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2,2′-Bis-[bis(4-substituted-phenyl)phosphino]-1,1′-binaphthyl derivatives in Rh(I)-catalyzed hydrogenation of acetamidoacrylic acid derivatives: Electronic effects

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Abstract

Electronic effects of electron-donating and electron-withdrawing substituents at the *para* position of the phenyl moieties of BINAP ligands were studied towards asymmetric hydrogenation of α-(acylamino)acrylic acids. Enantiomeric excesses varied as a linear relationship towards Hammett coefficients σ_p of electron-donating groups between 0 and −0.63.

Keywords: BINAP; Enantioselectivity; Hydrogenation; Electronic effect; Rhodium

1. Introduction

Chiral diphosphines play a central role as ligands for transition metals in homogeneous catalysis [1,2]. Among them, atropoisomeric diaryl-core diphosphanes like BINAP are attracting continued interest in view of their exceptional ability to induce asymmetry in transition metal-catalyzed reaction [3]. Atropoisomery is one of the most powerful tools for enantioselection. As described with MeO-BIPHEP [4–6], SYNPHOS [7,8] and SEGPHOS [9], BINAP [10,11] allows the formation of catalytic sites in which the chiral environment is controlled by classical steric and electronic factors, but also by the dihedral angle between the two aromatic cycles of the binaphthyl moiety [12].

Conveniently modification of the 3,3′ or 4,4′ positions of the naphthyl skeleton of BINAP influences strongly both the electronic density and the steric hindrance at the phosphorus atom [13,14]. According to the electron-donating or -withdrawing effects, we recently observed that the nature of substituents grafted in the 5,5′ position of BINAP affected the enantioselectivity of asymmetric hydrogenation of α-(acylamino)acrylic acids [15]. On the other hand, modification of the *para* position of the phenyl groups results in the change in the electronic density onto the phosphorus heteroatom [16–20]. Thus, electronic donor-acceptor properties of BINAP and its derivatives (*p*-Tol-, *p*-OMe-, *p*-F- and *p*-Cl-BINAP) were investigated towards the activity of rhodium and ruthenium catalysts. Generally, the π-acidic character of the diphosphine ligand incorporating electron-withdrawing substituents resulted in decreased catalytic activity and stereoselectivity of the asymmetric hydrogenation reactions [21,22]. Nevertheless, Genet described the use of an electrodeficient atropoisomeric diphosphane, difluorphos [23] which allowed for high levels of enantioselection in the hydrogenation of β-ketoesters. Electron-donating substituents exert positive effects on catalytic activity and stereoselectivity of these reactions. In order to investigate the effects of substituents on the four phenyl rings of BINAP, we examined the electronic effects on the enantioselectivity of the Rh(I)-catalyzed asymmetric hydrogenation of α-(acylamino)acrylic acids 1 (Scheme 1). Substituents, which could influence the electronic features of the catalysts,

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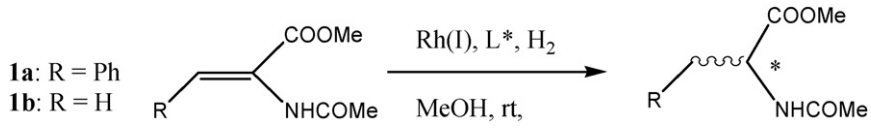


Scheme 1. Hydrogenation of α-(acylamino)acrylic acids 1a and 1b.

were incorporated at the *p*-position of the phenyl groups of BINAP.

Already described with high e.e. when 1 mol% of [Rh(-binap)(norbornadiene)]ClO_4 was used under 3–4 atm [24,25], the generally low enantioselectivities of this reaction with less than 0.1 mol% of Rh(I) is actually a desirable property because, in principle, statistically significant changes in enantioselectivities can be expected.

To better understand the effects of *para*-substituents on metal coordination, spectral data of the carbonyl stretching frequencies of RhCl(BINAP)-(CO) species were frequently studied in asymmetric reactions [20,23]. In the hydrogenation of 2-benzamidomethyl-3-oxobutanoate catalyzed by cationique BINAP-ruthenium(II) complexes, Takaya et al. described a linear relationships between the values of ν_{CO} and Hammet σ-values values of BINAP derivatives [24,25]. Since Jacobsen studied the effect of electronic properties of salen ligands in the asymmetric epoxidation [26,27], recent examples demonstrated that electronic tuning of a ligand system could be connected to the enantioselectivity [28,29] with linear relationships in many cases [30–33].

2. Experimental

2.1. Chemicals

The solvents used in the syntheses were purchased as extra dry from Acros organics and Aldrich and used without further purification. Commercially available starting materials (organic and organomettalic reagents) were used as received, unless stated. 5a and 5b were purchased from Stem Chemicals. (*R*)-2,2′-bis(trifluoromethanesulfonyloxy)-1,1′ binaphthyl was prepared as described in literature [34].

2.2. Characterizations

^1H, ^{13}C and ^{31}P NMR spectra were recorded with a Bruker AM300 (^1H, 300 MHz, ^{13}C, 75 MHz) in $CDCl_3$ as solvent. Polarimetric measurements were performed on a Perkin-Elmer 241 apparatus, at ambient temperature).

2.3. Synthesis of BINAP 5c and 5d

2.3.1. Bis(4-methoxyphenyl)phosphine oxide

A solution of magnesium (4.125 g, 0.171 mol) in THF (10 mL) was stirred under Ar at room temperature for 1 h. A solution of 4-bromoanisole (19.53 mL, 0.156 mol) in THF (30 mL) was slowly added at 45 °C and the mixture was stirred at 5 °C for 1 h. Then, diethyl phosphite (10 mL, 0.78 mol) was added and the mixture was stirred at 45 °C for 2 h. After cooling (0 °C), water (50 mL), ethyl acetate (100 mL) and HCl 10% (50 mL) were successively added. The mixture was stirred at room temperature for 30 min. The reaction mixture was portioned, and the aqueous layer was extracted three times with ethyl acetate (60 mL). The combined organic layers were washed with HCl 2% (200 mL) and Brine (100 mL), and dried over anhydrous magnesium sulphate. The solution was then filtered and the filtrate concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel using ethyl acetate as the eluent to give the product (11 g, white crystal, 54%). Mp = 124–125 °C; ^1H NMR (300 MHz, $CDCl_3$): δ: 3.71 (s, 6H, OCH_3), 6.92 (d, J = 7 Hz, 4H, H_{arom}), 7.55 (dd, J = 14.2, 7 Hz, 4H, H_{arom}), 7.94 (d, J = 480 Hz, 1H, HP); ^{13}C NMR (300 MHz, $CDCl_3$): 55.8, 114.7 (d, J = 20), 123.5 (d, J = 110), 133.0 (d, J = 20), 163.2 (d, J = 10); $^{31}P\{^1H\}$ NMR (81 MHz, $CDCl_3$): δ: 20.9 (s).

2.3.2. Bis(4-methoxyphenyl)phosphine-borane complex 3

A solution of cerium chloride (11.27 g, 45.75 mmol) in THF (35 mL) was stirred under Ar at room temperature (25 °C) for 30 min. Sodium borohydride (1.8 g, 47.28 mmol) was added and the mixture was stirred at room temperature for 1 h. Then, bis(4-methoxyphenyl)phosphine oxide (4 g, 15.25 mmol) and lithium alumina hydride (0.7 g, 18.3 mmol) were successively added at 5 °C and the mixture was stirred at room temperature for 3 h. 3N NaOH (50 mL) was added at 3 °C, followed by ethyl acetate (50 mL), water (20 mL) and cellite. The mixture was stirred at room temperature for 30 min and then filtered. The filtrate was partitioned, and the aqueous layer was extracted three times with ethyl acetate (90 mL). The combined organic layers were washed with water (2 × 100 mL), Brine (100 mL), dried over anhydrous magnesium sulphate, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent *n*-hexane/ethyl acetate 5/1 → 2/1) to give 3 (2.4 g, white crystal, 60%). ^1H NMR (300 MHz, $CDCl_3$): 0.43–1.57 (m, 3H, BH_3), δ: 3.82 (s, 6H, OCH_3), 6.24 (dq, J = 377.9, 6.78 Hz, 1H, HP), 6.95 (dd, J = 8.71, 1.72 Hz, 4H, H_{arom}), 7.53–7.60 (m, 4H, H_{arom}); $^{31}P\{^1H\}$ NMR (81 MHz, $CDCl_3$): δ: −4.53 to 2.73 (m), −1.26 to 0.40 (m), −4.15 (m).

2.3.3. (R)-2,2′-bis[bis(4-methoxyphenyl)phosphino]-1,1′-binaphthyl 5c

Under an argon atmosphere, to a solution (5 mL) of [1,2-bis-(diphenylphosphino)-ethane]dichloronickel (53 mg, 0.1 equivalent), (*R*)-2,2′-bis(trifluoromethanessulfonyloxy)-1,1′binaphthyl (500 mg, 0.91 mmol) and 1,4-diazabicyclo[2,2,2]octane (613 mg, 6.0 equivalents) in DMF was added at room temperature bis(4-methoxyphenyl)phosphine-borane complexe (543 mg, 2.3 equivalent) and the mixture was stirred at room temperature for 30 min and then at 110 °C for 48 h. DMF was

evaporated under reduced pressure and methanol was added to the residue to give the title compound 5c (444 mg, white crystal, 66%). $[\alpha]_D^{25} = +107.6$ (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ: 3.73 (s, 12H, CH_3), 6.64 (d, $J = 8.35$ Hz, 4H, H_{arom}), 6.69 (d, $J = 8.19$ Hz, 4H, H_{arom}), 6.80 (d, $J = 8.49$ Hz, 2H, H_{arom}), 6.92–7.03 (m, 10H, H_{arom}), 7.30–7.38 (m, 2H, H_{arom}), 7.40–7.45 (m, 2H, H_{arom}), 7.82 (d, $J = 8.13$ Hz, 2H, H_{arom}), 7.87(d, $J = 8.52$ Hz, 2H, H_{arom}); $^{31}P\{^1H\}$ NMR (81 MHz, $CDCl_3$): δ: −16.86(s).

2.3.4. (R)-2,2′-bis[bis(4-hydroxyphenyl)phosphino]-1,1′-binaphthyl 5d

A solution of (*R*)-2,2′-bis[bis(4-methoxyphenyl)phosphino]-1,1′-binaphthyl (433 mg, 0.56 mmol) in dry CH_2Cl_2 (20 mL) was cooled at 0 °C. A 1 M solution of BBr_3 in CH_2Cl_2 (5.6 mL, 5.6 mmol) was added, and the reaction mixture was stirred at 0 °C for 1 h, and then at room temperature for 24 h. The solution was cooled to 5 °C and CH_3OH (10 mL) was carefully added. After removal of the organic solvents, the residue was recrystallized from hot CH_3OH (10 mL) by adding cold water (5 mL) to give 5d (380 mg, 95%). White solid; mp >220 °C; $[\alpha]_D^{25} = +29$ (*c* 0.9, MeOH); ^1H NMR (300 MHz, DMSO-*d*6): δ: 6.55 (d, $J = 8.6$ Hz, 2H, H_{arom}), 6.65–6.69 (m, 6H, H_{arom}), 6.82 (bt, $J = 7.5$ Hz, 2H, H_{arom}), 7.13 (dd, $J = 11.5$, 8.6 Hz, 4H, H_{arom}), 7.31 (dd, $J = 11.5$, 8.6 Hz, 2H, H_{arom}), 7.38 (bt, $J = 7.5$ Hz, 2H, H_{arom}), 7.44 (dd, $J = 11.5$, 8.6 Hz, 2H, H_{arom}), 7.86–7.92 (m, 4H, H_{arom}), 9.95 (s, 4H, OH); $^{31}P\{^1H\}$NMR (81 MHz, DMSO-*d*6): −18.42(s).

2.3.5. Bis(4-dimethylaminophenyl)phosphine oxide

A solution of magnesium (2.0 g, 81.6 mmol) in THF (5 mL) was stirred under Ar at room temperature for 1 h. A solution of 4-bromo-*N*,*N*-dimethylaniline (14.85 g, 74.2 mmol) in THF (25 mL) was slowly added at 45 °C and the mixture was stirred at 5 °C for 1 h. Then, diethyl phosphite (4.75 mL, 37.1 mmol) was added and the mixture was stirred at 45 °C for 2 h. After cooling (0 °C), water (25 mL), ethyl acetate (50 mL) and HCl 10% (25 mL) were successively added. The mixture was stirred at room temperature for 30 min. The reaction mixture was neutralized with NaOH, portioned, and the aqueous layer was extracted three times with ethyl acetate (30 mL). The combined organic layers were washed with HCl 2% (100 mL) and Brine (50 mL), and dried over anhydrous magnesium sulphate. The solution was then filtered and the filtrate concentrated under reduced pressure. The residue was recrystallized from *t*-butylmethyl ether to give the product (6.25 g, white crystal, 58.4%). Mp = 152 °C; ^1H NMR (300 MHz, $CDCl_3$): δ: 3.01 (s, 12H, CH_3), 6.71 (d, $J = 8.94$ Hz, 2H, H_{arom}), 6.72 (d, $J = 8.94$ Hz, 2H, H_{arom}), 7.48 (d, $J = 8.91$ Hz, 2H, H_{arom}), 7.52 (d, $J = 8.88$ Hz, 2H, H_{arom}), 7.96 (d, $J = 470$ Hz, 1H, HP); ^{13}C NMR (300 MHz, $CDCl_3$): 40.38, 111.72, 111.90, 116.88, 118.37, 132.54, 132.72, 153.03, 153.06; $^{31}P\{^1H\}$ NMR (81 MHz, $CDCl_3$): δ: 23.3 (s).

2.3.6. Bis(4-dimethylaminophenyl)phosphine-borane complex 4

A solution of cerium chloride (7.69 g, 31.2 mmol) in THF (35 mL) was stirred under Ar at room temperature (25 °C) for 30 min. Sodium borohydride (1.22 g, 37.8 mmol) was added and the mixture was stirred at room temperature for 1 h. Then bis(4-dimethylaminophenyl)phosphine oxide (3 g, 10.4 mmol) and lithium alumina hydride (0.47 g, 12.48 mmol) were successively added at 5 °C and the mixture was stirred at room temperature for 3 h. 3N NaOH (40 mL) was added at 3 °C, followed by ethyl acetate (40 mL), water (20 mL) and cellite. The mixture was stirred at room temperature for 30 min and then filtered. The filtrate was partitioned, and the aqueous layer was extracted three times with ethyl acetate (60 mL). The combined organic layers were washed with water (2 × 30 mL), Brine (2 × 30 mL), dried over anhydrous magnesium sulphate, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent *n*-hexane/ethyl acetate, 1/1) to give 4 (0.6 g, white crystal, 20%). Mp = 142.5 °C; ^1H NMR (300 MHz, $CDCl_3$): δ: 0.41–1.34 (m, 3H, BH_3), 3.07 (s, 12H), 6.3 (dq, $J = 376.1$ Hz, 1H, HP), 7.5 (d, $J = 8.81$ Hz, 4H, H_{arom}), 7.53 (d, $J = 8.79$ Hz, 4H, H_{arom}); $^{31}P\{^1H\}$ NMR (81 MHz, $CDCl_3$): δ: −6.38–4.73 (m), −3.3–1.6 (m).

2.3.7. (R)-2,2′-bis[bis(4-dimethylaminophenyl)phosphino]-1,1′- binaphthyl 5e

To a solution of [1,2-bis(diphenylphosphino)-ethane] dichloronickel (164 mg, 0.311 mmol) in dry DMF (15 mL), (*R*)-2,2′-bis(trifluoromethanesulfonyloxy)-1,1′ binaphthyl (1.7 g, 3.1 mmol) and 1,4-diazabicyclo[2,2,2]octane (2.1 g, 18.7 mmol) and bis(4-dimethylaminophenyl)phosphine–borane complexe (2.05 g, 7.16 mmol) were added under Ar at room temperature. The mixture was stirred at room temperature for 30 min and then at 110 °C for 5 days. DMF was evaporated under reduced pressure. One millilitre EtOAc and 10 mL methanol were added to the residue to give the title compound 5e (1.3 g, white crystal, 52.9%). $[\alpha]_D^{25} = 13.05$ (*c* 0.95, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): δ: 2.9 (s, 24H, CH_3), 6.42 (d, $J = 6.8$ Hz, 4H, H_{arom}), 6.52–6.6 (m, 4H, H_{arom}), 6.75–7.05 (m, 12H, H_{arom}), 7.13–7.25 (m, 2H, H_{arom}), 7.5 (d, $J = 7.13$ Hz, 2H, H_{arom}), 7.75 (d, $J = 7.55$ Hz, 2H, H_{arom}), 7.82 (d, $J = 8.29$ Hz, 2H, H_{arom}); $^{31}P\{^1H\}$ NMR (81 MHz, $CDCl_3$): δ: −17.5 (s).

2.4. Synthesis of catalysts 6a–f′

2.4.1. [Rh(BINAP)(COD)]BF_4 6a–6e

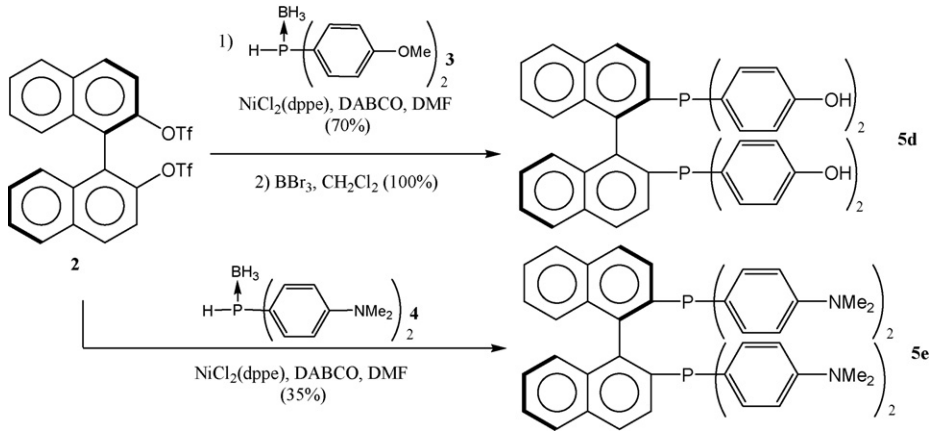
Stock solution of 6a–e catalysts were prepared in a glove box under argon by stirring a mixture of $[Rh(COD)_2]BF_4$ (1 eq/mmol) and 5a–d and 5f derivatives (1.05 eq mmol) in degassed methanol at room temperature during 1 h. Catalysts were stored in methanolic solution at 0 °C before used.

2.4.2. [Rh(BINAP)(COD)]BF_4 6f′

To a methanolic solution of 6e (0.2 mmol), $MeOSO_2CF_3$ (0.8 mmol) was added and the mixture was stirred at room temperature for 5 h. Catalyst was stored in methanolic solution at 0 °C before used.

2.5. Hydrogenation

Hydrogenation experiments were performed in a mini-autoclave of stainless of 15 mL from Amtec (www.amtec-



Scheme 2. Synthesis of ligands 5d and 5e.

chemnitz.de). Conversions and enantiomeric excesses were determined by GC analysis on a chiral CHIRASILVAL column.

A solution of 1a (1b) (0.1 M) in MeOH (4 mL) was stirring (2200 rpm) at 35 °C with catalysts 6a–f′ (10^{-3} or 10^{-4} M) under H_2 (P_{H_2} = 5 or 30 bar). After the reaction time, the autoclave was cooled to room temperature and depressurized. Conversion and enantiomeric excess were determined from on time sampling of the reaction mixture by GC analysis on a CHIRASILVAL column.

3. Results and discussion

3.1. Preparation of the catalysts

Although 5a-b were commercially available, 5c was obtained by a coupling reaction from the di-*p*-anisylphosphine-borane 3 [35] (Scheme 2) and 2 in the presence of DABCO and $NiCl_2$dppe in DMF, as an alternative faster and more efficient route than those proposed in literature [19,36].

Treatment of 5c with BBr_3 afforded 5d [36] in quantitative yield. 5e [37] was prepared in the same manner from the *p*-anilinephosphine [38] *via* the coupling reaction between 2 and the *p*-anilinephosphine borane analogue 4 [37].

Rh(I)-BINAP complexes 6a–e were used in the hydrogenation of substituted olefins 1a and 1b, and the results were given in Table 1. Catalysts 6a–e were prepared *in situ* by stirring a solution of $[Rh(COD)_2]BF_4$ precursor and the diphosphine ligands (Scheme 3) prior to introduction of the olefin and being pressurized under H_2.

3.2. Catalytic hydrogenation

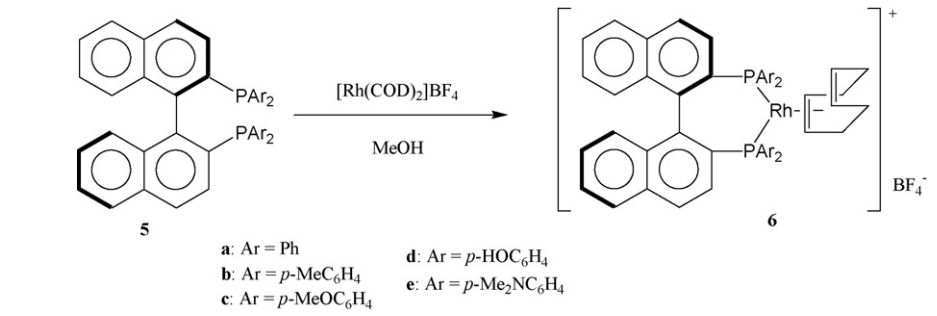
Each catalyst/H_2 pressure/substrate ((α-acylamino)acrylic esters 1a and 1b) combination was examined under our hydrogenation conditions, and the results are presented in Table 1.

Regardless of the ligands and the hydrogen pressure were used, methyl-2-acetamidoacrylate 1b was hydrogenated faster than (Z)-methyl-α-acetamidocinnamate 1a due to the higher reactivity of 1b. E.e's were moderate and varied from 15% in favour of the (*S*) enantiomer to 57% in favour of the (*R*) enantiomer with very low values of 5 and 3% of (*S*) product with Tol-BINAP 6b (Fig. 1). Moreover, the effects of hydrogen pressure on the hydrogenation of 1a seemed to be marginal with maximum variations of 3% with 6e. On the contrary, increasing the H_2 pressure from 5 to 30 bars led to more significant variations of e.e.s in the hydrogenation of 1b (from 1 to 9%).

Table 1
Asymmetric hydrogenation of 1a and 1b

Catalyst	Substrate[a]	Time[b] (min)	Conversion[b] (%)	Ee[b,c] (% *R*)	Log[*R*/*S*)$_X$/(*R*/*S*)$_H$][b]	σ_p[39–42]
6a	1a	23 (2.5)	99 (98)	−14 (−14)	0 (0)	0
	1b	1.5 (0.6)	99 (99)	−15 (−8)	0 (0)	
6b	1a	9 (2)	98 (98)	− 5 (−5)	0.065 (0.73)	−0.14
	1b	1 (0.6)	99 (99)	− 3 (− 2)	0.106 (0.104)	
6c	1a	26.5 (7)	99 (99)	15 (14)	0.242 (0.241)	−0.28
	1b	1 (0.6)	96 (96)	13 (18)	0.252 (0.228)	
6d	1a	22 (6)	97 (97)	37 (36)	0.458 (0.445)	−0.38
	1b	2 (0.6)	99 (99)	30 (39)	0.401 (0.431)	
6e	1a	24 (5)	97 (95)	57 (54)	0.679 (0.642)	−0.63
	1b	2 (0.6)	99 (96)	48 (48)	0.587 (0.518)	

[a] With 1a: Rh(I) 0.1 mol%; with 1b: Rh(I) 0.01 mol%.
[b] Pressure, 5 bar. Values in parentheses refer to results obtained at 30 bar.
[c] Determined by chiral HPLC.



Scheme 3. General procedure of BINAP complexes synthesis.

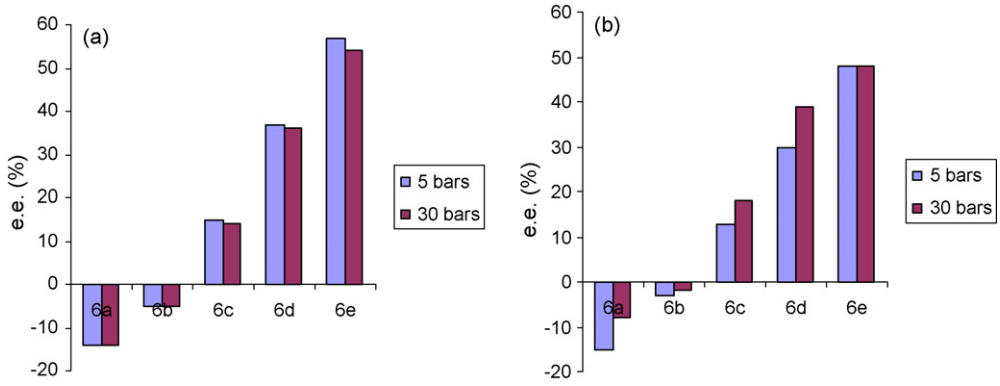


Fig. 1. H_2 pressure effect on the e.e.s of the hydrogenation of 1a and 1b.

3.3. Electronic effects

These results showed that the efficiency and the sense of the enantioselective hydrogenation were highly influenced by the electronic density on the phosphorus atom of the catalyst.

From these data, we determined the influence of the electronic density of the metal catalyst on the enantiomeric ratio, i.e. *R*/*S*. When the results were reported in Hammett plots of $\log[(R/S)_X/(R/S)_H]$ versus σ_p [39–42] (Fig. 2), the slope of the obtained strengths (ρ) could be interpreted as the reflection of the influence of the *p*-substituents on the BINAP towards the sensitivity of the asymmetric induction. With a ρ value of −1.03, asymmetric hydrogenation of 1a could be considered to be more influenced by the nature of the BINAP catalyst than the hydrogenation of 1b with a smaller value of −0.92. This can be explained in terms of the Hammond postulate, as demonstrated for salen or porphyrins type catalysts [30,31]. Thus, lower reactivity leads to a comparatively late transition state accompanied of a higher selectivity. The largest $|\rho|$ value of 1a suggested that the interaction between catalyst and substrate was the greatest, because the lower reactivity of 1a leads to a transition state with the most product-like conformation. Nevertheless, with $\rho = \log[(R/S)_X/(R/S)_H]/\sigma$ values close to 1, it seemed to be possible and interesting to correlate directly the *R*/*S* ratios with σ_p (Fig. 3).

Indeed, when the *R*/*S* are reported were reported *versus* Hammett coefficients (Fig. 3), the same trend was observed with electron-donating groups on the catalyst leading to higher enantioselectivities. With five-point Hammett plots, we found clear linear relationships ($R^2 > 0.95$) between the electronic constants and enantioselectivities. As shown in Fig. 3, *R*/*S* ratios decreased following the sequence $NMe_2 > OH > OMe > Me > H$. With ρ

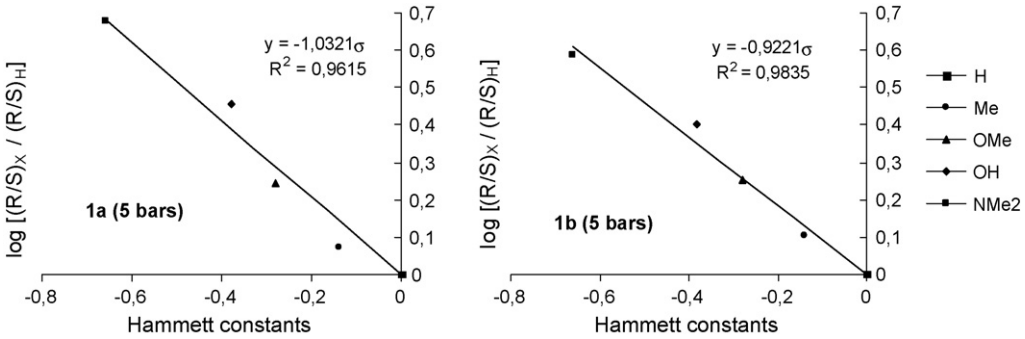


Fig. 2. $\log[(R/S)_X/(R/S)_H]$ as a function of phosphine electronics.

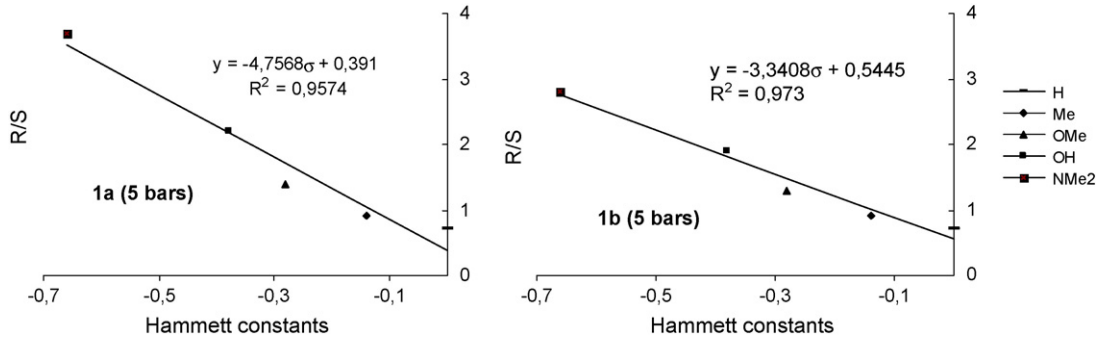
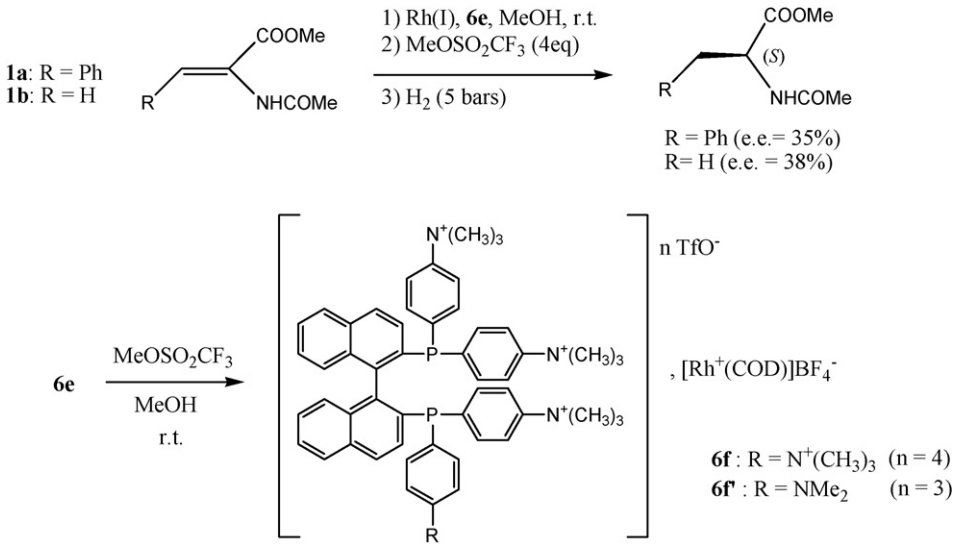


Fig. 3. *R* and *S* ratio as a function of phosphine electronics.



Scheme 4. Hydrogenation of 1a and 1b with the ammonium BINAP derivative prepared in situ.

values of −4.76 and −3.34, respectively for 1a and 1b, we confirmed that the asymmetric induction in the hydrogenation reaction of (α-acylamino)acrylic esters was governed by the electronic density on the phosphorus atom with a higher influence in the asymmetric induction of 1a.

In order to confirm the surprising change in the enantioselectivity, a BINAP bearing electron-withdrawing group was evaluated.

When the Rh-catalyst 6e was treated *in situ* with methyl trifluoromethanesulfonate before its use in the hydrogenation of 1a and 1b, *N*-acetyl-L-phenylalanine methyl ester and *N*-acetyl-L-alanine methyl ester were predominantly obtained with e.e.s of 35 and 38%, respectively (Scheme 4). This supplementary result confirmed the change in the sense of the enantioselectivity from electron-donating to electron-withdrawing substituents.

When e.e.s were reported as a function of Hammett coefficients (Fig. 4), a linear relationship was also observed with ligands 6a–e. The experimental e.e. with the implied ammonium ligand 6f does not respect the linearity and corresponds to an e.e. theoretically obtained with the ligand 6f', incorporating three ammonium groups and one NMe_2. If we consider that 6e was partially alkylated, the medium Hammett coefficient of 6f' could be given by $\sigma_p(\text{medium}) = [3\sigma_p(N^+(CH_3)_3 + \sigma_p(NMe_2)]/4$ with values of σ_p $N^+(CH_3)_3$ and σ_p (NMe_2) of 0.82 and −0.63, respectively. Then, the calculated Hammett constant was 0.45 and the corresponding e.e. (experimental) fits with the straight line.

From the knowledge of the σ_p of the phenylene substitutents, it was possible to predict the e.e.s of the hydrogenation reaction

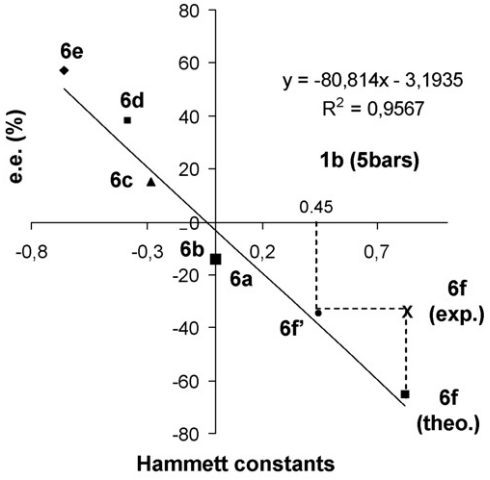


Fig. 4. E.e. as a function of phosphine electronics in the hydrogenation of 1b.

of (α-acylamino)acrylic esters. Thus, a theoretical e.e. of 65% of the (*S*) enantiomer would be reached with the ammonium catalyst 6f.

4. Conclusions

In conclusion, the electronic effects of electron-donating substituents at the *para* position of the phenyl moieties of BINAP ligands have been evaluated towards asymmetric hydrogenation of α-(acylamino)acrylic acids. Enantiomeric excesses were highly dependant of the nature of the substitutents and varied experimentally from 38% of (*S*) compound to 57% of (*R*) compound as an unexpected linear relationship towards Hammett coefficients (between −0.63 and 0). The changes in the sense of the enantioselectivity can be explained from electronic factors as confirmed when electron-withdrawing substituents were introduced on the phenyl fragment. The change in the sense of the enantioselectivity could be connected to favoured kinetic or thermodynamic transition states. The modification of the dihedral angle between the two naphthyl moieties which is known to be a nonetheless important parameter [7] certainly influences the selectivity. Future work aiming at using molecular modelling for a more fundamental understanding of these results and for more directed asymmetric catalyst design is ongoing.

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