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Enantioselective Allylic Amination with Chiral (Phosphino-oxazoline)Pd Catalysts

Peter von Matt, Olivier Loiseleur, Guido Koch, and Andreas Pfaltz*#

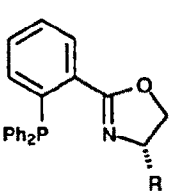
Institut für Organische Chemie, Universität Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

Claudia Lefeber, Thomas Feucht, and Günter Helmchen*#

Institut für Organische Chemie der Universität, Im Neuenheimer Feld 270, D-69120 Heidelberg, Germany

Abstract: *Chiral (phosphinophenyl-oxazoline)palladium complexes have been studied as enantioselective catalysts for allylic amination using benzylamine or the sodium salts of p-toluenesulfonamide, benzoylhydrazine, and $(Boc)_2NH$ as nucleophiles. In the reactions with 1,3-diphenyl- and 1,3-dialkyl-2-propenyl acetates, carbonates, or phosphates, moderate to high enantiomeric excesses of up to 97% have been obtained.*

Independent studies at the Universities of Basel,[1] Heidelberg,[2] and Loughborough[3] have shown that palladium complexes with chiral phosphino-oxazoline ligands are very effective catalysts for enantioselective allylic alkylation.[4] In the reaction of racemic 1,3-diphenyl-2-propenyl acetate **2** (R = Ph) with dimethyl malonate, phosphino-oxazolines of type **1**[5] induce enantiomeric excesses as high as 99% (Scheme 1). Similar levels of enantioselectivity are obtained with acetylacetonate and diethyl acetamidomalonate as nucleophiles.[1] The more demanding 1,3-dialkyl-substituted substrates **2** (R = alkyl) afford moderate to high enantiomeric excesses with these catalysts.[1] Here we report an extension of our studies to enantioselective allylic amination reactions with various nitrogen nucleophiles.



1a R = Ph
1b R = *t*-Bu
1c R = *i*-Pr
1d R = Benzyl
1e R = (3-Indolyl)methyl

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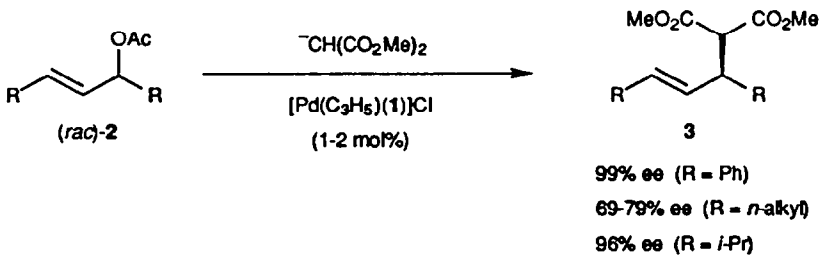
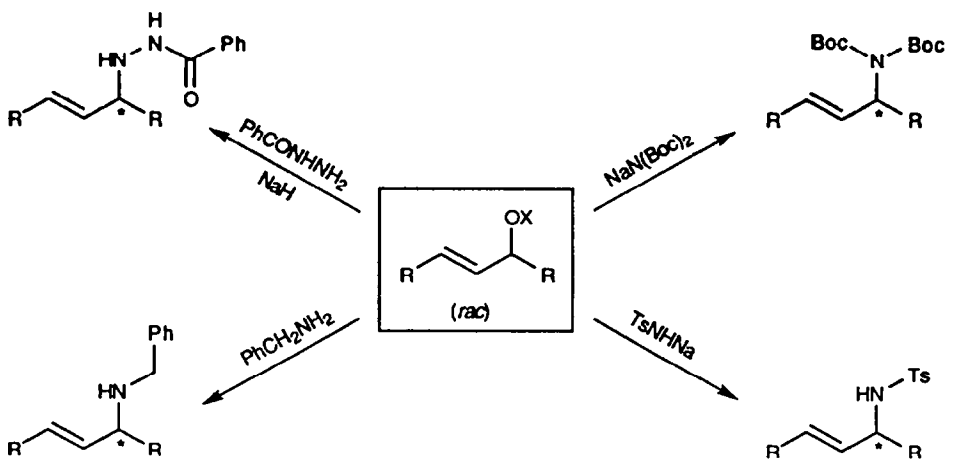
Scheme 1



Palladium-catalyzed allylic amination is a well-established process in organic synthesis.[6] Various nitrogen compounds including primary and secondary amines, sodium azide, phthalimide, sulfonamides, and di-*tert*-butyl iminodicarboxylate have been employed as nucleophiles.[7] The resulting allylic amines or related derivatives are useful compounds which can be converted to a wide range of products, e.g. by functionalization, cleavage, or reduction of the C=C bond.[8] There are several examples of enantioselective allylic aminations catalyzed by chiral diphosphine-palladium complexes.[9] The most promising results have been reported by Hayashi, Ito and coworkers[9a] for reactions of 1,3-diphenyl- and 1,3-dialkyl-2-propenyl carbonates and phosphinates with benzylamine, and by Trost *et al.*[9d] using substrates derived from *meso*-2-alkene-1,4-diols.

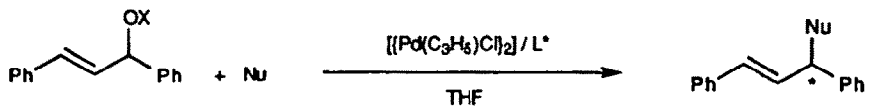
Scheme 2



The *N*-nucleophiles used in this study are shown in Scheme 2. Reactions of these nucleophiles were found to be slower than analogous allylic alkylations with dimethyl malonate or related stabilized carbanions. In general, heating to 40-60 °C and/or long reaction times proved to be necessary for achieving satisfactory yields. As for the corresponding reactions of *C*-nucleophiles,[1] the best results were obtained with 1,3-diphenyl-2-

propenyl acetate and carbonate as substrates (Table 1). Under optimized conditions, benzylamine and the sodium salts of *p*-toluenesulfonamide and benzoylhydrazine all reacted to give the expected products with excellent enantioselectivity and in essentially quantitative yield. The resulting *N*-allyl-*p*-toluenesulfonamide could be readily obtained in enantiomerically pure form by recrystallization from chloroform/hexane (99.7% ee after one recrystallization). The sodium salt of di-*tert*-butyl iminodicarboxylate also gave high yields but somewhat lower enantiomeric excesses. The absolute configuration of the benzylamine-derived product (-)-**5** (Nu = $NHCH_2Ph$) is known to be (*R*) from the sign of its optical rotation.[9a] The absolute configuration of the other products has not been determined experimentally but is assumed to be (*R*) as well, based on the mechanism of these reactions.[4]

Table 1. Enantioselective Allylic Amination of 1,3-Diphenyl-Substituted Substrates (*rac*)-**4**

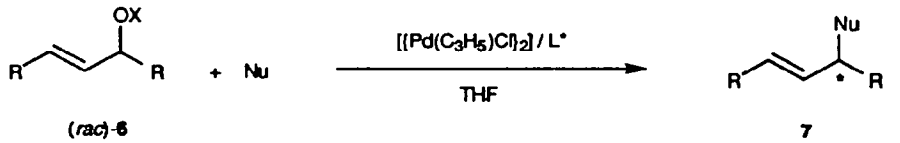


(*rac*)-**4** **5**

Nucleophile	Ligand L* (mol%)	[Pd][a] [mol%]	X	Temp. [°C]	Reaction Time [h]	yield [%]	ee [%]
$TsNH^-Na^+$	**1b** (2.5)	2.0	Ac	50	48	96	97[b]
	1a (2.5)	2.0	Ac	50	24	97	95[b]
$PhCONHNH_2$/NaH	**1b** (2.5)	2.0	Ac	50	96	95	97[b]
	1a (2.5)	2.0	Ac	50	48	63	95[b]
$(Boc)_2N^-Na^+$	**1b** (2.5)	2.0	Ac	50	96	90	67[c]
	1a (2.5)	2.0	Ac	50	96	98	86[c]
$PhCH_2NH_2$	**1b** (2.5)	2.0	Ac	23	96	87	89[d]
	1a (2.5)	2.0	Ac	23	96	97	73[c]
	1a (3.0)	3.0[e]	CO_2Me	40	1	98	94[f]
	1b (3.0)	3.0[e]	CO_2Me	40	2	93	88[f]
	1c (3.0)	3.0[e]	CO_2Me	40	0.5	97	87[f]
	1d (3.0)	3.0[e]	CO_2Me	40	6	78	74[f]
	1e (3.0)	3.0[e]	CO_2Me	40	2.5	96	83[f]

a) 2 mol% of [Pd] corresponds to 1 mol% of $[\{(\eta^3\text{-}C_3H_5)PdCl\}_2]$. b) Determined by HPLC (Chiralcel OJ). c) HPLC (Chiralcel OD). d) Reaction in DME; HPLC (Chiralcel OD). e) 1.5 mol% of $[Pd_2(dba)_3\cdot CHCl_3]$. f) HPLC of the corresponding (*R*)-2-methoxy-2-phenylacetamides.

Table 2. Enantioselective Allylic Amination of 1,3-Dialkyl-Substituted Substrates (*rac*)-**6**



Nucleophile	Ligand L* (mol%)	[Pd][a] [mol%]	R	X	Temp. [°C]	Reaction Time [h]	Yield [%]	ee [%]
$TsNH^-Na^+$	**1b** (2.5)	2.0	Me	Ac	23	91	61	66[b]
	1b (2.5)	2.0	Pr	Ac	50	90	90	66[c]
	1b (2.5)	2.0	*i*-Pr	CO_2Et	60	112	39	88[c]
	1b (2.5)	2.0	*i*-Pr	$PO(OEt)_2$	23	230	57	90[c]
	1b (2.5)	2.0	*i*-Pr	$PO(OEt)_2$	50	72	55	88[c]
$PhCONHNH_2$/ NaH	**1b** (2.5)	2.0	Me	Ac	23	91	52	73[d]
	1b (2.5)	2.0	Me	Ac	50	59	52	66[d]
	1b (2.5)	2.0	Pr	Ac	50	90	56	72[d]
	1b (2.5)	2.0	*i*-Pr	CO_2Et	60	112	17	84[e]
	1b (2.5)	2.0	*i*-Pr	$PO(OEt)_2$	23	230	23	92[e]
	1b (2.5)	2.0	*i*-Pr	$PO(OEt)_2$	50	112	20	86[e]
$(Boc)_2N^-Na^+$	**1b** (2.5)	2.0	Me	Ac	23	91	7	64[f]
	1b (2.5)	2.0	Me	Ac	50	59	28	12[f]
	1a (2.5)	2.0	Me	Ac	23	91	44	75[f]
	1b (2.5)	2.0	Pr	Ac	50	96	60	59[g]
	1a (2.5)	2.0	Pr	Ac	50	96	66	54[g]
	1b (2.5)	2.0	*i*-Pr	$PO(OEt)_2$	23	194	29	97[g]
	1b (2.5)	2.0	*i*-Pr	$PO(OEt)_2$	50	70	23	95[g]
	1a (2.5)	2.0	*i*-Pr	$PO(OEt)_2$	50	70	27	89[g]
$PhCH_2NH_2$	**1a** (10)	3.0[h]	Me	CO_2Me	40	15	93	30[i]
	1b (10)	3.0[h]	Me	CO_2Me	40	96	87	57[i]
	1c (10)	3.0[h]	Me	CO_2Me	40	35	84	51[i]
	1d (10)	3.0[h]	Me	CO_2Me	40	34	82	35[i]
	1e (10)	3.0[h]	Me	CO_2Me	40	8	91	50[i]
	1e (10)	3.0[h]	Me	CO_2Me	25	36	85	50[i]

a) 2 mol% of [Pd] corresponds to 1 mol% of $[\{(\eta^3\text{-}C_3H_5)PdCl\}_2]$. b) Determined by HPLC (Chiralcel OJ) after derivatization with cinnamoyl chloride. c) HPLC (Chiralcel OD). d) HPLC (Chiralcel OJ). e) Derivatization with cinnamoyl chloride, HPLC (Chiralcel OD). f) Cleavage of one Boc group with TFA, GC (Chiraldex γ-CD-TFA). g) Cleavage of one Boc group with TFA, GC (MSP β-CD-*tert*-butyl-dimethylsilylated). h) 1.5 mol% of $[Pd_2(dba)_3\cdot CHCl_3]$. i) Derivatization with 1-naphthoyl chloride, HPLC (Pirkle CSP 2).

Analogous 1,3-di-*n*-alkyl-substituted substrates **6** (R = Me, *n*-Pr) undergo allylic substitution with moderate enantioselectivities in the range of 50-75% ee (Table 2). In the reactions of the 1,3-dimethylallyl derivatives **6** (R = Me), ca. 5% of the (Z)-isomers are formed according to ^{1}H- and ^{13}C-NMR analyses. In all other cases listed in Tables 1 and 2, the (Z)-products could not be detected. As expected, the low reactivity of the 1,3-diisopropyl-substituted allylic substrates proved to be a problem. Under the usual conditions in various solvents, the acetate **6** (R = *i*-Pr, X = OAc) did not react with the nucleophiles listed in Table 2. However, acceptable yields and good selectivities of up to 90% ee could be obtained with the corresponding diethyl phosphate and sodium *p*-toluenesulfonamide as nucleophile. The sodium salts of benzoylhydrazine and di-*tert*-butyl iminodicarboxylate also gave high enantioselectivities with this substrate, but the yields were below 30%.

For most substrate/nucleophile combinations, the *tert*-butyl-oxazoline derivative **1b** was found to be the most effective ligand. With 1,3-dimethylallyl methyl carbonate and benzylamine, the highest reaction rate was observed using the (3-indolyl)methyl-oxazoline **1e**. In terms of enantioselectivity, however, this ligand was less effective than the *tert*-butyl derivative **1b**.

In summary, we have demonstrated that palladium complexes derived from chiral phosphino-oxazoline ligands are efficient catalysts for allylic aminations with various nitrogen nucleophiles. The observed enantiomeric excesses are in the same range as in analogous reactions with chiral (ferrocenyl-diphosphine)-palladium catalysts reported by Hayashi *et al.*[9a] Interestingly, in the (ferrocenyl-diphosphine)palladium-catalyzed reactions, benzylamine gave higher yields and enantioselectivities than *p*-toluenesulfonamide, whereas with phosphino-oxazoline-based catalysts the best results were obtained using the sodium salt of *p*-toluene-sulfonamide as nucleophile.

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EXPERIMENTAL

General. DME (*Fluka puriss.*), THF (*Fluka puriss.*), and diethyl ether (*Scharlau*) were distilled from Na/benzophenone. Benzylamine, crotonaldehyde, (*R*)-2-methoxy-phenylacetic acid: *Fluka puriss.*; acetic anhydride, benzoylhydrazine, di-*tert*-butyl iminodicarboxylate, isopropyl bromide, and 4-toluenesulfonamide: *Fluka purum*; diethyl chlorophosphate: *Fluka pract.*; methyllithium: *Merck*, 1.6 M in Et_2O; butyllithium: *Aldrich*, 1.6 M in hexanes. (*E*)-1,3-Diphenyl-2-propenyl acetate and carbonate, (*E*)-1-propyl-2-hexenyl acetate and (*E*)-1-(1-methylethyl)-4-methyl-2-pentenyl ethyl carbonate were synthesized using literature procedures.[9a] $[\{(\eta^3\text{-}C_3H_5)PdCl\}_2]$ was synthesized according to Dent *et al.*[10] Reactions were carried out under argon using dried glassware. Flash column chromatography (FC): silica gel C 560, 0.035-0.070 mm, *Chemische Fabrik Uetikon*. TLC: silica gel 60 *Merck*, 0.25mm, F 254, staining with basic $KMnO_4$ or vanillin in H_2SO_4. Specific rotation: *Perkin-Elmer-241* polarimeter; l = 10 cm, 23 °C, concentration in g/100 mL, estimated error: ± 5%. IR ($CHCl_3$): selected bands in cm^{-1}. NMR ($CDCl_3$): δ in ppm *vs.* TMS, *J* in Hz; ^{1}H: 300 MHz, ^{13}C: 75 MHz, ^{31}P: 121 MHz, triphenyl phosphate as external reference (–18.0 ppm). MS: selected peaks; *m/z* (%); matrix for FAB-MS: 3-nitrobenzyl alcohol (NBA). High resolution mass spectra (HRMS) were recorded on a Varian MAT 711 instrument.

Substrates. *(E)-1-Methyl-2-butenyl acetate.* Crotonaldehyde (4.1 g, 58 mmol) was dissolved in 120 mL of THF under nitrogen. Over a period of 3 h, 38 mL (61 mmol) of a solution of methyllithium (1.6 M in Et_2O) were added at –78 °C. The reaction mixture was stirred at –40 °C for 1 h and cooled again to –78 °C. A

solution of Ac_2O (6.2 g, 61 mmol) in 50 mL of THF was then added. After warming to room temperature and stirring for an additional 1 h, the reaction mixture was poured onto ice-water and extracted with ether. The organic layer was washed with saturated aqueous NH_4Cl solution and dried over $MgSO_4$. The solvent was removed *in vacuo* at 0 °C. FC (5 cm x 32 cm, pentane/ether 10 : 1) and kugelrohr distillation (100 °C/30 mbar) afforded 3.9 g (52%) of (*E*)-1-methyl-2-butenyl acetate as a colorless oil. *Analytical data:* IR: 1730s, 1680w, 1450m, 1375s, 1260s, 1100s, 1045s, 1020s, 970s, 950w. ^{1}H-NMR: 1.28 (d, J = 6.4, 3 H, $H_3C(1')$); 1.69 (br d, J = 6.5, 3 H, $H_3C(4)$); 2.03 (s, 3 H, Ac); 5.26-5.78 (m, 1 H, HC(1)); 5.48 (ddq, J = 15.3, 6.8, 1.6, 1 H, HC(2)); 5.66-5.78 (m, 1 H, HC(3)). ^{13}C-NMR: 17.6/20.1/21.3 (CH_3); 71.0 (HC(1)); 128.0/130.8 (HC=CH); 170.2 (C=O). TLC: R_f = 0.39 (pentane/Et_2O 10:1).

(E)-2,6-Dimethyl-4-hepten-3-ol. To a solution of isopropylmagnesium bromide, prepared from 7.3 g (0.3 mol) of magnesium and 36.9 g (0.3 mol) of isopropylbromide in 200 mL of Et_2O, at –40 °C under nitrogen, was added dropwise a solution of 17.2 g (175 mmol) of *(E)*-4-methyl-2-pentenal[11] in 100 mL of Et_2O over 45 min. The solution was warmed to room temperature, stirred for 4 h, and refluxed for an additional 2 h. The reaction mixture was poured onto ice-water and washed with saturated cold NH_4Cl solution. The aqueous layer was extracted twice with ether. The combined ether extracts were dried over $MgSO_4$. Evaporation of the solvent followed by FC (7 cm x 45 cm; hexane/ EtOAc 6:1) gave 16.5g (66%) of 2,6-dimethyl-4-hepten-3-ol contaminated by 14% of the corresponding homoallylic alcohol, as a colorless oil. IR: 1465s, 1380m, 1365m, 1170w, 1000s, 970s, 910w, 835w. ^{1}H-NMR: 0.87 (d, J = 6.9, 3 H, $(CH_3)_2HC(2)$); 0.93 (d, J = 6.6, 3 H, $(CH_3)_2HC(2)$); 1.00 (d, J = 6.6, 6 H, $(CH_3)_2HC(6)$); 1.64-1.75 (m, 2 H, HC(2), OH); 2.29 (septet d, J = 6.6, 1.2, 1 H, HC(6)); 3.77 (br t, J = 6.6, 1 H, HC(3)); 5.40 (ddd, J = 15.5, 7.2, 1.2, 1 H, HC(4)); 5.60 (ddd, J = 15.5, 6.6, 0.8, HC(5)). ^{13}C-NMR: 18.1/18.2/22.3/22.4 (CH_3); 30.8/33.9 (HC(2,6)); 78.3 (HC(3)); 128.1/140.0 (HC=CH). Additional signals of 2,6-dimethyl-5-hepten-3-ol are observed. MS (CI, NH_3): 141(56), 125(100). TLC: R_f = 0.13 (hexane/EtOAc 6:1).

(E)-1-(1'-Methylethyl)-4-methyl-2-pentenyl diethyl phosphate. To a solution of *(E)*-2,6-dimethyl-4-hepten-3-ol (1.31g, 9.21 mol) in 90 mL of THF at –78 °C was added dropwise 10 mL of a 1.6 M solution of butyllithium (16 mmol, 1.70 equiv.) in hexane over a period of 30 minutes. After 10 min, 4.0 mL of diethyl chlorophosphate (27.6 mmol, 3.0 equiv.) were added dropwise at the same temperature. The reaction mixture was stirred for 1 h at –78 °C and another 3 h at ambient temperature. After addition of cold brine at 0 °C, the aqueous layer was extracted three times with ether. The organic layers were washed with cold brine and dried over $MgSO_4$. Evaporation of the solvent followed by FC (hexane/AcOEt 1:1) and kugelrohr distillation (100-120 °C/10^{-3} mbar) afforded 1.79g (70%) of allylic phosphate (*rac*)-**6** (R = *i*-Pr, X = $PO(OEt)_2$)[1)] as a colorless oil. IR: 2470w, 1467m, 1425w, 1390m, 1370m, 1166w, 1100m, 1034s, 994s, 881w, 820w. ^{1}H-NMR: 0.90 (d, J = 6.9, 3 H, $(CH_3)_2HC(1')$); 0.93 (d, J = 6.9, 3 H, $(CH_3)_2HC(1')$); 1.00 (d, J = 6.6, 6 H, $(CH_3)_2HC(4)$); 1.30 (dt, J = 7.2, 0.9, 3 H, $PO(OCH_2CH_3)_2$); 1.32 (dt, J = 7.2, 0.9, 3 H, $PO(OCH_2CH_3)_2$); 1.89 (m, 1 H, HC(1')); 2.32 (octet d, J = 6.6, 1.2, 1 H, HC(4)); 4.07 (m, 4 H, $PO(OCH_2CH_3)_2$); 4.48 (br q, J = 8, 1 H, HC(1)); 5.39 (ddd, J = 15.3, 8.4, 1.2, 1 H, HC(2)); 5.71 (ddm, J = 15.3, 6.6, 1 H, HC(3)). ^{13}C-NMR: 15.96/16.06 (2 d, $J_{P,C}$ = 6.7, $PO(OCH_2CH_3)_2$); 17.6/18.0/22.0/22.1 ($(CH_3)_2HC(1',4)$); 30.7 (HC(4)); 33.3 (d, $J_{P,C}$ = 6.9, HC(1')); 63.17 (d, $J_{P,C}$ = 5.8, $PO(OCH_2CH_3)_2$); 63.23 (d, $J_{P,C}$ = 5.7, $PO(OCH_2CH_3)_2$); 84.9 (d, $J_{P,C}$ = 5.7, HC(1)); 123.8 (d, $J_{P,C}$ = 2.3, HC(2)); 142.4 (HC(3)). Additional signals of *(E)*-1-(1-methylethyl)-4-methyl-3-pentenyl diethyl phosphate are observed. ^{31}P-NMR: –1.83 (m). MS (FAB): 279([M + H]$^+$, 5), 155(100). TLC: R_f = 0.33 (hexane/AcOEt 1:1).

Palladium-Catalyzed Allylic Amination. Procedure A: In an ampule equipped with a magnetic stirring bar, 1.80 mg (4.92 µmol) of $[\{(\eta^3\text{-}C_3H_5)PdCl\}_2]$ and 4.8 mg (12.3 µmol, 1.25 equiv./Pd) of (–)-(*S*)-2-[2-(diphenylphosphino)phenyl]-4-*tert*-butyl-3,4-dihydrooxazole **1b**[12] were dissolved under nitrogen in 0.5 mL of THF. The homogeneous, slightly yellow solution was degassed at 0.01 torr by three freeze-thaw cycles. The evacuated ampule was sealed with a vacuum-tight teflon stopper and the solution was stirred at 50 °C for 2 h. To 16.5 mg (0.70 mmol) of dry NaH in 4.5 mL of THF, 4-toluenesulfonamide (152 mg, 0.90 mmol) was slowly added. The foaming suspension was stirred for 2 h at 23 °C under N_2. A solution of 124.1 mg (0.492

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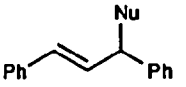
1) The product contained 14% of the corresponding homoallylic phosphate. This isomer is inert under the conditions used for allylic amination and can be readily separated from the substitution products **7h-k** by FC.

mmol) (*rac*)-(*E*)-1,3-diphenyl-2-propenyl acetate in 0.5 mL of THF and the freshly prepared suspension of 4-toluenesulfonamide-sodium salt were added to the catalyst solution at room temperature under N_2. The reaction mixture was degassed immediately at 0.01 torr by three freeze-thaw cycles. The evacuated ampule was sealed with a vacuum-tight teflon stopper and the solution was stirred at 50 °C. After 48 h, the reaction mixture was diluted with ether, transferred to a separatory funnel, and washed twice with ice-cold saturated aqueous NH_4Cl solution. The organic phase was dried over $MgSO_4$, concentrated *in vacuo*, and purified by FC (4 cm x 26 cm, hexane/EtOAc 5:2) to afford 172 mg (96%) of analytically pure sulfonamide **5a** as a white crystalline solid (mp 152 °C, 97.4% ee by HPLC).



5a Nu = NHTs **5c** Nu = $N(Boc)_2$

5b Nu = NHNHCOPh **5d** Nu = $NHCH_2Ph$

(–)-(E)-N-(1,3-diphenyl-2-propenyl)-4-toluenesulfonamide **5a**. The product was recrystallized from $CHCl_3$/hexane (white crystals, mp 152 °C). $[\alpha]_D$ = –34.4 (c = 0.8, $CHCl_3$, 23 °C, 99.7% ee (HPLC)). IR: 3375m, 3270m, 1730m, 1600m, 1495m, 1450m, 1405m, 1330s, 1305s, 1160s, 1095s, 1045s, 1030m, 965s, 865s. ^{1}H-NMR: 2.32 (s, 3 H, CH_3); 4.97 (br d, *J*=7, 1 H, NH); 5.11 (br t, *J* = 6.8, 1 H, HC(1)); 6.07 (dd, *J* = 15.8, 6.8, 1 H, HC(2)); 6.35 (d, *J* = 15.8, 1 H, HC(3)); 7.09-7.27 (m, 12 H, aromatic CH); 7.63-7.66 (m, 2 H, aromatic CH). ^{13}C-NMR: 21.4 (CH_3); 59.8 (HC(1)); 126.4/126.9/127.2/127.6/127.7/128.1/128.3/128.5/129.3/131.9 (HC=CH, aromatic CH); 135.9/137.6/139.5/143.0 (aromatic C). MS (EI): 363(M^+, 1.5), 208(100), 193(14), 181(11). TLC: R_f = 0.29 (hexane/EtOAc 5:2). HPLC: t_R = 45 min; (+)-enantiomer: 37 min (Chiralcel OJ, hexane/*i*-PrOH 75:25, 0.5 mL/min, 254 nm). Anal. Calcd for $C_{22}H_{21}NO_2S$: C, 72.70; H, 5.82; N, 3.85. Found: C, 72.45; H, 5.76; N, 3.96.

(–)-(E)-N-(1,3-Diphenyl-2-propenyl)-N'-benzoylhydrazine **5b**. Mp 128 °C. $[\alpha]_D$ = –36.9 (c = 1.6, $CHCl_3$, 23 °C, 95% ee (HPLC)). IR: 3690w, 3445m, 3290w, 1890w, 1810w, 1660s, 1600m, 1580m, 1510s, 1495s, 1450s, 1440s, 1685m, 1300m, 1290m, 1025m, 965s. ^{1}H-NMR: 4.85 (d, *J* = 8.0, 1 H, HC(1)); 5.23 (br d, *J* = 4.7, 1 H, NH); 6.37 (dd, *J* = 15.8, 8.0, 1 H, HC(2)); 6.68 (d, *J* = 15.8, 1 H, HC(3)); 7.21-7.69 (m, 16 H, aromatic CH, NH). ^{13}C-NMR: 67.2 (HC(1)); 126.5/126.8/127.66/127.72/127.8/128.4/128.6/128.7/129.4/131.7/132.5 (aromatic CH, HC=CH); 132.7/136.5/140.3 (aromatic C); 167.3 (C=O). MS (CI, NH_3): 329([M+H]$^+$, 3), 299(10), 208(17), 193(100). TLC: R_f = 0.34 (hexane/EtOAc 2:1). HPLC: t_R = 43 min; (+)-enantiomer: 37 min (Chiralcel OJ, hexane/*i*-PrOH 85:15, 0.5 mL/min, 254 nm). Anal. Calcd for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14; N, 8.53. Found: C, 80.29; H, 6.19; N, 8.56.

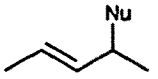
(+)-(E)-Di-tert-butyl N-(1,3-diphenyl-2-propenyl)iminodicarboxylate **5c**. Mp 96 °C. $[\alpha]_D$ = +43.2 (c = 1.4, $CHCl_3$, 23 °C, 86% ee (HPLC)). IR: 1775s, 1740s, 1695s, 1495m, 1480w, 1450m, 1395m, 1370s, 1350s, 1310m, 1145s, 1120s, 1095s, 970m, 865s. ^{1}H-NMR: 1.39 (s, 18 H, *t*-Bu); 6.10 (d, *J* = 8.1, 1 H, HC(1)); 6.67 (d, *J* = 16.0, 1 H, HC(3)); 6.79 (dd, *J* = 16.0, 8.1, 1 H, HC(2)); 7.23-7.47 (m, 10 H, aromatic CH). ^{13}C-NMR: 27.9 (*t*-Bu); 61.3 (HC(1)); 82.4 (*t*-Bu); 126.3/126.5/126.8/127.0/127.8/128.1/ 128.5/134.2 (aromatic CH, HC=CH); 136.6/140.6 (aromatic C); 152.3 (C=O). MS (CI, NH_3): 400([M+H]$^+$, 0.1), 209(16), 193(100). TLC: R_f = 0.33 (hexane/EtOAc 10:1). HPLC: t_R = 10 min; (–)-enantiomer: 21 min (Chiralcel OD, hexane/*i*-PrOH 99:1, 0.5 mL/min, 254 nm).

(–)-(R,E)-N-Benzyl-(1,3-diphenyl-2-propenyl)amine **5d**[9a] (prepared from acetate **4** (X = Ac) using procedure A with $PhCH_2NH_2$ instead of NaNHTs). Colorless oil. $[\alpha]_D$ = –21.6 (c = 1.2, $CHCl_3$, 23 °C, 89% ee (HPLC)). IR: 1955w, 1880w, 1810w, 1600s, 1495s, 1455s, 1305m, 1120m, 1070m, 1030m, 965s, 910m. ^{1}H-NMR: 1.78 (br s, 1 H, NH); 3.75/3.81 (AB, *J* = 13.3, 2 H, H_2CPh); 4.39 (d, *J* = 7.4, 1 H, HC(1)); 6.31 (dd, *J* = 15.9, 7.4, 1 H, HC(2)); 6.58 (d, *J* = 15.9, 1 H, HC(3)); 7.17-7.45 (m, 15 H, aromatic CH). ^{13}C-NMR: 51.4 (H_2CPh); 64.6 (HC(1)); 126.4/126.9/127.31/127.35/127.41/128.1/128.2/128.5/128.6/130.3/132.6 (aromatic CH, HC=CH); 137.0/140.4/142.9 (aromatic C). MS (EI): 299(M^+, 27), 222(15), 208(66), 193(16), 178(7), 115(26), 104(32), 91(100). TLC: R_f = 0.40 (hexane/EtOAc 3:1). HPLC: t_R = 46 min (*R*), 51 min (*S*) (Chiralcel OD, hexane/*i*-PrOH 200:1, 0.5 mL/min, 254 nm).

Procedure B: *(–)-(R,E)-N-Benzyl-(1,3-diphenyl-2-propenyl)amine* **5d**. A solution of 15 mg (0.015 mmol) of $[Pd_2(dba)_3{\cdot}CHCl_3]$[14] and 0.03 mmol of chiral ligand **1**[12] in 10 mL of THF was stirred for 20 min at room temperature. Then 144 mg (1.00 mmol) of *(E)*-1-methyl-2-butenyl methyl carbonate, 190 mg (1.78 mmol) of benzylamine, and 8 mg (0.03 mmol) of tetrabutylammonium chloride were added. The solution was

warmed to 40 °C and stirring was continued until the TLC indicated complete conversion of the starting material. The solvent was evaporated under reduced pressure and the crude product was purified by FC (petroleum ether 40-60/EtOAc 95:5 + 1% triethylamine) to yield a colorless oil.

The ee was determined by HPLC analysis of the corresponding *(R)*-2-methoxy-2-phenylacetamides. Oxalyl chloride (317 mg, 2.5 mmol) was added to a stirred solution of 83 mg (0.5 mmol) of *(–)-(R)*-2-methoxy-2-phenylacetic acid and a catalytic amount of DMF in 1 mL of dry benzene. After stirring for 2 h at room temperature, the solvent was evaporated under reduced pressure. The residue was dissolved in dry benzene and the solvent evaporated *in vacuo*. This procedure was repeated. The crude acid chloride was dissolved in 5 mL of dry CH_2Cl_2 and the solution slowly added to a solution of 150 mg (0.5 mmol) of *(–)-(R,E)-N*-benzyl-(1,3-diphenyl-2-propenyl)amine **5d**, 111 mg (1.40 mmol) of dry pyridine, and a catalytic amount of 4-(dimethylamino)pyridine in 5 mL of dry CH_2Cl_2. The solvent was evaporated under reduced pressure and the residue was filtered through a small pad of silica gel to yield 137 mg (61%) of the diastereomeric amides as a colorless solid foam. *Analytical Data*: ^{1}H-NMR (two diastereoisomers, both existing as two conformers in a ratio of 1:1 for the *(R,R)*- and 2:1 for the *(R,S)*-isomer): *(R,R)*-isomer: 3.28 (s, 3 H, H_3CO); 3.50 (s, 3 H, H_3CO); 4.36 (d, J = 15.3, 1 H, HC-N); 4.72 (d, J = 15.3, 1 H, HC-N); 4.46/4.58 (AB, J = 17.9, H_2CPh); 4.82 (s, 1 H, H_3COHC); 5.99-6.52 (m, 2 H, HC=CH); 6.98-7.53 (m, 20 H, aromatic CH). *(R,S)*-Isomer, major conformer: 3.27 (s, 3 H, H_3CO); 4.15 (d, J = 15.3, 1 H, HC-N); 4.37/4.42 (AB, J = 18.2, H_2CPh); 4.77 (s, 1 H, H_3COHC); 6.02-6.28 (m, 2 H, HC=CH); 6.96-7.54 (m, 20 H, aromatic CH). *(R,S)*-Isomer, minor conformer: 3.49 (s, 3 H, H_3CO); 5.03 (d, J = 15.7, 1 H, HC-N); 4.37/4.43 (AB, J = 18.2, H_2CPh); 5.20 (s, 1 H, H_3COHC); 6.67-6.78 (m, 2 H, HC=CH); 6.96-7.54 (m, 20 H, aromatic CH). HRMS: Calcd for $C_{33}H_{33}NO_2$: 447.2198. Found: 447.2191. HPLC: t_R = 16.7 min (*R,R*), 19.7 min (*R,S*) (Merck Lichrosorb, petroleum ether/EtOAc 95:5 + 1% AcOH, 1.5 mL/min, 254 nm).



7a Nu = NHTs **7c** Nu = $N(Boc)_2$
7b Nu = NHNHCOPh **7d** Nu = $NHCH_2Ph$

(–)-(E)-N-1-(Methyl-2-butenyl)-4-toluenesulfonamide **7a**. Colorless oil. $[\alpha]_D$ = –15.8 (c = 0.96, $CHCl_3$, 23 °C, 66% ee (HPLC)). IR: 3278s br, 1590m, 1496w, 11428s, 1326s, 1160s, 1095s, 1069s, 966s, 667s. ^{1}H-NMR: 1.14 (d, J = 6.8, 3 H, $H_3C(1')$); 1.50 (d, J = 6.4, 3 H, $H_3C(4)$); 2.41 (s, 3 H, CH_3/Ts); 3.79-3.86 (m, 1 H, HC(1)); 5.00 (d, J = 7.4, 1 H, NH); 5.18 (dd, J = 15.3, 6.6, 1 H, HC(2)); 5.41 (dq, J = 14.6, 6.5, 1 H, HC(3)); 7.28 (d, J = 8.5, 2 H, aromatic CH); 7.76 (d, J = 8.3, 2 H, aromatic CH). ^{13}C-NMR: 17.3 ($H_3C(1')$); 21.4 (CH_3/Ts); 21.8 ($H_3C(4)$); 51.4 (HC(1)); 126.3/127.1/129.3/131.8 (aromatic CH, HC=CH); 138.1/142.9 (aromatic C). MS (CI, NH_3): 257([M+NH_4]$^+$, 15), 240([M+H]$^+$, 14), 224(15), 189(42), 155(6), 108(9), 91(6), 86(100). TLC: R_f = 0.30 (hexane/EtOAc 3:1).

The ee was determined by HPLC analysis of the *N*-cinnamoyl derivative: To a solution of **7a** (33.6 mg, 0.140 mmol), 4-(dimethylamino)pyridine (5 mg), and triethylamine (30 µL, 0.211 mmol) in 3.0 mL methylenechloride under argon at 23 °C, was added 28.5 mg (0.170 mmol) of cinnamoyl chloride. After 21 h at 23 °C, the reaction mixture was poured onto ice-water and extracted three times with ether. The combined organic extracts were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by FC (hexane/EtOAc 6:1) afforded 26.9 mg (52%) of a colorless oil. *Analytical Data:* $[\alpha]_D$ = –3.4 (c = 1.8, $CHCl_3$, 23 °C, 66% ee (HPLC)). IR: 1778m, 1674s, 1617s, 1353s, 1160s, 1088s. ^{1}H-NMR: 1.58 (d, J = 7.0, 3 H, $H_3C(1')$); 1.68 (d, J = 6.5, 3 H, $H_3C(4)$); 2.41 (s, 3 H, CH_3/Ts); 5.07-5.12 (m, 1 H, HC(1)); 5.63 (dq, J = 15.4, 6.4, 1 H, HC(3)); 5.85-5.93 (m, 1 H, HC(2)); 7.19 (d, J = 15.4, 1 H, *H*C=CHPh); 7.30 (d, J = 8.0, 2 H, aromatic CH/Ts); 7.35-7.37 (m, 3 H, aromatic CH); 7.42-7.47 (m, 2 H, aromatic CH); 7.58 (d, J = 15.4, 1 H, HC=C*H*Ph); 7.82 (d, J = 8.4, 2 H, aromatic CH/Ts). ^{13}C-NMR: 17.6 ($H_3C(1')$); 20.0 ($H_3C(4)$); 21.6 (H_3C/Ts); 57.2 (HC(1)); 120.1 (*H*C=CHPh); 127.6/128.2/128.4/128.6/128.9/129.0/129.6/130.3/131.2 (HC(2), HC(3), HC=*C*HPh, aromatic CH, aromatic C); 134.6/144.6 (aromatic C/Ts); 166.2 (C=O). MS (CI, NH_3): 370([M+H]$^+$, 39), 319(22), 302(100). TLC: R_f = 0.26 (hexane/EtOAc 6:1). HPLC: t_R = 37 min; (+)-enantiomer: 32 min (Chiralcel OJ, hexane/*i*PrOH 93:7, 0.5 mL/min, 254 nm).

(–)-(E)-N-(1-Methyl-2-butenyl)-N'-benzoylhydrazine **7b**. The product was recrystallized from petroleum ether (white crystals, mp 90 °C). $[\alpha]_D$ = –82.4 (c = 0.96, $CHCl_3$, 23 °C, 91% ee (HPLC)). IR: 3447m, 3289w, 1657s, 1580m, 1517s, 1460s, 1438s, 1282m, 969s. ^{1}H-NMR: 1.17 (d, J = 6.5, 3 H, $H_3C(1')$); 1.67

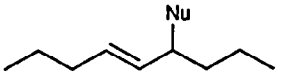
(d, J = 6.4, 3 H, $H_3C(4)$); 3.55-3.60 (m, 1 H, HC(1)); 4.89 (br s, 1 H, NH); 5.36 (dd, J = 15.3, 8.0, 1 H, HC(2)); 5.63 (dq, J = 15.2, 6.5, 1 H, HC(3)); 7.40-7.53 (m, 3 H, aromatic CH); 7.71-7.75 (m, 2 H, aromatic CH); 7.95 (br s, 1 H, NH). ^{13}C-NMR: 17.8 ($H_3C(1')$); 19.2 ($H_3C(4)$); 58.3 (HC(1)); 126.8/128.1/128.6/131.7/132.7 (HC=CH, aromatic CH); 133.0 (aromatic C); 167.1 (C=O). MS (EI): 204(M^+, 1), 136(11), 122(19), 105(100). TLC: R_f = 0.12 (hexane/EtOAc 3:1). HPLC: t_R = 47 min; (+)-enantiomer: 50 min (Chiralcel OJ, hexane/*i*-PrOH 99:1, 0.5 mL/min, 254 nm). Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.89; N, 13.71. Found: C, 70.91; H, 8.01; N, 13.67.

(–)-(E)-Di-tert-butyl N-(1-methyl-2-butenyl)iminodicarboxylate **7c**. Colorless oil. $[\alpha]_D$ = –5.3 (c = 0.98, $CHCl_3$, 23 °C, 44% ee (GC)). IR: 1734s, 1369s, 1350s, 1128s. ^{1}H-NMR: 1.35 (d, J = 7.0, 3 H, $H_3C(1')$); 1.49 (s, 18 H, *t*-Bu); 1.69 (d, J = 5.8, 3 H, $H_3C(4)$); 4.72-4.80 (m, 1 H, HC(1)); 5.53-5.73 (m, 2 H, HC=CH). ^{13}C-NMR: 17.6 ($H_3C(1')$); 18.8 ($H_3C(4)$); 28.0 (*t*-Bu); 53.5 (HC(1)); 81.9 (*t*-Bu); 126.6/131.7 (HC=CH); 152.9 (C=O). MS (CI, NH_3): 286([M+H]$^+$, 26), 247(21), 230(47), 191(100). TLC: R_f = 0.24 (hexane/EtOAc 50:1).

The ee was determined by GC analysis after selective removal of one *tert*-butyloxycarbonyl group[7h] using the procedure described for **7g**. Yield: 69%. *(E)-tert-butyl N-(1-methyl-2-butenyl)iminocarboxylate*. Colorless oil. IR: 3446m, 1706s, 1497s, 1453m, 1368s, 1169s. ^{1}H-NMR: 1.18 (d, J = 6.8, 3 H, $H_3C(1')$); 1.44 (s, 9 H, *t*-Bu); 1.67 (d, J = 6.3, 3 H, $H_3C(4)$); 4.13-4.16 (m, 1 H, NH); 4.38-4.44 (m, 1 H, HC(1)); 5.41 (dd, J = 15.4, 5.6, 1 H, HC(2)); 5.58 (dq, J = 15.3, 6.3, 1 H, HC(3)). ^{13}C-NMR: 17.6 ($H_3C(1')$); 21.2 ($H_3C(4)$); 28.4 (*t*-Bu); 47.7 (HC(1)); 79.1 (*t*-Bu); 124.9/133.1 (HC=CH); 155.1 (C=O). TLC: R_f = 0.37 (hexane/EtOAc 6:1). GC: t_R = 48.4 min; minor enantiomer: 49.2 min (Chiraldex γ-CD-TFA-, 70-160 °C, 0.2 °C/min).

(–)-N-Benzyl-(1-methyl-2-butenyl)amine **7d**. The reaction of *(E)*-1-methyl-2-butenyl methyl carbonate with benzylamine was carried out as described in procedure B, but with 0.100 mmol of the chiral ligand. Ratio of the (*E*/*Z*)-isomers = 95:5. $[\alpha]_D$ = –14.6 (c = 2.0, $CHCl_3$, 23 °C, 57% ee for the (*E*)-isomer (HPLC)). ^{1}H-NMR: (*E*)-Isomer: 1.17 (d, J = 6.4, 3 H, $H_3C(1')$); 1.35 (br s, 1 H, NH); 1.70 (dd, J = 6.4, 1.5, 3 H, $H_3C(4)$); 3.20 (q, J = 6.4, 1 H, HC(1)); 3.69/3.81 (AB, J = 13.2, 2 H, H_2C-Ph); 5.36 (ddq, J = 15.3, 6.4, 1.5, 1 H, HC(2)); 5.57 (dq, J = 15.3, 6.4, 1 H, HC(3)); 7.21-7.33 (m, 5 H, aromatic CH). (*Z*)-Isomer: 1.63 (dd, J = 6.9, 1.8, 3 H, $H_3C(4)$). Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 81.99; H, 9.74; N, 7.83.

The ee was determined by HPLC analysis of the *N*-naphthoyl derivative. 1-Naphthoyl chloride (48 mg, 0.25 mmol) was added to a solution of 35 mg (0.20 mmol) of (–)-*N*-benzyl-(1-methyl-2-butenyl)amine, 50 mg (0.50 mmol) of triethylamine, and a catalytic amount of 4-(dimethylamino)pyridine in 1 mL of dry CH_2Cl_2 at 0 °C. After 30 min, the solution was allowed to reach room temperature and stirring was continued for an additional 15 h. After hydrolysis with 1 N HCl, the organic layer was washed with saturated $NaHCO_3$ solution, brine, and dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the crude product was purified by FC (petroleum ether 40-60/EtOAc 9:1) to yield 63 mg (95%) of the amide as a yellowish oil. *Analytical Data:* $[\alpha]_D$ = –30.2 (c = 1.8, $CHCl_3$, 23 °C, 57% ee for the (*E*)-isomer (HPLC)). ^{1}H-NMR (two conformers in a ratio of 1:1.1): major conformer: 1.09 (d, J = 7.8, 3 H, $H_3C(1')$); 1.60 (dd, J = 6.1, 1.4, 3 H, $H_3C(4)$); 4.19-4.28 (m, 1 H, HC(1)); 4.58/5.04 (AB, J = 15.1, 2 H, H_2C-Ph); 5.24-5.46 (m, 2 H, HC=CH); 7.03-7.57 (m, 9 H, aromatic CH); 7.76-8.00 (m, 3 H, aromatic CH). Minor conformer: 1.05 (d, J = 6.9, 3 H, $H_3C(1')$); 1.55 (dd, J = 4.9, 1.4, 3 H, $H_3C(4)$); 4.19-4.28 (m, 1 H, HC(1)); 4.58/5.04 (AB, J = 15.1, 2 H, H_2C-Ph); 5.24-5.46 (m, 2 H, HC=CH); 7.03-7.57 (m, 9 H, aromatic CH); 7.76-8.00 (m, 3 H, aromatic CH). HPLC: t_R = 47.6 min (*S*), 52.9 min (*R*) (Pirkle CSP 2, petroleum ether 60-95/ethanol/methanol 99.3:0.5:0.2, 1.0 mL/min, 254 nm). Anal. Calcd for $C_{23}H_{23}NO$: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.78; H, 7.18; N, 4.36.



7e Nu = NHTs
7f Nu = NHNHCOPh
7g Nu = N(Boc)$_2$

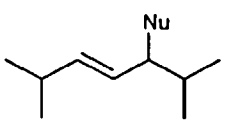
(–)-(E)-N-(1-Propyl-2-hexenyl)-4-toluenesulfonamide **7e**. Colorless oil. $[\alpha]_D$ = –11.2 (c = 0.98, $CHCl_3$, 23 °C, 66% ee (HPLC)). IR: 3381m, 3274m br, 1711w, 1560m, 1327s, 1159s, 1094m, 968m. ^{1}H-NMR: 0.77 (t, J = 7.4, 3 H, CH_2CH_3); 0.83 (t, J = 7.3, 3 H, CH_2CH_3); 1.13-1.46 (m, 6 H, $H_2C(1',2',5)$);

1.72-1.85 (m, 2 H, $H_2C(4)$); 2.40 (s, 3 H, CH_3/Ts); 3.66-3.71 (m, 1 H, HC(1)); 4.59 (d, J = 7.8, 1 H, NH); 5.04 (dd, J = 15.4, 7.6, 1 H, HC(2)); 5.28 (dd, J = 15.4, 6.6, 1 H, HC(3)); 7.26 (d, J = 8.3, 2 H); 7.74 (d, J = 8.2, 2 H, aromatic CH). ^{13}C-NMR: 13.5/13.5 ($H_3C(3',6)$); 18.6 (H_2C); 21.3 (CH_3/Ts); 21.9/34.0/38.2 (H_2C); 55.9 (HC(1)); 127.2/129.3/129.5/132.3 (aromatic CH, HC=CH); 138.4/142.8 (aromatic C). MS (CI, NH_3): 313([M+NH_4]$^+$, 8), 296([M+H]$^+$, 4), 252(37), 204(24), 189(52), 142(100). TLC: R_f = 0.38 (hexane/EtOAc 3:1). HPLC: t_R = 25 min; (+)-enantiomer: 22 min (Chiralcel OD, hexane/*i*-PrOH 95:5, 0.5 mL/min, 254 nm).

(–)-(E)-N-(1-Propyl-2-hexenyl)-N'-benzoylhydrazine **7f**. The product was recrystallized from petroleum ether (white needles, mp 66 °C). $[\alpha]_D$ = –80.2 (c = 1.1, $CHCl_3$, 23 °C, 94% ee (HPLC)). IR: 3448m, 3286m br, 1655s, 1580m, 1517m, 1456s, 972m. ^{1}H-NMR: 0.87 (t, J = 7.4, 3 H, CH_3); 0.92 (t, J = 6.9, 3 H, CH_3); 1.25-1.45 (m, 5 H, $H_2C(5,1',2')$); 1.53-1.57 (m, 1 H, $H_2C(1')$); 1.96-2.04 (m, 2 H, $H_2C(4)$); 3.41-3.39 (m, 1 H, HC(1)); 4.90-4.94 (br s, 1 H, NH); 5.26 (dd, J = 15.2, 8.7, 1 H, HC(2)); 5.60 (dt, J = 15.1, 6.9, 1 H, HC(3)); 7.38-7.53 (m, 3 H, aromatic CH); 7.71-7.75 (m, 2 H, aromatic CH); 7.82-7.84 (br s, 1 H, NH). ^{13}C-NMR: 13.6/14.1 (CH_3); 19.1/22.4 ($H_2C(2',5)$); 34.4/35.5 ($H_2C(1',4)$); 63.5 (HC(2)); 126.7/128.5/130.6/131.6/134.8 (aromatic CH, HC=CH); 133.1 (aromatic C); 166.8 (C=O). MS (EI): 260 (M^+, 2), 217(56), 140(28), 137(13), 136(11), 125(14), 124(14), 122(24), 105(97), 96(13), 83(72), 77(44), 69(100). TLC: R_f = 0.18 (hexane/EtOAc 3:1). HPLC: t_R = 68 min; (+)-enantiomer: 60 min (Chiralcel OD, hexane/*i*-PrOH 98:2, 0.5 mL/min, 254 nm). Anal. Calcd for $C_{16}H_{24}N_2O$: C, 73.81; H, 9.29; N, 10.76. Found: C, 73.75; H, 8.88; N, 10.79.

(–)-(E)-Di-tert-butyl N-(1-propyl-2-hexenyl)iminodicarboxylate **7g**. Colorless oil. $[\alpha]_D$ = –4.0 (c = 1.1, $CHCl_3$, 23 °C, 54% ee (GC)). IR: 1769m, 1694s, 1457m, 1393s, 1369s, 1348s, 1134s, 972m. ^{1}H-NMR: 0.88 (t, J = 7.5, 3 H, CH_2CH_3); 0.91 (t, J = 7.1, 3 H, CH_2CH_3); 1.23-1.42 (m, 4 H, $H_2C(2',5)$); 1.49 (s, 18 H, *t*-Bu); 1.57-1.96 (m, 2 H, $H_2C(1')$); 1.98-2.02 (m, 2 H, $H_2C(4)$); 4.57 (dt, J = 7.5, 6.3, 1 H, HC(1)); 5.59-5.68 (m, 2 H, HC=CH). ^{13}C-NMR: 13.7/13.8 ($H_3C(2',6)$); 19.7/22.2 ($H_2C(2',5)$); 28.0 (*t*-Bu); 34.3/35.3 ($H_2C(1',4)$); 58.7 (HC(1)); 81.7 (*t*-Bu); 129.5/133.1 (HC=CH); 153.1 (C=O). MS (CI, NH_3): 342(M^+, 1.8), 303(13), 286(6), 247(100). TLC: R_f = 0.63 (hexane/EtOAc = 3/1).

The ee was determined after selective removal of one *tert*-butyloxycarbonyl group[7h]: *(–)-(E)*-Di-*tert*-butyl *N*-(1-propyl-2-hexenyl)iminodicarboxylate **7g** (80 mg, 0.234 mmol) in 2.3 mL of methylene chloride was treated with 24.5 µL (0.321 mmol) of trifluoroacetic acid. After stirring under argon at 23 °C for 16 h, the solution was diluted with ether and washed with 5% NaOH and saturated aqueous NaCl. The aqueous layers were extracted twice with ether. The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to provide a colorless oil, which was purified by FC (hexane/EtOAc 1:20). Yield: 34.5 mg (71%) of *(E)*-*tert*-butyl *N*-(1-propyl-2-hexenyl)iminocarboxylate. $[\alpha]_D$ = –8.5 (c = 1.0, $CHCl_3$, 23 °C, 59% ee (GC)). IR: 3444m, 1707s, 1498s, 1368m, 1168s, 970m. ^{1}H-NMR: 0.88 (t, J =7.5, 3 H, CH_2CH_3); 0.91 (t, J = 7.1, 3 H, CH_2CH_3); 1.32-1.42 (m, 6 H, $H_2C(1',2',5)$); 1.44 (s, 9 H, *t*-Bu); 1.99 (dt, 2 H, J = 7.1, 7.0, $H_2C(4)$); 3.99 (br m, 1 H, NH); 4.00-4.01 (m, 1 H, HC(1)); 5.30 (dd, J = 15.3, 6.4, 1 H, HC(2)); 5.55 (ddd, J = 15.1, 7.1, 6.9, 1 H, HC(3)). ^{13}C-NMR: 13.6/13.9 ($H_3C(3',6)$); 19.0/22.4 ($H_2C(2',5)$); 28.4 (*t*-Bu); 34.3/37.9 ($H_2C(1',4)$); 52.1 (HC(1)); 79.0 (*t*-Bu); 130.9 (HC(2) and HC(3)); 155.4 (C=O). MS (FAB): 242([M+H]$^+$, 9), 198(6), 186(100). TLC: R_f = 0.24 (hexane/EtOAc = 20:1). GC: t_R = 23.7 min; (–)-enantiomer: 23.2 min (MSP TBDMS-β-CD, 120-160 °C, 1.0 °C/min).



7h Nu = NHTs
7i Nu = NHNHCOPh
7k Nu = N(Boc)$_2$

(+)-(E)-N-[1-(1'-Methylethyl)-4-methyl-2-pentenyl]-4-toluenesulfonamide **7h**. The product was recrystallized from hexane/$CHCl_3$ (white crystals, mp 107 °C, 88% ee). $[\alpha]_D$ = +13.7 (c = 1.1, $CHCl_3$, 23 °C, 88% ee (HPLC)). IR($CHCl_3$): 3383w, 1599w, 1495w, 1414m, 1387m, 1330m,1305m, 1289m, 1159s, 1094m, 1039m, 971m. ^{1}H-NMR: 0.76/0.77/0.84/0.86 (4 d, J = 6.9, 12 H, CH_3); 1.71/2.04 (2 m, 2 H, HC(1',4)); 2.40 (s, 3H, CH_3/Ts); 3.53 (m, 1H, HC(1)); 4.31 (d, J = 8.4, 1 H, NH); 4.97 (ddd, J = 15.6, 7.5, 1.2, 1 H, HC(2 or 3)); 5.16 (ddd, J = 15.6, 6.6, 0.9, HC(2 or 3)); 7.22-7.28 (m, 2 H, aromatic CH); 7.70 (br dt, J = 8.4, 2.0, 2 H, aromatic CH). ^{13}C-NMR: 18.2/18.3/21.99/22.05 (CH_3); 21.4 (CH_3/Ts); 30.6/33.1

(HC(1',4)); 61.4 (HC(1)); 124.2/127.2/129.4 (aromatic CH, HC(2)); 138.4 (aromatic C); 140.5 (HC(3)); 142.9 (aromatic C). MS (CI, NH_3): 296([M+H]$^+$, 6), 253(6), 252(39), 126(10), 125(100). TLC: R_f = 0.34 (hexane/EtOAc 2.5:1). HPLC: t_R = 35 min; (–)-enantiomer: 30 min (Chiralcel OD, hexane/*i*-PrOH 98:2, 0.5 mL/min, 254 nm). Anal. Calcd for $C_{16}H_{25}NO_2S$: C, 64.83; H, 8.50; N, 4.72. Found: C, 65.05; H, 8.34; N, 4.75.

(+)-(E)-N-[1-(1'-Methylethyl)-4-methyl-2-pentenyl)]-N'-benzoylhydrazine **7i**. Colorless oil. $[\alpha]_D$ = +49.8 (c = 1.1, $CHCl_3$, 23 °C, 80% ee (HPLC)). IR: 3450m, 1710w, 1656s, 1580w, 1518w, 1455m, 1438m, 1385,w, 1367w, 1280w, 1069w, 1026w, 977m, 908w. ^{1}H-NMR: 0.94 (d, *J* = 6.9, 3 H, $(CH_3)_2$HC(1')); 0.980 (d, *J* = 6.6, 3 H, $(CH_3)_2$HC(4)); 0.986 (d, *J* = 6.6, 3 H, $(CH_3)_2$HC(4)); 0.992 (d, *J* = 6.9, 3 H, $(CH_3)_2$HC(1')); 1.81 (m, HC(1')); 2.32 (octet d, *J* = 6.6, 1.2, 1H, HC(4)); 3.18 (br dd, *J* = 8.7, 6.0, 1 H, HC(1)); 4.97 (br, 1 H, NH); 5.28 (ddd, *J* = 15.3, 8.7, 1.2, 1 H, HC(2)); 5.58 (dd, *J* = 15.3, 6.6, 1H, HC(3)); 7.39 (br, 1 H, NHCO); 7.39-7.75 (m, 5 H, aromatic CH). ^{13}C-NMR: 18.0/19.5/22.5/22.6 (CH_3); 30.6/31.1 (HC(1',4)); 69.1 (HC(1)); 166.7/125.0/126.7/128.6/131.6 (aromatic CH, HC(2)); 133.2 (aromatic C); 143.0 (HC(3)); 166.7 (HNCO). MS (CI, NH_3): 262(15), 261([M+H]$^+$, 82), 217(30), 140(5), 138(8), 137(100). TLC: R_f = 0.31 (hexane/EtOAc 2.5:1).

The ee was determined by HPLC analysis of the *N*-cinnamoyl derivative (see procedure for **7a**). Yield: 45% of a colorless glassy solid. *Analytical Data:* $[\alpha]_D$ = –13.4 (c = 1.0, $CHCl_3$, 23 °C, 80% ee (HPLC)). IR: 3402w, 1702s, 1654s, 1617s, 1578w, 1498m, 1479m, 1450m, 1388s, 1340w, 1270m, 1070w, 1026w, 977m, 933w. ^{1}H-NMR (55°C): 0.70-1.30 (br m, 12 H, $(CH_3)_2$HC(1',4)); 1.93/2.24 (2 br m, 2 H, HC(1',4)); 4.70 (br m, 1 H, HC(1)); 5.37 (br dd, *J* = 15.3, 7.8, 1 H, HC(2 or 3)); 5.68 (br dd, *J* = 15.3, 6.3, 1 H, HC(2 or 3)); 6.73 (d, *J* = 15.3, 1 H, *H*C=CHPh); 7.10-7.90 (m, 12 H, HC=C*H*Ph, aromatic CH, HNCO); at 25 °C, only very broad signals are observed. ^{13}C-NMR: 19.7 /20.3(br)/22.1(br)/22.3(br) (CH_3); 29.9(br)/31.1 (HC(1',4)); 64.9(br, HC(1)); 116.8/122.7(br)/127.2/127.9/128.7/129.0/129.7/132.5/135.1/ 144.0 (HC=CH, HC=CHPh, aromatic CH); 132.3/143.1(br) (aromatic C); 166.4(br)/167.9 (C = O). MS (CI, NH_3): 392 (12), 391([M+H]$^+$, 12), 373(5), 268(18), 267(100). TLC: R_f = 0.23 (hexane/AcOEt 3:1). HPLC: t_R = 44 min; minor enantiomer: 28 min (Chiralcel OD, hexane/*i*-PrOH 9:1, 0.5 mL/min, 254 nm).

(+)-(E)-Di-tert-butyl N-[1-(1'-methylethyl)-4-methyl-2-pentenyl]iminodicarboxylate **7k**. Colorless oil. $[\alpha]_D$ = +8.4 (c = 0.98, $CHCl_3$, 23 °C. 95% ee (GC). IR: 3497w, 1769w, 1732m, 1691s, 1467w, 1450w, 1383w, 1369s, 1350m, 1167w, 1127m, 1111w, 1084w, 976w. ^{1}H-NMR: 0.85/0.89/0.969/0.975 (4 d, *J* = 6.6, 12 H, CH_3); 1.49 (s, 18 H, *t*-Bu); 2.08-2.36 (2 m, 2 H, HC(1',4)); 4.11 (m, 2 H, HC(1)); 5.53-5.67 (m, 2 H, HC=CH). ^{13}C-NMR: 19.5/20.9/22.29/22.32 (CH_3); 30.5/30.9 (HC(1',4)); 28.1 (*t*-Bu); 66.1 (HC(1)); 81.7 (*t*-Bu); 125.5 (HC(2)); 141.7 (HC(3)); 153.3 (C = O). MS (NBA + KCl): 380([M + K]$^+$, 25), 322(13), 230(14), 229(6), 228(15), 184(8), 149(6), 142(15) 125(21), 123(8), 116(6), 107(6), 106(5), 91(11), 89(7), 81(8),79(7), 77(14), 71(6), 69(30), 67(6), 63(7), 57(100). TLC: R_f = 0.28 (hexane/EtOAc) 25:1).

The ee was determined after selective removal of one *tert*-butyloxycarbonyl group[7h] using the procedure described for **7g**. Yield: 80%: *(–)-tert-Butyl-N-[1-(1'-methylethyl)-4-methyl-2-pentenyl]iminocarboxylate.* White needles, mp: 49-52 °C. $[\alpha]_D$ = –1.1 (c = 1.09, $CHCl_3$, 95% ee (GC)). IR: 3448m, 1706s, 1499s, 1466m, 1391s, 1367s, 1297w, 1167s, 1095w, 1042w, 1006m, 972m, 867w. ^{1}H-NMR: 0.866/0.873 (2 d, *J* = 6.9, 6 H, CH_3); 0.98 (d, *J* = 6.6, 6 H, CH_3); 1.45 (s, 9 H, *t*-Bu); 1.74/2.29 (2 m, 2 H, HC(1',4)); 3.90 (br m, HC(1)); 4.46 (br, NH); 5.24 (ddd, *J* = 15.3, 6.6, 0.9, 1 H, HC(2 or 3)); 5.53 (ddd, *J* = 15.3, 6.6, 1.2, 1 H, HC(2 or 3)). ^{13}C-NMR: 18.2/18.6/22.4/22.5 (CH_3); 28.4 (*t*-Bu); 30.9/32.6 (HC(1',4)), 57.4 (HC(1)); 79.0 (*t*-Bu); 126.6 (HC(2)); 138.9 (HC(3)); 155.5 (C = O). MS (CI, NH_3): 242([M+H]$^+$, 6), 203(38), 186(29), 143(10), 142(100). TLC: R_f = 0.37 (hexane/EtOAc 9:1). GC: t_R = 13.2 min; minor enantiomer: 12.9 min (MSP β-CD-*t*-butyl-dimethylsilylated, 120-160 °C, 2 °C/min).

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