Asymmetric Palladium-Catalyzed Allylic Alkylation Using Bis(Oxazoline) Ligands: Phenomenal Reversal of Enantioselectivity with a Single Chiral Backbone

Olivier Hoarau, Hassan Aït-Haddou,*,† Jean-Claude Daran, Dimitri Cramailère, and Gilbert G. A. Balavoine*

Laboratoire de Chimie de Coordination CNRS, UPR 8241, 205 Route de Narbonne, 31077 Toulouse Cedex, France

Received June 7, 1999

Chiral bis(oxazoline) ligands with four stereogenic centers were tested in the asymmetric palladium-catalyzed allylic alkylation of the *rac*-1,3-diphenyl-2-propenyl esters with sodium dimethyl malonate. A remarkable effect on the enantioselectivity was observed: the dihydroxy bis(oxazoline) ligands gave the ***(S)***-product with 92% ee, while the diester led to the ***(R)***-product with 90% ee. This change in direction of chiral induction sense with the dihydroxy ligand is due to the regioselection of the nucleophilic attack on the palladium(II) π-allyl complex. Implication of the interaction of a hydroxy group with the dimethyl malonate anion is considered to explain the change in the regiochemistry of the nucleophilic attack. X-ray structures of the η^3-1,3-diphenylallyl-[(2,2-bis[2-((4*S*)-((1*S*)-1-hydroxy-1-phenylmethyl)-1,3-oxazolinyl)]propane)-*N,N′*]palladium(II) tetrafluoroborate **7** and the η^3-1,3-diphenylallyl-[(2,2-bis[2-((4*S*)-((1*S*)-1-methyloxy-1-phenylmethyl)-1,3-oxazolinyl)]propane)-*N,N′*]palladium-(II) tetrafluoroborate **8** are presented, which clearly show the occurrence of hydrogen bonding in complex **7**.

Introduction

The enantioselective palladium-catalyzed substitution of allylic acetates or carbonates with soft nucleophiles is among the most important methods for C−C bond formation in asymmetric synthesis. Several chiral ligands that efficiently induce asymmetry in this reaction have been reported.[1] Usually, ligands with phosphorus as donor atoms have been used, but in recent years, different nitrogen-containing ligands have proven to be useful as well. In particular, high enantioselectivities were obtained with C_2-symmetric nitrogen-containing ligands.[2]

The origin of the enantioselectivity in this reaction is still discussed, and several parameters are involved. In the case of asymmetric allylic substitution of the *rac*-1,3-diphenyl-2-propenyl esters **1**, the enantioselection should be dependent on the regioselection of the nucleophilic attack on the palladium(II) π-allyl complex. With C_2-symmetric nitrogen-containing ligands it is generally accepted that the repulsive interaction between the chiral ligand and the substrate discriminates the two enantiotopic termini of the allylic intermediate.[3]

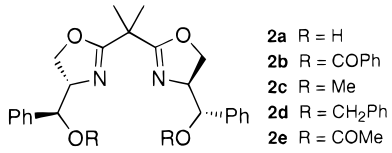


Figure 1. Bis(oxazoline) ligands from (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol.

According to this analysis and to the recent report of successful results obtained when using hydroxyalkyl- and alkoxyalkylpyridinooxazolines containing two asymmetric centers in these catalytic processes,[4] we decided to investigate the effectiveness of the bis(oxazoline)[5] ligands **2** recently described (Figure 1).[6] These bis(oxazolines) allow the tuning of the stereoelectronic properties around the same chiral backbone. In this paper we discribe the important effect exerted by the functional side chain on the control of the enantio-

† Fax: 00 (33) 5 61 55 30 03. E-mail: aithad@lcc-toulouse.fr.

(1) (a) Hayashi, T. In *Catalytic Asymmetric Synthesis*, Ojima, I., Ed.; VCH: Weinheim, New York, 1993; pp 325. (b) Reiser, O. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 547. (c) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron Lett.* **1992**, *3*, 1089. (d) Trost, B. M.; van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395.

(2) (a) Müller, D.; Umbricht, U.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232. (b) Leutenegger, U.; Umbricht, G.; Fahrni, C.; von Matt, P.; Pfaltz, A. *Tetrahedron* **1992**, *48*, 2143. (c) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339. (d) Kubota, H.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1993**, *34*, 8135. (e) Tanner, D.; Anderson, P. G.; Harden, A.; Somfai, P. *Tetrahedron Lett.* **1994**, *35*, 4631. (f) Kang, J.; Cho, W. O.; Cho, H. G. *Tetrahydron: Asymmetry* **1994**, *5*, 1347.

(3) von Matt, P.; Lloyd-Jones, G. C.; Minidis, A. B. E.; Pfaltz, A.; Macko, L.; Neuburger, M.; Zehnder, M.; Rüegger, H.; Pregosin, P. S. *Helv. Chim. Acta* **1995**, *78*, 265; see also ref 2d.

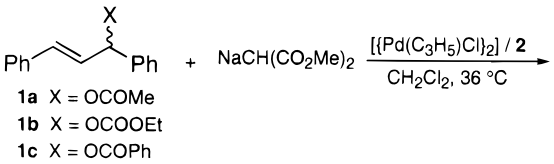
(4) (a) Nordström, K.; Macedo, E.; Moberg, C. *J. Org. Chem.* **1997**, *62*, 1604. (b) Bremberg, U.; Rahm, F.; Moberg, C. *Tetrahedron: Asymmetry* **1998**, *9*, 3437.

(5) For the recent use of the bis(oxazoline) ligands in the asymmetric catalysis see: (a) Evans, D. A.; Kozlowski, M. C.; Murry, J. A.; Burgey, C. S.; Campos, K. R.; Connell, B. T.; Staples, R. J. *J. Am. Chem. Soc.* **1999**, *121*, 669. (b) Evans, D. A.; Burgey, C. S.; Kozlowski, M. C.; Tregay, S. W. *J. Am. Chem. Soc.* **1999**, *121*, 686. (c) Ghosh, A. K.; Mathivanan, P.; Cappiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1−45. (d) Yao, S.; Johannsen, M.; Audrain, H.; Hazell, R. G.; Jørgensen, K. A. *J. Am. Chem. Soc.* **1998**, *120*, 8599. (e) Yao, S.; Johannsen, M.; Audrain, H.; Hazell, R. G.; Jørgensen, K. A. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 3121. (f) Schulze, V.; Hoffmann, R. W. *Chem. Eur. J.* **1999**, *5*, 337.

(6) Hoarau, O.; Aït-Haddou, H.; Castro, M.; Balavoine, G. G. A. *Tetrahedron: Asymmetry* **1997**, *8*, 3755.

10.1021/om990437j CCC: $18.00
Publication on Web 10/22/1999

Scheme 1. Enantioselective palladium-catalyzed allylic alkylation of *rac*-1 with bis(oxazoline) 2.



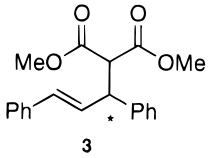


Table 1. Enantioselective Allylic Alkylation of Substrates 1a−c with 2a−e[a]

entry	S	L	*t* (h)	ee[b]	abs config[c]	yield[d]
1	**1a**	**2a**	2	92%	*S*	98%
2	**1a**	**2b**	24	90%	*R*	98%
3	**1a**	**2c**	96	85%	*R*	65%
4	**1a**	**2d**	96	n.r.[e]		n.r.
5	**1a**	**2e**	24	77%	*R*	99%
6	**1b**	**2a**	1	84%	*S*	90%
7	**1b**	**2b**	12	84%	*R*	90%
9	**1c**	**2a**	24	45%	*S*	99%
10	**1c**	**2b**	36	45%	*R*	95%

[a] S = substrate (1 equiv), $H_2C(CO_2Me)_2$ (3 equiv), NaH (3 equiv), [{$Pd(C_3H_5)Cl$}$_2$] (1 mol %), L = ligand (4 mol %), CH_2Cl_2, 36 °C. [b] The ee values were determined by HPLC using a chiral column (Pharmacir 7C, flow rate 0.7 mL min^{-1}, *n*-BuOH/*n*-hexane 1:9). [c] The absolute stereochemistry of the product was determined by comparison of the optical rotation with the literature values.[7] [d] Yields refer to purified product after column chromatography. [e] No reaction.

selectivity in the case where the nucleophile was sodium dimethyl malonate (Scheme 1). Also, experimental efforts for determining the origin of this reversal in the enantioselectivity are investigated.

Results and Discussion

Allylic substitutions of **1a−c** were performed in CH_2Cl_2 at 36 °C in the presence of the palladium(II) complex generated in situ from bis[(π-allyl)palladium chloride] and the appropriate ligand. The results of catalytic reactions are summarized in Table 1.

It appears that the most efficient ligands are **2a** and **2b**, which gave the product **3** in high yields and with good enantioselectivities. To our surprise, the use of the dihydroxy bis(oxazoline) **2a** led to ***(S)*** selectivity with 92% ee (entry 1), while **2b** gave the ***(R)*** selectivity with 90% ee (entry 2).[8] Furthermore, except for **2d**,[9] the other ligands led to the product ***(R)*-3** with moderate to good enantioselectivity. Examination of other substrates such as ethyl carbonate **1b** and benzoate **1c** (entries 6−10) showed that in all case the use of the dihydroxy ligand **2a** resulted in the preferred formation of ***(S)*-3**, while the use of the diester ligand **2b** resulted in ***(R)*-3**. It is noteworthy to mention that the verification of other solvents such as diethyl ether, tetrahydrofuran, toluene, and acetonitrile did not show any effect on the direction of chiral induction, but affected the level of enantioselectivity. For example, in acetonitrile **2a** led to ***(S)*-3** (89% ee, 98% yield) and **2b** afforded ***(R)*-3** (78% ee, 98% yield), whereas in THF **2a** led to ***(S)*-3** (77% ee, 98 yield) and **2b** gave ***(R)*-3** (73% ee, 99% yield).

The generally accepted mechanism for this reaction with soft nucleophiles such as sodium dimethyl malonate is a nucleophilic attack on the π-allylic palladium complex on the side opposite the palladium center. According to this mechanism, the ***(R)*-3** product was formed by nucleophilic addition on C1 from the side opposite the palladium center (Scheme 2**,** A). We may assume that the enantioselection in favor of ***(R)*-3** with ligands bearing functional groups other than hydroxyl was mainly due to steric effects. Furthermore, the hydroxyalkyl group results in a completely different stereochemistry, leading to **(*S*)-3**. The effects of hydroxy or other functional group in asymmetric allylic substitutions have been previously investigated.[10,11] In the present case, formation of ***(S)*-3** with the dihydroxy ligand **2a** may be due to an interaction between one of the hydroxy groups and the dimethyl malonate anion, inducing an effect either on the regioselectivity of the nucleophilic attack (Scheme 2, B) or on the configuration of the π-allyl intermediate (Scheme 2, C). However, at this stage we cannot exclude the third possibility of an attack on the carbon 1 from the palladium side leading to ***(S)*-3** as a consequence of an interaction between the nucleophile and the hydroxy group (Scheme 2, D). It is important to point out that these three hypotheses are undiscernible with 1,3-diphenyl propenyl ester **1** as substrate because the two allylic termini are identical. For this reason, we have decided to study the stereochemical course of the reaction **1a** → **3** by using the enantiomerically pure 1-(4-tolyl)-3-phenylprop-2-enyl acetate ***(S)*-4** as a close analogue of the *rac*-**1a** substrate (Scheme 3). This enantiomerically pure material, prepared by a known method,[3] offers the possibility to obtain a single enantiopure π-allyl intermediate bearing two distinct allylic termini.

In a preliminary experiment we used 2,2′-bipyridine (bpy) as an *N*,*N*-chelating achiral ligand. The ***(R)*-5** product was obtained with a slight excess over ***(S)*-6**, reflecting a moderate electronic effect of the p-Me group as observed by Pfaltz with triphenyl phosphine.[3] With the dihydroxy ligand **2a** a 15:85 ratio of ***(R)*-5** and ***(S)*-6** was obtained. Using the diester **2b**, the regioisomers ***(R)*-5** and ***(S)*-6** were obtained in a reverse ratio of 97:03. It is noteworthy to mention that in all cases the reactions were quantitative and compounds ***(R)*-5** and ***(S)*-6** were optically pure.

It is thus clear that the **2b** diester ligand favors a nucleophilic attack of the dimethyl malonate anion from

(7) (a) Hayashi, T.; Yamamoto, A.; Hagihara, T.; Ito, Y. *Tetrahedron Lett.* **1986**, *27*, 191. (b) von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566.

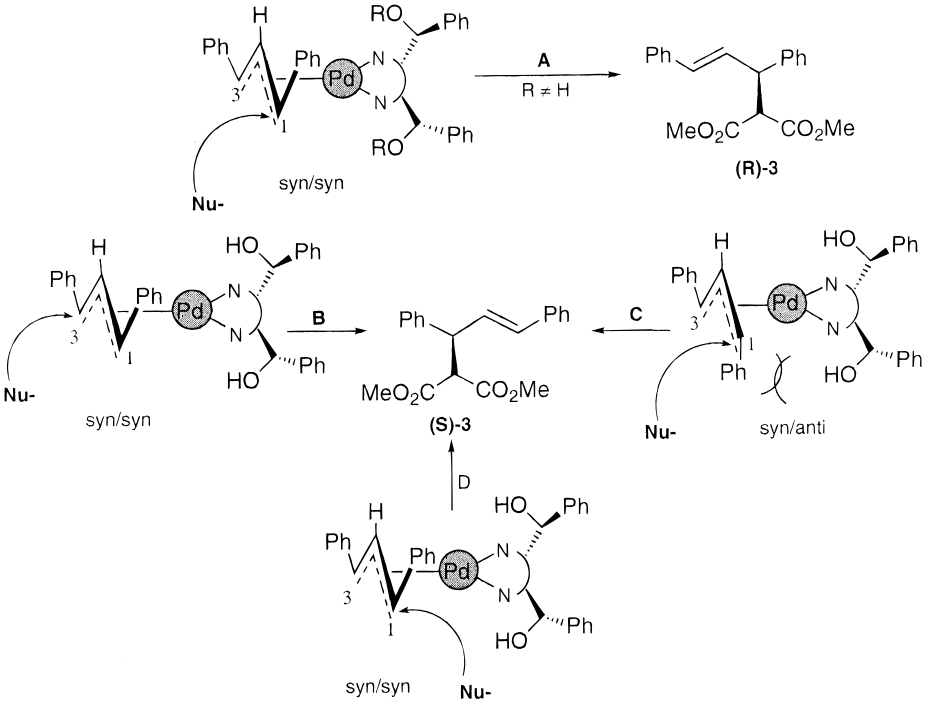
(8) Reversal in enantioselectivity with bis(oxazoline)−metal catalysts depending on the oxazoline ring substituent was very recently observed in other reactions see: (a) Evans, D. A.; Johnson, J. S.; Burgey, C. S.; Campos, K. R. *Tetrahedron Lett.* **1999**, *40*, 2879. (b) Johannsen, M.; Jørgensen, K. A. *J. Org. Chem.* **1995**, *60*, 5757. (c) Johannsen, M.; Yao, S.; Jørgensen, K. A. *Chem. Commun.* **1997**, 2169. (d) Johannsen, M.; Yao, S.; Graven, A.; Jørgensen, K. A. *Pure Appl. Chem.* **1998**, *70*, 1117.

(9) Complete decomposition of the catalyst was observed when the dimethyl malonate anion was added.

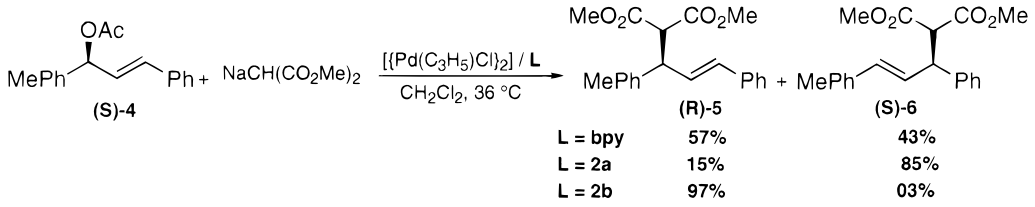
(10) (a) Sawamura, M.; Ito, Y. *Chem. Rev.* **1992**, *92*, 857. (b) Hayashi, T.; Kanehira, K.; Hagihara, T.; Kumada, M. *J. Org. Chem.* **1988**, *53*, 113. (c) Hayashi, T.; Yamamoto, A.; Ito, Y.; Nishioka, E.; Miura, H.; Yanagi, K. *J. Am. Chem. Soc.* **1989**, *111*, 6301. (d) Yamazaki, A.; Morimoto, T.; Achiwa, K. *Tetrahedron Lett.* **1993**, *4*, 2287.

(11) (a) Togni, A.; Burkhardt, U.; Gramlich, V.; Pregosin, P. S.; Salzman, R. *J. Am. Chem. Soc.* **1996**, *118*, 1031. (b) Nomura, N.; Mermet-Bouvier, Y. C.; Rajanbabu, T. V. *Synlett* **1996**, 745.

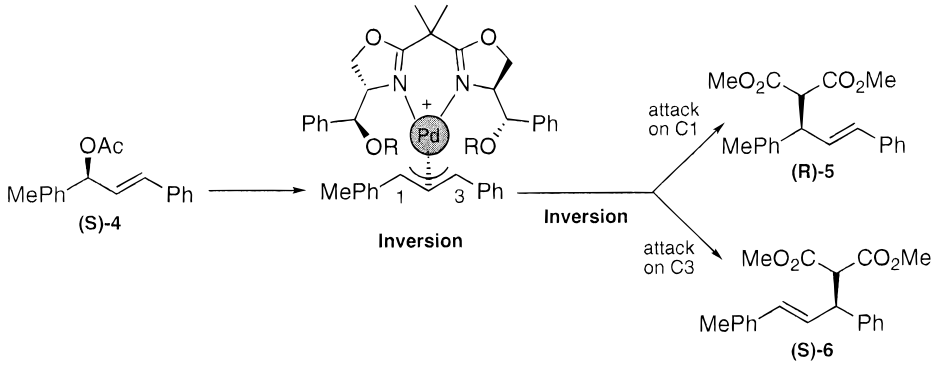
Scheme 2. Different hypothesis explaining the switch of enantioselectivity with the ligand 2a.



Scheme 3. Use of (*S*)-4 for the study of the stereochemical course of the reaction 1 → 3.



Scheme 4. Allylic alkylation of (*S*)-4 using 2a and 2b.



the side opposite the palladium center on C1 of the π-allyl intermediate, while the **2a** dihydroxy ligand leads to the attack on C3 (Scheme 4). The results obtained on ***(S)*-4** with ligand **2a** demonstrate that the reversal in the enantioselectivity observed with this dihydroxy ligand in the reaction **1a** → **3** is due to the change in regiochemistry of the nucleophilic attack depicted in Scheme **2,** B. On the other hand, these results clearly rule out the stereochemical pathways illustrated in Scheme **2,** C and D, which lead to the formation of the regioisomer ***(S)*-5** from ***(S)*-4**.

We have been able to obtain crystals of the tetrafluoroborate 1,3-diphenylallyl palladium complexes with ligands **2a** and **2c**.[12] X-ray structural determinations were carried out for both complexes **7** and **8** in view of comparing their stereochemical characteristics. Their molecular structures are shown in Figures 2 and 3, respectively. Both complexes crystallize in the $P2_1$ chiral space group, and their structures are closely related, the only difference being the presence of a hydroxyl group in **2a** compared to a methoxy group in **2c**. As shown in Figures 2 and 3, the $[PdC_3N_2]$ framework is identical within experimental error for both compounds and compares well with the one in the related $[Pd(C_{23}H_{26}N_2O_2)(C_{15}H_{13})]PF_6$ complex.[13] In all three compounds the bis(oxazoline) ligands adopt a strongly

(12) For the preparation of the (π-allyl)−palladium−ligand complexes **7** and **8** see: refs 9c and 3.

(13) Zehnder, M.; von Matt, P.; Pfaltz, A. *Acta Crystallogr., Sect. C* **1995**, 1109.

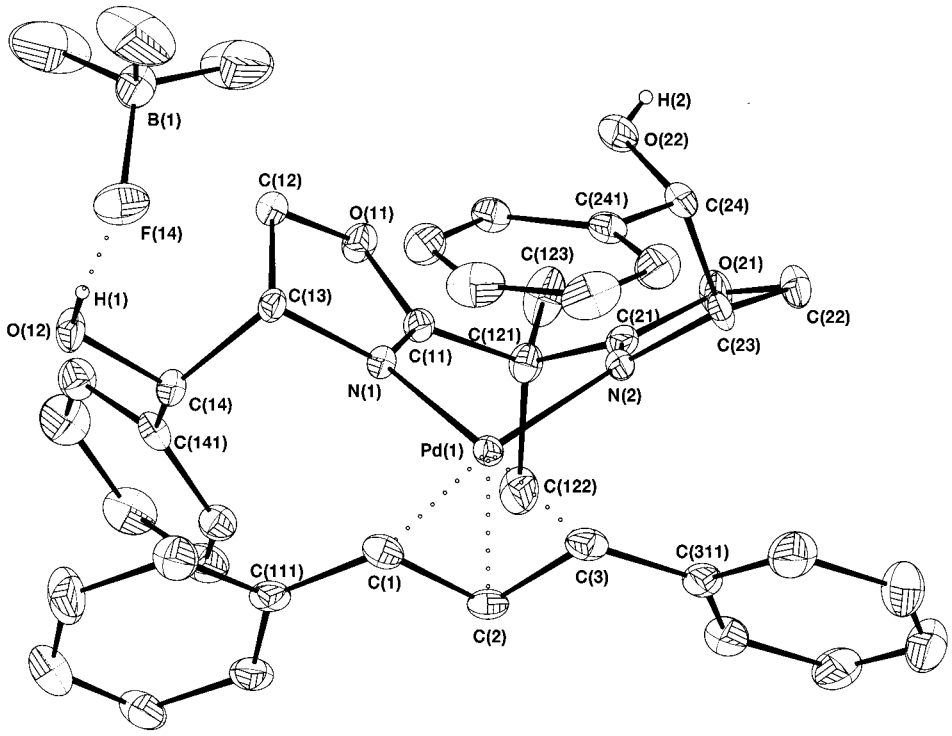


Figure 2. Molecular view of complex **7** (cation + anion) with atom-labeling scheme. Ellipsoids are drawn at 30% probability.

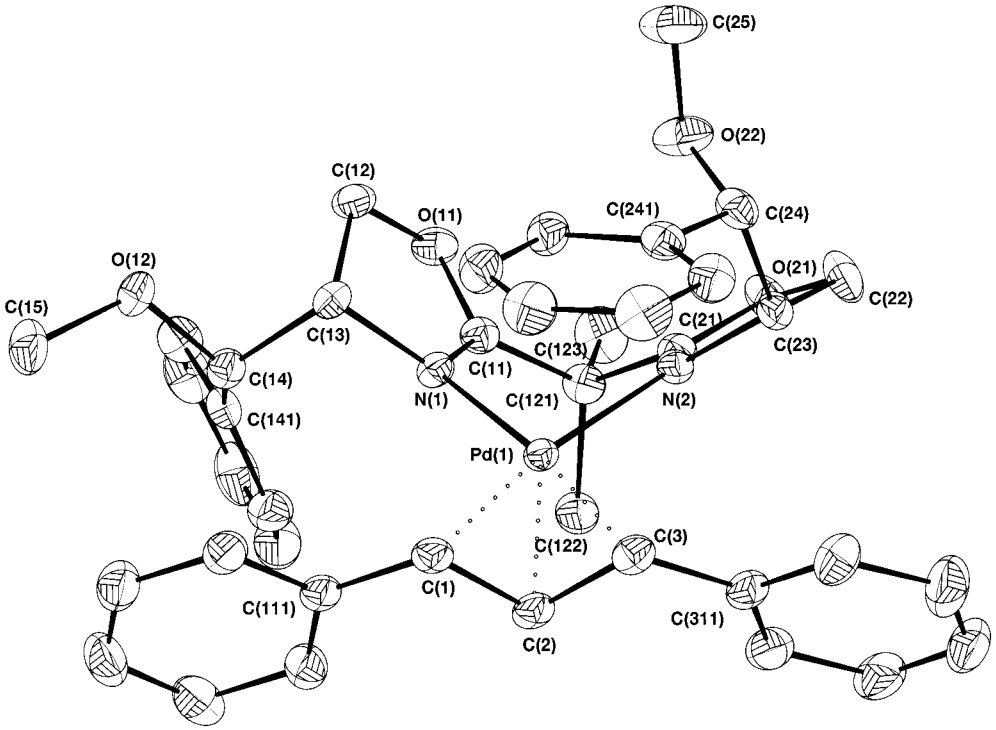


Figure 3. Molecular view of complex **8** (cation) with atom-labeling scheme. Ellipsoids are drawn at 30% probability.

distorted nonplanar conformation with a dihedral angle of 131.3°, 126.3°, and 127.3°, respectively, between the two oxazoline rings. It is also worth pointing out that in all these complexes the allyl fragment is not symmetrically bonded to palladium. One Pd−C bond is significantly longer, and the corresponding angle with the adjacent Pd−N bond is larger:

	Pd−C(1)	Pd−C(3)	C(2)−Pd−N(1)
compound **7**	2.201(3)	2.145(3)	109.4(1)
compound **8**	2.181(3)	2.155(3)	107.6(1)
ref 13	2.169(3)	2.118(3)	108.0

The largest increase in bond lengths and angle from Pd−C(1) and Pd−C(3) and the largest dihedral angle are observed for complex **7**. The reason for this may be related to the occurrence of the hydrogen bond between the hydroxyl group and BF_4. According to this observation, we may suppose that the shift in regioselectivity from carbon 1 to carbon 3 with the dihydroxy ligand **2a** can originate from an interaction between the nucleophile and the hydroxy group. A and B in Figure 4 illustrate the rationalization for the nucleophile attack of the enolate on the π-allylpalladium intermediate

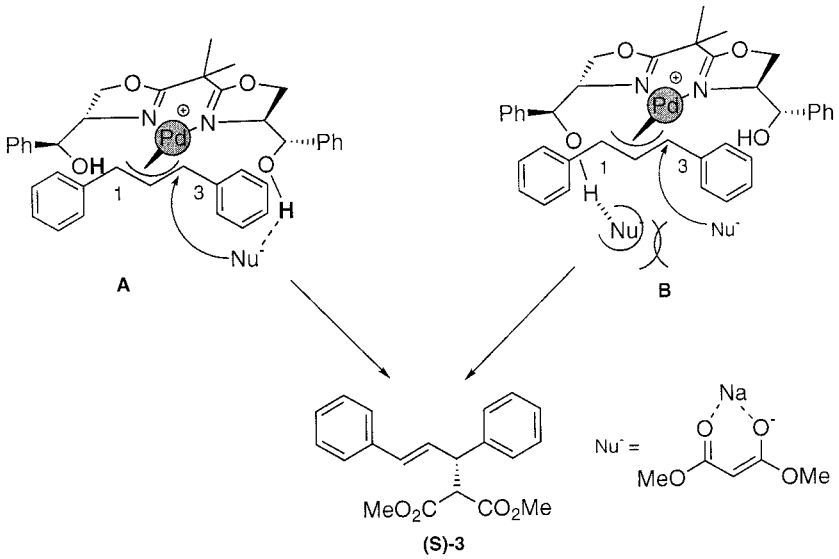


Figure 4. Rationalization of the reversal in the enantioselectivity with **2a**.

including ligand **2a**. If a hydrogen bond allows interaction between the complex and the enolate, two different hypotheses may be suggested: either the H bond involves the hydroxy group close to carbon 3, which brings the enolate close to this carbon and favors the nucleophilic attack (Figure 4, A), or the H bond occurs with the hydroxy group close to carbon 1, which favors the attack on carbon 3 by preventing the attack on carbon 1 (Figure 4, B). However, at this stage, we do not have any clue to favor any of these hypotheses.

In conclusion we have discovered an example of asymmetric synthesis leading to the formation of ***(R)*** or ***(S)*** isomers, both in high enantiomeric excess by using an enantiogenic catalyst based on ligand **2a** or **2b** characterized by the same chiral backbone and configuration. We have demonstrated that this shift in the control of the enantioselectivity was due to the presence of a hydroxy group on the side chain. Possibly, one of the hydroxy groups interacts with the nucleophile, inducing the change in the regiochemistry of the nucleophilic attack. A reversal of chiral induction sense caused by the ligand containing a hydroxyl group has been previously observed in asymmetric catalysis. However, to the best of our knowledge this is the first report concerning the high influence of a hydroxy group located in the side chain on the stereoselectivity in asymmetric allylic alkylation reactions using the same C_2-symmetric chiral ligand building blocks. New dihydroxy bis(oxazoline) ligands are currently under investigation to clarify the effect of the ligand structures on this change of enantioselectivity.[14]

Experimental Section

Materials. All reagents and solvents were dried and purified before use by usual procedures. All syntheses were carried out under an atmosphere of dry argon by standard Schlenk techniques unless otherwise specified. Allylic ester **2a**, allylic benzoate **2b**, and allylic carbonate **2c** were prepared by reaction of (*E*)-1,3-diphenyl-2-propen-1-ol with acetic anhydride, benzoyl chloride, or ethyl chloroformiate according to the literature methods.[15] Allylic acetate ***(S)*-4** was prepared according to the published method.[3] $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ was purchased from Aldrich; $[Pd(\eta^3\text{-PhCHCHCHPh})Cl]_2$ was prepared according to the published method.[16] Syntheses and NMR data for the ligands **1a**−**f** have previously been reported.[6]

General Methods. ^{1}H NMR and ^{13}C NMR spectra were measured on Brücker AC200 and AM250 spectrometers using Me_4Si as an internal standard. HPLC analyses were performed with a chiral column (Pharmacir 7C, 4.6 mm × 250 mm) eluted with *n*-BuOH/*n*-hexane; 10:90; flow rate 0.7 mL min^{-1} (or 1.0 mL min^{-1} when specified) using a Waters 600 pump and a Waters 486 detector operating at 254 nm.

Alkylation of (*E*)-1,3-Diphenyl-2-propenyl Acetate with Sodium Malonate. Dimethyl malonate (0.170 mL, 1.5 mmol) and sodium hydride (43 mg of 80% suspension, 1.5 mmol, washed three times with pentane) were mixed in 3 mL of dichloromethane under argon. In a separate flask, the chiral ligand **1a** (7.9 mg, 0.02 mmol), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.8 mg, 0.005 mmol), and racemic (*E*)-1,3-diphenyl-2-propenyl-1-acetate **2a** (126 mg, 0.5 mmol) in 2 mL of dichloromethane were stirred for 20 min and then added dropwise to the above mixture. The resulting mixture was refluxed, and the reaction was monitored by thin-layer chromatography on a silica plate (eluant ethyl acetate/pentane; 15:85). After consumption of (*E*)-1,3-diphenyl-2-propenyl-1-acetate **2a**, the reaction mixture was diluted with a saturated aqueous solution of NH_4Cl and washed twice with dichloromethane. The organic layer was separated, dried over $MgSO_4$, and concentrated under vacuum. The crude was purified by flash chromatography (ethyl acetate/pentane; 15:85) to yield **3**. The enantiomeric excess was determined by HPLC analysis with a chiral column. ^{1}H NMR ($CDCl_3$) for **3**: δ 3.53 (s, 3H), 3.70 (s, 3H), 3.95 (d, J = 11 Hz, 1H), 4.27 (dd, J = 11 Hz, 8 Hz, 1H), 6.32 (dd, J = 15 Hz, 8 Hz, 1H), 6.48 (d, J = 15 Hz, 8 Hz, 1H), 7.15−7.44 (m, 10 H). $[\alpha]^{20}_D$ = +19.2 (c = 1.30, $CHCl_3$) (+)-(R). HPLC Pharmacir 7C (*n*-BuOH/*n*-hexane; 10:90; 0.7 mL min^{-1}): t_R (*S*) 10.66 min and t_R (*R*) 11.88 min.

Alkylation of (*S*,*E*)-1-(4-Methylphenyl)-3-phenylprop-2-enyl Acetate with Sodium Malonate. General Procedure. Dimethyl malonate (0.170 mL, 1.5 mmol) and sodium hydride (43 mg of 80% suspension, 1.5 mmol, washed three times with pentane) were mixed in 3 mL of dichloromethane.

(14) Hoarau, O.; Cramailère, D.; Aït-Haddou, H.; Pezet, F.; Daran, J.-C.; Balavoine, G. G. A. To be submitted.

(15) For the preparation of the carbonate **1b** see: Gais, H.-J.; Eichelmann, H.; Spalthoff, N.; Gerhards, F.; Frank, M.; Raabe, G. *Tetrahydron: Asymmetry* **1998**, *9*, 235.

(16) $[Pd(1,3\text{-diphenyl-}\pi\text{-allyl})Cl]_2$ was prepared according to Bosnich's procedure; see: (a) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033. (b) Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046.

In a separate flask, chiral ligand **1a** (7.9 mg, 0.02 mmol), [Pd(η^3-C_3H_5)Cl]$_2$ (1.8 mg, 0.005 mmol), and (*S*,*E*)-1-(4-methylphenyl)-3-phenylprop-2-enyl acetate (126 mg, 0.5 mmol) in 2 mL of dichloromethane were stirred for 20 min and then added dropwise to the above mixture. The resulting mixture was refluxed, and the reaction was monitored by thin-layer chromatography on a silica plate (eluant ethyl acetate/pentane; 15:85). After consumption of ***(S)*-4**, the reaction mixture was diluted with a saturated aqueous solution of NH_4Cl and washed twice with dichloromethane. The organic layer was separated, dried over $MgSO_4$, and concentrated under vacuum. The mixture was analyzed by HPLC to determine the product ratio.

Dimethyl 2-[(*R*,*E*)-1-(4-Methylphenyl)-3-phenylprop-2-enyl] propanedioate (5). ^{1}H NMR ($CDCl_3$): δ 2.32 (s, 3H, PhCH_3), 3.56 (s, 3H, OCH_3), 3.70 (s, 6H, OCH_3), 3.94 (d, J = 10.9 Hz, 1H, H (CO_2CH_3)$_2$), 4.26 (dd, J = 10.9 and 8.5 Hz, 1H, PhCH=CH CH), 6.32 (dd, J = 15.7 and 8.5 Hz, 1H, PhCH=CH), 6.47 (d, J = 15.7 Hz, 1H, PhCH=CH), 7.33−7.11 (m, 9H). ^{13}C NMR ($CDCl_3$): δ = 168.1, 167.7, 137.1, 136.9, 131.6, 129.4, 129.3, 128.4, 127.7, 127.5, 126.3, 57.6, 52.5, 52.3, 48.7, 21.1. R_f = 0.30 (hexane/ethyl acetate; 3:1). HPLC Pharmacir 7C (*n*-BuOH/*n*-hexane; 10:90; 1.0 mL min^{-1}): t_R (*R*) 7.0 min, (t_R (*S*) 8.4 min).

Dimethyl 2-[(*S*,*E*)-3-(4-Methylphenyl)-1-phenylprop-2-enyl]propanedioate (6). ^{1}H NMR ($CDCl_3$): δ 2.31 (s, 3H, PhCH_3), 3.52 (s, 3H, OCH_3), 3.70 (s, 6H, OCH_3), 3.95 (d, J = 10.9 Hz, H (CO_2Me)$_2$), 4.25 (dd, J = 10.9 and 8.5 Hz, 1H, PhCH=CHCH), 6.27 (dd, J = 15.7 and 8.7 Hz, PhCH=CH), 6.45 (d, J = 15.7 Hz, 1H, PhCH=CH), 7.33−7.07 (m, 9H). ^{13}C NMR ($CDCl_3$): δ 168.2, 167.8, 137.1, 136.9, 136.7, 131.6, 129.4, 129.3, 128.4, 127.7, 127.5, 126.3, 57.7, 52.6, 52.4, 48.8, 21.0. R_f = 0.30 (hexane/ethyl acetate; 3:1). HPLC Pharmacir 7C, (*n*-butanol/hexane; 10:90, 1.0 mL min^{-1}): t_R (*S*) 9.9 min, (t_R (*R*) 12.3 min).

***η*^{3}-1,3-Diphenylallyl[(2,2-bis-[2-((4*S*)-((1*S*)-1-hydroxy-1-phenylmethyl)-1,3-oxazolinyl)] propane)-*N*,*N*′]palladium-(II) Tetrafluoroborate (7).** To a solution of the preformed ligand **1a** (85 mg, 0.21 mmol) and [Pd(η^3-PhCHCHCHPh)Cl]$_2$ (65 mg, 0.09 mmol) in a mixture of CH_3OH/CH_2Cl_2/THF (5 mL/6 mL/5 mL) was added a solution of $AgBF_4$ (60 mg) in 5 mL of THF. The resulting mixture was stirred for 30 min, and the formed solid was filtered off. The yellow filtrate was concentrated to afford complex **7** (147 mg, 91%). Crystals were grown from a solution of THF/diethyl ether/ethyl acetate. ^{1}H NMR (CD_3COCD_3): δ 1.15 (s, 3H, $C_{(122)}H_3$), 1.66 (s, 3H, $C_{(123)}H_3$), 3.26 (d, J = 10.7 Hz, 1H, $C_{allyl(3)}H$), 3.41 (m, 1H, $C_{(14)}H$), 3.51 (m, 1H, $C_{(23)}H$), 4.04 (t, J = 9.7 Hz, 1H, $C_{(22)}H_2$), 4.41 (m, 1H, $C_{(12)}H$ and $C_{(14)}OH$), 4.53 (m, 1H, $C_{(13)}H$), 4.70 (d, J = 12.0 Hz, 1H, $C_{allyl(1)}H$), 4.77 (m, 2H, $C_{(22)}H_2$ and $C_{(12)}H_2$), 5.00 (m, 2H, $C_{(24)}H$ and $C_{(24)}OH$), 6.90 (dd, J = 10.7 and 12.0 Hz, $C_{allyl(2)}H$), 7.12−7.88 (m, 18 H), 8.13 (m, 2 H). ^{13}C NMR (CD_3COCD_3): δ 20.71 ($C_{(122)}$), 27.66 ($C_{(123)}$), 39.57 ($C_{(121)}$), 68.60 ($C_{(14)}$), 70.24 ($C_{(24)}$), 70.87 ($C_{(13)}$), 71.06 ($C_{(12)}$), 72.58 ($C_{(24)}$), 72.69 ($C_{(22)}$), 73.93 ($C_{allyl(3)}$), 81.96 ($C_{allyl(1)}$), 106.93 ($C_{allyl(2)}$), 127.06, 127.54, 127.89, 128.11, 128.56, 128.93, 129.24, 129.51, 130.05, 138.21, 138.56, 175.81 ($C_{(11)}$), 175.93 ($C_{(21)}$).

***η*^{3}-1,3-Diphenylallyl-[(2,2-Bis[2-((4*S*)-((1*S*)-1-methyloxy-1-phenylmethyl)-1,3-oxazolinyl)]propane)-*N*,*N*′]palladium-(II) Tetrafluoroborate (8).** This compound was obtained in 87% yield. ^{1}H NMR (CD_3COCD_3): δ 1.01 (s, 3H, $C_{(122)}H_3$), 1.17 (s, 3H, $C_{(123)}H_3$), 3.09 (s, 3H, $OC_{(25)}H_3$), 3.29 (s, 3H, $OC_{(15)}H_3$), 3.45 (d, J = 4.7 Hz, 1H, $OC_{(14)}H$), 3.60 (ddd, J = 3.5, 3.8, and 9.5 Hz, 1H, $C_{(23)}H$N), 4.07 (t, J = 9.5 Hz, 1H, $C_{(22)}H$), 4.13 (d, J = 10.6 Hz, 1H, $C_{allyl(3)}H$), 4.20 (ddd, J = 3.1, 4.7, and 9.4 Hz, 1H, $C_{(13)}H$N), 4.40 (d, J = 3.8 Hz, 1H, $OC_{(24)}H$), 4.43 (t, J = 9.4 Hz, 1H, $C_{(12)}H_2$), 4.81 (dd, J = 3.5 and 9.5 Hz, 1H, $C_{(22)}H_2$), 4.86 (dd, J = 3.1 and 9.4 Hz, 1H, $C_{(12)}H_2$), 5.22 (d, J = 12.2 Hz, 1H, $C_{allyl(1)}H$), 6.99 (dd, J = 12.2 and 10.6 Hz, $C_{allyl(2)}H$), 7.30 (m, 2H), 7.45 (m, 4H), 7.55−7.75 (m, 10H), 8.00 (m, 2H), 8.20 (m, 2H). ^{13}C NMR (CD_3COCD_3): δ 22.83 ($C_{(122)}$), 25.34 ($C_{(123)}$), 39.54 ($C_{(121)}$), 56.68 ($C_{(15)}$), 56.86 ($C_{(25)}$), 67.49 ($C_{(23)}$), 68.02 ($C_{(13)}$), 70.62 ($C_{(12)}$), 71.51 ($C_{(22)}$), 73.79 ($C_{(3)}$), 79.97 ($C_{(14)}$), 81.47 ($C_{(24)}$), 83.30 ($C_{(1)}$), 107.87 ($C_{(2)}$), 128.04, 128.16, 128.54, 128.65, 128.77, 128.98, 129.69, 129.73, 130.28, 135.49, 136.85, 137.89, 138.90, 174.52 ($C_{(11)}$), 174.73 ($C_{(21)}$).

X-ray Crystallographic Study. Data for **7** and **8** were collected on a Stoe IPDS (imaging plate diffraction system) diffractometer. The final unit cell parameters were obtained by least-squares refinement of 5000 reflections. Only statistical fluctuations were observed in the intensity monitors over the course of data collections.

The two structures were solved by direct methods (SIR92)[17] and refined by least-squares procedures on F_{obs}. H atoms were located on difference Fouriers maps. The H atoms of the OH groups for **7** were refined isotropically, the others were introduced in the calculation with idealized positions (d(CH) = 0.96 Å), and their atomic coordinates were recalculated after each cycle. They were given isotropic thermal parameters 20% higher than those of the carbon to which they are attached. Least-squares refinements were carried out by minimizing the function $\sum w(|F_o| - |F_c|)^2$, where F_o and F_c are the observed and calculated structure factors. The weighting scheme used in the last refinement cycles was $w = w'[1 - \{\Delta F/6\sigma(F_o)\}^2]^2$, where $w' = 1/\sum_1^n \mathrm{ArTr}(x)$ with three coefficients Ar for the Chebyshev polynomial ArTr(x), where x was F_c/F_c(max).[18] Models reached convergence with $R = \sum(|F_o| - |F_c|)/\sum(|F_o|)$ and $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w(F_o)^2]^{1/2}$, having the values listed in Table 1. Criteria for a satisfactory complete analysis were the ratios of rms shift to standard deviation less than 0.1 and no significant features in final difference maps. Details of data collection and refinement are given in the Supporting Information.

The calculations were carried out with the CRYSTALS package program[19] running on a PC. The drawings of the molecules were made with the CAMERON software.[20] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited at the Cambridge Crystallographic Data Center as supplementary publication XXX. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 IEZ, U.K. [fax int. code + 44(1223)336-033; e-mail deposit@ccdc.cam.ac.uk].

Acknowledgment. This work was supported by the Centre National de Recherche Scientifique (CNRS) and the "Ministère de l'Education Nationale, de la Recherche et de la Technologie" with a doctoral fellowship for O.H. H.A.-H. thanks Prof. Jean-Pierre Tuchagues for his help.

Supporting Information Available: This material is available free of charge via the Internet at http://pubs.acs.org.

OM990437J

(17) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Poidori, G. SIR92−a program for automatic solution of crystal structures by direct methods. *J. Appl. Crystallogr.* **1994**, *27*, 435.

(18) Prince, E. *Mathematical Techniques in Crystallography*; Springer-Verlag: Berlin, 1982.

(19) Watkin, D. J.; Prout, C. K.; Carruthers, J. R.; Betteridge, P. W. *CRYSTALS Issue 10*; Chemical Crystallography Laboratory: University of Oxford, Oxford, 1996.

(20) Watkin, D. J.; Prout, C. K.; Pearce, L. J. *CAMERON*; Chemical Crystallography Laboratory: University of Oxford, Oxford, 1996.