Carboranyl phosphites: the electronic effect in the Suzuki—Miyaura reaction

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Isomeric carborane-containing phosphite ligands possessing different electronic properties have been synthesized. Their use in the Pd-catalyzed Suzuki—Miyaura reaction involving activated aryl bromides showed that phosphite with 9-*o*-carborane substituent has proved more efficient, with carboranyl phosphite having 1-*m*-carborane fragment being more efficient in the reactions with nonactivated aryl bromides.

Key words: carboranes, cross-coupling, phenylboronic acid, aryl halides, phosphites.

Activity of a metal complex catalyst considerably depends on the steric and electronic structure of the ligands used. Bulky ligands can have a positive effect on the catalytic process.[1—4] Usually, it is more difficult to evaluate electronic effect of the ligand, which also affects properties of the catalyst,[5—7] since introduction of electron-donating or electron-withdrawing substituents into it is frequently accompanied by the change in the ligand shape and size.

Dicarba-*closo*-dodecaboranes, existing in the *ortho*-, *meta*-, and *para*-isomeric forms, are bulky spherical structures, whose electronic properties change within a wide range depending on position of boron atoms in the carborane framework.[8] In this case, spatial structure of the isomers remains virtually unchanged, that makes them attractive objects for the study of electronic effects of ligands. Recently,[9—13] we have reported on the synthesis and use in metal complex catalysis of a series of mono- and bidentate phosphite-type ligands containing isomeric carborane substituents. It was shown that catalytic characteristics of the ligands can be optimized by varying a carborane fragment on the phosphorus atom. In this work, we report on the results of testing isomeric phosphite ligands containing 9-*o*-carborane and 1-*m*-carborane groups in the Suzuki—Miyaura reaction, which is a convenient method for the creation of carbon—carbon bonds, in particular, in biaryls widely used for the preparation of biologically active drugs, as well as in polymeric materials.[14,15]

Results and Discussion

The reaction of phosphorylating agent **1** with 1-hydroxy-*m*-carborane **2** and 9-hydroxy-*o*-carborane **3** afforded new carborane-containing phosphites **4** and **5** (Scheme 1). Compounds **4** and **5** are white powders stable on prolonged standing.

Their efficiency as ligands was studied in the Pd-catalyzed cross-coupling reactions of phenylboronic acid **6** with aryl bromides **7—12**, leading to the formation of biaryls **13—18** (Scheme 2, Table 1).

Scheme 1

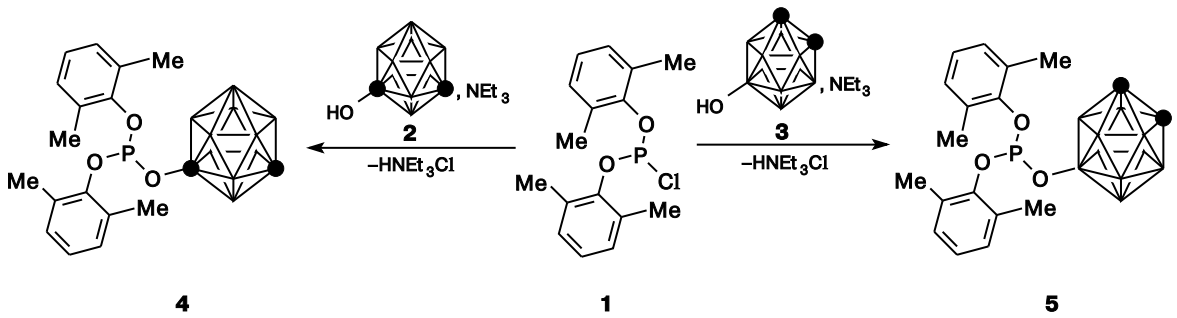

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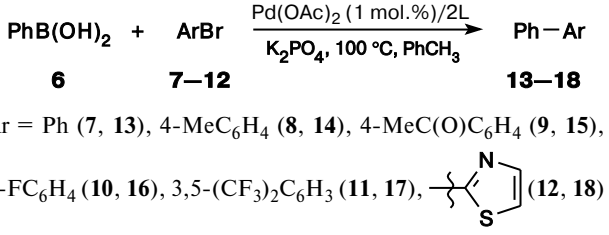
Table 1. Pd-Catalyzed cross-coupling of phenylboronic acid with aryl bromides*

Entry	Ligand	Substrate	Conversion of ArBr (%)
1	**4**	**7**	60
2	**5**	**7**	45
3	**4**	**8**	62
4	**5**	**8**	35
5	**4**	**9**	75
6	**5**	**9**	97
7	**4**	**10**	43
8	**5**	**10**	60
9	**4**	**11**	97
10	**5**	**11**	99
11	**4**	**12**	55
12	**5**	**12**	80

* 1.0 equiv. of ArBr, 1.4 equiv. of $PhB(OH)_2$, 3 equiv. of K_3PO_4, 5 mL of toluene, 0.01 equiv. of $Pd(OAc)_2$, 0.02 equiv. of L, 100 °C, 4 h.

Scheme 2



Ar = Ph (**7**, **13**), 4-MeC_6H_4 (**8**, **14**), 4-$MeC(O)C_6H_4$ (**9**, **15**), 4-FC_6H_4 (**10**, **16**), 3,5-$(CF_3)_2C_6H_3$ (**11**, **17**), (**12**, **18**)

The reaction outcome depends on the donor-acceptor characteristics of the ligands. In the reaction with involvement of bromobenzene **7** and 4-bromotoluene **8**, the conversion in the presence of phosphite **4** containing electron-withdrawing 1-*m*-carboranyl group ($\delta_i = +0.21$)[8] was higher than in the presence of ligand **5** bearing electron-donating 9-*o*-carborane fragment ($\delta_i = -0.23$)[8] (Table 1, entries *2*, *4*). In the reactions with involvement of aryl bromides containing electron-withdrawing substituents, *i.e.*, 4-bromoacetophenone (**9**), 1-bromo-4-fluorobenzene (**10**), and 1-bromo-3,5-bis(trifluoromethyl)benzene (**11**), as well as 2-bromotoluene (**12**), another situation was observed (see Table 1, entries *5—12*). In these cases, when ligand **5** with a donating 9-*o*-carborane group was used, higher conversion was observed than upon use of carboranyl phosphite **4**.

In conclusion, we have synthesized isomeric carboranyl phosphite ligands containing electron-donating 9-*o*-carborane and electron-withdrawing 1-*m*-carborane group. The use of these ligands in the Pd-catalyzed cross-coupling reaction of phenylboronic acid with activated aryl bromides showed higher efficiency of phosphite with 9-*o*-carborane substituent. Conversely, in the reactions with nonactivated aryl bromides carboranyl phosphite with 1-*m*-carborane fragment gives better results.

Experimental

^{31}P and ^1H NMR spectra (^{31}P, 121.49 MHz; ^1H, 300.13 MHz) were recorded on an Avance 400 spectrometer, ^{11}B NMR spectra (128.4 MHz), on an Avance 300 spectrometer, relatively to 85% aqueous H_3PO_4 in D_2O, Me_4Si, and $BF_3 \cdot OEt_2$, respectively (for solutions in $CDCl_3$). Elemental analysis was performed in the Laboratory of Microanalysis of the A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences.

All the reactions were carried out under dry argon in anhydrous solvents. Bis(2,6-dimethylphenyl) chlorophosphite (**1**),[16] 1-hydroxy-*m*-carborane (**2**),[17] 9-hydroxy-*o*-carborane (**3**)[18] were obtained according to the known procedures. Phenylboronic acid **6**, aryl bromides **7—12**, and palladium acetate were commercially available from Aldrich.

Synthesis of ligands 4 and 5. Hydroxycarborane **2** or **3** (160 mg, 1 mmol) and triethylamine (0.135 mL, 1 mmol) were added to a solution of phosphorylating agent **1** (309 mg, 1 mmol) in benzene (20 mL) with stirring. The reaction mixture was heated to boiling point and cooled to ~20 °C. A precipitate of $HNEt_3Cl$ was filtered off. A solution obtained was subjected to flash-chromatography on silica gel (benzene). The solvent was evaporated *in vacuo* to obtain ligand **4** or **5** as an oil solidified on standing.

Bis(2,6-dimethylphenyl)-*m*-carboran-1-yl phosphite (4). The yield was 380 mg (88%). Found (%): C, 49.80; H, 6.92; P, 7.02. $C_{18}H_{29}B_{10}O_3P$. Calculated (%): C, 49.99; H, 6.78; P, 7.16. ^1H NMR, δ: 7.12—6.91 (m, 6 H, Ar); 2.72 (s, 1 H, CH carb.); 2.30 (s, 12 H, 4 Me); 3.74—1.02 (m, 10 H, BH). $^{31}P\{^1H\}$ NMR, δ: 141.8. $^{11}B\{H\}$ NMR, δ: −4.89 (s, 1 B); −11.67 (s, 1 B); −12.93 (s, 2 B); −14.70 (s, 1 B); −15.98 (m, 5 B).

Bis(2,6-dimethylphenyl)-*o*-carboran-9-yl phosphite (5). The yield was 302 mg (70%). Found (%): C, 50.12; H, 6.85; P, 7.06. $C_{18}H_{29}B_{10}O_3P$. Calculated (%): C, 49.99; H, 6.78; P, 7.16. ^1H NMR, δ: 7.02—6.85 (m, 6 H, Ar); 3.25 (s, 2 H, CH carb.); 2.29 (s, 12 H, 4 Me); 3.11—0.98 (m, 9 H, BH). $^{31}P\{^1H\}$ NMR, δ: 141.8 (q, $J_{P,B}$ = 16.7 Hz). $^{11}B\{H\}$ NMR, δ: 12.14 (s, 1 B); −3.80 (s, 1 B); −10.51 (s, 2 B); −13.45—19.50 (m, 6 B).

Suzuki—Miyaura cross-coupling reaction. Palladium diacetate (2 mg, 0.01 mmol), ligand **4** or **5** (8 mg, 0.02 mmol), and toluene (5 mL) were placed into a Schlenk vessel, followed by addition of the corresponding haloarene **7—12** (1 mmol), phenylboronic acid (**6**) (171 mg, 1.4 mmol), and K_3PO_4 (637 mg, 3 mmol). The mixture was stirred for 4 h at 100 °C, cooled to 20 °C, diluted with hexane (10 mL), filtered through a layer of silica gel, and analyzed by GC and ^1H NMR spectroscopy after isolation of the reaction products by column chromatography.

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