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New chiral 1,3-diphosphine ligands for Rh-catalyzed enantioselective hydrogenation: a search for electronic effects

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Abstract—New electron-rich chiral 1,3-diphosphines of the BDPP type were prepared from 1,3-diphenylpropane-1,3-diol by an economically feasible synthetic approach. The σ-donor properties of the phosphines were determined by measurement of $J(^{31}P–^{77}Se)$ coupling constants in the corresponding phosphine selenides. For comparison related, but electronically different, 1,3-diphosphines were considered. The new diphosphines showed good enantioselectivities as ligands in the Rh-catalyzed enantioselective hydrogenation of benchmark substrates and β-amino acid precursors (up to 98% ee). The electronic effects on the outcome of the enantioselective catalysis have been analyzed.

1. Introduction

The enantioselective Rh-catalyzed hydrogenation of prochiral olefins is a key step in several industrial processes.[1] In particular, chiral trivalent phosphorus compounds have been applied as ancillary ligands, which can confer to the catalyst a powerful stereodiscriminating ability.[2] To date, literally thousands of P-ligands have been tested in this transformation.[3] In spite of the vast number of ligands and substrates investigated, understanding about how the enantioselectivity can be controlled is limited. Besides steric effects, electronic influences have also been noted in several cases. Achiwa was the first, who showed that electron-rich phosphines may have a beneficial effect on the enantioselectivity.[4] RajanBabu et al. found enhanced enantioselectivities in the Rh-catalyzed hydrogenation of α-acetamido acrylates with C_1-symmetric arylphosphinites as ligands bearing electron-donating groups at the *meta*- or *para*-position of the aryl groups.[5] Recently, Bakos et al. reported on some interesting results with C_2-symmetric 1,3-diphosphine ligands of the BDPP-type (BDPP = skewPHOS[6a] = chiral 2,4-bis(diphenylphosphino)pentane).[6b] Thus, incorporation of one or more electron-donating groups in the P-aryl rings significantly decreased the enantioselectivity in the hydrogenation of itaconic acid and its dimethyl ester. In contrast, by employment of α-acetamido acrylates as substrates electron-rich phosphines performed superior as ligands.

These results prompted us to report herein our results on Rh-catalyzed hydrogenation with ligands of types **1** and **2**. These diphosphines bear electronically different substituents at the 1-position (phenyl vs *p*-tolyl) and 2-position (phenyl vs cyclohexyl), respectively, to the phosphorus atom. These investigations were facilitated by a simple and economically feasible access to diphosphine **1a**, which represents the pivotal component of a catalytic cross self-replicating system.[7] Herein, **1a** has been advantageously employed for the stereoselective production of the other chiral diphosphines.

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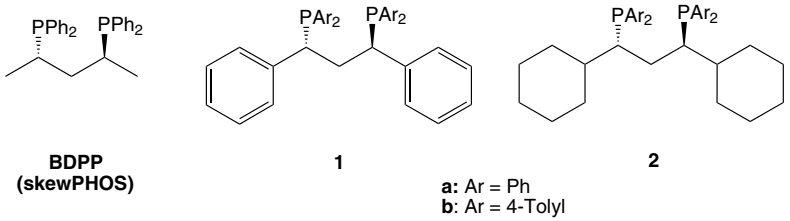


2. Results and discussion

New diphosphines **2a** and **b** were synthesized via chiral diol **4** (Scheme 1). The key step of our approach is the highly stereoselective hydrogenation of 1,3-diketone **3** by using a Ru(II)-catalyst based on *ent*-**1a** as a chiral ligand ('cross self replicating process') which affords the ligand precursor 1,3-diphenyl-propane-1,3-diol **4** in more than 99% de and 99% ee. This compound was transformed into diphosphines **1a** and **b** by the procedure already detailed.[7] It was envisaged to reduce the benzylic rings of **4** with a heterogeneous catalyst in order to obtain diol **5**. This reaction has already been described by Donovan and Roos who relied their approach on the use of a Rh-chloride catalyst.[8]

This method however is hampered by the high price of the metal used and long reaction time (22 h). To our surprise, we found that inexpensive Ru/Al_2O_3 can also be used for the smooth saturation of the aromatic rings.[9] The heterogeneous catalyst gave the desired 1,3-dicyclohexylpropane-1,3-diol **5** in quantitative yield within 3 h. HPLC-analysis indicated that epimerization did not occur during the reaction. Neither the corresponding *meso*-diol nor the opposite enantiomer was detected. Subsequent incorporation of arylphosphine groups via dimesylate **6** afforded diphosphines **2a** and **b**.

For the characterization of the σ-donor properties of phosphines, the measurement of phosphorus–selenium coupling constants $J(^{77}Se–^{31}P)$ in the ^{31}P NMR spectroscopy has been suggested.[10] In general, the higher the magnitude of the coupling constant, the lower the basicity of the phosphine.[10a] Suitable diselenides were prepared in a NMR tube by treating bisphosphines **1** and **2** with an excess of elemental selenium in $CDCl_3$ at room temperature. For comparison, the phosphine selenide of BDPP was also synthesized. Coupling constants are summarized in Table 1.

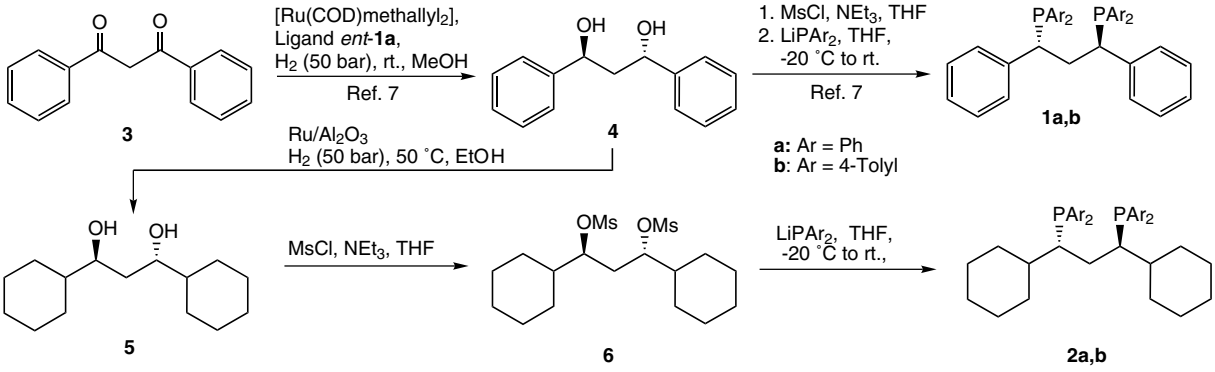
Table 1. $^{31}P–^{77}Se$ coupling constants (Hz) for phosphine selenides

Diselenides derived from diphosphine	$J(^{31}P–^{77}Se)$[a]
1a	744
1b	736
2a	724
2b	716
BDPP	722

[a] Measured in $CDCl_3$.

Selenides of diphosphines **1a** and **b** are characterized by the largest coupling constants amongst the compounds investigated herein indicating their low σ-donor capability. As expected, the replacement of the P-phenyl groups by the electron donating *p*-tolyl groups diminished the coupling constant. This permutation resulted in a constant decrease of 8 Hz. Interestingly, the saturation of the β-phenyl rings has an even more pronounced effect. Thus, the coupling constants of selenides derived from 1,3-dicyclohexyl derivatives **2a** and **b** are 20 Hz smaller than those derived from related 1,3-diphenyl-bis(diarylphosphino)propanes **1a** and **b**. When considering only the electronic properties, it becomes clear that BDPP is more related to the 1,3-dicyclohexyl compounds **2a** and **b** than to the 1,3-diphenyl analogues **1a** and **b**.

Cationic Rh(I)-precatalysts of the type [Rh(COD)-(ligand)]BF_4 were prepared by the reaction of diphosphines with [Rh(COD)acac] and subsequent addition of HBF_4. Purification of these complexes was accomplished by recrystallization from THF/Et_2O. Yellow



Scheme 1.

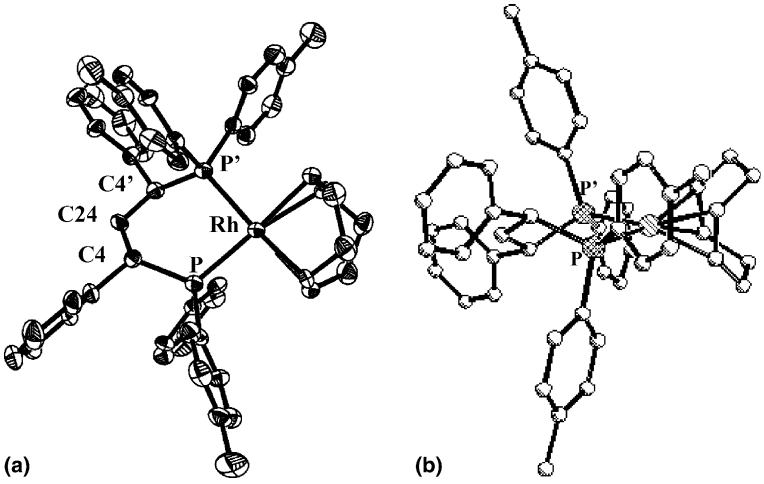


Figure 1. Crystal structure of the cation of [Rh(COD)(*R*,*R*-**1b**)]$^+$. (a) Top-view; ORTEP plot. Hydrogen atoms have been omitted for clarity. (b) Side view, ball and stick model. Selected interatomic distances (Å) and intramolecular angles (deg): P′-Rh = 2.311(2), P-Rh = 2.312(2), P-Rh-P′ = 89.37 (10); C4–C24–C4′ = 123.1(8).

crystals of [Rh(COD)(**1b**)]BF_4 obtained were suitable for a X-ray structural analysis. The structure of the cation is shown in Figure 1 along with the selected bond lengths and intramolecular angles. Similar to the related [Rh(COD)(**BDPP**)]$^+$ complex, this cation also adopted a λ-skew conformation, which was forced by the two 1,3-diphenyl groups attached to the six-membered chelate ring.[6a,11] The P(*p*-tolyl) rings are in a chiral array with alternate quasi-axial and quasi-equatorial position.

The new bidentate chiral phosphines were tested as ligands in the Rh-catalyzed asymmetric hydrogenation of benchmark substrates and β-dehydroamino acid derivatives (Figs. 2–7, for exact values see Tables 2–4). For comparison, some results obtained with the closely related BDPP precatalyst are also given. In general, catalysts based on the ligands considered herein show strongly varying enantiodiscriminating ability. In most cases, the best results were obtained in CH_2Cl_2 as the solvent for the hydrogenation.

In the hydrogenation of the benchmark substrate, methyl (*Z*)-α-*N*-acetylamino cinnamate, low or moderate enantioselectivities were observed (Fig. 2). Differences were in the range of 20% ee for the (*S*)-product to 76% ee for the formation of the (*R*)-product. Best results were obtained with electron-rich diphosphines as ligands. Unexpectedly, the less bulky ligand BDPP gave the highest ees independent of the solvent used.

In the reduction of the other commonly used benchmark substrate dimethyl itaconate, enantioselectivities of up to 96% were achieved (Fig. 3). It is remarkable that in strong contrast to the hydrogenation of the α-amino acid precursor for this substrate, the catalyst based upon the less basic diphosphine ligands **1a** and **b** was superior and the catalyst derived from BDPP gave low ees.

As industrially important substrates, we also tested β-amino acid precursors. Recent investigations have shown that the course of the reaction as well as

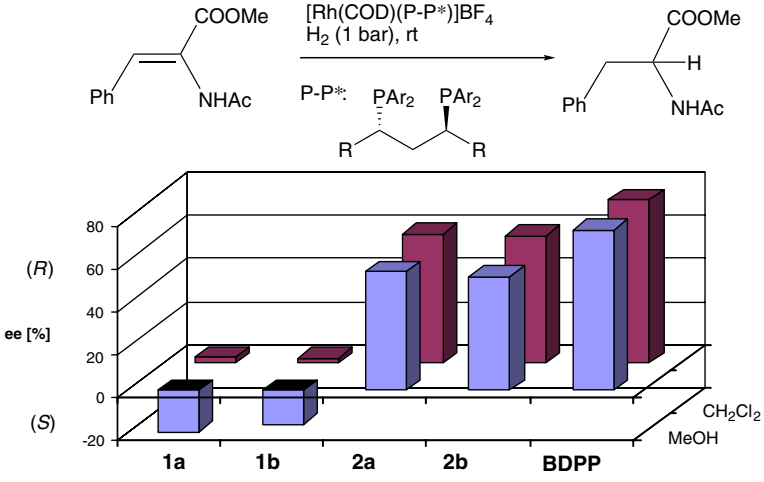


Figure 2. Enantioselective hydrogenation of methyl (*Z*)-α-*N*-acetylamino cinnamate.

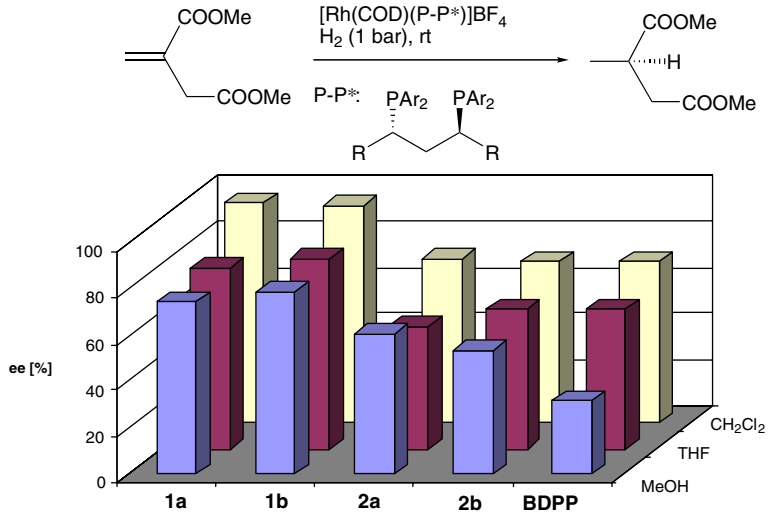


Figure 3. Enantioselective hydrogenation of dimethyl itaconate.

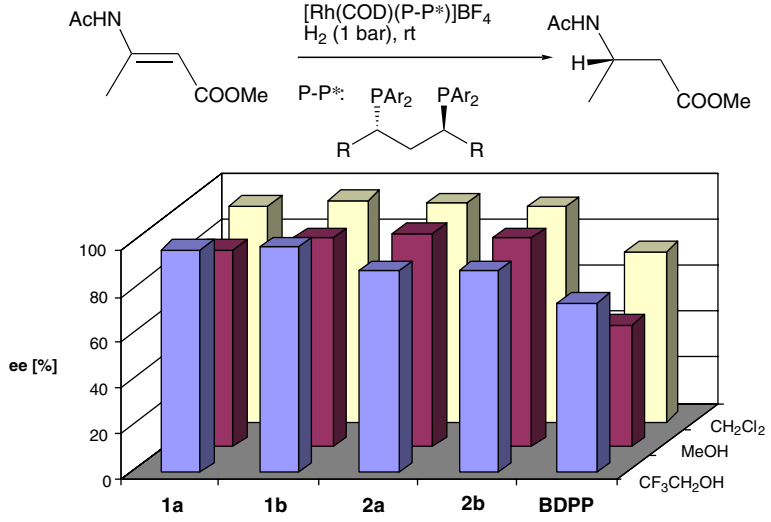


Figure 4. Enantioselective hydrogenation of methyl (*E*)-β-acetylamino butenoate.

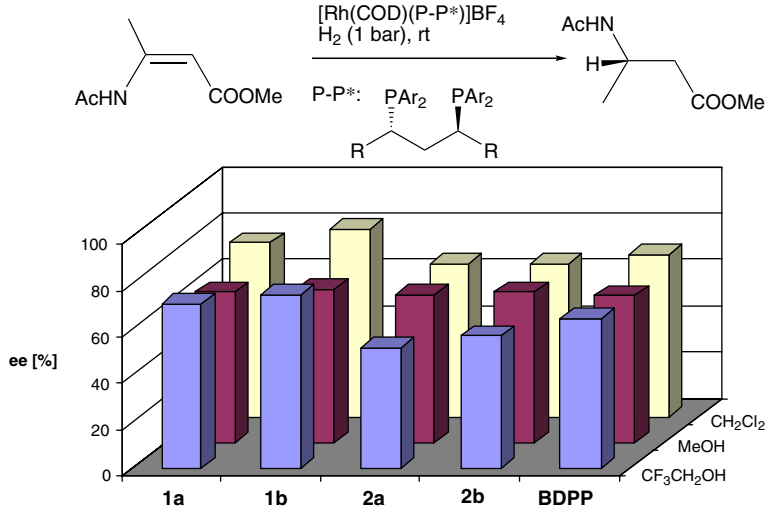


Figure 5. Enantioselective hydrogenation of methyl (*Z*)-β-acetylamino butenoate.

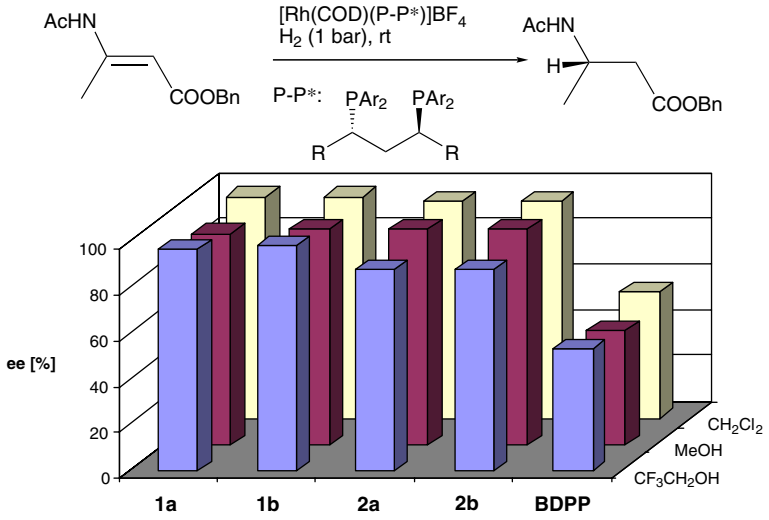


Figure 6. Enantioselective hydrogenation of benzyl (*E*)-β-acetylamino butenoate.

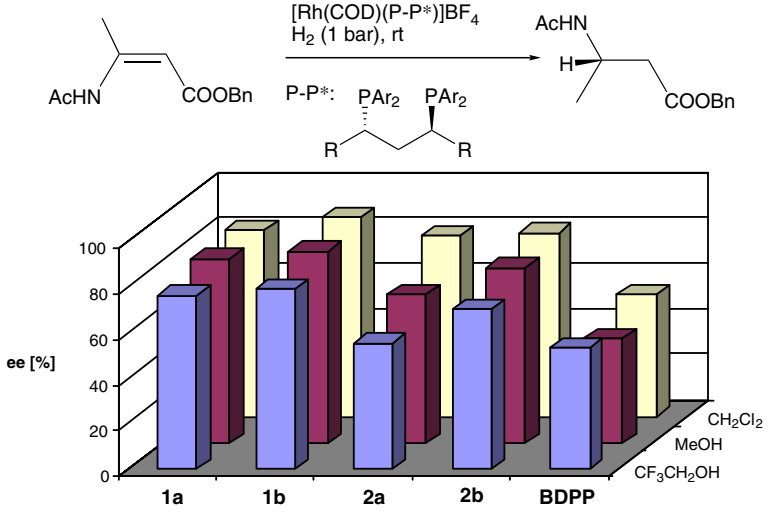


Figure 7. Enantioselective hydrogenation of benzyl (*Z*)-β-acetylamino butenoate.

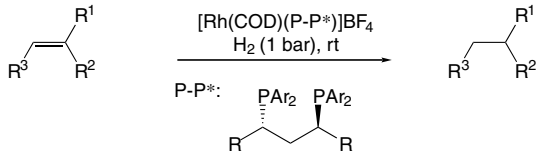
enantioselectivities achievable may be strongly dependent on the *E*–*Z* geometry in the substrate.[12] Relevant results are detailed in Figures 4–7.

In general, with *E*-configured substrates, excellent ees were achieved (Fig. 4). A further improvement could be achieved by employment of the corresponding benzyl instead of methyl ester (Fig. 6). Good results were also obtained in the strongly polar solvent CF_3CH_2OH. The important protected β-amino acids could be produced by up to 98% ee (ligand **1b**). With *Z*-configured substrates, lower ees were obtained (Figs. 5 and 7). It seems that electronic effects in the catalyst do not play such a dominant role as noted with benchmark substrates discussed above. Only a slight decrease in the ee occurred due to the saturation of the 1,3-phenyl rings (ligands **2a** and **b**). Comparison of the results obtained with the electronically equivalent, but sterically less crowded catalysts (ligand **2a**,**b** vs BDPP) shows a slight decrease in the enantioselectivity (compare Figs. 4, 6 and 7). Obviously, the hydrogenation of this type of substrate is more dependent on the steric features of the catalysts than on the electronic effects of the ligand.

3. Conclusions

New chiral electron-rich C_2-symmetric substituted 1,3-diphosphines of the BDPP-type have been prepared by a short and economically feasible pathway. In order to assess their σ-donor properties, ^{31}P–^{77}Se coupling constants of the corresponding phosphine selenides were measured. For comparison, relevant coupling constants of related 1,3-diphenyl and 1,3-dimethyl compounds were likewise determined. Differences by up to 28 Hz were noted dependent on the substitution pattern. In the Rh-catalyzed enantioselective

Table 2. Enantioselective hydrogenations of benchmark substrates with [Rh(COD)((*R*,*R*)-ligand)]BF_4[a]



Run	Ligand, R	Ar	R^1	R^2	R^3	Solvent	ee [%][b]
1	**1a**, Ph	Ph	COOMe	NHAc	Ph	MeOH	20 (*S*)[c]
2	**1a**, Ph	Ph	COOMe	NHAc	Ph	CH_2Cl_2	3 (*R*)[c]
3	**1b**, Ph	*p*-Tol	COOMe	NHAc	Ph	MeOH	16 (*S*)[c]
4	**1b**, Ph	*p*-Tol	COOMe	NHAc	Ph	CH_2Cl_2	2 (*R*)[c]
5	**2a**, Cy	Ph	COOMe	NHAc	Ph	MeOH	55 (*R*)[c]
6	**2a**, Cy	Ph	COOMe	NHAc	Ph	CH_2Cl_2	60 (*R*)[c]
7	**2b**, Cy	*p*-Tol	COOMe	NHAc	Ph	MeOH	53 (*R*)[c]
8	**2b**, Cy	*p*-Tol	COOMe	NHAc	Ph	CH_2Cl_2	59 (*R*)[c]
9	Me	Ph	COOMe	NHAc	Ph	MeOH	75 (*R*)[c]
10	Me	Ph	COOMe	NHAc	Ph	CH_2Cl_2	76 (*R*)[c]
11	**1a**, Ph	Ph	COOMe	CH_2COOMe	H	CH_2Cl_2	96 (*R*)[d]
12	**1a**, Ph	Ph	COOMe	CH_2COOMe	H	MeOH	75 (*R*)[d]
13	**1a**, Ph	Ph	COOMe	CH_2COOMe	H	THF	79 (*R*)[d]
14	**1a**, Ph	Ph	COOH	CH_2COOH	H	CH_2Cl_2	87 (*R*)[e]
15	**1a**, Ph	Ph	COOH	CH_2COOH	H	MeOH	88 (*R*)[e]
16	**1a**, Ph	Ph	COOH	CH_2COOH	H	THF	94 (*R*)[e]
17	**1b**, Ph	*p*-Tol	COOMe	CH_2COOMe	H	CH_2Cl_2	95 (*R*)[d]
18	**1b**, Ph	*p*-Tol	COOMe	CH_2COOMe	H	MeOH	80 (*R*)[d]
19	**1b**, Ph	*p*-Tol	COOMe	CH_2COOMe	H	THF	83 (*R*)[d]
20	**1b**, Ph	*p*-Tol	COOH	CH_2COOH	H	CH_2Cl_2	82 (*R*)[e]
21	**1b**, Ph	*p*-Tol	COOH	CH_2COOH	H	MeOH	85 (*R*)[e]
22	**1b**, Ph	*p*-Tol	COOH	CH_2COOH	H	THF	88 (*R*)[e]
23	**2a**, Cy	Ph	COOMe	CH_2COOMe	H	CH_2Cl_2	71 (*R*)[d]
24	**2a**, Cy	Ph	COOMe	CH_2COOMe	H	MeOH	61 (*R*)[d]
25	**2a**, Cy	Ph	COOMe	CH_2COOMe	H	THF	53 (*R*)[d]
26	**2b**, Cy	*p*-Tol	COOMe	CH_2COOMe	H	CH_2Cl_2	70 (*R*)[d]
27	**2b**, Cy	*p*-Tol	COOMe	CH_2COOMe	H	MeOH	54 (*R*)[d]
28	**2b**, Cy	*p*-Tol	COOMe	CH_2COOMe	H	THF	61 (*R*)[d]
29	Me	Ph	COOMe	CH_2COOMe	H	CH_2Cl_2	70 (*R*)[d]
30	Me	Ph	COOMe	CH_2COOMe	H	MeOH	32 (*R*)[d]

[a] Conditions: 0.01 mmol precatalyst, 1.0 mmol of prochiral olefin in 15.0 ml solvent at 25.0 °C, 1.0 atm overall pressure over the solution.
[b] Measured after consumption of the calculated amount of H_2.
[c] Determined by GC, 25 m Lipodex E, 145 °C.
[d] Determined by GC, 25 m Lipodex E, 80 °C.
[e] After esterification with diazomethane as dimethyl methylmalonate.

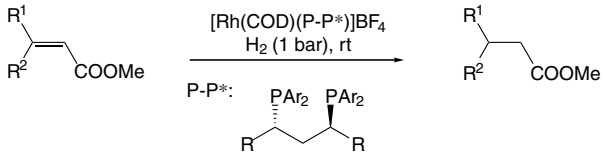
hydrogenations of benchmark substrates, such as α-dehydroamino acid precursors and dimethyl itaconate as well as of pharmaceutically important β-dehydroamino acid precursors up to 98% ee could be achieved (Tables 2–4). Interestingly, the electronic features in the ligands affect the enantioselectivity in different ways. Thus, with methyl (*Z*)-α-*N*-acetylamino cinnamate, electron-rich phosphine ligands in the catalyst performed better. In strong contrast, the hydrogenation of dimethyl itaconate benefits from electron-poor phosphines as ligands. These results match well the tendency noted by Bakos et al. with related catalysts.[6b] Moreover, it also confirms tendencies described by Rajan-Babu with structurally entirely different catalysts based on seven-membered Rh-bisphosphinite complexes in hand.[5] The hydrogenation of β-dehydroamino acids is less sensitive to the electronic properties in the ligand and predominantly governed by steric effects. However, it can be concluded that no general correlation between the electronic effects and enantioselectivity in the hydrogenation exist for catalysts and substrates investigated herein.

4. Experimental

4.1. General

All reagents unless otherwise mentioned were purchased from commercial sources and used without additional purification. Solvents were dried and freshly distilled under argon before use. Ru/Al_2O_3 (5%) was purchased from Degussa AG (G 204 R/D 5%). All reactions involving phosphines were performed under an argon atmosphere by using standard Schlenk techniques. Thin-layer chromatography was performed on precoated TLC plates (silica gel). Melting points are corrected. The optical rotations were measured on a 'gyromat-HP' instrument (Fa. Dr. Kernchen). NMR spectra were recorded at the following frequencies:

Table 3. Enantioselective hydrogenations of methyl β-acetylamino butenoates with [Rh(COD)((*R*,*R*)-ligand)]BF_4[a]



Run	Ligand, R	Ar	R^1	R^2	Solvent	ee [%][b]
1	**1a**, Ph	Ph	NHAc	Me	CF_3CH_2OH	97 (*S*)
2	**1a**, Ph	Ph	NHAc	Me	CH_2Cl_2	94 (*S*)
3	**1a**, Ph	Ph	NHAc	Me	CH_3OH	86 (*S*)
4	**1a**, Ph	Ph	Me	NHAc	CF_3CH_2OH	71 (*S*)
5	**1a**, Ph	Ph	Me	NHAc	CH_2Cl_2	75 (*S*)
6	**1a**, Ph	Ph	Me	NHAc	CH_3OH	65 (*S*)
7	**1b**, Ph	*p*-Tol	NHAc	Me	CF_3CH_2OH	98 (*S*)
8	**1b**, Ph	*p*-Tol	NHAc	Me	CH_2Cl_2	96 (*S*)
9	**1b**, Ph	*p*-Tol	NHAc	Me	CH_3OH	91 (*S*)
10	**1b**, Ph	*p*-Tol	Me	NHAc	CF_3CH_2OH	75 (*S*)
11	**1b**, Ph	*p*-Tol	Me	NHAc	CH_2Cl_2	81 (*S*)
12	**1b**, Ph	*p*-Tol	Me	NHAc	CH_3OH	66 (*S*)
13	**2a**, Cy	Ph	NHAc	Me	CF_3CH_2OH	88 (*S*)
14	**2a**, Cy	Ph	NHAc	Me	CH_2Cl_2	95 (*S*)
15	**2a**, Cy	Ph	NHAc	Me	CH_3OH	93 (*S*)
16	**2a**, Cy	Ph	Me	NHAc	CF_3CH_2OH	52 (*S*)
17	**2a**, Cy	Ph	Me	NHAc	CH_2Cl_2	66 (*S*)
18	**2a**, Cy	Ph	Me	NHAc	CH_3OH	64 (*S*)
19	**2b**, Cy	*p*-Tol	NHAc	Me	CF_3CH_2OH	88 (*S*)
20	**2b**, Cy	*p*-Tol	NHAc	Me	CH_2Cl_2	93 (*S*)
21	**2b**, Cy	*p*-Tol	NHAc	Me	CH_3OH	91 (*S*)
22	**2b**, Cy	*p*-Tol	Me	NHAc	CF_3CH_2OH	57 (*S*)
23	**2b**, Cy	*p*-Tol	Me	NHAc	CH_2Cl_2	66 (*S*)
24	**2b**, Cy	*p*-Tol	Me	NHAc	CH_3OH	65 (*S*)
25	Me	Ph	NHAc	Me	CF_3CH_2OH	74 (*S*)
26	Me	Ph	NHAc	Me	CH_2Cl_2	74 (*S*)
27	Me	Ph	NHAc	Me	CH_3OH	53 (*S*)
28	Me	Ph	Me	NHAc	CF_3CH_2OH	65 (*S*)
29	Me	Ph	Me	NHAc	CH_2Cl_2	70 (*S*)
30	Me	Ph	Me	NHAc	CH_3OH	63 (*S*)

[a] Conditions: 0.01 mmol precatalyst, 1.0 mmol of prochiral olefin in 15.0 ml solvent at 25.0 °C, 1.0 atm overall pressure over the solution.
[b] Measured after consumption of the calculated amount of H_2. Determined by GC, 50 m, Chiraldex β-PH.

400.13 MHz (^{1}H), 100.63 MHz (^{13}C), 161.98 MHz (^{31}P). Chemical shifts of ^{1}H and ^{13}C NMR spectra are reported in ppm downfield from TMS as an internal standard. Chemical shifts of ^{31}P NMR spectra are referred to H_3PO_4 as the external standard. Coupling constants in Table 1 were determined from ^{31}P NMR spectra with an estimated uncertainty of ±1 Hz. Elemental analyses were performed with a LEGO CHNS-932. Mass spectra were recorded on an AMD 402 spectrometer.

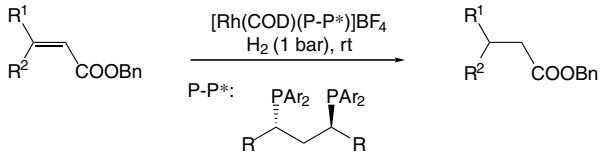
4.2. (*S*,*S*)-1,3-Dicyclohexylpropane-1,3-diol 5

A mixture of (*S*,*S*)-diphenylpropan-1,3-diol **4**[7] (ee > 98%, 4.00 g, 17.5 mmol) and Ru/Al_2O_3 (4.00 g, 100 mass%) in ethanol (30 ml) was hydrogenated at 50 °C and 50 bar initial H_2 pressure for 3 h. The catalyst was then filtered off and the solution evaporated to give the enantiomerically pure product as white crystals. Enantiomeric excess was determined by HPLC (Chiraldex β-PH, 50 m) and NMR spectroscopy. Yield: 4.20 g (quantitative); an analytically pure sample was obtained by recrystallization from EtOH. Mp 138–139 °C, $[\alpha]_D^{20} = -45.0$ (*c* 0.6, CH_3OH); Ref. 8a $[\alpha]_D = -40.9$ (*c* 0.2, CH_3OH).

4.3. (*S*,*S*)-1,3-Bis(methanesulfonyloxy)-1,3-dicyclohexylpropane 6

To the mixture of (*S*,*S*)-1,3-dicyclohexylpropane-1,3-diol **5** (0.98 g, 4.00 mmol) and Et_3N (1.32 g, 12.00 mmol) in THF (40 ml) was added under stirring methanesulfonyl chloride (0.92 g, 8.00 mmol) at 0 °C. The mixture was stirred at 0 °C for 8 h. Then, water (50 ml) was added and the product was extracted with diethyl ether (3 × 50 ml). The organic layer was washed with water (3 × 50 ml) and the solvent was removed under reduced pressure to give **5** as a colorless oil. Yield: 1.58 g (quantitative); $[\alpha]_D^{20} = -62.4$ (*c* 1.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.01–1.32 (12H, m, C_6H_{11}), 1.65–1.86 (10H, m), 1.93 (2H, t, CH), 3.09 (6H, s, CH_3), 4.72 (2H, m); ^{13}C NMR ($CDCl_3$) δ 26.3, 26.4, 26.7, 27.8, 28.6 (CH_2, C_6H_{11}), 32.7 (CH_2O), 39.2 (CH_3), 42.8 (CH), 84.4 (CH); $C_{17}H_{32}O_6S_2$ ($M = 396.56$); MS (70 eV) *m*/*z* (%) 221 (21), 204 (33), 139 (21), 121 (100), 108 (44), 95 (52).

Table 4. Enantioselective hydrogenations of benzyl β-acetylamino butenoates with [Rh(COD)((*R*,*R*)-ligand)]BF_4[a]



Run	Ligand, R	Ar	R^1	R^2	Solvent	ee [%][b]
1	**1a**, Ph	Ph	NHAc	Me	CF_3CH_2OH	96 (*S*)
2	**1a**, Ph	Ph	NHAc	Me	CH_2Cl_2	97 (*S*)
3	**1a**, Ph	Ph	NHAc	Me	CH_3OH	92 (*S*)
4	**1a**, Ph	Ph	Me	NHAc	CF_3CH_2OH	76 (*S*)
5	**1a**, Ph	Ph	Me	NHAc	CH_2Cl_2	82 (*S*)
6	**1a**, Ph	Ph	Me	NHAc	CH_3OH	81 (*S*)
7	**1b**, Ph	*p*-Tol	NHAc	Me	CF_3CH_2OH	98 (*S*)
8	**1b**, Ph	*p*-Tol	NHAc	Me	CH_2Cl_2	97 (*S*)
9	**1b**, Ph	*p*-Tol	NHAc	Me	CH_3OH	94 (*S*)
10	**1b**, Ph	*p*-Tol	Me	NHAc	CF_3CH_2OH	79 (*S*)
11	**1b**, Ph	*p*-Tol	Me	NHAc	CH_2Cl_2	88 (*S*)
12	**1b**, Ph	*p*-Tol	Me	NHAc	CH_3OH	84 (*S*)
13	**2a**, Cy	Ph	NHAc	Me	CF_3CH_2OH	88 (*S*)
14	**2a**, Cy	Ph	NHAc	Me	CH_2Cl_2	95 (*S*)
15	**2a**, Cy	Ph	NHAc	Me	CH_3OH	94 (*S*)
16	**2a**, Cy	Ph	Me	NHAc	CF_3CH_2OH	55 (*S*)
17	**2a**, Cy	Ph	Me	NHAc	CH_2Cl_2	80 (*S*)
18	**2a**, Cy	Ph	Me	NHAc	CH_3OH	65 (*S*)
19	**2b**, Cy	*p*-Tol	NHAc	Me	CF_3CH_2OH	88 (*S*)
20	**2b**, Cy	*p*-Tol	NHAc	Me	CH_2Cl_2	95 (*S*)
21	**2b**, Cy	*p*-Tol	NHAc	Me	CH_3OH	94 (*S*)
22	**2b**, Cy	*p*-Tol	Me	NHAc	CF_3CH_2OH	70 (*S*)
23	**2b**, Cy	*p*-Tol	Me	NHAc	CH_2Cl_2	81 (*S*)
24	**2b**, Cy	*p*-Tol	Me	NHAc	CH_3OH	77 (*S*)
25	Me	Ph	NHAc	Me	CF_3CH_2OH	53 (*R*)
26	Me	Ph	NHAc	Me	CH_2Cl_2	56 (*R*)
27	Me	Ph	NHAc	Me	CH_3OH	50 (*R*)
28	Me	Ph	Me	NHAc	CF_3CH_2OH	53 (*R*)
29	Me	Ph	Me	NHAc	CH_2Cl_2	54 (*R*)
30	Me	Ph	Me	NHAc	CH_3OH	46 (*R*)

[a] Conditions: 0.01 mmol precatalyst, 1.0 mmol of prochiral olefin in 15.0 ml solvent at 25.0 °C, 1.0 atm overall pressure over the solution.
[b] Determined by HPLC, Chiralcel OD-H.

4.4. Synthesis of 1,3-diphosphines 2a and b. General procedure

A solution of $LiPAr_2$ (prepared from 17.6 mmol of chlorodiphenylphosphine or chloro-bis(*p*-tolyl)phosphine[13] and 106 mmol of Li) was added under stirring to a solution of 1,3-dimesylate **6** (1.69 g, 4.27 mmol) in THF (30 ml) at −20 °C. The resulting solution was allowed to warm to room temperature (5 h) and then the solvent removed under reduced pressure. Methanol (10 ml) was then added. The solvent was evaporated and the residue extracted with *n*-hexane to give the product as a colorless oil. The crude phosphines were purified as BH_3 complexes by flash chromatography (*n*-hexane/ethylacetate 5:1). Subsequently, the borane group was removed by treatment with DABCO.[14] Phosphines were used directly for the formation of Rh complexes.

4.5. (*R*,*R*)-Bis(diphenylphosphino)-1,3-dicyclohexylpropane 2a

Yield: 0.84 g (34.1%); $[\alpha]_D^{20} = -58.0$ (*c* 0.6, C_6H_6); ^1H NMR ($CDCl_3$) δ 1.11–1.86 (20H, m), 2.02 (2H, m), 2.27 (1H, m), 2.48 (1H, m), 2.71 (2H, m), 7.12–7.28 (12H, m, arom. H), 7.64 (4H, m, arom. H), 7.76 (4H, m, arom. H); ^{13}C NMR ($CDCl_3$) δ 27.1 (CH_2, C_6H_{11}), 27.6–27.8, (CH_2, C_6H_{11}), 31.5 (CH_2, C_6H_{11}), 32.3 (CH_2), 40.6 (CH), 40.9 (CH), 128.7–129.1 (arom. C), 134.1–135.4 (arom. C), 139.0 (arom. C); ^{31}P NMR (C_6D_6) δ −5.0 (s); $C_{39}H_{46}P_2$ ($M = 576.73$); MS (70 eV) *m/z* (%) 576 $[M]^+$ (10), 500 (26), 499 (59), 391 $[M-PPh_2]^+$ (100), 185 $[PPh_2]^+$ (37).

The phosphine was purified as its BH_3 complex: ^1H NMR ($CDCl_3$) δ 0.41–1.78 (28H, m), 1.92 (2H, m), 2.53 (2H, m), 7.34–7.49 (8H, m, arom. H), 7.59–7.76 (12H, m, arom. H); ^{13}C NMR ($CDCl_3$) δ 23.5, 26.4, 26.9, 27.9, 29.5 (CH_2, C_6H_{11}), 35.3 (CH_2), 38.1 (CH), 39.5 (CH), 128.9–129.3 (arom. C), 131.5 (arom. C), 133.0 (arom. C), 134.1 (arom. C); ^{31}P NMR ($CDCl_3$) δ 24.9 (m). MS (70 eV) *m/z* (%) 408 $[M-PPh_2BH_3]^+$ (37), 282 $[PPh_2CH_2Cy]^+$ (100), 200 $[HPPh_2BH_3]^+$ (60), 199 $[PPh_2BH_3]^+$ (25), 186 $[HPPh_2]^+$ (69), 185 $[PPh_2]^+$ (24); $C_{39}H_{52}B_2P_2$ ($M = 604.40$); calcd: C, 77.50; H, 8.67; P, 10.25; found: C, 76.21; H, 8.96; P, 10.22.

4.6. (*R*,*R*)-Bis[(di-*p*-tolyl)phosphino]-1,3-dicyclohexylpropane 2b

Yield: 0.85 g (31.7%); $[\alpha]_D^{22} = -18.0$ (*c* 0.6, C_6H_6). ^1H NMR (C_6D_6) δ 1.13–2.05 (22H, m), 2.21 (d, 12H, CH_3), 2.31 (2H, m), 3.14 (2H, m), 3.65 (2H, m), 6.73–6.82 (8H, m, arom. H), 7.48–7.54 (8H, m, arom. H); ^{13}C NMR ($CDCl_3$) δ 21.4 (CH_3, *p*-Tol), 26.7, 26.9, 27.1, 27.4, 27.7, 28.0, 28.5, 29.7, 31.5, 33.4 (CH_2, C_6H_{11}), 33.7 (CH_2), 37.9 (CH), 40.5 (CH), 129.7 (arom. C), 134.3 (arom. C), 135.3 (arom. C), 138.8 (arom. C); ^{31}P NMR ($CDCl_3$) δ −9.3 (s); $C_{43}H_{54}P_2$ ($M = 632.84$); MS (70 eV) *m*/*z* (%) 618 $[M-CH_3]^+$ (6), 323 $[M-(p\text{-Tol})_2PCHCy]^+$ (13), 310 $[(p\text{-Tol})_2PCHCy]^+$ (100), 227 $[(p\text{-Tol})_2PCH_2]^+$ (48), 228 $[(p\text{-Tol})_2PCH_3]^+$ (73), 214 $[HP(p\text{-Tol})_2]^+$ (85).

The compound was purified as its BH_3 adduct. ^1H NMR ($CDCl_3$) δ 0.48–1.96 (28H, m), 2.35 (12H, d, CH_3), 2.85 (2H, m), 3.42 (2H, m), 7.15–7.25 (8H, m, arom. H), 7.66–7.74 (8H, m, arom. H); ^{13}C NMR ($CDCl_3$) δ 21.9 (CH_3, *p*-Tol), 26.4–27.0, 27.8, 28.4, 29.4, 30.1, 30.8, (CH_2, C_6H_{11}), 36.4 (CH_2), 38.2 (CH, C_6H_{11}), 129.8 (d, arom. C), 132.7–133.2 (arom. C), 141.5 (arom. C); ^{31}P NMR ($CDCl_3$) δ 22.8 (m). MS (70 eV) *m*/*z* (%) 437 (48), 436 (100), 434 $[M-P(p\text{-Tol})_2BH_3]^+$ (12), 310 $[P(p\text{-Tol})_2CH_2Cy]^+$ (38), 228 $[HP(p\text{-Tol})_2BH_3]^+$ (64), 227 $[P(p\text{-Tol})_2BH_3]^+$ (29), 214 $[HP(p\text{-Tol})_2]^+$ (17). $C_{43}H_{60}B_2P_2$ ($M = 660.51$); calcd: C, 78.19; H, 9.16; P, 9.38; found: C, 77.51; H, 9.53; P, 8.68.

4.7. General procedure for the preparation of [Rh(COD)(ligand)]BF_4

A solution of diphosphine **1b** and **2a** and **b** (2.37 mmol) in THF (30 ml) was slowly added to a solution of Rh(COD)acac (0.74 g, 2.37 mmol) in THF (30 ml). The solution was stirred for 15 min. Then, a stoichiometric amount of aq 40% HBF_4 was added and stirring continued for another 15 min. The complex was precipitated with diethyl ether.

4.8. [Rh(COD)(1b)]BF_4

Yield: 1.93 g (75%); ^{13}C NMR ($CDCl_3$) δ 20.4 (CH_3), 28.0, 30.6 (CH_2,COD), 34.5 (CH_2), 39.2 (CH), 98.0, 100.4 (=CH,COD), 125.1–133.4 (arom. C), 136.7 (arom. C), 138.2 (arom. C), 139.2 (arom. C); ^{31}P NMR ($CDCl_3$) δ 23.5 (d, $J(P,Rh) = 141.5$ Hz); $C_{51}H_{54}BF_4P_2Rh$ ($M = 918.64$); FAB MS *m*/*z* (%) 831 $[M-BF_4]^+$, 723 $[M-BF_4-COD]^+$.

Crystal structure analysis of [Rh(COD)(**1b**)]BF_4: Data were collected with a STOE-IPDS-diffractometer using graphite-monochromated Mo Kα radiation. The structure was solved by direct methods (SHELXS-86)[15] and refined by full-matrix least-squares techniques against F^2 (SHELXL-93).[16] XP (BRUKER AXS) was used for structure representation. Space group $C222_1$, orthorhombic, $a = 10.683(2)$, $b = 31.762(6)$, $c = 13.117(3)$ Å, $V = 4451(2)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.371$ g cm^{-3}, 8340 reflections measured, 2336 were independent of symmetry and 1964 were observed ($I > 2\sigma(I)$), $R1 = 0.044$, wR^2 (all data) = 0.112, 254 parameters.

4.9. [Rh(COD)(2a)]BF_4

Yield: 1.40 g (67.5%); ^{13}C NMR ($CDCl_3$) δ 26.0, 26.3 26.6, 27.4 29.3 (CH_2, C_6H_{11}), 29.8, 31.9 (CH_2,COD), 35.5 (CH_2), 38.0 (CH, C_6H_{11}), 40.1 (CH), 97.6, 103.7 (=CH,COD), 129.4–129.9 (arom. C), 131.9 (arom. C), 136.9 (arom. C); ^{31}P NMR ($CDCl_3$) δ 30.3 (d, $J(P,Rh) = 141.5$ Hz); $C_{47}H_{58}BF_4P_2Rh$ ($M = 874.62$); FAB MS *m*/*z* (%) 787 $[M-BF_4]^+$, 679 $[M-BF_4-COD]^+$.

4.10. [Rh(COD)(2b)]BF_4

Yield: 1.51 g (68.3%); ^{13}C NMR ($CDCl_3$) δ 22.1 (CH_3, *p*-Tol), 27.5, 27.9, 28.1, 30.1, 30.8, (CH_2, C_6H_{11}), 29.8, 31.8 (CH_2,COD), 36.4 (CH_2), 38.2 (CH, C_6H_{11}), 43.3 (CH), 98.2, 102.0 (=CH,COD), 129.5–129.9 (arom. C), 134.0–135.5 (arom. C), 138.6 (arom. C); ^{31}P NMR ($CDCl_3$) δ 28.5 (d, $J(P,Rh) = 141.5$ Hz); $C_{51}H_{66}BF_4P_2Rh$ ($M = 930.73$); FAB MS *m*/*z* (%) 843 $[M-BF_4]^+$, 735 $[M-BF_4-COD]^+$.

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