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Communication

Carborane-derived diphosphites: New ligands for Pd-catalyzed allylic amination

Sergey E. Lyubimov [a,*], Andrey A. Tyutyunov [a], Pavel A. Vologzhanin [b], Anton S. Safronov [a], Pavel V. Petrovskii [a], Valery N. Kalinin [a], Konstantin N. Gavrilov [b], Vadim A. Davankov [a]

[a] Institute of Organoelement Compounds, Russian Academy of Sciences, 28 Vavilov Street, 119991 Moscow, Russia
[b] Department of Chemistry, Ryazan State University, 46 Svoboda Street, 390000 Ryazan, Russia

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ABSTRACT

A series of chiral diphosphite ligands bearing sterically congested carborane fragments have been prepared and applied in the Pd-catalyzed allylic amination of 1,3-diphenylallyl acetate with pyrrolidine and di-*n*-propylamine (up to 83% ee).

1. Introduction

Carborane-containing organophosphorus derivatives represent an interesting class of compounds that has been insufficiently investigated. Nevertheless, there are several practical uses of the substances. First of all, it has been reported that organophosphorus carborane derivatives were used in the neutron-capture therapy of cancer [1]. Pesticide, bactericide and ferment-inhibition properties of the compounds were also known [2,3]. Despite the encouraging performance of many achiral carborane organophosphorus ligands, especially phosphines [4,5], chiral phosphorus derivatives of carboranes are rare and represented only by our recent work related to the synthesis and first successful application of chiral phosphite derivatives of carboranes in the asymmetric hydrogenation of prochiral olefins (up to 99.8% ee) [6,7]. Encouraged by excellent enantioselectivities in the asymmetric hydrogenation processes and motivated by our continuing efforts in the design of novel chiral carboranylphosphite ligands, we have prepared a series of sterically congested carborane-phosphite derivatives for an application in other important asymmetric catalytic transformations, namely Pd-catalyzed allylic substitution. The high synthetic utility of this catalytic process is now well established through numerous efficient syntheses of enantiopure natural and unnatural products [8].

2. Results and discussion

The novel carboranylphosphites **4**, **5** bearing cyclic 1,2-carborane[1,2-*d*]-1,3,2-dioxaphosphepine fragment were easily obtained by direct phosphorylation of BINOL **2** and 1,4:3,6-dianhydro-D-mannitol **3** in the presence of NEt_3 in toluene (Scheme 1).

Additionally, we have prepared ligands **8**, **9** with bulky acyclic phosphorus centers by phosphorylation of 1-hydroxy-*ortho*-carborane (**6**) and 1-methyloxy-*ortho*-carborane (**8**) followed by treatment of the intermediate phosphochloridites (**8**, **9**, generated *in situ*) with corresponding diols (**2**, **3**, Scheme 2). All compounds are white solids, which are stable on prolonged storage.

To study the potential of carboranylphosphite ligands (**4**, **5** and **10**, **11**), we tested them in the Pd-catalyzed allylic substitution of (*E*)-1,3-diphenylallyl acetate **13** (which is widely used as a model substrate) with N-containing nucleophiles (Scheme 3).

The reactions were performed in THF or CH_2Cl_2 at room temperature (with $[Pd(allyl)Cl]_2$ as precatalyst, L/Pd = 1 or 2) according to the published procedures [8,9]. In the allylic amination of **12** with pyrrolidine (Table 1), ligand **4** showed excellent conversion but nearly racemic product. On the contrary, 1,4:3,6-dianhydro-D-mannitol based ligand **5** bearing the same phosphorus center gave good enantioselectivity but the activities were from moderate to good. The use of the ligands **10**, **11** with acyclic phosphorus centers showed the opposite trend. The bulky BINOL-based tetracarboranylphosphite **10** is a good enantioselector (up to 83% ee) but shows moderate conversion. Apparently from this, 1,4:3,6-dianhydro-D-mannitol based ligand **5** has an excellent activity but very low enantioselectivity. It should be noted, that in all cases

* Corresponding author. Tel./fax: +7 495 135 6471.
E-mail address: lssp452@mail.ru (S.E. Lyubimov).

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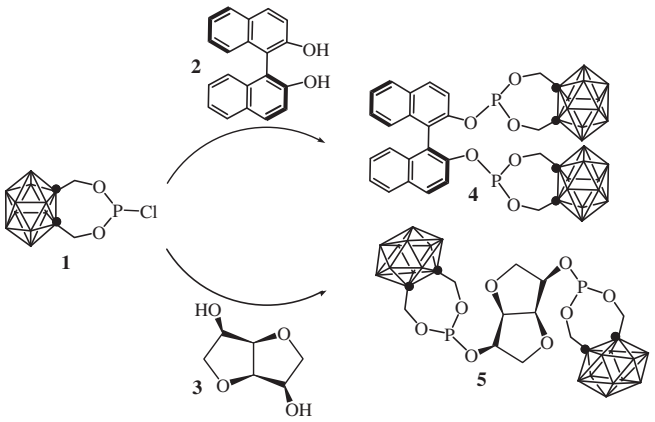


Scheme 1. Synthesis of ligands **4**, **5**.

Table 1
Allylic amination of **12** with pyrrolidine

Entry	Ligand	L/Pd	Solvent	Conv. (%)	ee of **13** (%)
1	**4**	1/1	THF	100	3 (*R*)
2	**4**	2/1	THF	100	5 (*R*)
3	**4**	1/1	CH_2Cl_2	100	5 (*R*)
4	**4**	2/1	CH_2Cl_2	100	6 (*R*)
5	**5**	1/1	THF	30	43 (*R*)
6	**5**	2/1	THF	20	53 (*R*)
7	**5**	1/1	CH_2Cl_2	45	20 (*R*)
8	**5**	2/1	CH_2Cl_2	90	73 (*R*)
9	**10**	1/1	THF	30	63 (*R*)
10	**10**	2/1	THF	45	82 (*R*)
11	**10**	1/1	CH_2Cl_2	50	35 (*R*)
12	**10**	2/1	CH_2Cl_2	54	**83** (*R*)
13	**11**	1/1	THF	100	4 (*R*)
14	**11**	2/1	THF	100	5 (*R*)
15	**11**	1/1	CH_2Cl_2	100	6 (*R*)
16	**11**	2/1	CH_2Cl_2	100	7 (*R*)

Table 2
Allylic amination of **12** with di-*n*-propylamine

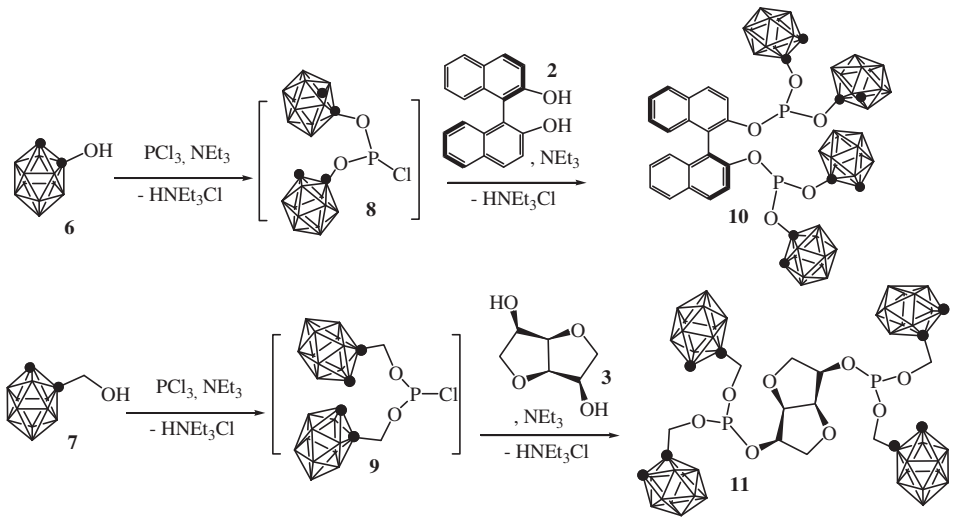
Entry	Ligand	L/Pd	Solvent	Conv. (%)	ee of 14 (%)[a]
1	**4**	2/1	CH_2Cl_2	30	20 (–)
2	**5**	2/1	CH_2Cl_2	60	41 (–)
3	**10**	2/1	CH_2Cl_2	90	**60** (–)
4	**11**	2/1	CH_2Cl_2	64	41 (–)

[a] The sign of specific rotation of the product **14** is given in parentheses.

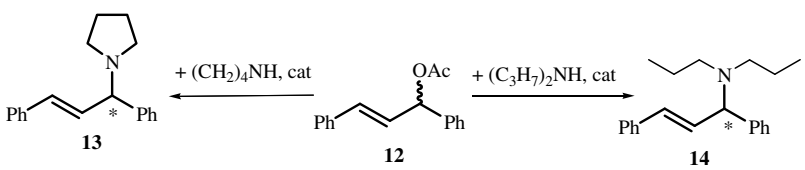
the best combination of activity and enantioselectivity was achieved with dichloromethane as solvent and L/Pd molar ratio (2/1).

We also screened ligands **4**, **5** and **10**, **11** in the closely related reaction of **12** with di-*n*-propylamine (Scheme 3 and Table 2) using conditions that provided optimum tradeoff between enantioselectivities and reaction rates, i.e., a ligand-to-palladium ratio of 2/1 and CH_2Cl_2 as solvent. In general, they follow the same trends as for the allylic alkylation with pyrrolidine. However, the enantiomeric excesses were slightly lower (ee's up to 60%), the most sterically congested ligand **10** providing maximum enantioselectivity and conversion.

In summary, we have designed and synthesized the first representatives of sterically congested carborane-containing chiral diphosphite ligands for asymmetric catalysis. It has been found that in allylic amination of (*E*)-1,3-diphenylallyl acetate with pyrrolidine and di-*n*-propylamine maximum enantioselectivities (up to 83% ee) were obtained with the bulkiest diphosphite **10** bearing tetracarboranyl phosphorus center. Further modification of carboranyl part, for example, introduction of different organic substituents in the $C_2B_{10}H_{12}$ fragment or modification of carboranyl part itself (e.g. use of *meta*- or *para*-carboranes which have very



Scheme 2. Synthesis of ligands **10**, **11**.



Scheme 3. Pd-catalyzed allylic amination of **12** with benzylamine and di-*n*-propylamine (20 °C).

different electronic properties [7]), may improve enatioselectivity. Such experiments are in progress.

3. Experimental

All reactions were carried out under a dry argon atmosphere in freshly dried and distilled solvents. ^{1}H (400.13 MHz), ^{13}C (100.61 MHz), ^{11}B (128.38 MHz) and ^{31}P (161.98 MHz) NMR spectra were recorder with a Avance 400 instrument. Complete assignment of all the resonances in ^{13}C NMR spectra was achieved by the use of *J*-mode techniques. Chemical shifts (ppm) are given relative to Me_4Si (^{1}H and ^{13}C), 85% H_3PO_4 (^{31}P NMR) and $BF_3{}^{*}Et_2O$ (^{11}B NMR). Elemental analyses were performed at the Laboratory of Microanalysis (Institute of Organoelement Compounds, Moscow). 2-Chloro-5,6-carborano-1,3,2-dioxaphosphepine (**1**) [9], 1-hydroxy-*ortho*-carborane (**6**) and 1-methyloxy-*ortho*-carborane (**8**) were prepared as published [10]. Enantiomeric excesses of the product **13** and conversion of **12** were determined by HPLC (Chiralcel OD-H, 200/1/0.1 hexane/*i*-PrOH/$HNEt_2$), 1 mL/min, 254 nm, *t*(*R*-**13**) = 5.2 min, *t*(*S*-**13**) = 6.1 min, *t*(*R*,*S*-**12**) = 12.2 and 13.9 min. Enantiomeric excesses of the product **14** was determined by HPLC (Chiralcel OD-H, 1000/1/1 hexane/*i*-PrOH/$HNEt_2$), 0.4 mL/min, 254 nm, *t*("+" **14**) = 8.0 min, *t*("−" **14**) = 9.1 min, *t*(*R*,*S*-**12**) = 12.2 and 13.9 min. The conversion of **12** was determined according to ^{1}H NMR.

3.1. Preparation of ligands *4*, *5* (general technique)

The phosphorylating reagent **1** 0.269 g (1 mmol) was added to a vigorously stirred solution of **2** or **3** (0.5 mmol) and NEt_3 (1 mmol) in toluene (20 ml). The mixture was then heated to the boiling point, stirred for 0.5 h and cooled to 20 °C. Solid HEt_3NCl was filtered off, and the filtrates concentrated in vacuo (40 Torr). The crude products **4**, **5** were purified by flash column chromatography (silica gel, toluene) to give the desired products. Yields: 65% for **4** and 68% for **5**.

3.2. (Sa,Sa)-2,2′-bis-(1,2-Carborano[1,2-d]-1,3,2-dioxaphosphepine-4-yloxy)-1,1′-binaphthyl (*4*)

White solid, m.p. 130–132 °C (dec). ^{31}P {H} NMR ($CDCl_3$): = 120.99. ^{11}B NMR ($CDCl_3$): −3.33 (m, 4B), −10.97 (м, 16B). ^{13}C {H} NMR ($CDCl_3$): 63.63 (d, *J* = 5.9, CH_2O), 75.92 (d, *J* = 9.1 Hz, C carborane), 119.58 (d, *J* = 12.1 Hz), 121.99, 125.41, 125.57, 127.41, 128.15, 130.48, 130.61, 133.43, 147.27 (d, *J* = 9.5 Hz, aryl all). Anal. Calc. for $C_{28}H_{40}B_{20}O_6P_2$: C, 44.79; H, 5.37; B, 28.80. Found: C, 44.92; H, 5.48; B, 28.72%.

3.3. 3,6-bis-(1,2-Carborano[1,2-d]-1,3,2-dioxaphosphepine-4-yloxy)-(3R,3S,6R,6S)-hexahydrofuro[3,2-b]furan (*5*)

White solid, m.p. 108–110 °C (dec). ^{31}P {H} NMR ($CDCl_3$): = 133.91. ^{11}B NMR ($CDCl_3$): −3.33 (m, 4B), −10.52 (m, 16B). ^{13}C {H} NMR ($CDCl_3$): 63.70 (s, CH_2O), 71.50 (d, *J* = 6.6 Hz, CH_2O), 74.08 (d, *J* = 16.4 Hz, CHOP), 76.28 (d, *J* = 12.6 Hz, C carborane), 80.94 (d, *J* = 2.0 Hz, CH). Anal. Calc. for $C_{14}H_{36}B_{20}O_8P_2$ (%): C, 27.54; H, 5.94; B, 35.14. Found: C, 27.68; H, 5.87; B, 35.02%.

3.4. Preparation of ligands *10*, *11* (general technique)

A solution of corresponding 1-hydroxy-*ortho*-carborane (**6**) (4.5 mmol) or 1-methyloxy-*ortho*-carborane (**8**) and Et_3N 0.63 ml (4.5 mmol) in toluene (15 ml) was added dropwise at 20 °C over 20 min to a vigorously stirred solution of PCl_3 0.2 ml (2.25 mmol) in toluene (25 ml). The mixture was then heated to the boiling point, stirred for 10 min and cooled to 20 °C. To a solution of intermediate **8** or **9** was added corresponding diol **2** or **3** (1.125 mmol) and Et_3N 0.315 ml (2.25 mmol). The mixture was then heated to the boiling point, stirred for 30 min and cooled to 20 °C. Solid HEt_3NCl was filtered off, and the filtrates concentrated in vacuo (40 Torr). The crude products **10**, **11** were purified by flash column chromatography (silica gel, toluene) to give the desired products. Yields: 50% for **10** and 45% for **11**.

3.5. (Sa)-2,2′-bis-(di-1-Carboranylphosphito)-1,1′-binaphthyl (*10*)

White solid moderately soluble in organic solvents, m.p. 144–148 °C (dec). ^{31}P {H} NMR ($CDCl_3$): = 144.56. ^{11}B NMR ($CDCl_3$): 2.38 (s, 8B), −9.21 (s, 8B), −13.61 (m, 20B), −14.74 (s, 4B). ^{1}H NMR ($CDCl_3$): 1.25–2.81 (м, 40 H, BH); 3.53 (c, 4H, CHcarborane); 7.09–7.99 (м, 12 H, Aryl). Anal. Calc. for $C_{28}H_{56}B_{40}O_6P_2$: C, 34.12; H, 5.74; B, 43.99. Found: C, 34.23; H, 5.89; B, 43.80%.

3.6. 3,6-bis-(di-Carboran-1-ylmethylphosphito)-(3R,3S,6R,6S)-hexahydrofuro[3,2-b]furan (*11*)

White solid, m.p. 102–104 °C (dec). ^{31}P {H} NMR ($CDCl_3$): = 137.26. ^{11}B NMR ($CDCl_3$): −2.24 (s, 4B), −4.26 (s, 4B), −8.84 (m, 8B), −10.23–15.36 (m, 24B). ^{13}C {H} NMR ($CDCl_3$): 58.26 (s, CHcarborane), 64.44 (d, *J* = 12.8 Hz, CH_2O-carborane), 68.62 (s, Ccarborane), 71.76 (d, *J* = 5.14 Hz, CH_2O), 73.76 (d, *J* = 11.7 Hz, CHOP), 80.92 (s, CH). Anal. Calc. for $C_{18}H_{60}B_{40}O_8P_2$: C, 24.05; H, 6.73; B, 48.10. Found: C, 24.18; H, 6.82; B, 48.01%.

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