Short communication

# Chiral cationic diamidophosphite: Novel effective ligand for Pd-catalysed enantioselective allylic substitution

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## Abstract

Novel diamidophosphite ligand bearing alkylammomium fragment was prepared by a one-step phosphorylation of a quaternised aminoalcohol. The ionic ligand demonstrated high enantioselectivity in the Pd-catalysed allylic substitution of 1,3-diphenylallyl acetate (up to 99% ee).
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## 1. Introduction

Chiral monodentate phosphites and diamidophosphites represent very attractive group of ligands for asymmetric metal-complex catalysis because of their synthetic availability, high resistance to oxidative destruction and their low cost [1]. No less important, P-monodentate phosphite-type compounds showed excellent results in enantioselective Rh-catalysed hydrogenation, Cu-catalysed addition of organozinc reagents, Ir- and Pd-catalysed allylic substitution, Pd-catalysed hydrosilylation-oxidation and Ru-catalysed hydrogenation of ketones [2–8]. In comparison with traditional phosphines, optically active phosphites and amidophosphites seem to be more versatile ligands. Indeed, electronic properties of the traditional for phosphines PPh$_2$-fragment can be regulated basically only by introduction of electron-donor or electron-acceptor substituents into the phenyl rings. In contrast, phosphites provide broad opportunities for fine tuning of their donor–acceptor and steric properties by incorporation of oxygen and/or nitrogen into the first coordination sphere of phosphorus and wide variation of the O- and N-containing building blocks [9]. This approach is now considered most practical to developing one universal ligand for different types of asymmetric catalytic reactions.

We have developed a new effective chiral monodentate cationic diamidophosphite ligand that is derived from a readily accessible quaternised aminoalcohol. It should be noted, that synthesis and catalytic use of achiral ionic phosphites is known (see [10] and the references cited therein), while there are practically no examples of chiral ionic phosphite-type ligands. The only exception are imidazolium-phosphites derived from (*1R,2R*)-*trans*-diaminocyclohexane, used in the synthesis of their carbene derivatives [11]. This is rather surprising, because optically active cationic phosphines and phosphinites have been successfully tested in asymmetric hydrogenation and allylic substitution (see [12,13] and references cited therein).

## 2. Experimental

### 2.1. General methods

$^1$H, $^{31}$P and $^{13}$C NMR spectra were recorded on a Bruker AMX-400 instrument at 400.13, 162.0 and 100.6 MHz, respectively. Chemical shifts (ppm) are given relative to Me$_4$Si ($^1$H, $^{13}$C NMR) and 85% H$_3$PO$_4$ ($^{31}$P NMR). Complete assignment of all the resonances in $^{13}$C NMR spectra was achieved by the use of DEPT techniques. Electrospray ionization (ESI) mass spectra were measured on a Finnigan LCQ Advantage mass spectrometer. Elemental analyses were performed at the Laboratory of Microanalysis (Institute of Organoelement Compounds, Moscow). Optical yields and conversion of product **7**,

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**8**, **9**, were determined using HPLC (Daicel Chiralcel OD-H column) according to the literature [6,14]. Optical yields of product **10** were determined using HPLC ((*R,R*)-WHELK-01 column)) according to the literature [6].

All reactions were carried out under a dry argon atmosphere in freshly dried and distilled solvents; Et$_3$N, Pr$_2$NH and pyrrolidine were twice distilled over KOH and then over a small amount of LiAlH$_4$ before use. Starting substrate **6** was synthesized as published [15]. Dimethyl malonate (dimethylamino)ethanol, BSA (*N,O*–bis(trimethylsilyl) acetamide), sodium *para*-toluene sulfinate were commercially available.

[Pd(allyl)Cl]$_2$ are synthesized using literature procedure [16]. The syntheses of palladium(II) complexes **3–5** were performed by techniques similar to that reported [6,14]. Catalytic experiments: allylic sulfonylation of substrate **6** with sodium *para*-toluene sulfinate, allylic alkylation with dimethyl malonate, allylic amination with pyrrolidine and with di-*n*-propylamine were performed according to the appropriate procedures [6,14].

## 2.2. Synthesis

### 2.2.1. N-(2-hydroxyethyl)-N,N-dimethylheptylammonium tetrafluoroborate (1)

A mixture of *N*-(2-hydroxyethyl)-*N,N*-dimethylheptyl-ammonium bromide (obtained similar to [10] without characterization) (10 g, 37 mmol), KBF$_4$ (14 g, 111 mmol) and dry acetonitrile (50 ml) was heated to reflux with stirring for 48. Upon cooling, the white precipitate was filtered off and washed with acetonitrile (3 × 20 ml). The organic filtrate was concentrated in vacuum to give paraffin-like product (8.652 g, 85% yield).

$^1$H NMR (CDCl$_3$, *J*(H,H)/Hz): $\delta$ = 0.85 (t, 3H, $^3J$ = 6.8), 1.24–1.32 (m, 8H), 1.71 (m, 2H), 3.23 (s, 6H), 3.42 (m, 2H), 3.58 (t, 2H, $^3J$ = 4.8), 4.05 (s, 2H), 4.61 (s, 1H). ESI-MS (CH$_3$CN): *m/z* (%): 188 (100) [M- BF$_4$]$^+$, 87 (100) [BF$_4$]$^-$. Anal. Calc. for C$_{11}$H$_{26}$NOBF$_4$ (%): C, 48.02, H, 9.52, N, 5.09%; found C, 48.14, H, 9.64, N, 5.17%.

### 2.2.2. (2R,5S)-1-(2-(3-phenyl-1,3-diaza-2-phosphabicyclo[3.3.0]octane)oxyethyl)-N,N–dimethyl-heptylammonium tetrafluoroborate (2)

A solution of the phosphorylating reagent [6] 1 g (4.2 mmol) in CH$_2$Cl$_2$ (15 ml) was added to a vigorously stirred solution of **1** 1.14 g (4.2 mmol) and NEt$_3$ 0.56 ml (4.2 mmol) in CH$_2$Cl$_2$ (15 ml). The mixture was stirred for additional 3 h. Obtained solution was washed with water (100 ml), dried over Na$_2$SO$_4$, filtered, and concentrated. The residue was purified by flash column chromatography (silica gel, CH$_2$Cl$_2$) to give the desired product as yellow oil. Yield: 1.47 g, 65%.

$^{31}$P {H} NMR (CDCl$_3$): $\delta_P$ = 121.82. 13. $^{13}$C NMR (CDCl$_3$): 13.49, 21.88, 22.00, 25.43, 25.65 (d, $^2J_{C,P}$ = 6.66 Hz), 28.11, 30.93, 31.78, 48.11(d, $^2J_{C,P}$ = 38.14 Hz), 50.94, 51.08, 54.11 (d, $^2J_{C,P}$ = 7.3 Hz), 54.95 (d, $^2J_{C,P}$ = 5.13 Hz), 62.96, 63.09 (d, $^2J_{C,P}$ = 8.80), 64.78, 114.30(d, $^3J_{C,P}$ = 12.40 Hz), 118.98, 128.85, 144.39 (d, $^2J_{C,P}$ = 14.6 Hz). ESI-MASS (CH$_3$CN): *m/z* (%): 392 (100) [M − BF$_4$]$^+$. Anal. Calc. for C$_{22}$H$_{39}$BF$_4$N$_3$OP: C, 55.12, H 8.20, N, 8.77%; found C 55.18, H 8.24, N, 8.72(%).

## 2.3. Palladium complexes

*Characterization data for* **3**: $^{31}$P {H} NMR (CDCl$_3$): $\delta_P$ = 123.5. ESI-MASS (CH$_3$CN): *m/z* (%): 576 (82) [M − BF$_4$]$^+$), 625 (100) [M − Cl ]$^+$. Anal. Calc. for C$_{25}$H$_{44}$BClF$_4$N$_3$OPPd: C 45.34, H 6.70, N 6.34%; found: C 45.41, H 6.81, N 6.25%.

*Characterization data for* **4**: $^{31}$P {H} NMR (CDCl$_3$): $\delta_P$ = 115.5 (broad) ppm. Anal. Calc. for C$_{47}$H$_{83}$B$_3$F$_{12}$N$_6$O$_2$P$_2$Pd: C 47.32, H 7.01, N 7.04%; found C 47.41, H 7.14, N 6.91%.

## 3. Results and discussion

The quaternised tetrafluoroborate aminoalcohol **1** was easily prepared by anion exchange from its bromide precursor (Scheme 1).

Novel cationic diamidophosphite ligand **2** was synthesized by a direct phosphorylation of the corresponding substrate **1** in CH$_2$Cl$_2$ (Scheme 2).

Interestingly, despite the ionic nature, compound **2** is readily soluble in commonly used solvents such as CH$_2$Cl$_2$, CHCl$_3$ or THF and stable enough to tolerate washing of its solute in CH$_2$Cl$_2$ with water.
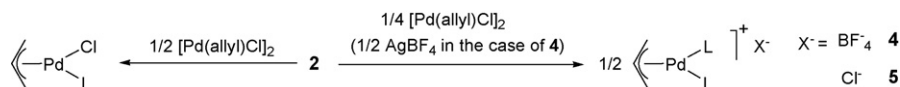
The required palladium catalysts (Scheme 3) were prepared from the ionic diamidophosphite **2**. Compounds **3**, **4**, as well as the complex **5** formed from [Pd(allyl)Cl]$_2$ and the corresponding ligand **2** *in situ*, were tested in the asymmetric Pd-catalysed
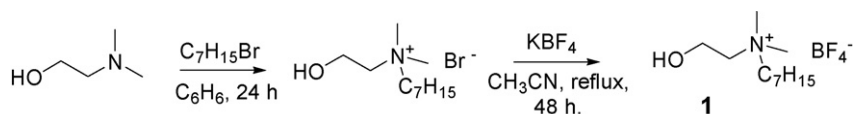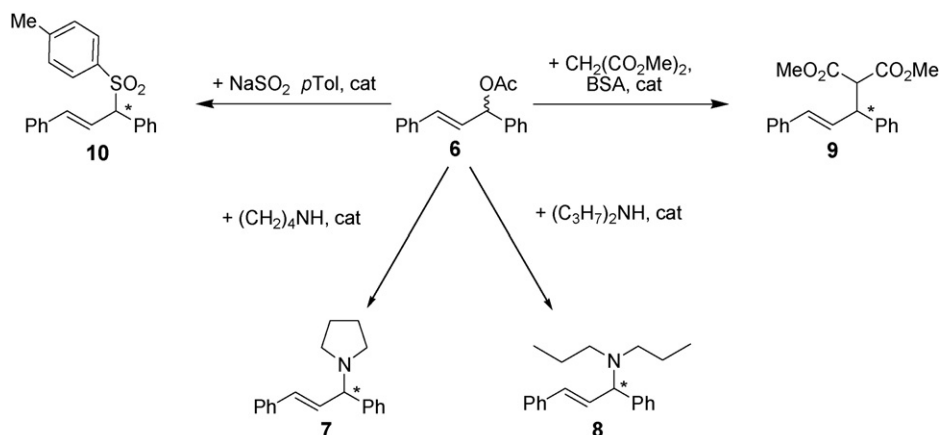


Scheme 1. Synthesis of quaternised aminoalcohol.
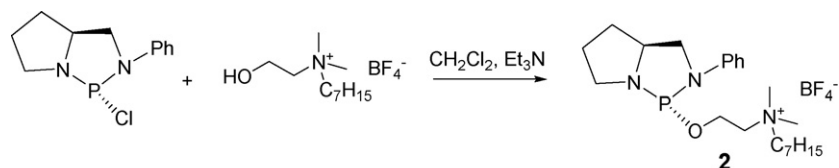


Scheme 2. Synthesis of cationic ligand.

Scheme 3. Complexation of the ligand with Pd (II).



Scheme 4. Pd-catalysed enantioselective allylic substitution.

allylic allylation using 1,3-diphenyl-2-propenyl acetate **6** as substrate.

The neutral **3** and cationic **4**, **5** palladium complexes showed from good to excellent enantioselectivities in the asymmetric Pd-catalysed allylic amination, alkylation and sulfonylation (Scheme 4).

In the Pd-catalysed allylic amination of 1,3-diphenylallyl acetate **6** with pyrrolidine (Scheme 4 and Table 1), cationic complex **5** demonstrated high asymmetric induction (90% ee, Table 1, entry (6) in THF. Its tetrafluoroborate analogue **4** was less efficient (up to 77% ee, Table 1, entry (4). Interestingly, when THF was used as a solvent instead of $CH_2Cl_2$, the enantioselectivities in all cases were better.

The maximum described so far optical yield (99% ee) for product **8** (Scheme 4) was obtained by the use of the cationic palladium complex **5** in THF (Table 2, entry 4). Neutral complex **3** provided up to 93% ee in the same solvent (Table 2, entry 2). It is remarkable, that this cationic monodentate diamidophosphite ligand **2** exceeds the best previously reported result (90% ee) obtained with its analogues not containing any ionic fragment [14]. Cationic complex **4** was also tested as catalysts for the allylic amination in an ionic liquid medium (1-butyl-3-methylimidazolium tetrafluoroborate (IL)). In the first catalytic cycle, 74% ee and quantitative conversion were obtained in 12 h (Table 2, entry 5). However, a second cycle suffered from a

Table 2
Enantioselective allylic amination of **6** with di-$n$-propilamine (20 °C, 48 h)

| Entry | Catalyst | Solvent | Conversion (%) | ee[a] (%) |
|---|---|---|---|---|
| 1 | **3** | $CH_2Cl_2$ | 100 | 91 (+) |
| 2 | **3** | THF | 70 | 93 (+) |
| 3 | **4** | $CH_2Cl_2$ | 68 | 94 (+) |
| 4 | **4** | THF | 95 | **99** (+) |
| 5 | **4** | IL (first cycle)[b] | 100 | 73 (+) |
| 6 | **4** | IL (second cycle)[b] | 35 | 74 (+) |
| 7 | **5** | $CH_2Cl_2$ | 95 | 90 (+) |
| 8 | **5** | THF | 40 | 77 (+) |

[a] The sign of specific rotation of the product **8** is given in parentheses.
[b] 12 h.

considerable drop in activity of the recovered catalyst (Table 2, entry 6).

In allylic alkylation of **6** with dimethyl malonate, neutral complex **3** afforded product **9** with low ee's (Table 3, entries 1 and 2). On the contrary, cationic complex **4** provided up to 90% ee (Table 3, entry 3). Its chloride analogue **5** showed an almost equal enantioselectivity (up to 89% ee, Table 3, entry 5) and good conversion in $CH_2Cl_2$. It should be noted, that under the conditions of catalytic allylic alkylation comparable with those described for ligand **2**, carben-derivatives of (*1R,2R*)-*trans*-diaminocyclohexane-based imidazolium-phosphites ensures 42% ee [11] only.

Table 1
Enantioselective allylic amination of **6** with pyrrolidine (20 °C, 48 h)

| Entry | Catalyst | Solvent | Conversion (%) | ee (%) |
|---|---|---|---|---|
| 1 | **3** | $CH_2Cl_2$ | 68 | 73 (R) |
| 2 | **3** | THF | 70 | 80 (R) |
| 3 | **4** | $CH_2Cl_2$ | 35 | 23 (R) |
| 4 | **4** | THF | 70 | 77 (R) |
| 5 | **5** | $CH_2Cl_2$ | 92 | 87 (R) |
| 6 | **5** | THF | 70 | **90** (R) |

Table 3
Enantioselective allylic alkylation of **6** with with dimethyl malonate (BSA, KOAc, 20 °C, 48 h)

| Entry | Catalyst | Solvent | Conversion (%) | ee (%) |
|---|---|---|---|---|
| 1 | **3** | $CH_2Cl_2$ | 65 | 20 (S) |
| 2 | **3** | THF | 100 | 1 (S) |
| 3 | **4** | $CH_2Cl_2$ | 70 | **90** (S) |
| 4 | **4** | THF | 61 | 86 (S) |
| 5 | **5** | $CH_2Cl_2$ | 85 | 89 (S) |
| 6 | **5** | THF | 3 | 1 (S) |

Table 4
Pd-catalysed allylic sulfonylation of **6** with NaSO$_2$*p*Tol (20 °C, 48 h, THF)

| Entry | Catalyst | Yield (%) | ee (%) |
|-------|----------|-----------|--------|
| 1 | **3** | 74 | **83** (*S*) |
| 2 | **4** | 22 | 3 (*S*) |
| 3 | **5** | 50 | 64 (*S*) |

The ionic diamidophosphite **2** has been found to be a good stereoselector in the Pd-catalysed allylic sulfonylation of **6**, generating up to 83% ee (Table 4, entry 1). In this case, the neutral complex **3** was the most effective. Cationic catalysts **4**, **5** afforded moderate to poor enantioselectivity for product **10**.

## 4. Conclusions

In summary, we have prepared and characterized the first representative of a new class of monodentate phosphite-type ligands bearing an alkylammonium fragment. The advantage for using such ligands is that they can be made from cheap aminoalcohols. No less important, the ionic diamidophosphite is an excellent ligand in the Pd-catalysed allylic substitution (up to 99% ee). It is also attractive candidate for other asymmetric transition-metal-catalysed reactions, and for development of reusable catalytic systems (for example see [13,17]).

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