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Niew Bidentate Diphosphine Ligands on the Basis of Diphenyl Ether

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Abstract—A new procedure has been developed for the preparation of new bidentane diphosphine ligands, 2,2′-diphosphinodiphenyl ethers containing various substituents on the phosphorus, which differ in both electron-donor and steric parameters.

In the recent years, bidentate P,P- and P,N-ligands derived from *o*,*o′*-disubstituted aromatic and heteroaromatic compounds (such as biphenyl, binaphthyl, ferrocene, and diphenyl ether and its analogs linked through positions *6* and *6′* by a heteroatom bridge), have become of specific importance [1–3] for metal-complex catalysis. These ligands are capable of forming complexes with transition metals, which possess a rigid skeleton having 4–5 units between the donor atoms. As compared with monophosphine ligands, as well as with those based on α,ω-diphosphinoalkanes, the above complexes turned out to be more effective; they ensured mild conditions and high conversion and regio- and stereoselectivity of a number of reactions, e.g., hydroformylation [4] and hydrocyanation of alkenes [5, 6], allylic alkylation [7] and arylation of amines [8, 9], etc. Sagighi *et al.* [8] studied cross coupling of aniline with 4-bromo-*N*,*N*-dimethylaniline and found that replacement of the diphenylphosphino groups in the catalyst, 2,2′-bis-(diarylphosphino)diphenyl ether complex with Pd(0), by di(*o*-tolyl)phosphino groups increases the conversion from 30 to 80%. The effect of steric properties of such ligands on the catalytic activity and selectivity of metal complexes in the arylation of amines was discussed in [10–12]. It was presumed [10] that complexes with sterically hindered ligands favor the oxidative addition stage due to ready dissociation of one of the phosphine centers; however, in the reactions with fatty amines β-hydride reduction of allyl bromide is considerably accelerated [11].

The lack of sufficient data on the effect of steric parameters of complexes on their catalytic activity prompted us to synthesize a number of new bidentate ligands on the basis of diphenyl ether. Unlike the known [13] ligand with diphenylphosphino groups, we obtained its analogs having secondary or tertiary radicals or both these on the phosphorus, as well as petafluorophenyl group which is a stronger electron acceptor than phenyl. Comparison of the catalytic activities of palladium complexes with ligands in which both steric and donor parameters of the phosphorus atom are varied could allow us to estimate the role of key stages (such as oxidative addition of aromatic substrate and, especially, the subsequent nucleophile replacement in the palladium complex) in cross coupling reactions.

2,2′-Diphosphinodiphenyl ethers **IIa**–**IIg** were synthesized by a modified procedure [13]. Diphenyl ether was treated with butyllithium in the presence of *N*,*N*,*N′*,*N′*-tetramethylethylenediamine (TMEDA), and the resulting dilithium derivative **I** was treated with appropriate chlorophosphine (Scheme 1). Our procedure differed from that reported in [13] by the following. First of all, we used 2 equiv of butyllithium instead of 2.2 equiv of more difficultly accessible *s*-butyllithium. Second, the phosphorylation of salt **I** was also effected with 2 rather than 2.2 equiv (as in [13]) of halophosphine. Under optimal conditions, the yields of products **II** were almost quantitative (according to the ^{31}P NMR data), except for ligand **IIe** (72%, ^{31}P NMR); moreover, our procedure ensured easier isolation of the target products. The yields of the isolated products were 55–75% because of their ready oxidation in solution. However, often there is no need of isolating pure ligands, for palladium complexes can be prepared from crude products **II**.

The reaction of butyllithium with TMEDA is accompanied by a strong exothermic effect (the mixture warms up to 50–55°C) and formation of a colorless

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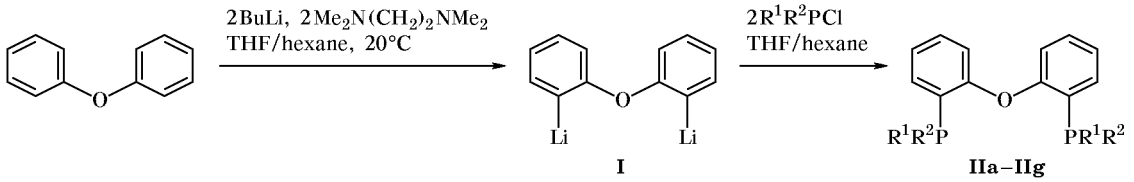
Scheme 1.



$R^1 = R^2$ = Ph (**a**), *cyclo*-C_6H_{12} (**b**), *i*-Pr (**c**), *t*-Bu (**d**), C_6F_5 (**e**); R^1 = *i*-Pr, R^2 = *t*-Bu (**f**); R^1 = *t*-Bu, R^2 = Ph (**g**).

precipitate. The latter dissolves completely by the end of addition of TMEDA. After cooling to room temperature, 1 equiv of diphenyl ether was added, and the mixture was stirred for 16–24 h at 20°C. Salt **I** thus obtained was treated with 2 equiv of appropriate chlorophosphine in hexane. The reactions with dialkylchlorophosphines having secondary and especially tertiary alkyl radicals required elevated temperature because of reduced electrophilicity and (what is more important) increased steric hindrance at the phosphorus atom. For example, diphenylchlorophosphine reacts with salt **I** at 20°C in several hours, whereas reactions with branched dialkylchlorophosphines occurred at 60°C (reaction time 2–4 h); the conversion of diisopropylchlorophosphine at 20°C in 24 h was 70%. The most electrophilic bromobis(pentafluorophenyl)phosphine reacts with salt **I** very vigorously even at room temperature; the reaction is accompanied by strong heat evolution and profound tarring, presumably as a result of reaction of butyllithium with fluorine atoms in the pentafluorophenyl groups. By carrying out the reaction at low temperature (–50°C) we succeeded in obtaining ligand **IIe** in a good yield.

When treating the reaction mixtures and isolating products **II**, thoroughly degassed solvents and distilled water should be used; otherwise, ligands **II** undergo fast oxidation in solution. The isolation procedures and solvents for crystallization of the products were different for particular compounds **II** (see Experimental). Pure ligands **II** are colorless or light pink solid, amorphous, or finely crystalline substances (except for **IIf**). They are readily soluble in methylene chloride and chloroform and poorly soluble in ethanol. Solid ligands **II** can be stored for a long time under argon. The melting points of compounds **II** increase in going from *tert*-alkyl- to secondary alkyl-substituted derivatives and with rise in the number of phenyl groups on the phosphorus.

Ligands **II** ($R^1 = R^2$ = Alk) show in the ^{31}P NMR spectra narrow singlets in the range from –20 to +12 ppm, which are typical of tertiary phosphines like R^1R^2PPh. When $R^1 \neq R^2$ (compounds **IIf** and **IIg**), signals from diastereoisomeric ligands are broadened. The signal width is about 5 ppm; it is consistent with the difference between the ^{31}P chemical shifts of the *meso*-form and racemate ($\Delta\delta_P$ 0.5 to 10 ppm) [12]. The spectrum of **IIe** contains an anomalously upfield multiplet signal at δ_P –56.2 ppm due to coupling with fluorine nuclei.

The synthesis of palladium complexes with ligands **IIa**–**IIg** and study of their catalytic activity in the amination of aryl halides are now in progress.

EXPERIMENTAL

The ^{31}P NMR spectra were obtained on Varian FT-80A (32.2 MHz) and Varian VXR-400 (161.9 MHz) instruments using 85% H_3PO_4 as external reference. The ^1H NMR spectra were measured on Varian VXR-400 spectrometer relative to tetramethylsilane as internal reference. All operations were performed under dry argon. The solvents were purified by standard procedures. Chlorodiisopropylphosphine [14], di-*tert*-butylchlorophosphine [14], dicyclohexylchlorophosphine [14], chlorodiphenylphosphine [15], bromobis(pentafluorophenyl)phosphine [16], *tert*-butyl(chloro)phenylphosphine [17], and *tert*-butyl(chloro)isopropylphosphine [18] were synthesized by known methods.

General procedure for preparation of ligands II. A two-necked flask equipped with a dropping funnel and a reflux condenser was filled with argon and charged with 4.5 ml of a 2.64 N solution of butyllithium (11.8 mmol). *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine, 1.36 g (11.8 mmol), was added dropwise with stirring. The mixture spontaneously warmed up to 50–60°C, and a colorless material separated. The mixture became homogeneous by the end of addition of TMEDA. It was cooled to room temperature, and a solution of 1 g (5.9 mmol) of diphenyl ether in 3 ml of tetrahydrofuran was slowly added. The mixture was stirred for 16 h at 20°C. Further procedures were different for each particular ligand.

2,2′-Bis(diphenylphosphino)diphenyl ether (IIa). A solution of 2.6 g (11.8 mmol) of chlorodiphenylphosphine in 3.5 ml of petroleum ether was added dropwise with stirring to a mixture containing 5.9 mmol of dilithium salt **I** (see above). After 10 min, a colorless material began to separate from the solution. The mixture was stirred for 24 h at 20°C, 10 ml of degassed distilled water and 10 ml of methylene chloride were added, and the organic phase was separated, dried over sodium sulfate, and the solvent was removed under reduced pressure. After 1 h, the residue crystallized. It was dissolved in 10 ml of acetone at 40–45°C, the solution was cooled to room temperature, and the colorless precipitate was filtered off through a glass filter and dried under reduced pressure. Yield 2.4 g (78%), mp 183–184°C. ^{31}P NMR spectrum (CH_2Cl_2): δ_P –18.0 ppm. Published data [13]: mp 175–176°C; δ_P –16.4 ppm (in $CHCl_3$).

2,2′-Bis(dicyclohexylphosphino)diphenyl ether (IIb). A solution of 2.7 g (11.8 mmol) of chlorodicyclohexylphosphine in 3 ml of petroleum ether was added dropwise with stirring at 10°C to a solution of salt **I**. The mixture was heated for 4 h at 60°C, cooled, and treated as described above for ligand **IIa**. A light brown oily substance was isolated. It was treated with 5 ml of methanol, and the mixture was kept for a long time at –50°C for crystallization. The product was quickly filtered off through a glass filter, washed with acetone and petroleum ether cooled to –50°C (2 ml each), and dried under reduced pressure. Yield 1.9 g (59%), mp 159–160°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.07–1.26 m (24H), 1.54–1.73 m (16H), 1.84 d.m (4H), 6.73 d.d (2H, J = 2.9, 8.1 Hz), 7.07 d.t (2H, J = 0.7, 7.3 Hz), 7.25 d.t (2H, J = 1.1, 8.9 Hz), 7.52 d.t (2H, J = 1.1, 7.0 Hz). ^{31}P NMR spectrum (CH_2Cl_2): δ_P –7.06 ppm. Found, %: C 76.22; H 9.11. $C_{36}H_{52}OP_2$. Calculated, %: C 76.87; H 9.25.

2,2′-Bis(diisopropylphosphino)diphenyl ether (IIc). A solution of 1.83 g (11.8 mmol) of chlorodiisopropylphosphine in 2 ml of petroleum ether was added to a solution of salt **I** on cooling with water. The mixture was heated for 40 min at 55°C and cooled to room temperature, 10 ml of distilled water and 10 ml of methylene chloride were added, and the organic phase was separated and dried over magnesium sulfate. The solvent was removed under reduced pressure to leave an oily residue which was treated with 3 ml of methanol and 0.3 ml of ether. The mixture was kept for a long time at –10 to –15°C, and the colorless precipitate was filtered off, washed on a filter with methanol and acetone (2 ml) cooled to –20°C, and dried under reduced pressure. Yield 1.4 g (58%), mp 81.5–82°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.08 d.d (24H, J = 7.2, 14.0 Hz), 2.28–2.36 m (4H), 1.84 d.m (4H), 6.73 d.d (2H, J = 2.9, 8.1 Hz), 7.08 d.t (2H, J = 0.7, 8.0 Hz), 7.24 d.t (2H, J = 0.7, 8.2 Hz), 7.50 d.t (2H, J = 0.6, 6.8 Hz). ^{31}P NMR spectrum (CH_2Cl_2): δ_P 1.48 ppm. Found, %: C 72.29; H 9.12. $C_{24}H_{36}OP_2$. Calculated, %: C 71.64; H 8.96.

2,2′-Bis(di-*tert*-butylphosphino)diphenyl ether (IId). Following the above procedure, from 2.12 g (11.8 mmol) of di-*tert*-butylchlorophosphine and a solution of salt **I** (2.5 h at 60°C) we obtained 1.9 g (72%) of ligand **IId** as a yellow noncrystallizable oily substance, bp 170–175°C (1 mm). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.10–1.22 m (36H); the aromatic region of the spectrum was almost identical to that of ligand **IIc**. ^{31}P NMR spectrum (CH_2Cl_2): δ_P 11.23 ppm. Found, %: C 72.95; H 9.57. $C_{28}H_{44}OP_2$. Calculated, %: C 73.36; H 9.61.

2,2′-Bis[bis(pentafluorophenyl)phosphino]diphenyl ether (IIe). A solution of 2.6 g (5.88 mmol) of bromobis(pentafluorophenyl)phosphine in 3 ml of petroleum ether was added dropwise at –50°C to a mixture containing 2.94 mmol of salt **I**. When the entire amount of bromobis(pentafluorophenyl)phosphine was added, the mixture was allowed to slowly warm up to room temperature and was stirred for 1.5 h. We isolated 1.85 g (72%) of ligand **IIe** as an oily substance which crystallized on addition of 3 ml of acetone and cooling to –60°C. mp 151–154°C (decomp.). ^{31}P NMR spectrum (CH_2Cl_2): δ_P –56.2 ppm. Found, %: C 48.72; H 1.09. $C_{36}H_8F_{20}OP_2$. Calculated, %: C 48.11; H 0.89.

2,2′-Bis[*tert*-butyl(isopropyl)phosphino]diphenyl ether (IIf). Following the procedure described above for ligand **IId**, from 1.96 g (11.8 mmol) of *tert*-butyl(chloro)isopropylphosphine (4 h at 60°C) we obtained a light yellow mobile oily substance. It was subjected to vacuum distillation to isolate 1.5 g (65%) of ligand **IIf**, bp 162–168°C (1 mm) as a light yellow viscous oil which did not crystallize on prolonged storage at 20°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.98–1.38 m (32H); the aromatic region of the spectrum was almost identical to that of **IId**. ^{31}P NMR spectrum (CH_2Cl_2): δ_P 1.90–6.90 ppm. Found, %: C 71.97; H 9.15. $C_{26}H_{40}OP_2$. Calculated, %: C 72.59; H 9.30.

2,2′-Bis[*tert*-butyl(phenyl)phosphino]diphenyl ether (IIg). In a similar way, by reaction of 2.6 g (11.8 mmol) of *tert*-butyl(chloro)phenylphosphine with salt **I** on heating for 4 h at 55°C and appropriate treatment we obtained a brown oily substance which crystallized on addition of 3 ml of acetone and cooling

to 0°C. The colorless precipitate of ligand **IIg** was filtered off, washed on a filter with 1 ml of acetone, and dried. Yield 1.55 g (54%), mp 134–135°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.23–1.26 d (9H, J = 12.5 Hz), 6.47 d.d (2H, J = 2.7, 8.0 Hz), 6.83 d.t (2H, J = 0.7, 7.6 Hz), 7.03 d.t (2H, J = 0.5, 7.4 Hz), 7.15 d.t (2H, J = 0.8, 7.5 Hz), 7.28 m (6H), 7.50 m (4H). ^{31}P NMR spectrum (CH_2Cl_2): δ_P 0.2–1.3 ppm. Found, %: C 77.53; H 7.32. $C_{32}N_{36}OP_2$. Calculated, %: C 77.11; H 7.23.

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