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A General Method for the Enantioselective Hydrogenation of β-Keto Esters using Monodentate Binaphthophosphepine Ligands

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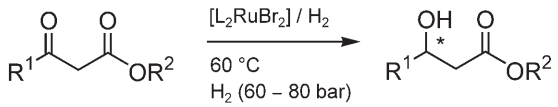
Abstract: 17 monodentate phosphepine ligands with a 4,5-dihydro-3*H*-dinaphtho[2,1-*c*;1′,2′-*e*]phosphepine structural motif have been synthesized and tested in the asymmetric hydrogenation of various β-keto esters. By variation of the substituents of the aryl group on the phosphorus atom a fine tuning of the selectivity of the catalytic system is possible. Quantitative yield and enantioselectivities up to 95% ee have been achieved for the hydrogenation of methyl acetoacetate (**7a**), methyl 3-oxovalerate (**7b**) and ethyl 4-phenyl-3-oxo-propionate (**7d**) using 4-(4-methoxyphenyl)-4,5-dihydro-3*H*-dinaphtho-[2,1-c;1′,2′-*e*]phosphepine (**4g**) as ligand. Best enantioselectivities were obtained at comparably high temperatures (100–120 °C), which had the advantage of increased reaction rates.

Keywords: enantioselective hydrogenation; β-hydroxy esters; β-keto esters; monodentate ligands; phosphine

Introduction

Transition metal-catalyzed asymmetric reactions constitute an important tool for the synthesis of enantiomerically pure compounds.[1] With regard to practical applications enantioselective hydrogenations offer the most efficient and elegant possibility for the synthesis of pharmaceutical intermediates among the different available catalytic methods.[2] In addition to the enantioselective hydrogenation of prochiral olefins, especially the asymmetric reduction of carbonyl compounds has attracted significant interest in the last decade. Here, apart from simple ketones the hydrogenation of β-keto esters is an actual and important topic (Scheme 1).[3]

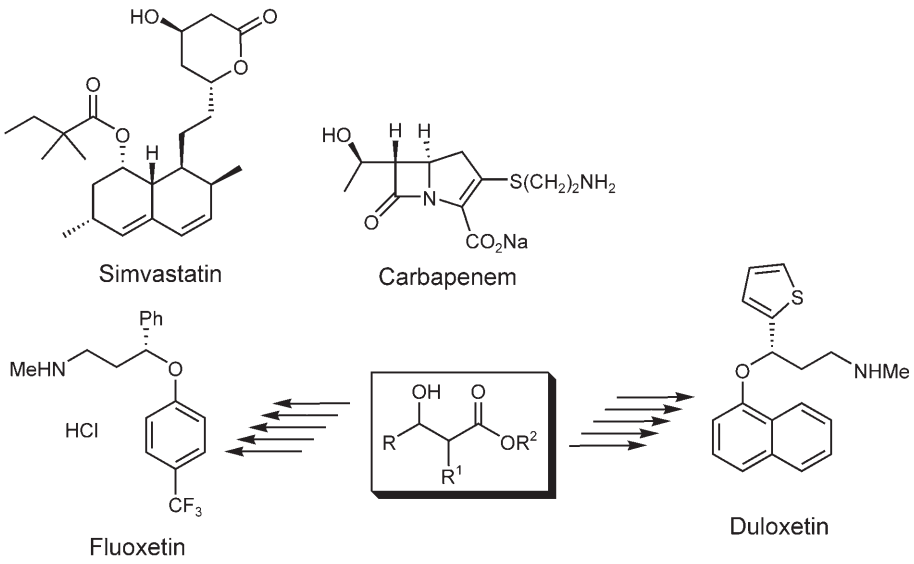


Scheme 1. Ruthenium-catalyzed hydrogenation of β-keto esters.

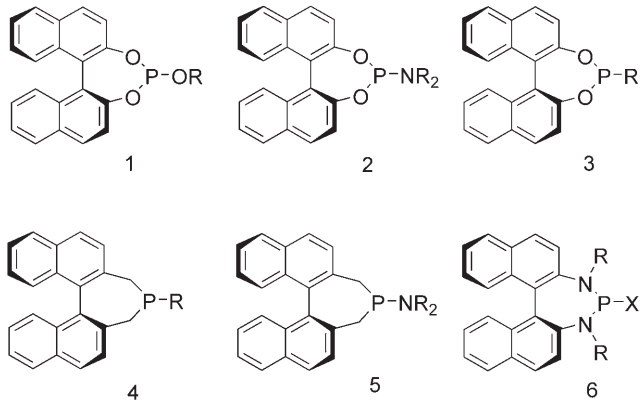
The resulting chiral β-hydroxy esters are found as a structural motif in a number of current pharmaceuticals, most notably atorvastatin. In addition, they serve as useful building blocks for the synthesis of a variety of naturally occurring and biologically active compounds such as fluoxetin and duloxetin (Scheme 2).[4]

Until very recently optically active diphosphines were essential as chiral ligands in order to achieve high enantioselectivity in the hydrogenation of β-keto esters. For example, pioneering work by Noyori and co-workers introduced BINAP as a highly selective ligand for this transformation.[5] Later on, important developments of chiral bidentate ligands for this transformation were reported by the groups of Genet,[6] Weissensteiner and Spindler,[7] Imamoto,[8] Knochel,[9] Zhang[10] and others.[11] To the best of our knowledge only one example[12] is known using a monodentate ligand for this application.

The situation changed for catalytic hydrogenations in 2000, when Reetz et al. (phosphites **1**[13]), Feringa and de Vries et al. (phosphoramidites **2**[14]) and Pringle and Claver et al. (phosphonites **3**[15]) introduced several monodentate phosphorous ligands[16] with a 2,2′-binaphthol core (Scheme 3) for the hydrogenation of prochiral olefins. An important advantage of such ligands is the easier preparation and tunability compared to diphosphines. Unfortunately, none of these ligands has been applied successfully for the hydrogenation of β-keto esters. Here, a special problem seems to be the hydrolytic



Scheme 2. A selection of pharmaceutically important β-hydroxy ester derivatives.



Scheme 3. Chiral monodentate phosphorous ligands with 2,2′-binaphthyl core.

stability of **1**–**3**, because β-keto ester hydrogenation requires in general protolytic solvents.

Recently, we became interested in the synthesis and catalytic application of chiral monodentate phosphines **4** with a 4,5-dihydro-3*H*-dinaphtho[2,1-*c*;1′,2′-*e*]phosphepine motif, which resemble the 2,2′-binaphthol-type ligands **1**–**3**. Despite the more complicated synthesis of **4**, these phosphines have advantages compared to **1**–**3**, **5**[17] and **6**[18] with regard to isolation, purification and hydrolytic stability even at higher temperatures (> 120 °C). Based on an initial account of Gladiali,[19] and parallel to the work of Zhang,[20] we established the use of **4** as highly enantioselective ligands for asymmetric hydrogenation of α-amino acid precursors, itaconic esters[21] and enamides.[22]

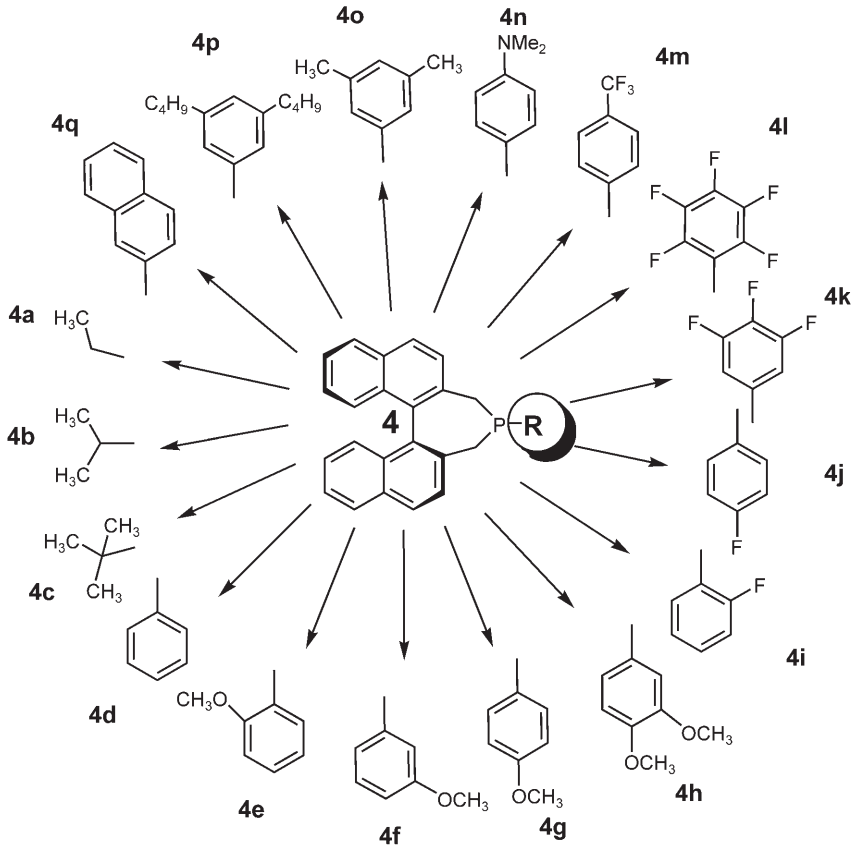
In a preliminary communication we compared the activity and selectivity of different ligands **3** and **4** for the ruthenium-catalyzed asymmetric hydrogenation of β-keto esters.[23] Here, we report a full account of our studies using 17 different 4,5-dihydro-3*H*-dinaphtho[2,1-*c*;1′,2′-*e*]phosphepines in the hydrogenation of various β-keto esters. In addition, the synthesis of new ligands of type **4** is described.

Results and Discussion

In Scheme 4 the various 4,5-dihydro-3*H*-dinaphtho[2,1-*c*;1′,2′-*e*]phosphepine ligands **4** used in this study are shown. Basically all ligands were prepared in 1–2 steps from optically pure 2,2′-dimethylbinaphthyl (ee > 99%), which we have prepared on a 20 g-scale from 2,2′-binaphthol *via* esterification with trifluoromethanesulfonic acid anhydride in the presence of pyridine (99% yield) and subsequent nickel-catalyzed Grignard reaction with methylmagnesium bromide in diethyl ether (95% yield).

Double metallation of 2,2′-dimethylbinaphthyl with *n*-butyl lithium, quenching with diethylaminodichlorophosphine and reaction with HCl gives 4-chloro-4,5-dihydro-3*H*-dinaphtho-[2,1-*c*;1′,2′-*e*]phosphepine in 76% overall yield (from 2,2′-binaphthol). This chlorophosphepine is a valuable building block for the synthesis of a variety of substituted 4,5-dihydro-3*H*-dinaphtho[2,1-*c*;1′,2′-*e*]phosphepines (Scheme 4) by simple Grignard reaction. Here, for the first time ligands **4k**, **4l**, and **4m** were synthesized by this sequence in moderate to good yields (45–83%).

With a number of chiral monodentate ligands in hand we were interested in their catalytic behavior in the hydrogenation of β-keto esters. All experiments were run either in a 100-mL pressure reactor or in an 8-fold parallel reactor array (5 mL). As pre-catalyst a mixture of 1 mol % [Ru(coD)(methallyl)$_2$] in the presence of 2 mol % of the respective ligand was used. Initially hydrogenation experiments with methyl acetoacetate



Scheme 4. A library of 4,5-dihydro-3*H*-dinaphtho[2,1-*c*;1′,2′-*e*]phosphepines.

(**7a**) as substrate have been carried out using different solvents such as methanol, toluene, dichloromethane, 2-propanol and THF. However, methanol was the only reaction medium which showed significant conversion (Table 1). At 60 bar initial hydrogen pressure full conversion required temperatures $>60\,^{\circ}C$ and a comparably long reaction time (>10 h). Nevertheless, we were pleased to find that under these conditions good enantioselectivities (84% ee) were achieved (Table 1, entry 4). Applying ligand **4d**[24] also a variation of the hydrogen pressure (20, 40, 60 and 80 bar H_2) has been done. At 60 °C and 20 bar initial hydrogen pressure only 25% yield of **8a** and 53% ee are observed, while at 60 bar 51% yield and 74% ee are obtained. Using a higher pressure than 60 bar of H_2 did not improve the enantioselectivity. Hence, an initial hydrogen pressure of 60 bar H_2 was used throughout of this study. It is important to note that all ligands were tested routinely at three different temperatures (60, 80, and 100 °C). In general, in Table 1 only the best result obtained is shown.

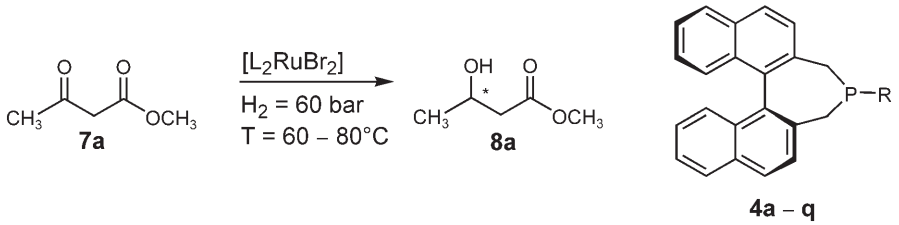
A comparison of the structures of ligands **4** demonstrates the necessity of a P-aryl group for obtaining good enantioselectivity. This might be due to the possible coordination of this aromatic rest to the ruthenium center.[25] Hence, alkyl-substituted phosphepine ligands **4a**–**c** give only disappointing enantioselectivities (46–60%) in the model reaction.

Interestingly, both substitution of electron-donating (OMe) as well as electron-withdrawing substituent (F) at the 4-position of the phenyl group results in an increase of enantioselectivity (Table 1, entries 7, 8, 11–13). However, the 4-trifluoromethylphenyl (**4m**) and the 4-dimethylaminophenyl phosphepines (**4n**) give similar or lower enantioselectivity compared to **4d**. The significant loss in selectivity for **4n** (Table 1, entry 17) is attributed to a possible coordination of the nitrogen to the ruthenium.

In all cases substitution at the *ortho*-position of the phenyl group significantly reduces the enantioselectivity (Table 1, entries 5, 10). Also, using substituents at the 3- and 5-positions led to a similar (Table 1, entries 6, 20) or a significantly decreased enantioselectivity (Table 1, entries 14, 18, 19). A comparison of 4-(2,3,4,5,6-pentafluorophenyl-4,5-dihydro-3*H*-dinaphtho-[2,1-*c*;1′,2′-*e*]phosphepine **4l** (25% yield; 6% ee) and 4-phenyl-4,5-dihydro-3*H*-dinaphtho-[2,1-*c*;1′,2′-*e*]phosphepine **4d** (>99% yield; 84% ee) as ligands demonstrates the importance of electronic effects for obtaining high yield and optimized enantioselectivity (Table 1, entries 4, 15).

Interestingly, for most ligands the enantioselectivity is increased with increasing reaction temperature, show-

Table 1. Screening of various ligands in the hydrogenation of methyl acetoacetate (**7a**).



Entry	Ligand	R	Time [h]	Temperature [°C]	Yield [%]	ee [%] (R)
1	**4a**	Et	16	100	90	46
2	**4b**	*i*-propyl	48	60	>99	60
3	**4c**	*t*-butyl	16	60	99	49
4	**4d**	C_6H_5	16	80	>99	84
5	**4e**	2-$CH_3OC_6H_4$	16	80	90	11
6	**4f**	3-$CH_3OC_6H_4$	48	80	93	84
7	**4g**	4-$CH_3OC_6H_4$	16	80	>99	92
8	**4g**	4-$CH_3OC_6H_4$	8	100	>99	95
9	**4h**	3,4-$(CH_3O)_2C_6H_3$	48	80	94	74
10	**4i**	2-FC_6H_4	16	80	89	58
11	**4j**	4-FC_6H_4	16	80	>99	82
12	**4j**	4-FC_6H_4	1	120	>99	95
13	**4j**	4-FC_6H_4	1	130	>99	91
14	**4k**	3,4,5-$F_3C_6H_2$	16	80	69	25
15	**4l**	C_6F_5	16	80	25	6
16	**4m**	4-$CF_3C_6H_4$	16	100	94	81
17	**4n**	4-$Me_2NC_6H_4$	16	80	>99	33
18	**4o**	3,5-$Me_2C_6H_3$	16	100	89	61
19	**4p**	3,5-(*t*-butyl)$_2$-C_6H_3	16	80	16	10
20	**4q**	2-naphthyl	16	80	>99	85

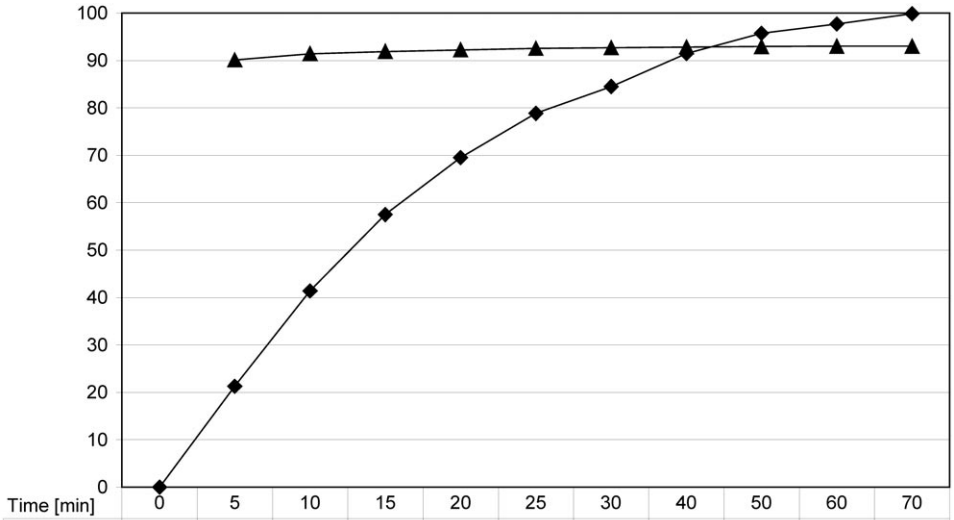
Reaction conditions: solvent (20 mL), 3.8 mmol substrate; 3.8×10^{-2} mmol [Ru(COD)methallyl)$_2$]; 7.6×10^{-2} mmol ligand; 60 bar initial hydrogen pressure; *reaction conditions if run in 8-fold parallel reactor array:* solvent (2 mL, 3.8×10^{-1} mmol substrate; 3.8×10^{-3} mmol [Ru(COD)methallyl)$_2$]; 7.6×10^{-3} mmol ligand; 60 bar initial hydrogen pressure; methanolic HBr.

ing an optimum at 80–100 °C. This temperature dependence of the selectivity is of special importance for applied synthesis because it is easier and more economical to perform a reaction at 100 °C than at room temperature. In case of the 4-fluorophenyl ligand **4j** best selectivity is obtained even at 120 °C (Table 1, entries 11–13)! More specifically, on applying **4j** the ee is increased from 59% at 60 °C to 82% at 80 °C to 95% at 120 °C. In order to take a closer look at this reaction we took samples out of the running reaction *via* an autosampler (Figure 1). The somewhat lower enantioselectivity in the beginning of the reaction (90 *vs.* 93% ee) is explained by the slow formation of the most selective catalyst species, which is apparently not fully formed in the preformation phase but after the addition of the substrate. At this point one should note that the detailed mechanism for the ruthenium-catalyzed asymmetric hydrogenation of β-keto esters and the knowledge about the active catalyst is still vague.

Next, the asymmetric hydrogenation of methyl 3-oxovalerate (**7b**), ethyl 4-chloro-3-oxobutyrate (**7c**) and ethyl 4-phenyl-3-oxopropionate (**7d**) was investigated in more detail (Table 2). Again all ligands have been tested at three different temperatures (60, 80 and 100 °C) and only the best result for the respective ligand is shown in Table 2. Using an appropriate ligand the different substrates were hydrogenated with excellent conversion and yield. In general, for **7b** similar ees are obtained compared to the hydrogenation of **7a**, while **7d** gave similar or slightly lower ee values.

Again the alkyl-substituted derivatives **4a**–**c** gave low enantioselectivity (Table 2, entries 1, 3, 4, 6, 7, 9). Also the influence of the different substituents on the P-phenyl group is not much different for the three substrates. An exception is ligand **4k**, for which the effect cannot be rationalized. The best enantioselectivity (95% ee for **7a** and **7d**) is obtained in the presence of **4g** with a methoxy group in the 4-position of the phenyl ring (Table 2, entries 18, 20).

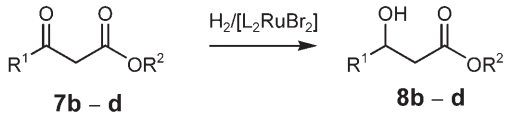
High selectivities (>80% ee) were also obtained with the phenyl-, 3-methoxyphenyl- and 4-fluorophenyl-substituted ligands **4d**, **4f** and **4j** (Table 2, entries 10, 15, 17, 27). Clearly, the asymmetric hydrogenation of **7c** proved to be the most difficult test reaction. Here, in the presence of all P-aryl ligands lower enantioselectivity is obtained. In addition, in most cases reductive dehalogena-



Time [min]	0	5	10	15	20	25	30	40	50	60	70
yield [%]	0	21	41	57	70	79	85	91	96	98	100
ee [%]		90,1	91,4	91,9	92,3	92,5	92,7	92,8	92,9	93,0	93,0

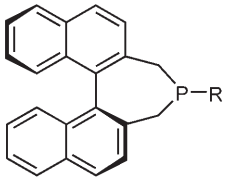
Figure 1. Online-analysis of the hydrogenation of **7a** with ligand **4j**.

Table 2. Hydrogenation of other substrates.



7b – d **8b – d**

7b, **8b**: R^1 = Et; R^2 = Me
7c, **8c**: R^1 = Cl-CH_2; R^2 = Et
7d, **8d**: R^1 = Ph; R^2 = Et



4a – q

Entry	Substrate	Ligand	Time [h]	Temperature [°C]	Yield [%]	ee [%]
1	**7b**	**4a**	16	80	95	31 (*R*)
2	**7c**	**4a**	16	80	50	9 (*S*)
3	**7d**	**4a**	8	100	99	47 (*S*)
4	**7b**	**4b**	48	60	60	56 (*R*)
5	**7c**	**4b**	16	60	87	54 (*S*)
6	**7d**	**4b**	16	80	88	37 (*S*)
7	**7b**	**4c**	16	60	>99	67 (*R*)
8	**7c**	**4c**	16	80	87	54 (*S*)
9	**7d**	**4cc**	16	80	88	37 (*S*)
10	**7b**	**4dc**	16	80	97	86 (*R*)
11	**7c**	**4dc**	16	60	81	13 (*S*)
12	**7d**	**4dc**	16	60	>99	73 (*S*)
13	**7b**	**4ec**	16	80	91	10 (*R*)
14	**7d**	**4e**	16	80	85	17 (*S*)
15	**7b**	**4f**	48	80	97	83 (*R*)
16	**7c**	**4f**	48	80	43	20 (*S*)
17	**7d**	**4f**	48	80	99	81 (*S*)
18	**7b**	**4g**	**8**	**100**	**>99**	**95 (*R*)**
19	**7c**	**4g**	16	80	98	6 (*S*)
20	**7d**	**4g**	**8**	**100**	**>99**	**95 (*S*)**
21	**7b**	**4h**	48	80	98	61 (*R*)
22	**7c**	**4h**	48	80	46	16 (*S*)
23	**7d**	**4h**	48	80	>99	80 (*S*)
24	**7b**	**4i**	16	80	89	58 (*R*)
25	**7c**	**4i**	16	80	>99	6 (*S*)

Table 2 (cont.)

Entry	Substrate	Ligand	Time [h]	Temperature [°C]	Yield [%]	ee [%]
26	**7d**	**4i**	16	80	>99	42 (*S*)
27	**7b**	**4j**	16	80	>99	91 (*R*)
28	**7c**	**4j**	16	80	97	6 (*S*)
29	**7d**	**4j**	16	80	>99	76 (*S*)
30	**7b**	**4k**	16	80	82	28 (*R*)
31	**7c**	**4k**	16	80	99	20 (*S*)
32	**7d**	**4k**	16	80	99	79 (*S*)
33	**7b**	**4l**	16	80	40	6 (*R*)
34	**7c**	**4l**	16	80	35	5 (*S*)
35	**7d**	**4l**	16	80	40	9 (*S*)
36	**7b**	**4m**	16	100	98	80 (*R*)
37	**7c**	**4m**	16	80	46	5 (*S*)
38	**7d**	**4m**	16	100	99	52 (*S*)
39	**7b**	**4n**	16	80	99	30 (*R*)
40	**7c**	**4n**	16	80	95	20 (*S*)
41	**7d**	**4n**	16	80	93	57 (*S*)
42	**7b**	**4o**	48	60	98	53 (*R*)
43	**7c**	**4o**	16	100	56	14 (*S*)
44	**7d**	**4o**	16	100	86	58 (*S*)
45	**7b**	**4p**	16	80	12	10 (*R*)
46	**7c**	**4p**	16	80	12	9 (*S*)
47	**7d**	**4p**	16	80	62	4 (*S*)
48	**7b**	**4q**	16	80	>99	81(*R*)
49	**7d**	**4q**	16	80	>99	55 (*S*)

Reaction conditions: solvent (20 mL), 3.8 mmol substrate; 3.8×10^{-2} mmol [Ru(COD)methallyl)$_2$]; 7.6×10^{-2} mmol ligand; 60 bar initial hydrogen pressure; *reaction conditions if run in 8-fold reactor array:* solvent (2 mL), 3.8×10^{-1} mmol substrate; 3.8×10^{-3} mmol [Ru(COD)methallyl)$_2$]; 7.6×10^{-3} mmol ligand; 60 bar initial hydrogen pressure; methanolic HBr.

tion is observed as a side-reaction. Surprisingly, the highest enantioselectivity is observed for ligand **4b** with moderate ee (54% ee) (Table 2, entry 5).

Conclusion

In conclusion, we have synthesized a library of monodentate chiral ligands containing a 4,5-dihydro-3*H*-dinaphtho[2,1-*c*;1′,2′-*e*]phosphepine structure. These ligands can be synthesized on multi-10 g-scale from 2,2′-binaphthol and are tuned easily by variation of the substitutent on the phosphepine ring. Some of the prepared ligands (**4g**, **4j**) can be used efficiently for the ruthenium-catalyzed hydrogenation of β-keto esters. With regard to practical organic synthesis especially the temperature tolerance of the catalysts is remarkable. Even at 100–120 °C enantioselectivities up to 95% were achieved.

Experimental Section

General

Unless otherwise noted, all chemicals are commercially available and were used without further purification. The β-keto esters **7a**–**d** were distilled under an argon atmosphere. New products were fully characterized (bp, IR, MS, EA, NMR). Catalytic hydrogenation experiments were carried out in a Parr stainless steel autoclave (100 mL) or in an 8-fold autoclave array of 3-mL reactors provided by the IAT Rostock-Warnemünde.

General Procedure

In situ ***preparation of ruthenium catalyst:***[5] [Ru(coD)(methallyl)$_2$] and ligand **4** (7.6×10^{-5} mol) were placed in a dried 25-mL Schlenk tube under an argon atmosphere and anhydrous and degassed acetone (5 mL) was added. After dropwise addition of a solution of HBr in methanol (0.33 mL, 0.29 M) a brown precipitate was formed. Stirring was continued over 30 min, and the solvent was removed under vacuum and methanol (20 mL) (for substrates **7a**, **b**) or ethanol (for substrates **7c**, **d**) respectively was added.

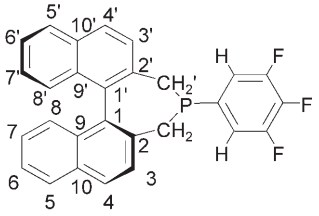
Asymmetric hydrogenation of β-keto esters **7a**–**d**: In a typical experiment, a 100-mL autoclave was charged with a mixture of the *in situ* prepared catalyst [L$_2$RuBr$_2$] and 3.8×10^{-3} mol substrate **7** and an internal standard (diglyme) in 20 mL solvent under an argon stream. The autoclave was charged with 60 bar hydrogen and heated up to reaction temperature followed by addition of substrate **7**.

In the case of the reactor array the autoclaves were filled with 1.0 mL *in situ* prepared catalyst [L$_2$RuBr$_2$] containing 3.8×10^{-6} mol Ru(COD)methallyl$_2$ and 7.6×10^{-6} mol of the

corresponding ligand **4**. Afterwards the reactor vessels are charged with 1.0 mL stock solution containing 3.8×10^{-4} mol substrate **7**. The reaction solutions were transferred to the reactor *via* syringe under an argon stream. It is possible to run 8 different reactions at the same reaction temperature with different pressures. The advantage lies furthermore in the use of stock solutions and the minimized usage of catalyst. In general all substrates **7** have been tested in the autoclave array with repeat determination at once and scrutinized in the 100 mL autoclave.

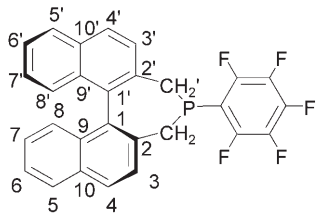
The autoclave/reactor array was stirred at 40 to 80 bar hydrogen pressure and 60–130 °C for 1–48 h. The autoclave/reactor array was cooled to room temperature and the hydrogen was released.

The reaction mixtures were filtered over silica gel and the enantiomeric excess was determined by GC (Lipodex E) or HPLC (Chiracel OD-H). Most of the hydrogenation products have been previously described. Methyl 3-hydroxybutyrate (**8a**): GC (25 m Lipodex E) 95 °C isothermal: t_r(min) = 4.9 (*S*), 5.7 (*R*); methyl 3-hydroxyvalerate (**8b**): GC (25 m Lipodex E) 85 °C isothermal: t_r(min) = 10.9 (*S*), 11.6 (*R*); ethyl 3-hydroxy-4-chlorobutyrate (**8c**): GC (25 m Lipodex E) 95 °C isotherm: t_r(min) = 20.4 (*R*), 20.6 (*S*); ethyl 3-hydroxy-3-phenylpropionate (**8d**): HPLC (OD-H002 short, hexane/ethanol = 95:5, 0.5 mL/min), t_r(min) = 10.1 (*S*), 11.5 (*R*).



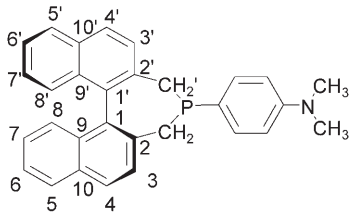
4-(3,4,5-Trifluorophenyl)-4,5-dihydro-3*H*-dinaphtho-[2,1-c;1′,2′-e]phosphepine (4k)

Yield: 82%; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.70 [dd, 1H, $J_{H,H}$ = 14.5 Hz, $J_{P,H}$ = 4.8 Hz, CH_2′(a)], 2.77 [dd, 1H, $J_{H,H}$ = 11.8 Hz, $J_{P,H}$ = 3.2 Hz, CH_2 (b)], 2.88 [dd, 1H $J_{P,H}$ = 13.2 Hz, CH_2′(b)], 3.02 [dd, 1H, $J_{P,H}$ = 17.6 Hz, CH_2(a)], 6.87 (m, 2H, *o*-$PC_6H_2F_3$), 6,93 (d, 1H, $J_{3',4'}$ = 8.5 Hz, H-3), 7.24–7.27 (m, 4H, H-7,7′,8,8′), 7.44–7.47 (m, 2H, H-6,6′), 7.64 (dd, 1H, $J_{3,4}$ = 8.5 Hz, H-3), 7.78 (d, 1H, H-4′), 7.92–7.95 (m, 3H, H-4,5,5′); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 30.5 (d, *J* = 16.5 Hz, CH_2), 32.1 (d, *J* = 22.0 Hz, CH_2′), 115.4 (m, *o*-$PC_6H_2F_3$), 124.9 (C-6′), 125.2 (C-6), 126.0, 126.1 (C-7,7′), 126.7 (C-8,8′), 127.4 (C-3), 127.5 (C-H′), 128.0 (C-3′), 128.3, 128.6, 128.7 (C-4,5,5′), 131.9–133.8 (C-1,1′,2′,9,9′,10,10′), 134.3 (C-2), carbon signals for *i*-, *m*-, *p*-$PC_6H_2F_3$ are not given; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 7.6; IR (KBr): ν = 3050 w, 2915 w, 1610 m, 1592 w, 1519 s, 1458 w, 1410 m, 1315 m, 1235 w, 1081 w, 1043 s, 863 w, 850 w, 824 m, 752 m, 671 w, 621 w, 603 cm^{-1} w. MS (ESI): *m/z* (%) = 443 ([M^+], 100), 312 (3), 283 (42), 265 (52), 252 (15), 183 (3), 138 (9), 132 (12), 9 (5), 75 (4), 58 (4), 43 (5); HR-MS: calcd. for $C_{28}H_{18}PF_3$: 442.1105; found: 442.1098; optical rotation: [α]^{21}: −18 (*c* 0.05, toluene).



4-(2,3,4,5,6-Pentafluorophenyl-4,5-dihydro-3*H*-dinaphtho-[2,1-*c*;1′,2′-*e*]phosphepine (4l)

Yield: 83%; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.79 [dd, 1H, *J* = 17.6 Hz, *J* = 15.1 Hz CH_2′(a)], 3.16 [dd, 1H, *J* = 12.3 Hz, *J* = 2.8 Hz, CH_2 (b)], 3.34–3.41 [m, 2H, CH_2 (a), CH_2′ (b)], 7.20 (d, 1H, $J_{3',4'}$ = 8.5 Hz, H-3′), 7.24–7.28 (m, 4H, H-7,7′,8,8′), 7.42–7.48 (m, 2H, H-6,6′), 7.65 (dd, 1H $J_{3,4}$ = 8.5 Hz, $J_{P,H}$ = 1.3 Hz, H-3), 7.81 (d, 1H, H-4′), 7.90–7.96 (m, 3H, H-4,5,5′); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 28.8–29.4 (m, CH_2, CH_2′), 124.8 (C-6′), 125.2 (C-6), 126.1 (C-7,7′), 126.6, 126.7 (C-8,8′), 127.4–128.7 (C-3,3′,4,4′,5,5′), 131.9–133.5 (C-1,1′,2′,9,9′,10,10′), 134.2 (C-2), carbon signals for PC_6F_5 are not given; ^{31}P NMR (162 MHz, $CDCl_3$): δ = 7.7; IR (KBr): ν = 3050 w, 2921 w, 1639 w, 1619 w, 1610 w, 1593 w, 1515 s, 1464 s, 1425 w, 1377 w, 1283 w, 1249 s, 1226 w, 1083 s, 976 s, 865 w, 823 m, 748 m, 670 w, 622 cm^{-1} w; MS (ESI): *m/z* (%) = 479 ([M^+], 100), 311 (1), 283 (5), 265 (44), 239 (10), 183 (2), 138 (9), 126 (7), 93 (1); HR-MS calcd. for $C_{28}H_{16}PF_5$: 478.0910; found: 478.0930; optical rotation: [α]^{21}: −84 (*c* 0.05, toluene).



4-(4-Dimethylaminophenyl)-4,5-dihydro-3*H*-dinaphtho-[2,1-*c*;1′,2′-*e*]phosphepine (4n)

Yield: 45%; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.64 [dd, 1H, $J_{H,H}$ = 14.2 Hz, $J_{P,H}$ = 4.5 Hz, CH_2′(a)], 2.83 [dd, 1H, $J_{P,H}$ = 11.0 Hz, CH_2′(b)], 2.89 [dd, 1H, $J_{P,H}$ = 16.0 Hz, $J_{H,H}$ = 12.0 Hz, CH_2(a)], 2.95 [dd, 1H, $J_{P,H}$ = 2.8 Hz, CH_2(b)], 2.98 (s, 6H, NMe_2), 6.63 (br s, 2H, *m*-PC_6H_4), 7.03 (d, 1H, $J_{3',4'}$ = 8.5 Hz, H-3′), 7.10 ("t", *o*-PC_6H_4), 7.22–7.30 (m, 4H, H-7,7′,8,8′), 7.41–7.45 (m, 2H, H-6,6′) 7.65 (dd, 1H $J_{3,4}$ = 8.5 Hz, $J_{P,H}$ = 1.0 Hz, H-3), 7.80 (d, 1H, H-4′), 7.93 ("d", 3H, H-4,5,5′); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 31.2 (d, *J* = 14.7 Hz, CH_2), 33.1 (d, *J* = 22.0 Hz, CH_2′), 40.3 (br, NMe_2), 112.0 (br, *m*-PC_6H_4), 121.8 (br, *i*-PC_6H_4), 124.7 (C-6′), 124.9 (C-6), 125.7–125.8 (C-7,7′), 126.70, 126.72 (C-8,8′), 127.4 (C-4′); 127.4 (d, *J* = 1.8 Hz, C-3), 128.1, 128.2, 128.3, 128.7 (C-3′,4,5,5′), 132.0, 132.3 (2×), 132.9 (C-9,9′,10,10′), 132.8 (d, *J* = 2.0 Hz, C-1′), 133.5 (d, *J* = 4.5 Hz, C-1), 133.7 (d, *J* = 21.9 Hz, *o*-PC_6H_4), 134.0 (C-2′), 135.0 (C-2), 151.1 (br, *p*-PC_6H_4); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 4.3; IR (KBr): ν = 3041 m, 3002 s,

2900 m, 2797 s, 1593 s, 1543 s, 1509 s, 1478 w, 1440 m, 1417 m, 1358 s, 1331 w, 1249 w, 1225 m, 1209 w, 1180 m, 1097 s, 1062 w, 1023 w, 945 w, 938 w, 865 w, 828 s, 795 m, 773 w, 751 s, 733 w, 670 w, 619 w, 567 w, 519 cm^{-1} m; MS (ESI): *m/z* (%) = 432 ([M^+], 100), 311, 283 (1), 277 (10), 265 (7), 166 (3), 151 (5), 121 (9), 91 (3), 77 (2), 42 (2); HR-MS: calcd. for $C_{30}H_{26}NP$: 431.1824; found: 431.1803; optical rotation: $[\alpha]^{22}$: −251 (*c* 0.05, toluene).

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