P-Chiral monodentate diamidophosphites as ligands for Rh-catalyzed asymmetric reactions

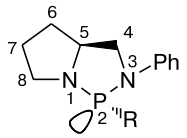
S. E. Lyubimov, V. A. Davankov, P. V. Petrovskii, and N. M. Loim*

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. Fax: +7 (499) 135 6471. E-mail: lssp452@mail.ru

A series of *P*-chiral monodentate diamidophosphite ligands of the 1,3-diaza-2-phosphabicyclo[3.3.0]octane family was tested in the Rh-catalyzed hydrogenation of dimethyl itaconate and addition of phenylboronic acid at the carbonyl group of *trans*-cinnamaldehyde. The enantioselectivities and conversions of these reactions are strongly dependent on the nature of the exo-cyclic substituent of the ligand.

Key words: 1,3-diaza-2-phosphabicyclo[3.3.0]octanes, *P*-chirality, diamidophosphites, metal complex catalysis, rhodium complexes, asymmetric hydrogenation, phenylboronic acid, *trans*-cinnamaldehyde.

P-Chiral monodentate phosphites and amidophosphites belong to the new class of efficient ligands for asymmetric catalysis. At present, there are just few examples of application of this type of ligands in the Rh-catalyzed hydrogenation of prochiral unsaturated esters,[1,2] as well as in the Pd-catalyzed allylic substitution.[3—5] Thus, the synthesis of new *P*-chiral monodentate ligands of phosphite type, as well as the research on the possibility of their use in the other catalytic asymmetric reactions are of much interest. Recently, we have shown[3] that the synthetically available diamidophosphite monodentate ligands **1a**—**d** can provide a high level of enantiomeric excess in the Pd-catalyzed allylic substitution of 1,3-diphenylprop-2-enyl acetate (to 97% *ee*).



1a—e

R = OMe (**a**), OPr^i (**b**), OCH(CF$_3$)$_2$ (**c**), OPh (**d**), OCH[C$_5$H$_4$Mn(CO)$_3$]$_2$ (**e**)

In the present work, the results of testing of *P*-chiral diamidophosphite ligands of 1,3-diaza-2-phosphabicyclo[3.3.0]octane family in the reaction of asymmetric hydrogenation of dimethyl itaconate, as well as in the addition of phenylboronic acid at the carbonyl group of *trans*-cinnamaldehyde are reported. The structural features of the chiral ligands, promoting the increase in enantioselectivity and conversion in the reactions under consideration, are revealed.

Results and Discussion

Ligands **1a**—**d** were synthesized according to the procedure published by us earlier.[3] Diamidophosphite **1e** bearing sterically bulky dicymantrenylmethanol residue was obtained similarly. According to the ^{31}P NMR spectrum, ligand **1e** is a mixture of phosphorus epimers in the ratio 77 : 23 with the main stereoisomer having the pseudoequatorial orientation of the dicymantrenylmethoxy substituent, *i.e.,* the *R*-configuration of the chiral phosphorus center. This follows from the spin-spin coupling constant value $^2J_{C(8),P}$ = 37.0 Hz in the ^{13}C NMR spectrum and from the known correlation between value of $^2J_{C(8),P}$ constant and dihedral angle between the lone electron pair of the phosphorus atom and C(8) (see Refs 3—6). When the lone electron pair of the phosphorus atom and C(8) are in *cis*-position to each other (substituent R has the pseudoequatorial orientation), the $^2J_{C(8),P}$ values are the maximal (32—40 Hz). The minimal values of this spin-spin coupling constant (3.1—4.0 Hz) correspond to the *trans*-orientation of the lone electron pair of the phosphorus atom and C(8), which is characteristic of the minor *S*p-epimer (3.5 Hz). The presence of the chiral phosphorus fragment in ligand **1e** is responsible for the two diastereotopic cymantrenyl groups and, consequently, for the nonequivalence of all the carbon atoms of Cp-rings in the ^{13}C NMR spectrum.

Diamidophosphites **1a**—**e** were tested in the reaction of asymmetric Rh-catalyzed hydrogenation of dimethyl itaconate (**2**) (Scheme 1 and Table 1). In case of ligand **1a** with the smallest exo-cyclic substituent (R = OMe), the conversion was the most complete, however, the enan-

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 10, pp. 2023—2025, October, 2007.

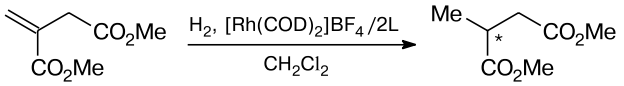
Table 1. Rh-Catalyzed asymmetric hydrogenation of dimethyl itaconate

Entry	Ligand	*t*/h	Conversion (%)	*ee* (%)
1	**1a**	24	100	4 (*R*)
2	**1b**	24	75	4 (*S*)
3	**1c**	24	78	55 (*S*)
4	**1c**	36	98	54 (*S*)
5	**1d**	24	80	6 (*S*)
6	**1e***	24	50	33 (*S*)
7	**1e***	36	80	34 (*S*)

* Mixture of diastereomers.

tioselectivity was only 4% *ee* (*S*). It is worthy to note that, when ligands **1b**—**e** were used, product **3** was obtained in the opposite configuration, despite of the same type of the phosphorus center in **1a**—**e** and the absence of additional chirality in exo-cyclic substituent (see Table 1). A comparison of the enantiomeric excess of product **3**, obtained with the use of ligands **1a**—**e**, showed that the best result (55% *ee*) was provided by ligand **1c** with electron-withdrawing exo-cyclic substituent. The prolongation of the experiment with participation of **1c** to 36 h made the conversion of substrate **2** virtually complete (see Table 1, entries *3* and *4*).

Scheme 1



2 **3**

Conditions: H_2 at 5 atm.

Ligands **1a**—**e** were also tested in the addition of phenylboronic acid to *trans*-cinnamaldehyde (**4**) (Scheme 2 and Table 2) with the use of $[Rh(COD)Cl]_2$ as the pre-catalyst. Such an approach opens the access to valuable allylic alcohols, used as the intermediates in the synthesis of biologically active compounds.[7] It should be noted that for the reaction under consideration, there is the only example of application of the phosphite type monodentate ligands, synthesized on the basis of the poorly available 1,1′-spirobiindane-7,7-diol.[8]

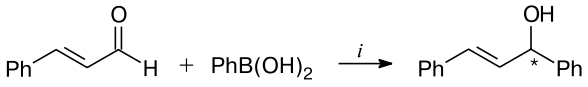
Table 2. Rh-Catalyzed asymmetric addition of phenylboronic acid to *trans*-cinnamaldehyde

Entry	Ligand	*t*/h	*T*/°C	Conversion (%)	*ee* (%)
1	**1a**	24	20	40	4 (*R*)
2	**1b**	24	20	35	17 (*R*)
3	**1b**	24	60	49	12 (*R*)
4	**1c**	24	20	40	0
5	**1c**	24	60	51	0
6	**1d**	24	20	52	0
7	**1e***	24	20	60	14 (*R*)
8	**1e***	24	60	54	11 (*R*)

* Mixture of diastereomers.

When the reaction was carried out at 20 °C and ligand **1e** was used, the maximal yield of product **5** was 60%, however, the enantioselectivity in this case did not exceed 14% *ee* (see Table 2, entry *7*). The higher optical yield was provided by diamidophosphite **1b** (17% *ee*), though, with the lower yield of the reaction product (35%, see Table 2, entry *2*). The temperature increase to 60 °C promoted the increase in the product yield, however, the enantioselectivity of the process fell to 12% *ee* (see Table 2, entry *3*).

Scheme 2



4 **5**

Reagents and conditions: $[Rh(COD)Cl]_2$/4L, toluene—H_2O (1 : 1), 2 KF, 24 h.

In conclusion, for the first time we showed the possibility of application of the *P*-chiral diamidophosphite ligands in the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate and addition of phenylboronic acid at the carbonyl group of *trans*-cinnamaldehyde. In the first reaction, the maximal enantioselectivity can be reached by the introduction of the electron-withdrawing exo-cyclic substituent at the phosphorus atom, whereas, in the second reaction, the highest conversion is favored by the introduction of the sterically bulky group, though, with the low enantioselectivity of the reaction.

Experimental

^{31}P, ^{1}H, and ^{13}C NMR spectra were recorded on a Avance AMX-400 spectrometer (161.98, 400.13, and 100.61 MHz) relatively to 85% aq. H_3PO_4 in D_2O and Me_4Si, respectively. Signal assignments in the ^{13}C NMR spectra were performed by the *J*-modulated echo method. Hydrogenation was carried out on a Parr 4843 autoclave (25 mL). Elemental analyses were performed in the Organic Microanalysis Laboratory of the A. N. Nesmeyanov Institute of Organoelement Compounds of RAS.

All the reactions were carried out under dry argon in anhydrous solvents. Dimethyl itaconate, phenylboronic acid, and *trans*-cinnamaldehyde were purchased from Aldrich.

(2*R*,5*S*,S_a)-2-Dicymantrenylmethoxy-3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane (1e) was obtained from dicymantrenylmethanol[9] similarly to the described procedures.[3—5] The yield was 70%, slowly crystallizing yellow oil. Found (%): C, 52.78; H, 3.87; N, 4.12. $C_{28}H_{23}N_2O_7PMn_2$. Calculated (%):

C, 52.52; H, 3.62; N, 4.37. ^{31}P NMR ($CDCl_3$), δ: 128.4 (77%, *R*p), 123.5 (23%, *S*p). ^{13}C NMR **1e** (*R*p) ($CDCl_3$), δ: 25.7 (s, C(7)); 31.6 (s, C(6)); 48.8 (d, C(8), J = 37.0 Hz); 53.7 (d, C(4), J = 6.5 Hz); 63.1 (d, C(5), J = 8.4 Hz); 65.7 (s, COP); 79.7 (d, Cp, J = 48.2 Hz); 80.4 (d, Cp, J = 17.6 Hz); 84.1 (d, Cp, J = 22.1 Hz); 84.9 (d, Cp, J = 38.2 Hz); 104.4 (d, C_{ipso} Cp, J = 8.8 Hz); 115.1 (d, Ar, J = 12.6 Hz); 118.9 (s, Ar); 128.7 (s, Ar); 144.9 (d, Ar, J = 16 Hz); 224.4 (s, CO); 224.5 (d, CO, J = 20.3 Hz). ^{13}C NMR **1e** (*S*p) ($CDCl_3$), δ: 28.3 (s, C(7)); 31.7 (s, C(6)); 43.8 (d, C(8), J = 3.5 Hz); 50.7 (d, C(4), J = 6.9 Hz); 64.1 (d, C(5), J = 8.8 Hz); 65.4 (s, COP); 79.5 (d, Cp, J = 48.2 Hz); 80.3 (d, Cp, J = 17.4 Hz); 84.0 (d, Cp, J = 21.7 Hz); 84.8 (d, Cp, J = 38.2 Hz); 104.3 (d, C_{ipso} Cp, J = 17.2 Hz); 116.6 (d, Ar, J = 14.1 Hz); 119.7 (s, Ar); 129.0 (s, Ar); 145.3 (d, Ar, J = 14.5 Hz); 224.3 (d, CO, J = 20.1 Hz).

Asymmetric hydrogenation of dimethyl itaconate. Complex $[Rh(COD)_2]BF_4$ (2.5 mg, 0.006 mmol) and the corresponding ligand **1a—e** (0.012 mmol) were dissolved in CH_2Cl_2 (4 mL). Then, dimethyl itaconate **2** (0.1 g, 0.6 mmol) was added and this was placed in an autoclave. The capped autoclave was blown through with argon, then, trice with hydrogen and then hydrogenation was performed at 5 atm and 20 °C for 24—36 h (see Table 1). The reaction mixture was diluted with hexane (8 mL) and filtered through a short layer of silica gel. The solvents were evaporated under reduced pressure (40 Torr), the residue was dried *in vacuo* (10 Torr). The conversion was determined by ^{1}H NMR spectroscopy. Enantiomeric excess of the product was determined on a Chiralcel OD-H column according to the published data.[10]

Addition of phenylboronic acid to *trans*-cinnamaldehyde. Complex $[Rh(COD)Cl]_2$ (2 mg, 0.004 mmol) was dissolved in toluene (0.5 mL), the corresponding ligand **1** (0.016 mmol) in toluene (0.5 mL) was added to this mixture. The mixture was stirred for 15 min under argon, after that, $PhB(OH)_2$ (102 mg, 0.8 mmol), $KF \cdot 2H_2O$ (78 mg, 0.8 mmol), water (1 mL), and *trans*-cinnamaldehyde (55 mg, 0.4 mmol) were sequentially added. The mixture was kept at the corresponding temperature for 24 h, then, extracted with toluene (3×2 mL), the extracts were dried with Na_2SO_4 and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel (hexane—ethyl acetate, 9 : 1, as the eluent). The structure of product **5** was confirmed by ^{1}H NMR spectroscopy and mass spectrometry data and was in complete accordance with the published data.[8] Enantiomeric excess of the product **5** was determined on a Chiralcel OD-H column according to the known procedure.[8]

This work was financially supported by the INTAS (INTAS Open Call 2005-2006 Grant, Ref. No. 05-1000008-8064).

References

1. M. T. Reetz, J. Ma, and R. Goddard, *Angew. Chem. Int. Ed.*, 2005, **3**, 412.
2. O. G. Bondarev and R. Goddard, *Tetrahedron Lett.*, 2006, **47**, 9013.
3. V. N. Tsarev, S. E. Lyubimov, A. A. Shiryaev, S. V. Zheglov, O. G. Bondarev, V. A. Davankov, A. A. Kabro, S. K. Moiseev, V. N. Kalinin, and K. N. Gavrilov, *Eur. J. Org. Chem.*, 2004, 2214.
4. S. E. Lyubimov, V. A. Davankov, and K. N. Gavrilov, *Tetrahedron Lett.*, 2006, **47**, 2721.
5. S. E. Lyubimov, V. A. Davankov, M. G. Maksimova, P. V. Petrovskii, and K. N. Gavrilov, *J. Mol. Catal. A: Chemical,* 2006, **259**, 183.
6. J. M. Brunel, O. Legrand, S. Reymond, and G. Buono, *J. Am. Chem. Soc.*, 1999, **121**, 5807.
7. M. Fontes, X. Verdaguer, L. Sola, M. A. Pericas, and A. Riera, *J. Org. Chem.,* 2004, **69**, 2532.
8. H. Duan, J. Xie, W. Shi, Q. Zhang, and Q. Zhou, *Org. Lett.*, 2006, **7**, 1479.
9. N. Loim, P. Kondrat´ev, N. Solov´eva, V. Antanovich, P. Petrovskii, Z. Parnes, and D. Kursanov, *J. Organomet. Chem.,*1981, **209**, 233.
10. G. Argouarch, O. Samuel, and H. B. Kagan, *Eur. J. Org. Chem.*, 2000, **16**, 2885.

Received February 15, 2007;
in revised form April 12, 2007