Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters
Tetrahedron Letters 45 (2004) 8327–8330

Suzuki reactions catalyzed by palladium complexes bearing the bulky (2,6-dimesitylphenyl)dimethylphosphine

Rhett C. Smith,[a] Robert A. Woloszynek,[a] Weizhong Chen,[b] Tong Ren[b] and John D. Protasiewicz[a,*]

[a]*Department of Chemistry, Case Western Reserve University, Cleveland, OH 44106, USA*
[b]*Department of Chemistry, University of Miami, Coral Gables, FL 33146, USA*

Received 23 July 2004; revised 4 September 2004; accepted 9 September 2004
Available online 28 September 2004

Abstract—A new bulky and stable phosphine (2,6-dimesitylphenyl)dimethylphosphine, and representative palladium complexes have been prepared and structurally characterized; some of these complexes prove efficient for coupling of aryl chlorides with arylboronic acids.

Sterically encumbered phosphines are a subject of current interest,[1] especially for use in catalytic C–C coupling reactions. In particular, it has been shown that bulky *ortho*-biphenyldialkylphosphines (**A**, Fig. 1) have led to some spectacular successes in this area of chemistry.[2–7] For example, a recent report announced that when R = Cy and R′ = 2,6-$(OMe)_2$ even palladium catalyzed Suzuki–Miyaura couplings involving normally unreactive hindered chloroarenes with arylboronic acids can be highly efficient.[2] The success of this hindered biarylphosphine was attributed in part to the increased steric bulk of the *ortho*-biphenyl group. Development of phosphines based on various *meta*-terphenyls and quaterphenyls has also yielded other interesting ligands.[8,9,13]

We have previously examined the use of *meta*-terphenyls for the development of low coordinate (multiply bonded) phosphorus centres in pi-conjugated materials.[10,11] One such material, $DmpPCl_2$ (Fig. 1, X = Cl, Dmp = 2,6-dimesitylphenyl)[12] seemed particularly suited for serving as a precursor to new dialkylphosphines of the form $DmpPR_2$. Like (biaryl)dialkylphosphines **A**, (triaryl)dialkylphosphines might also find applications as ligands for catalysis. We herein report on the synthesis of $DmpPMe_2$ (**1**) and of its corresponding palladium complexes. These materials have been fully characterized, and preliminary studies reveal that such palladium complexes can effect efficient coupling of aryl halides with arylboronic acids.

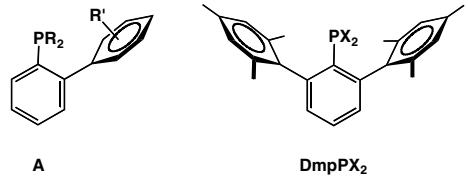


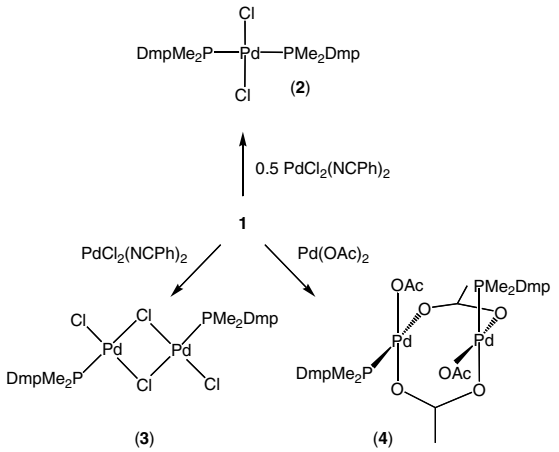
Figure 1.

Phosphine **1** was readily prepared in 65% yield by reaction of $DmpPCl_2$ with 2.2 equiv of MeLi at low temperature in diethyl ether.[18] Attesting to the steric protection afforded by the Dmp unit, crystalline **1** is stable to oxidation even after standing open to the atmosphere at room temperature for at least one month. Crystallographic analysis of **1** (see Supplementary data) shows it to possess a geometry similar to the related structurally characterized *meta*-terphenylphosphine 2,6-$(4\text{-}^tBuC_6H_4)_2C_6H_3PCl_2$.[14]

Phosphine **1** was found to yield a variety of complexes depending upon the particular palladium source used. Complex **2**, *trans*-$[(\mathbf{1})_2PdCl_2]$, was readily prepared in essentially quantitative yield by stirring 2 equiv of **1** with $PdCl_2(NCPh)_2$ in CH_2Cl_2 at room temperature for 30 min.[18] By contrast, addition of the reagents in a 1:1 ratio led to the isolation of $[(\mathbf{1})PdCl(\mu\text{-}Cl)]_2$ (**3**) in 92% yield[18] (Scheme 1).

Keywords: Phosphines; Suzuki reaction; Palladium catalyst.
* Corresponding author. Tel.: +1 216 368 5060; fax: +1 216 368 3006; e-mail: protasiewicz@case.edu

0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.09.069



Scheme 1.

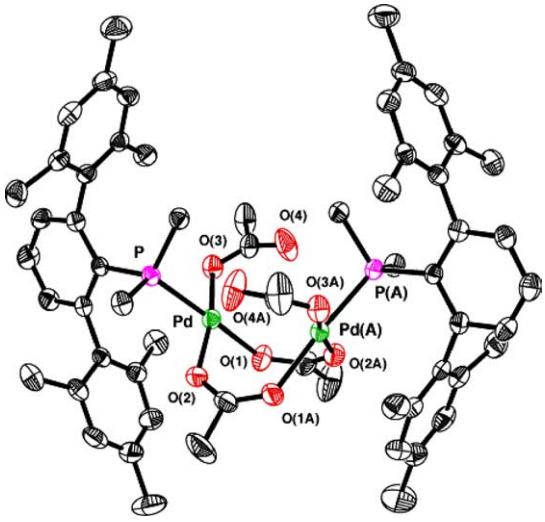


Figure 2. X-ray structure of **4** (H atoms and cocrystallized THF molecule have been omitted for clarity). Select bond lengths (Å) and angles (°): P–Pd 2.2120(13); Pd–O3, 2.025(3); Pd–O2, 2.020(3); Pd–O1, 2.103(3); Pd–Pd(A) 3.427; P–Pd–O1, 173.60(11); O3–Pd–O2, 169.43(15).

Reaction of **1** with $Pd(OAc)_2$ also led to dimeric complex **4** that was isolated in 85%.[18] Compounds **3** and **4** (1:1 Pd:phosphine ratio) are attractive materials, as under catalytic conditions they might generate highly active monophosphine Pd species, perhaps stabilized by interaction of Pd with the π system of a flanking mesityl group, as has been noted for Pd·**A**-type complexes.[9,15]

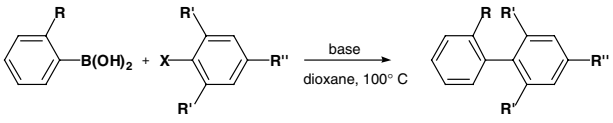
An X-ray structural analysis of complex **4**·THF (see Supplementary data) confirms a dimeric structure (Fig. 2), and also reveals a number of additional features of note. The global coordination mode, in which the μ-acetato moieties are distributed *cis* to one another, is in line with many other structurally characterized complexes featuring a diacetato-bridged dipalladium core.

The phosphines are oriented in the presumably more sterically favourable (noneclipsed) orientation, with a nonbridging acetate completing the pseudo-square planar coordination sphere at each Pd centre. The Pd lies above the ligand plane by 0.154 Å as the ligands tilt slightly away from the dipalladium core. The structural impact of the bulky phosphine substituent is perhaps most easily discerned by comparison to the related structure of $[PdCl(\mu\text{-}OAc)(PMe_2Ph)]_2$ (**B**).[16]

The Pd–P bond length in **4** (2.2120(13) Å) is essentially the same as that in **B** (2.213 Å), while the Pd–Pd distance in **4** (3.427 Å) is the longest among structurally characterized complexes featuring the diacetato-bridged dipalladium core (cf. 3.080 Å for **B**). This spreading of the core is likely a response to steric forces imposed by the convex Dmp groups.

Having confirmed the expected formulation of these materials, preliminary investigations into the catalytic efficacy of **3** and **4** were carried out (Table 1). Initial screening indicated that **3** was a more potent catalyst, and reactions with this complex were thus more thoroughly pursued. These promising early (nonoptimized) results are comparable to those obtained with catalysts containing ligands of type **A** when phenylboronic acid

Table 1. Suzuki couplings catalyzed by 1 mol% **3**



Entry	R	X	R′	R″	Base	Yield (%)[17]
1	H	Cl	H, H	H	Cs_2CO_3	97
2	H	Br	H, H	CH_3	Cs_2CO_3	100
3	H	Cl	CH_3, H	H	CsF	72
4	H	Br	CH_3, H	H	CsF	91
5	H	Cl	CH_3, CH_3	CH_3	CsF	75
6	CH_3	Cl	H, H	H	CsF	46
7	CH_3	Br	H, H	CH_3	CsF	48
8	CH_3	Cl	H, CH_3	H	CsF	31
9	CH_3	Br	H, CH_3	H	CsF	48
10	CH_3	Cl	CH_3, CH_3	CH_3	CsF	40

is one of the reaction partners. Notably, moderate to high yields are observed for the coupling of aryl chlorides with phenylboronic acid (97% for chlorobenzene using 1 mol% **3**). The successful coupling of phenylboronic acid with either 2-chlorotoluene (72%) or 2-chloromesitylene (75%) indicates that coupling of bulkier aryl halides is also accessible despite the bulk of the phosphine. This finding may reflect the aforementioned in situ formation of less bulky and more reactive monophosphine complexes, although this is currently speculative and additional studies must therefore be carried out.

Depressed yields are observed when the bulkier *ortho*-tolylboronic acid is employed under the same conditions, however. Optimization of reaction conditions and/or variation of alkyl/*meta*-terphenyl combination may lead to additional improvements.

In conclusion, a bulky *meta*-terphenyl substituted dialkylphosphine has been prepared and structurally characterized. Three palladium complexes of this phosphine have been prepared and one has been structurally characterized. These complexes hold promise for use in high yield Suzuki coupling of aryl chlorides and boronic acids, including sterically hindered aryl chlorides. Further investigations into catalytic applications employing **1** and other *meta*-terphenyl phosphines are currently underway.

Acknowledgements

The authors thank the National Science Foundation (CHE-0202040) for support.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.09.069. The supplementary data is available online with the paper in ScienceDirect (crystallographic details in .cif format for **1** and **4**).

References and notes

1. (a) Some recent references: Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553; (b) Hartwig, J. F.; Richards, S.; Baranano, D.; Paul, F. *J. Am. Chem. Soc.* **1996**, *118*, 3626; (c) Chen, H.-P.; Liu, Y.-H.; Peng, S.-M.; Liu, S.-T. *Dalton Trans.* **2003**, 1419; (d) Bell, N. A.; Coles, S. J.; Constable, C. P.; Hursthouse, M. B.; Light, M. E.; Mansor, R.; Salvin, N. J. *Polyhedron* **2002**, *21*, 1845; (e) Albert, J.; Bosque, R.; Cadena, J. M.; Delgado, S.; Granell, J.; Muller, G.; Ordinas, J. I.; Bardia, M. F.; Solans, X. *Chem. Eur. J.* **2002**, *8*, 2279; (f) Xu, X.; Nieuwenhuyzen, M.; James, S. L. *Angew. Chem., Int. Ed.* **2002**, *41*, 764; (g) Matsumoto, T.; Kasai, T.; Tatsumi, K. *Chem. Lett.* **2002**, *3*, 346; (h) Stuer, W.; Wolf, J.; Werner, H. *J. Organomet. Chem.* **2002**, *641*, 203; (i) Alyea, E. C.; Ferguson, G.; Kannan, S. *Polyhedron* **2000**, *19*, 2211; (j) Yamamoto, Y.; Kawasaki, K.; Nishimura, S. *J. Organomet. Chem.* **1999**, *587*, 49; (k) Nagata, K.; Takeda, N.; Tokitoh, N. *Chem. Lett.* **2003**, *32*, 170.
2. Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 1871.
3. Miura, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2201.
4. Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176.
5. Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722.
6. Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 2413.
7. Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550.
8. Tang, W.; Chi, Y.; Zhang, X. *Org. Lett.* **2002**, *4*, 1695.
9. Aikawa, K.; Mikami, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 5455.
10. Smith, R. C.; Protasiewicz, J. D. *Eur. J. Inorg. Chem.* **2004**, *5*, 998.
11. Smith, R. C.; Protasiewicz, J. D. *J. Am. Chem. Soc.* **2004**, *126*, 2268.
12. Urnezius, E.; Protasiewicz, J. D. *Main Group Chem.* **1996**, *1*, 369.
13. Matsumoto, T.; Kasai, T.; Tatsumi, K. *Chem. Lett.* **2002**, 346.
14. Wehmschulte, R. J.; Khan, M. A.; Hossain, S. I. *Inorg. Chem.* **2001**, *40*, 2756.
15. Reid, S. M.; Boyle, R. C.; Mague, J. T.; Fink, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 7816.
16. Wong-Ng, W.; Cheng, P.-T.; Kocman, V.; Luth, H.; Nyburg, S. C. *Inorg. Chem.* **1979**, *18*, 2620.
17. Yields and product identities were determined by GC–MS analysis of product mixtures using a Hewlett Packard 5890 Series II gas chromatograph coupled to a Hewlett Packard 5971A mass spectroscopic detector. Analysis and calibration procedures are detailed in: McMaster, M. C.; McMaster, C. *GC/MS: A Practical User's Guide*; John Wiley and Sons: New York, 1998.
18. Experimental and physical data for **1**–**4**:**1**: To a solution of $DmpPCl_2$ (1.0 g, 2.5 mmol) in diethyl ether (30 mL) at −78 °C was added MeLi (1.6 M in diethyl ether, 3.4 mL, 5.4 mmol) and the resultant was allowed to come to room temperature. The solution was filtered and volatiles removed in vacuo to give a light orange solid. The solid was taken up in a minimum amount of ether and cooled to −35 °C for 24 h, after which time large white crystals had formed. The crystals were collected and dried to give **1** (0.585 g, 65%). ^1H NMR ($CDCl_3$): δ 0.72 (d, 6H, $J = 4$ Hz), 2.03 (s, 12H), 2.34 (s, 6H), 6.92 (s, 4H), 6.95 (d, 2H, $J = 7$ Hz), 7.36 (t, 1H, $J = 7$ Hz); ^{31}P NMR ($CDCl_3$): δ −36.9. Anal. Calcd for $C_{26}H_{31}P$: C, 83.39; H, 8.34. Found: C, 83.14; H, 8.11.
Compound **2**: To a mixture of solids **1** (50 mg, 0.13 mmol) and $PdCl_2(NCPh)_2$ (25 mg, 0.067 mmol) was added 3 mL of anhydrous dichloromethane. Upon addition of solvent, the solution became orange in colour, then quickly faded to yellow. After 30 min of stirring at room temperature, the volatiles were removed in vacuo to give a pale yellow solid. The solid was rinsed with hexanes and dried to give **2** (61 mg, 98%) as a pale yellow solid. ^1H NMR (CD_2Cl_2): δ 1.13 (virtual t, 12H, $J = 3$ Hz), 2.05 (s, 24H), 2.27 (s, 12H), 6.84 (s, 8H), 6.88 (d, 4H, $J = 7$ Hz), 7.42 (t, 2H, $J = 7$ Hz); ^{31}P NMR (CD_2Cl_2): δ −10.1. Anal. Calcd for $C_{52}H_{62}Cl_2P_2Pd$: C, 67.42; H, 6.75. Found: C, 68.01; H, 6.62.
Compound **3**: To a solution of $PdCl_2(NCPh)_2$ (51 mg, 0.13 mmol) in 3 mL of anhydrous dichloromethane was added a dichloromethane (3 mL) solution of **1** (50 mg, 0.13 mmol) over 1.5 min. During addition, the solution became deep orange in colour. The solution was allowed to stir at room temperature for 3 h and solvent volume was

then reduced in volume to incipient crystallization. The solution was allowed to stand for 16 h, over which time a microcrystalline orange-brown solid formed, which was collected and dried in vacuo to give **3** (93 mg, 92%). Analytically pure material was obtained by slow evaporation from a saturated dichloromethane solution. ^{1}H NMR ($CDCl_3$): δ 1.19 (d, 12H, J = 13 Hz), 2.12 (s, 24H), 2.43 (s, 12H), 7.01 (s, 8H), 7.05 (dd, 4H, J_{HH} = 8 Hz, J_{HP} = 3 Hz), 7.42 (t, 2H, J = 8 Hz); ^{31}P NMR ($CDCl_3$):δ 8.7. Anal. Calcd for $C_{53}H_{64}Cl_6P_2Pd_2$ (**3**·CH_2Cl_2): C, 53.86; H, 5.21. Found: C, 54.31; H, 5.36.

Compound **4**: To a solution of $Pd(OAc)_2$ (60 mg, 0.26 mmol) in dichloromethane (6 mL) was added a dichloromethane (6 mL) solution of **1** (100 mg, 0.26 mmol) over about 3 min at −35 °C. After 1 h the mixture was allowed to come to room temperature and solvent removed until incipient crystallization. The mixture was allowed to stand at −35 °C overnight, over which time brown crystals formed. The crystals were collected and dried in vacuo, yielding **4** (140 mg, 85%). ^{1}H NMR ($CDCl_3$): δ 1.06 (d, 12H, J = 13 Hz), 1.76 (s, 12H), 2.10 (s, 24H), 2.35 (s, 12H), 7.01 (s, 8H), 7.06 (dd, 4H, J_{HH} = 7 Hz, J_{HP} = 3 Hz), 7.61 (t, 2H, J = 7 Hz); ^{31}P NMR ($CDCl_3$): δ 3.7. Anal. Calcd for $C_{61}H_{76}Cl_2O_8P_2Pd_2$ (**4**·CH_2Cl_2): C, 57.11; H, 5.97. Found: C, 57.75; H, 5.85.