First chiral [2.2]paracyclophane-derived phosphite ligands: synthesis and application in asymmetric reactions

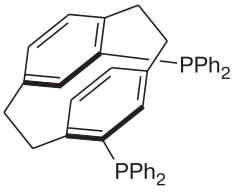
S. E. Lyubimov, R. P. Zhuravskii, V. I. Rozenberg, A. S. Safronov, P. V. Petrovskii, and V. A. Davankov*

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

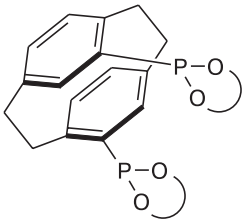
First representatives of chiral phosphite ligands derived from 4,5-dihydroxy[2.2]paracyclophane have been synthesized. A possibility of the use of these compounds in the reactions of asymmetric Pd- and Ir-catalyzed allylic amination of 1,3-diphenylprop-2-enyl acetate with pyrrolidine and Rh-catalyzed hydrogenation of dimethyl itaconate has been demonstrated.

Key words: paracyclophanes, phosphites, metal complex catalysis, allylic amination, asymmetric hydrogenation.

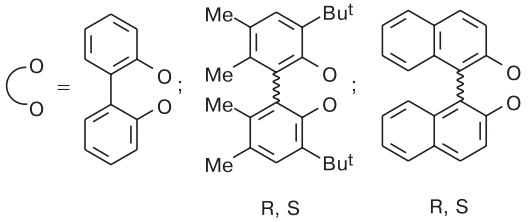
[2.2]Paracyclophane-derived P,P-bidentate ligands are attractive for the use in asymmetric catalysis, which provide high values of enantiomeric excess and conversion in the reactions of the Rh-catalyzed hydrogenation and hydroboration of cyclopropenes, as well as in the Pd-catalyzed allylic amination.[1,2] In these cases, ligands of such a type are represented only by phosphines and phosphinites, such as bis(diphenylphosphino)[2.2]paracyclophane (**1**) and its phosphinite analogs **2** (see Refs 3, 4). In addition, it is known that ligands of the phosphite type are also capable of being efficient chiral inductors in various asymmetric reactions and on the whole are more synthetically available as compared with their phosphine and phosphinite analogs.[5,6] In this way, the synthesis of phosphite ligands derived from [2.2]paracyclophane, as well as the testing their applicability in asymmetric catalysis seemed reasonable.



1



2



In the present work, we synthesized phosphite ligands on the basis of 4,5-dihydroxy[2.2]paracyclophane (**3**) and tested them in the asymmetric Pd- and Ir-catalyzed allylic amination of 1,3-diphenylprop-2-enyl acetate with pyrrolidine and in the Rh-catalyzed hydrogenation of dimethyl itaconate.

Results and Discussion

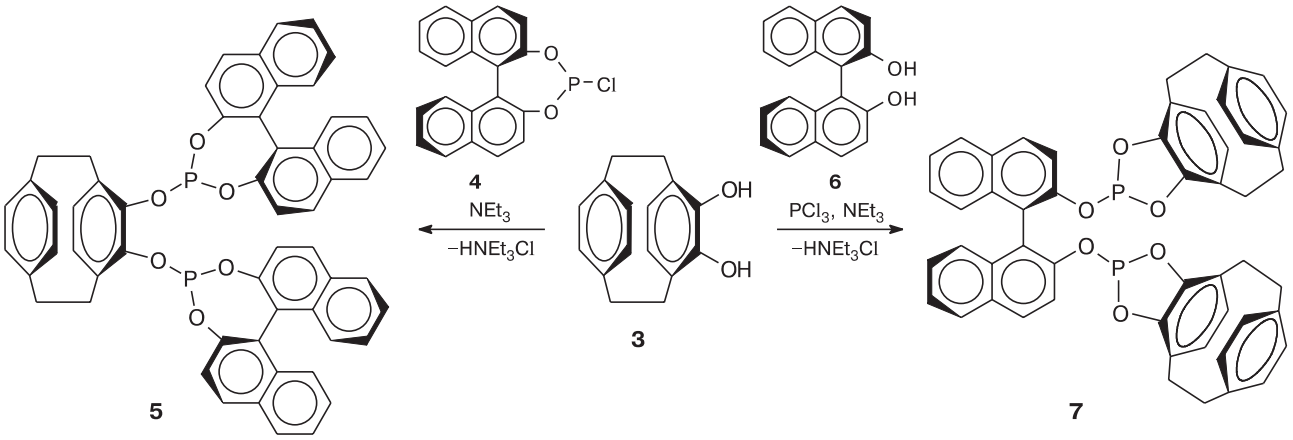
Ligand **5** was obtained by the one-step phosphorylation of achiral 4,5-dihydroxy[2.2]paracyclophane (**3**) with the axially chiral phosphorylating reagent **4** (Scheme 1). It is worth to note that the published synthesis of phosphine (**1**) and phosphinite ligands **2** on the basis of [2.2]paracyclophane includes three and more steps.[3,4] We proposed the synthesis of phosphite **7** in one technological step, which does not require isolation of the intermediate phosphorylating reagent (see Scheme 1 and Experimental). Ligands **5** and **7** are stable in air powders, which can be stored for a long time in dry atmosphere.

Phosphites **5** and **7** were tested as the ligands in asymmetric allylic amination of 1,3-diphenylprop-2-enyl acetate (**8**) with pyrrolidine (Scheme 2). Compounds $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and $Ir(COD)Cl]_2$ (COD is cycloocta-1,5-diene) were used as the source of transition metals, which showed high regio- and enantioselectivity in the amination of unsymmetric allylic systems.[7,8] It should be noted that the use of this source of iridium in the asymmetric allylation of symmetric allylic substrates such as **8**, was the only literature precedent.[9]

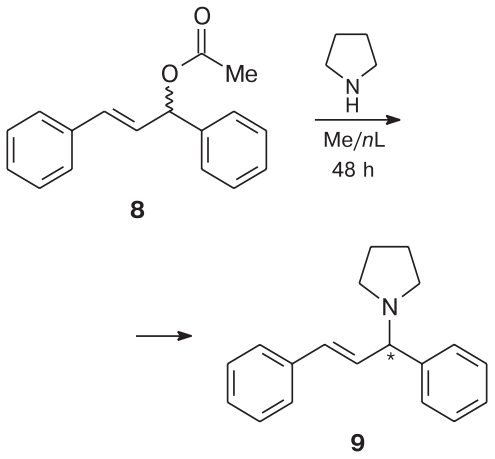
In the palladium-catalyzed amination of compound **8** (Table 1, entries *1—4*) with participation of ligands **5** and **7**, we succeeded in rising the conversion to the quantitative values when THF was used as the solvent, however,

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 1, pp. 132—134, January, 2008.

Scheme 1



Scheme 2



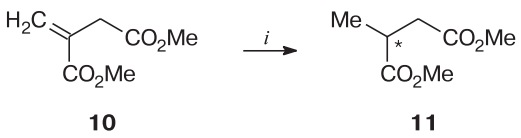
enantioselectivity did not exceed 30%. In case of the iridium-based catalysts (see Table 1, entries *5*—*8*) with the same ligands, the high values of enantiomeric excess (up to 90% *ee*) were achieved in dichloromethane, while the conversion was lower. Unfortunately, such iridium catalysts are virtually inactive in THF (Table 1, entries *6* and *8*).

Table 1. Data on the Pd- and Ir-catalyzed asymmetric allylic amination of 1,3-diphenylprop-2-enyl acetate

Entry	Catalyst	Solvent	Conversion (%)	*ee* (%)
1	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/**5**	CH_2Cl_2	70	20 (*S*)
2	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/**5**	THF	100	30 (*S*)
3	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/**7**	CH_2Cl_2	52	12 (*S*)
4	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/**7**	THF	100	5 (*S*)
5	$[Ir(COD)Cl]_2$/**5**	CH_2Cl_2	20	90 (*S*)
6	$[Ir(COD)Cl]_2$/**5**	THF	10	5 (*S*)
7	$[Ir(COD)Cl]_2$/**7**	CH_2Cl_2	24	81 (*S*)
8	$[Ir(COD)Cl]_2$/**7**	THF	6	3 (*S*)

Ligands **5** and **7** were also tested in the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate **10** (Scheme 3, Table 2).

Scheme 3



i. H_2, $[Rh(COD)_2]BF_4$/L, CH_2Cl_2, 24 h.

It was found that the enantioselectivity of this process strongly depends on the hydrogen pressure. An increase in pressure facilitates an increase in conversion of dimethyl itaconate, however, the *ee* value of the reaction product decreases. In this reaction, like in case of allylic amination, the values of enantioselectivity and conversion, obtained when ligand **5** (having two axially chiral substituents) was used, were higher than when phosphite **7** was used.

In conclusion, we have synthesized the first representatives of chiral phosphite ligands on the basis of paracyclophane. Their testing in allylic amination of 1,3-diphenylprop-2-enyl acetate showed that they are able

Table 2. Data on the Rh-catalyzed hydrogenation of dimethyl itaconate

Entry	Catalyst	Pressure of H_2 /atm	Conversion (%)	*ee* (%)
1	$[Rh(COD)_2]BF_4$/**5**	5	50	47 (*R*)
2	$[Rh(COD)_2]BF_4$/**5**	20	87	29 (*R*)
3	$[Rh(COD)_2]BF_4$/**7**	5	35	38 (*R*)
4	$[Rh(COD)_2]BF_4$/**7**	20	62	20 (*R*)

to provide the high values of enantiomeric excess (up to 90% *ee*) with moderate conversion in case of the iridium complex, whereas a traditional palladium catalysis with the use of these ligands facilitates the high values of conversion but with low enantioselectivity. In addition, we found that, in comparison with phosphite **7**, having only one chiral center in the molecule, ligand **5**, possessing two elements of chirality, leads to the higher values of conversion and enantiomeric excess of the product in both reactions studied.

Experimental

^{31}P, ^{1}H, and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer (161.98, 400.13, and 100.61 MHz) relatively to 85% H_3PO_4 in D_2O and Me_4Si, respectively. Elemental analysis was performed in the Organic Microanalysis Laboratory of the A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences. Hydrogenation of dimethyl itaconate (**10**) was carried out on a Parr 4843 machine equipped with 25-mL autoclave. Optical rotation was determined on a Perkin—Elmer-141 polarimeter. Enantiomeric excess of product **9** and conversion of **8** were determined according to the known procedure.[10] Conversion of dimethyl itaconate was determined with the help of ^{1}H NMR spectroscopy, enantiomeric excess of product **11** was determined by HPLC according to available procedure.[11] Dihydroxy[2.2]paracyclophane (**3**)[12] and (*R*)-2-chlorodinaphtho[2,1:*d*:1′,2′-*f*][1,3,2]dioxaphosphepane (**4**)[13] were synthesized according to the described procedures. All the reactions were carried out in the atmosphere of dry argon and in anhydrous solvents. Commercially available (*R*)-BINOL (**6**) and dimethyl itaconate (**10**) (Aldrich) were used without additional purification.

4,5-Bis{(*R*)-dinaphtho[2,1-*d*:1′,2′-*f*][1,3,2]dioxaphosphepan-2-yloxy}[2.2]paracyclophane (5). A solution of dihydroxy[2.2]paracyclophane (0.2 g, 0.831 mmol) in benzene (5 mL) was added dropwise to a solution of phosphorylating reagent (**4**) (0.476 g, 1.662 mmol) and triethylamine (0.224 mL, 1.662 mmol) in the same solvent (10 mL). The mixture obtained was heated to the boiling point, cooled to room temperature, and $HNEt_3Cl$ was removed by filtration. The filtrate was concentrated *in vacuo*. The product was purified by column chromatography on silica gel, eluent: hexane/CH_2Cl_2, 1:1. The yield was 0.56 g (78%), white powder, m.p. 152—156 °C, $[\delta]_D^{25}$ −152° (*c* 0.8, CH_2Cl_2). Found (%): C, 77.62; H, 4.18; P, 7.01. $C_{58}H_{38}P_2O_6$. Calculated (%): C, 77.41; H, 4.41; P, 7.13. ^{31}P NMR ($CDCl_3$), δ: 132.33 (d, $J_{P,P}$ = 7.1 Hz); 144.97 (d, $J_{P,P}$ = 7.1 Hz). ^{1}H NMR ($CDCl_3$), δ: 2.39—2.48 (m, 2 H); 2.73—2.86 (m, 4 H); 2.94—3.01 (m, 2 H); 6.10—8.04 (m, 30 H). ^{13}C NMR ($CDCl_3$), δ: 28.93 (d, $J_{C,P}$ = 2.9 Hz); 33.47 (d, $J_{C,P}$ = 8.4 Hz); 117.63—147.50 (aryl).

(*R*,*R*)-2,2′-Bis{[2.2]paracyclophano[*d*][1,3,2]dioxaphospholan-2-yloxy}-1,1′-binaphthyl (7). A mixture of dihydroxy[2.2]paracyclophane (0.384 g, 1.6 mmol) and triethylamine (0.431 mL, 3.2 mmol) in benzene (6 mL) was added dropwise to a solution of PCl_3 (0.14 mL, 1.6 mmol) in benzene (6 mL), the mixture was heated to boiling, then cooled to ~20 °C. A solution of (*R*)-BINOL (0.229 g, 0.8 mmol) (**6**) and triethylamine (0.216 mL, 1.6 mmol) in benzene (8 mL) was slowly added to the *in situ* obtained phosphorylating reagent. The mixture was heated to boiling, cooled to 24 °C, $HNEt_3Cl$ was filtered off, and the product was concentrated *in vacuo* (40 Torr). The residue was purified by column chromatography on silica gel, eluent: hexane—CH_2Cl_2 (3 : 2). The yield was 0.54 g (68%), white powder, m.p. 168—170 °C, $[\alpha]_D^{25}$ −128° (*c* 0.74, CH_2Cl_2). Found (%): C, 76.18; H, 4.79; P, 7.39. $C_{52}H_{40}O_6P_2$. Calculated (%): C, 75.90; H, 4.90; P, 7.53. ^{31}P NMR ($CDCl_3$), δ: 131,73. ^{1}H NMR ($CDCl_3$), δ: 2.39—3.22 (m, 16 H); 6.07—8.03 (m, 24 H). ^{13}C NMR ($CDCl_3$), δ: 28.97, 33.53, 117.63—147.52 (aryl).

Allylic amination of 1,3-diphenylprop-2-enyl acetate with pyrrolidine. A solution of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (3.7 mg, 0.01 mmol) or $[Ir(COD)Cl]_2$ (6.7 mg, 0.01 mmol) and the corresponding ligand (0.02 mmol) in 2 mL of a solvent (THF or CH_2Cl_2) was stirred for 20 min. Then 1,3-diphenylprop-2-enyl acetate (0.1 mL, 0.5 mmol) was added, the reaction mixture was stirred for additional 15 min, pyrrolidine (0.12 mL, 1.5 mol) was added. The mixture obtained was stirred for 48 h at 20 °C, then diluted with hexane (4 mL), and filtered through a layer of silica gel. The solvent was evaporated *in vacuo* (40 Torr). The residue was analyzed as pointed out above.

Asymmetric hydrogenation of dimethyl itaconate. Compound $[Rh(COD)_2]BF_4$ (2.5 mg, 0.006 mmol) and ligand **5** or **7** (0.006 mmol) were dissolved in CH_2Cl_2 (3 mL). Then dimethyl itaconate (**2**) (0.1 g, 0.6 mmol) was added and the mixture was placed in autoclave. The sealed autoclave was blown through with argon, then, 2 times with hydrogen, and kept for 24 h under pressure of hydrogen of 5 or 20 atm. The reaction mixture was diluted with hexane (6 mL) and filtered through a short layer of silica gel. The solvent was evaporated at reduced pressure (40 Torr), the residue was dried *in vacuo* (6 Torr) and analyzed as pointed out above.

This work was financially supported by the Russian Foundation for Basic Research (Project No. 06-03-33086) and INTAS (Open Call Grant 05-1000008-8064).

References

1. S. E. Gibson, J. D. Knight, *Org. Biomol. Chem.*, 2003, **1**, 1256.
2. B. Dominguez, A. Zanotti-Gerosa, W. Hems, *Org. Lett.*, 2004, **6**, 1927.
3. P. J. Pye, K. Rossen, R. A. Reamer, N. N. Tsou, R. P. Volante, P. J. Reider, *J. Am. Chem. Soc.*, 2002, **119**, 6207.
4. A. Zanotti-Gerosa, C. Malan, D. Herzberg, *Org. Lett.*, 2001, **3**, 3687.
5. J. Ansell, M. Wills, *Chem. Soc. Rev.*, 2002, **31**, 259.
6. K. N. Gavrilov, O. G. Bondarev, A. I. Polosukhin, *Usp. Khim.*, 2004, **73**, 726 [*Russ. Chem. Rev.*, 2004, **73**, 671 (Engl. Transl.)].
7. T. Ohmura, J. Hartwig. *J. Am. Chem. Soc.*, 2002, **124**, 15164.
8. C. Kiener, C. Shu, C. Incarvito, J. Hartwig, *J. Am. Chem. Soc.*, 2003, **125**, 14272.
9. D. Polet, A. Alexakis, K. Tissot-Croset, C. Corminboeuf, K. Ditrich, *Chem. Eur. J.*, 2006, **12**, 3596.
10. D. Smyth, H. Tye, C. Eldred, N. W. Alcock, M. Wills, *J. Chem. Soc., Perkin Trans. 1*, 2001, 2840.
11. G. Argouarch, O. Samuel, H. B. Kagan, *Eur. J. Org. Chem.*, 2000, 2885.
12. V. Rozenberg, R. Zhuravsky, E. Sergeeva, *Chirality*, 2006, **18**, 95.
13. G. Francio, C. G. Arena, F. Faraone, C. Graiff, M. Lanfranchi, A. Tiripicchio, *Eur. J. Inorg. Chem.*, 1999, 1219.

Received August 16, 2007;
in revised form October 24, 2007