Pergamon

Tetrahedron Vol. 51, No. 8, pp. 2305-2324, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4020/95 $9.50+0.00

0040-4020(94)01100-1

Enantioselective Conjugate Addition of Primary Dialkylzinc Reagents to 2-Aryl- and 2-Heteroaryl-nitroolefins Mediated by Titanium-TADDOLates Preparation of Enantioenriched 2-Aryl-alkylamines

Harald Schäfer[1] and Dieter Seebach*

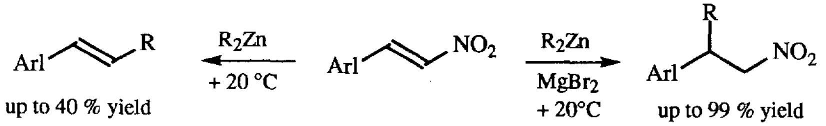
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, ETH-Zentrum,
Universitätstrasse 16, CH-8092 Zürich, Switzerland.

Abstract: The addition of dialkylzinc to nitroolefins is catalyzed by *Lewis* acids such as $MgBr_2$, MgI_2, and chlorotitanates. Using the (*R,R*)-Ti-TADDOLates the addition of diethyl-, dibutyl-, and dioctyl zinc to 2-aryl-nitroethenes is shown to be enantioselective with yields near 90% and enantiomer ratios of *ca.* 9:1 (products **3-12**; enantiomer enrichment by crystallization is possible in some cases). Reduction of the 2-aryl-nitroalkanes thus obtained by catalytic hydrogenation over Pd/C or *Raney*-Ni leads to the corresponding enantioenriched 2-aryl-alkylamines (products **13-21**). The enantiopurity of the nitroalkanes and amines was determined by chromatography on chiral columns. The configuration of the products is assigned (*S*) by optical comparison and by analogy (comparison of five different types of physical data). The relative topicity of the process is *unlike* (*ul* = *R,R*/*Si* or *S,S*/*Re*).

INTRODUCTION

Due to their multiple reactivities organic nitro compounds remain to be important intermediates for the synthesis of nitro-free products[2-6]. The reactions of nitroalkanes and nitroalkenes and their derivatives are especially attractive from a synthetic point of view because they provide building blocks with reactivity *umpolung* for the preparation of carbonyl compounds and of amines. Very often, intriguing conversions are observed with nitroaliphatic derivates[7]. Thus, we have recently discovered a truely novel reaction (*Scheme 1*): the replacement of the nitro group in simple ω-nitrostyrenes by an alkyl group[8] using dialkylzinc reagents[9]. This result is the more surprizing if one considers that nitroolefins are the strongest *Michael* acceptors known[2,6,10]. For poor yields in reactions of nitroolefins with aggressive organometallic reagents such as alkyl or aryl lithium or magnesium derivatives radical reactions (SET processes)[11], oligomerization/polymerization[12], or attack of these reagents on the primarily formed nitronates[13] are commonly blamed, and these can only partially be suppressed by carrying out the reactions at very low temperatures[14-16]. In connection with mechanistic investigations and optimizations of the above mentioned NO_2/alkyl substitution we noticed that dialkyzinc adds

Scheme 1



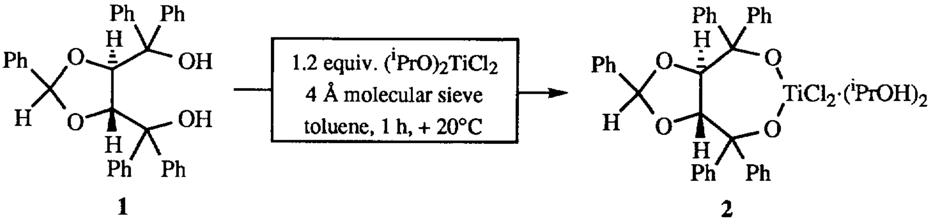
in high yields to ω-nitroolefins in the presence of magnesium bromide at room temperature in diethyl ether as solvent (cf. *Scheme 1* and GP-I, Experimental Part). Having chiral *Lewis* acids, the Mg^{17} and Ti$^{18-21}$ alkoxides of TADDOLs, available which proved highly effective in *Grignard*^{17}, R_2Zn^{18-20}, and $RTi(OR')_3$ additions^{21} to aldehydes and ketones, as well as in (4+2) and (2+2) cycloadditions and ene reactions^{22,23}, we tested whether the *Michael* additions to nitroolefins could be performed enantioselectively in the presence of those auxiliaries. The chiral ligands (TADDOLs = α,α,α',α'-tetraaryl-1,3-dioxolan-4,5-dimethanols) are readily available in two steps from (*R*,*R*)- or (*S*,*S*)-tartrate ester, an aldehyde or ketone, and an aryl *Grignard* reagent$^{20,22-25}$.

PREPARATIVE RESULTS

For the present investigation we chose the diol **1** bearing five phenyl groups^{20b,23,24c,e} as the standard chiral auxiliary which was converted to the titanate **2** as indicated in *Scheme 2*. The recipe involves an *in-situ* preparation of the chiral *Lewis* acid in toluene from the TADDOL and dichloro-diisopropoxy-titanium, without removal of isopropanol, and in the presence of 4 Å molecular sieve^{22,23,24c}. The nitrostyrene was added to a 20% molar excess of the Ti-TADDOLate, both as toluene solutions, and then an almost fourfold excess of a dialkylzinc solution was added at -90°C (*Scheme 2*). After six hours at -75°C the reaction was quenched, and the 2-aryl-1-nitroalkanes **3**-**12** isolated in pure form by column chromatography or distillation; the ratio of enantiomers was determined by high pressure liquid or by gas chromatography on chiral columns (*vide infra* and Experimental Part). The standard conditions as specified in *Scheme 2* have to be strictly followed^{26} in order to obtain the results presented in *Table 1*. For assignment of the chirality sense of the major products (*S*)-**3**-**10** and (*R*)-**11**, **12** formed with the (*R*,*R*)-TADDOL **1**, see a later section. It appears that all additions occur with an enantioselectivity of *ca.* 9:1 (the enantiomer excesses range from 68 to 90%). This magic limit could not be surpassed by any of the measures we took so far. An improvement "after the facts" was, however, achieved by low-temperature crystallization in the case of three of the aryl-nitroalkanes. *Table 1* also reveals that

Scheme 2

Preparation of the Chiral *Lewis* Acid



Standard Conditions for Enantioselective *Michael* Additions

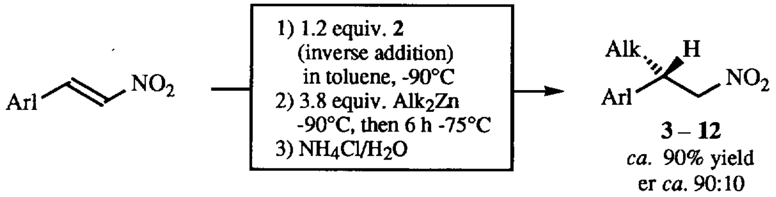
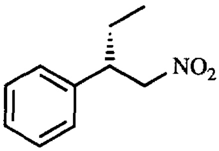
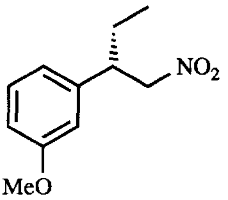


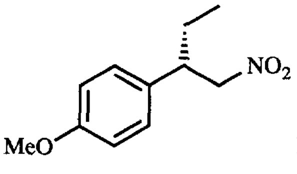
Table 1. Enantioenriched 2-Aryl-1-nitroalkanes 3-12 from ω-Nitrostyrenes and Heteroaryl Analogs and Dialkylzinc Reagents under the Conditions Specified in Scheme 2. The yields are those of pure chromatographed or distilled samples isolated from 1-34 mmolar runs. The enantiomer ratios er were all determined by high pressure liquid or by gas chromatography. Enantiomer enrichments of the products **3**, **7**, and **8** were achieved by crystallization from Et_2O/pentane at dry-ice temperature.



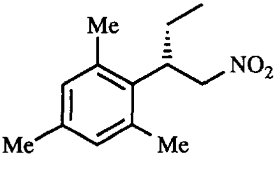
3 92% y, er 87:13
(er 99:1 by cryst.)



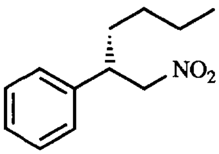
4 94% y, er 88:12



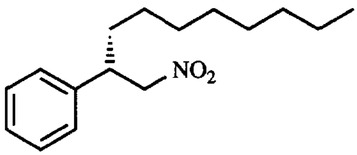
5 95% y, er 88:12



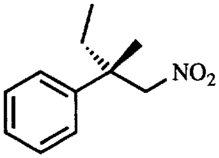
6 92% y, er 95:5



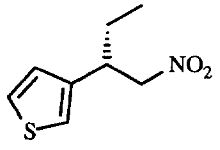
7 98% y, er 89:11
(er 99.5:0.5 by cryst.)



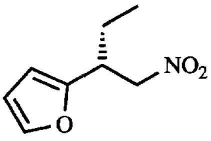
8 87% y, er 88:12
(er 94:6 by cryst.)



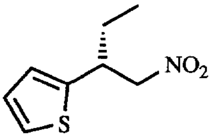
9 35% y, er 84:16



10 90% y, er 89:11



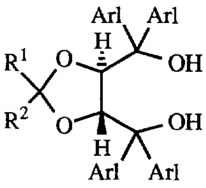
11 88% y, er 87:13



12 83% y, er 90:10

heteroaromatic substitution of the nitroolefin starting material (products **10-12**) or methyl substitution at the *Michael* acceptor carbon (product **9**) do not lead to dramatic changes of the selectivity[27], neither does the increase of chain length in the nucleophilic R_2Zn reagent. TADDOLs other than **1** produced very little variation of the enantioselectivity: the results obtained with six different diols of this type are collected in *Table 2*: most er values are identical within experimental error with the 91:9 er obtained under the standard conditions specified in *Scheme 2*.

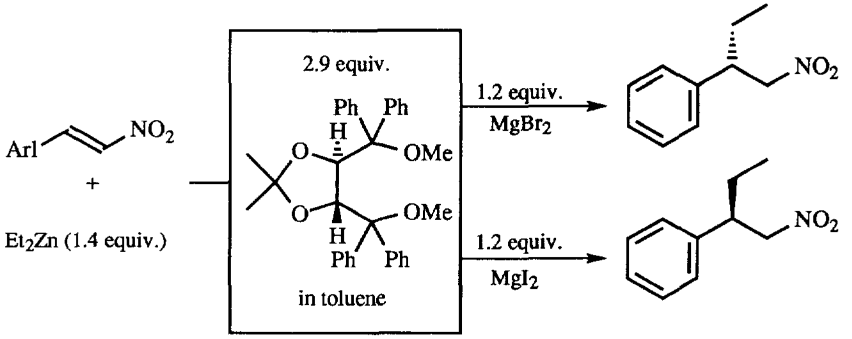
Table 2. Other TADDOLs [22-25] Tested in the Standard Reaction Producing Nitrocompound 3 (cf. Scheme 2). The TADDOL with $R^1 = R^2 =$ Me, Arl = 1-naphthyl did not give an active catalyst at all.



er of **3**	89:11	88:12	83:17	90:10	88:12	87:13
Arl	Ph	2-Naph	Ph	Ph	Ph	Ph
R^1	Me	Me	Ph	4-CF_3-Ph	^{t}Bu	Ph
R^2	Me	Me	Ph	H	H	Me

Finally, we have also done experiments with the dimethyl ether of the original TADDOL[20a,28a], see *Scheme 3*. Addition of diethylzinc to nitrostyrene in toluene containing *ca.* 3 equiv. of this diether and 1.2 equiv. magnesium halide gave the phenyl-nitrobutane **3** in enantioenriched form: 70% preferentially (*S*) with $MgBr_2$ and 75% (*R*) with MgI_2, an intriguing result and a hard nut to crack for those who like to propose mechanisms[28b]! The enantioselectivities observed with the diether auxiliary were not high enough to warrant extensive optimization experiments [it is just worth mentioning that a substoichiometric amount of the TADDOL dimethyl ether (0.29 equiv.) still gave an (*S*)/(*R*) ratio of 60:40].

Scheme 3

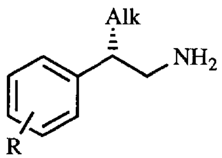


3 (93%)
(*S*)/(*R*) 70:30

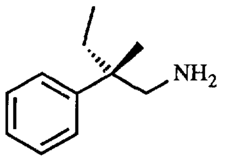
ent-**3** (60%)
(*R*)/(*S*) 75:25

A major interest in the chemistry of organic nitro compounds stems from the fact that they are readily reduced to amines. We chose catalytic hydrogenation[29,30] for the conversion of the enantioenriched aryl-nitroalkanes **3**-**11** to the corresponding amines **13**-**21**. The results are collected in *Table 3*. As heterogeneous catalysts we used Pd on charcoal or *Raney* nickel. Interestingly, the aryl-nitrobutanes **3**-**6** (the products from Et_2Zn additions) were reduced readily at room temperature and at normal H_2 pressure over Pd/C within three days to give the amines **13**-**16** in good yields, while the higher homologs, the nitrohexane **7** and -decane **8** were recovered under these conditions, even when we applied higher pressure and used $H_2/Pd(OH)_2$.

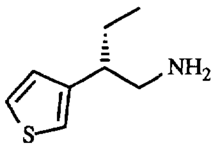
Table 3. Enantioenriched Amines by Catalytic Hydrogenation of 3-11 Using 10%-Pd on Charcoal or Raney-*Ni*. The enantiopurities of these amines are identical to those of the precursor 2-aryl-nitroalkanes (see accompanying text and Experimental Part).



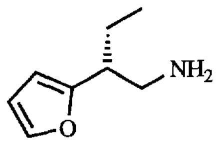
13 – **18**



19 73% y (H_2/Ry-Ni)



20 23% y (H_2/Pd-C)



21 2% y (H_2/Ry-Ni)
(er 87:13)

No.	13	14	15	16	17	18
Alk	Et	Et	Et	Et	Bu	Oct
R	H	3-MeO	4-MeO	2,4,6-Me_3	H	H
H_2/Cat.	Pd-C	Pd-C	Pd-C Ry-Ni	Pd-C	Ry-Ni	Ry-Ni
% y	73	76	91 80	66	71	78

On the other hand, *Raney* nickel at 30 bar H_2 pressure for 24 h at ambient temperature led to the reduction of all types of aryl-nitroalkanes, including the β-branched compound **9** (cf. *Table 3*, products **15**, **17-19** and **21**). The amines thus formed were difficult to obtain in analytically pure form: they are air-sensitive (reacting with O_2 and CO_2), and their hydrochloride and hydrogen oxalate salts did not lend themselves for purification purposes. The most sensitive amine, which is also very volatile, was the furan derivative **21**, most of which we lost during purification (see yield in *Table 3*). The enantiopurity of the amines **13-18**, **20**, **21** was determined by preparing amides of (*R*)- and (*S*)-α-methoxy-α-(trifluoromethyl)-phenylacetic acid (*Mosher* amides)[31] and doing an HPLC or ^{19}F-NMR analysis, which showed that the enantiomer ratios were identical within experimental error (± 1%) with those determined of the corresponding aryl-nitroalkanes **3-10** (*vide supra* and *Table 1*).

CONFIGURATIONAL ASSIGNMENT

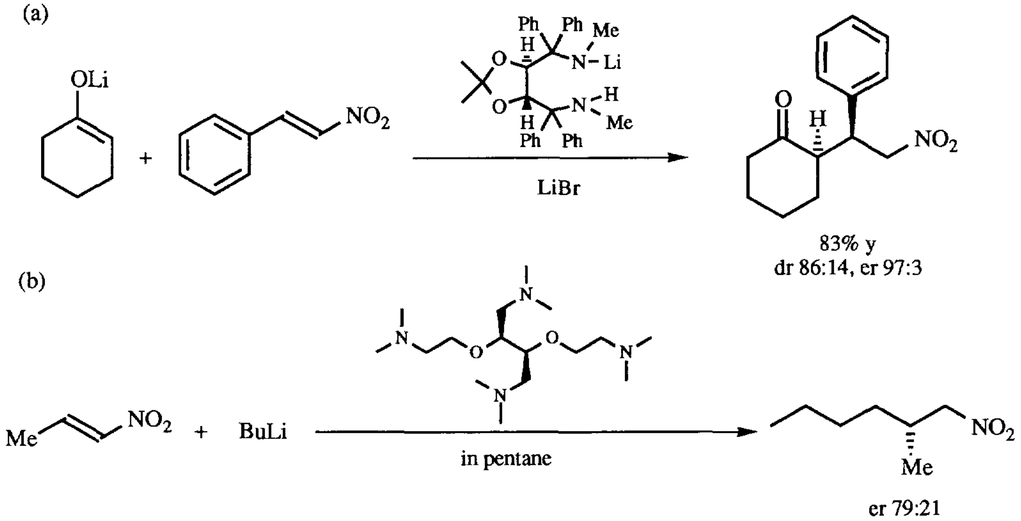
The parent compound of our aryl-nitroalkanes, 2-phenyl-nitrobutane (**3**), has been prepared in enantiopure form before. *Ohta et al.* have shown that *E*-2-aryl-nitropropene, -butene, and -pentene, but not higher homologs can be reduced (23-64%) enantioselectively (er 95:5 to 99:1) to the nitroalkanes by yeast reduction[30]; by optical comparison, the product thus obtained is *ent*-**3**. Both enantiomers have been reduced to 2-phenyl-butylamine, which in turn had been prepared from 2-phenylbutanoic acid by *Kirmse et al.*[32] and correlated with glyceraldehyde by *Pettersen*[33]. Thus, our compounds, the laevorotatory nitroalkane **3** and its reduction product, the dextrorotatory amine **13** can be safely assigned (*S*)-configuration.

The *major* enantiomers of the nitroalkanes (**3-12**) are laevorotatory[34a], and they have the larger retention time on Chiralcel OD (HPLC)[34b] and the smaller retention time on FS-Lipodex E (GC)[34c]; furthermore, their reduction products (the amines **13-21**) are dextrorotatory[34d] and the amides of (*S*)-*Mosher* acid[31] prepared from the amines show a higher-field ^{19}F-NMR signal[34e]. From the constitutional similarity of the 2-aryl-nitroalkanes and those common features of five independent physical properties we assign all our major products as resulting from *Si*-face addition to the nitroolefin, by analogy[35] [see the *formulae* of *Scheme 2*, *Table 1*, and *Table 3*; (*S*)-configuration for compounds **3-10**, (*R*)-configuration for the homochiral compounds **11** and **12**].

CONCLUSION AND DISCUSSION

There are numerous examples described in the literature of highly diastereoselective C,C-bond-forming *Michael* additions of chiral nucleophiles, such as enamines[36,37] and enolates[38], to nitroolefins, as well as of achiral nucleophiles to chiral nitroolefins[39]. Also, stereoselective additions of nitrogen[6,40], oxygen[41], and sulfur[42] nucleophiles to nitroolefins can be highly efficient. A special case is the enantioselective addition of two achiral components, an enolate and a nitroolefin, under the influence of a chiral Li-amido-amine[43] (TADDAMIN derivative), see (a) in *Scheme 4*. The addition of simple alkyl nucleophiles to nitroolefins was much less successful so far, with Li, Mg, Zn, and Cu derivatives having been tested[15,44,45]. An example from our own work is shown in *Scheme 4* (b)[44].

Scheme 4



The Ti-TADDOLate-mediated dialkylzinc addition to aryl-nitroolefins described herein occurs with the highest enantioselectivities hitherto observed for this particular type of process. Without further investigations, as they have been done in the case of Ti-TADDOLate-catalyzed nucleophilic additions to aldehydes[18-21] and *Diels-Alder* reactions[23], we consider it improper to even speculate about the mechanism of the reaction. It is intriguing and appropriate to point out, however, that the R_2Zn reagent adds to the *Si*-face of the trigonal center in the nitroolefins as it does in the case of aldehydes[18-21], see accompanying Figure (a) and (b).

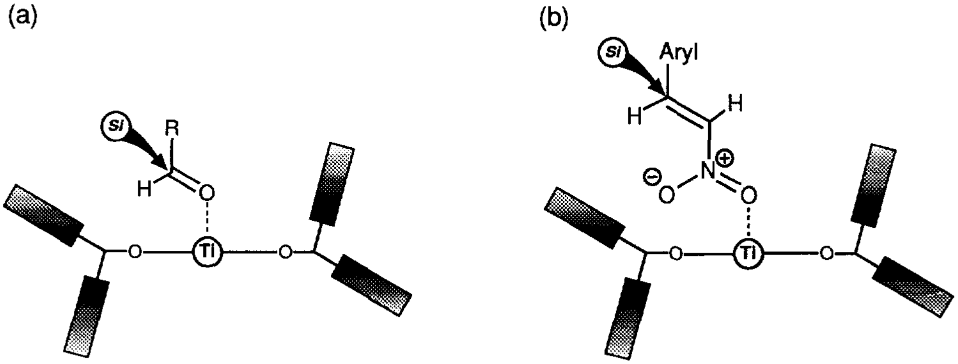


Figure. Comparison of Possible Complexations of Aldehydes (a) and Nitrostyrenes (b) to the Lewis *Acidic Site of an (R,R)-Ti-TADDOLate.* The ligand sphere of Ti may be octahedral or trigonal bipyramidal. The shaded rectangles symbolize the typical axial and equatorial phenyl groups on the seven-membered Ti-TADDOLate ring[20,23]. The back side is occupied by the dioxolane ring (not shown). The experimentally observed topicity of the nucleophilic attack is *Si*.

Acknowledgements: We thank for a Kekulé-Stipendium granted to H. S. by the Stiftung Stipendien-Fonds des Verbandes der Chemischen Industrie (Oct. 1990 - Sept. 1992) as well as for support by the Studienstiftung des deutschen Volkes (Jan. - Dec. 1991). We thank *A. K. Beck* and *S. Sigrist* for thorough corrections and *F. Kühnle* and *Y. M. Wang* for drawing some schemes. The *Witco GmbH* (D-Bergkamen) supplied us generously with diethylzinc and the *Hüls AG* (D-Rheinfelden) with tetraisopropoxytitanium. Continuous financial support by the Sandoz Pharma and Agro AG (CH-Basel) is gratefully acknowledged.

EXPERIMENTAL PART

General: Abbreviations: GP (general Procedure), HV (high vacuum, 0.01-0.1 Torr), MS (molecular sieve), MTPACl (α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride), RV (evaporator), R_f (retention factor), R_t (retention time in minutes).

Starting materials and reagents: Nitroolefins are commercially available or were obtained according to the literature[46a]. Due to poor yields which we obtained using reported procedures[46b,c] we modified the conditions for the preparation of the heteroaromatic nitroolefins. 2-(2-Furyl)-nitroethene, 2-(2-thienyl)-nitroethene and 2-(3-thienyl)-nitroethene were prepared according to ref.[46b-d] using NaOMe (*Fluka*, 95 %) in MeOH at -10°C for the nitro aldol addition[46b], dissolving the adduct in the minimum amount of chilled water and pooring it onto chilled *ca.* half concentrated aqueous HCl[46c,d]. Nevertheless only moderate yields were achieved (56, 44, and 65 % respectively). Right after preparation or after long storage periods, the nitroolefins were sublimed at 80°C/HV or filtered over silicagel with CH_2Cl_2 as eluant to yield brightly yellow compounds. A stock soln. of Et_2Zn (2 M) was prepared from 20.5 ml Et_2Zn (freshly distilled, ref.[47]) and 79.5 ml of toluene or of Et_2O (**CAUTION**: pure Et_2Zn reacts violently with air and water). Diethyl ether-free Bu_2Zn was obtained from a soln. of BuMgBr in Et_2O and a 1.0 M soln. of $ZnCl_2$ in Et_2O (*Aldrich*) by filtration of the reaction mixture under argon, and fractional distillation (b.p.: 100 °C/4 Torr (ref.[47]: 61°C/4 Torr)). Ether free Oct_2Zn was obtained according to ref.[48] or, preferably, to ref.[49]. $TiCl_2(O^iPr)_2$ was prepared according to ref.[50] and stored as stock solution in toluene (0.322 M). Molecular sieve 4 Å (MS)was ground and dried for 8 h at 160°C under HV directly before use. Sat. $MgBr_2$ in Et_2O (*ca.* 2.1 M)[51] was obtained from 1,2-dibromoethane and magnesium. Sat. MgI_2 soln. in Et_2O (*ca.* 1.29 M)[52] was obtained from 1,2-diiodoethane and magnesium. Toluene and Et_2O used in the reactions were dried immediately before use by refluxing and distillation over metallic potassium or sodium, respectively with benzophenone as indicator. The solvents used for workup and purification were distilled: Et_2O (KOH, $FeSO_4$); CH_2Cl_2, hexane (P_2O_5).

Equipment: All reactions were performed under an inert argon atmosphere in oven-dried equipments. The addition reactions at low temperature were performed using a bath of toluene, cooled by liquid nitrogen (*ca.* -90°C) and dry ice (*ca.* -75°C), respectively. Thinlayer chromatography (**TLC**): precoated silica gel 60 F_{254} plates (*Merck*); visualization by UV_{254} light extinction, development using phosphomolybdic acid soln. (25 g phosphomolybdic acid, 10 g $Ce(SO_4)_2{\cdot}4H_2O$, 60 ml H_2SO_4, 940 ml H_2O) or ninhydrin soln. (600 mg ninhydrin, 285 ml BuOH, 2 ml AcOH, 13 ml H_2O). Flash chromatography (**FC**): SiO_2 60 (0.040 - 0.063 mm, *Fluka*), pressure: 0.2-0.4 bar. $[\alpha]_D^{r.t.}$ (*ca.* 20°C): *Perkin-Elmer 241* polarimeter (*p.a.* solvents, *Fluka*). Distillation of the products: *Büchi GKR-50* bulb-to-bulb distillation apparatus. Boiling points (**b.p.**): correspond to uncorrected air bath temp. Melting points (**m.p.**): open glass capillaries, *Büchi 510* (*Tottoli* apparatus), 50°C range *Anschütz* thermometers, uncorrected. High-pressure liquid chromatography (**HPLC**): *Kontron, Uvikon LCD 725*; two pumps *Kontron*, LC Pump 414; Chiralcel OD *Daicel, Chemical Industries, Ltd*; 230 nm; 0.5 ml/min. Capillary gas chromatography (CGC): *HRGC* (*Carlo Erba*); injector temp.: 220°C; detector temp.: 250°C; γ-CD: FS-Lipodex® E, 2,6-O-pentyl-3-O-butyryl-γ-CD, 50 m x 0.25 mm (*Macherey-Nagel AG*), 1.5 kPa (H_2); *ibid.* 45 m x 0.19 mm (30 % precoated in OV1701V; self-made), 2.0 kPa (H_2). **IR**: film; *Perkin-Elmer 1600*; $\tilde{\nu}$ in cm^{-1}. **^{1}H- and ^{13}C-NMR** spectra: *Varian Gemini 200* (200 and 50 MHz, resp.), *Varian Gemini 300* or *Bruker WM 300* (300 and 75 MHz, resp.), *Bruker AMX 400* (400 and 100 MHz, resp.), *Bruker AMX 500* (500 and 125 MHz, resp.); δ in ppm downfield of TMS (δ = 0) in $CDCl_3$; J in Hz. DEPT spectra and a ^{13}C-NMR calculation programm[53] were used for the assignment of ^{13}C-NMR signals. **^{19}F-NMR** spectra: *Varian Gemini 300* (282 MHz), δ in ppm downfield of CCl_3F (δ = 0) in $CDCl_3$. ^{19}F-NMR spectra of *Mosher* amides were measured at -70.24 to -68.64 ppm with a high density of points (NP = 16000) at 55°C. MS: VG-*Tribrid* spectrometer, fragment ions in *m/z* with relative intensities (%) in parentheses. Elemental analysis were performed at the *Microanalytical Service Laboratory of the Laboratorium für Organische Chemie (ETH Zürich).*

I. Preparation of racemic *Michael* adducts by addition of Et_2Zn to nitroolefins in the presence of $MgBr_2$ (GP-I): To a stirred soln. of 1.2 equiv. of sat. $MgBr_2$ were added 20-30 ml of Et_2O, 1.4 equiv. of a 2 M Et_2Zn soln. in Et_2O and, within 30 min, a soln. of 1.2-7.2 mmol of the nitroolefin in 25-30 ml Et_2O. The reaction mixture was stirred for 1 h at r.t. and then carefully quenched by addition of 20 ml sat. NH_4Cl soln. at 0°C. The mixture was stirred for 30 min at r.t., while adding 2 M HCl in portions to dissolve the precipitate (pH 1). The organic layer was washed with sat. NaCl. soln., dried over $MgSO_4$ and evaporated (RV, at the end of evaporation HV was applied for a short period of time). The residue was then purified by FC (15x3 cm, pentane/CH_2Cl_2 5:1) yielding the *Michael* adducts in 65-99%.

II. Enantioselective addition of dialkylzinc to nitroolefins mediated by titanium-TADDOLates (GP-II): 30-200 ml of toluene and 1.2 equiv. of 0.32 M $TiCl_2(O^iPr)_2$ in toluene were added to 0.3-1.5 g of MS and 1.2 equiv. of **1**. This mixture was stirred for 1 h at r.t. and then cooled to -90°C. A soln. of 1.3-33.5 mmol nitroethen (1 equiv.) in toluene (9-50 ml) was added, keeping the temperature below -80°C. At -90 ± 3°C a soln. of 3.8 equiv. dialkylzinc (2 M for Et_2Zn; otherwise 1-2 M) was added within 30-45 min. The reaction mixture was allowed to warm to -75°C and kept at this temperature. Upon completion of the reaction (6 h for Et_2Zn) the reaction mixture was poured into 50-200 ml of sat. NH_4Cl soln., stirred for *ca.* 1.5 h and then filtered through celite. The organic layer was washed with sat. NaCl soln., then dried over $MgSO_4$ and evaporated (RV, at the end of evaporation HV was applied for a short period of time). The residue was dissolved in Et_2O or CH_2Cl_2, 50 ml of hexanes were added and the more volatile Et_2O or CH_2Cl_2 was evaporated (RV). The solution was decanted from residual TADDOL. The TADDOL was washed with 2x20 ml of hexanes and the combined fractions were evaporated. The residue was then purified by FC (15x3 cm; pentane/CH_2Cl_2 5:1) or bulb-to-bulb distillation.

III. Preparation of 2-aryl-butylamines by catalytic hydrogenation of 2-aryl-1-nitrobutanes using 10%-Pd on charcoal (GP-III): A soln. of 5.58 mmol of the 2-aryl-butylamine in ethyl acetate was stirred with 10%-Pd/C for 3 d at ambient temperature and at normal pressure of hydrogen. The reaction mixture was filtered through celite and the amine was extracted with 1 M H_2SO_4. The aqueous phase was made alkaline by addition of 2.5 M NaOH and the amine was extracted three times with Et_2O.[54] The organic layer was dried over $MgSO_4$ and evaporated.

IV. Preparation of 2-aryl-alkylamines by catalytic hydrogenation of 2-aryl-1-nitroalkanes using *Raney*-Ni (GP-IV): Neutral *Raney*-Ni (activity W2) was prepared according to ref.[55] from 3.5 g of *Raney*-Ni alloy and was washed with water to pH 6 and then six times with ethanol (**CAUTION**: activated *Raney*-Ni is pyrophoric). The amine (5 mmol) was hydrogenated in 20 ml of ethanol in an shaken autoclave for 24 h at ambient temperature and 30 bar. The solution was filtered through celite and evaporated (RV, at the end of evaporation HV was applied for a short period of time). The residue was purified by FC (17x3 cm; with CH_2Cl_2/MeOH/Et_3N 95:5:0.5 as eluant, eventually changing to a ratio of 90:10:1 after *ca.* 400 ml; ninhydrine) and distillation. The purified amines were stored at -10°C under an inert atmosphere.

V. Preparation of *Mosher* amides (GP-V): *Mosher* amides used for HPLC analysis were prepared and purified according to ref.[30]. *Mosher* amides used for ^{19}F-NMR analysis were prepared in an NMR tube simply by mixing 15 mg of the amine with 1.5 equiv. of (*R*)- or (*S*)-MTPACl and a trace of N,N-dimethyl-4-amino pyridine in 0.4 ml $CDCl_3$ and shaking the mixture shortly.

2-Aryl-nitroalkanes

2-Phenyl-nitrobutane (3): a) Following GP-I, a soln. of 1.00 g (6.71 mmol) 2-phenyl-nitroethene and 4.7 ml (9.4 mmol) of Et_2Zn soln. with 3.8 ml (7.98 mmol) of $MgBr_2$ soln. gave 1.10 g (92%) of *rac*-**3** as colourless liquid.

b) Following GP-II, 2.55 ml (5.1 mmol) of Et_2Zn soln. and a soln. of 200 mg (1.34 mmol) 2-phenyl-nitroethene in 15 ml toluene with 828 mg (1.61 mmol) **1**, 300 mg MS, 30 ml of toluene and 5 ml (1.61 mmol) of $TiCl_2(O^iPr)_2$ soln. gave after distillation 227 mg (95%) of **3** as colourless liquid [(*S*)/(*R*) = 91:9; Chiralcel OD; hexane/^{i}PrOH 95:5; R_t:17.4 (*R*), 23.5 (*S*)]; [89:11; FS-Lipodex E; 1.5 bar, 100°C + 0.3°C/min; R_t: 55.2 (*S*), 57.9 (*R*); moderate peak separation]. Compound **3** has been described by *Ohta et al.* with ^1H-NMR data (in CCl_4) and an er of 98.5:1.5 (*R*)[30], having the opposite sign of optical rotation as compared to **3** prepared herein (cf. *Table 6*).

Table 4. Determination of the Enantiomer Ratios (er) of the Michael *Adducts. by HPL or Gas Chromatography.* The relative peak areas are given in the order of elution. For details see the corresponding procedures. For nitroalkane **11** see its hydrogenation product **21** in *Table 5*.

Column	HPLC: Chiralcel OD		GC: Lipodex E	
No.	R_t [min]	er	R_t [min]	er
3	17.4; 23.5	9:91	55.2; 57.9	89:11
4	28.7; 67.0	12.5:87.5		
5	20.9; 33.7	12:88		
6	16.1; 22.8	5:95		
7	16.0; 23.2	11.5:88.5		
8	15.1; 20.8	12:88		
9			86.7; 87.2	84:16
10	37.3; 41.3	11:89	79.2; 79.6	88:12
12			73.7; 75.2	90:10

c) Large-Scale Run: following GP-II, 38.2 ml (76.4 mmol) of Et_2Zn soln. and a soln. of 3.00 g (20.1 mmol) 2-phenyl-nitroethene in 40 ml toluene with 12.41 g (24.1 mmol) **1**, 900 mg MS, 120 ml of toluene and 75 ml (24.1 mmol) of $TiCl_2(O^iPr)_2$ soln. gave after distillation 3.30 g (92%) of **3** as colourless liquid [(*S*)/(*R*) = 87:13; Chiralcel OD; hexane/^{i}PrOH 95:5; R_t:17.8 (*R*), 26.1 (*S*)]. Compound **3** was crystallized several times by dissolving it in a *ca.* ten fold volume of pentane/Et_2O 1:1, keeping the mixture at -75°C for 1-2 h and then removing the mother liquor with a syringe to yield 1.46 g (41%) with an er 99.2:0.8. – **B.p.**: 100°C/0.2 Torr. – **IR**: $\tilde{v}$ = 3030w, 2967m, 2933m, 2876w, 1552s, 1495m, 1454m, 1431m, 1380s, 760m, 701s. – **^{1}H-NMR** (300 MHz): δ = 0.84 (t, J = 7.4, 3 H, 4-H), 1.61-1.84 (m, 2 H, 3-H), 3.31-3.41 (m, 1 H, 2-H), 4.57 (J_{AB} = 12.1, J_{AX} = 7.9, J_{BX} = 7.6, 2 H, 1-H), 7.16-7.20 (m, 2 H, arom. H), 7.23-7.36 (m, 3 H, arom. H). – **^{13}C-NMR** (75 MHz): δ = 11.6 (C-4), 26.2 (C-3), 46.0 (C-2), 80.8 (C-1), 128.9, 127.6 (arom. CH), 139.4 (C-1'). – **MS**: m/z = 179 (1) [M^+], 132 (82) [$M^+ - HNO_2$], 117 (32), 104 (32), 91 (100).

d) Preparation of **3** and *ent*-**3** in the presence of the TADDOL dimethyl ether according to *Scheme 3*. - d1) With $MgBr_2$ as *Lewis* acid: 1.92 g (3.88 mmol) of the dimethyl ether, 200 mg (1.34 mmol) 2-phenylnitroethene and 40 ml of toluene were added to $MgBr_2$, which had been prepared by evaporating 0.77 ml (1.62 mmol) of sat. $MgBr_2$ soln. in Et_2O. The reaction mixture was stirred for 1 h at r.t. and then cooled to -75°C. Within 5 min, 0.94 ml (1.88 mmol) of Et_2Zn soln. were added. The reaction mixture was then stirred for 14 h with gradual warming to r.t. At 0°C, 20 ml of sat. NH_4Cl soln. were addded carefully. The mixture was stirred for 30 min at r.t., while adding 2 M HCl in portions to dissolve the precipitate (pH 1). The organic layer was washed with sat. NaCl. soln., dried over $MgSO_4$ and evaporated (RV, at the end of evaporation HV was applied for a short period of time). The residue was dissolved in Et_2O, 25 ml of MeOH were added and the more volatile Et_2O was evaporated (RV). At 0°C, the solution was decanted from residual TADDOL dimethyl ether which was washed three times with MeOH (0°C). The combined MeOH fractions were evaporated after addition of some silicagel. The resulting residue was then purified by FC (15x3 cm; pentane/CH_2Cl_2 5:1) yielding 223 mg (93%) of **3** as colourless liquid [(*S*)/(*R*) = 71:29; FS-Lipodex E]. – d2) With MgI_2 as *Lewis* acid: Following the same procedure, but using 1.25 ml (1.62 mmol) of sat. MgI_2 soln. in ether instead of the $MgBr_2$, gave 145 mg (60%) of **3** [(*S*)/(*R*) = 25.5:74.5; FS-Lipodex E].

2-(3-Methoxyphenyl)-nitrobutane (4): a) Following GP-I, a soln. of 0.20 g (1.16 mmol) 2-(3-methoxyphenyl)-nitroethene and 0.8 ml (1.6 mmol) of Et_2Zn soln. with 0.64 ml (1.34 mmol) of $MgBr_2$ soln. gave 164 mg (70%) of *rac*-**4** as colourless liquid. – b) Following GP-II, 5.1 ml (10.2 mmol) of Et_2Zn soln. and a soln. of 481 mg (2.68 mmol) of the nitroolefin in 20 ml toluene with 1.656 g (3.22 mmol) **1**, 500 mg MS, 60 ml of toluene and 10 ml (3.22 mmol) of $TiCl_2(O^iPr)_2$ soln. gave after distillation and FC 529 mg (94%) of **4** as colourless liquid [(*S*)/(*R*) = 87.5:12.5; Chiralcel OD; hexane/^{i}PrOH 95:5; R_t: 28.7 (*R*), 67.0 (*S*)]. – Racemic **4** has been reported by *von Angerer et al.* (with ^{1}H-NMR data)[56]. – **B.p.**: 140°C/0.1 Torr. – **IR**: $\tilde{v}$ = 2965s, 2935s, 2876m, 2837m, 1602s, 1586s, 1552s, 1490s, 1456s, 1435s, 1381s, 1263s, 1161s, 1043s, 782s, 701s. – **^{1}H-NMR** (200 MHz): δ = 0.84 (t, J(3-H) = 7.4, 3 H, 4-H), 1.58-1.79 (m, 2 H, 3-H), 3.25-3.40 (m, 1 H, 2-H), 3.79 (s, 3 H, OCH_3), 4.53 (m, 2 H, 1-H), 6.71-6.82 (3 H, arom. H), 7.25 (dd, 1 H, arom. H). – **^{13}C-NMR** (50 MHz): δ = 11.5 (C-4), 26.1 (C-3), 46.0 (C-2), 55.2 (OCH_3), 80.7 (C-1), 112.8, 113.7 (C-2', C-4'), 119.8 (C-6'), 129.9 (C-5'), 140.9 (C-1'), 159.9 (C-3').

2-(4-Methoxyphenyl)-nitrobutane (5): a) Following GP-I, a soln. of 1.00 g (5.58 mmol) 2-(4-methoxyphenyl)-nitroethene and 3.9 ml (7.8 mmol) of Et_2Zn soln. with 3.2 ml (6.7 mmol) of $MgBr_2$ soln. gave 1.11 g (95%) of *rac*-**5** as slightly yellow liquid. – b) Following GP-II, 2.55 ml (5.1 mmol) of Et_2Zn soln. and a soln. of 240 mg (1.34 mmol) of the nitroolefin in 15 ml toluene with 828 mg (1.61 mmol) **1**, 300 mg MS, 30 ml of toluene and 5 ml (1.61 mmol) of $TiCl_2(O^iPr)_2$ soln. gave after 8 h at -78°C, distillation and FC 266 mg (95%) of **5** as slightly yellow liquid which slowly crystallized upon storage [(*S*)/(*R*) = 88:12; Chiralcel OD;

hexane/^{i}PrOH 95:5; R$_t$: 20.9 (*R*), 33.7 (*S*)]. – **B.p.**: 130°C/0.1 Torr. – **M.p.**: 27.6-28.0°C – **IR**: $\tilde{\nu}$ = 2966m, 2934m, 2877w, 2838w, 1612m, 1552s, 1514s, 1381m, 1253s, 1180m, 1034m, 832m. – **^{1}H-NMR** (300 MHz): δ = 0.83 (t, *J*(3-H) = 7.3, 3 H, 4-H), 1.58-1.78 (m, 2 H, 3-H), 2.26-3.36 (m, 1 H, 2-H), 3.79 (s, 3 H, OCH$_3$), 4.46-4.59 (m, 2 H, 1-H), 6.84-6.89 (m, 2 H, arom. H), 7.08-7.13 (m, 2 H, arom. H). – **^{13}C-NMR** (75 MHz): δ = 11.5 (C-4), 26.2 (C-3), 45.3 (C-2), 55.2 (OCH$_3$), 81.0 (C-1), 114.3 (C-3', C-5'), 128.6 (C-2', C-6'), 131.2 (C-1'), 158.9 (C-4'). – **MS**: *m/z* = 209 (20) [M$^+$], 162 (63) [M$^+$ – HNO$_2$], 134 (58), 121 (100), 91 (18). – Anal. calcd. for C$_{11}$H$_{15}$NO$_3$ (209.25): C 63.14, H 7.23, N 6.69; found: C 63.28, H 7.44, N 6.70.

2-(2,4,6-Trimethylphenyl)-nitrobutane (6): a) Following GP-I, 1.1 ml (2.2 mmol) of Et$_2$Zn soln. and a soln. of 293 mg (1.53 mmol) 2-(2,4,6-trimethylphenyl)-nitroethene with 5.0 ml (1.61 mmol) of TiCl$_2$(OiPr)$_2$ soln. in toluene instead of MgBr$_2$-soln. in Et$_2$O were stirred for 2 h with gradual warming from -85°C to 6°C, to give after FC (pentane/CH$_2$Cl$_2$ 2:1) 268 mg (79 %) of *rac*-**6** as colourless liquid. – b) Following GP-II, 10.2 ml (20.4 mmol) of Et$_2$Zn soln. and a soln. of 1.026 g (5.36 mmol) of the nitroolefin in 30 ml toluene with 3.321 g (6.45 mmol) **1**, 700 mg MS, 80 ml of toluene and 20 ml (6.44 mmol) of TiCl$_2$(O^{i}Pr)$_2$ soln. gave after FC 1.10 g (92%) of **6** as colourless liquid [(*S*)/(*R*) = 95:5; Chiralcel OD; hexane/^{i}PrOH 98:2; R$_t$: 16.1 (*R*), 22.8 (*S*)]. – **IR**: $\tilde{\nu}$ = 2967s, 2875m, 1611m, 1553s, 1457m, 1379s, 853m. – **^{1}H-NMR** (300 MHz): δ = 0.86 (t, *J*(3-H) = 7.44, 3 H, 4-H), 1.74-1.95 (m, 2 H, 3-H), 2.23 (s, 3 H, CH$_3$), 2.34 (s, 3 H, CH$_3$), 2.36 (s, 3 H, CH$_3$), 3.98 (m, 1 H, 2-H), 4.69 (J_{AB} = 12.0, J_{AX} = 7.4, J_{BX} = 8.1, 2 H, 1-H), 6.82 (2 H, arom. H). – **^{13}C-NMR** (75 MHz): δ = 12.2 (C-4), 20.6, 21.2, 21.6 (3 CH$_3$), 24.6 (C-3), 40.8 (C-2), 80.8 (C-1) [*ca.* 80.8 - 81.0: (C-1)], 129.7, 131.3 (C-3', C-5'), 132.5, 135.7, 136.5, 137.7 (C-1', C-2', C-4', C-6'). – **MS**: *m/z* = 221 (17) [M$^+$], 174 (4) [M$^+$ – HNO$_2$], 159 (10), 146 (33), 133 (100). – Anal. calcd. for C$_{13}$H$_{19}$NO$_2$ (221.30): C 70.56, H 8.65, N 6.33; found: C 70.87, H 8.40, N 6.40.

2-Phenyl-nitrohexane (7): a) Following GP-I, a soln. of 400 mg (2.68 mmol) 2-phenyl-nitroethene and 1.9 ml (3.23 mmol) 1.70 M BuLi in hexane (instead of Et$_2$Zn and MgBr$_2$ soln.) gave after 13 h at -75°C in toluene 212 mg (38 %) of *rac*-**7** as colourless liquid. – b) Following GP-II, 40.8 ml (40.8 mmol) of 1 M Bu$_2$Zn in toluene and a soln. of 1.60 g (10.73 mmol) of the nitroolefin in 20 ml toluene with 6.624 g (12.9 mmol) **1**, 1.0 g MS, 80 ml of toluene and 40 ml (12.9 mmol) of TiCl$_2$(O^{i}Pr)$_2$ soln. gave after FC 2.18 g (98%) of **7** as colourless liquid [(*S*)/(*R*) = 88.5:11.5; Chiralcel OD; hexane/^{i}PrOH 95:5; R$_t$: 16.0 (*R*), 23.2 (*S*)]. – Compound **7** was crystallized several times by addition of a *ca.* ten fold volume of pentane/Et$_2$O 1:1, keeping the mixture at -75°C for 1-2 h and then removing supernatant liquid with a syringe to yield 995 mg (45%) of **7** with an er 99.4:0.6. – Enantioenriched **7**, which turned out to have an er of 79:21, has been prepared by *Seebach et al.* and reported with IR and ^{1}H-NMR (in CCl$_4$) data[15,44]. – **IR**:$\tilde{\nu}$ = 3031w, 2958m, 2932m, 2860m, 1553s (NO$_2$), 1454m, 1379s, 762m, 700s. – **^{1}H-NMR** (200 MHz): δ = 0.83 (t, *J*(5-H) = 6.9, 3 H, 6-H), 1.07-1.35 (m, 4 H, 4-H, 5-H), 1.67 (dt, *J*(2-H) = *J*(4-H) = 7.5, 2 H, 3-H), 3.43 (m, *J*(1-H) = *J*(3-H) = 7.6, 1 H, 2-H), 4.53 (J_{AB} = 12.2, J_{AX} = 7.8, J_{BX} = 7.6, 2 H, 1-H), 7.14-7.37 (m, 5 H, arom. H). – **^{13}C-NMR** (75 MHz): δ = 13.8 (C-6), 22.4 (C-5), 29.0 (C-4), 32.7 (C-3), 44.4 (C-2), 81.0 (C-1), 127.5, 128.9 (C-2' to C-6'), 139.6 (C-1'). – **MS**: *m/z* = 207 (0.4) [M$^+$], 160 (25) [M$^+$ – HNO$_2$], 118 (100), 117 (17), 105 (17), 104 (36), 103 (12), 91 (75).

2-Phenyl-nitrodecane (8): a) Following GP-II, 4.0 ml (13.7 mmol) Oct$_2$Zn[48] in 15 ml toluene and a soln. of 490 mg (3.28 mmol) 2-phenyl-nitroethene in 15 ml toluene with 2.027 g (3.94 mmol) **1**, 300 mg MS, 40 ml of toluene and 12.24 ml (3.94 mmol) of TiCl$_2$(O^{i}Pr)$_2$ soln. gave after FC 747 mg (87%) of **8** as colourless liquid [(*S*)/(*R*) = 87.5:12.5; Chiralcel OD; hexane/^{i}PrOH 95:5; R$_t$: 13.9 (*R*), 19.3 (*S*)]. – b) Following GP-II, 44 mmol Oct$_2$Zn (from 100 mmol OctI and excess Et$_2$Zn; 89 % conversion)[49] in 40 ml toluene and a soln. of 1.73 g (11.56 mmol) of the nitroolefin in 30 ml toluene with 7.15 g (13.9 mmol) **1**, 1.0 g MS, 100 ml of toluene and 43.2 ml (13.9 mmol) of TiCl$_2$(O^{i}Pr)$_2$ soln. gave after 2xFC (17x3 cm) 2.07 g (69 %) of **8** as colourless liquid [(*S*)/(*R*) = 88:12; Chiralcel OD; hexane/^{i}PrOH 95:5; R$_t$: 15.1 (*R*), 20.8 (*S*)]. – Compound **8** was crystallized twice by addition of 40 ml pentane/Et$_2$O 1:1, keeping the mixture at -75°C for 1-2 h and then removing supernatant liquid with a syringe to yield 744 mg (25%) of **8** with an er 94:6. – **IR**: $\tilde{\nu}$ = 3064w, 3030m, 2926s, 2855s, 1556s (NO$_2$), 1495m, 1455m, 1431m, 1378s, 761m, 700s. – **^{1}H-NMR** (300 MHz): δ = 0.86 (t, *J*(9-H) = 7.27, 3 H, 10-H), 1.1-1.35 (m, 12 H, 4-H to 9-H), 1.63-1.89 (m, 2 H, 3-H), 3.21-3.49 (m, 1 H, 2-H), 4.55 (J_{AB} = 12.1, J_{AX} = 8.0, J_{BX} = 7.6, 2 H, 1-H), 7.15-7.20 (m, 2 H, arom. H), 7.23-7.60 (m, 3 H, arom. H). – **^{13}C-NMR** (75 MHz): δ = 14.1 (C-10), 22.6 (C-9), 26.9, 29.2, 29.3, 31.8, 33.1 (C-3 to C-8), 44.4 (C-2), 81.1 (C-1), 127.5, 128.9, (C-2' to C-6'), 139.7 (C-1'). – **MS**: *m/z* = 263 (0.1) [M$^+$], 216 (13) [M$^+$ – HNO$_2$], 131 (11), 118 (100), 117 (20), 104 (22), 91 (59). – Anal. calcd. for $C_{16}H_{25}NO_2$ (263.38): C 72.97, H 9.57, N 5.32; found: C 73.18, H 9.78, N 5.36.

2-Methyl-2-phenyl-nitrobutane (**9**): Following GP-II, 23.1 ml (46.2 mmol) of Et$_2$Zn soln. and a soln. of 1.985 g (12.17 mmol) 2-phenyl-1-nitropropene in 30 ml toluene with 7.51 g (14.6 mmol) **1**, 700 mg MS, 100 ml of toluene and 45.4 ml (14.6 mmol) of TiCl$_2$(O^{i}Pr)$_2$ soln. gave after 2xFC (18x3 cm) 1.762 g (75%) of **9**, which contained some starting material due to incomplete conversion[57]. Two further FC (24x5 cm; pentane/Et$_2$O = 96:4) of 1.497 mg gave 689 mg (35%) of **9** (^{1}H-NMR purity >97%) as slightly yellow liquid [(*S*)/(*R*) = 84:16; FS-Lipodex E; 2 bar; 5 min 100°C, + 0.5°C/min; R$_t$: 86.7 (*S*), 87.2 (*R*)]. – **B.p.**: 100°C/0.1 Torr. – **IR**: $\tilde{\nu}$ = 3059w, 3031w, 2973m, 2937w, 2882w, 1549s (NO$_2$), 1446m, 1374m, 764m, 699s. – **^{1}H-NMR** (300 MHz): δ = 0.74 (t, *J*(3-H) = 7.39, 3 H, 4-H), 1.52 (s, 3 H, CH$_3$), 1.67-1.80 & 1.89-2.02 (2 m, 2 H, 3-H), 4.50-4.62 (m, 2 H, 1-H), 7.22-7.44 (m, 5 H, arom. H). – **^{13}C-NMR** (75 MHz): δ = 8.2 (C-4), 21.9 (CH$_3$), 32.3 (C-3), 42.6 (C-2), 86.1 (C-1), 126.2 (C-2', C-6'), 126.9 (C-4'), 128.6 (C-3', C-5'), 142.0 (C-1'). – **MS**: *m/z* = 193 (10) [M$^+$], 147 (11) [M$^+$ – NO$_2$], 133 (12), 118 (71), 117 (66), 105 (53), 91 (100).– Anal. calcd. for $C_{11}H_{15}NO_2$ (193.25): C 68.37, H 7.82, N 7.25; found: C 68.13, H 7.69, N 7.28.

2-(3-Thienyl)-nitrobutane (**10**): a) Following GP-I, a soln. of 300 mg (1.93 mmol) 2-(3-thienyl)-nitroethene and 1.4 ml (2.8 mmol) of Et$_2$Zn soln. with 1.1 ml (2.31 mmol) of MgBr$_2$ soln. gave 305 mg (85%) of *rac*-**10** (^{1}H-NMR purity *ca.* 97%) as slightly yellow liquid. – b) Following GP-II, 5.1 ml (10.2 mmol) of Et$_2$Zn soln. and a soln. of 416 mg (2.68 mmol) of the nitroolefin in 25 ml toluene with 1.656 g (3.22 mmol) **1**, 400 mg MS, 30 ml of toluene and 10 ml (3.22 mmol) of TiCl$_2$(O^{i}Pr)$_2$ soln. gave after FC 411 mg (90%) of **10** as slightly yellow liquid [(*S*)/(*R*) = 88:12; FS-Lipodex E; 2 bar; 100°C + 0.5°C/min; R$_t$: 79.2 (*S*), 79.6 (*R*); moderate peak separation] [(*S*)/(*R*) = 89:11; Chiralcel OD; hexane/^{i}PrOH = 99:1; R$_t$: 37.3 (*R*), 41.3 (*S*); moderate peak separation]. – **IR**: $\tilde{\nu}$ = 3105w, 2967s, 2933m, 2876m, 1556s (NO$_2$), 1462m, 1431m, 1380s, 780s, 663s. – **^{1}H-NMR** (300 MHz): δ = 0.87 (t, *J*(3-H) = 7.4, 3 H, 4-H), 1.59-1.93 (m, 2 H, 3-H), 3.48-3.59 (m, 1 H, 2-H), 4.53 (J_{AB} = 12.1, J_{AX} = 7.9, J_{BX} = 7.4, 2 H, 1-H), 6.96 (dd, *J*(5'-H) = 5.0, *J*(2'-H) = 1.3, 1 H, 4'-H), 7.06 (ddd, *J*(5'-H) = 3.0, *J*(4'-H) = 1.3, *J* = 0.3, 1 H, 2'-H), 7.32 (dd, *J*(4'-H) = 5.0, *J*(2'-H) = 2.9, 1 H, 5'-H). – **^{13}C-NMR** (75 MHz): δ = 11.5 (C-4), 26.2 (C-3), 41.3 (C-2), 80.5 (C-1), 122.0, 126.0, 126.5 (C-2', C-4', C-5'), 140.1 (C-3'). – **MS**: *m/z* = 185 (9) [M$^+$], 138 (86) [M$^+$ – HNO$_2$], 123 (23), 110 (49), 109 (11), 97 (100). – Anal. calcd. for $C_8H_{11}NO_2S$ (185.25): C 51.87, H 5.99, N 7.56, S 17.27; found: C 51.72, H 5.70, N 7.60, S 17.22.

2-(2-Furyl)-nitrobutane (11): a) Following GP-I, a soln. of 1.00 g (7.19 mmol) 2-(2-furyl)-nitroethene and 5.0 ml (10 mmol) of Et_2Zn soln. with 4.1 ml (8.6 mmol) of $MgBr_2$ soln. gave after 2xFC 790 mg (65 %) of *rac*-**11** (^{1}H-NMR purity *ca.* 95%) as slightly yellow liquid. – b) Following GP-II, 51 ml (102 mmol) of Et_2Zn soln. and a soln. of 3.73 g (26.8 mmol) of the nitroolefin in 60 ml toluene with 16.56 g (32.2 mmol) **1**, 1.0 g MS, 260 ml of toluene and 100 ml (32.2 mmol) of $TiCl_2(O^iPr)_2$ soln. gave after 2xFC 3.99 g (88%) of **11** as slightly yellow liquid [(*S*)/(*R*) = 86.5:13.5 (cf. **21**, determined with the product of hydrogenation)]. – **IR**: $\tilde{\nu}$ = 3120w, 2970m, 2936w, 2879w, 1556s (NO_2), 1379m, 1150m, 1010m, 738m. – **^{1}H-NMR** (300 MHz): δ = 0.91 (t, *J*(3-H) = 7.4, 3 H, 4-H), 1.60-1.85 (m, 2 H, 3-H), 3.47-3.57 (m, 1 H, 2-H), 4.58 (J_{AB} = 12.3, J_{AX} = 7.0, J_{BX} = 7.9, 2 H, 1-H), 6.14 (dd, *J*(4'-H) = 3.2, *J*(5'-H) = 0.6, 1 H, 3'-H), 6.30 (dd, *J*(3'-H) = 3.2, *J*(5'-H) = 1.9, 1 H, 4'-H), 7.35 (dd, *J*(4'-H) = 1.9, *J*(3'-H) = 0.8, 1 H, 5'-H). – **^{13}C-NMR** (75 MHz): δ = 11.3 (C-4), 24.2 (C-3), 39.5 (C-2), 78.3 (C-1), 107.3, 110.3 (C-3', C-4'), 142.2 (C-5'), 152.6 (C-2'). – **MS**: *m/z* = 169 (3) [M^+], 122 (100) [$M^+ - HNO_2$], 107 (20), 94 (31), 81 (42). – Anal. calcd. for $C_8H_{11}NO_3$ (169.18): C 56.80, H 6.55, N 8.28; found: C 56.84, H 6.40, N 8.23.

2-(2-Thienyl)-nitrobutane (12): a) Following GP-I, a soln. of 1.50 g (9.67 mmol) 2-(2-thienyl)-nitroethene and 7.0 ml (14 mmol) of Et_2Zn soln. with 5.5 ml (11.6 mmol) of $MgBr_2$ soln. gave after distillation, FC, and again distillation 1.33 g (74 %) of *rac*-**12** as slightly yellow liquid. – b) Following GP-II, 2.55 ml (5.1 mmol) of Et_2Zn soln. and a soln. of 208 mg (1.34 mmol) of the nitroolefin in 20 ml toluene with 828 mg (1.61 mmol) **1**, 300 mg MS, 30 ml of toluene and 5 ml (1.61 mmol) of $TiCl_2(O^iPr)_2$ soln. gave after FC and distillation 203 mg (83%) of **12** as slightly yellow liquid [(*S*)/(*R*) = 90:10; FS-Lipodex E; 1.5 bar; 100°C + 0.5°C/min; R_t: 73.7 (*S*), 75.2 (*R*)]. – **B.p.**: 75°C/0.2 Torr. – **IR**: $\tilde{\nu}$ = 3110w, 2967m, 2933m, 2876w, 1551s (NO_2), 1429m, 1381s, 1202w, 851m, 703s. – **^{1}H-NMR** (300 MHz): δ = 0.93 (t, *J*(3-H) = 7.4, 3 H, 4-H), 1.6-1.9 (m, 2 H, 3-H), 3.64-3.77 (m, 1 H, 2-H), 4.56 (J_{AB} = 12.2, J_{AX} = 7.8, J_{BX} = 7.4, 2 H, 1-H), 6.88 (m, 1 H, thienylH), 6.95 (m, 1 H, thienylH), 7.22 (m, 1 H, thienylH). – **^{13}C-NMR** (75 MHz): δ = 11.5 (C-4), 27.4 (C-3), 41.3 (C-2), 81.0 (C-1), 124.4, 125.5, 127.0 (C-3', C-4', C-5'), 142.4 (C-2'). – **MS**: *m/z* = 185 (3) [M^+], 138 (100) [$M^+ - HNO_2$], 123 (25), 110 (36), 109 (17), 97 (57). – Anal. calcd. for $C_8H_{11}NO_2S$ (185.25): C 51.87, H 5.99, N 7.56; found: C 51.88, H 6.02, N 7.34.

2-Aryl-alkylamines

2-Phenyl-butylamine (13): Following GP-III, 1.00 g (5.58 mmol) of **3** (er 80:20) was hydrogenated for 4 d to yield 612 mg (73 %) of **13** as slightly yellow liquid after distillation (er 81:19; eluent for HPLC hexane/^{i}PrOH 99:1). According to the sign of optical rotation, **13** was assigned (*S*)-configuration[33]. – $[\alpha]_D^{r.t.}$ = +5,6 (c = 1.2, Et_2O), corresponding to er 78:22; ref.[33]: $[\alpha]_D^{r.t.}$ = +10 (*c* = 1.2, Et_2O). – **Bp.**: 70-100°C/0.2 Torr. – **IR**: $\tilde{\nu}$ = 3373m, 3287m, 3061m, 3027s, 2959s, 2924s, 2873s, 1602m, 1493s, 1452s, 1378m, 839m, 758s, 701s. – **^{1}H-NMR** (300 MHz): δ = 0.80 (t, *J*(3-H) = 7.4, 3 H, 4-H), 1.11 (s, 2 H, NH_2) 1.47-1.78 (dm, 2 H, 3-H), 2.41-2.52 (m, 1 H, 2-H), 2.78-2.94 (J_{AB} = 12.6, J_{AX} = 8.7, J_{BX} = 5.5, 2 H, 1-H), 7.12-7.22 (m, 3 H, arom. H), 7.22-7.33 (m, 2 H, arom. H). – **^{13}C-NMR** (75 MHz): δ = 12.1 (C-4), 26.5 (C-3), 47.9 (C-1), 51.7 (C-2), 126.3 (C-4'), 128.0, 128.5 (C-2', C-3', C-5', C-6'), 143.5 (C-1'). – **MS**: *m/z* = 149 (44) [M^+], 132 (20), 118 (20), 91 (47).

Table 5: ***Determination of the Enantiomer Ratios (er) of the Amines 13 - 18, 20 and 21 by Analysis of the*** Mosher *MTPA Amides*. For details see general procedure V. The ^{19}F signals were used for NMR analysis. In the case of the amines **13** and **15** samples from non-optimized runs have been used for these experiments (compare the er of **3** and **5** in *Table 1*).

	^{19}F-NMR analysis			**HPLC analysis**			
No.	Chemical Shift of the *Mosher* amides δ [ppm]	er of the (*S*)-MTPA-amides[a]	er of the (*R*)-MTPA-amides[b]	R$_t$ of the (*S*)-MTPA-amides	er of the (*S*)-MTPA-amides	R$_t$ of the (*R*)-MTPA-amides	er of the (*R*)-MTPA-amides
13	-69.50 (*u*); -69.55 (*l*)	21.5:78.5	80.5:19.5	45.2; 51.3	78.5:21.5	51.3; 57.8	80.5:19.5
14	-69.48 (*u*); -69.54 (*l*)	12:88	87:13				
15	-69.46 (*u*); -69.49 (*l*)			48.4; 57.8	78:22	34.8; 40.9	21:79[c]
16	-69.38 (*u*); -69.50 (*l*)	5:95	95:5				
17	-69.48 (*u*); -69.54 (*l*)	<2:98	>98.:2				
18	-69.50 (*u*); -69.55 (*l*)	11.5:88.5	87.5:12.5				
20				32.3; 42.1	87.5:12.5	20.6; 29.0	87.5:12.5
21	-69.40 (*u*); -69.70 (*l*)	13.5:86.5	86.5:13.5				

a) Configuration of excess diastereoisomer (*l*); b) Configuration of excess diastereoisomer (*u*); c) See footnote[35].

2-(3-Methoxyphenyl)-butylamine (14): Following GP-III, 246 mg (1.18 mmol) of **4** (er 87.5:12.5) were hydrogenated. The crude amine was extracted with 2 M HCl instead of 1 N H_2SO_4 to yield 612 mg (76 %) of **14** as colourless liquid after FC with CH_2Cl_2/MeOH/Et_3N 90:10:1 as eluent (er = 88:12). – Racemic **14** has been reported by *von Angerer et al.*, with ^{1}H-NMR data[56]. – **IR**: $\tilde{\nu}$ = 3378w, 2958s, 2931s, 2873m, 2835m, 1600s, 1583s, 1486s, 1453s, 1437m, 1260s, 1159m, 1047s, 779s, 701s. – **^{1}H-NMR** (400 MHz): δ = 0.82 (t, *J*(3-H) = 7.39, 3 H, 4-H), 1.24 (s, 2 H, NH_2), 1.48-1.60 and 1.63-1.74 (dm, 2 H, 3-H), 2.42-2.51 (m, 1 H, 2-H), 2.86 (J_{AB} = 12.6, J_{AX} = 8.9, J_{BX} = 5.3, 2 H, 1-H), 3.80 (s, 3 H, OCH_3), 6.72-6.79 (m, 3 H, arom. H), 7.21-7.27 (m, 1 H, arom. H). – **^{13}C-NMR** (100 MHz): δ = 12.1 (C-4), 26.8 (C-3), 47.8 (C-1), 51.7 (C-2), 55.1 (OCH_3), 111.3, 114.0 (C-2', C-4'), 120.4 (C-6'), 129.4 (C-5'), 145.3 (C-1'), 159.7 (C-3'). – **MS**: *m*/*z* = 179 (15) [M^+], 150 (100), 135 (29), 134 (13), 122 (13), 121 (38), 91 (24).

2-(4-Methoxyphenyl)-butylamine (15): a) Following GP-III, 1.00 g (4.78 mmol) of **5** (er 79:21) gave 783 mg (91 %) of **15** as colourless liquid. – b) Following GP-IV, 1.046 g (5 mmol) of **5** gave 731 mg (80 %) of **15** which was distilled (er 78:22; solvent mixture used for HPLC analysis hexane/^{i}PrOH 98:2). – **IR**: $\tilde{\nu}$ = 3374w, 3298w, 2995w, 2958s, 2929m, 2872m, 2834m, 1611m, 1512s (NO_2), 1463m, 1248s, 1178m, 1036m, 828s. – **^{1}H-NMR** (300 MHz): δ = 0.80 (t, *J*(3-H) = 7.4, 3 H, 4-H), 1.39 (s, 2 H, NH_2), 1.43-1.58 and 1.60-1.75 (dm, 2 H, 3-H), 2.39-2.49 (m, 1 H, 2-H), 2.78 and 2.91 (J_{AB} = 12.6, J_{AX} = 8.9, J_{BX} = 5.3, 2 H, 1-H), 3.79 (s, 3 H, OCH_3), 6.83-6.89 (m, 2 H, 3'-H, 5'-H), 7.06-7.28 (m, 2 H, 2'-H, 6'-H). – **^{13}C-NMR** (75 MHz): δ = 12.1 (C-4), 26.9 (C-3), 47.9 (C-1), 50.7 (C-2), 55.2 (OCH_3), 114.0 (C-3', C-5'), 128.9 (C-2', C-6'), 135.5 (C-1'), 158.2 (C-4'). – **MS**: *m*/*z* = 179 (4) [M^+], 162 (16), 150 (59), 149 (100), 134 (14), 121 (84), 91 (20).

2-(2,4,6-Trimethylphenyl)-butylamine (16): Following GP-III, 636 mg (2.87 mmol) of **6** (er 95:5) gave crude **15** (562 mg, quantitative yield, without extraction). FC of 470 mg of this material with 400 ml of CH_2Cl_2/MeOH/Et_3N 75:25:1 and then with CH_2Cl_2/MeOH/Et_3N 90:10:1 as eluants gave 310 mg (66 %) of **16** as colourless liquid (analytically pure except for incorrect elemental analysis) (er 95:5). – **IR**: $\tilde{\nu}$ = 2962s, 2871s, 1611m, 1477m, 1457m, 1376m, 1024w, 850s. – ^{1}**H-NMR** (500 MHz): δ = 0.84 (t, J(3-H) = 7.44, 3 H, 4-H), 1.76 (m, 2 H, 3-H), 2.23 (s, 3 H, CH_3), 2.32 and 2.33 (2 s, 6 H, 2 CH_3), 2.41 (s, 2 H, NH_2), 3.03 (J_{AB} = 12.6, J_{AX} = 6.8, J_{BX} = 8.8, 2 H, 1-H), 3.16 (m, 1 H, 2-H), 6.78, 6.82 (2 s, 2 H, 3'-H, 5'-H). – ^{13}**C-NMR** (126 MHz): δ = 12.8 (C-4), 20.6 (CH_3), 21.3 (CH_3), 22.3 (CH_3), 24.8 (C-3), 45.2 (C-1), 45.7 (C-2), 129.3, 131.3 (C-3', C-5'), 135.4, 135.5, 136.1, 138.2 (C-1', C-2', C-4', C-6'). – **MS**: m/z = 191 (19) [M^+], 162 (45), 161 (51), 133 (100), 119 (19), 91 (14).

2-Phenyl-hexylamine (17): Following GP-IV, 486 mg (2.34 mmol) of **7** (er 99.4:0.6) gave 296 mg (71 %) of slightly impure **17** as colourless liquid (not distilled) (er ≥ 98:2). – **B.p.**: 50°C/0.02 Torr. – **IR**: $\tilde{\nu}$ = 3376w, 3284w, 3025m, 2957s, 2926s, 2857s, 1601m, 1491m, 1458m, 1452m, 1378m, 800s, 760m, 700s. – ^{1}**H-NMR** (300 MHz): δ = 0.83 (t, J(5-H) = 7.1, 3 H, 6-H), 1.02-1.39 (m, 4 H, 4-H, 5-H), 1.47-1.70 (s, m, 4 H, 3-H, NH_2), 2.52-2.69 (m, 1 H, 2-H), 2.81 and 2.92 (J_{AB} = 12.5, J_{AX} = 8.8, J_{BX} = 5.1, 2 H, 1-H), 7.14-7.61 (m, 5 H, arom. H). – ^{13}**C-NMR** (75 MHz): δ = 15.0 (C-6), 23.8 (C-5), 30.7 (C-4), 34.6 (C-3), 49.1 (C-1), 50.6 (C-2), 127.4 (C-4'), 129.0, 129.6 (C-2', C-3', C-5', C-6'), 144.7 (C-1'). – **MS**: m/z = 177 (4) [M^+], 146 (49), 117 (18), 105 (18), 104 (26), 103 (15), 91 (100), 30 (53).

Table 6. Optical Rotation of the 2-Aryl-nitroalkane and of Some 2-Aryl-alkylamine Samples. In most cases samples from non-optimized *Michael* additions were used for the measurements. Nitroalkanes in $CHCl_3$, amines in Et_2O.

No.	ee [%]	determined by	$[\alpha]_D^{r.t.}$	c
3	82	HPLC	-32.9 a)	1.10
4	75	HPLC	-22.3	0.99
5	56	HPLC	-25.0	0.96
6	90	HPLC	-48.2	1.00
7	98.7	HPLC	-24.4	0.99
8	80	HPLC	-11.1	1.00
9	68	FS-Lipodex E	-26.0	1.00
10	75	HPLC	-27.8	1.00
11	73	^{19}F-NMR (cf. **21**)	-21.6	1.00
12	80	FS-Lipodex E	-40.2	1.01
13	56	HPLC, ^{19}F-NMR	+ 5.6 b)	1.20
17	≥ 96	^{19}F-NMR	+15.3	1.12
18	76	^{19}F-NMR	+14.5	0.95
20	75	HPLC	+10.9	1.02

a) Ref.[30]: $[\alpha]_D^{r.t.}$ = +38.2 (c = 1.1, $CHCl_3$); ee 97%, (*R*); b) Ref.[33]: $[\alpha]_D^{r.t.}$ = +10 (c = 1.2, Et_2O), (*S*).

2-Phenyl-decylamine (18): Following GP-IV, 830 mg (3.15 mmol) of **8** (er 88:12) gave 577 mg (78 %) of **18** as colourless liquid (er 88.5:11.5). – **B.p**: 80°C/2·10^{-4} Torr. – **IR**: $\tilde{\nu}$ = 3376w, 3027w, 2924s, 2854s, 1603w, 1494w, 1452m, 1378w, 759m, 700s. – ^{1}**H-NMR** (300 MHz): δ = 0.86 (t, J(9-H) = 6.8, 3 H, 10-H), 1.01 (br, 2 H, NH_2), 1.21 (br, 12 H, 4-H to 9-H), 1.50-1.70 (m, 2 H, 3-H), 2.51-2.61 (m, 1 H, 2-H), 2.82 and 2.91 (J_{AB} = 12.6, J_{AX} = 8.6, J_{BX} = 5.5, 2 H, 1-H), 7.15-7.35 (m, 5 H, arom. H). – ^{13}**C-NMR** (75 MHz): δ = 14.1 (C-10), 22.7 (C-9), 27.5 (C-4), 29.3, 29.5, 29.7, 31.9, 33.9 (C-3, C-5 to C-8), 48.3 (C-1), 49.9 (C-2), 126.3 (C-4'), 128.0, 128.5 (C-2', C-3', C-5', C-6'), 143.9(C-1'). – **MS**: m/z = 233 (8) [M^+], 216 (11), 202 (100), 117 (29), 104 (62), 91 (97). – Anal. calcd. for $C_{16}H_{27}N$ (233.40): C 82.34, H 11.66, N 6.00; found: C 82.47, H 11.71, N 6.09.

2-Methyl-2-phenyl-butylamine (19): Following GP-IV, 450 mg (2.33 mmol) of **9** (er 84:16) gave 276 mg (73 %) of **19** (^{1}H-NMR purity 95 %) as colourless liquid **b.p.**: 70°C/0.08 Torr. – **IR**: $\tilde{\nu}$ =

3386w, 3300w, 3087w, 3057w, 3023w, 2965s, 2922s, 2878m, 1601w, 1497m, 1458m, 1379m, 759s, 700s. – **^{1}H-NMR** (300 MHz): δ = 0.70 (t, J(3-H) = 7.46, 3 H, 4-H), 0.85 (s, 2 H, NH_2), 1.29 (s, 3 H, CH_3), 1.52 and 1.77 (dm, 2 H, 3-H), 2.68 and 2.93 (dd, J_{AB} = 13.1, 2 H, 1-H), 7.15-7.21 (m, 1 H. arom. H), 7.25-7.36 (m, 4 H, arom. H). – **^{13}C-NMR** (75 MHz): δ = 8.4 (C-4), 21.3 (CH_3), 32.6 (C-3), 43.4 (C-2), 54.0 (C-1), 125.7, 126.8, 128.2 (C-2' to C-6'), 145.5 (C-1'). – **MS**: m/z = 163 (3) [M^+], 134 (28), 133 (63), 132 (100), 118 (25), 117 (60), 115 (39), 105 (87), 91 (51).

2-(3-Thienyl)-butylamine (20): Following GP-III, 2.41 g (13.01 mmol) of **10** (er 87.5:12.5) gave after FC (18x3 cm) with CH_2Cl_2/MeOH/Et_3N 90:10:1 as eluant and FC (18x3 cm) with 300 ml CH_2Cl_2/MeOH/Et_3N 95:5:1 and then with CH_2Cl_2/MeOH/Et_3N 90:10:1 (250-600 ml) as eluants and distillation 464 mg (23 %) of **20** as colourless liquid (er = 87.5:12.5; solvent mixture for HPLC hexane/^{i}PrOH 98:2).– **B.p.**: 100°C/0.1 Torr. – **IR**: $\tilde{\nu}$ = 3368w, 3300w, 3092w, 2960s, 2924s, 2872m, 1583s, 1462m, 846m, 775s, 656m. – **^{1}H-NMR**: δ = 0.84 (t, J(3-H) = 7.4, 3 H, 4-H), 1.13 (s, 2 H, NH_2), 1.46-1.76 (dm, 2 H, 3-H), 2.59-2.70 (m, 1 H, 2-H), 2.80 and 2.91 (J_{AB} = 12.5, J_{AX} = 8.4, J_{BX} = 5.2, 2 H, 1-H), 6.94 (m, J(2'-H) = 1.3, 1 H, 4'-H), 6.99 (ddd, J(5'-H) = 3.0, J(4'-H) = 1.3, J = 0.5, 1 H, 2'-H), 7.29 (ddd, J(4'-H) = 5.0, J(2'-H) = 2.9, J = 0.3, 1 H, 5'-H). – **^{13}C-NMR**: δ = 12.0 (C-4), 26.5 (C-3), 46.9 (C-2), 47.5 (C-1), 120.8 (C-2'), 125.6, 126.6 (C-5', C-4'), 144.6 (C-3'). – **MS**: m/z = 155 (4) [M^+], 126 (100), 111 (26), 97 (47), 30 (35). – Anal. calcd. for $C_8H_{13}NS$ (155.26): C 61.89, H 8.44, N 9.02; found: C 61.94, H 8.22, N 8.97.

2-(2-Furyl)-butylamine (21): Following GP-IV, 1.00 g (5.91 mmol) of **11** gave after two FC and distillation 19 mg (2 %) of **21** as colourless liquid, which quickly turned yellow (er = 86.5:13.5). – **B.p.**: 80°C/0.2 Torr. – **IR**: $\tilde{\nu}$ = 3371m, 2963s, 1593m, 1505m, 1458m, 1150m, 1008, 731m. – **^{1}H-NMR** (300 MHz): δ = 0.87 (t, J(3-H) = 7.4, 3 H, 4-H), 1.55-1.77 (m, 2 H, 3-H), 2.75-3.15 (m, br, 3 H, 2-H, 1-H), 4.88 (s, br, 2 H, NH_2), 6.15 (d, J(4'-H) = 3.1, 1 H, 3'-H), 6.31 (dd, J(3'-H) = 3.1, J(5'-H) = 1.9, 1 H, 4'-H), 7.36 (d, J(4'-H) = 1.1, 1 H, 5'-H). – **^{13}C-NMR** (126 MHz): δ = 11.6 (C-4), 24.4 (C-3), 42.1 (br), 44.0 (br) (C-1, C-2), 107.0, 110.0 (C-3', C-4'), 141.8 (C-5'), 155.0 (C-2'). – **MS**: m/z = 139 (0.25) [M^+], 109 (2), 94 (4), 81 (14), 30 (100).

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27. Under the standard conditions (*Scheme 2*), the aliphatic nitroolefin 3,3-dimethyl-1-nitrobutene and Et_2Zn gave a 13% yield of adduct (er 64:36).
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35. We are well aware of the possible pitfalls of this reasoning (which was also used by *Ohta et al.* for their configurational assignment[30]): When we analyzed the amides obtained from **13**, **15**, and **20** and *Mosher* (*R*) or (*S*) acid chloride on the Chiralcel OD HPLC column the major and minor diastereoisomers from 2-(4-methoxy-phenyl)-butylamine (**15**) and (*R*)-MTPACl showed a reversed order of elution as compared to that observed with the other 5 diastereoisomers (cf. *Table 5*)! The use of a chiral column for the separation of diastereoisomers is, of course, not necessary; the Chiralcel OD HPLC-column was used for practical purpose.
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(*Received in Germany* 24 *November* 1994; *accepted* 9 *December* 1994)