Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 715–740

TETRAHEDRON: *ASYMMETRY*

TETRAHEDRON: ASYMMETRY REPORT NUMBER 34

Recent applications of α-phenylethylamine (α-PEA) in the preparation of enantiopure compounds. Part 1: Incorporation in chiral catalysts. Part 2: α-PEA and derivatives as resolving agents

Eusebio Juaristi,* Jaime Escalante, José Luis León-Romo and Adelfo Reyes

Departamento de Química, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Apartado Postal 14-740, 07000 Mexico, D.F. Mexico

Received 20 January 1998; accepted 29 January 1998

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1. Introduction

Most organic natural products are chiral and Nature usually produces them in a single enantiomeric form. In contrast, both academic and industrial chemists aiming to synthesize enantiopure substances must 'pay the price' by using already available chiral auxiliaries, reagents, and catalysts.[1–8] In this regard, the general importance of chiral amines is well recognized and α-phenylethylamine (α-PEA) is well known as a simple, yet powerful, chiral adjuvant.[9] Furthermore, both enantiomers of α-PEA are readily produced via resolution of racemic PEA utilizing chiral acids such as tartaric acid[10] and (*S*)-carbamalactic acid,[11] among others. Several stereoselective syntheses have also been reported,[12] thus both enantiomers

* Corresponding author. E-mail: juaristi@chem.cinvestav.mx

PII: S0957-4166(98)00058-5

of α-PEA are commercially accessible at a low price, so that their recovery may not be critical even after large-scale use. Indeed, one advantage of α-PEA as an auxiliary is its possible reductive removal.

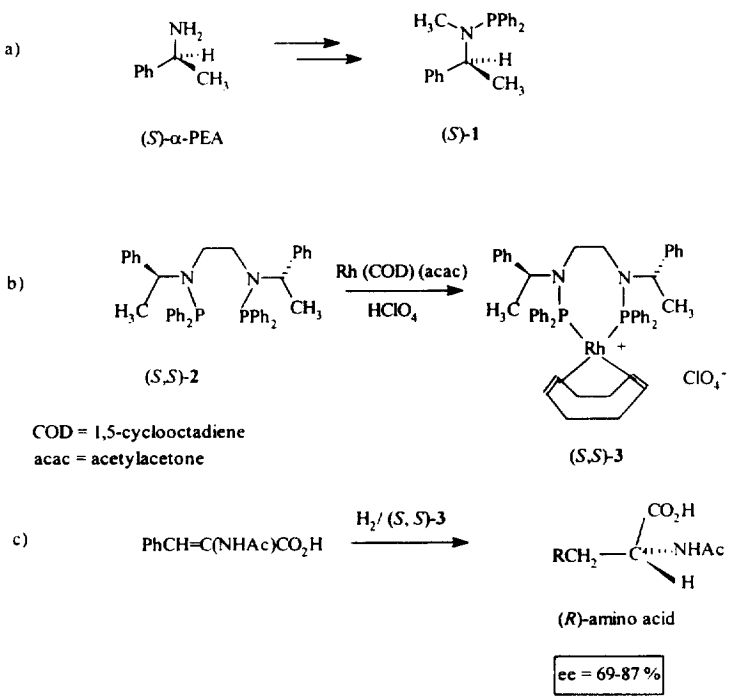
The purpose of this review is to highlight recent applications (1990–1997) of α-PEA and some of its derivatives as chiral adjuvants in the resolution of racemates and as ligands in asymmetric (or disymmetric) catalysts.[13,14] An upcoming report, including the use of α-PEA as a chiral auxiliary and as a chiral base, will be presented shortly.

2. Incorporation of α-PEA in chiral ligands for asymmetric catalysis

Following the great success of chiral phosphine–transition metal complexes in asymmetric synthesis,[15–20] intensive activity has been dedicated to the development of ligands containing chiral amines.[21] The derived catalysts have been particularly effective in the asymmetric hydrogenation of olefins, reduction of ketones, organometallic addition to aldehydes, organocuprate addition to enones, allylic alkylation, and cross-coupling reactions.

2.1. Enantioselective hydrogenation of olefins

In 1969, Sajus et al.[22] showed the effectiveness of several rhodium–aminophosphine complexes in catalytic olefin hydrogenation. Asymmetric modifications were then explored by Giongo and coworkers[23] who found the monodentate ligand (*S*)-**1** ineffective in terms of asymmetric induction, whereas the catalyst derived from the bidentate C_2-symmetric ligand (*S,S*)-**2** catalyzed the enantioselective hydrogenation of prochiral olefinic precursors of α-amino acids with good stereoselectivity (ee=69–87%, Scheme 1 and Table 1).

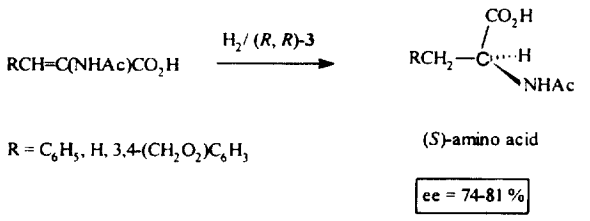


Scheme 1.

Table 1
Asymmetric hydrogenation catalyzed by (*S*,*S*)-**3**[23] (Scheme 1c)

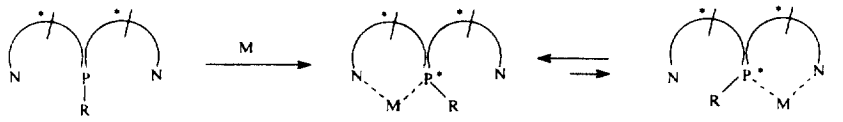
R	Temperature (°C)	Pressure (atm)	ee (%)
C_6H_5	25	1	77
C_6H_5	25	5	71
C_6H_5	25	10	69
C_6H_5	0	10	82
C_6H_5	-20	10	84
H	25	1	77
3,4-$(CH_2O_2)C_6H_3$	25	1	77
3-OCH_3-4-OAc-C_6H_3	25	1	87

As expected,[1,4,16–19] opposite configuration in the ligand, which is introduced when using (*R*)-PEA as the starting material, led to hydrogenation products of opposite configuration, thus providing a convenient method for the synthesis of either natural or unnatural chiral amino acids (Scheme 2).



Scheme 2.

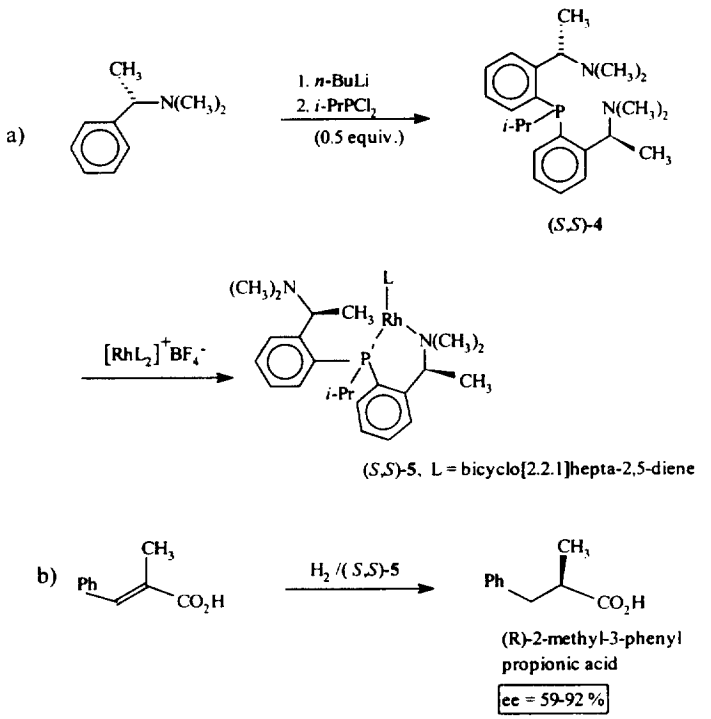
Chiral ligands possessing stereogenic phosphorus atoms, while quite effective for asymmetric transformations,[15,16] have unique problems associated with their synthesis.[24] Thus, Yamagishi et al.[25] have recently developed phosphinediamine ligands with *latent* chiral phosphorus atoms in the molecule. Indeed, selective coordination to a metal was anticipated to afford a stereogenic phosphorus atom as illustrated in Scheme 3.



Scheme 3.

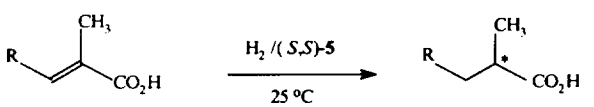
In the event, *o*-lithiation of (*S*)-*N*,*N*-dimethyl-1-phenylethylamine followed by reaction with dichloroisopropylphosphine afforded (*S*,*S*)-**4**, whose rhodium complexes proved effective for the asymmetric hydrogenation of acrylic acids (Scheme 4 and Table 2).

The authors[25] point out that enantioselectivities obtained with (*S*,*S*)-**5** (Table 2) are much higher than those obtained with rhodium–*diphosphine* catalysis. Also apparent in Table 2 is a bell-shaped dependency of enantioselectivity on the hydrogen pressure, the highest (92% ee) being obtained at a hydrogen pressure of 40 atm. This observation was unprecedented for rhodium catalysts. Finally, additional studies of solvent and substrate substituent effects[25b] led to the proposed structure of the catalyst system depicted in Fig. 1.



Scheme 4.

Table 2
Asymmetric hydrogenation of acrylic acid derivatives by rhodium (*S,S*)-**5** catalyst[25a]



R	H_2 Pressure (atm)	Time (h)	Conversion (%)	% ee
Ph	20	57	75	63 (*R*)
Ph	20	120	100	84 (*R*)
Ph	40	86	100	92 (*R*)
Ph	80	43	100	59 (*R*)
CH_3	20	94	100	75 (*S*)

2.2. *Enantioselective reduction of ketones*

Chiral amine–borane complexes are promising reagents for the asymmetric reduction of prochiral ketones, especially since the chiral amine can be recovered and reused. Although (*R*)- and (*S*)-α-phenylethylamine–borane complexes reduce prochiral ketones in very low (1–13%) enantiomeric excess,[26] the C_2-symmetric bis(α-phenylethyl)amine complex (*S,S*)-**6**·BH_3 has been reported to reduce acetophenone in the presence of $BF_3 \cdot OEt_2$ with 42% ee[27] (Scheme 5).

Recently, the borane complexes derived from chiral phenylethyl amines **7**–**11** (Fig. 2) were prepared and used to reduce prochiral aromatic ketones in the presence of $BF_3 \cdot OEt_2$.[28] Table 3 summarizes the results with the borane complex derived from (−)-**11**. It should be mentioned that the reactions were

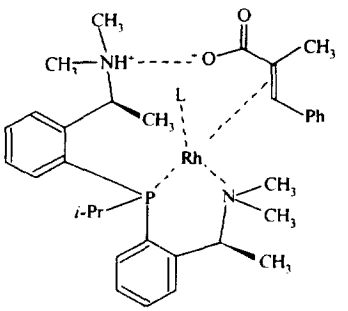
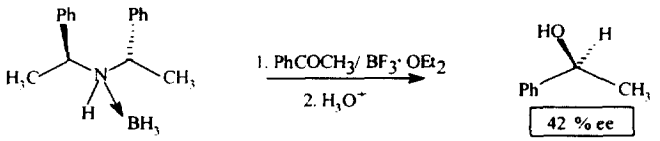
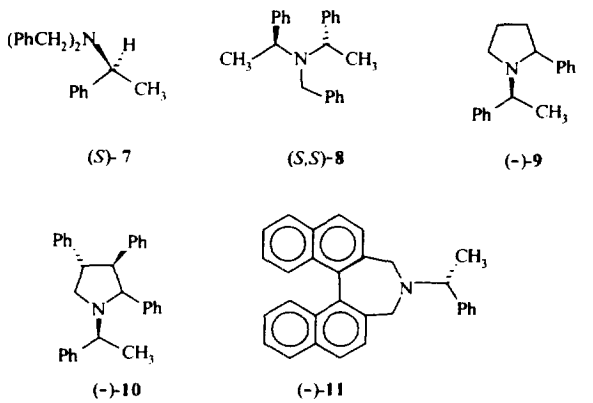


Fig. 1.



Scheme 5.



[a] For amines (−)-**9**, (−)-**10** and (−)-**11** only the configuration of the phenethyl group is certain.

Fig. 2.

carried out with a single stereoisomer of **10**; nevertheless, the configuration of the 1,1′-binaphthyl moiety was not determined by the researchers[28] (see also the footnote in Fig. 2).

As appreciated in Table 3, the configuration of the products was consistently *R*, with the asymmetric induction decreasing with increasing chain length of the alkyl moiety.

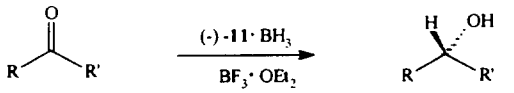
The transition state mode outlined in Fig. 3 was advanced by Periasamy and coworkers[28] in order to explain the role of $BF_3 \cdot OEt_2$. Nevertheless, the stereoinducing center(s) seem(s) too distant to the reacting carbonyl group in this model.

Recently, Wills and coworkers reported the use of novel catalysts (*R*)-**12** and **13**, containing an N–P=O phosphinamide structural unit, for the asymmetric reduction of ketones by borane, presumably via the mechanism outlined in Scheme 6.[29]

Reduction of ketones **14**–**17** (Fig. 4) afforded high yields of the corresponding alcohols, although enantiomeric excesses were low (ee=5–46%).[29]

In addition to rhodium(I), iridium(I) complexes with chiral ligands can be effective catalysts for asymmetric catalytic reduction of prochiral ketones. In this context, Zassinovich and coworkers[30] have

Table 3
Asymmetric reduction of prochiral ketones using amine (−)-**11**·borane complex, in benzene and at 0°C[28]



Substrate	Yield	% ee (Configuration)
R= Ph, R'= CH_3	82	51 (*R*)
R= Ph, R' = Et	81	41 (*R*)
R =Ph, R'= *n*-Pr	80	11 (*R*)
R= 1-naphthyl, R'= CH_3	78	57 (*R*)

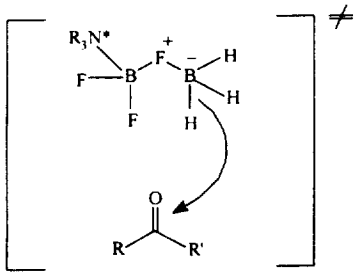
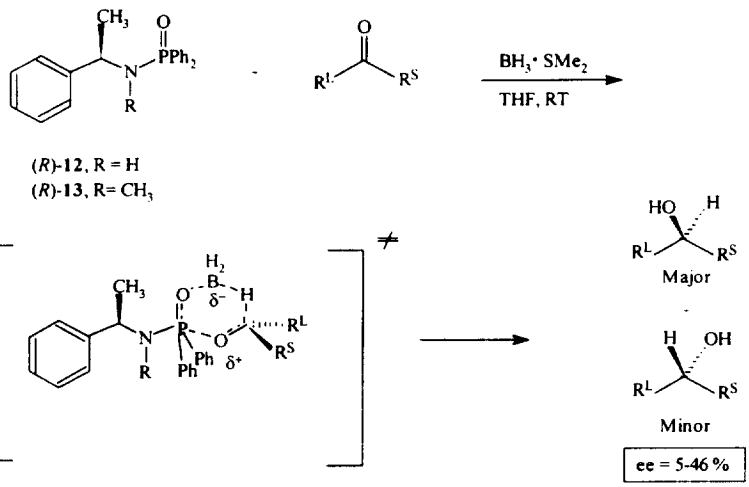


Fig. 3.

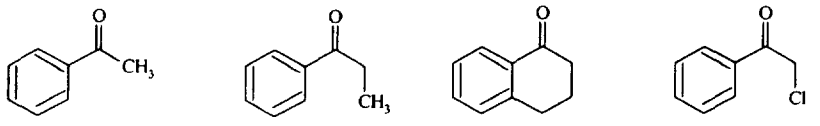


Scheme 6.

described the synthesis of pentacoordinate iridium complexes **18** and **19** (Fig. 5). These complexes were shown to be active and selective precatalysts for asymmetric hydrogen transfer from isopropanol to prochiral ketones, affording enantiomeric excesses of up to 80% (Scheme 7 and Table 4). The structure and absolute configuration of **18** and **19** were determined by X-ray crystallographic diffraction.

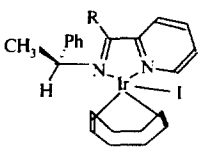
The proposed active species[30] is depicted in Fig. 6, where a stabilizing interaction between the phenyl ring in the substrate and that of the phenylethyl group of the chiral ligand could account for the preferred configuration in the observed products.

Related chiral aminodiphosphine ligands **20**, derived from (*R*) and (*S*)-α-PEA, were recently described by Bianchini and coworkers.[31] The catalytic hydrogen-transfer reduction of $PhCH{=}CHCOCH_3$ and other α,β-unsaturated ketones in the presence of $[Ir(COD)(OMe)]_2$ (COD=1,4-cyclooctadiene) proceeded with



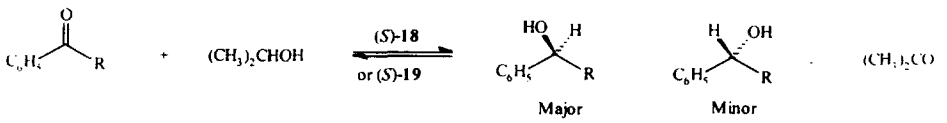
14 15 16 17

Fig. 4.



(*S*)-**18**, R= H
(*S*)-**19**, R= CH_3

Fig. 5.



R = CH_3, *i*-Pr, *t*-Bu

ee = 20-80 %

Scheme 7.

Table 4
Asymmetric reduction of alkyl phenyl ketones by isopropanol, in the presence of (*S*)-**18** or (*S*)-**19** precatalysts[30] (Scheme 7)

Precatalyst	Ketone	Conversion (%)	% ee (Configuration)
(*S*)-**18**	$C_6H_5COCH_3$	88	37 (*S*)
(*S*)-**18**	C_6H_5CO-*i*-Pr	91	52 (*S*)
(*S*)-**18**	C_6H_5CO-*t*-Bu	94	80 (*S*)
(*S*)-**19**	$C_6H_5COCH_3$	92	20 (*S*)
(*S*)-**19**	C_6H_5CO-*i*-Pr	92	27 (*S*)
(*S*)-**19**	C_6H_5CO-*t*-Bu	96	42 (*S*)

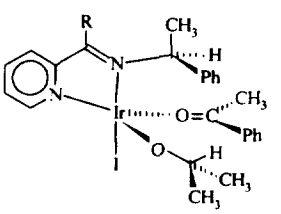
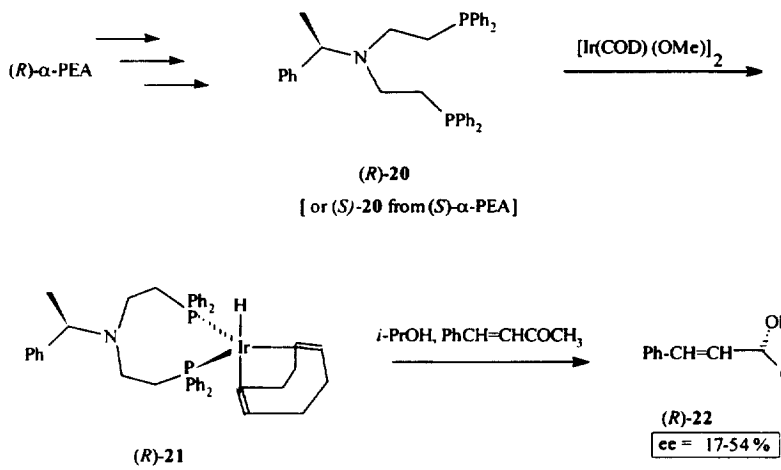


Fig. 6.

high carbonyl chemoselectivity and with moderate enantioselectivities (ee=17–54%) (Scheme 8 and Table 5).

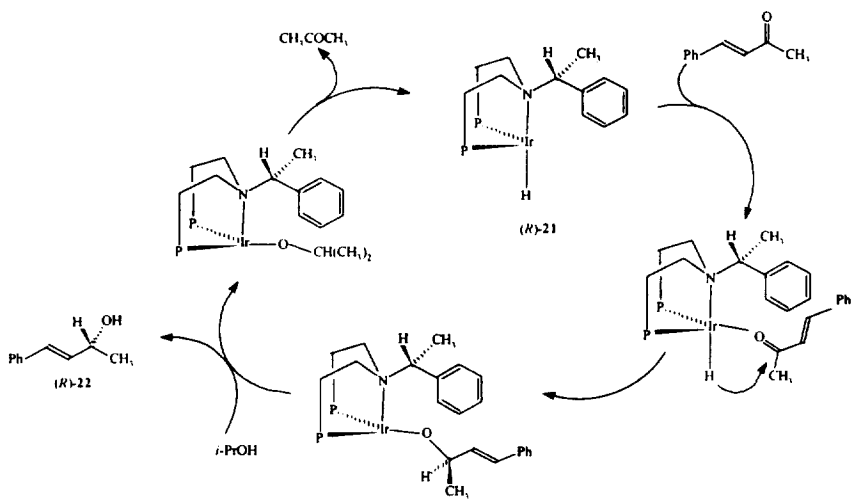
^1H and ^{31}P NMR studies of the catalytic system led Bianchini and coworkers to propose the mechanistic pathway presented in Scheme 9.



Scheme 8.

Table 5
Asymmetric reduction of *trans*-PhCH=CHCOCH$_3$ catalyzed by (*R*)- or (*S*)-**20** and [Ir(COD)(OMe)]$_2$[31]

Chiral ligand	Temp (°C)	Time (min.)	Conversion (%)	% ee (Configuration)
(*R*)-**20**	83	15	93	22 (*R*)
(*S*)-**20**	83	15	93	17 (*S*)
(*R*)-**20**	60	45	83	33 (*R*)
(*S*)-**20**	60	45	90	27 (*S*)
(*R*)-**20**	40	150	85	41 (*R*)
(*S*)-**20**	40	150	86	32 (*S*)
(*R*)-**20**	25	300	65	54 (*R*)
(*S*)-**20**	25	360	64	42 (*S*)

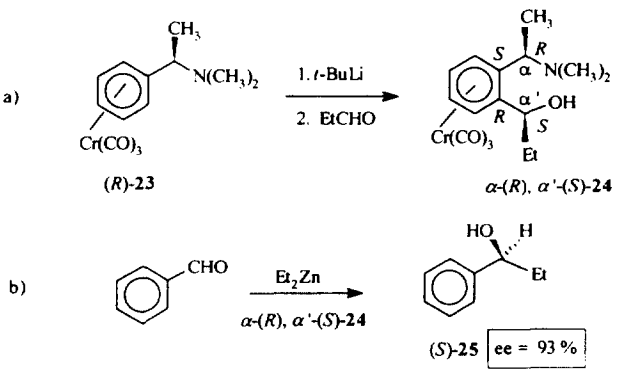


Scheme 9.

2.3. *Enantioselective organometallic addition to aldehydes*

It is well known that chiral aminoalcohols not only accelerate the alkylation of aldehydes with dialkylzincs but also dictate the absolute configuration of the secondary carbinols produced.[32] In

a series of publications, Uemura and coworkers[33] have shown that planar chirality in the ligand can compete with stereogenic centers for the achievement of enantioselective reactions. In particular, tricarbonyl(*N*,*N*-dimethyl-α-phenylethylamine)chromium (**23**) was selectively deprotonated[34] and treated with propionaldehyde to give aminoalcohol **24** as the main product (Scheme 10a). This chiral (arene)chromium complex was found to catalyze the enantioselective ethylation of benzaldehyde with diethylzinc (ee=93%, Scheme 10b).[33b] Table 6 shows additional results with analogous (arene)chromium complexes as catalysts for the enantioselective addition of diethylzinc to benzaldehyde.[33a]



Scheme 10.

The results presented in Table 6 demonstrate that the direction of $Cr(CO)_3$ complexation and the chirality of the benzylic alcohol are relevant factors for high stereoinduction. Uemura and coworkers[33a] suggest a model where the zinc atom is incorporated into a seven membered ring with a chair conformation in an *exo*-configuration to the $Cr(CO)_3$ group. Ethylation takes place via a six-membered ring transition state (Fig. 7). Nucleophilic addition of the ethyl group to the *Si* face of the aldehyde leads to the *S*-isomer.

Very recently, van Koten et al.[35] developed (*R*,*R*)-**25** as an efficient catalyst for the addition of dialkylzinc compounds to aliphatic and aromatic aldehydes to give the corresponding secondary alcohols in nearly quantitative yields and with enantiomeric purities of 69–99% (Scheme 11).

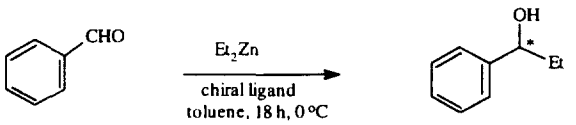
In this context, only recently have asymmetric versions of the Henry (nitroaldol) reaction been reported.[36] Nevertheless, Nájera and coworkers[37] prepared chiral derivatives of guanidine (*S*)-**26** and (*S*,*S*)-**27**, incorporating (*S*)-α-PEA, and obtained low to moderate enantioselectivities in various nitroaldol reactions (Scheme 12). An application of this asymmetric reaction yielded enantioenriched propranolol[37] (*S*-**28**, Scheme 12c).

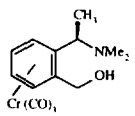
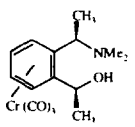
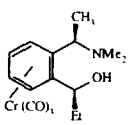
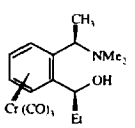
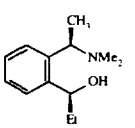
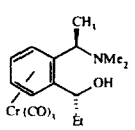
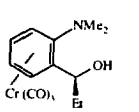
On the other hand, Salvadori et al.[38] prepared chiral aminoalcohols (*R*,*R*)- and (*R*,*S*)-**29** (Fig. 8), containing (*R*)- or (*S*)-α-PEA, and used them successfully as catalysts in the enantioselective addition of diethylzinc to arylaldehydes with enantiomeric excesses as high as 88% (Table 7).

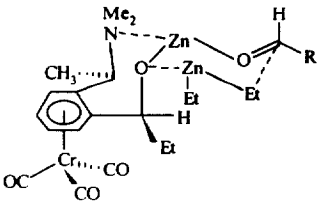
The results summarized in Table 7 show that aminoalcohols (*R*,*R*)- and (*R*,*S*)-**29** are efficient catalysts for the ethylation reaction. When the substrate is deactivated towards the nucleophilic addition (Ar=4-CH_3O–C_6H_4), both the reaction yield and ee are lower, probably due to competing uncatalyzed reactions giving the racemic product.[39] Following Noyori,[40] the mechanism outlined in Fig. 9 was assumed by Salvadori and coworkers.[38]

In this context, *N*-(*S*)-α-methylbenzyl-β-aminoalcohols **30**–**32** (Fig. 10) catalyzed the enantioselective alkylation of benzaldehyde by diethylzinc.[41] Interestingly, the extent and even the sense of the asymmetric induction were found to depend on the presence or absence of 'inert' lithium chloride[42] (Table 8).

Table 6
Asymmetric ethylation of benzaldehyde catalyzed by chiral (arene)$Cr(CO)_3$

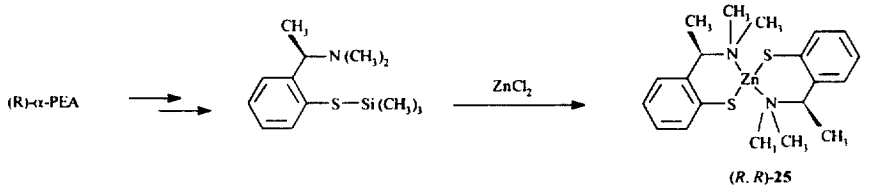


Chiral ligand	Conversion (%)	% ee (Configuration)
	70	15 (*S*)
	83	63 (*S*)
	87	93 (*S*)
	98	87 (*S*)
	79	30 (*R*)
	71	24 (*S*)
	87	50 (*S*)
	56	12 (*S*)

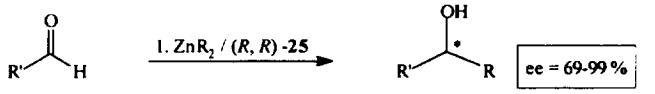


α -(*R*), α '-(*S*)-**24** / Et_2Zn / aldehyde activated complex

Fig. 7.

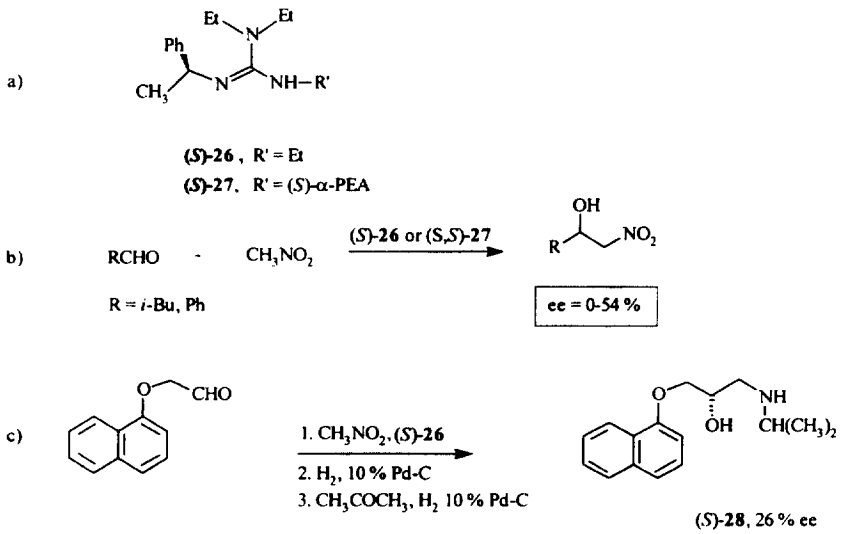


(*R*, *R*)-**25**



R'	R	Yield (%)	% ee (Configuration)
4-ClC_6H_4	Et	99	97 (*S*)
4-$MeOC_6H_4$	Et	94	95 (*S*)
4-MeC_6H_4	Et	99	99 (*S*)
2-Furyl	Et	99	89 (*S*)
$C_6H_5CH_2CH_2$	Et	98	69 (*S*)
C_6H_5	CH_3	88	94 (*S*)
C_6H_5	*i*-Pr	45	80 (*S*)

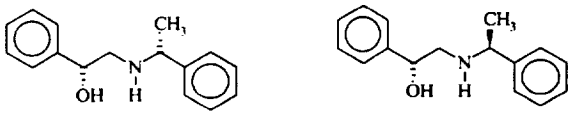
Scheme 11.



Scheme 12.

2.4. *Enantioselective organocuprate addition to enones*

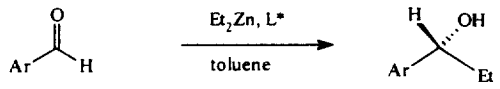
Organocopper reagents are very useful for C–C bond forming reactions. Pioneering work by Kretchmer[43] made use of the alkaloid (−)-sparteine as a chiral ligand of organocopper(I) compounds



(*R,R*)-**29** (*R,S*)-**29**

Fig. 8.

Table 7
Enantioselective addition of Et_2Zn to arylaldehydes[38]



(*R*)

Chiral ligand	Ar	Yield (%)	Time (h)	% ee
(*R,R*)-**29**	phenyl	78	6	88
(*R,R*)-**29**	2-naphthyl	75	6	82
(*R,R*)-**29**	4-CF_3-C_6H_4	80	6	82
(*R,R*)-**29**	4-CH_3O-C_6H_4	50	22	52
(*R,S*)-**29**	phenyl	90	6	78
(*R S*)-**29**	2-naphthyl	78	6	68
(*R,S*)-**29**	4-CF_3-C_6H_4	95	6	66
(*R,S*)-**29**	4-CH_3O-C_6H_4	70	22	33

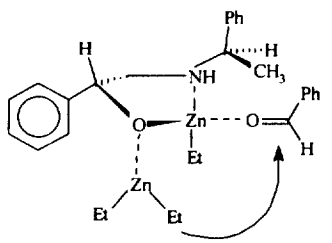


Fig. 9.

of the type $RCuMgX_2$ in the conjugate addition to enones, obtaining products of low enantiomeric purity (ee<10%). In 1986 Bertz et al.[44] described the use of (*R*)-and (*S*)-α-PEA in the preparation of chiral phenyl organocuprates, which reacted with 2-cyclohexenone in 30% ee (Scheme 13).

More recently, Jansen and Feringa[45] reported the asymmetric conjugate addition of Grignard reagents to α,β-enones catalyzed by chiral diamine–zinc(II) complex (*S,S*)-**33**, where 1.0 mol% of (*S,S*)-**33** at 0°C and isopropylmagnesium bromide is added to 2-cyclohexenone with an ee of 8% (Scheme 14).

In this regard, Lippard's research group reported that chiral complexes of phenethyl-containing aminotropone imine (*R,R*)-**34** catalyzed the conjugate addition of organocopper reagents to 2-cyclohexenone with modest enantioselectivity (15–20% ee).[46a] Nevertheless, a significant increase in enantioselectivity occurred when silyl reagents and hexamethylphosphoramide (HMPA) were added to the reaction mixture.[46b] (Scheme 15 and Table 9).

In their systematic study, Rossiter and coworkers[47] explored a total of 31 chiral amines as non-transferable ligands in lithium organo(amido)cuprates[$LiCu(L^*)R]_2$ capable of enantioselective conjugate addition to cycloalkenones. The most successful ligands were (*S*)-**35** and (*R*)-**36**, which contain a second site of chelation (Fig. 11). Table 10 summarizes some of the most salient results.

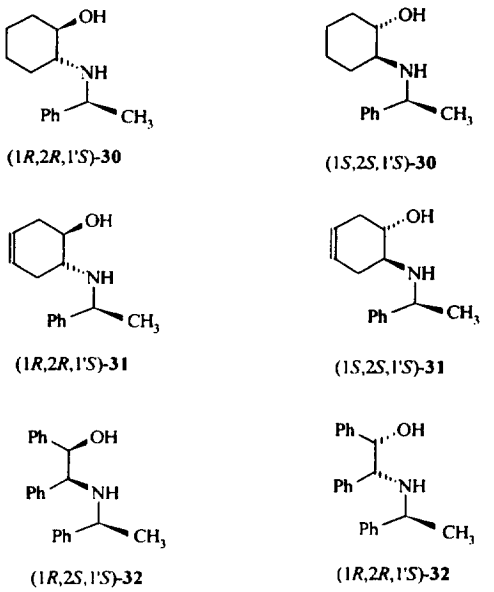
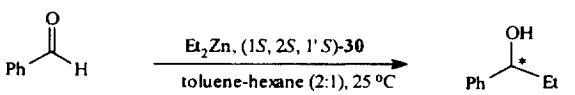
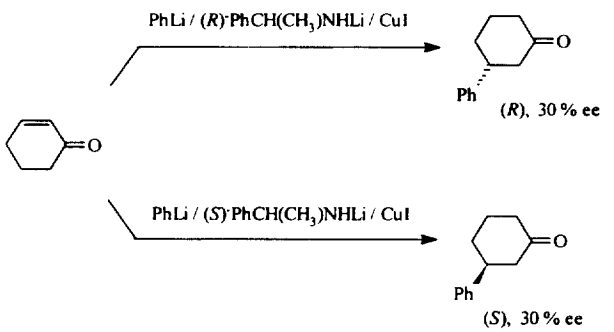


Fig. 10.

Table 8
Salt (LiCl) effect in the addition of Et_2Zn to benzaldehyde[41]



LiCl (%)	Yield (%)	% ee	Configuration
0	65	47	(*R*)
18	51	36	(*S*)

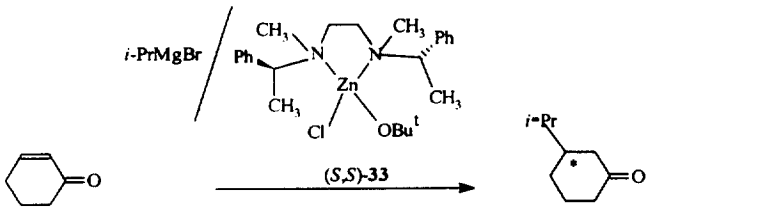


Scheme 13.

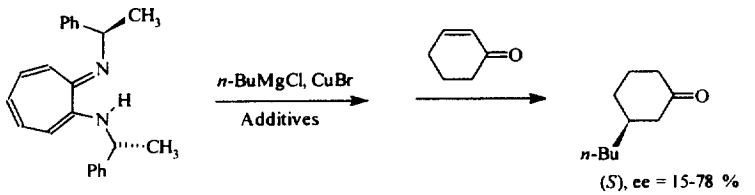
Figure 12 presents the proposed structure of *n*-butyl amidocuprate derived from (*S*)-**36**. Rossiter suggests a model for enantioselection based on enone complexation with a lithium cation, fixing the orientation of the substrate and activating it to addition.

On the other hand, Uemura and coworkers[48] have reported the enantioselective addition of diethylzinc to chalcone in the presence of $Ni(acac)_2$ complexed with chiral tricarbonyl-(1,2-disubstituted arene)chromium (Scheme 16).

Very recently, Wendisch and Sewald[49] described the Cu(I)-catalyzed 1,4-addition of diethylzinc in



Scheme 14.



Scheme 15.

Table 9
Asymmetric conjugate addition reactions of *n*-BuMgCl to 2-cyclohexenone[46] (Scheme 15)

Additives	Yield (%)	% ee
—	96	20
$Ph_2(t\text{-Bu})SiCl$	57	74
$Ph_2(t\text{-Bu})SiCl$/HMPA	97	78

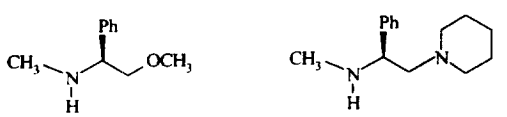


Fig. 11.

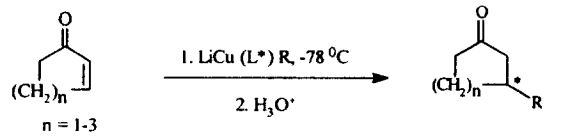
the presence of enantiopure phenethyl-containing sulfonamide (*R*)-**37** (Scheme 17). The structure of the actual catalytic species is unknown.

2.5. *Enantioselective allylic alkylation*

New chiral complexes containing tricarbonyl(arene)chromium were recently prepared by Uemura et al.[50] from (*R*)-α-PEA. The presence of an additional chelating group in (*R*)-**38** allowed the catalytic asymmetric allylic alkylation of 1,3-diphenyl-1-acetoxypropene with sodium dimethyl malonate in the presence of palladium(0) (Scheme 18).

In somewhat related studies,[51] chiral complex (*R*)-**39** catalyzed the asymmetric cross-coupling of 1-phenylethylmagnesium or -zinc reagent with vinyl bromides in the presence of palladium or nickel (Scheme 19).

Table 10
Enantioselective conjugate addition to enones with scalemic lithium organo(amido) cuprates[47]



Ligand, L*	Enone	R	% Yield	% ee (Configuration)
(*S*)-**35**	2-cyclohexenone	*n*-Bu	92	68 (*S*)
(*S*)-**36**	2-cyclohexenone	*n*-Bu	92	83 (*S*)
(*S*)-**36**	2-cyclohexenone	Ph	30	97 (*S*)
(*S*)-**36**	2-cyclopentenone	Me	40	32 (*R*)
(*S*)-**36**	2-cyclopentenone	*n*-Bu	51	45 (*S*)
(*S*)-**36**	2-cycloheptenone	Me	60	97 (*S*)
(*S*)-**36**	2-cycloheptenone	*n*-Bu	63	97 (*S*)

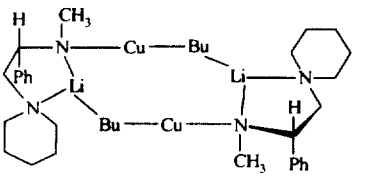
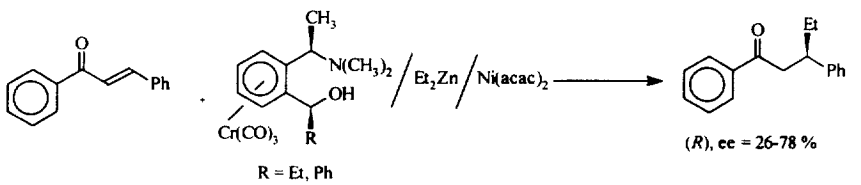


Fig. 12.

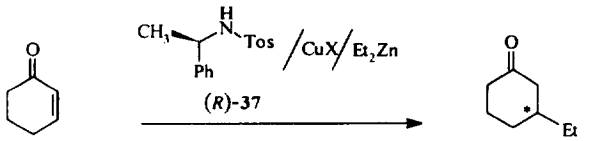


R	mol % $Ni(acac)_2$	Ratio of Ni (II) : L*	Yield (%)	% ee
Ph	1	1: 10	66	36
Ph	5	1: 10	90	62
Ph	100	1 : 1	70	78
Et	7	1 : 2.5	78	26
Et	5	1 : 10	91	43
Et	100	1 : 1	73	53

Scheme 16.

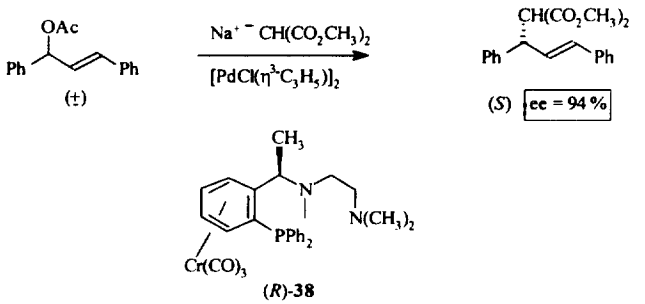
3. Phenylethylamines as resolving agents

In his classical review of resolving agents,[52] the late S. H. Wilen pointed out that naturally occurring alkaloids are the most common resolving agents for the resolution of racemic acids via diastereomeric salt formation. Indeed, α-PEA, quinine and brucine have been the leading resolving agents for chiral acids for more than 100 years. A large number of carboxylic acids have been resolved via their diastereomeric salts with (*R*)- or (*S*)-α-PEA. Alternatively, racemic acids have been resolved by covalent derivatization and separation of the resulting diastereoisomeric amides.

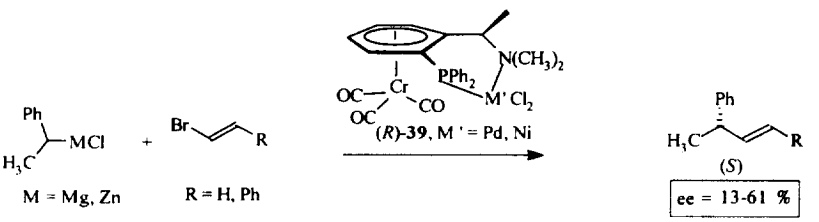


CuX	Main product	% ee
CuCN	(*R*)	17-30
CuOTf	(*S*)	16
CuSPh	(*S*)	16-22
CuI	(*S*)	28

Scheme 17.



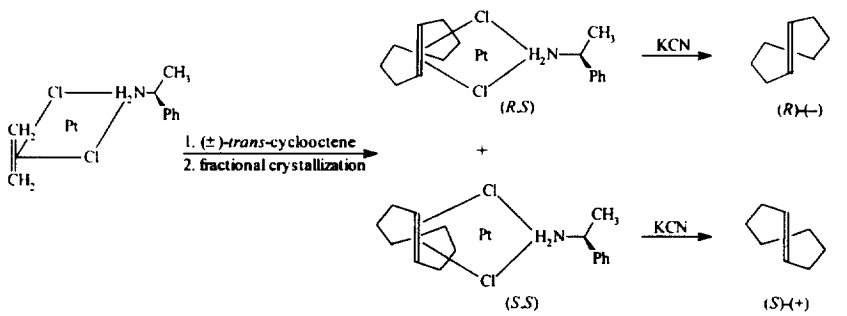
Scheme 18.



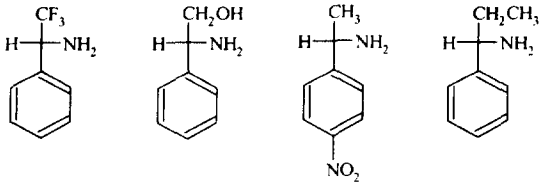
Scheme 19.

3.1. Covalent attachment of the resolving agent

Very interesting is Cope's resolution of (±)-cyclooctene through their diastereoisomeric complexes with platinum(II) derivatives of (*S*)-α-PEA.[53] Separation was achieved via fractional crystallization to constant optical rotation, and decomposition of the complexes with potassium cyanide furnished enantiopure (+)- and (−)-cyclooctene. (Scheme 20).[54]



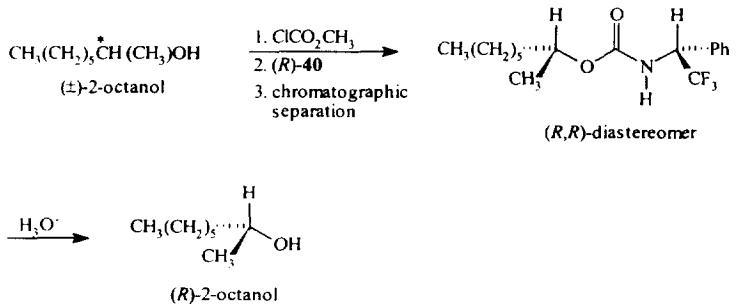
Scheme 20.



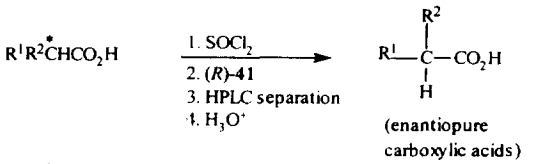
(*R*)-**40** (*R*)-**41** (*S*)-**42** (*S*)-**43**

Fig. 13.

Several enantiopure derivatives of α-PEA have proved to be valuable resolving agents. For example, 2,2,2-trifluoro-1-phenylethylamine (**40**, Fig. 13) was successfully used by Pirkle and Hauske for the chromatographic resolution of racemic alcohols via diastereomeric carbamates[55] (Scheme 21). (−)-(*R*)-Phenylglycinol (**41**, Fig. 13) was explored by Helmchen and coworkers[56] in the resolution of enantiomeric carboxylic acids through the separation of diastereomeric amides. Carbinol **41** has the additional bonus that the hydroxyl group facilitates the hydrolysis of the separated amides via neighboring group participation[56] (Scheme 22). Compounds (*R*)- and (*S*)-α-*p*-nitrophenylethylamines (**42**, Fig. 13) were used by Perry et al.[57] for the resolution of several racemates. These workers indicate that α-PEA failed under similar conditions. Finally, Nohira et al.[58] have recently recommended the use (*R*)- and (*S*)-α-ethylbenzylamine (**43**, Fig. 13) as an effective resolving agent of chiral carboxylic acids. (Section 3.2).



Scheme 21.



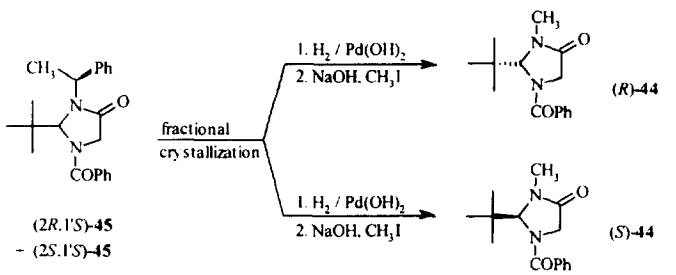
(a) $R^1 = n\text{-}C_3H_7$; $R^2 = CH_3$
(b) $R^1 = PhCH_2$; $R^2 = CH_3$
(c) $R^1 = Ph_2CH$; $R^2 = CH_3$

Scheme 22.

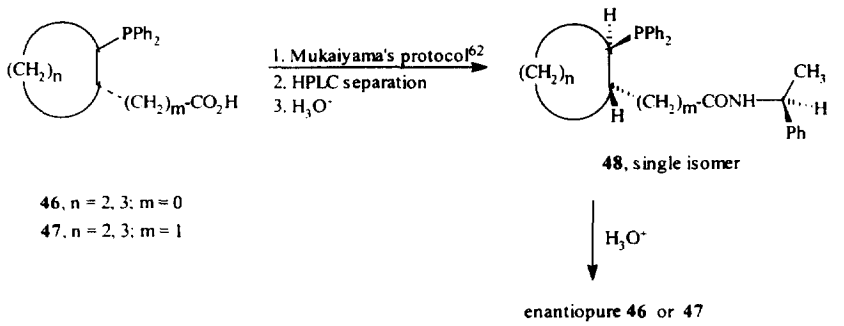
1-Benzoyl-2-*tert*-butyl-3-methyl-1,3-imidazolidin-4-one (**44**), a useful chiral precursor for the asymmetric synthesis of α-amino acids,[59] can be prepared in enantiomerically pure form via the separation of diastereomeric derivatives **45** incorporating (*S*)-α-PEA (Scheme 23).[60]

Racemic phosphinocarboxylic acids **46** and **47** were resolved through diastereomeric amides **48**,[61] derived from the chiral phosphines and (*S*)-PEA (Scheme 24).[62]

2-[4-(2-Oxocyclohexylidenemethyl)-phenyl]propionic acid **49**, a good anti-inflammatory and analgesic agent, was also resolved via diastereomeric separation (medium-pressure liquid chromatogra-

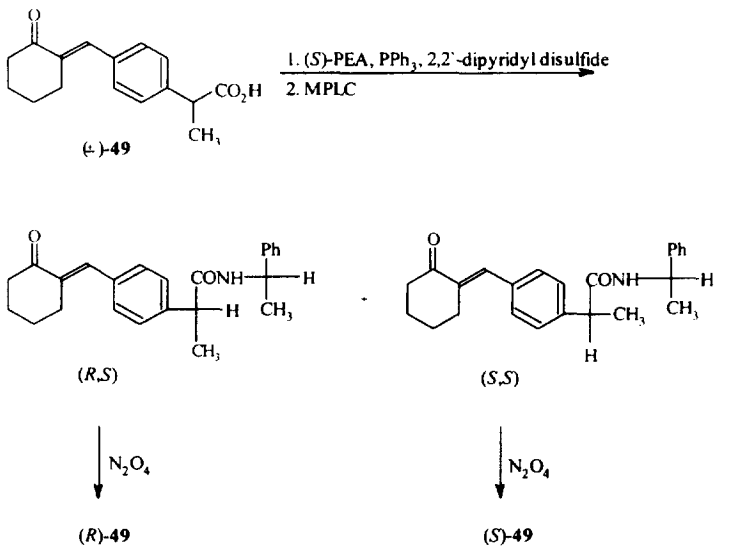


Scheme 23.



Scheme 24.

phy, MPLC) of the (*S*)-phenylethyl amide derivatives, followed by amide bond cleavage with N_2O_4[63] (Scheme 25).



Scheme 25.

Racemic azido acids **50**,[64] 2,4-dimethyl-5-oxopentanoates **51**,[65] glutamic acid analogues **52–54**,[66] and trimethylenemethane iron(tricarbonyl) esters **55**[67] were similarly resolved through the chromatographic separation of diastereomeric amides derived from (*R*)- or (*S*)-α-PEA (Fig. 14).

The preparation of enantiopure flosequinan **56**, a novel vasodilator containing an asymmetric sulfur, was accomplished via the separation of diastereomeric derivatives (*R,R*)- and (*R,S*)-**57**, which were prepared from racemic precursor (±)-**58** and (*R*)-α-PEA[68] (Scheme 26).

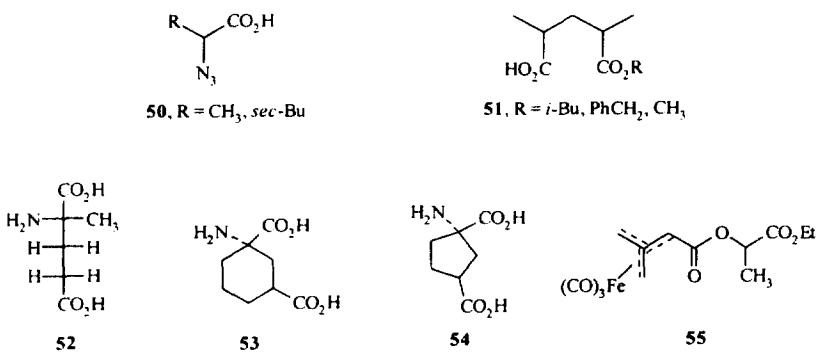
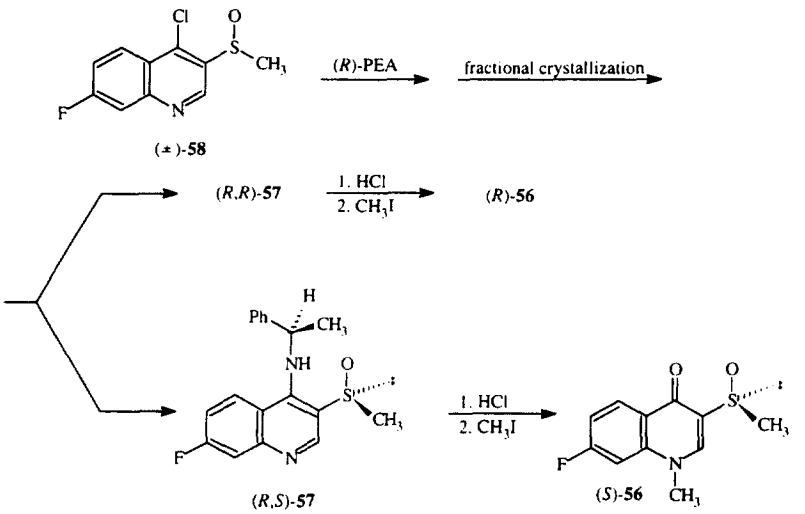


Fig. 14.



Scheme 26.

Recently, (*S*)- and (*R*)-4-formyl-5-hydroxy[2.2]paracyclophane, (*S*)- and (*R*)-**59**, were resolved via their Schiff's bases with (*R*)-α-PEA[69] (Scheme 27). Enantiopure [2.2]paracyclophanes **59** are useful chiral auxiliaries for the asymmetric synthesis of β-hydroxy-α-amino acids.[70]

Fractional crystallization of diastereoisomers (*S*,*S*)- and (*S*,*R*)-**60** followed by hydrogenolytic debenzylation afforded enantiopure 2-anilino-2-oxo-1,3,2-oxazaphosphorinanes (*S*)- and (*R*)-**61**[72] (Scheme 28).

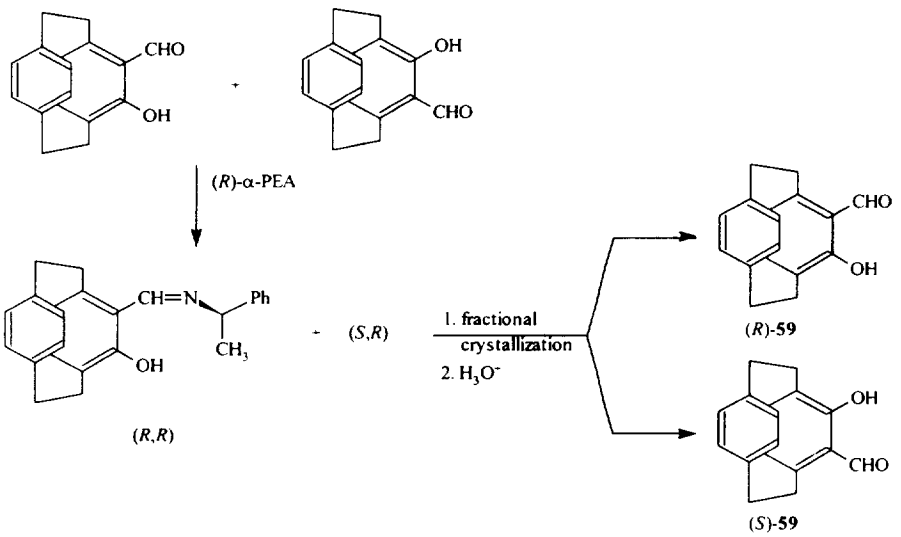
Application of the method described by Hu and coworkers for the resolution of 1,1′-binaphthalenyl-2,2′-diol (BINOL, **62**)[71] was successful for the separation by fractional crystallization of diastereomeric dibenzofuranyl analogues (*R*,*S*)- and (*S*,*S*)-**63**[72] (Fig. 15).

An interesting resolution procedure for biphenyl diphosphines (*R*)- and (*S*)-**64**, utilizing commercial (*S*)-dipalladium complex **65**, was reported by Jendralla and coworkers[73] (Scheme 29).

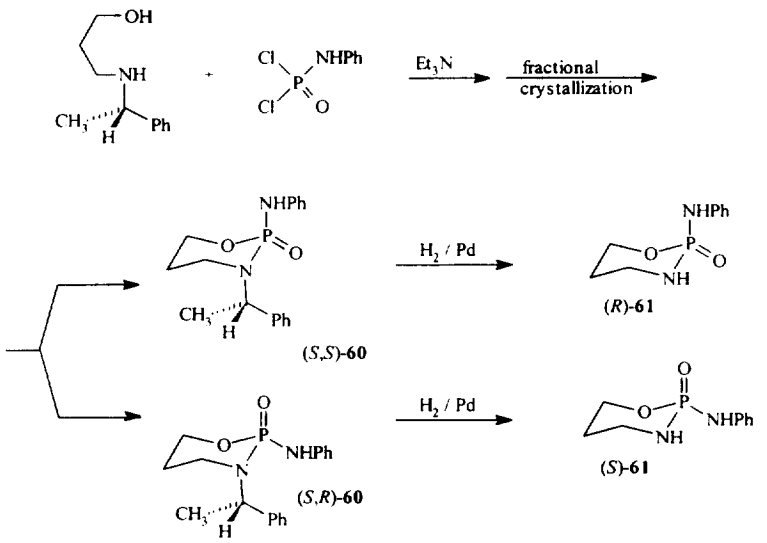
Finally, chromatographic separation of diastereomeric amides **66** (Scheme 30) permitted the preparation of enantiopure proline derivatives **67**.[74]

3.2. *Diastereomeric salt formation*

Among the classical developments, the resolution of aldehydes and ketones via amine bisulfite salts **68**, described by Adams and Garber,[75] illustrates an early application of α-PEA. Because a mixture of



Scheme 27.



Scheme 28.

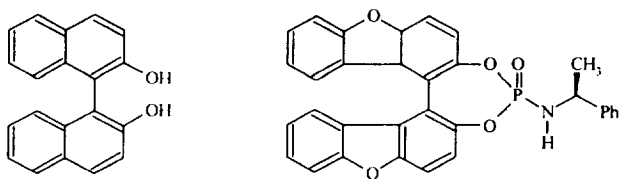
bisulfite stereoisomers is formed, resolution by this route has been limited to but a few cases, including 3-methylcyclohexanone (Scheme 31), 3-*t*-butylcyclohexanone, and β-methylcinnamaldehyde.

In 1967 Mosher described the resolution of four pairs of enantiomeric α-substituted phenylacetic acids with α-PEA,[76] by then already well established as a convenient resolving adjuvant (Scheme 32).

Seebach et al.[77] have recently reported the convenient resolution of 4,4,4-trifluoro-3-hydroxybutanoic acid (**69**) with α-PEA. Fractional crystallization of the *like* and *unlike* diastereomeric salts, followed by recovery of the free acid, led to the isolation of (*R*)- and (*S*)-**69** (Scheme 33).

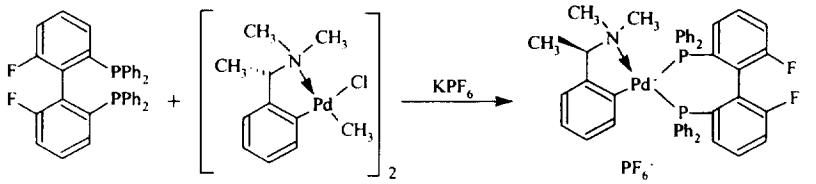
Classical resolution of racemic *E*-oxiranes **70** with α-PEA was essential in the synthesis of all four stereoisomers of methyl 3-phenyl-1H-aziridine-2-carboxylate (**71**) described by Zwanenburg and coworkers[78] (Scheme 34).

By the same token, the enantioselective preparation of spiro hydantoin (2*R*,4*S*)-**72** was accomplished by separation of the diastereomeric salts of acidic precursor **73** and (*S*)-benzyl-α-PEA (Scheme 35).[79]

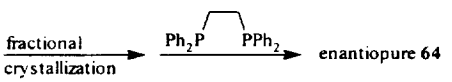


(±)-**62** (*R,S*)- and (*S,S*)-**63**

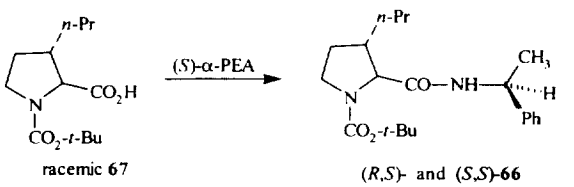
Fig. 15.



(±)-**64** (*S*)-**65** (diastereomeric pair)

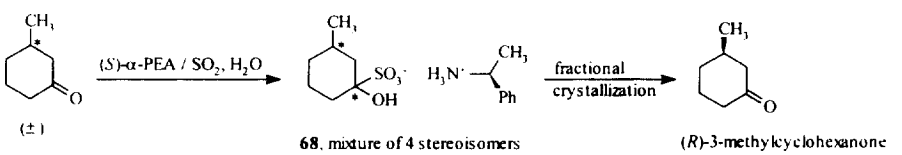


Scheme 29.



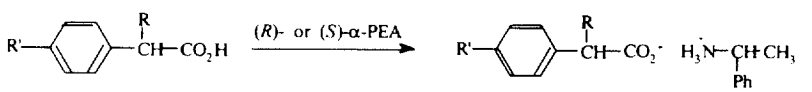
racemic **67** (*R,S*)- and (*S,S*)-**66**

Scheme 30.



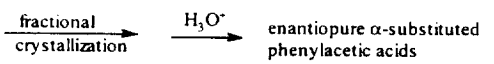
68, mixture of 4 stereoisomers (*R*)-3-methylcyclohexanone

Scheme 31.



R = CH_3, Et, *n*-Pr, *t*-Bu, CF_3
R' = H, OCH_3

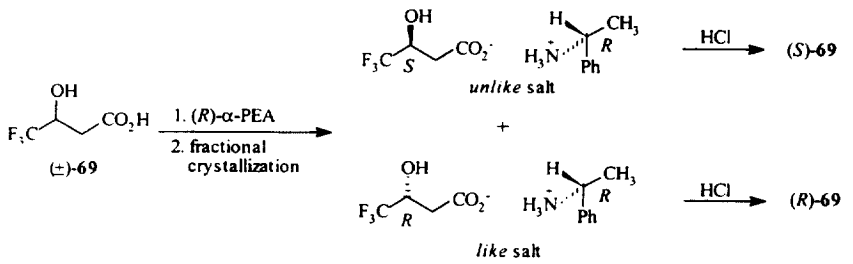
diastereomeric salts



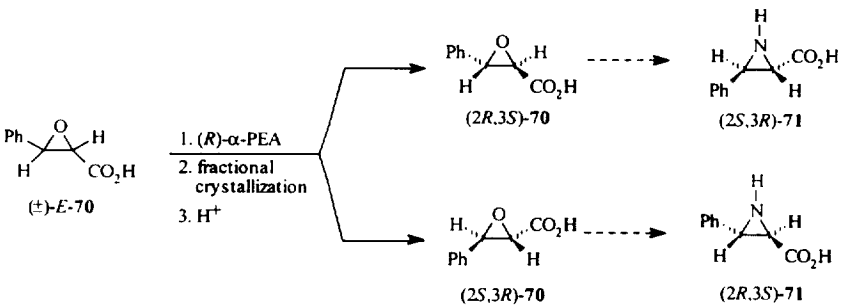
Scheme 32.

Additional chiral carboxylic acids that have been resolved via their diastereomeric salts with (*S*)- or (*R*)-α-PEA include 3-(4-methoxyphenyl)glycidic acid **74**,[80] 6-oxodecahydroisoquinoline-3-carboxylic acid **75**,[81] arylsuccinic acids **76**,[82] 5-dihydropyrimidinecarboxylic acids **77**,[83] phenylglycine derivative **78**,[84] and citric acid derivative **79**[85] (Fig. 16).

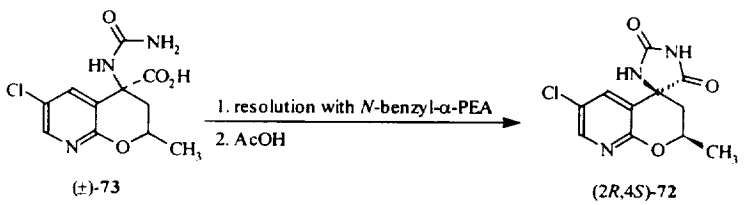
A useful procedure for the resolution of chiral alcohols involves conversion of the carbinol to



Scheme 33.



Scheme 34.



Scheme 35.

an alkyl hydrogen phthalate, followed by diastereomer salt formation with a chiral base such as α-PEA[86] or brucine.[87] Recent applications of this methodology have been described by Reyes and Juaristi[88] (2-octanol, Scheme 36), Hoffmann and Scharf[89] (all *trans*-2,3,4,5-tetramethylcyclopentanol, **80**, Fig. 17), Pallavicini et al.[90] (isopropyledene glycerol, **81**, Fig. 17), and Greene et al.[91] [1-(2,4,6-tri-isopropylphenyl)ethanol, **82**, Fig. 17].

3.3. Other resolution methods

In other recent developments, Bergbreiter and Zhang[92] have reported the use of ethylene oligomers containing (*R*)- or (*S*)-α-PEA (**83**, Fig. 18) for the resolution of racemic 10-camphorsulfonic acid.

Fogassy et al.[93,94] observed that the physical properties of diastereomeric derivatives of α-PEA in supercritical solvents such as CO_2 become more distinguishable than in traditional solvents, allowing more efficient resolution processes. For example, racemic aryl-acetic acids and cyclopropylcarboxylic acids were efficiently separated as diastereomeric pairs with (*R*)-α-PEA.

Kishikawa and coworkers[95] have developed a silica gel modified with a chiral acylurea containing two (*S*)-α-PEA moieties [(*S*, *S*)-**84**, Fig. 18]. The hydrogen bond acceptor centered in a pseudo-C_2 symmetric environment proved quite effective in the resolution of various racemic butanamides **85** (Fig. 18).

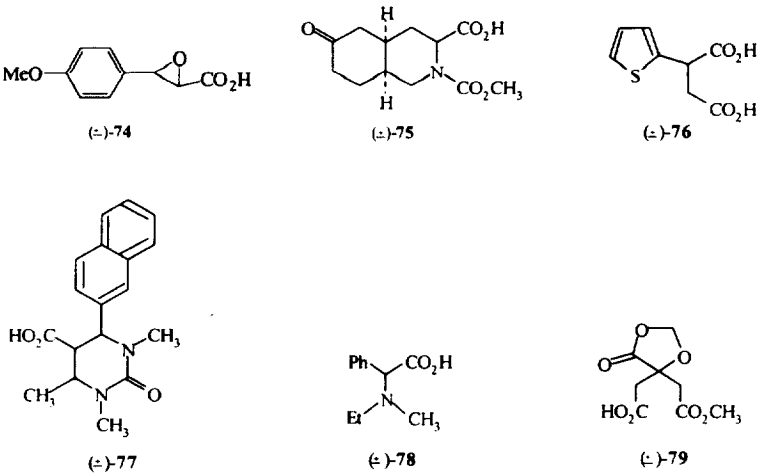
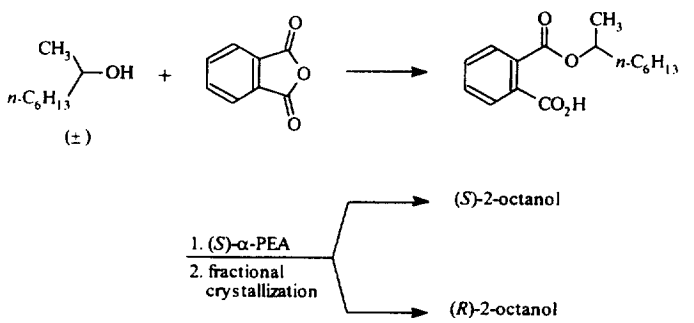


Fig. 16.



Scheme 36.

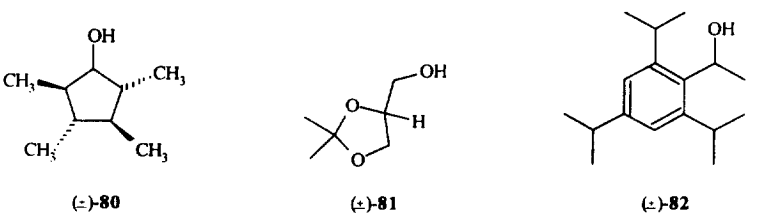


Fig. 17.

4. Concluding remarks

Due to the low price of both enantiomers of α-PEA, chemists will continue to use this chiral amine or derivatives therefrom in the preparation of enantiomerically pure compounds. The present summary of the application of α-phenylethylamine in the development of chiral catalysts, or as a resolving agent, may motivate the interest of chemists in academia and also in industry to take advantage of this simple but powerful chiral adjuvant.

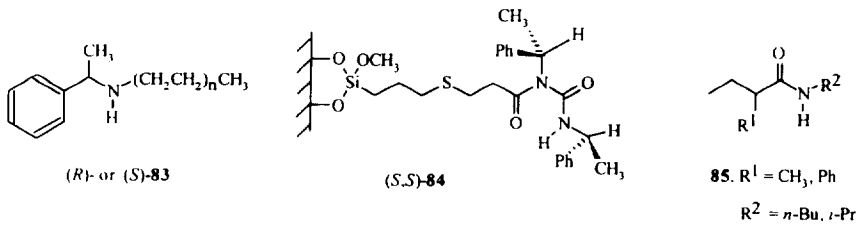


Fig. 18.

Acknowledgements

We are indebted to the Editor (Professor D. P. Curran) and one of the reviewers, for many useful recommendations.

References

1. Juaristi, E. *Introduction to Stereochemistry and Conformational Analysis*; Wiley: New York, 1991.
2. Crosby, J. *Tetrahedron* **1991**, *47*, 4789.
3. Sheldon, R. A. *Chirotechnology*; M. Dekker: New York, 1993.
4. Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994.
5. Seyden-Penne, J. *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; Wiley: New York, 1995.
6. Ager, D. J.; East, M. B. *Asymmetric Synthetic Methodology*; CRC Press: Boca Raton, 1996.
7. Gawley, R. E.; Aubé, J. *Principles of Asymmetric Synthesis*; Pergamon: Oxford, 1996.
8. Juaristi, E. *Anales Quím. Int. Ed.* **1997**, *93*, 135.
9. *N*-Alkylated derivatives of α-PEA are readily prepared: Juaristi, E.; Murer, P.; Seebach, D. *Synthesis* **1993**, 1243.
10. (a) Ault, A. *Organic Synthesis*; Wiley: New York, 1973, Coll. Vol. V, p. 932. (b) Newman, P. *Optical Resolution Procedures for Chemical Compounds*; O. R. I. C., Manhattan College: New York, 1978; Vol. 1, p. 79.
11. Brown, E.; Viot, F.; Le Floch, Y. *Tetrahedron Lett.* **1985**, *26*, 4451.
12. (a) Hua, D.; Miao, S. W.; Chen, J. S.; Iguchi, S. *J. Org. Chem.* **1991**, *56*, 4. (b) Wu, M.-J.; Pridgen, L. N. *J. Org. Chem.* **1991**, *56*, 1340.
13. For a short, recent review, see: Jaen, J. C. In *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 5, p. 3427.
14. Because of time and space limitations, this manuscript concentrates on literature published in the 1990–1997 period. Nevertheless, we want to apologize for relevant work not included here. We would appreciate it if the readers inform us about such missing references.
15. Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106.
16. Kagan, H. B. *Bull. Soc. Chim. Fr.* **1988**, 846.
17. Morrison, J. D., Ed. *Asymmetric Synthesis*; Academic Press: New York, 1985; Vol. 5.
18. (a) Ojima, I.; Clos, N.; Basto, C. *Tetrahedron* **1989**, *45*, 6901. (b) Ojima, I., Ed. *Catalytic Asymmetric Synthesis*; VCH Publishers: Weinheim, 1993.
19. (a) Brunner, H. *Top. Stereochem.* **1988**, *18*, 129. (b) Brunner, H.; Zettlemeier, W. *Handbook of Enantioselective Catalysis*; VCH Publishers: Weinheim, 1993.
20. Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994.
21. Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 497.
22. Chevallier, Y.; Stern, R.; Sajus, L. *Tetrahedron Lett.* **1969**, 1197.
23. Fiorini, M.; Marcati, F.; Giongo, G. M. *J. Mol. Catal.* **1978**, *4*, 125.
24. Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375.
25. (a) Yamada, I.; Yamaguchi, M.; Yamagishi, T. *Tetrahedron: Asymmetry* **1996**, *7*, 3339. (b) Yamada, I.; Ohkouchi, M.; Yamaguchi, M.; Yamagishi, T. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1869.
26. (a) Borch, R. F.; Levitan, S. R. *J. Org. Chem.* **1972**, *37*, 2347. (b) Grundon, M. F.; McCleery, D. G.; Wilson, J. W. *J. Chem. Soc., Perkin Trans. 1* **1981**, 231.
27. Hogeveen, H.; Elevald, M. B. *Tetrahedron Lett.* **1986**, *26*, 635.

28. Periasamy, M.; Kanth, J. V. B.; Reddy, C. K. *J. Chem. Soc., Perkin Trans. 1.* **1995**, 427.
29. (a) Burns, B.; Studley, J. R.; Wills, M. *Tetrahedron Lett.* **1993**, *34*, 7105. (b) Burns, B.; King, N. P.; Studley, J. R.; Tye, H.; Wills, M. *Tetrahedron: Asymmetry* **1994**, *5*, 801. (c) See also: Burns, B.; Merifield, E.; Mahon, M. F.; Molloy, K. C.; Wills, M. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2243.
30. (a) Zassinovich, G.; Bettella, R.; Mestroni, G.; Bresciani-Pahor, N.; Geremia, S.; Randaccio, L. *J. Organometal. Chem.* **1989**, *370*, 187. (b) See also: Zassinovich, G.; Mestroni, G.; Gladiali, S. *Chem. Rev.* **1992**, *92*, 1051.
31. Bianchini, C.; Farnetti, E.; Glendenning, L.; Graziani, M.; Nardin, G.; Peruzzini, M.; Rocchini, E.; Zanobini, F. *Organometallics* **1995**, *14*, 1489.
32. For recent discussions, see: (a) Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833. (b) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49. (c) Knochel, P. *Chemtracts* **1995**, *8*, 205. (d) van Koten, G. *Pure Appl. Chem.* **1994**, *66*, 1455.
33. (a) Uemura, M.; Miyake, R.; Hayashi, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 1696. (b) Uemura, M.; Miyake, R.; Shiro, M.; Hayashi, Y. *Tetrahedron Lett.* **1991**, *32*, 4569.
34. Blagg, J.; Davies, S. G.; Goodfellow, C. L.; Sutton, K. H. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1805.
35. Rijnberg, E.; Hovestad, N. J.; Kleij, A. W.; Jastrzebski, J. T. B. H.; Boersma, J.; Janssen, M. D.; Spek, A. L.; van Koten, G. *Organometallics* **1997**, *16*, 2847.
36. (a) van Aken, E.; Wynberg, H.; van Bolhuis, F. *Acta Chem. Scand.* **1993**, *47*, 122. (b) Sasai, H.; Suzuki, T.; Itoh, N.; Tanaka, K.; Date, T.; Okamura, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1993**, *115*, 10372, and references therein.
37. Chinchilla, R.; Nájera, C.; Sánchez-Agulló, P. *Tetrahedron: Asymmetry* **1994**, *5*, 1393.
38. Iuliano, A.; Pini, D.; Salvadori, P. *Tetrahedron: Asymmetry* **1995**, *6*, 739.
39. Corey, E. J.; Po-Wai, Y.; Hannon, F. J.; Wierda, D. A. *J. Org. Chem.* **1990**, *55*, 784.
40. Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028.
41. (a) Anaya de Parrodi, C.; Juaristi, E.; Quintero-Cortés, L.; Amador, P. *Tetrahedron: Asymmetry* **1996**, *7*, 1915. (b) Anaya de Parrodi, C.; Juaristi, E.; Quintero-Cortés, L. *Anales Quím. Int. Ed.* **1996**, *92*, 400.
42. For a recent discussion of lithium salt effects in organic synthesis, see: Seebach, D.; Beck, K. A.; Studer, A. *Modern Synthetic Methods 1995*; VCH Publishers: Basel, 1995; pp. 1–178.
43. Kretchmer, R. A. *J. Org. Chem.* **1972**, *37*, 2744.
44. Bertz, S. H.; Dabbagh, G.; Sundararajan, G. *J. Org. Chem.* **1986**, *51*, 4953.
45. Jansen, J. F. G. A.; Feringa, B. L. *J. Chem. Soc., Chem. Commun.* **1989**, 741.
46. (a) Villacorta, G. M.; Rao, C. P.; Lippard, S. J. *J. Am. Chem. Soc.* **1988**, *110*, 3175. (b) Ahn, K.-H.; Klassen, R. B.; Lippard, S. J. *Organometallics* **1990**, *9*, 3178.
47. Rossiter, B. E.; Eguchi, M.; Miao, G.; Swingle, N. M.; Hernández, A. E.; Vickers, D.; Fluckiger, E.; Patterson, R. G.; Reddy, K. V. *Tetrahedron* **1993**, *49*, 965.
48. Uemura, M.; Miyake, R.; Nakayama, K.; Hayashi, Y. *Tetrahedron: Asymmetry* **1992**, *3*, 713.
49. Wendisch, V.; Sewald, N. *Tetrahedron: Asymmetry* **1997**, *8*, 1253.
50. Hayashi, Y.; Sakai, H.; Kaneta, N.; Uemura, M. *J. Organometal. Chem.* **1995**, *503*, 143.
51. Uemura, M.; Miyake, R.; Nishimura, H.; Matsumoto, Y.; Hayashi, T. *Tetrahedron: Asymmetry* **1992**, *3*, 213.
52. Wilen, S. H. *Top. Stereochem.* **1971**, *6*, 107.
53. Cope, A. C.; Ganellin, C. R.; Johnson, H. W.; van Auken, T. V.; Winkler, H. J. S. *J. Am. Chem. Soc.* **1963**, *85*, 3276.
54. For the determination of the absolute configuration, see: Manor, P. C.; Shoemaker, D. P.; Parkes, A. S. *J. Am. Chem. Soc.* **1970**, *92*, 5260.
55. Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 2436.
56. Helmchen, G.; Nill, G.; Flockerzi, D.; Yonssef, M. S. K. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 63.
57. Perry, C. W.; Brossi, A.; Deitcher, K. H.; Tautz, W.; Teitel, S. *Synthesis* **1977**, 492.
58. Nohira, H.; Nohira, M.; Yoshida, S.; Osada, A.; Terunuma, D. *Bull. Chem. Soc. Jpn* **1988**, *61*, 1395.
59. Seebach, D.; Juaristi, E.; Miller, D. D.; Schickli, C.; Weber, T. *Helv. Chim. Acta* **1987**, *70*, 237.
60. Juaristi, E.; Rizo, B.; Natal, V.; Escalante, J.; Regla, I. *Tetrahedron: Asymmetry* **1991**, *2*, 821.
61. Okada, Y.; Minami, T.; Umezu, Y.; Nishikawa, S.; Mori, R.; Nakayama, Y. *Tetrahedron: Asymmetry* **1991**, *2*, 667.
62. Mukaiyama, T.; Usui, M.; Shimada, E.; Saigo, K. *Chem. Lett.* **1975**, 1045.
63. Naruto, S.; Terada, A. *Chem. Pharm. Bull.* **1991**, *39*, 190.
64. Hoffman, R. V.; Kim, H.-O. *Tetrahedron* **1992**, *48*, 3007.
65. Ozegowski, R.; Kumath, A.; Schick, H. *Tetrahedron: Asymmetry* **1993**, *4*, 695.
66. (a) Acher, F.; Azerad, R. *Tetrahedron: Asymmetry* **1994**, *5*, 731. (b) See also: Yamazaki, T.; Zhu, Y.-F.; Probst, A.; Chadha, R. K.; Goodman, M. *J. Org. Chem.* **1991**, *56*, 6644.
67. Franck-Neumann, M.; Stöber, P.; Passmore, G. *Tetrahedron: Asymmetry* **1996**, *7*, 3193.

68. Morita, S.; Ohtsubo, K.; Matsubara, J.; Ohtani, T.; Uchida, M.; Kido, M.; Shimizu, T. *Chem. Pharm. Bull.* **1994**, *42*, 2157.
69. Antonov, D. Y.; Belokon, Y. N.; Ikonnikov, N. S.; Orlova, S. A.; Pisarevsky, A. P.; Raevski, N. I.; Rozenberg, V. I.; Sergeeva, E. V.; Struchkov, Y. T.; Tararov, V. I.; Vorontsov, E. V. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1873.
70. Ouryupin, A. B.; Kadyko, M. I.; Petrovskii, P. V.; Fedin, E. I.; Okruszek, A.; Kinas, R.; Stec, W. J. *Tetrahedron: Asymmetry* **1995**, *6*, 1813.
71. Gong, B.; Chem, W.; Hu, B. *J. Org. Chem.* **1991**, *56*, 423.
72. Gelpke, A. E. S.; Fraanje, J.; Goubitz, K.; Schenk, H.; Hiemstra, H. *Tetrahedron* **1997**, *53*, 5899.
73. Jendralla, H.; Li, C. H.; Paulus, E. *Tetrahedron: Asymmetry* **1994**, *5*, 1297.
74. Chung, J. Y. L.; Wasicak, J. T.; Arnold, W. A.; May, C. S.; Nadzan, A. M.; Holladay, M. W. *J. Org. Chem.* **1990**, *55*, 270.
75. (a) Adams, R.; Garber, J. D. *J. Am. Chem. Soc.* **1949**, *71*, 522. (b) Adolphen, G.; Eisenbraun, E. J.; Keen, G. W.; Flanagan, P. W. K. *Org. Prep. Proced.* **1970**, *2*, 93.
76. Aaron, C.; Dull, D.; Schmiegel, J. L.; Jaeger, D.; Ohashi, Y.; Mosher, H. S. *J. Org. Chem.* **1967**, *32*, 2797.
77. Acs, M.; von dem Bussche, C.; Seebach, D. *Chimia* **1990**, *44*, 90.
78. Thijs, L.; Porskamp, J. J. M.; van Loon, A. A. W. M.; Derks, M. P. W.; Feenstra, R. W.; Legters, J.; Zwanenburg, B. *Tetrahedron* **1990**, *46*, 2611.
79. Sarges, R.; Goldstein, S. W.; Welch, W. M.; Swindell, A. C.; Siegel, T. W.; Beyer, T. A. *J. Med. Chem.* **1990**, *33*, 1859.
80. Yamamoto, M.; Hayashi, M.; Masaki, M.; Nohira, H. *Tetrahedron: Asymmetry* **1991**, *2*, 403.
81. Ornstein, P. L.; Arnold, M. B.; Augenstein, N. K.; Paschal, J. W. *J. Org. Chem.* **1991**, *56*, 4388.
82. Brunner, H.; Zettlmeier, W. *Bull. Soc. Chim. Belg.* **1991**, *100*, 259.
83. (a) Kappe, C. O.; Uray, G.; Roshger, P.; Lindner, W.; Kratky, C.; Keller, W. *Tetrahedron* **1992**, *48*, 5473. (b) See also: Moriarty, R. M.; Levy, S. G. *J. Heterocyclic Chem.* **1995**, *32*, 155.
84. Shiraiwa, T.; Baba, Y.; Miyazaki, H.; Sakata, S.; Kawamura, S.; Uehara, M.; Kurokawa, H. *Bull. Chem. Soc. Jpn* **1993**, *66*, 1430.
85. Ancliff, R. A.; Russell, A. T.; Sanderson, A. J. *Tetrahedron: Asymmetry* **1997**, *8*, 3379.
86. Gough, G. A. C.; Hunter, H.; Kenyon, J. *J. Chem. Soc.* **1926**, 2052.
87. Ingersoll, A. W. In *Organic Reactions*, Adams, R., Ed.; Wiley: New York, 1944; Vol. 2, Chapter 9.
88. Reyes, A.; Juaristi, E. *Synth. Commun.* **1995**, *25*, 1053.
89. Hoffmann, N.; Scharf, H.-D. *Tetrahedron: Asymmetry* **1991**, *2*, 977.
90. Pallavicini, M.; Valoti, E.; Villa, L.; Piccolo, O. *Tetrahedron: Asymmetry* **1994**, *5*, 5.
91. Delair, P.; Kanazawa, A. M.; de Azevedo, M. B. M.; Greene, A. E. *Tetrahedron: Asymmetry* **1996**, *7*, 2707.
92. Bergbreiter, D. E.; Zhang, L. *J. Chem. Soc., Chem. Commun.* **1993**, 596.
93. Fogassy, E.; Acs, M.; Szili, T.; Simandi, B.; Sawinsky, J. *Tetrahedron Lett.* **1994**, *35*, 257.
94. Kozma, D.; Acs, M.; Fogassy, E. *Tetrahedron* **1994**, *50*, 6907.
95. (a) Kishikawa, K.; Otake, K.; Kohmoto, S.; Yamamoto, M.; Yamada, K. *Tetrahedron: Asymmetry* **1995**, *6*, 329. (b) Kishikawa, K.; Takada, Y.; Kawashima, K.; Kohmoto, S.; Yamamoto, M.; Yamada, K. *Tetrahedron: Asymmetry* **1996**, *7*, 1733.