 126.6, 127.2, 127.7, 127.8, 128.3, 128.5, 128.6, 128.7, 128.9, 130.0, 130.8, 131.0, 132.0, 133.4, 143.4, 150.2, 150.6, 150.8.

^{31}P NMR (81 MHz): δ = 146.5 (t, *J* = 11.5 Hz).

MS (EI): *m*/*z* (%) = 434 (100), 105 (77), 268 (21), 79 (16), 77 (13), 239 (9), 315 (7), 252 (6), 391 (5); Anal. Calcd for $C_{36}H_{30}NO_2P$ (539.62): C, 80.13, H, 5.60, N, 2.60, O, 5.93. Found: C, 80.24, H, 5.75, N, 2.48, O, 5.52.

***O,O′*-(*P*)-1,1′-Binaphthyl-2,2′-diyl)-*N*,*N*-(*S*,*S*)-bis(1-phenylethyl)phosphoramidite [(*P*,*S*,*S*)-L1]**
Colorless crystals; yield: 54% (1.35 g); mp 87–89 °C; $[\alpha]_D$ +15.5 (*c* = 0.8, $CHCl_3$).

IR (KBr): 3057 (w), 2970 (w), 2927 (w), 1590 (m), 1460 (m), 1327 (m), 1231 (s), 1204 (m), 947 (s) cm^{-1}.

^1H NMR (200 MHz): δ = 1.74 (6 H, d, *J* = 7.1 Hz), 4.47 (2 H, dq, *J* = 11.0, 7.1 Hz), 7.12–7.68 (18 H, m), 7.75–8.09 (4 H, m).

^{13}C NMR (50 MHz): δ = 23.5 (d, *J* = 11.8 Hz), 55.0 (d, *J* = 11.1 Hz), 121.7, 121.8, 123.0, 123.1, 124.7, 124.7, 125.0, 125.1, 126.4, 126.6, 127.3, 127.7, 127.9, 128.3, 128.5, 128.6, 128.7, 128.9, 130.2, 130.9, 131.0, 131.9, 133.4, 133.4, 143.7, 150.4, 151.0, 151.2.

^{31}P NMR (81 MHz): δ = 151.6 (t, *J* = 11.0 Hz).

MS (EI): *m*/*z* (%) = 434 (100), 105 (77), 268 (21), 79 (16), 77 (13), 239 (9), 315 (7), 252 (6), 391 (5).

***O,O′*-(*P*)-3,3′-Dimethyl-1,1′-binaphthyl-2,2′-diyl)-*N*,*N*-(*R*,*R*)-bis(1-phenylethyl)phosphoramidite [(*P*,*R*,*R*)-L2]**
Colorless crystals; yield: 49% (0.39 g); mp 116–123 °C; $[\alpha]_D^{29}$ +467.9 (*c* = 2.96, $CHCl_3$).

IR (KBr): 3056 (w), 2962 (m), 2921 (m), 1498 (m), 1448 (m), 1411 (m), 1240 (m), 1205 (m), 1141 (m), 1085 (m), 900 (s), 773 (s), 746 (s), 696 (m) cm^{-1}.

^1H NMR (500 MHz): δ = 1.48–1.80 (6 H, br m), 2.40 (3 H, s), 2.72 (3 H, s), 4.55 (2 H, br m), 6.96–7.37 (16 H, m), 7.74–7.82 (4 H, m).

^{13}C NMR (126 MHz): δ = 17.7, 18.9, 23.3, 23.3, 52.6 (d, *J* = 12.2 Hz), 122.5, 122.5, 124.3, 124.3, 124.8, 125.0, 125.4, 125.5, 127.0, 127.3, 127.5, 127.7, 127.9, 129.8, 130.1, 130.4, 130.7, 130.8, 131.7, 132.1, 132.3, 149.3, 149.5, 149.6.

^{31}P NMR (202 MHz): δ = 143.9 (s).

MALDI-ToF MS: *m*/*z* calcd for $C_{39}H_{34}NO_2P$ $[M + H]^+$, 568.66; found: 569.00.

Anal. Calcd for $C_{38}H_{34}NO_2P$ (567.66): C, 80.40, H, 6.04, N, 2.47. Found: C, 80.35, H, 6.74, N, 2.36.

***O,O′-(M)*-3,3′-Dimethyl-1,1′-binaphthyl-2,2′-diyl)-*N*,*N*-(*R*,*R*)-bis(1-phenylethyl)phosphoramidite [(*M*,*R*,*R*)-L2]**
Colorless crystals; yield: 49% (0.39 g); mp 171–173 °C; $[\alpha]_D^{29}$ –92.0 (*c* = 2.98, $CHCl_3$).

IR (KBr): 3019 (w), 2958 (m), 2917 (m), 2850 (m), 1596 (m), 1498 (m), 1465 (m), 1409 (m), 1236 (m), 1130 (m), 1093 (s), 900 (s), 775 (s), 748 (s), 692 (s) cm^{-1}.

^1H NMR (500 MHz): δ = 1.62 (6 H, d, *J* = 7.0 Hz), 1.91 (3 H, s), 2.67 (3 H, s), 4.54 (2 H, m), 6.98–7.04 (4 H, m), 7.06–7.36 (12 H, m), 7.67–7.86 (4 H, m).

^{13}C NMR (126 MHz): δ = 17.5, 17.5, 23.1 (br), 54.8 (d, *J* = 10.9 Hz), 121.6, 121.7, 124.0, 124.1, 124.3, 124.6, 124.8, 125.0, 126.9, 126.9, 127.0, 127.3, 127.5, 127.9, 128.1, 129.1, 129.7, 130.1, 130.3, 131.2, 131.2, 131.7, 131.8, 143.2, 149.0, 149.2, 149.2.

^{31}P NMR (202 MHz): δ = 147.8 (s).

MALDI-ToF MS: *m*/*z* calcd for $C_{38}H_{34}NO_2PK$ $[M + K]^+$, 606.75; $C_{39}H_{34}NO_2P$ $[M+H]^+$, 568.66; found: 606.79 $[M + K]^+$; 568.88 $[M + H]^+$.

Anal. Calcd for $C_{38}H_{34}NO_2P$ (567.66): C, 80.40, H, 6.04, N, 2.47. Found: C, 80.39, H, 6.04, N, 2.54.

Phosphoramidite/Copper(I) Catalyzed Conjugate Addition of Dialkylzinc Compounds to Nitroolefins; General Procedure
Copper(II) triflate (0.5–2.0 mol% referring to nitroolefin) and the corresponding phosphoramidite (1.0–4.1 mol%) were dissolved in a corresponding dry solvent (catalyst concentration: ca. 5 mM) and stirred for 1 h at r.t. under argon. The clear solution was cooled to the appropriate temperature and the solution of Et_2Zn (1.5 equiv; 1 M in hexane) was added dropwise followed by a solution of nitroolefin (ca. 1 M in the corresponding solvent). Dodecane was used as an inner standard for determination of the conversion. The reaction progress was monitored by GC analysis. The reaction was quenched by addition of a solution of sat. aq NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with Et_2O (2 ×). The combined organic layers were washed with brine, dried (over Na_2SO_4 or $MgSO_4$) and filtered. The solvents were removed under reduced pressure and the resulting oil was purified by column chromatography to afford the product.

Methyl 2-(Nitromethyl)butanoate (12)
Colorless oil; yield: 94% (2.89 g).

IR (neat): 2971 (m), 2881 (w), 1737 (s), 1556 (s), 1438 (m), 1380 (s), 1257 (s), 1205 (s), 1182 (s), 971 (w), 848 (w) cm^{-1}.

^{1}H NMR (200 MHz): δ = 0.98 (3 H, t, *J* = 7.5 Hz), 1.71 (2 H, m), 3.17 (1 H, m), 3.75 (3 H, s), 4.43 (1 H, dd, *J* = 14.3, 4.4 Hz), 4.75 (1 H, dd, *J* = 14.3, 9.2 Hz).

^{13}C NMR (50 MHz): δ = 11.5, 23.0, 44.6, 52.8, 75.4, 173.1.

MS (EI): *m*/*z* (%) = 130 (15), 87 (22), 83 (48), 73 (25), 59 (91), 56 (13), 55 (100), 45 (16), 41 (29), 39 (22), 30 (19), 29 (31), 27 (34), 15 (30).

Anal. Calcd for $C_6H_{11}NO_4$ (161.16): C, 44.72; H, 6.88, N, 8.69. Found: C, 45.00; H, 6.94; N 8.55.

Ethyl 2-Ethyl-3-nitrobutanoate (13d)
Colorless oil; yield: 57% (101 mg, both diastereomers).

IR (neat): 2979 (m), 1734 (s), 1555 (s), 1460 (m), 1390 (m), 1273 (m), 1190 (m), 1107 (m) cm^{-1}.

Anal. Calcd for $C_8H_{15}NO_4$ (189.21): C, 50.78; H, 7.99; N, 7.40. Found: C, 51.35; H, 8.38; N, 6.90.

Diastereomer 1:

^{1}H NMR (500 MHz): δ = 0.94 (3 H, t, *J* = 7.5 Hz), 1.29 (3 H, t, *J* = 7.2 Hz), 1.55 (3 H, d, *J* = 6.6 Hz), 1.56 (1 H, m), 1.70 (1 H, m), 2.92 (1 H, ddd, *J* = 9.2, 9.2, 4.2 Hz), 4.20 (2 H, q, *J* = 7.2 Hz), 4.74 (1 H, dq, *J* = 9.2, 6.7 Hz).

^{13}C NMR (126 MHz): δ = 11.2, 14.2, 17.5, 22.8, 51.2, 61.2, 84.0, 171.4;

MS (EI): *m*/*z* (%) =191 (9), 190 (100), 159 (4), 144 (7), 145 (5), 143 (8), 115 (6).

Diastereomer 2

^{1}H NMR (500 MHz): δ = 0.95 (3 H, t, *J* = 7.5 Hz), 1.27 (3 H, t, *J* = 7.1 Hz), 1.59 (3 H, d, *J* = 6.9 Hz), 1.63 (2 H, m), 2.99 (1 H, ddd, *J* = 9.1, 9.1, 4.2 Hz), 4.18 (2 H, q, *J* = 7.1 Hz), 4.82 (1 H, dq, *J* = 9.1, 6.9 Hz).

^{13}C NMR (126 MHz): δ = 11.1, 14.2, 17.4, 22.8, 51.4, 61.2, 84.1, 172.0.

Ethyl 2-Ethyl-3-nitropentanoate (13e)
Colorless oil; yield: 74% (276 mg, both diastereomers).

IR (neat): 2969 (m), 2939 (m), 1731 (s), 1554 (s), 1461 (m), 1376 (m), 1272 (m), 1184 (m), 1025 (w); cm^{-1}.

Anal. Calcd for $C_9H_{17}NO_4$ (203.24): C, 53.19; H, 8.43; N, 6.89. Found: C, 53.35; H, 8.39; N, 6.89.

Diastereomer 1

^{1}H NMR (500 MHz): δ = 0.92 (3 H, t, *J* = 7.5 Hz), 0.96 (3 H, t, *J* = 7.3 Hz), 1.29 (3 H, t, *J* = 7.2 Hz), 1.54 (1 H, m), 1.71 (2 H, m), 1.98 (1 H, m), 2.87 (1 H, ddd, *J* = 10.0, 10.0, 3.5 Hz), 4.20 (2 H, q, *J* = 7.2 Hz), 4.59 (1 H, ddd, *J* = 10.4, 10.4, 3.5 Hz).

^{13}C NMR (126 MHz): δ = 10.3, 11.0, 11.0, 14.2, 23.0, 25.7, 50.6, 61.2, 91.0, 171.6.

MS (EI): *m*/*z* (%) = 205 (11), 204 (100), 173 (4), 159 (7), 158 (10), 157 (19), 129 (12).

Diastereomer 2

^{1}H NMR (500 MHz): δ = 0.94 (3 H, t, *J* = 7.5 Hz), 0.97 (3 H, t, *J* = 7.1 Hz), 1.26 (3 H, t, *J* = 7.0 Hz), 1.63 (1 H, m), 1.75 (1 H, m), 1.91 (1 H, m), 2.02 (1 H, m), 3.00 (1 H, dt, *J* = 9.3, 4.2 Hz), 4.17 (2 H, q, *J* = 7.0 Hz), 4.71 (1 H, dt, *J* = 9.3, 3.6 Hz).

^{13}C NMR (126 MHz): δ = 9.5, 10.8, 10.8, 14.1, 21.6, 24.1, 48.4, 61.2, 89.1, 172.1.

Methyl 2-[(*tert*-Butoxycarbonyl)aminomethyl]butanoate (15)
Dried ammonium formate (296 mg, 4.69 mmol) and Pd/C (56 mg, 10%) were added under an argon atmosphere to a solution of the nitro compound (0.86 mmol) in abs. MeOH (2.0 mL). While the mixture was stirred for 30 min, gas evolution was observed. The solution was then filtered through a plug of Celite®. The Celite® plug was washed with abs. MeOH (8 mL). Anhyd Et_3N (0.25 mL, 1.80 mmol) and Boc_2O (242 mg, 1.11 mmol) were added to the filtrate and the mixture was stirred under an argon atomsphere for 12 h at r.t. Then H_2O (8 mL) was added, the solution was cooled to 0 °C, and acidified to ca. pH 3 with 1 N $KHSO_4$ solution. The mixture was extracted with EtOAc (5 × 15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and evaporated in vacuo. The Boc protected β^2-homoaminoacid ester **15** was purified by flash chromatography.

Colorless oil; yield for 2 steps: 79% (395 mg); $[\alpha]_D^{26}$ –23.9 (*c* = 1.0, $CHCl_3$).

IR (neat): 3379 (m), 2973 (s), 1718 (s), 1520 (s), 1457 (w), 1438 (w), 1366 (m), 1272 (s), 1252 (s), 1173 (s) cm^{-1}.

^{1}H NMR (250 MHz): δ = 0.94 (3 H, t, *J* = 7.5 Hz), 1.43 (9 H, s), 1.60 (2 H, m), 2.53 (1 H, m), 3.28 (2 H, m), 3.70 (3 H, s), 4.86 (1 H, br s).

^{13}C NMR (126 MHz): δ = 11.5, 22.9, 28.4, 41.4, 47.2, 51.7, 79.4, 155.9, 175.4.

MS (EI): *m*/*z* (%) = 184 (32), 176 (92), 158 (79), 144 (33), 133 (15), 132 (100), 126 (63), 100 (20).

Anal. Calcd for $C_{11}H_{21}NO_4$ (231.29): C, 57.12; H, 9.15; N, 6.06. Found: C, 57.43; H, 9.10; N, 5.80.

2-[(*tert*-Butoxycarbonyl)aminomethyl]butanoic Acid (16)
$LiOH·H_2O$ (629 mg, 15.0 mmol) was added at 0 °C to a solution of **15** (360 mg, 1.56 mmol) in THF (35 mL). The mixture was stirred at 0 °C for 6 h and then allowed to warm up to r.t. Stirring was continued for further 18 h. H_2O (5 mL) was added and the mixture was acidified to ca. pH 3 with 1N HCl. The solution was extracted with EtOAc (4 × 30 mL) and the combined organic layers were dried over $MgSO_4$, filtered, and evaporated in vacuo to afford the product.

White powder; yield: 95% (322 mg); mp 51–53 °C; $[\alpha]_D^{26}$ –17.3 (*c* = 1.3, MeOH).

^{1}H NMR (250 MHz): δ = 1.03 (3 H, t, *J* = 7.5 Hz), 1.46 (9 H, s), 1.75 (2 H, m), 3.18 (1 H, m), 4.44 (1 H, dd, *J* = 14.4, 5.0 Hz), 4.75 (1 H, dd, *J* = 14.4, 8.9 Hz), 5.20 (br s, 1 H), 9.57 (br s, 1 H).

IR (KBr): 3385 (m), 2972 (m), 1686 (s), 1528 (s), 1270 (s), 1171 (s) cm^{-1}.

^{13}C NMR (126 MHz): δ = 11.0, 22.4, 28.3, 44.1, 74.7, 80.8, 158.4, 176.9.

Anal. Calcd for $C_{10}H_{19}NO_4$ (217.26): C, 55.28; H, 8.81; N, 6.45. Found: C, 55.24. H, 8.69; N, 6.00.

Acknowledgment

We gratefully acknowledge support from the Konrad Adenauer Foundation, the University of Bielefeld (Ph.D. grants to A.R.), and Fonds der Chemischen Industrie. Prof. Dr. Andreas Pfaltz generously provided a sample of the chiral ligand (*M*,*S*)-**L3**.

References

(1) Present address: Oklahoma State University, Department of Chemistry, Stillwater, OK 74078, USA.
(2) (a) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon Press: Oxford, **1992**. (b) Jung, M. E. *Comprehensive Organic Synthesis*, Vol. 4; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, **1991**, 1–67.
(3) (a) Krause, N.; Hoffmann-Röder, A. *Synthesis* **2001**, *2*, 171. (b) Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346. (c) Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033. (d) Rossiter, B. E.; Swingle, N. M. *Chem. Rev.* **1992**, *92*, 771.
(4) (a) Seebach, D.; Colvin, E. W.; Lehr, F.; Weller, T. *Chimia* **1979**, *33*, 1. (b) Ono, N. *The Nitro Group in Organic Synthesis*; Wiley-VCH: New York, **2001**. (c) Berner, O. M.; Tedeschi, L.; Enders, D. *Eur. J. Org. Chem.* **2002**, 1877. (d) Barrett, A. G. M. *Chem. Soc. Rev.* **1991**, *20*, 95. (e) Rosini, G.; Ballini, R. *Synthesis* **1988**, *11*, 833.
(5) (a) Barrett, A. G. M.; Grabowski, G. *Chem. Rev.* **1986**, *86*, 751. (b) Kabalka, G. W.; Varma, R. S. *Org. Prep. Proced. Int.* **1987**, *19*, 283. (c) Perekalin, V. V.; Lipina, E. S.; Berestovitskaya, V. M.; Efremov, D. A. *Nitroalkenes: Conjugated Nitrocompounds*; John Wiley & Sons: New York, **1994**.
(6) Rimkus, A.; Sewald, N. *Org. Lett.* **2003**, *5*, 79.
(7) Sewald, N.; Wendisch, V. *Tetrahedron: Asymmetry* **1998**, *9*, 1341.
(8) Rimkus, A.; Sewald, N. *Org. Lett.* **2002**, *4*, 3289.
(9) Duursma, A.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2003**, *125*, 3700.
(10) (a) Eilitz, U.; Leßmann, F.; Seidelmann, O.; Wendisch, V. *Tetrahedron: Asymmetry* **2003**, *14*, 189. (b) Luchaco-Cullis, C. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 8192. (c) Ongeri, S.; Piarulli, U.; Jackson, R. F. W.; Gennari, C. *Eur. J. Org. Chem.* **2001**, 803. (d) Alexakis, A.; Benhaim, C. *Org. Lett.* **2000**, *2*, 2579. (e) Duursma, A.; Minnaard, A. J.; Feringa, B. L. *Tetrahedron* **2002**, *58*, 5773. (f) Versleijen, J. P. G.; van Leusen, A. M.; Feringa, B. L. *Tetrahedron Lett.* **1999**, *40*, 5803.
(11) Knochel, P.; Singer, R. D. *Chem. Rev.* **1993**, *93*, 2117; and references cited therein.
(12) (a) Knochel, P.; Perea, J. J. A.; Jones, P. *Tetrahedron* **1998**, *54*, 8275; and references cited therein. (b) Arnold, L. A.; Naasz, R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2001**, *123*, 5842. (c) Alexakis, A.; Benhaim, C.; Fourniuox, X.; van den Heuvel, A.; Leveque, J.-M.; March, S.; Rosset, S. *Synthesis* **1999**, 1811.
(13) (a) Knochel, P.; Jones, P.; Langer, F. *Organozinc Reagents: A Practical Approach In The Practical Approach in Chemistry Series*; Knochel, P.; Jones, P., Eds.; University Press: Oxford, **1999**. (b) Langer, F.; Schwink, L.; Devasagayaraj, A.; Chavant, P.-Y.; Knochel, P. *J. Org. Chem.* **1996**, *61*, 8229. (c) Stevenson, T. M.; Prasad, B. A. S.; Citineni, J. R.; Knochel, P. *Tetrahedron Lett.* **1996**, *37*, 8375. (d) Rieke, R. D.; Hanson, M. V. *Tetrahedron* **1997**, *53*, 1925.
(14) (a) Jones, P.; Reddy, Ch. K.; Knochel, P. *Tetrahedron* **1998**, *54*, 1471. (b) Jones, P.; Knochel, P. *J. Chem. Soc., Perkin Trans. 1* **1997**, *21*, 3117. (c) Reddy, Ch. K.; Davasagayaraj, A.; Knochel, P. *Tetrahedron Lett.* **1996**, *37*, 4495.
(15) For synthesis of (TMSM)ZnR see: Berger, S.; Langer, F.; Lutz, C.; Knochel, P.; Mobley, T. A.; Reddy, Ch. K. *Angew. Chem. Int. Ed.* **1997**, *36*, 1496.
(16) TMSM group as a non-transferrable ligand: Bertz, S. H.; Eriksson, S. H.; Miao, G.; Snyder, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 10906.
(17) (a) Shin, C.; Yamaura, M.; Inui, E.; Ishida, Y.; Yoshimura, J. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2618. (b) Shechter, H.; Conrad, F. *J. Am. Chem. Soc.* **1953**, *75*, 5610. (c) Piet, J. C.; Le Hetet, G.; Cailleux, P.; Benhaoua, H.; Carrié, R. *Bull. Soc. Chim. Belg.* **1996**, *105*, 33.
(18) (a) Rosini, G. *Comprehensive Organic Synthesis*, Vol. 2; Trost, B. M., Ed.; Pergamon: New York, **1991**, 321–340. (b) Modified procedure: Wollenberg, R. H.; Miller, S. J. *Tetrahedron Lett.* **1978**, *19*, 3219.
(19) For the original procedures see: (a) TFAA/Et_3N method: Denmark, S. E.; Marcin, L. R. *J. Org. Chem.* **1993**, *58*, 3853. (b) DCC/Cu(I)Cl method: Knochel, P.; Seebach, D. *Synthesis* **1982**, *12*, 1017.
(20) (a) Worrall, D. E. *Org. Synth.*, Vol. 1; J. Wiley & Sons Inc.: New York, **1941**, 413. (b) Gairaud, C. B.; Lappin, G. P. *J. Org. Chem.* **1953**, *18*, 1; nitrostyrene **1a** is also commercially available.
(21) (a) Wendisch, V.; Sewald, N. *Tetrahedron: Asymmetry* **1997**, *8*, 1253. (b) Alexakis, A.; Benhaim, C.; Rosset, S.; Humam, M. *J. Am. Chem. Soc.* **2002**, *124*, 5262.
(22) Rozema, M. J.; Sidduri, A.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 1956.
(23) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.
(24) For the synthesis of 1-trimethylsilyloxy-1-ethoxycyclopropane see: Rühlmann, K. *Synthesis* **1971**, 236.
(25) (a) Rappoport, Z.; Gazit, A. *J. Org. Chem.* **1985**, *50*, 3184. (b) Jubert, C.; Knochel, P. *J. Org. Chem.* **1994**, *59*, 1053; and references cited therein.
(26) Seebach, D.; Schäfer, H.; Schmidt, B.; Schreiber, M. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1587.
(27) Synthesized from trimethylsilylmethyllithium [(TMSM)Li] and the corresponding iodide. See also ref. [15].
(28) Schäfer, H.; Seebach, D. *Tetrahedron* **1995**, *51*, 2305.
(29) Alexakis, A.; Vastra, J.; Mangeney, P. *Tetrahedron Lett.* **1997**, *38*, 7745.
(30) (a) de Vries, A. H. M.; Meetsma, A.; Feringa, B. L. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2374. (b) Feringa, B. L.; Pineschi, M.; Arnold, L. A.; Imbos, R.; de Vries, A. H. M. *Angew. Chem. Int. Ed.* **1997**, *36*, 2620.
(31) Arnold, L. A.; Imbos, R.; Mandoli, A.; de Vries, A. H. M.; Naasz, R.; Feringa, B. L. *Tetrahedron* **2000**, *56*, 2865.
(32) Kazlauskas, R. J. *Org. Synth.* **1992**, *71*, 60.
(33) Dennis, M. R.; Woodward, S. *J. Chem. Soc., Perkin Trans. 1* **1998**, *6*, 1081.
(34) The data of (*P*,*S*,*S*)-**L1** have been confirmed (private communications) by Prof. A. Alexakis, University of Geneva, Switzerland {$[\alpha]_D$ +8.3 (*c* = 0.75, $CHCl_3$)} and Prof. N. Krause, University of Dortmund, Germany {$[\alpha]_D$ +10.5 (*c* = 0.75, $CHCl_3$)}.
(35) Jubert, C.; Knochel, P. *J. Org. Chem.* **1992**, 5431.
(36) (a) *Enantioselective Synthesis of β-Amino Acids*; Juaristi, E., Ed.; Wiley-VCH: New York, **1997**. (b) Cardillo, G.; Tomasini, C. *Chem. Soc. Rev.* **1996**, *25*, 117.
(37) (a) Mayachi, N.; Shibasaki, M. *J. Org. Chem.* **1990**, *55*, 1975. (b) Tanner, D.; Somfai, P. *Tetrahedron* **1988**, *44*, 613.
(38) Cheng, R. P.; Gellman, S. H.; DeGrado, W. F. *Chem. Rev.* **2001**, *101*, 3219.
(39) Langer, F.; Devasagayaraj, A.; Chavant, P.-Y.; Knochel, P. *Synlett* **1994**, *6*, 410.