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Synthesis of Chiral 2-Hydroxy-1-methylpropanoates by Rhodium-Catalyzed Stereoselective Hydrogenation of α-(Hydroxymethyl)-acrylate Derivatives

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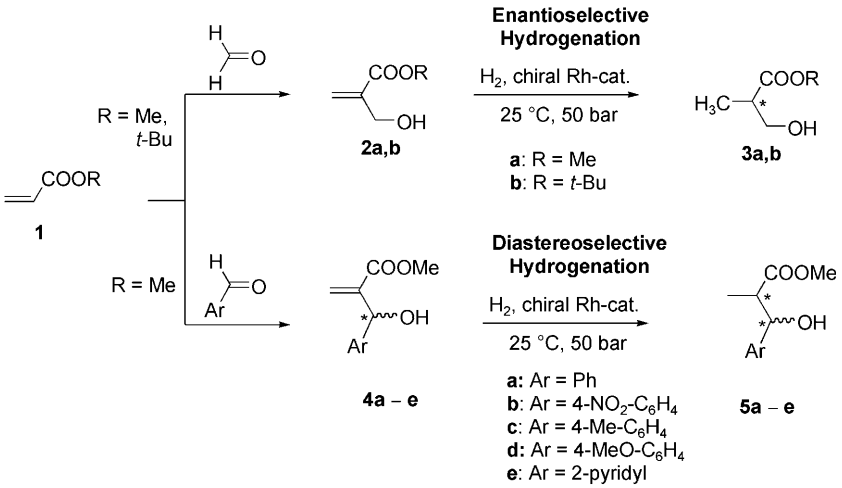
Abstract: The synthesis of chiral 3-hydroxy-2-methylpropanoic acid esters (e.g., "Roche ester" **3a**) based on the rhodium-catalyzed stereoselective hydrogenation of Baylis–Hillman reaction products was investigated. Full conversions and enantioselectivities of up to 99% at a substrate/catalyst ratio of up to 500/1 were achieved by application of bisphospholanes of the cat*AS*ium M series as ancillary ligands. An interesting kinetic resolution was observed by the diastereoselective hydroxy-directed hydrogenation of related racemic β-branched precursors affording mainly *anti*-isomers with up to 96% ee.

Keywords: asymmetric catalysis; hydrogenation; kinetic resolution; phospholanes; rhodium

Introduction

Enantiomerically pure 3-hydroxy-2-methylpropionates of the general formula **3** (Scheme 1, R = H, alkyl) represent versatile C_4-building blocks for the synthesis of natural products as well as for the construction of other biologically active compounds. These compounds have seen, for example, application in the synthesis of (+)-13-deoxytedanolide,[1] (−)-dictyostatin,[2] spiculoic acid A,[3] and discodermolide,[4] respectively. In spite of their huge synthetic potential, the number of synthetic venues is strongly limited.[5] Recently, Ratovelomanana-Vidal and Genêt showed that the homogeneous enantioselective hydrogenation of the unsaturated precursor α-(hydroxymethyl)-acrylic acid ester (**2**) represents a synthetic methodol-



Scheme 1. Synthesis of functionalized olefins **2** and **4** by Baylis–Hillman reaction and their subsequent stereoselective hydrogenation.

Table 1. Preliminary results of the asymmetric hydrogenation of **2a**, **b**.[a]

Entry	Substrate Precatalyst		**2a**			**2b**		
		pH_2 [bar]	Solvent	ee[b] [%]	pH_2 [bar]	Solvent	ee[b] [%]
1	[Rh(COD)((*R*)-SYNPHOS)]BF_4	25	MeOH; THF	4.2 (*R*); 33.5 (*R*)	50	MeOH; THF	23.0 (*R*); 20.1 (*R*)
2	[Rh(COD)((*S*)-(*R*)-JOSIPHOS)]BF_4	25	MeOH; THF	64.5 (*S*); 76.7 (*S*)	50	MeOH; THF	32.6 (*S*); 43.0 (*S*)
3	[Rh(COD)((*R*)-(*S*)-DPPF^{t}BP)]BF_4	25	MeOH; THF	11.0 (*R*); 10.6 (*R*)	50	MeOH; THF	8.2 (*S*); 4.3 (*S*)
4	[Rh(COD)((*R*)-(S_a)-BoPHOZ)]BF_4	25	MeOH; THF	1.2 (*R*); 31.8 (*S*)	50	MeOH; THF	3.2 (*R*); 1.0 (*R*)

[a] *Conditions*: 0.5 mmol substrate, 5 mL solvent, 25 °C, 12 h.
[b] Complete conversion was confirmed by ^{1}H NMR spectroscopy and the enantiomeric excess was analyzed by HPLC: for **3a**: CHIRACEL OD-H (150×4.6 mm), hexane:2-propanol = 97:3, 1.2 mL min^{-1}, detection at 215, 220 and 225 nm, t_R = 5.9 min (*R*-enantiomer), t_R = 6.6 min (*S*-enantiomer); for **3b**: CHIRACEL OD-H (150×4.6 mm), hexane:2-propanol = 99:1, 1.1 mL min^{-1}, detection at 215, 220 and 225 nm, t_R = 5.3 min (*R*-enantiomer), t_R = 5.8 min (*S*-enantiomer).

ogy of high potential. By using a chiral Ru-(SYNPHOS) hydrogenation catalyst pertinent chiral esters yielded by up to 94% *ee*.[5,6] Interestingly, only two example exist in the literature which are concerned with the use of rhodium complexes. Thus, Reek et al. achieved up to 98% *ee* with an INDOL-PHOS ligand with TOFs over 5500 h^{-1} by application of low temperatures (−40 °C).[7] Saito and co-workers reported 90% *ee* with DuPHOS and BeePHOS as chiral ligands.[8] The latter belong to the large family of bisphospholanes.[9]

Inspired by these investigations and taking our own observations in mind that small changes in the structure of bisphospholane ligands may cause dramatic effects in the outcome of the asymmetric hydrogenation,[10] herein we report our results on the Rh-catalyzed asymmetric hydrogenation of α-(hydroxymethyl)acrylates (**2**) with cat*A*Sium M ligands.[11] These bisphospholanes belong to a large family of commercially available and strongly related ligands. Therefore, fine tuning of the reaction can be easily achieved. The required prochiral olefins **2** are available by Baylis–Hillman reaction of the corresponding acrylates **1** with formaldehyde.[12a] Moreover, this synthetic approach also allows the preparation of racemic (α-branched hydroxymethyl)acrylates of type **4** which are highly challenging substrates for the diastereoselective hydrogenation of the olefinic group.

Results and Discussion

In order to identify the most efficient ligand types for the asymmetric transformation in the beginning of our research we screened the hydrogenation of substrate **2a** with rhodium catalysts bearing ferrocene ligands JOSIPHOS,[13] DPPF^{t}BP[13] and BoPHOZ[14] as well as the atropisomeric ligand SYNPHOS.[15] Required cationic precatalysts of the type [Rh(COD)(P–P)]BF_4 were prepared prior to the asymmetric reaction. The hydrogenations were carried out with a ratio of substrate/catalyst of 100:1 at 25 or 50 bar initial H_2 pressure at 25 °C over a period of 12 h. The results (Table 1) show that full conversion, but disappointingly low *ee* values were achieved. Only the catalyst based on JOSIPHOS gave the so-called "Roche ester" **3a** as well as *t*-butyl ester **3b** (entry 2) with moderate *ee* values (33–77%).

Next, we turned our attention to the use of the of cat*A*Sium ligands **6**–**11** (Figure 1).[11b] Differences in the substitution pattern and ring size of the backbone of the ligands should provide some information about electronic and/or steric effects. The results are summarized in Table 2.

In most reactions full conversion was achieved in less than 90 min. The *ee* values are in the range from 0–98%. Our results clearly evidence that the ring size

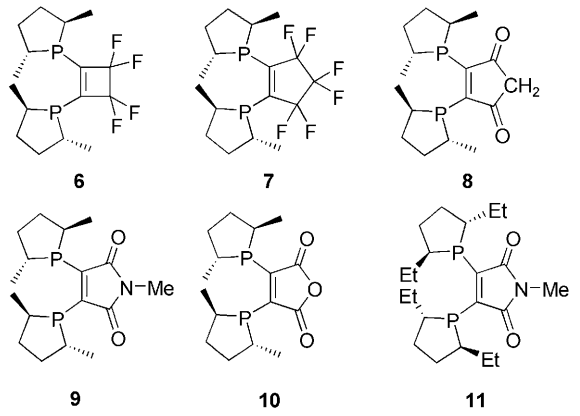


Figure 1. Structures of ligands **6**–**11**.

of the ligand backbone does not dramatically influence the stereodifferentiating properties of the catalyst.[16] Also, the replacement of the 2,5-dimethyl substituents at the phospholane by ethyl groups (ligands **9** *vs.* **11**) did not strongly affect the enantioselectivities.

A much stronger effect can be attributed to the solvent (e.g.. entries 14/30 *vs.* 16/32). In general, the use of aprotic solvents (tetrahydrofuran, dichloromethane) was superior in comparison to methanol. In the latter several hours were required to achieve full conversion. It is remarkable to note that the catalysts derived from the fluorinated ligand **7** gave nearly racemic mixtures of **3a** or **3b** in methanol (entries 3 and 19) whereas in aprotic solvents 90–98% *ee* resulted (entries 4, 5, 20, 21). The reason for this disparate behaviour is not clear and currently under investigation.

In methanol the Rh catalysts based on ligand **10** bearing an anhydride structure in the backbone showed varying results in dependence on the time of pretreatment. Thus, after stirring of the precatalyst [Rh(COD)(**10**)]BF_4 in methanol for one hour the enantioselectivity differed from the values noted by using the same precatalyst without preformation (entries 10/26 *vs.* entries 11/27). This result might be attributed to the ring opening reaction and transesterification with methanol.[17]

In general, hydrogenation at elevated H_2 pressure, which proceeded faster than at 1 bar, is recommended in order to avoid the formation of traces of by-products due to oligomerization of the starting olefin and dehydroxylation of the product. In regard to enantioselectivity the pressure effect is small. In some examples a slight increase (entries 8, 15) or a slight decrease was observed (e.g., entries 1, 2, 9, 17). In methanol the influence of the applied pressure is more pronounced than in aprotic solvents (entries 10, 14, 26).

In the next step of our optimization approach we investigated the influence of the initial hydrogen pressure and the substrate:catalyst ratio on the asymmetric hydrogenation using the precatalyst based on ligand **11**. All reactions were carried out at 25 °C in THF and conducted over a period of two hours. The results in Table 3 illustrate that a decrease of the pressure influences the *ee* values in the product only marginally. The reactions can be carried out even with higher ratios of substrate to catalyst (entries 5 and 7). However to our surprise in the hydrogenation of substrate **2b** with an S/C ratio of 500 only traces of the desired product were formed (entries 14 and 16).

Table 2. Results of the asymmetric hydrogenation of **2a**, **b** (1 and 50 bar, up to 90 min).[a]

			2a			**2b**	
Entry	Ligand	Solvent	*ee* [%] at 1 bar	*ee* [%] at 50 bar	Entry	*ee* [%] at 1 bar	*ee* [%] at 50 bar
1	**6**	THF	90 (*S*)	84 (*S*)	17	95 (*S*)	81 (*S*)
2	**6**	CH_2Cl_2	92 (*S*)	85 (*S*)	18	93 (*S*)	89 (*S*)
3	**7**	MeOH	racemic	racemic	19	28 (*S*)	19 (*S*)
4	**7**	THF	91 (*S*)	90 (*S*)	20	96 (*S*)	97 (*S*)
5	**7**	CH_2Cl_2	94 (*S*)	95 (*S*)	21	98 (*S*)	98 (*S*)
6	**8**	THF	93 (*S*)	95 (*S*)	22	97 (*S*)	95 (*S*)
7	**8**	CH_2Cl_2	95 (*S*)	94 (*S*)	23	95 (*S*)	92 (*S*)
8	**9**	THF	89 (*S*)	95 (*S*)	24	97 (*S*)	96 (*S*)
9	**9**	CH_2Cl_2	97 (*S*)	91 (*S*)	25	97 (*S*)	96 (*S*)
10	**10**	MeOH	79 (*S*)	84 (*S*)	26	93 (*S*)	77 (*S*)
11	**10**	MeOH	–	79 (*S*)[b]	27	–	92 (*S*)[b]
12	**10**	THF	92 (*S*)	93 (*S*)	28	96 (*S*)	95 (*S*)
13	**10**	CH_2Cl_2	95 (*S*)	93 (*S*)	29	95 (*S*)	95 (*S*)
14	**11**	MeOH	40 (*R*)	80 (*R*)	30	61 (*R*)	57 (*R*)
15	**11**	THF	88 (*R*)	94 (*R*)	31	99 (*R*)	95 (*R*)
16	**11**	CH_2Cl_2	93 (*R*)	95 (*R*)	32	94 (*R*)	93 (*R*)

[a] For other reactions conditions and analytics of the reaction product, see Table 1.

[b] The precatalyst with ligand **10** was stirred in MeOH for 60 min. Under these conditions the anhydride was opened quantitatively.[16]

Table 3. Influence of reaction conditions on the hydrogenation with ligand **11** in THF.[a]

	2a				**2b**		
Entry	S:C	pH_2 [bar]	*ee* [%]	Entry	S:C	pH_2 [bar]	*ee* [%]
1	100	90	96 (*R*)	10	100	90	95 (*R*)
2	100	60	93 (*R*)	11	100	60	94 (*R*)
3	100	30	92 (*R*)	12	100	30	93 (*R*)
4	250	50	94 (*R*)	13	250	50	97 (*R*)
5	500	50	93 (*R*)	14	500	50	n. d.[b]
6	250	25	95 (*R*)	15	250	25	97 (*R*)
7	500	25	96 (*R*)	16	500	25	n. d.[b]

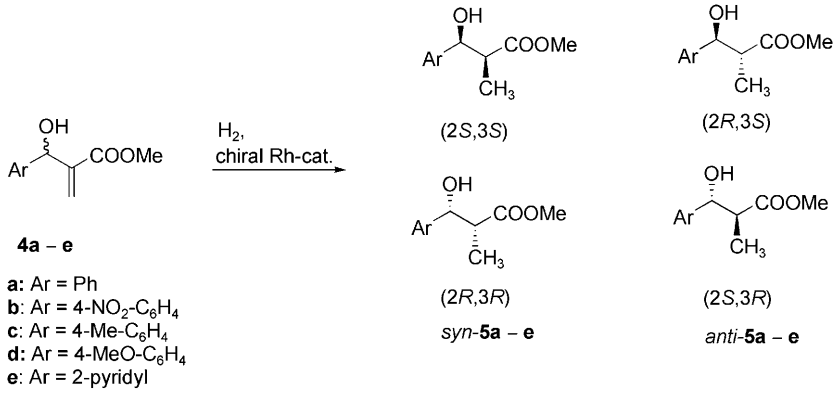
[a] For other conditions and analytics of the reaction products, see Table 1.
[b] Only traces of the product were formed.

As announced in the introduction, in order to extend the range of substrates, we also used as substrates olefins **4a–e** which are likewise available by Baylis–Hillman reaction of aromatic aldehydes and methyl acrylate.[12] Among others, products of the hydrogenation have importance in drugs with antiproliferative activity.[18] Due to the already established stereocentre in the substrate the hydrogenation with chiral catalysts should provide interesting information as to whether the stereochemistry in the final product is governed by the substrate or by the catalyst. Principally, the hydrogenation of racemic **4** with an achiral rhodium catalyst may afford a mixture of two pairs of racemic diastereomers **5** where hydroxy group and the newly created methyl substituent are placed either in a *syn*(*erythro*)- or an *anti*(*threo*)-arrangement (Scheme 2).

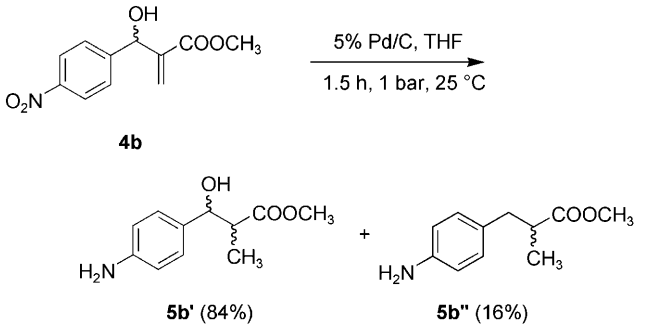
The hydrogenation of **4a** was already investigated by Brown et al. with the homogeneous Rh catalyst in hand.[19] It was found that in methanol the *anti*-product was preferentially formed. This preference was attributed to attractive stereodirecting interactions between hydroxy group in the substrate and the metal centre during the transfer of hydrogen. Protection of the polar group led to a significant decrease of the *anti*:*syn* ratio.[20] In contrast, by application of a heterogeneous Pd catalyst the *anti/syn* ratio was diminished. When a chiral Rh(DiPAMP)[19a–c] or Ru(BINAP) catalyst[21] was employed diastereoselective hydrogenation could be achieved caused by different reaction rates of the enantiomeric substrates.[22]

In order to confirm these pioneering results we hydrogenated the olefins with an initial H_2 pressure at 20 bar in methanol at room temperature. In first trials substrates **4a–e** were reduced until full conversion (20 h). By application of the achiral precatalyst [Rh(dppb)(COD)]BF_4 the racemic mixtures of the diastereomers *anti*-**5a,c,d,e** were obtained in a *anti/syn* ratio of > 90/10. Exceptionally, under these conditions the hydrogenation of **4b** afforded not only **5b**. As a side product the corresponding aniline derivative *anti*-**5b′** was formed as a result of the reduction of the nitro group (see also Scheme 3). The expected *anti*-geometry of **5b** was evidenced by X-ray structural analysis (Figure 2).[23]

The application of Pd on charcoal as a heterogeneous catalyst at ambient pressure in THF led predominantly to the formation of the aniline derivative **5b′**, but under these conditions significant hydrogenolysis of the benzylic alcohol took place to give **5b″** (Scheme 3). The compound *anti*-**5b′** was detected as a by-product in the homogeneous hydrogenation of racemic mixture of **4b**.



Scheme 2. Possible hydrogenation products derived from **4a–e**.



Scheme 3. Products of the heterogeneous Pd-catalyzed hydrogenation of **4b**.

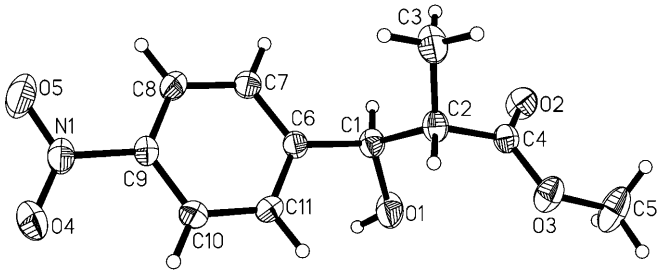


Figure 2. X-ray structural analysis of *anti*-**5b**. The thermal ellipsoids correspond to 30% probability.

The *anti*-geometry for the other main products **5a, c–e** could be established by comparison of the NMR spectra.[24] Thus, the signal of the C*H*O proton is shifted downfield for the *syn*-isomer (region of 4.95 to 5.15 ppm *vs.* 4.60 to4.85 ppm for the *anti*-isomer). Also the relevant coupling constant of the *anti*-derivatives is larger than for the corresponding *syn*-isomer (~8 Hz *vs.* 4 Hz).

In general, by employment of the chiral Rh catalysts based on ligands **6**, **8**–**10** or **11** only poor *ee* values were noted (Table 4). This observation gives proof that the stereodifferentiating addition of H_2 is dominated by the adjacent chiral centre in the substrate and not by the chiral catalyst. Also under our conditions the *syn*-products were formed in less than 4%. Surprisingly in the hydrogenation of the (2-pyridyl)-substituted derivative **4e** with the achiral [Rh(dppb)(COD)]BF_4 and the chiral Rh catalyst of **9** we observed an increase in the formation of the *syn*- over the *anti*-compound (79:21 and 68:32, respectively). This change nicely illustrates that the decisive secondary interaction of the substrate with the Rh centre is now governed by the pyridine nitrogen instead of the hydroxy group.

Under the precondition evidenced above, that the stereochemical course of the hydrogenation is dominated by the chiral substrate, interruption of the hydrogen uptake at *ca.* 50% conversion opens up the opportunity of a diastereoselective reaction provided a highly stereoselective catalyst can be found which reacts much faster with one enantiomer of the racemic substrate. In this case the classical situation of a kinetic resolution is established.[26] In order to test this hypothesis we stopped the reaction of **4a** with catalysts based on ligands **9** and **11** after varying periods of hydrogen uptake and determined conversion (NMR, HPLC) as well as enantiomeric composition of the reaction mixture (HPLC). From Figure 3 it is apparent that during the first half of the reaction (*ca.* 50% conversion) mainly *anti*-product **5a** was formed.

Table 4. Results of the asymmetric hydrogenation of **4a–e** at room temperature.[a]

Entry	Substrate	Ligand	Solvent	pH_2 [bar]	*ee* [%][25]
1	**4a**	**9**	MeOH	1	17 (+)[b]
2	**4b**	**6**	THF	50	9 (+)
3	**4b**	**8**	THF	50	2 (+)
4	**4b**	**9**	THF	50	1 (+)
5	**4b**	**10**	MeOH	50	27 (+)
6	**4b**	**10**	THF	50	4 (+)
7	**4b**	**11**	MeOH	50	2 (−)
8	**4b**	**11**	THF	50	5 (−)
9	**4c**	**9**	THF	1	8 (+)
10	**4c**	**11**	THF	50	7 (−)
11	**4d**	**11**	THF	50	7 (−)
12	**4e**	**9**	MeOH	1	25(−)/90(+)[c]
13	**4e**	**9**	THF	1	47(−)/94(+)[d]

[a] *Conditions:* 0.33 mmol substrate, 0,0033 mmol Rh catalyst, 5 mL solvent, 25 °C, 120 min (50 bar) or until completion of hydrogen consumption (1 bar). For other reaction conditions and analytics of the hydrogenation products, see Experimental Section.

[b] (+) = (2*S*,3*R*)-configuration, (−) = (2*R*,3*S*)-configuration.

[c] *syn/anti* = 76:24; absolute configuration could not be determined.

[d] *syn/anti* = 68:32; absolute configuration could not be determined.

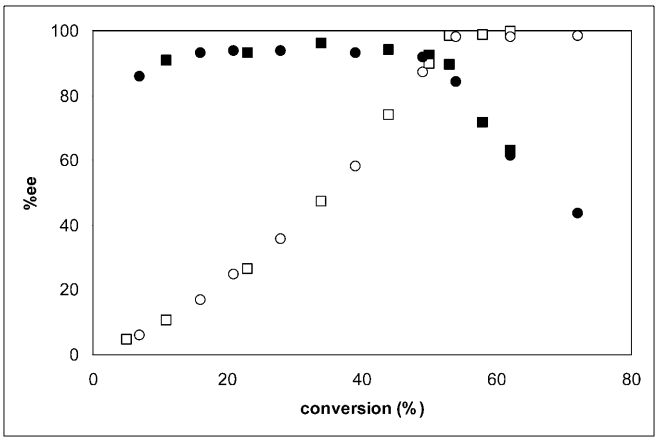


Figure 3. Selective hydrogenation of **4a** (□/○) to *anti*-**5a** (■/●) with [Rh(**9**)(COD)]BF_4 (●/○) and [Rh(**11**)(COD)]BF_4 (●/□) (15 bar, 25 °C, S/C = 200, THF).

In this stage the product was generated with nearly constant enantiomeric excess and the starting product **4a** became enantiomerically enriched with the less favoured enantiomer. The maximum *ee* value of both enantiomeric compounds was found around a conversion of 48–52%. As expected in the second half of the reduction also the less favoured enantiomeric starting product reacts to give the *anti*-product with the opposite configurations, hence in the end nearly racemic product is obtained.

A similar behaviour was found in other solvents (MeOH, CH_2Cl_2), with substrates **4b–e** (Table 5).

Obviously the difference in the hydrogenation rates of the enantiomeric starting products is large enough to allow for a good stereodifferentiation. Proof for this assumption can be easily derived from the hydrogen uptake curves (Figure 4), which are clearly separated into two parts. Figure 4 a and b (bold lines) illustrates the hydrogen consumption in the reaction with **4a** and **4c** under ambient reaction conditions (25 °C, 1 bar) using [Rh(**9**)(COD)]BF_4. In the first part, for example, after *ca.* 50% of required H_2 volume uptake, the preferred (*S*)-enantiomers are consumed rapidly followed by a slow reaction of the less-favored (*R*)-enantiomers. A different behaviour is noted in the hydrogenation of the 2-pyridyl-substituted substrate **4e** (Figure 4 b, empty squares). This hydrogenation is characterized by a continuous uptake of hydrogen without deceleration after *ca.* 50% conversion. Apparently, both the hydroxy group and the 2-pyridyl group compete for coordination with the rhodium centre. Therefore both enantiomeric substrates are hydrogenated by the same catalyst with similar rates and kinetic resolution is impossible. The predominant formation of the *syn*-isomer of **5e** (e.g., *anti*-isomer relative to the pyridyl group) indicates that the coordinating ability of the 2-pyridyl group is stronger.

In a preparative trial we interrupted the hydrogenation reaction of **4a** with ligand **9** at *ca.* 50% conver-

Table 5. Chiral composition of mixtures after *ca.* half conversion of **4a–e**.[a]

Entry	Substrate	Ligand	Solvent	Conversion [%][b]	*anti:syn*[b]	ee_{Educt} [%][c]	$ee_{Product}$ [%][d]
1	**4a**	**9**	THF	52	98:2	96 (−)	91 (+)
2	**4a**	**9**	MeOH	53	98:2	85 (−)	80 (+)
3	**4a**	**9**	CH_2Cl_2	47	>99:1	77 (−)	93 (+)
4	**4a**	**11**	THF	51	97:3	88 (+)	88 (−)
5	**4a**	**11**	MeOH	53	97:3	91 (+)	82(−)
6	**4a**	**11**	CH_2Cl_2	49	99:1	83 (+)	89 (−)
7	**4b**[e]	**9**	THF	51	>99:1	93 (−)	92 (+)
8	**4b**[e]	**9**	MeOH	54	>99:1	94 (−)	82 (+)
9	**4b**[e]	**11**	THF	40	>99:1	54 (+)	88 (−)
10	**4b**[e]	**11**	MeOH	52	>99:1	88 (+)	84 (−)
11	**4c**	**9**	THF	52	98:2	95 (−)	89 (+)
12	**4c**	**11**	THF	48	98:2	82 (+)	90 (−)
13	**4d**	**9**	THF	49	99:1	85 (−)	84 (+)
14	**4d**	**11**	THF	50	97:3	73 (+)	84 (−)
15	**4e**	**9**	THF	58	32:68	10 (+)[f]	99 (+)/54 (−)[f]
16	**4e**	**11**	THF	59	29:71	14 (−)[f]	99 (−)/40 (+)[f]

[a] *Reaction conditions:* H_2 (1 bar, isobar), 0.5 mmol substrate, 0.005 mmol precatalyst, 7.5 mL solvent, 25 °C.
[b] Conversion was determined by ^{1}H NMR spectroscopy and/or HPLC.
[c] (+) = (*S*)-configuration, (−) = (*R*)-configuration.
[d] (+) = (2*S*,3*R*)-configuration, (−) = (2*R*,3*S*)-configuration.
[e] Less than 4% of *anti*-**5b′** was formed.
[f] *anti*/*syn*; absolute configurations could not be determined. Conclusions by comparison with optical rotations of the related *anti*- and *syn*-derivatives of **5a–d** may fail due to the unique hydrogenation mechanism, which covers competitive interactions of pyridyl and hydroxy group with Rh.

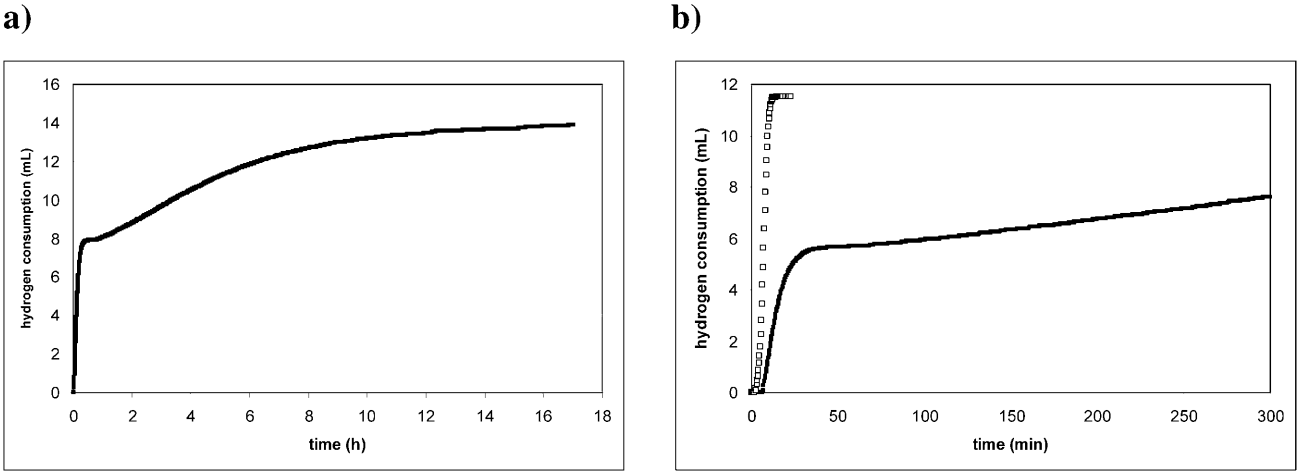


Figure 4. Consumption of hydrogen during the reaction of a) **4a** with [Rh(**9**)(COD)]BF_4 and b) **4c** (bold line, continued up to 17 h with 11.5 mL H_2 consumption) and **4e** (□) with [Rh(**9**)(COD)]BF_4 [S/C = 100, 25 °C, H_2 (1 bar, isobar), 10 mL THF].

sion (nearly half of H_2 consumption; additionally confirmed by NMR and HPLC analysis) in order to generate a mixture consisting of (*R*)-**4a** (93.9% *ee*) and (2*S*,3*R*)-**5a** (91.5% *ee*) as described above (Scheme 4). Both compounds could be separated by flash chromatography. Subsequently compound (*R*)-**4a** was individually hydrogenated with [Rh(**11**)(COD)]BF_4 bearing a ligand with opposite configuration in comparison to ligand **9** to produce (2*R*,3*S*)-**5a** in 94.4% *ee*.

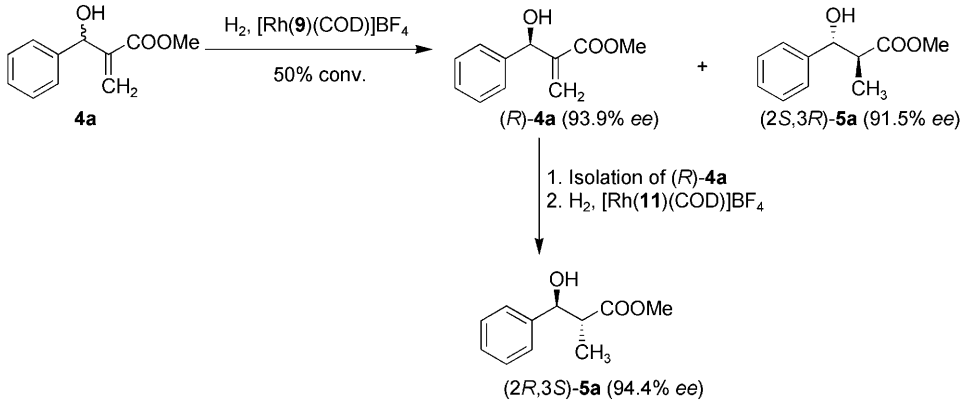
Conclusions

The Rh-catalyzed enantioselective hydrogenation of α-(hydroxymethyl)acrylates proceeds with up to >99% *ee* with bisphospholanes of the cat*A*Sium M family as ancillary ligands, which are the highest enantioselectivities reported up to now. Moreover, in the diastereoselective hydrogenation of related racemic β-hydroxy-β-aryl-substituted precursors kinetic resolution is possible under the conditions that the hydrogenation is stopped after *ca.* 50% conversion. Starting products and hydrogenation products can be obtained by this methodology in high enantioselectivity. In general, with the exception of a pertinent pyridine derivative the steric course is governed by the hydroxy group in the chiral substrate and not by the chiral catalyst. It proceeds in an *anti*-manner. By separation of enantiomerically enriched starting product and hydrogenation product after *ca.* half conversion and subsequent individual hydrogenation of the former with a catalyst of opposite chirality both enantiomers could be produced in >91% *ee*.

Experimental Section

General Remarks

Solvents were dried and freshly distilled under argon before use. All reactions were performed under an argon atmos-



Scheme 4. Production of both enantiomers of **5a** by two consecutive diastereoselective hydrogenations with different chiral catalysts.

phere. Thin layer chromatography was performed on precoated TLC plates (silica gel). Flash chromatography was carried out with silica gel 60 (particle size 0.040–0.063 mm). Melting points are uncorrected. NMR spectra were recorded at a Bruker ARX 400 spectrometer at the following frequencies: 400.13 MHz (^{1}H) and 100.63 MHz (^{13}C). Chemical shifts of ^{1}H and ^{13}C NMR spectra are reported in ppm downfield from TMS as internal standard. Signals are quoted as s (singlet), d (doublet), br (broad) and m (multiplet).

General Procedures for the Synthesis of 2-Hydroxymethylacrylates 2a, b and 4b, e

Following the procedure of Hu et al.[12a] relevant aldehydes (30 mmol), acrylates **1** (90 mmol) and DABCO (30 mmol) were dissolved in 300 mL of 1,4-dioxane/water (1:1 v/v) and the mixture was stirred at ambient temperature. After completion of the reaction MTBE (500 mL) and water (250 mL) were added to the mixture. After phase separation the organic layer was washed with brine (2×100 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by distillation (**3a, b**) and crystallization (**4b** from ethanol) to yield the desired product.

General Procedures for Synthesis of Methyl 2-Aryl-2-hydroxymethylacrylates 4a, c, d

According to the method of Zheng et al.[12b] methyl acrylate (**1a**) (1.61 g, 18.7 mmol), the corresponding aromatic aldehyde (15 mmol) and DABCO (1.68 g, 15 mmol) were stirred without any solvent for 24 h at room temperature. After dilution with diethyl ether (200 mL) the mixture was washed with HCl, $NaHCO_3$ and water. The organic phase was dried (Na_2SO_4) and concentrated to remove the solvent and the excess of methyl acrylate. The yielded crude products were purified by chromatography to yield the desired racemic mixtures of **4a, c, d**.

Methyl (2-hydroxymethyl)acrylate (2a): Yield: 2.4 g (69%); colourless oil; bp 60–62 °C/2 mbar; ^{1}H NMR ($CDCl_3$): δ = 6.21 (m, 1H, =CH), 5.81 (m, 1H, =CH), 4.27 (m, 2H, CH_2O), 3.73 (s, 3H, OCH_3), 2.82 (s, br), 1H, OH); ^{13}C NMR ($CDCl_3$): δ = 166.7 (C=O), 139.4 (=C), 125.6 (=CH_2), 62.1 (CH_2O), 51.8 (OCH_3); HPLC analysis: Chiralcel OD-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 97:3, t_R = 7.6 min at 210, 215 and 225 nm.

***tert*-Butyl (2-hydroxymethyl)acrylate (2b):** Yield: 8.8 g (56%); colourless oil; bp 72 °C/2 mbar or purification by colum chromatography (heptane/AcOEt = 2:1, R_f = 0.25); ^{1}H NMR ($CDCl_3$): δ = 6.12 (m, 1H, =CH), 5.72 (m, 1H, =CH), 4.25 (m, 2H, CH_2O), 2.51 (t, J = 6.5 Hz, 1H, OH); 1.48 (s, 9H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 165.7 (C=O), 140.8 (=C), 124.7 (=CH_2), 81.3 (O−C), 62.6 (CH_2O), 28.0 (CH_3); HPLC analysis: Chiralcel OD-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 99:1, t_R = 8.0 min at 210, 215 and 225 nm.

***rac*-Methyl 2-[hydroxy(phenyl)methyl]acrylate (4a):** Yield: 2.70 g (94%), colourless oil by colum chromatography (heptane/AcOEt = 8:1 to 2:1; R_f = 0.25); ^{1}H NMR ($CDCl_3$): δ = 7.24–7.43 (m, 5H, arom. H), 6.34 (m, 1H, =CH), 5.84 (m, 1H, =CH), 5.55 (d, J = 5.6, 1H, CHO), 3.71 (s, 3H, OCH_3), 3.14 (d, J = 5.6 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$): δ = 166.7 (C=O), 141.9 (=C), 141.2 (arom. =C), 128.4 (arom. =CH), 127.8 (arom. =CH), 126.5 (arom. =CH), 126.0 (=CH_2), 73.1 (CHO), 51.9 (OCH_3); HPLC analysis: Reprosil 100 NR 8 μm (250×4.6 mm), flow rate 1.25 mL/min; eluant hexane/2-propanol = 95:5, t_R = 7.7 min (*R*)-(−)-**4a** and t_R = 9.3 min (*S*)-(+)-**4a** at 210, 215 and 225 nm.

***rac*-Methyl 2-[hydroxy(4-nitrophenyl)methyl]acrylate (4b):** Yield: 2.75 g (77%); mp 72–74 °C; yellow solid by crystallization from ether; ^{1}H NMR ($CDCl_3$): δ = 8.17 (m, 2H, arom. H), 7.55 (m, 2H, arom. H), 6.38 (m, 1H, =CH), 5.86 (m, 1H, =CH), 5.61 (d, br, 1H, CHO), 3.72 (s, 3H, OCH_3), 3.14 (d, br, 1H, OH); ^{13}C NMR ($CDCl_3$): δ = 166.4 (C=O), 148.6 (arom. =C), 147.4 (arom. =C), 140.9 (=C), 127.3 (arom. =CH), 127.3 (=CH_2), 123.6 (arom. =CH), 72.7 (CHO), 52.2 (OCH_3); HPLC analysis: Chiralpak AS-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 85:15, t_R = 5.9 min (*R*)-(−)-**4b** and t_R = 17.2 min (*S*)-(+)-**4b** at 210, 240 and 255 nm.

***rac*-Methyl 2-[hydroxy(4-methylphenyl)methyl]acrylate (4c):** Yield: 2.87 g (93%); colourless oil by column chromatography (heptane/AcOEt = 4:1; R_f = 0.55); ^{1}H NMR ($CDCl_3$): δ = 7.24 (m, 2H, arom. H), 7.14 (m, 2H, arom. H), 6.31 (m, 1H, =CH), 5.84 (m, 1H, =CH), 5.51 (d, J = 5.4 Hz, 1H, CHO),3.70 (s, 3H, OCH_3), 3.05 (d, J = 5.4 Hz, 1H, OH), 2.33 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 166.7 (C=O), 142.0 (=C), 138.3 (arom. =C), 137.4 (arom. =C), 129.0 (arom. =CH), 126.5 (arom. =CH), 125.7 (=CH_2), 72.9 (CHO), 51.8 (OCH_3), 21.0 (CH_3); HPLC analysis: Reprosil 100 NR 8 μm (250×4.6 mm), flow rate 1.00 mL/min; eluant hexane/2-propanol = 90:10, t_R = 7.7 min (*R*)-(−)-**4c** and t_R = 9.5 min (*S*)-(+)-**5c** at 210, 215 and 220 nm.

***rac*-Methyl 2-[hydroxy(4-methoxyphenyl)methyl]acrylate (4d):** Yield: 2.90 g (87%); mp 62–63 °C; white solid by column chromatography (heptane/AcOEt = 4:1; R_f = 0,15); ^{1}H NMR ($CDCl_3$): δ = 7.20 (m, 2H, arom. H), 6.78 (m, 2H, arom. H), 6.23 (m, 1H, =CH), 5.77 (m, 1H, =CH), 5.44 (d, J = 5.3 Hz, 1H, CHO),3.71 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 2.89 (d, J = 5.4 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$): δ = 166.7 (C=O), 159.2 (arom. =C), 142.2 (=C), 133.5 (arom. =C), 127.9 (arom. =CH), 125.5 (=CH_2), 113.8 (arom. =CH), 72.6 (CHO), 55.2 (OCH_3), 51.8 (OCH_3); Chiralpak AD-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 95:15, t_R = 11.6 min (*S*)-(+)-**4d** and t_R = 12.7 min (*R*)-(−)-**4d** at 210, 215 and 220 nm.

***rac*-Methyl 2-[hydroxy(2-pyridyl)methyl]acrylate (4e):** Yield: 3.42 g (59%); mp 50–51 °C; pale yellow solid by column chromatography (heptane/AcOEt = 1:1; R_f = 0.45); ^{1}H NMR ($CDCl_3$): δ = 8.52 (m, 1H, arom. H), 7.66 (m, 1H, arom. H), 7.40 (m, 1H, arom. H), 7.17 (m, 1H, arom. H), 6.33 (m, 1H, =CH), 5.94 (m, 1H, =CH), 5.60 (s, br, 1H, CHO), 2.89 (s, br, 1H, OH), 3.72 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$): δ = 166.4 (C=O), 159.5 (arom. =C), 148.2 (arom. =C), 141.6 (=C), 136.7 (arom. =CH), 125.5 (=CH_2), 122.5 (arom. =CH), 121.1 (arom. =CH), 72.0 (CHO), 51.7 (OCH_3); Chiralpak OD-H (150×4.6 mm), flow rate 1.30 mL/min; eluant hexane/2-propanol = 97:3, t_R = 9.1 min *syn*-(+)-**4e** and t_R = 11.8 min *syn*-(−)-**4e** at 215, 255 and 270 nm.

General Procedure for Synthesis of Racemates of 3a, b and 4a-e

A solution of substrates **2a, b** or **4a–e** (0,5 mmol) and achiral [Rh(dppb)(COD)]BF_4 (3.5 mg, 0.005 mmol) in methanol (7.5 mL) was stirred at ambient temperature under a hydrogen pressure of 60 bar for 20 h. After decompression the mixture was directly used for HPLC analysis and the residue after evaporation was investigated by NMR. In all cases full conversion was observed.

***rac*-Methyl 3-hydroxy-2-methyl-propanoate (3a):** ^{1}H NMR ($CDCl_3$): $\delta = 3.68$ (m, 2H, CH_2O), 3.68 (s, 3H, OCH_3), 2.65 (m, 1H, CH), 2.50 (s, br, 1H, OH), 1.14 (d, $J = 7.2$ Hz, 3H, CH_3; ^{13}C NMR ($CDCl_3$): $\delta = 176.1$ (C=O), 64.5 (CH_2O), 51.8 (OCH_3), 41.6 (CH), 13.4 (CH_3); HPLC analysis: Chiralcel OD-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 97:3, $t_R = 5.8$ min (*R*)-**3a** and $t_R = 6.6$ min (*S*)-**3a** at 210, 215 and 225 nm.

***rac-tert*-Butyl 3-hydroxy-2-methyl-propanoate (3b):** ^{1}H NMR ($CDCl_3$): $\delta = 3.63$ (m, 2H, CH_2O), 2.55 (m, 1H, CH), 2.44 (s, br, 1H, OH), 1.44 (s, 9H, CH_3),1.11 (d, $J = 7.2$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 175.1$ (C=O), 80.8 (C-O), 64.6 (CH_2O), 42.4 (CH), 28.0 (CH_3), 13.5 (CH_3); HPLC analysis: Chiralcel OD-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 99:1, $t_R = 5.5$ min (*R*)-**3b** and $t_R = 6.1$ min (*S*)-**3b** at 210, 215 and 225 nm.

rac-Methyl 3-Hydroxy-2-methyl-3-phenyl-propanoate (5a) [*anti*:*syn* = 90:10]

***anti*-5a:** ^{1}H NMR ($CDCl_3$): $\delta = 7.23$–7.38 (m, 5H, arom. H), 4.72 (d, $J = 8.8$ Hz, 1H, CHO), 3.70 (s, 3H, OCH_3), 3.09 (s, br, 1H, OH), 2.80 (m, 1H, CH), 0.97 (d, $J = 7.2$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 176.3$ (C=O), 145.6 (arom. =C), 128.4 (arom. =CH), 128.0 (arom. =CH), 126.6 (arom.=CH), 76.4 (CHO), 51.9 (OCH_3), 47.1 (CH), 14.4 (CH_3); HPLC analysis: Reprosil 100 NR 8 μm (250×4.6 mm), flow rate 1.00 mL/min; eluant hexane/2-propanol = 95:5, $t_R = 8.8$ min (2*R*,3*S*)-(−)-**5a** and $t_R = 10.5$ min (2*S*,3*R*)-(+)-**5a** at 210, 215 and 225 nm.

***syn*-5a:** ^{1}H NMR ($CDCl_3$): $\delta = 7.23$–7.38 (m, 5H, arom. H), 5.06 (d, $J = 4.3$ Hz, 1H, CHO), 3.64 (s, 3H, OCH_3), 3.09 (s, br, 1H, OH), 2.80 (m, 1H, CH), 1.11 (d, $J = 7.2$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 176.1$ (C=O), 141.4 (arom. =C), 128.2 (arom. =CH), 127.4 (arom. =CH), 125.9 (arom.=CH), 73.6 (CHO), 51.8 (OCH_3), 46.4 (CH), 10.7 (CH_3); HPLC analysis: Reprosil 100 NR 8 μm (250×4.6 mm), flow rate 1.00 mL/min; eluant hexane/2-propanol = 95:5, $t_R = 7.6$ min and $t_R = 8.0$ min s*yn*-**5a** at 210, 215 and 225 nm.

Racemic *anti*-Methyl 3-Hydroxy-2-methyl-3-(4-nitrophenyl)propanoate (5b), *rac*-Methyl 3-(4-Aminophenyl)-3-hydroxy-2-methylpropanoate (5b′) and *rac*-Methyl 3-(4-Aminophenyl)-2-methylpropanoate (5b″) [*anti*-5b:*anti*-5b′ = 89:11]

Separation by chromatography (eluant heptane:AcOEt = 2:1 to 1:1).

***anti*-5b**: mp 105 °C; $R_f = 0.32$ (heptane:AcOEt = 2:1); ^{1}H NMR ($CDCl_3$): $\delta = 8.13$ (m, 2H, arom. H), 7.45 (m, 2H, arom. H), 4.81 (d, $J = 7.7$ Hz, 1H, CHO), 3.67 (s br, 1H, OH), 3.64 (s, 3H, OCH_3), 2.76 (m, 1H, CH), 1.00 (d, $J = 7.2$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 175.5$ (C=O), 148.9 (arom. =C), 147.4 (arom. =C), 127.4 (arom. =CH), 123.5 (arom. =CH), 75.0 (CHO), 52.0 (OCH_3), 46.7 (CH), 14.1 (CH_3); MS (EI, 70 eV): $m/z = 239$ [M^+, 2], 152 [$C_7H_6NO_3^+$, 21]; 88 [$C_4H_8O_2^+$, 100], HPLC analysis: Chiralpak AS-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 85:15, $t_R = 6.8$ min (2*S*,3*R*)-(+)-**5b** and $t_R = 9.2$ min (2*R*,3*S*)-(−)-**5b** at 210, 240 and 270 nm.

***anti*-5b′**: mp 154 °C; $R_f = 0.13$ (heptane:AcOEt = 2:1); ^{1}H NMR ($CDCl_3$): $\delta = 7.11$ (m, 2H, arom. H), 6.65 (m, 2H, arom. H), 4.63 (d, $J = 9.0$ Hz, 1H, CHO), 3.73 (s, 3H, OCH_3), 3.67 (s, br, 1H, OH), 2.76 (m, 1H, CH), 0.95 (d, $J = 7.2$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 176.5$ (C=O), 146.3 (arom. =C), 131.5 (arom. =C), 127.8 (arom. =CH), 115.0 (arom. =CH), 76.3 (CHO), 51.9 (OCH_3), 47.2 (CH), 14.5 (CH_3); MS (EI, 70 eV): $m/z = 209$ [M^+, 8], 191 [$(M-H_2O, 40)^+$ 122 [$C_7H_8NO^+$, 100]; HPLC analysis: Chiralpak AS-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 85:15, $t_R = 11.9$ min (2*S*,3*R*)-(+)-**5b′** and $t_R = 15.6$ min (2*R*,3*S*)-(−)-**5b′** at 210, 240 and 270 nm.

Application of Pd/C (5%) as catalyst (1 bar, 90 min, S:C = 100:1, THF, 25 °C) leads to the predicted formation of a mixture of the *anti*-**5b′** and *syn*-**5b′** diastereomers with a ratio of 56:44 (84%). In contrast to the observation of Coelho et al.[17a] we observed also the hydrogenolysis of the C–OH bond to form the racemic methyl 3-(4-aminophenyl)-2-methylpropanoate (**5b″**) (16%). All products could be separated by colum chromatography (heptane:AcOEt = 2:1).

***syn*-5b′**: mp 89 °C; $R_f = 0.16$ (heptane:AcOEt = 2:1); ^{1}H NMR ($CDCl_3$): $\delta = 7.07$ (m, 2H, arom. H), 6.60 (m, 2H, arom. H), 4.88 (d, $J = 4.7$ Hz, 1H, CHO), 3.60 (s, 3H, OCH_3), 3.60 (s, br, 1H, OH), 2.72 (m, 1H, CH), 1.13 (d, $J = 6.7$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 176.0$ (C=O), 145.7 (arom. =C), 131.6 (arom. =C), 127.0 (arom. =CH), 114.9 (arom. =CH), 73.8 (CHO), 51.7 (OCH_3), 46.7 (CH), 11.3 (CH_3); HPLC analysis: Chiralpak AS-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 85:15, $t_R = 8.5$ min (*S*,*S*)-(−)-**5b′** and $t_R = 13.7$ min (*R*,*R*)-(+)-**5b′** at 210, 240 and 270 nm;

***rac*-5b″**: oil; $R_f = 0.32$ (heptane:AcOEt = 2:1); ^{1}H NMR ($CDCl_3$): $\delta = 6.93$ (m, 2H, arom. H), 6.60 (m, 2H, arom. H), 3.62 (s, 3H, OCH_3), 3.57 (s, br, 1H, OH), 2.90 (dd, $J = 13.2$, 6.6 Hz, 1H, H_b-CH_2), 2.65 (m, 1H, CH), 2.54 (dd, $J = 13.2$, 7.6 Hz, 1H, H_a-CH_2),1.11 (d, $J = 6.8$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 176.8$ (C=O), 144.6 (arom. =C), 129.7 (arom. =CH), 129.3 (arom. =C), 115.1 (arom. =CH), 51.5 (OCH_3), 41.7 (CH), 38.9 (CH_2), 16.6 (CH_3); MS (EI, 70 eV): $m/z = 193$ [M^+, 12], 106 [$C_7H_8N^+$, 100]; HPLC analysis: Chiralpak AS-H (150×4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 85:15, $t_R = 4.3$ min *rac*-**5b″** at 220, 240 and 255 nm and Chiralcel OD-H (150×4.6 mm), flow rate 1.20 mL/min, eluant hexane/2-propanol = 85:15, $t_R = 8.8$ min (*S*)-(+)-**5b″** and $t_R = 11.0$ min (*R*)-(−)-**5b″** at 220, 240 and 255 nm.

rac-Methyl 3-Hydroxy-2-methyl-3-(4-methylphenyl)propanoate (5c) [*anti*:*syn* = 97:3]

***anti*-5c**: ^{1}H NMR ($CDCl_3$): $\delta = 7.19$ (m, 2H, arom. H), 7.13 (m, 2H, arom. H), 4.67 (d, $J = 8.5$ Hz, 1H, CHO), 3.70 (s, 3H, OCH_3), 3.04 (s, br, 1H, OH), 2.77 (m, 1H, CH), 2.32 (s, 3H, CH_3), 0.95 (d, $J = 7.2$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$):

δ = 176.3 (C=O), 138.6 (arom. =C), 137.7 (arom. =C), 129.1 (arom. =CH), 126.5 (arom. =CH), 76.2 (CHO), 51.8 (OCH_3), 47.1 (CH), 21.0 (CH_3), 14.3 (CH_3); HPLC analysis: Reprosil 100 NR 8 μm (250 × 4.6 mm), flow rate 1.00 mL/min; eluant hexane/2-propanol = 90:10, t_R = 7.2 min (2*R*,3*S*)-(−)-**5c** and t_R = 8.5 min (2*S*,3*R*)-(+)-**5c** at 210, 215 and 220 nm.

***syn*-5c:** ^{1}H NMR ($CDCl_3$): δ = 7.19 (m, 2H, arom. H), 7.13 (m, 2H, arom. H), 5.00 (d, *J* = 4.5 Hz, 1H, CHO), 3.62 (s, 3H, OCH_3), 3.04 (s, br, 1H, OH), 2.77 (m, 1H, CH), 2.32 (s, 3H, CH_3), 1.11 (d, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 176.0 (C=O), 138.6 (arom. =C), 137.7 (arom. =C), 128.8 (arom. =CH), 125.8 (arom. =CH), 73.6 (CHO), 51.7 (OCH_3), 46.5 (CH), 21.0 (CH_3), 10.9 (CH_3); HPLC analysis: not detectable.

rac-Methyl 3-Hydroxy-2-methyl-3-(4-methoxyphenyl)propanoate (5d) [*anti:syn* = 96:4]

***anti*-5d**: ^{1}H NMR ($CDCl_3$): δ = 7.22 (m, 2H, arom. H), 6.86 (m, 2H, arom. H), 4.67 (d, *J* = 8.7 Hz, 1H, CHO), 3.77 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 2.89 (s, br, 1H, OH), 2.75 (m, 1H, CH), 0.95 (d, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 176.3 (C=O), 159.3 (arom. =C), 133.7 (arom. =C), 127.8 (arom. =CH), 113.8 (arom. =CH), 75.9 (CHO), 55.2 (OCH_3), 51.8 (OCH_3), 47.2 (CH), 14.4 (CH_3); Chiralpak AD-H (150 × 4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 95:15, t_R = 16.7 min (2*S*,3*R*)-(+)-**5d** and t_R = 17.8 min (2*R*,3*S*)-(−)-**5d** at 210, 215 and 220 nm.

***syn*-5d**: ^{1}H NMR ($CDCl_3$): δ = 7.22 (m, 2H, arom. H), 6.86 (m, 2H, arom. H), 4.97 (d, *J* = 4.8 Hz, 1H, CHO), 3.77 (s, 3H, OCH_3), 3.62 (s, 3H, OCH_3), 2.89 (s, br, 1H, OH), 2.75 (m, 1H, CH), 1.13 (d, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 176.0 (C=O), 159.3 (arom. =C), 133.7 (arom. =C), 127.1 (arom. =CH), 113.6 (arom. =CH), 73.5 (CHO), 55.2 (OCH_3), 51.7 (OCH_3), 46.6 (CH), 11.1 (CH_3); HPLC analysis: Chiralpak AD-H (150 × 4.6 mm), flow rate 1.20 mL/min; eluant hexane/2-propanol = 95:15, t_R = 9.3 min and t_R = 10.2 min at 210, 215 and 220 nm.

rac-Methyl 3-Hydroxy-2-methyl-3-(2-pyridyl)-propanoate (5e) [*anti:syn* = 21:79]

***anti*-5e**: ^{1}H NMR ($CDCl_3$): δ = 8.47 (m, 1H, arom. H), 7.63 (m, 1H, arom. H), 7.26 (m, 1H, arom. H), 7.14 (m, 1H, arom. H), 4.80 (m, 1H, CHO), 4.42 (s, br, 1H, OH), 3.61 (s, 3H, OCH_3), 2.96 (m, 1H, CH), 1.05 (d, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 175.3 (C=O), 159.8 (arom. =C), 148.5 (arom. =CH), 136.5 (arom. =CH), 122.6 (arom. =CH), 121.3 (arom. =CH), 75.2 (CHO), 51.6 (OCH_3), 46.2 (CH), 13.5 (CH_3); HPLC analysis: Chiralpak AS-H (150 × 4.6 mm), flow rate 1.00 mL/min; eluant hexane/2-propanol = 97:3, t_R = 13.0 min *anti*-(+)-**5e** and t_R = 14.5 min *anti*-(−)-**5d** at 215, 255 and 270 nm.

***syn*-5e**: ^{1}H NMR ($CDCl_3$): δ = 8.47 (m, 1H, arom. H), 7.63 (m, 1H, arom. H), 7.30 (m, 1H, arom. H), 7.14 (m, 1H, arom. H), 5.30 (m, 1H, CHO), 4.42 (s, br, 1H, OH), 3.64 (s, 3H, OCH_3), 2.89 (m, 1H, CH), 0.97 (d, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 175.2 (C=O), 159.7 (arom. =C), 148.2 (arom. =CH), 136.6 (arom. =CH), 122.4 (arom. =CH), 120.6 (arom. =CH), 73.1 (CH), 51.7 (OCH_3), 45.7 (CHO), 10.0 (CH_3); HPLC analysis: Chiralpak AS-H (150 × 4.6 mm), flow rate 1.00 mL/min; eluant hexane/2-propanol = 97:3, t_R = 8.6 min *syn*-(+)-**5e** and t_R = 11.9 min *syn*-(−)-**5e** at 215, 255 and 270 nm.

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