

## 2,2'-Bis(diphenylphosphino)biphenyl revisited

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Received 5 May 1995

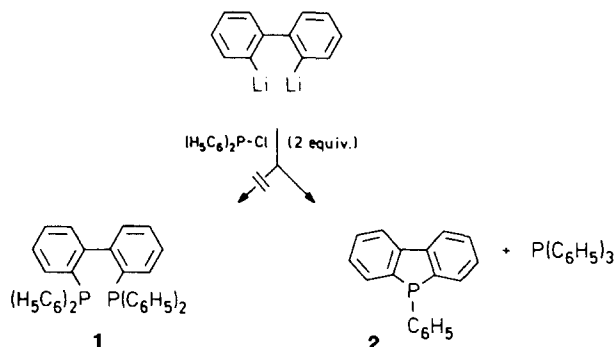
### Abstract

The reaction between 2,2'-dilithiobiphenyl and two equivalents of chlorodiphenylphosphine is confirmed to afford equal amounts of 9-phenyl-9-phosphafluorene (**2**) and triphenylphosphine. 2,2'-Bis(diphenylphosphino)biphenyl (1,1'-biphenyl-2,2'-diylbis(diphenylphosphine) (**1**)) can be conveniently prepared by Ullmann coupling of 2-iodophenyldiphenylphosphine oxide and subsequent reduction with trichlorosilane.

**Keywords:** 2,2'-Bis(diphenylphosphino)biphenyl; Phosphorus; Organolithium intermediates; Nucleophilic substitution

### 1. Introduction

“For the practical preparation of large amounts of ... (2,2'-bisdiphenylphosphinobiphenyl) a different ... (method) is obviously required”. This discouraging statement is the end of a communication by Miyamoto et al. [1] summarizing unsuccessful attempts to make this ligand according to a published procedure [2]. Treatment of 2,2'-biphenylenedilithium with two equivalents of chlorodiphenylphenylphosphine did not produce 2,2'-bis(diphenylphosphino)biphenyl (1,1'-biphenyl-2,2'-diylbis(diphenylphosphine oxide) bpbp (**1**)) as claimed by Uehara and Bailar [2] but rather gave a 1:1 mixture of 9-phenyl-9-phosphafluorene (5-phenyl-5*H*-benzo[*b*]-phosphindole (**2**)) and triphenylphosphine:



In the same article [2], the coordination of bisphosphine **1** with rhodium, the subsequent racemate resolution of the complex and its eventual utilization as a catalyst for the hydrogenation of 2-(acetamido)acrylic acid and 2-(acetamido)cinnamic acid to produce *N*-acetyl-(*R*)-alanine and *N*-acetyl-(*R*)-phenylalanine with measurable, although poor optical activities (13% ee at best) were described. Since this work was, and still is, considered to be a milestone in asymmetric synthesis, we wanted to check it.

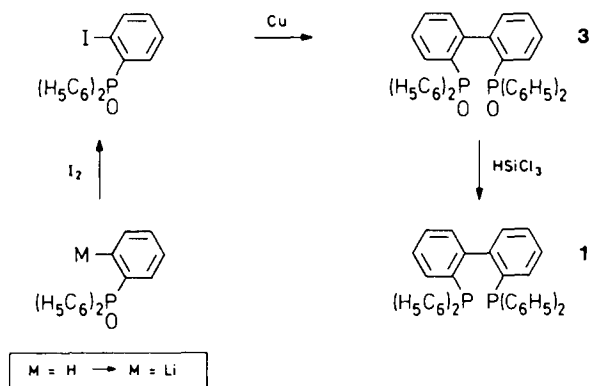
### 2. Results and discussion

First, our findings fully confirm the conclusions drawn by Miyamoto et al. [1]. 2,2'-Dilithiobiphenyl quantitatively condenses with chlorodiphenylphosphine to give equal amounts of 9-phenyl-9-phosphafluorene (**2**) and triphenylphosphine. The outcome of the reaction is independent of the mode of addition. When the lithium reagent is converted into a di(chloromagnesium) species prior to the addition of chlorodiphenylphosphine, biphenyl is the only identified product (90% or more) in tetrahydrofuran while a 1:2:2 mixture of the bisphosphine **1**, the phosphafluorene **2** and triphenylphosphine is formed in diethyl ether.

Next, we have found a convenient way of obtaining the elusive bisphosphine **1**, by taking the Ullmann route previously explored by Schmid et al. [3] and Brown and Woodward [4]. (2-Iodophenyl)diphenylphosphine oxide, prepared by *ortho*-lithiation [5] of triphenylphosphine

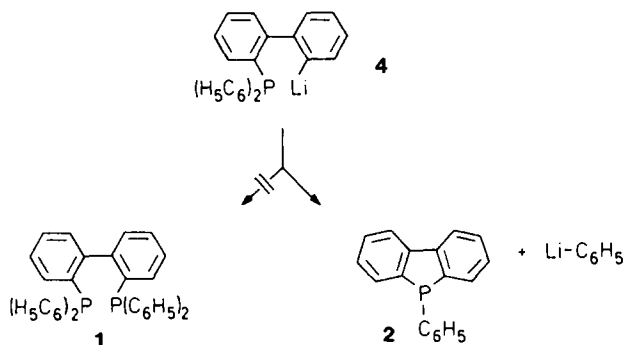
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oxide followed by iodolysis of the organometallic intermediate, was submitted to the copper promoted, reductive coupling. The resulting 2,2'-bis(diphenylphosphoryl)biphenyl (**3**) (70%) was reduced with trichlorosilane in boiling xylene to afford bisphosphine **1** (71%):



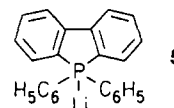
Bisphosphine **1** was found to melt at 211–212°C, very close to the melting “point” (m.p.) of 212°C reported by Bennett et al. [6], who had isolated a small amount (less than 0.3 mmol) of **1** after the oxidation of dimeric 2-(diphenylphosphino)phenylgold(I) with bromine or iodine and subsequent thermal decomposition of the adduct. In contrast, the 1:1 mixture of 9-phenyl-9-phosphafluorene (m.p. 93–95°C) and triphenylphosphine (m.p. 79–81°C) melts in the range 73–75°C.

Finally, we have attempted to understand why the reaction between 2,2'-dilithiobiphenyl and chlorodiphenylphosphine has taken such an unexpected course. The transient monolithio-monophosphine **4** formed by reaction of the 2,2'-dilithiobiphenyl with one molecule of chlorodiphenylphosphine has two options: it may either undergo a second intermolecular condensation with chlorodiphenylphosphine (to give the bisphosphine **1**) or proceed by an intramolecular attack of the aryllithium moiety onto the phosphorus atom from where a phenyl anion is ejected (thus affording the cyclic phosphine **2** and phenyllithium which eventually reacts with chlorodiphenylphosphine to give triphenylphosphine).



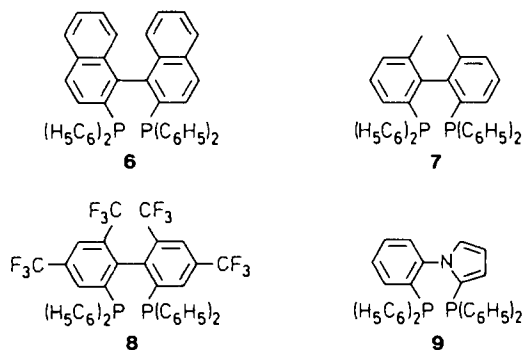
Obviously, the latter  $S_N2(P)$  type process outperforms, in terms of rates, the former. How can this be rationalized?

As carbon-by-carbon replacement reactions are notoriously slow [7], even their intramolecular variety should ordinarily not be able to compete with an intermolecular chlorine-by-carbon replacement. Thus one feels tempted to invoke a special mechanistic situation. The intermediacy of a lithium phosphoranide **5**, a species belonging to a class of compounds discovered by Hellwinkel [8], could indeed explain the failure of the second substitution:



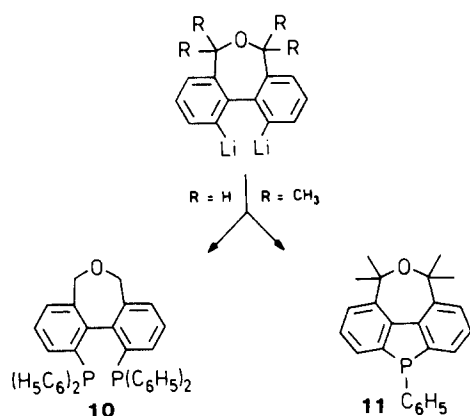
As both the *o*- and the *o'*-position are occupied, elimination of phenyllithium remains as the only plausible reaction mode.

It can also be immediately perceived why this option does not always exist. The planarization of the biphenyl moiety, a prerequisite for ring closure affording the phosphoranide, would generate intolerable strain due to steric repulsion or angle compression when chlorodiphenylphosphine (or its oxide, diphenylphosphoryl chloride) is allowed to react with 2,2'-dilithio-1,1'-binaphthyl [9], 2,2'-dilithio-6,6'-dimethylbiphenyl [10], 2,2'-dilithio-4,4',6,6'-tetrakis(trifluoromethyl)biphenyl [11] or 6,6'-dilithio-3-methoxy-2,4-dimethyl-2',4'-bis(trifluoromethyl)biphenyl [11]. In all these cases only the bisphosphines “BINAP” (**6**), “BIPHEMP” (**7**), “BIFUP” (**8**) and “FUBMOP” (**9**) [11] are obtained:



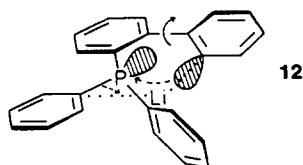
Nevertheless we have to reject the hypothesis of transient phosphoranides since it cannot account for a puzzling discrepancy. The unbranched 5,7-dihydro-1,11-dilithiodibenz[*c,e*]oxepin smoothly reacts with chlorodiphenylphosphine to form bisphosphine **10** [8,12]

while the 5,5,7,7-tetramethyl-substituted derivative [13] resolutely swerves to the phosphafluorene **11** [14]:



Considering the planarization energies of the corresponding hydrocarbons, 5,7-dihydrodibenz[*c,e*]oxepin ( $E_{\text{tors}} \approx 9$  kcal mol [15]) and 5,7-dihydro-5,5,7,7-tetramethyldibenz[*c,e*]oxepin ( $E_{\text{tors}} \approx 13$  kcal mol [16]), one might rather have predicted the opposite behavior.

We now tentatively postulate concertedness for the carbon-by-carbon substitution at phosphorus. That the latter process occurs with inversion [17] does not necessarily imply a coaxial alignment of the phenyl–P and Li–aryl bonds. A skew geometry (**12**) showing an antiparallel orientation of the organometallic bond with respect to the phosphorus lone pair is conceivably more favorable:



In this way, the collinear rear attack which is characteristic for nucleophilic substitution at carbon centers would be replaced by a winding-in motion that couples the shortening of the distance between the phosphorus and the metal-bearing *ortho*-carbon atom to a rotation around the central biphenyl axis. This elaborate trajectory offers a twofold advantage. It minimizes the repulsion between loosely bound electrons (“lone pairs” and “carbanionic” bonds) and it allows the lithium to switch easily from its former to its future binding site, i.e. from the *ortho*-carbon of the biphenyl moiety to the *ipso*-carbon of the nucleofugal phenyl ring.

Special structural features have to be considered to explain the case of the 5,5,7,7-substituted dibenzoxepin. As the inspection of molecular models reveals, severe steric interactions destabilize not only the transition state of ring inversion but also the ground state. Pla-

narization of the biphenyl core forces two methyl groups into uncomfortably close axial positions (C–C distances of about 1.6 Å before angle deformation), whereas one methyl group on each side collides with one half of the biphenyl entity each (H–C<sup>*ipso*</sup> and H–C<sup>*ortho*</sup> distances of about 1.9 Å before structure relaxation), if the latter is oriented at a dihedral angle of roughly 50°, as usual. In order to attenuate the intolerable repulsion thus produced, the dihedral angle has to shrink to, say, 30°. This partial untwisting of the biphenyl system, brings the two accessible *ortho* positions close to each other, thus disfavoring the introduction of two bulky diphenylphosphino moieties there and paving the way to phosphafluorene formation. In summary, phosphafluorene formation requires only a moderately twisted but not a completely planarized biphenyl moiety at the transition state. There are two ways to diminish the ordinary torsional angles at low cost: either avoid any 6,6'-substituents or tailor them so that they destabilize the fully twisted ground-state structure.

### 3. Experimental details

#### 3.1. Generalities

Starting materials have been purchased from Fluka AG (Buchs), Aldrich-Chemie (Steinheim), or Merck-Schuchardt (Hohenbrunn), unless literature references or details of the preparation are given. All commercial reagents were used without further purification.

Tetrahydrofuran was obtained as anhydrous by distillation from sodium wire after the characteristic blue color of in-situ-generated sodium diphenyl ketyl [18] was found to persist. Etheral extracts were dried with sodium sulfate. Before distillation of compounds prone to radical polymerization or sensitive to acids, a spatula tip of hydroquinone or potassium carbonate respectively was added.

The temperature of dry-ice–methanol baths is consistently indicated as  $-75^{\circ}\text{C}$  and “room temperature” ( $22\text{--}26^{\circ}\text{C}$ ) as  $25^{\circ}\text{C}$ . Melting ranges (m.p.) are reproducible after resolidification, unless stated otherwise (“decomposition”) and are corrected using a calibration curve which was established with authentic standards. If no m.p.s. are given, this means that all attempts to crystallize the liquid product have failed, even at temperatures as low as  $-75^{\circ}\text{C}$ .

<sup>1</sup>H NMR spectra were recorded at 400 MHz and <sup>31</sup>P NMR spectra at 162 MHz, both in deuteriochloroform solutions. Chemical shifts refer to the signal of tetramethylsilane in the case of <sup>1</sup>H spectra and to 85% aqueous phosphoric acid in the case of <sup>31</sup>P spectra. Abbreviations of coupling patterns are as follows: s, singlet; d, doublet; t, triplet; q, quadruplet; td, triplet of

doublets; m, multiplet. High resolution NMR spectroscopy commonly produces signals showing fine structure due to long-range coupling. Except in very special cases, coupling constants smaller than 1 Hz have little informative value and hence are neglected.

Mass spectrometry (MS) was carried out at 70 eV ionization potential maintaining a source temperature of 200°C. When no molecular peak was visible under electron impact, chemical ionization (CI) was applied in an ammonia atmosphere at 95.3 eV. Elementary analyses were made by the laboratory of I. Beetz, D-96'302 Kronach, Germany.

### 3.2. 2,2'-Dilithiobiphenyl as the key intermediate

(a) As reported in the literature [2], a solution of 2,2'-dibromobiphenyl [19] (6.2 g, 20 mmol) in diethyl ether (90 ml) was cooled to 0°C before it was mixed with a 1.5 M solution of butyllithium in hexane (30 ml, 45 mmol). After 4 h at 25°C, chlorodiphenylphosphine (7.4 ml, 8.8 g, 40 mmol) was added and a light-red color appeared which faded away to a pale yellow towards the end. Gas chromatography analysis (glass column) 2 m long and of 2 mm inner diameter; 5% SE-30 silicon rubber; 8 min at 160°C; then with 10°C min heating rate to 230°C; tetradecane as an internal standard for calibration) of a known fraction of the reaction mixture showed the presence of biphenyl (approximately 1%), triphenylphosphine (85%) and 9-phenyl-9-phosphafluorene (2) (90%) [20]. After removal of the solvents, the residue was partitioned between dichloromethane (50 ml) and water (10 ml). Upon evaporation of the organic layer, a pale-yellow solid was isolated, yield 10 g (96% with respect to  $C_{18}H_{15}P + C_{18}H_{13}P$ ); m.p. 66–72°C.  $^1H$  NMR:  $\delta$  7.94 (2H, d,  $J = 7.8$  Hz), 7.69 (2H, dd,  $J = 7.7$  Hz, 5.1), 7.44 (2H, td,  $J = 7.6$  Hz, 1.2), 7.3 (19H, m), 7.2 (3H, m) ppm.  $^{31}P$  NMR:  $\delta$  -4.8 (s, broad), -9.6 (s, broad) ppm.

(b) At -75°C, 2,2'-dibromobiphenyl (6.2 g, 20 mmol) was added to *tert*-butyllithium (80 mmol) dissolved in neat diethyl ether (50 ml) after the original solvent (pentane) had been stripped off. The turbid red reaction mixture was slowly poured into a vigorously stirred solution of chlorodiphenylphosphine (7.4 ml, 8.8 g, 40 mmol) in diethyl ether (20 ml), no color change being observed. According to gas chromatography (see above), biphenyl (approximately 5%), triphenylphosphine (75%) and the phosphafluorene 2 (85%) had been formed.  $^{31}P$  NMR:  $\delta$  -4.8 (s, broad), -9.6 (s, broad) ppm.

(c) The reaction was repeated as described above (Section 3.2(b)), but magnesium dichloride (5.7 g, 60 mmol) was added to the organolithium intermediate, before the pale-grey suspension was allowed to reach 25°C and was poured into the ethereal solution of chlorodiphenylphosphine. By gas chromatography (see

Section 3.2(a)), biphenyl (6.5%), triphenylphosphine (46%) and the phosphafluorene 2 (50%) were identified as reaction products.  $^{31}P$  NMR:  $\delta$  -4.9 (triphenylphosphine; s, broad), -9.7 (2; s, broad) and -13.9 (1; s, broad) ppm; integrals in the ratio of 1.1 : 1.0 : 1.2.

### 3.3. 2-(Diphenylphosphoryl)phenyllithium as the key intermediate

(a) To obtain (2-iodophenyl)diphenylphosphine oxide, a suspension of triphenylphosphine oxide (70 g, 0.25 mol) in a lithium-bromide-containing ethereal solution (0.40 l) of phenyllithium [21] was stirred for 72 h at -25°C, before iodine (70 g, 0.28 mol) was added to the deep-red mixture. The diethyl ether was evaporated and replaced by dichloromethane (0.30 l). The organic extract was washed with a 10% aqueous solution (0.15 l) of sodium thiosulfate and brine (0.20 l). The solvent was removed and the solid residue crystallized from ethyl acetate (yield, 73%; m.p., 150–159°C (crude product); m.p. 159–161°C (after recrystallization from toluene)).  $^1H$  NMR:  $\delta$  8.04 Hz (1H, ddm,  $J = 7.9$ , 3.0 Hz), 7.70 (4H, ddm,  $J = 11.9$ , 8.0 Hz), 7.58 (2H, tq,  $J = 7.4$ , 1.4 Hz), 7.49 (4H, tm,  $J = 7.3$  Hz), 7.33 (1H, tm,  $J = 7.6$  Hz), 7.2 (2H, m) ppm.  $^{31}P$  NMR:  $\delta$  33.6 ppm. MS: 404 (100%,  $M^+$ ), 327 (6%), 277 (86%). Anal. Found: C, 53.59; H, 3.53.  $C_{18}H_{14}IOP$  Calc. (404.18); C, 53.49; H, 3.49%.

(b) To obtain 1,1'-biphenyl-2,2'-diylbis(diphenylphosphine oxide) (2,2'-bis(diphenylphosphoryl)biphenyl (3)) a mixture of (2-iodophenyl)diphenylphosphine oxide (40 g, 100 mmol) and activated [22] copper (38 g, 0.60 mol) in dimethylformamide (0.40 l) was heated for 48 h to reflux. Kieselgur (diatomite) was added, the solvent evaporated and the residue extracted with ethyl acetate (0.50 l) in a Soxhlet apparatus. Upon cooling, the colorless product crystallized from the filtrate yield 78%; m.p., 221–223°C.  $^1H$  NMR:  $\delta$  7.7 (8H, m), 7.51 (2H, tm,  $J = 7.4$  Hz), 7.44 (4H, tm,  $J = 7.1$  Hz), 7.3 (6H, m), 7.2 (6H, m), 7.1 (2H, m) ppm.  $^{31}P$  NMR:  $\delta$  28.6 (s, broad) ppm. MS: 554 (0.2%), 477 (1%), 353 (100%).  $^{31}P$  NMR:  $\delta$  28.6 (s, broad) ppm. MS: 554 (0.2%), 477 (1%), 353 (100%). Anal. Found: C, 78.45; H, 5.17.  $C_{36}H_{28}O_2P_2$  Calc. (554.57): C, 77.97; H, 5.09%.

(c) To obtain 1,1'-biphenyl-2,2'-diylbis(diphenylphosphine) (2,2'-bis(diphenylphosphino)biphenyl (bpbp) (bpbp) (1)), bis(phosphine oxide) (3) (11 g, 20 mmol), freshly distilled trichlorosilane (8.1 ml, 11 g, 80 mmol) and triethylamine (13 ml, 9.1 g, 90 mmol) in xylene (0.30 l) were heated for 1 h to 100°C, 1 h to 125°C and 1 h to reflux. At 25°C, a 30% aqueous solution (0.15 l) of sodium hydroxide was added slowly and the turbid two-phase mixture was stirred at 50°C until, after 1 h, the organic phase became clear. Dichloromethane (0.20 l) was added and the combined organic layer vigorously

shaken with a 30% aqueous solution (0.15 l) of sodium hydroxide. The combined aqueous phases were extracted with a 1:1 (v/v) mixture ( $2 \times 0.10$  l) of dichloromethane and toluene and the combined organic layers were washed with brine ( $2 \times 0.10$  l) before being evaporated to dryness. The residue was recrystallized from a 1:2 (v/v) mixture of ethanol and toluene to afford a white powder (yield, 71%; m.p., 211–212°C).  $^1\text{H}$  NMR ( $[\text{H}_8]$ tetrahydrofuran):  $\delta$  7.2 (2H, m), 7.07(2H, td,  $J = 7.5, 1.5$  Hz), 7.03 (2H, dm,  $J = 7.5$  Hz), 6.79 (2H, dm,  $J = 7.5$  Hz) ppm.  $^{31}\text{P}$  NMR:  $\delta$  -14.1 (s, broad) ppm. MS (CI): 555 (2%,  $M^+ + 2\text{NH}_4 - 3$ ), 540 (1%,  $M^+ + \text{NH}_4$ ), 523 (100%,  $M^+ + 1$ ), 445 (3%), 337 (42%), 261 (83%), 187 (90%). Anal. Found: C, 82.93; H, 5.20.  $\text{C}_{36}\text{H}_{28}\text{P}_2$  Calc. (522.57): C, 82.74; H, 5.40%.

### Dedication and Acknowledgment

The authors congratulate Professor Rolf Huisgen on the occasion of his 75th birthday (to be celebrated on 13 June 1995). They are indebted to the Schweizerische Nationalfonds für wissenschaftliche Forschung for financial support in the framework of the ordinary subsidiaries (Grant 20-36'385-92) and the "chiral-2" project (Grants 21-36'736-92 and 20-41'221-94).

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