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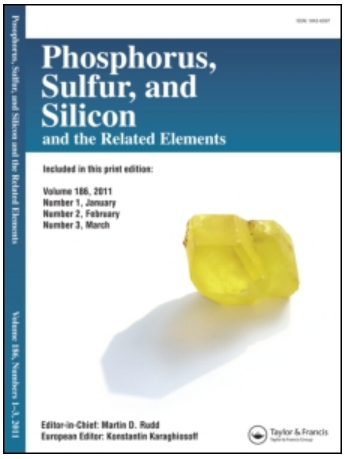

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SYNTHESIS OF ENANTIOMERICALLY ENRICHED α-AMINOPHOSPHINIC ACID DERIVATIVES VIA ASYMMETRIC HYDROGENATION

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SYNTHESIS OF ENANTIOMERICALLY ENRICHED α-AMINOPHOSPHINIC ACID DERIVATIVES VIA ASYMMETRIC HYDROGENATION

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For the first time, the biological interesting enantiomerically enriched α-aminophosphinic acids and their derivatives were prepared by asymmetric hydrogenation of suitable precursors and saponification of the obtained products. Enantiomeric excesses of up to 99 % were obtained.

Keywords: α-aminophosphinic acids; hydrogenation; rhodium; catalysis

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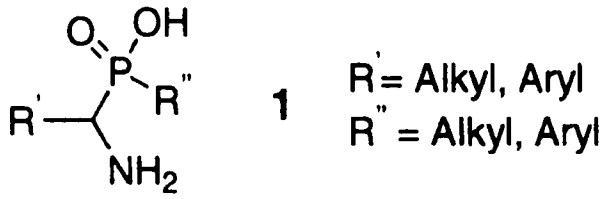
INTRODUCTION

α-Aminophosphinic acids as analogs of amino acids may have biological and pharmacological properties and may be an effective constituent in herbicides, bactericides and antibiotics.[1] Therefore, the significance of these compounds increases permanently and the search for new, more efficient synthetic protocols continues unabated. The synthesis and application of α-aminophosphonic acids has been recently reviewed.[2] The preparation of racemic α-aminophosphinic acids **1** (Scheme 1) has been often described.[1g,3]

* Correspondence author.



SCHEME 1 α-Aminophosphinic acids

However, only a few authors reported the synthesis of the corresponding enantiomerically enriched compounds.[4] A catalytic route, especially catalytic asymmetric hydrogenation to enantiomerically pure derivatives of the α-aminophosphinic acids has not been described in the literature until now.

In this article, we summarize the preparation of the unsaturated precursors of the α-aminophosphinic acid derivatives (A) and their hydrogenation under various conditions (B). In part C we report the isolation of enantiomerically pure derivatives of the α-aminophosphinic acids.

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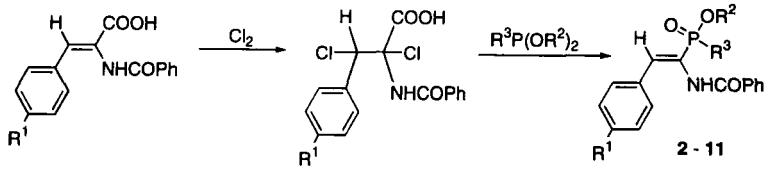
RESULTS AND DISCUSSION

The asymmetric hydrogenation of dehydroamino acids catalyzed by chiral rhodium(I) complexes is an elegant method to produce enantiomerically enriched unusual amino acids.[5] However, this method needs suitable precursors. Therefore, we describe the preparation of the vinyl-phosphinic acid derivatives.

A. Synthesis of (*E*)-(1-*N*-Acylamino-2-aryl)vinyl-aryl(or alkyl)-phosphinic Acids and Their Esters

In 1993 BROVARETS et al.[6] reported a synthesis of (1-*N*-benzoylamino-2-phenyl)vinyl-phenylphosphinic acid ethyl ester. Firstly, they chlorinated the double bond of *N*-benzoylaminocinnamic acid and the following ARBUZOV reaction led to the desired product. Only products with an (*E*)-configuration are observed, which is important for the subsequent rhodium catalyzed hydrogenation step. We also used this method.

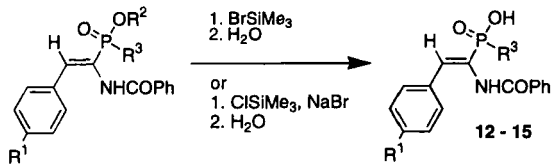
The various cinnamic acid derivatives were prepared by the classical ERLENMEYER synthesis.[7] In all cases the chlorination of the double bond occurred nearly quantitatively. The obtained products were often unstable to heat and light and were used without recrystallization. After the ARBUZOV reaction with different phosphonites, we obtained the (*E*)-(1-*N*-benzoylamino-2-aryl)vinyl-aryl(or alkyl)phosphinic acid esters **2** – **11** in moderate yields (10–35 %, Scheme 2).



	R^1	R^2	R^3		R^1	R^2	R^3
2	H	Et	Ph	**7**	H	Me	Ph
3	Me	Et	Ph	**8**	Me	Me	Ph
4	*i*Pr	Et	Ph	**9**	F	Me	Ph
5	F	Et	Ph	**10**	H	Et	Me
6	NO_2	Et	Ph	**11**	H	Et	*n*Bu

SCHEME 2 Preparation of the (*E*)-(1-*N*-benzoylamino-2-aryl)vinyl-aryl(or alkyl)-phosphinic acid esters

The corresponding (*E*)-(1-*N*-benzoylamino-2-aryl)vinyl-aryl(or alkyl) phosphinic acids **12** – **15** were prepared in good yields (over 80 %) by transesterification with halogenotrimethylsilane at room temperature followed by saponification of the trimethylsilyl ester (Scheme 3).



	R^1	R^3		R^1	R^3
12	H	Ph	**14**	Me	Ph
13	F	Ph	**15**	H	Me

SCHEME 3 Preparation of the (*E*)-(1-*N*-benzoylamino-2-aryl)vinyl-aryl(or alkyl)-phosphinic acids

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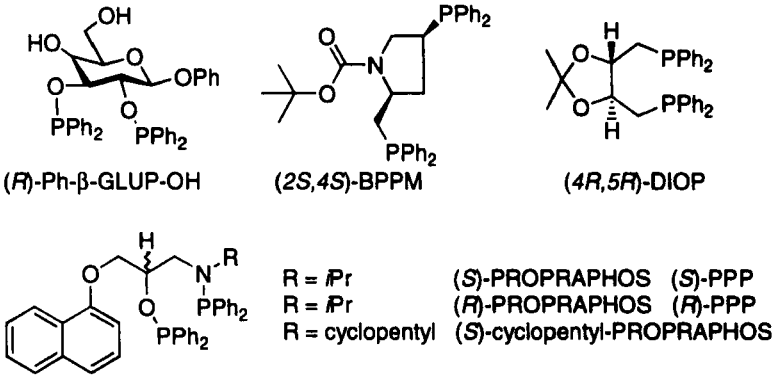
B. Asymmetric Hydrogenation of the (*E*)-(1-*N*-Acylamino-2-aryl)-vinyl-aryl (or alkyl)phosphinic Acids and Their Esters with Chiral Rhodium Complexes

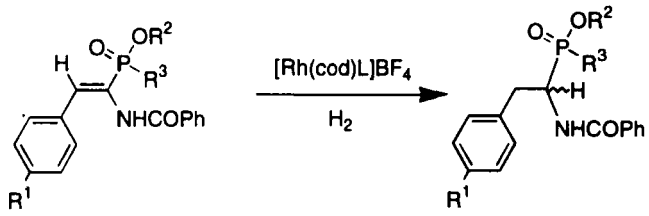
Catalytic asymmetric hydrogenations with chiral rhodium complexes are frequently used reactions with excellent enantioselectivities and activities.[5] The ligands for the asymmetric hydrogenation of the (*E*)-(1-*N*-acylamino-2-aryl)vinyl-aryl(or alkyl)phosphinic acid derivatives are depicted in Scheme 4. The diphosphines (*R,R*)-DIOP[8], (*S,S*)-BPPM[9], bisphosphinite (*R*)-Ph-β-Glup-OH[10] and aminophosphine phosphinites (*R*)-PROPRAPHOS[11], (*S*)-PROPRAPHOS[11], (*S*)-cyclopentyl-PROPRAPHOS[12] constitute seven-membered chelate rings with rhodium. The diphosphines were used with $[Rh(cod)_2]BF_4$ *in situ*, whereas the other ligands were utilized as cationic rhodium complexes $[Rh(cod)L]BF_4$.



SCHEME 4 Applied ligands for the asymmetric hydrogenation

Detailed instructions for the hydrogenation (Scheme 5) are described in the EXPERIMENTAL section.

The rhodium complexes of (*2S,4S*)-BPPM, (*4R,5R*)-DIOP, (*S*)-PROPRAPHOS, (*S*)-cyclopentyl-PROPRAPHOS resulted in the (*S*)-configuration of the newly formed stereogenic center as proved by X-ray structure analysis. (*R*)-Ph-β-GLUP-OH, (*R*)-PROPRAPHOS afforded consequently the corresponding (*R*)-configurations.[13] The ee values with respect to the



SCHEME 5 Asymmetric hydrogenation of the (*E*)-(1-*N*-acylamino-2-aryl)vinyl-aryl(or alkyl)phosphinic acid derivatives by chiral rhodium complexes

α-C-atom (ee_C) were determined from the enantiomeric excesses of the diastereomeric pairs of the ester.[13]

1. Asymmetric catalytic hydrogenation in methanol as solvent

A comparison of the activities ($t_{1/2}$: time necessary to consume half of the theoretical amount of hydrogen – halflife; was taken as a measure for the activity) and enantioselectivities of various catalysts in Table I shows, that the combination Rh-(*S,S*)-BPPM gave the best results (up to 86 % ee_C). In the case of acid, the rate increased concommitant with a decrease in ee.

TABLE I Hydrogenation results of (*E*)-(1-*N*-benzoylamino-2-phenyl)vinyl-phenylphosphinic acid and their esters by use of different catalysts

	R^1	R^2	R^3	*L*	$t_{1/2}$ *[h]*	*t [h]*	ee_C *[%] (configuration*
12	H	H	Ph	(*S*)-PROPRAPHOS	0.3	2.1	65 (*S*)
	H	H	Ph	(*R*)-PROPRAPHOS	0.3	0.7	60 (*R*)
	H	H	Ph	(*S*)-cyclopentyl-PROPRAPHOS	0.2	0.7	63 (*S*)
	H	H	Ph	(*S,S*)-BPPM	0.5	4.2	**76 (*S*)**
	H	H	Ph	(*R,R*)-DIOP	0.9	4.4	60 (*S*)
	H	H	Ph	(*R*)-Ph-β-Glup-OH	2.0	7.0	12 (*R*)
7	H	Me	Ph	(*S*)-PROPRAPHOS	0.9	4.2	69 (*S*)
	H	Me	Ph	(*R*)-PROPRAPHOS	0.9	3.0	72 (*R*)
	H	Me	Ph	(*S*)-cyclopentyl-PROPRAPHOS	2.5	23.0	68 (*S*)
	H	Me	Ph	(*S,S*)-BPPM	1.0	12.6	**85 (*S*)**
	H	Me	Ph	(*R,R*)-DIOP	1.2	14.0	48 (*S*)

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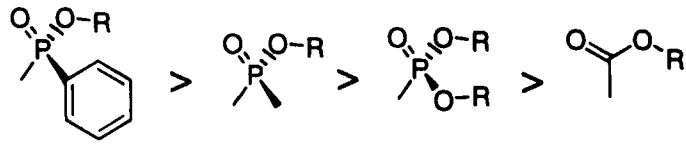
	R^1	R^2	R^3	L	$t_{1/2}$ [h]	t [h]	ee_C [%] (configuration
	H	Me	Ph	(*R*)-Ph-β-Glup-OH	7.2	39.7	78 (*R*)
2	H	Et	Ph	(*S*)-PROPRAPHOS	2.2	16.5	71 (*S*)
	H	Et	Ph	(*R*)-PROPRAPHOS	1.7	13.1 1	61 (*R*)
	H	Et	Ph	(*S*)-cyclopentyl-PROPRAPHOS	1.5	6.5	59 (*S*)
	H	Et	Ph	(*S,S*)-BPPM	1.6	19.6	**86 (*S*)**
	H	Et	Ph	(*R,R*)-DIOP	1.8	9.8	59 (*S*)
	H	Et	Ph	(*R*)-Ph-β-Glup-OH	3.2	22.0	71 (*R*)

Conditions: 25 °C, 1 bar H_2-pressure, 15 ml methanol, 1 mmol substrate, 0.01 mmol [Rh(cod)L]BF_4, for R^1, R^2, R^3 see Scheme 5

An interesting aspect should be given by a comparison of hydrogenation results of unsaturated amino acid[12,14], aminophosphonic acid[15,16] and aminophosphinic acid derivatives.

The Figures 1 and 2 clearly indicate a trend of the activities and enantioselectivities for the ligand (*S*)-PROPRAPHOS in methanol. Both the activities and selectivities decrease in the order of the aminocarboxylic, aminophosphonic and aminophosphinic acid precursors. The sterical effect of the tetrahedral phenylphosphino, methylphosphino and phosphono groups in contrast to the planar carboxylic group may be responsible for these results (Scheme 6).



SCHEME 6 Structure of the phenylphosphinic, methylphosphinic, phosphonic and carboxylic acid ester group

2. Hydrogenation in other organic solvents

It is well known, that selectivities and rates in asymmetric hydrogenation reactions strongly depend on the solvent used. Normally, the asymmetric catalytic hydrogenation proceeds as well as in polar and apolar solvents. Therefore, the unsaturated aminophosphinic acid and their methyl and ethyl ester derivatives were hydrogenated in methanol, dichlo-

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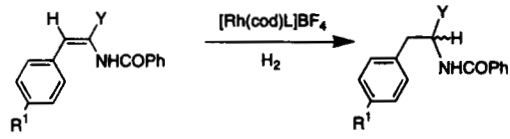

$Y = COOR^2, P(O)(OR^2)_2, P(O)R^3(OR^2)$

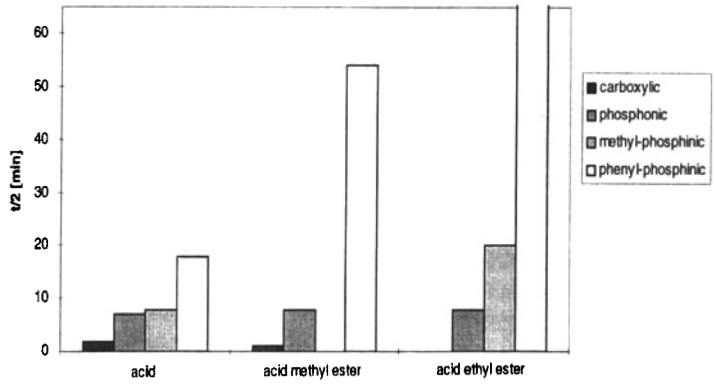

FIGURE 1 Halflifes of hydrogenation with (*S*) PROPRAPHOS as ligand of the precursors of amino, aminophosphonic and aminophosphinic acid derivatives

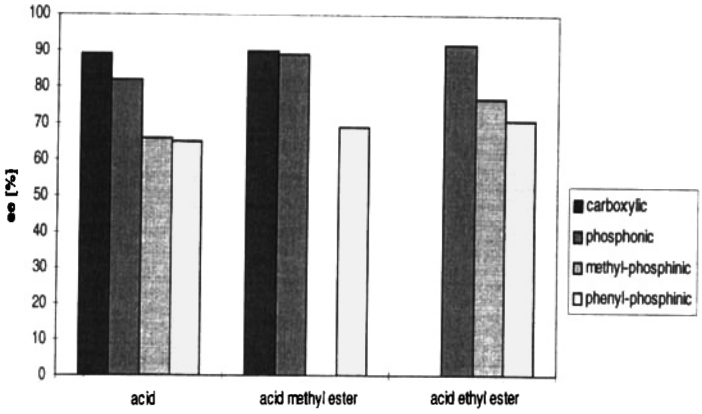

FIGURE 2 Enantioselectivities of the hydrogenations of the precursors of amino, aminophosphonic and aminophosphinic acid derivatives with (*S*)-PROPRAPHOS as ligand

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romethane, tetrahydrofuran, benzene, toluene, dioxane and 1,2-dimethoxyethane. The results are summarized in Table II.

TABLE II Hydrogenation results of (*E*)-(1-*N*-benzoylamino-2-phenyl)vinyl-phenylphosphinic acid and their esters by use of different catalysts

	R^1	R^2	R^3	*solvent*	*L – (S)-PPP*			*L – (S,S)-BPPM*		
					$t_{1/2}$ [h]	t [h]	ee_C [%] (S)	$t_{1/2}$ [h]	t [h]	ee_C [%] (S)
12	H	H	Ph	methanol	0.2	0.9	56	0.3	1.4	81
	H	H	Ph	dioxane	0.4	3.0	20	0.2	1.5	69
	H	H	Ph	dichloromethane	0.3	1.5	63	0.4	2.2	76
	H	H	Ph	tetrahydrofuran	0.2	1.0	10	0.3	2.1	14[a]
	H	H	Ph	benzene	1.2	5.5	19	2.0	8.2	70
	H	H	Ph	toluene	2.0	15.3	18	2.4	11.2	76
7	H	Me	Ph	methanol	0.6	3.4	76	0.1	1.0	86
	H	Me	Ph	dioxane	0.2	10.2	32	0.1	0.9	87
	H	Me	Ph	1,2-dimethoxyethane	2.3	10.2	67	0.4	2.5	84
	H	Me	Ph	dichloromethane	0.5	2.8	83	0.8	3.9	79
	H	Me	Ph	tetrahydrofuran	1.8	15.3	19	0.6	3.0	34
	H	Me	Ph	benzene	0.3	1.7	43	0.8	3.4	90
	H	Me	Ph	toluene	2.0	17.3	26	0.6	2.8	83
2	H	Et	Ph	methanol	0.7	3.8	75	0.2	1.9	87
	H	Et	Ph	dioxane	3.0	24.0	23	0.2	1.6	90
	H	Et	Ph	dichloromethane	0.7	11.7	79	0.3	1.7	79
	H	Et	Ph	tetrahydrofuran	5.0	28.8	18	0.5	11.9	69
	H	Et	Ph	benzene	0.3	1.5	31	0.5	2.4	91
	H	Et	Ph	toluene	2.5	20.4	25	1.2	6.3	82

a. (*R*)-configuration. Conditions : 25 °C, 1 bar H_2-pressure, 7.5 ml organic solvent, 0.5 mmol substrate, 0.01 mmol $[Rh(cod)L]BF_4$, for R^1, R^2, R^3 see Scheme 5

In each case, hydrogenations with the ligand (*S,S*)-BPPM gave better enantioselectivities than with (*S*)-PROPRAPHOS. In general, the PROPRAPHOS-ligand should be used in the solvents methanol and dichloromethane, whereas ee_C-values > 80 % for the esters were observed with (*S,S*)-BPPM in all tested solvents, except tetrahydrofuran. Hydrogenations in acetonitrile gave no hydrogenation products of the substrates.

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3. Hydrogenation reactions under variation of the substrate to catalyst ratios

A high substrate to catalyst ratio is decisive for the use of a catalytic reaction under industrial conditions. Therefore, we tried to increase the substrate to catalyst ratio without loss of ee.

Table III shows the dependence of enantioselectivity and activity of the catalysts [Rh(cod)(*S,S*)-bppm]BF_4 and [Rh(cod)(*S*)-propraphos]BF_4 on the substrate to catalyst ratio within the hydrogenation of the unsaturated aminophosphinic acid derivatives.

TABLE III Hydrogenation results of the unsaturated aminophosphinic acid derivatives with change of the substrate to catalyst ratio

	R^1	R^2	R^3	substrate:cat.	*L – (S)-PPP*			*L – (S,S)-BPPM*		
					$t_{1/2}$ [h]	T [h]	ee_C [%] (S)	$t_{1/2}$ [h]	t [h]	ee_C [%] (S)
12	H	H	Ph	50 : 1[a]	0.2	0.9	56	0.3	1.4	81
	H	H	Ph	100 : 1[b]	0.3	2.1	65	0.5	4.2	76
	H	H	Ph	200 : 1[c]	1.8	12.9	18	1.7	24.8	79
7	H	Me	Ph	50 : 1	0.6	3.4	76	0.1	1.0	86
	H	Me	Ph	100 : 1	0.9	4.2	69	1.0	12.6	85
	H	Me	Ph	200 : 1	3.5	6.7	52	1.4	26.3	78
	H	Me	Ph	300 : 1[d]	5.8	44.2	49	4.7	41.2	63
2	H	Et	Ph	50 : 1	0.7	3.8	75	0.2	1.9	87
	H	Et	Ph	100 : 1	2.2	16.5	71	0.7	2.0	87
	H	Et	Ph	200 : 1	5.0	19.0	43	0.8	5.3	86
	H	Et	Ph	300 : 1	6.5	24.0	46	4.0	23.0	61
10	H	Et	Me	50 : 1	0.3	9.9	77	0.1	0.9	93
	H	Et	Me	100 : 1	1.7	18.0	64	0.2	1.0	94
	H	Et	Me	200 : 1	3.3	21.0	66	1.6	3.0	94

a. 0.5 mmol substrate, 7.5 ml methanol.
b. 1.0 mmol substrate, 15 ml methanol.
c. 2.0 mmol substrate, 30 ml methanol.
d. 3.0 mmol substrate, 45 ml methanol.
Conditions : 25 °C, 1 bar H_2-pressure, 0.01 mmol cat.=[Rh(cod)L]BF_4, for R^1, R^2, R^3 see Scheme 5

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Although [Rh(cod)(*S,S*)-bppm]BF_4 was the more active catalyst, we measured a lower activity when the substrate to catalyst ratio was increased (see Table III). In general, the loss of enantioselectivity was accompanied by a loss of activity. Good results were obtained up to a substrate to catalyst ratio of 100 for the ligand (*S*)-PROPRAPHOS, and 200 for (*S,S*)-BPPM. We think that lower enantioselectivities with higher substrate to catalyst ratios (>200) are caused by impurities in the substrate (halogenide from former steps of the substrate synthesis). Again, the ee_C-values were higher for the esters than for the corresponding acids.

4. Dependence of the activity and enantioselectivity on temperature and hydrogen pressure

The consequences of a variation of the reaction conditions, temperature and hydrogen pressure have been described for various catalyst systems, but no general trend could be found for activities or enantioselectivities.[17]

We observed incomplete hydrogen uptake, rhodium precipitation and long reaction times especially at higher temperatures (between 30 and 50 °C, solvents : dioxane, 1,2-dimethoxyethane). In addition, decreasing enantioselectivities or poor reproducibility of the ee_C-values were usually observed.

Increasing hydrogen pressure often increases the activity, but also decreases the selectivity. We examined experiments using pressures up to 50 bar. Although the reaction rate increased, the enantioselectivities decreased significantly in the case of the ligand (*S*)-PROPRAPHOS, and less in the case of (*S,S*)-BPPM.

5. Hydrogenations of modified substrates

The unsaturated substrates used were distinguished by varying the substituents at the 2-phenyl group (R^1) and at the phosphorus atom (R^3).

Table IV shows the influence of the substituent R^1 on the rate and the selectivity of the hydrogenation.

Once more, the ligand (*S,S*)-BPPM was more active and selective than (*S*)-PROPRAPHOS (*t*/2 0.1...0.3 h vs. 0.2...2.3 h and 76...90 % ee_C vs. 56...77 % ee_C). However, in general, no significant influence of electron-donating (R^1 = Me, R^1 = iPr) or electron-withdrawing (R^1 = F, $R^1 = NO_2$) substituents were observed on the activity and the enantioselectivity, respectively.

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TABLE IV Influence of the substitution on the hydrogenation results of the various (*E*)-(1-*N*-benzoylamino-2-aryl)vinyl-phenylphosphinic acids and their esters

	R^1	R^2	R^3	*L – (S)-PPP*			*L – (S,S)-BPPM*		
				$t_{1/2}$ [h]	t [h]	ee_C [%] (S)	$t_{1/2}$ [h]	t [h]	ee_C [%] (S)
12	H	H	Ph	0.2	0.9	56	0.3	1.4	81
13	F	H	Ph	0.2	0.9	65	0.1	0.9	76
14	Me	H	Ph	0.3	1.0	70	0.2	0.7	80
7	H	Me	Ph	0.6	3.4	76	0.1	1.0	86
9	F	Me	Ph	0.6	3.3	77	0.1	0.6	90
8	Me	Me	Ph	1.0	13.0	68	0.2	1.3	89
2	H	Et	Ph	0.7	3.8	75	0.2	1.9	87
5	F	Et	Ph	1.0	6.2	64	0.3	2.6	87
6	NO_2	Et	Ph	0.7	5.0	60	0.3	2.6	81
3	Me	Et	Ph	2.0	10.6	60	0.2	2.4	85
4	*i*Pr	Et	Ph	2.3	16.8	60	0.3	1.8	87

Conditions : 25 °C, 1 bar H_2-pressure, 7.5 ml methanol, 0.5 mmol substrate, 0.01 mmol $[Rh(cod)L]BF_4$, for R^1, R^2, R^3 see Scheme 5

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The substituent at the phosphorus atom, which is situated more closely to the reaction center, has more influence on the enantioselectivity. The results are compiled in Table V. The hydrogenation of the unsaturated compounds with the small methyl group as substituent at the phosphorus atom gave the highest rate and best enantioselectivity. Similar rates and ee's were observed with the P-methyl and P-phenyl derivatives in the series of the ethyl esters. However, the *n*-butyl derivative gave lower ee and slower rates. In order to ascertain whether sterical and/or electronical effects are responsible, more P-alkyl and P-aryl derivatives have to be tested.

TABLE V Influence of the substitution on the hydrogenation results of the various (*E*)-(1-*N*-benzoylamino-2-phenyl)vinyl-phenyl(or alkyl)phosphinic acid and their esters

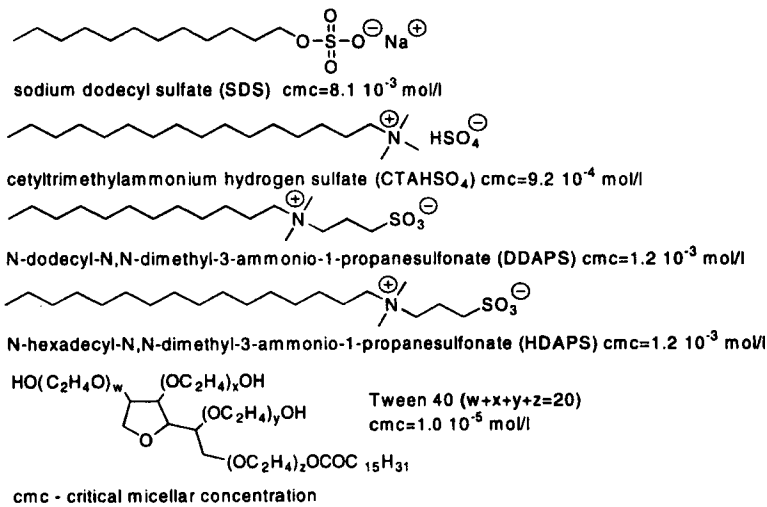
	R^1	R^2	R^3	*L – (S)-PPP*			*L – (S,S)-BPPM*		
				$t_{1/2}$ [h]	t [h]	ee_C [%] (S)	$t_{1/2}$ [h]	t [h]	ee_C [%] (S)
12	H	H	Ph	0.2	0.9	56	0.3	1.4	81
15	H	H	Me	0.1	0.5	66	0.1	0.3	90
7	H	Me	Ph	0.6	3.4	76	0.1	1.0	86

	R^1	R^2	R^3	*L – (S)-PPP*			*L – (S,S)-BPPM*		
				$t_{1/2}$ [h]	t [h]	ee_C [%] (S)	$t_{1/2}$ [h]	t [h]	ee_C [%] (S)
2	H	Et	Ph	0.7	3.8	75	0.2	1.9	87
10	H	Et	Me	0.3	9.9	77	0.1	0.9	93
11	H	Et	*n*Bu	3.0	21.9	39	0.7	11.5	67

Conditions : 25 °C, 1 bar H_2-pressure, 7.5 ml methanol, 0.5 mmol substrate, 0.01 mmol $[Rh(cod)L]BF_4$, for R^1, R^2, R^3 see Scheme 5

6. Hydrogenations in aqueous micellar media

Hydrogenations were normally carried out in organic solvents, mostly in alcohols. However, water would be an attractive alternative, because it is a non-toxic and non-polluting solvent.[18] In general, hydrogenation reactivities and enantioselectivities are lower in water than in organic solvents.[19] Nevertheless, activity and selectivity increase if the reaction is carried out with addition of a surfactant.[18a,20] The influence of the amphiphiles seems to be connected with the ability to form micelles and to solubilize substrate and complex, which are both slightly soluble in water. Scheme 7 shows surfactants that have been used for the asymmetric catalytic hydrogenation of α-aminophosphinic acid precursors in aqueous micellar media.



SCHEME 7 Surfactants used in hydrogenation reactions

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For the hydrogenation in this system we used the catalyst with the ligand (*S,S*)-BPPM. Initial experiments indicated, that the reaction could be carried out most efficiently with a surfactant:substrate:catalyst ratio of 100:50:1. We hydrogenated the substrate acid as the sodium salt because of its suitable solubility in water.

Table VI exhibits the results for the hydrogenations in aqueous micellar media in the presence of different surfactants (anionic, cationic, zwitterionic and non-ionic). The high enantiomeric excesses (>90 %) for the substrates used, are the conspicuous result. Unfortunately, we often observed no quantitative conversion, even after 20 h.

The experiments with the cationic ($CTAHSO_4$ – cetyltrimethylammonium hydrogen sulfate) and the anionic (SDS – sodium dodecyl sulfate) surfactants were especially successful. Here, we had over all (ee_C and conversion) a high yield of the optical active product. The substrate esters with $R^1 = H$ gave the best results. Nearly 100 % ee_C of compound **10** ($R^1 = H$, $R^2 = Et$, $R^3 = Me$) was obtained.

TABLE VI Hydrogenation results of unsaturated α-aminophosphinic acid derivatives in water in presence of various surfactants

substrate	R^1	R^2	R^3	*solvent – water*		
				t [h]	*ee_C [%] (S)*	*Conversion [%]*
				SDS : sub. : cat. = 100 : 50 : 1		
12	H	H	Ph	6.5[a)]	53[a]	–
7	H	Me	Ph	2.6	**97**	96
8	Me	Me	Ph	18.0	**97**	80
2	H	Et	Ph	2.0	**96**	100
5	F	Et	Ph	18.0	**96**	66
3	Me	Et	Ph	19.0	**96**	100
4	*i*Pr	Et	Ph	18.0	**93**	95
10	H	Et	Me	0.3	**98**	100
				$CTAHSO_4$: sub. : cat. = 100 : 50 : 1		
7	H	Me	Ph	3.5	**97**	85
8	Me	Me	Ph	18.0	**97**	30
2	H	Et	Ph	18.0	**95**	95
5	F	Et	Ph	22.0	79	65

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substrate	R^1	R^2	R^3	*solvent – water*		
				t [h]	*ee$_C$ [%] (S)*	*Conversion [%]*
4	*i*Pr	Et	Ph	19.0	**93**	75
10	H	Et	Me	1.5	**99**	100
				Tween 40 : sub. : cat. = 100 : 50 : 1		
7	H	Me	Ph	9.0	81	95
8	Me	Me	Ph	8.0	88	50
2	H	Et	Ph	20.0	29	85
5	F	Et	Ph	21.0	81	62
4	*i*Pr	Et	Ph	19.0	47	40
10	H	Et	Me	25.0	**97**	100
				HDAPS : sub. : cat. = 100 : 50 : 1		
7	H	Me	Ph	5.0	**93**	83
8	Me	Me	Ph	20.0	89	50
2	H	Et	Ph	18.0	78	60
5	F	Et	Ph	18.0	86	62
4	*i*Pr	Et	Ph	7.0	86	80

Conditions : 25 °C, 1 bar H_2-pressure, 7.5 ml water, 1 mmol surfactant, 0.5 mmol substrate, 0.01 mmol [Rh(cod)(*S,S*)-bppm]BF_4, for R^1, R^2, R^3 see Scheme 5

[a] addition of 0.1 N NaOH, substrate acid were hydrogenated as sodium salt

Figure 3 shows a comparison of the best hydrogenation results in representative organic solvents and in aqueous micellar media.

In general, we found higher enantiomeric excesses in aqueous micellar media compared to organic solvents (I-III and IV, V). Nevertheless, if we consider the conversion of the hydrogenation, the reaction in water/SDS gave a higher yield of optically active product than in organic solvents.

C. Synthesis of Free α-Aminophosphinic Acids

After separation of the hydrogenation product and catalyst (and surfactant), we obtained the *N*-protected α-aminophosphinic acid derivatives. We prepared the free α-aminophosphinic acid by hydrolytical removal of the benzoyl group with half concentrated hydrochloric acid. The obtained hydrochloride was converted with butylene oxide into the α-aminophosphinic acid (see Scheme 8).

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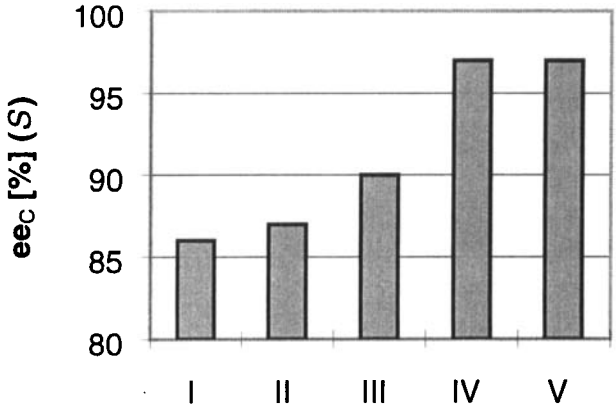
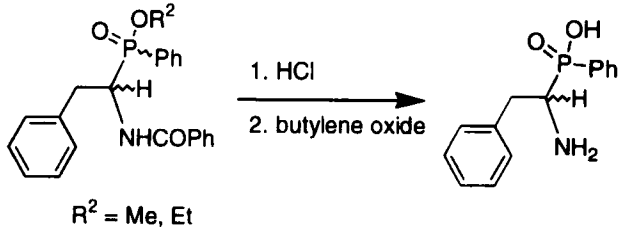


FIGURE 3 Enantioselectivities of the hydrogenation in organic solvent and aqueous micellar media. Solvent : I methanol, II dioxane, III benzene, IV water/SDS, V water/CTAHSO$_4$



SCHEME 8 Synthesis of the free α-aminophosphinic acid

D. NMR Spectra

For structure elucidation and characterization of compounds **2–29** the ^{1}H, ^{13}C and ^{31}P spectra have been recorded. In some cases, for the unambiguous assignment of signals in the aromatic part, recording of DEPT and 2D-COR spectra was necessary. Because of diastereomeric mixtures in the case of compounds **16–25** we found a doubling of signals. An outstanding feature of the ^{1}H as well as ^{13}C spectra is the splitting of various signals due to the coupling with the phosphorus atom. Some characteristic couplings or ranges of couplings, respectively, are summarized in Table VII.

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TABLE VII Coupling constants $J_{H,H}$, $J_{P,C}$ and $J_{F,C}$ of the substrates and products

coupling constants	***2 – 15***	***16 – 29***
$^{3}J_{OCH2,CH3}$	7.0 – 7.2	7.0 – 7.1
$^{3}J_{CH2,CH3}$	7.2 (**11**)	7.5 (**25**)
$^{2}J_{P,CH3}$	15.0 – 15.1	13.7 – 14.7
$^{3}J_{P,-OCH3}$	11.0 – 11.3	10.7 – 11.0
$^{3}J_{P,=CH-}$	13.5 – 15.0	–
$^{3}J_{P,NH}$	3.2 – 4.5	10.0
$^{1}J_{P,=C<}$	135.0 – 154.8	–
$^{1}J_{P,CH}$	–	96.5 – 115.4
$^{1}J_{P,CH3}$	100.8 – 104.0	88.8 – 91.6
$^{1}J_{P,C-1'}$	140.5 – 141.2	122.3 – 125.8
$^{2}J_{P,=CH-}$	18.0 – 22.1	–
$^{2}J_{P,CH2}$	–	1.5 – 7.0
$^{2}J_{P,OCH3}$	5.7–6.0	5.7 – 7.6
$^{2}J_{P,OCH2}$	5.7 – 6.5	6.7 – 8.2
$^{2}J_{P,C-2'}$	10.3 – 10.5	9.7 – 10.2
$^{3}J_{P,C-1}$	14.7 – 16.4	11.0 – 13.6
$^{3}J_{P,OCH2CH3}$	6.0 – 6.7	5.3 – 6.0
$^{3}J_{P,C-3'}$	13.4 – 13.9	12.5 – 12.8
$^{3}J_{P,CO}$	1.5 – 3.3	2.9 – 4.8
$^{4}J_{P,C-4'}$	2.7 – 3.0	2.7 – 2.8
$^{1}J_{F,C-4}$	250.2 – 251.0	243.2 – 245.1
$^{2}J_{F,C-3}$	21.8 – 22.1	21.0 – 21.9
$^{3}J_{F,C-2}$	7.2 (**5**)	8.0 (**19**)
$^{4}J_{F,C-1}$	3.3 (**5**)	3.2 – 3.3

The couplings $^{3}J_{P,=CH}$ of about 14 Hz for compounds **2–15** prove the *cis*-arrangement of the H and P at the C=C double bond and, therefore, the existence of the *E*-isomers. In the case of *trans*-arrangement (*Z*-configuration) a higher coupling constant should be expected.[21] Couplings of carbon to the phosphorus were found up to four bonds. The coupling constants $^{1}J_{P,CH}$ and $^{2}J_{P,CH2}$ for the diastereomeric compounds are dependent on the configuration at the phosphorus atom. In comparison to the NMR data of the analogous phosphonic acid derivatives,[22] the cou-

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plings $^{1}J_{P,=C<}$ and $^{1}J_{P,\underline{C}H}$ of the phosphinic acid derivatives were found to be significantly lowered ($^{1}J_{P,=C<} \approx$ 135–154.8 (**2–15**), 207.5–212.6 (Table II in Ref. 22); $^{1}J_{P,\underline{C}H} \approx$ 96.5–115.4 (**16–29**), 155.8–157.5 (Table II in Ref. 22) (Note : The ranges for $^{2}J_{\underline{C}H=,P}$ and $^{3}J_{C\text{-}1,P}$ (compounds **2–11**) given in Table II of Ref. 22 must be changed, $^{2}J_{\underline{C}H=,P} \approx$ 21.0–22.9 Hz and $^{3}J_{C\text{-}1,P} \approx$ 18.5–19.1 Hz, due to the assignment for C-1 and =CH- of the phosphonate **9** have to be reversed).

SUMMARY

We described the preparation of 11 new unsaturated α-aminophosphinic acid derivatives based on a method by BROVARETS.[6] For the first time these compounds were successfully used as substrates for the asymmetric catalytic hydrogenation to enantiomerically enriched α-aminophosphinic acids, now readily available. The enantioselectivity and activity is lower than for α-amino or α-aminophosphonic acid substrates. We found optimal conditions for the reaction by variation of the type of catalyst, the solvent, the substrate-catalyst ratio, temperature and hydrogen pressure. Best enantioselectivities (up to 99 %) were reached in aqueous micellar media. The free α-aminophosphinic acids are available by hydrolytical removal of the *N*-protective group.

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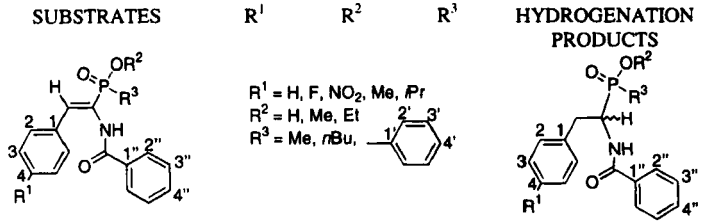
EXPERIMENTAL

Melting points were taken on a Kofler/Boetius apparatus. IR-spectra were recorded in KBr pellets on a Nicolet Magna 550 spectrometer. ^{1}H NMR-, ^{13}C NMR- (both relative to $Si(CH_3)_4$) and ^{31}P NMR-spectra (relative to 85% H_3PO_4) were recorded on Bruker AC 250, ARX 300 and ARX 400 spectrometers. Calibration of the ^{1}H and ^{13}C spectra was carried out by means of solvent peaks ($CDCl_3$: $\delta^{1}H = 7.25$; $\delta^{13}C = 77.0$). The coupling constants were determined using Gaussian multiplication and first-order analysis. The enantiomeric excesses were determined for the esters by HPLC (chiral stationary phase : Chiralpak AD, column : 250x4.6 mm^2, DAICEL; eluent : hexane/ethanol (9/1); Liquid Chromatograph 1090, Hewlett Packard) and for the acids by capillary electrophoresis (boric acid

buffer, 10 mM β-cyclodextrin, 0.05 % polyvinylalcohol, pH 9.6, U = 15 kV, capillary : 30 cm × 50 μm, BioFocus 3000 Capillary Electrophoresis system, BIORAD).



2	H	Et	Ph	**16**
3	Me	Et	Ph	**17**
4	*i*Pr	Et	Ph	**18**
5	F	Et	Ph	**19**
6	NO_2	Et	Ph	**20**
7	H	Me	Ph	**21**
8	Me	Me	Ph	**22**
9	F	Me	Ph	**23**
10	H	Et	Me	**24**
11	H	Et	*n*Bu	**25**
12	H	H	Ph	**26**
13	F	H	Ph	**27**
14	Me	H	Ph	**28**
15	H	H	Me	**29**

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2-*N*-Benzoylamino-2,3-dichloro-3-aryl-propionic acids

0.04 mol of the corresponding 2-*N*-benzoylamino-3-aryl-acrylic acid was suspended in 40 ml of carbon tetrachloride. Then 100 ml of a saturated solution of chlorine in carbon tetrachloride was added. The suspension was stirred for 24 hours at room temperature. The solid was filtered off, washed with carbon tetrachloride and dried. The crude products was quickly used for the following reactions without recrystallization.

(*E*)-(1-*N*-Benzoylamino-2-aryl)vinyl-aryl(or alkyl)phosphinic acid esters 2–11

25 mmol of dialkylaryl(or alkyl)phosphonite was added slowly at room temperature to a stirred suspension of 25 mmol of the 2-*N*-benzoylamino-2,3-dichloro-3-aryl-propionic acid in 40 ml of benzene. The stirring was continued up to the end of gas evolution. After standing overnight the formed precipitate was filtered off and the filtrate was concen-

trated under reduced pressure. Ether was added to the residue to yield a precipitation. The recrystallization was carried out in aqueous ethanol.

(*E*)-(1-*N*-Benzoylamino-2-phenyl)vinyl-phenylphosphinic acid ethylester 2

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-phenyl-propionic acid and diethyl phenylphosphonite.

Yield : 4.6 g (47 %); mp: 153–155 °C (lit.[6] 158–160 °C); anal. calc. for $C_{23}H_{22}NO_3P$: C 70.58; H 5.67; N 3.58; P 7.91; found : C 70.54; H 5.44; N 3.6; P 7.95, FT-IR : 1662, 1440, 1286, 1026; for approximate NMR data see the analogous methyl ester **7** and Table VII.

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(*E*)-(1-*N*-Benzoylamino-2-(4-methylphenyl)vinyl-phenylphosphinic acid ethylester 3

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-(4-methylphenyl)-propionic acid and diethyl phenylphosphonite.

Yield : 2.9 g (29 %); mp: 177–180 °C; anal. calc. for $C_{24}H_{24}NO_3P$: C 71.10; H 5.97; N 3.46; P 7.64; found : C 70.39; H 5.95; N 3.48; P 7.76, FT-IR : 1669, 1439, 1280, 1023; ^{1}H NMR ($CDCl_3$) : δ 1.37 (t, 3H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3); 2.28 (s, 3H, Ar-CH_3); 4.20 (m, 2H, OCH_2); 7.07 (m, 2H, H-3); 7.31 (d, 1H, $J_{P,H}$ = 14.8 Hz, =CH-); 7.34–7.56 (m, 8H, H-2, H-3′, H-3″, H-4′, H-4″); 7.65 (br d, $J_{P,H}$ = 3.2 Hz, 1H, NH); 7.68–7.75 (m, 2H, H-2″); 7.81–7.91 (m, 2H, H-2′); ^{13}C NMR ($CDCl_3$): δ 16.4 (d, $J_{P,C}$ = 6.5 Hz, CH_3); 21.3 (Ar-CH_3); 61.7 (d, $J_{P,C}$ = 6.0 Hz, OCH_2); 124.7 (d, $J_{P,C}$ = 152.0 Hz, =C<); 127.2 (C-2″); 128.5 (d, $J_{P,C}$= 13.5 Hz, C-3′); 128.6 (C-3″); 129.2 (C-3); 129.5 (C-2); 129.9 (d, $J_{P,C}$ = 140.8 Hz, C-1′); 131.3 (d, $J_{P,C}$= 16.0 Hz, C-1); 131.6 (d, $J_{P,C}$ = 10.3 Hz, C-2′); 131.8 (C-4″); 132.4 (d, $J_{P,C}$ = 2.8 Hz, C-4′); 133.9 (C-1″); 138.6 (d, $J_{P,C}$ = 20.3 Hz, =CH-); 139.6 (C-4); 164.9 (CO); ^{31}P NMR ($CDCl_3$): δ 29.2.

(*E*)-(1-*N*-Benzoylamino-2-(4-isopropylphenyl))vinyl-phenylphosphinic acid ethylester 4

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-(4-isopropylphenyl)propionic acid and diethyl phenylphosphonite.

Yield : 3.5 g (32 %); mp: 164–166 °C; anal. calc. for $C_{26}H_{28}NO_3P$: C 72.04; H 6.51; N 3.23; P 7.14; found : C 71.69; H 6.37; N 3.19; P 7.12, FT-IR : 1671, 1439, 1281, 1023; ^{1}H NMR ($CDCl_3$): δ 1.18 (d, 6H, $J_{CH3,CH}$ = 7.0 Hz, CH_3); 1.36 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3); 2.84 (sept, 3H, $J_{CH,CH3}$ = 7.0 Hz, C<u>H</u>$(CH_3)_2$); 4.21 (m, 2H, OCH_2); 7.13 (m, 2H, H-3); 7.33 (d, 1H, $J_{P,H}$ = 14.6 Hz, =CH-); 7.36–7.55 (m, 8H, H-2, H-3′, H-3″, H-4′, H-4″); 7.59 (d, $J_{P,H}$ = 3.2 Hz, 1H, NH); 7.69–7.75 (m, 2H, H-2″); 7.82–7.91 (m, 2H, H-2′); ^{13}C NMR ($CDCl_3$) : δ 16.4 (d, $J_{P,C}$= 6.5 Hz, CH_3); 23.60, 23.62 (CH(<u>C</u>$H_3)_2$); 33.9 (<u>C</u>H$(CH_3)_2$); 61.7 (d, $J_{P,C}$ = 6.0 Hz, OCH_2); 124.0 (d, $J_{P,C}$ = 152.0 Hz, =C<); 126.6 (C-3); 127.2 (C-2″); 128.5 (d, $J_{P,C}$ = 13.8 Hz, C-3′); 128.6 (C-3″); 129.7 (C-2); 130.5 (d, $J_{P,C}$ = 141.0 Hz, C-1′); 131.6 (d, $J_{P,C}$ = 10.4 Hz, C-2′); 131.7 (d, $J_{P,C}$ = 15.8 Hz, C-1); 131.8 (C-4″); 132.4 (d, $J_{P,C}$ = 3.0 Hz, C-4′); 133.9 (C-1″); 138.9 (d, $J_{P,C}$ = 20.2 Hz, =CH-); 150.6 (C-4); 165.1 (CO); ^{31}P NMR ($CDCl_3$) : δ 29.3.

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(*E*)-(1-*N*-Benzoylamino-2-(4-fluorophenyl))vinyl-phenylphosphinic acid ethylester 5

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-(4-fluorophenyl)propionic acid and diethyl phenylphosphonite.

Yield : 3.4 g (33 %); mp: 193–194 °C; anal. calc. for $C_{23}H_{21}FNO_3P$: C 67.48; H 5.17; N 3.42; P 7.57; found : C 67.5; H 5.16; N 3.37; P 7.75, FT-IR : 1665, 1439, 1282, 1234, 1021; ^{1}H NMR ($CDCl_3$) : δ 1.36 (t, 3H, $J_{CH3,CH2}$ = 7.1 Hz, CH_3); 4.20 (m, 2H, OCH_2); 6.95 (m, 2H, H-3); 7.27 (d, 1H, $J_{P,H}$ = 15.0 Hz, =CH-); 7.35–7.57 (m, 8H, H-2, H-3′, H-3″, H-4′, H-4″); 7.66 (br d, 1H, $J_{P,H}$ = 3.5 Hz, NH); 7.68–7.73 (m, 2H, H-2″); 7.80–7.89 (m, 2H, H-2′); ^{13}C NMR ($CDCl_3$) : δ 16.5 (d, $J_{P,C}$ = 6.5 Hz, CH_3); 61.9 (d, $J_{P,C}$ = 6.0 Hz, OCH_2); 115.5 (d, $J_{F,C}$= 21.9 Hz, C-3); 125.4 (d, $J_{P,C}$ = 151.0 Hz, =C<); 127.2 (C-2″); 128.6 (d, $J_{P,C}$ = 13.7 Hz, C-3′); 128.7 (C-3″); 129.5 (d, $J_{P,C}$ = 140.5 Hz, C-1′); 130.5 (dd, $J_{P,C}$= 15.3 Hz, $J_{F,C}$ = 3.3 Hz, C-1); 131.4 (d, $J_{F,C}$= 7.2 Hz, C-2); 131.7 (d, $J_{P,C}$ = 10.3 Hz, C-2′); 132.0 (C-4″); 132.6 (d, $J_{P,C}$ = 2.8 Hz, C-4′); 133.7 (C-1″); 136.9 (d, $J_{P,C}$ = 20.2 Hz, =CH-);163.0 (d, $J_{F,C}$ = 251.0 Hz, C-4); 165.5 (br, CO); ^{31}P NMR ($CDCl_3$): δ 29.1.

(*E*)-(1-*N*-Benzoylamino-2-(4-nitrophenyl))vinyl-phenylphosphinic acid ethylester 6

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-(4-nitrophenyl)-propionic acid and diethyl phenylphosphonite.

Yield : 1.3 g (12 %); mp: 168–172 °C; anal. calc. for $C_{23}H_{21}N_2O_3P$: C 63.3; H 4.85; N 6.42; P 7.10; found: C 63.26; H 4.72; N 6.31; P 7.49, FT-IR : 1670, 1439, 1348, 1024; ^{1}H NMR ($CDCl_3$): δ 1.40 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3); 4.23 (dq, 2H, $J_{P,CH2}$ = 7.7 Hz, $J_{CH3,CH2}$ = 7.0 Hz, OCH_2); 7.20 (d, 1H, $J_{P,H}$ = 15.0 Hz, =CH-); 7.39–7.60 (m, 8H, H-2, H-3′, H-3″, H-4′, H-4″); 7.67–7.73 (m, 2H, H-2″); 7.80–7.90 (m, 3H, H-2′, NH); 8.12 (m, 2H, H-3); ^{13}C NMR ($CDCl_3$): δ 16.5 (d, $J_{P,C}$ = 6.5 Hz, CH_3); 62.3 (d, $J_{P,C}$ = 6.0 Hz, OCH_2); 123.6 (C-3); 127.2 (C-2″); 128.8 (d, $J_{P,C}$ = 140.9 Hz, C-1′); 128.9 (C-3″); 128.9 (d, $J_{P,C}$ = 13.7 Hz, C-3′); 129.3 (d, $J_{P,C}$ = 146.6 Hz, =C<); 129.6 (C-2); 131.7 (d, $J_{P,C}$ = 10.5 Hz, C-2′); 132.5 (C-4″); 132.7 (d, $J_{P,C}$ = 19.2 Hz, =CH-); 133.1 (d, $J_{P,C}$ = 2.9 Hz, C-4′); 133.3 (C-1″); 141.4 (d, $J_{P,C}$ = 16.4 Hz, C-1); 147.3 (C-4); 164.1 (d, $J_{P,C}$ = 3.3 Hz, CO); ^{31}P NMR ($CDCl_3$) : δ 28.5.

(*E*)-(1-*N*-Benzoylamino-2-phenyl)vinyl-phenylphosphinic acid methylester 7

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-phenyl-propionic acid and dimethyl phenylphosphonite.

Yield : 2.9 g (31 %); mp: 156–158 °C (lit.[6] 140–142 °C); anal. calc. for $C_{22}H_{20}NO_3P$: C 70.02; H 5.34; N 3.71; P 8.21; found: C 69.89; H 5.38; N 3.71; P 8.05, FT-IR : 1663, 1440, 1289, 1019; ^{1}H NMR ($CDCl_3$): δ 3.81 (d, 3H, $J_{P,H}$ = 11.0 Hz, OCH_3); 7.22–7.29 (m, 3H, H-3, H-4); 7.35 (d, 1H, $J_{P,H}$ = 14.5 Hz, =CH-); 7.36–7.55 (m, 8H, H-2, H-3′, H-3″, H-4′, H-4″); 7.68–7.72 (m, 2H, H-2″); 7.73 (d, 1H, $J_{P,H}$ = 4.5 Hz, NH); 7.80–7.89 (m, 2H, H-2′); ^{13}C NMR ($CDCl_3$): δ 52.0 (d, $J_{P,C}$= 6.0 Hz, OCH_3); 125.6 (d, $J_{P,C}$ = 149.5 Hz, =C<); 127.3 (C-2″); 128.5 (C-3); 128.5 (d, $J_{P,C}$ = 13.9 Hz, C-3′); 128.6 (C-3″); 129.2 (d, $J_{P,C}$ = 141.2 Hz, C-1′), 129.4 (C-2, C-4); 131.7 (d, $J_{P,C}$ = 10.3 Hz, C-2′); 131.9 (C-4″); 132.6 (d, $J_{P,C}$ = 2.8 Hz, C-4′); 133.7 (C-1″); 133.9 (d, $J_{P,C}$ = 15.8 Hz, C-1), 139.1 (d, $J_{P,C}$ = 20.2 Hz, =CH-); 165.1 (CO); ^{31}P NMR ($CDCl_3$): δ 31.0.

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(*E*)-(1-*N*-Benzoylamino-2-(4-methylphenyl))vinyl-phenylphosphinic acid methylester 8

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-(4-methylphenyl)propionic acid and dimethyl phenylphosphonite.

Yield : 2.3 g (24 %); mp: 144–146 °C; anal. calc. for $C_{23}H_{22}NO_3P$: C 70.58; H 5.67; N 3.58; P 7.91; found : C 69.89; H 5.56; N 3.63; P 7.89, FT-IR : 1665, 1438, 1283, 1022; for approximate NMR data see the analogous ethyl ester **3** and Table VII.

(*E*)-(1-*N*-Benzoylamino-2-(4-fluorophenyl))vinyl-phenylphosphinic acid methylester 9

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-(4-fluorophenyl)propionic acid and dimethyl phenylphosphonite.

Yield : 2.6 g (26 %); mp: 155–157 °C; anal. calc. for $C_{22}H_{19}FNO_3P$: C 66.83; H 4.84; N 3.54; 7.83; found: C 66.90; H 4.78; N 3.52; P 8.04, FT-IR : 1670, 1440, 1284, 1021; for approximate NMR data see the analogous ethyl ester **5** and Table VII.

(*E*)-(1-*N*-Benzoylamino-2-phenyl)vinyl-methylphosphinic acid ethylester 10

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-phenyl-propionic acid and diethyl methylphosphonite. The crude product was purified by column chromatography. Eluent : ethyl acetate, $r_f = 0.13$.

Yield : 2.6 g (31 %); mp: 138–141 °C; anal. calc. for $C_{18}H_{20}NO_3P$: C 65.64; H 6.12; N 4.25; P 9.41; found: C 65.57; H 6.12; N 4.24; P 9.45, FT-IR : 1660, 1289, 1034; ^{1}H NMR ($CDCl_3$): δ 1.28 (t, 3H, $J_{CH3,CH2} = 7.0$ Hz, CH_3); 1.70 (d, 3H, $J_{P,H} = 15.0$ Hz, P-CH_3); 4.05 (m, 2H, OCH_2); 7.21 (d, 1H, $J_{P,H} = 13.8$ Hz, =CH-); 7.24–7.32 (m, 3H, H-3, H-4); 7.36–7.53 (m, 5H, H-2, H-3″, H-4″); 7.80–7.86 (m, 2H, H-2″); 8.07 (d, $J_{P,H} = 4.5$ Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 15.0 (d, $J_{P,C} = 104.0$ Hz, P-CH_3); 16.4 (d, $J_{P,C} = 6.5$ Hz, CH_3); 60.9 (d, $J_{P,C} = 6.3$ Hz, OCH_2); 127.4 (C-2″); 127.9 (d, $J_{P,C} = 141.8$ Hz, =C<); 128.6 (C-3, C-3′); 129.3 (C-2, C-4); 132.0 (C-4″); 133.4 (C-1″); 133.8 (d, $J_{P,C} = 15.0$ Hz, C-1); 137.1 (d, $J_{P,C} = 19.5$ Hz, =CH-); 165.7 (d, $J_{P,C} = 1.5$ Hz, CO); ^{31}P NMR ($CDCl_3$): δ 41.2.

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(*E*)-(1-*N*-Benzoylamino-2-phenyl)vinyl-*n*-butylphosphinic acid ethylester 11

Synthesis was started from 2-*N*-benzoylamino-2,3-dichloro-3-phenyl-propionic acid and diethyl *n*-butylphosphonite. The crude product was purified by column chromatography. eluent : ethyl acetate, $r_f = 0.31$.

Yield : 2.4 g (26 %); mp: 129–132 °C; anal. calc. for $C_{21}H_{26}NO_3P$: C 67.91; H 7.06; N 3.77; P 8.34; found : C 67.68; H 7.05; N 3.77; P 8.44, FT-IR : 1667, 1280, 1029; ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3H, $J_{CH3,CH2}$ = 7.2 Hz, P-CH_2-CH_2-CH_2-CH_3); 1.32 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3); 1.39 (m, 2H, P-CH_2-CH_2-CH_2-); 1.63 (m, 2H, P-CH_2-CH_2-); 1.96 (m, 2H, P-CH_2-); 4.09 (m, 2H, OCH_2); 7.14 (d, 1H, $J_{P,H}$ = 13.5 Hz, =CH-); 7.23–7.33 (m, 3H, H-3, H-4); 7.39–7.55 (m, 5H, H-2, H-3″, H-4″); 7.80–7.85 (m, 2H, H-2″); 7.87 (d, $J_{P,H}$ = 4.5 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$) : δ 13.5 (P-CH_2-CH_2-CH_2-CH_3); 16.5 (d, $J_{P,C}$ = 6.0 Hz, CH_3); 23.6 (d, $J_{P,C}$ = 4.0 Hz, P-CH_2-CH_2-); 23.8 (d, $J_{P,C}$ = 16.7 Hz, P-CH_2-CH_2-CH_2-); 28.2 (d, $J_{P,C}$= 101.0 Hz, P-CH_2-); 60.9 (d, $J_{P,C}$= 6.5 Hz, OCH_2); 126.6 (d, $J_{P,C}$ = 135.0 Hz, =C<); 127.4 (C-2″); 128.6 (C-3″); 128.7 (C-3); 129.2 (C-4); 129.3 (C-2); 132.0 (C-4″); 133.7 (C-1″); 134.2 (d, $J_{P,C}$ = 14.7 Hz, C-1); 136.5 (d, $J_{P,C}$ = 18.0 Hz, =CH-); 165.2 (d, $J_{P,C}$ = 2.0 Hz, CO); ^{31}P NMR ($CDCl_3$) : δ 44.2.

(*E*)-(1-*N*-Benzoylamino-2-aryl)vinyl-aryl(or alkyl)phosphinic acids 12–15

a) 10 mmol of the corresponding ester and 20 mmol bromotrimethylsilane were stirred in 20 ml of chloroform for 30 min at room temperature. The solvent and volatile reaction products were removed under reduced pressure. After the addition of aqueous ethanol to the residue the solution was concentrated *in vacuo*, and the acid precipitated as colorless crystals. The recrystallization was carried out from ethanol/water.

b) 10 mmol of the corresponding ester, 10 mmol chlorotrimethylsilane and 10 mmol sodium bromide were stirred in 30 ml of dry acetonitrile at room temperature for 1 hour. Then, the solution was evaporated to dryness and worked up as given in a.).

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(*E*)-(1-*N*-Benzoylamino-2-phenyl)vinyl-phenylphosphinic acid 12

Synthesis was started from **2** or **7**.

Yield : 2.8 g (74 %); mp: 95–98 °C; anal. calc. for $C_{21}H_{18}NO_3P \times H_2O$: C 66.14; H 5.29; N 3.67; P 8.12; found : C 66.09; H 5.29; N 3.65; P 7.76, FT-IR : 1649, 1440, 1185; for approximate NMR data see the analogous methyl ester **7** and Table VII.

After removal of the crystal water:

Mp : 163–166 °C (lit.[6] 168–170 °C); anal. calc. for $C_{21}H_{18}NO_3P$: C 69.42; H 4.99; N 3.86; P 8.53; found: C 69.44; H 4.95; N 3.87; P 9.16, FT-IR : 1684, 1438, 1198.

(*E*)-(1-*N*-Benzoylamino-2-(4-fluorophenyl))vinyl-phenylphosphinic acid 13

Synthesis was started from **5** or **9**.

Yield : 2.3 g (57 %); mp: 105–108 °C; anal. calc. for $C_{21}H_{17}FNO_3P \times H_2O$: C 63.16; H 4.80; N 3.51; P 7.76; found: C 63.11; H 4.78; N 3.54; P 7.60, FT-IR : 1649, 1439, 1196; for approximate NMR data see the analogous ethyl ester **5** and Table VII.

(*E*)-(1-*N*-Benzoylamino-2-(4-methylphenyl)vinyl-phenylphosphinic acid 14

Synthesis was started from **3** or **8**.

Yield : 3.3 g (83 %); mp: 102–104 °C; anal. calc. for $C_{22}H_{20}NO_3P \times H_2O$: C 66.83; H 5.61; N 3.54; P 7.83; found: C 66.65; H 5.78; N 3.59; P 7.75, FT-IR: 1651, 1439, 1185; for approximate NMR data see the analogous ethyl ester **3** and Table VII.

(*E*)-(1-*N*-Benzoylamino-2-phenyl)vinyl-methylphosphinic acid 15

Synthesis was started from **10**.

Yield : 2.1 g (71 %); mp: 168–170 °C; anal. calc. for $C_{16}H_{16}NO_3P$: C 63.75; H 5.35; N 4.65; P 10.28; found : C 63.11; H 5.47; N 4.61; P 10.36, FT-IR : 1676, 1172; for approximate NMR data see the analogous ethyl ester **10** and Table VII.

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Hydrogenation

Hydrogenation was performed usually under normal pressure (or necessaryly at higher hydrogen pressure) and at 25 °C (or necessaryly at other temperature). A suspension of 1 mmol of substrate (unsaturated compounds **2–15**) and 0.01 mmol of catalyst ([Rh(cod)L]BF_4, for L see Scheme 4) and in the case of hydrogenation in water 0.5 mmol of substrate, 0.01 mmol of catalyst and 1 mmol of surfactant (see Scheme 7) in 15 ml of deaerated solvent was stirred for 15 min under argon in a hydrogenation flask. Then, stirring was stopped, the argon replaced by hydrogen at atmospheric pressure, and the hydrogenation was started by stirring. The reaction was followed volumetrically. The reaction was continued up to the theoretically expected hydrogen uptake. The solvent was removed *in vacuo* (in the case of water, the mixture was extracted 3 times with 5 ml chloroform and then the organic phase was used for removal), and the residue was dissolved in a little dichloromethane/methanol (29/1) and filtered through a 3 cm plug of silica gel in order to remove the rhodium complex quantitatively. After concentration of the filtrate, the product was obtained in 90 – 96 % yield (in the case of water 70 – 95 %). The enantiomeric excess with respect to the formed center of chirality was determined by HPLC or by capillary electrophoresis.

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(1-*N*-Benzoylamino-2-phenyl)ethyl-phenylphosphinic acid ethylester 16

Synthesis was started from **2** by catalytical hydrogenation.

Mp : 134–137 °C; anal. calc. for $C_{23}H_{24}NO_3P$: C 70.22; H 6.15; N 3.56; P 7.87; found : C 70.15; H 6.17; N 3.53; P 7.84, $[\alpha]_D^{25}$ 53.3 (c = 0.13, CH_3OH, ee = 93 % (S)), FT-IR : 1661, 1439, 1025; for approximate NMR data see the analogous ethyl ester **24** and Table VII.

(1-*N*-Benzoylamino-2-(4-methylphenyl))ethyl-phenylphosphinic acid ethylester 17

Synthesis was started from **3** by catalytical hydrogenation.

Mp : 143–146 °C; anal. calc. for $C_{24}H_{26}NO_3P$: C 70.75; H 6.43; N 3.44; P 7.6; found: C 70.20; H 6.38; N 3.44; P 7.43, FT-IR : 1661, 1441, 1025; ^1H NMR ($CDCl_3$) : δ 1.16 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz), 1.30 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz)(2xCH_3); 2.21 (s, 3H), 2.25 (s, 3H)(2xAr-CH_3); 2.91–3.51 (m, 4H, 2xCH_2); 3.79–4.23 (m, 4H, 2xOCH_2); 5.13 (m, 2H, 2xCH);

6.92–7.08 (m, 6H, 2xH-2, 4xH-3); 7.15–7.26 (m, 4H, 2xH-2, 2xH-3″); 7.27–7.51 (m, 9H, 2xH-2″, 2xH-3″, H-4′, 2xH-4″, 2xNH); 7.52–7.60 (m, 1H, H-4″); 7.69–7.79 (m, 4H, 2xH-2′, 2xH-2″); 7.79–7.90 (m, 2H, 2xH-2′); ^{13}C NMR ($CDCl_3$): δ 16.37 (d, $J_{P,C}$ = 5.6 Hz), 16.42 (d, $J_{P,C}$ = 5.6 Hz)(2xCH_3); 20.89, 20.94 (2xAr-CH_3); 33.8 (d, $J_{P,C}$ = 1.8 Hz), 34.3 (d, $J_{P,C}$ = 6.5 Hz)(2xCH_2); 48.7 (d, $J_{P,C}$ = 114.5 Hz), 49.7 (d, $J_{P,C}$ = 107.5 Hz)(2xCH); 61.5 (d, $J_{P,C}$ = 7.1 Hz, OCH_2); 126.9, 127.1 (2xC-2″); 128.0 (C-3″); 128.2 (d, $J_{P,C}$ = 124.8 Hz, C-1′); 128.3 (C-3″); 128.3 (d, $J_{P,C}$ = 12.6 Hz), 128.7 (d, $J_{P,C}$ = 12.6 Hz)(2xC-3′); 128.86, 128.95, 129.0, 129.04 (2xC-2, 2xC-3); 129.1 (d, $J_{P,C}$ = 122.3 Hz, C-1′); 131.0, 131.3 (2xC-4″); 132.0 (d, $J_{P,C}$ = 9.8 Hz), 132.2 (d, $J_{P,C}$ = 10.2 Hz)(2xC-2′); 132.5 (d, $J_{P,C}$ = 2.7 Hz), 132.7 (d, $J_{P,C}$ = 2.7 Hz)(2xC-4′); 133.4 (d, $J_{P,C}$ = 13.1 Hz), 133.8 (d, $J_{P,C}$ = 11.8 Hz)(2xC-1); 134.2, 134.3 (2xC-1″); 136.0 (C-4); 166.9 (d, $J_{P,C}$ = 4.2 Hz), 167.1 (d, $J_{P,C}$ = 4.0 Hz)(2xCO); ^{31}P NMR ($CDCl_3$) : δ 39.7, 41.3.

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(1-*N*-Benzoylamino-2-(4-isopropylphenyl))ethyl-phenylphosphinic acid ethylester 18

Synthesis was started from **4** by catalytical hydrogenation.

Mp : 133–135 °C; anal. calc. for $C_{26}H_{30}NO_3P$: C 71.70; H 6.94; N 3.22; P 7.11; found : C 72.43, H 6.92; N 3.09; P 7.13, FT-IR : 1660, 1439, 1030; ^{1}H NMR ($CDCl_3$) : δ 1.16 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3); 1.18 (d, 12H, $J_{CH3,CH}$ = 7.0 Hz, CH_3); 1.27 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3); 2.81 (m, 2H, 2xC<u>H</u>$(CH_3)_2$); 2.98–3.50 (m, 4H, 2xCH_2); 3.84–4.16 (m, 4H, 2xOCH_2); 5.14 (m, 2H, 2xCH); 6.75 (d, 1H, $J_{P,H}$ = 10.0 Hz), 6.90 (d, 1H, $J_{P,H}$ = 10.0 Hz)(2xNH); 7.62–7.85 (m, 6H, 4xH-2′, 2xH-2″); 7.00–7.50 (m, 18H, 4xH-2, 2xH-2″, 4xH-3, 4xH-3″, 2xH-4′, 2xH-4″); ^{13}C NMR ($CDCl_3$) : δ 16.4 (d, $J_{P,C}$ = 6.0 Hz, CH_3); 23.9, 24.0 (2xCH(<u>C</u>$H_3)_2$); 33.61, 33.66 (2x<u>C</u>H$(CH_3)_2$); 34.0 (d, $J_{P,C}$ = 1.5 Hz, CH_2); 48.5 (d, $J_{P,C}$ = 114.5 Hz, CH); 61.5 (d, $J_{P,C}$ = 7.1 Hz, OCH_2); 126.3, 126.4 (2xC-3); 126.7, 127.0 (2xC-2″); 128.3, 128.4 (2xC-3″); 128.4 (d, $J_{P,C}$ = 124.8 Hz, C-1′); 128.4 (d, $J_{P,C}$ = 12.5 Hz, C-3′); 128.7 (d, $J_{P,C}$ = 12.5 Hz, C-3′); 129.1 (2xC-2); 131.1, 131.4 (2xC-4″); 132.1: (d, $J_{P,C}$= 9.7 Hz), 132.3 (d, $J_{P,C}$ = 10.0 Hz)(2xC-2′); 132.6 (d, $J_{P,C}$ = 2.8 Hz), 132.7 (d, $J_{P,C}$ = 2.8 Hz)(2xC-4′); 133.7 (d, $J_{P,C}$ = 12.0 Hz), 134.1 (d, $J_{P,C}$ = 11.0 Hz)(2xC-1); 134.3, 134.4 (2xC-1″); 147.1, 147.2 (2xC-4); 166.9 (d, $J_{P,C}$ = 4.5 Hz, CO); ^{31}P NMR ($CDCl_3$): δ= 39.7, 41.2.

(1-*N*-Benzoylamino-2-(4-fluorophenyl))ethyl-phenylphosphinic acid ethylester 19

Synthesis was started from **5** by catalytical hydrogenation.

Mp : 141–145 °C; anal. calc. for $C_{23}H_{23}FNO_3P$: C 67.15; H 5.63; N 3.40; P 7.53; found : C 66.78; H 5.31; N 3.26; P 7.44, FT-IR : 1661, 1439, 1216, 1029; for approximate NMR data see the analogous methyl ester **23** and Table VII.

(1-N-Benzoylamino-2-(4-nitrophenyl))ethyl-phenylphosphinic acid ethylester 20

Synthesis was started from **6** by catalytical hydrogenation.

Mp : 192–195 °C; anal. calc. for $C_{23}H_{23}N_2O_5P$: C 63.01; H 5.29; N 6.39; P 7.07; found : C 62.74; H 5.31; N 6.42; P 6.69, FT-IR : 1661, 1439, 1346, 1029; ^{1}H NMR ($CDCl_3$): δ 1.10 (t, 3H, $J_{CH3,CH2}$ = 7.1 Hz), 1.31 (t, 3H, $J_{CH3,CH2}$ = 7.1 Hz)(2xCH_3); 3.00–3.60 (m, 4H, 2xCH_2); 3.80–4.20 (m, 4H, 2xOCH_2); 5.10–5.30 (m, 2H, 2xCH); 7.14 (m, 2H, 2xH-3″); 7.25–7.62 (m, 15H, 4xH-2, 2xH-2″, 4xH-3′, 2xH-3″, 2xH-4′, H-4″); 7.64–7.73 (m, 2H, 2xH-2′); 7.76–7.89 (m, 4H, 2xH-2′, 2xH-2″); 7.95–8.10 (m, 2H, 2xH-3); 8.13 (d, 4H, $J_{P,H}$ = 10.0 Hz, NH); ^{13}C NMR ($CDCl_3$) : δ 16.3 (d, $J_{P,C}$= 5.5 Hz), 16.4 (d, $J_{P,C}$ = 5.5 Hz)(2xCH_3); 34.0 (d, $J_{P,C}$ = 2.0 Hz), 34.6 (d, $J_{P,C}$ = 7.0 Hz)(2xCH_2); 48.3 (d, $J_{P,C}$ = 114.5 Hz), 49.3 (d, $J_{P,C}$ = 108.5 Hz)(2xCH); 61.7 (d, $J_{P,C}$ = 7.0 Hz), 61.8 (d, $J_{P,C}$ = 7.0 Hz)(2xOCH_2); 123.3, 123.4 (2xC-3); 126.9, 127.2 (2xC-2″); 127.3 (d, $J_{P,C}$ = 125.8 Hz, C-1′); 127.9, 128.3 (2xC-3″); 128.3 (d, $J_{P,C}$ = 12.8 Hz, C-3′); 128.5 (d, $J_{P,C}$ = 123.0 Hz, C-1′); 128.9 (d, $J_{P,C}$ = 12.5 Hz, C-3′); 129.9, 130.1 (2xC-2); 131.2, 131.5 (2xC-4″); 131.5 (d, $J_{P,C}$ = 10.1 Hz), 132.1 (d, $J_{P,C}$ = 10.2 Hz)(2xC-2′); 132.8 (d, $J_{P,C}$= 2.8 Hz), 133.1 (d, $J_{P,C}$ = 2.8 Hz)(2xC-4′); 133.7, 133.8 (2xC-1″); 144.8 (d, $J_{P,C}$ = 13.6 Hz), 145.3 (d, $J_{P,C}$ = 12.3 Hz)(2xC-1); 146.7, 146.8 (2xC-4); 167.0 (d, $J_{P,C}$ = 4.3 Hz), 167.3 (d, $J_{P,C}$ = 3.9 Hz)(2xCO); ^{31}P NMR ($CDCl_3$) : δ 38.9, 40.9.

(1-*N*-Benzoylamino-2-phenyl)ethyl-phenylphosphinic acid methylester 21

Synthesis was started from **7** by catalytical hydrogenation.

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Mp : 157–160 °C; anal. calc. for $C_{22}H_{22}NO_3P$: C 69.65; H 5.84; N 3.69; P 8.16; found : C 68.94; H 5.83; N 3.63; P 7.61, $[\alpha]_D^{25}$ 32.8 (c = 0.13, CH_3OH, ee = 86 % (S)); FT-IR: 1660, 1439, 1035; for approximate NMR data see the analogous ethyl ester **24** and Table VII.

(1-*N*-Benzoylamino-2-(4-methylphenyl))ethyl-phenylphosphinic acid methylester 22

Synthesis was started from **8** by catalytical hydrogenation.

Mp : 137–140 °C; anal. calc. for $C_{23}H_{24}NO_3P$: C 70.22; H 6.15; N 3.56; P 7.87; found : C 70.35; H 6.06; N 3.78; P 8.04, FT-IR : 1648, 1439, 1030; for approximate NMR data see the analogous ethyl ester **17** and Table VII.

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(1-*N*-Benzoylamino-2-(4-fluorophenyl))ethyl-phenylphosphinic acid methylester 23

Synthesis was started from **9** by catalytical hydrogenation.

Mp : 154–157 °C; anal. calc. for $C_{22}H_{21}FNO_3P$: C 66.49; H 5.33; N 3.53; P 7.80; found : C 66.52; H 5.43; N 3.55; P 7.82, FT-IR : 1651, 1439, 1033; ^1H NMR ($CDCl_3$): δ 2.91–3.47 (m, 4H, 2xCH_2); 3.55 (d, 3H, $J_{P,H}$ = 10.8 Hz), 3.67 (d, 3H, $J_{P,H}$ = 11.0 Hz)(2xOCH_3); 5.05–5.21 (m, 2H, 2xCH); 6.82 (m, 2H), 6.92 (m, 2H, 2xH-3); 7.10 (m, 2H, 2xH-2); 7.16–7.23 (m, 2H, 2xH-3″); 7.26–7.53 (m, 14H, 2xH-2, 2xH-2″, 2xH-3′, 4xH-3″, H-4′, 2xH-4″, NH); 7.64 (d, 1H, $J_{P,H}$ = 10.0 Hz, NH); 7.55–7.62 (m, 1H, H-4′); 7.86–7.89 (m, 6H, 4xH-2′, 2xH-2″); ^{13}C NMR ($CDCl_3$) : δ 33.5 (d, $J_{P,C}$= 1.8 Hz), 34.1 (d, $J_{P,C}$ = 6.5 Hz)(2xCH_2); 48.6 (d, $J_{P,C}$ = 115.0 Hz), 49.6 (d, $J_{P,C}$ = 108.0 Hz)(2xCH); 51.8 (d, $J_{P,C}$ = 7.0 Hz), 51.9 (d, $J_{P,C}$ = 7.0 Hz)(2xOCH_3); 115.1 (d, $J_{F,C}$ = 21.2 Hz), 115.2 (d, $J_{F,C}$ = 21.2 Hz)(2xC-3); 126.9 (C-2″); 127.0 (d, $J_{P,C}$ = 125.0 Hz, C-1′); 127.2 (C-2″); 127.9 (d, $J_{P,C}$ = 123.0 Hz, C-1′); 128.1, 128.4 (2xC-3″); 128.5 (d, $J_{P,C}$ = 12.7 Hz), 128.9 (d, $J_{P,C}$ = 12.5 Hz)(2xC-3′); 130.5 (d, $J_{F,C}$ = 8.0 Hz), 130.7 (d, $J_{F,C}$ = 8.0 Hz)(2xC-2); 131.2, 131.5 (2xC-4″); 132.1 (d, $J_{P,C}$ = 10.0 Hz, C-2′); 132.2 (dd, $J_{P,C}$= 13.1 Hz, $J_{F,C}$ = 3.2 Hz, C-1); 132.3 (d, $J_{P,C}$ = 10.0 Hz, C-2′); 132.6 (dd, $J_{P,C}$ = 12.3 Hz, $J_{F,C}$ = 3.3 Hz, C-1); 132.9 (d, $J_{P,C}$ = 2.7 Hz), 133.0 (d, $J_{P,C}$ = 2.7 Hz)(2xC-4′); 133.9 (C-1″); 161.7 (d, $J_{F,C}$ = 244.7 Hz), 161.8 (d,

$J_{F,C}$ = 244.7 Hz)(2xC-4); 166.9 (d, $J_{P,C}$ = 4.5 Hz), 167.2 (d, $J_{P,C}$ = 4.0 Hz)(2xCO); ^{31}P NMR ($CDCl_3$) : δ 41.4, 43.2.

(1-*N*-Benzoylamino-2-phenyl)ethyl-methylphosphinic acid ethylester **24**

Synthesis was started from **10** by catalytical hydrogenation.

Mp : 199–201 °C; anal. calc. for $C_{18}H_{22}NO_3P$: C 65.25; H 6.69; N 4.23; P 9.35; found : C 64.9, H 6.68; N 4.18; P 9.04, FT-IR : 1633, 1043; for approximate NMR data see the analogous *n*-butyl-phosphinic acid ethyl ester **25** and Table VII.

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(1-*N*-Benzoylamino-2-phenyl)ethyl-*n*-butylphosphinic acid ethylester **25**

Synthesis was started from **11** by catalytical hydrogenation.

Mp : 130–132 °C; anal. calc. for $C_{21}H_{28}NO_3P$: C 67.54; H 7.56; N 3.75; P 8.30; found : C 67.48; H 7.63; N 3.79; P 8.38, FT-IR : 1656, 1027; ^{1}H NMR ($CDCl_3$) : δ 0.78 (t, 3H, $J_{CH3,CH2}$ = 7.5 Hz), 0.88 (t, 3H, $J_{CH3,CH2}$ = 7.5 Hz)(2xP-CH_2-CH_2-CH_2-$C\underline{H}_3$); 1.15 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3); 1.20–1.60 (m, 8H, 2xP-CH_2-CH_2-$C\underline{H}_2$-, 2xP-CH_2-$C\underline{H}_2$-); 1.33 (t, 3H, $J_{CH3,CH2}$ = 7.0 Hz, CH_3); 1.60–1.85 (m, 4H, 2xP-$C\underline{H}_2$-); 3.00–3.35 (m, 4H, 2xCH_2); 3.42–3.59 (m, 4H, 2xOCH_2); 4.80–4.95 (m, 2H, 2xCH); 7.10–7.45 (m, 17H, 4xH-2, 4xH-3, 4xH-3″, 2xH-4, 2xH-4″, NH); 7.67–7.80 (m, 4H, 2xH-2″); 7.98 (d, 1H, $J_{P,H}$ = 10.0 Hz, NH); ^{13}C NMR ($CDCl_3$): δ 13.37, 13.44 (2xP-CH_2-CH_2-CH_2-$\underline{C}H_3$); 16.6 (d, $J_{P,C}$= 5.3 Hz), 16.7 (d, $J_{P,C}$ = 5.5 Hz)(2xCH_3); 23.5 (d, $J_{P,C}$ = 4.6 Hz), 23.6 (d, $J_{P,C}$ = 4.6 Hz)(2xP-CH_2-$\underline{C}H_2$-); 23.8 (d, $J_{P,C}$ = 15.3 Hz), 23.9 (d, $J_{P,C}$ = 15.3 Hz)(2xP-CH_2-CH_2-$\underline{C}H_2$-); 26.5 (d, $J_{P,C}$ = 87.5 Hz), 26.9 (d, $J_{P,C}$ = 87.7 Hz)(2xP-$\underline{C}H_2$-); 33.5 (s, CH_2); 34.9 (d, $J_{P,C}$ = 4.0 Hz, CH_2); 48.9 (d, $J_{P,C}$ = 96.5 Hz), 49.0 (d, $J_{P,C}$ = 104.6 Hz)(2xCH); 61.1 (d, $J_{P,C}$ = 7.1 Hz), 61.2 (d, $J_{P,C}$= 7.1 Hz)(2xOCH_2); 126.5, 126.8 (2xC-4); 127.0, 127.3 (2xC-2"); 128.1, 128.3 (2xC-3″); 128.3, 128.4 (2xC-3); 129.07, 129.1 (2xC-2); 131.3, 131.4 (2xC-4″); 134.1 (C-1′); 136.7 (d, $J_{P,C}$ = 11.0 Hz), 137.1 (d, $J_{P,C}$ = 11.2 Hz)(2xC-1); 166.9 (d, $J_{P,C}$ = 3.8 Hz), 167.4 (d, $J_{P,C}$ = 4.0 Hz)(2xCO); ^{31}P NMR ($CDCl_3$): δ 53.5, 54.8.

(1-*N*-Benzoylamino-2-phenyl)ethyl-phenylphosphinic acid 26

Synthesis was started from **12** by catalytical hydrogenation.

Mp : 201–204 °C; anal. calc. for $C_{21}H_{20}NO_3P$: C 69.03; H 5.52; N 3.63; P 8.48; found : C 68.97; H 5.49; N 3.84; P 8.52, $[\alpha]_D^{25}$ 51.7 (c = 0.12, glacial acetic acid, ee = 99 % (S)), FT-IR : 1627, 1438, 1203; for approximate NMR data see the analogous ethyl ester **24** and Table VII.

(1-*N*-Benzoylamino-2-(4-fluorophenyl))ethyl-phenylphosphinic acid 27

Synthesis was started from **13** by catalytical hydrogenation.

Mp : 195–198 °C; anal. calc. for $C_{21}H_{19}FNO_3P$: C 65.79; H 5.00; N 3.65; P 8.08; found : C 65.88; H 5.0; N 3.66; P 8.06, FT-IR : 1650, 1438, 1201; for approximate NMR data see the analogous methyl ester **23**and Table VII.

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(1-*N*-Benzoylamino-2-(4-methylphenyl))ethyl-phenylphosphinic acid 28

Synthesis was started from **14** by catalytical hydrogenation.

Mp : 227–230 °C; anal. calc. for $C_{22}H_{22}NO_3P$: C 69.65; H 5.84; N 3.69; P 8.16; found : C 69.49; H 5.61; N 3.60; P 8.20, FT-IR : 1643, 1440, 1197; for approximate NMR data see the analogous ethyl ester **17** and Table VII.

(1-*N*-Benzoylamino-2-phenyl)ethyl-methylphosphinic acid 29

Synthesis was started from **15** by catalytical hydrogenation.

Mp : 197–200 °C; anal. calc. for $C_{16}H_{18}NO_3P$: C 63.36; H 5.98; N 4.62; P 10.21; found : C 63.37, H 5.81; N 4.52; P 10.26, FT-IR : 1641, 1162; for approximate NMR data see the analogous ethyl ester **24** and Table VII.

(1-Amino-2-phenyl)ethyl-phenylphosphinic acid 30

10 mmol **16** or **21** were refluxed for 20 hours with 6N hydrochloric acid. Then the solution was filtered and the filtrate was extracted three times

with ether. The aqueous phase was concentrated under reduced pressure. The residue was dissolved in a small amount of dry methanol and then heated shortly. After that, butylene oxide was added, the solution was concentrated again and the compound **30** precipitated.

Yield : 1.9 g (72 %); mp: 240–244 °C; anal. calc. for $C_{14}H_{16}NO_2P$: C 64.36; H 6.17; N 5.36; P 11.86; found: C 64.07; H 6.24; N 5.29; P 11.46; pK_{OH} = 1.3, pK_{NH2} = 7.7; FT-IR : 1619, 1437, 1217; ^{1}H NMR (D_2O) : δ 2.49–2.62 (m, 2H, CH_2); 3.07–3.49 (m, 1H, CH); 7.07–7.71 (m, 10H, 2xPh); ^{13}C NMR (D_2O): δ 38.8 (CH_2); 58.1 (d, $J_{P,C}$ = 95.4 Hz, CH); 132.0–140.7 (2xPh); ^{31}P NMR (D_2O) : δ 23.7.

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