

View Article Online View Journal

RSC Advances

This article can be cited before page numbers have been issued, to do this please use: Y. Sun, M. Yan, Y. Liu, Z. Lian, T. Meng, J. chen, S. Liu and G. Yu, *RSC Adv.*, 2015, DOI: 10.1039/C5RA11778J.



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. This Accepted Manuscript will be replaced by the edited, formatted and paginated article as soon as this is available.

You can find more information about *Accepted Manuscripts* in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard <u>Terms & Conditions</u> and the <u>Ethical guidelines</u> still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.



www.rsc.org/advances

RSCPublishing

COMMUNICATION

Journal Name

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2015, Accepted 00th January 2015

DOI: 10.1039/x0xx00000x

www.rsc.org/

Published on 11 August 2015. Downloaded by University of Sussex on 15/08/2015 15:40:03.

Phenylphosphinacalix[3]trifuran: synthesis, coordination and application in the Suzuki-Miyaura cross-coupling reaction in water[†]

Yue Sun,^a Meng-Qi Yan,^c Yan Liu,^c Ze-Yu Lian,^b Tong Meng,^a Sheng-Hua Liu,^a Jian Chen,^a Guang-Ao Yu^{*a}

Phenylphosphinacalix[3]trifuran and supramolecular assemblies with palladium have been synthesized. Phenylphosphinacalix[3]trifuran affords turnover numbers as high as 3.05×10^7 in Suzuki-Miyaura cross-coupling reactions in pure water.

The development of methods for construction of supramolecular architectures offers chemists the ability to synthesize many potentially useful species. Ultimately, control over the synthesis of compounds containing well-defined cavities enables the design of species that can arrange molecules in a specific and predictable fashion for catalysis.¹ Indeed, chemists are now beginning to utilize supramolecular chemistry as a tool toward the realization of catalytic systems with enzyme-like properties.² Acyclic phosphine compounds play an important role in catalysis³ and supramolecular chemistry. However, studies on phospha macrocycles are relatively limited.⁴ Recently, Edwards established a metal-template hydrophosphination method to construct a cyclic structure on a metal center by a self-coupling reaction of primary or secondary alkenylphosphines. Using this ingenious template method, a dozen phospha macrocycles were prepared.⁵ Herein, the we report preparation of phenylphosphinacalix[3]trifuran, the construction of supramolecular assemblies via metal coordination chemistry, and application in palladium-promoted Suzuki cross-coupling reactions using pure water as solvent.

The facile deprotonation of thiophene or furan by a strong base such as "BuLi is a well-known process. A wide variety of bis-electrophiles react with these anions to give bis-substituted compounds in high yields, and extension of this reaction to dianions allows the synthesis of cyclic compounds.⁶ Using this procedure, compound 1, a white solid, was obtained as the main product from a one-pot synthesis (Scheme 1). TLC on silica showed that there were three minor by-products in the reaction mixture, but the yields were too low for them to be isolated. The essential absence of larger cyclic oligomers suggests that

the trimeric macrocycle may be the thermodynamically favored product.



Scheme 1 One-pot four-step synthesis of 1.

of proposed mechanism for the formation The phenylphosphinacalix[3]trifuran (1) is shown in Scheme 2. The reaction between 2-furyllithium and phenylphosphorus dichloride should yield the di(2-furyl)phenyl phosphine (A). Reaction of A with "BuLi would then provide intermediate B. Diphosphine intermediate C would then be produced by the reaction of **B**, 2-furyllithium and phenylphosphorus dichloride. C would react with "BuLi to give the dianion D. Finally, 1 would be generated by the reaction between dianion **D** and phenylphosphorus dichloride. To confirm the reaction mechanism, ³¹P NMR spectra of the reaction mixture at every were studied. In addition, sten 2,4-bis(2furylphenylphosphino)furan (C) was isolated from the reaction mixture (see ESI[†]).

Compound 1 is stable in air, so no special precautions are required to handle it under ordinary laboratory conditions. It is also sufficiently soluble in common organic solvents (*e.g.*, dichloromethane, chloroform, benzene, and THF) to permit routine spectroscopic analysis. In ¹H NMR and ³¹P{¹H} NMR spectra, only one furan proton signal and a sharp phosphorus signal were observed, indicating that 1 has a symmetric cyclic structure.

The corresponding trioxide (2) of compound 1 could be produced by reaction of 1 with H_2O_2 in CH_2Cl_2 . 1 could also be

Published on 11 August 2015. Downloaded by University of Sussex on 15/08/2015 15:40:03.

converted cleanly to the corresponding trisulfide (3) by reaction with elemental sulfur or to triselenide by reaction with elemental selenium in 91% and 92% yield, respectively. The molecular structures of 2, 3 and 4 were initially elucidated based upon ${}^{31}P{}^{1}H$ NMR spectra. The ${}^{31}P{}^{1}H$ NMR spectra of 2 and 3 contained singlets at 2.62 and 9.01 ppm, respectively. The ${}^{31}P{}^{1}H$ NMR spectra of 4 displayed one major signal with selenium satellites at -5.17 ppm, due to the P atoms bonded to magnetically inactive Se nuclei, and a doublet ($J_{P-Se} = 821$ Hz) stemming from the P nucleus bonded to ${}^{77}Se$ (7.5% natural abundance, I = 1/2).⁷



Figure 1 Molecular structure of 2 with 30% probability level ellipsoids.

The structure of **2** was confirmed by X-ray crystallographic analysis (Figure 1). Compound **2** is $C_{3\nu}$ symmetric, and looks like a type of three-legged Chinese Bronze Tripod (an ancient cauldron) (see ESI†), wherein three furan units and three Ph–P groups are alternately linked to form a conical framework. Atoms C(2), C(3), C(6), C(7), C(10) and C(11) form the upper rim, and all six atoms are nearly coplanar with a mean deviation of 0.0225 Å. The three oxygen atoms bonded to phosphorus atoms are all directed to the upper rim of the cone. The P(1)– C(13), P(2)–C(19) and P(3)–C(25) bonds are almost perpendicular to the plane mentioned above, so the three benzene rings bonded to the phosphorus atoms form three legs.

The molecular structures of **3** and **4** were also confirmed by X-ray crystallography (see ESI†). The structures of **3** and **4** are very similar to that of **2**. For example, (i) they also look like Chinese Bronze Tripods, (ii) the average distance between the two O atoms of the furan rings is about 2.87 Å for **2**, 2.80 Å for **3** and 2.81 Å for **4**, and the three O atoms of the furan ring form an equilateral triangle, (iii) the P atoms in **3** and **4** possess a tetrahedral configuration with comparable C–P–C bond angles, and (iv) P=O, P=S and P=Se bonds are directed to the upper rim of the cone, and O, S or Se, together with the 3- and 4-position carbons of the furan ring form the upper rim of the cone.

The propensity of **1** toward chelation was tested through its reaction with $PdCl_2(NCCH_3)_2$. The single product was assigned as dinuclear $[cis-PdCl_2(1)]_2$ (**5**) on the basis of (i) broken C_3 symmetry



Figure 2 Molecular structure of 5 with 30% probability level ellipsoids.

Compound 5 is $C_{2\nu}$ symmetric, and looks like a Si Muwu square vessel (an ancient cauldron with four legs) (see ESI⁺). Four benzene rings bonded to the coordinated phosphine atoms form four legs. The palladium atom is coordinated in a distorted square planar geometry with a cis arrangement of two P-donors and two Cl atoms. The average Pd-Cl and Pd-P bond lengths are comparable with those observed in other phosphinopalladium(II) chloride complexes.⁸ A pseudo-rectangular geometry, where the four corners are occupied by coordinated P atoms, has dimensions of approximately 5.50 × 3.53 Å. The internal geometry of the cyclophane ligands in 5 is different from that in 1. The two furanyl moieties in the metallamacrocycle are almost parallel and separated by 3.385 Å, similar to other compounds that contain π - π stacking interactions.⁸ Both furanyl oxygen atoms point towards the cavity of the metallamacrocycle. Structural effects due to the formation of the metallamacrocycle also result in different P–P distances (P(1)-P(2) = 5.512 Å, P(2)-P(2A) = 5.453 Å).



Scheme 2 Possible mechanism for the formation of 1.

Published on 11 August 2015. Downloaded by University of Sussex on 15/08/2015 15:40:03

Table 1 The Suzuki-Miyaura coupling of various aryl halides with
arylboronic acid in the presence of 1/Pd(OAc) ₂ in water ^a

Entry	Halide	Boronic acid	Product	Yield
1	Br	⟨−B(OH)₂	\sim	90
2	O₂N-⟨}−Br	B(OH) ₂	0 ₂ N-	92
3	СНО СНО	⟨¯}−B(OH) ₂	Сно	94
4	о ————————————————————————————————————	—B(OH) ₂	$\rightarrow \bigcirc \rightarrow \bigcirc$	98
5	∏ Br	⟨		61
6	O₂N-⟨◯>−CI	⟨−B(OH) ₂	02N-	21
7	CI-CI	B(OH)2	\sim	0
8	H ₂ N- Br	B(OH) ₂	H ₂ N	85
9	Br NH ₂	⟨−B(OH)₂	$\underset{NH_2}{}$	82
10	Br	B(OH) ₂	$\bigcirc - \bigcirc$	65
11	Br	⟨	\sim	81
12	Br	B(OH)2	$\rightarrow \rightarrow$	87
13	H₃co-⟨>–Br	—B(OH) ₂	н₃со-⟨⟩⟨⟩	87
14		⟨		89
15	H3CO H3COBr	⟨−B(OH)₂	H3CO	91
16	H3CO Br H3CO	B(OH) ₂	H3CO H3CO	93
17	°→−−Br	H3CO B(OH)2	О→ОСН₃	63
18	о >—{{}-Br	C-B(OH) ₂ OCH ₃		72
19	O →→→Br	B(OH) ₂	°+⊖-∽	87
20	°→-{S−Br	B(OH) ₂	\sim	97

^aReaction conditions: 1.0 mmol of aryl halide, 1.2 mmol of boronic acid, 0.5 mol% Pd(OAc)₂, 1.5 mol% **1**, 3.0 mmol of $K_3PO_4 \cdot 3H_2O$, 2.0 mL H₂O, 100°C, reaction time 8 h. ^bIsolated yield (%).

Since the original discovery and development of Pd-catalyzed coupling reactions that led to the recent chemistry Nobel Prize being awarded to Heck, Suzuki and Negishi, a great deal of attention has focused on the development of catalytic systems that would improve their efficiency.⁹ The use of phosphine ligands allows very high turnover numbers (TONs) to be reached in Suzuki-Miyaura couplings, and the search for catalytic systems allowing ultra-low loadings is an ongoing field.¹⁰ In addition, there has been increasing interest in the use of water as a solvent for many homogeneously catalyzed reactions. Cost, environmental benefits, and safety are among the reasons most often used to justify the replacement of organic solvents by water in organic transformations.¹¹

Recently, cavity-shaped ligands have been shown to add value to the efficiency of the Suzuki-Miyaura coupling reaction.¹² With compound 1 in hand, we then studied the scope and limitations of 1/Pd as a catalyst in Suzuki-Miyaura coupling in water at low loadings. We applied similar conditions to those reported for the α -Cytep tetraphosphine. Using Pd(OAc)₂ as a palladium precursor together with compound 1 in a 3:2 ratio, but at a slightly higher (2×10⁻⁸%) loading than the lowest used with α -Cytep, and K₃PO₄·3H₂O in refluxing water for 3 days led to TONs of up to 3.05×10^7 . While the TONs is up to 2.55×10^7 , using bromobenzene and 2-methoxyphenylboronic acid as reactant. The TONs is just 1.50×10^7 , using Pd(OAc)₂ and phenyldifuranphosphine as catalyst to the reaction of bromobenzene with phenylboronic acid (see ESI[†]). However, this catalytic system is not as efficient as Buchwald's ligand for aryl chlorides. This observation suggests that these high TONs are not due to a facilitated oxidative addition step but, as previously noted, longevity of the catalyst can be a key to reach high TONs.¹²

Under the optimized reaction conditions, a wide array of aryl bromides reacted smoothly with phenylboronic acid to provide the corresponding products (see ESI[†]). For example, bromobenzene reacted efficiently with phenylboronic acid within 8 h, providing a 90% yield of the desired product (Table 1, entry 1). The reaction of aryl bromides bearing electron-withdrawing groups, such as -NO₂, -CHO, and -COCH₃, with phenylboronic acid also gave the required products in good to excellent yields (Table 1, entries 2-4). It is also noteworthy that the present protocol is applicable to the cross-coupling reaction of 2bromothiophene with phenylboronic acid, providing the desired heterocyclic product in 61% yield (Table 1, entry 5). Furthermore, cross-coupling reactions of aryl chlorides with phenylboronic acid resulted in low yields (Table 1, entries 6, 7). The reaction of phenylboronic acid with aryl bromides bearing electron-donating substituents such as -NH2, -CH3, -OCH3 gave the desired products in moderate to high yields (Table 1, entries 8-16). This catalyst system can also be used in the coupling reactions of moderately hindered aryl boronic acids with aryl bromides. For example, the reaction of 2-methoxyphenylboronic acid with 4'bromoacetophenone proceeded smoothly to give the biaryl product in 72% yield (Table 1, entry 18). 2-methylphenylboronic acid and 2-naphthylboronic acid also reacted efficiently with 4'bromoacetophenone to give the desired products in good yields (Table 1, entries 19, 20).

In summary, we have developed a one-pot synthesis of phenylphosphinacalix[3]furan (1), representing the first example of a P-bridged heteracalix[3]arene and expanding the range of heteracalixarenes. The reaction of 1 with $PdCl_2(NCCH_3)_2$ gives

the binuclear trimacrocyclic system 5. Compound 5 represents the first example of a metallamacrocycle containing a P-bridged cavity-shaped ligand. Compound 1 does not display exceptionally high yield. The complex generated with $Pd(OAc)_2$ and ligand 1 that exhibit high activities in Suzuki-Miyaura cross-coupling. This property could be associated with its ability of the ligand in stabilizing the catalytic species by coordination through multiple binding sites. We have therefore shown that P-bridged heteracalixarenes can serve as interesting platforms for catalysis under aqueous conditions.

Acknowledgements

The authors would like to thank the National Natural Science Foundation of China (Nos. 21472060, 21072071 and 21272088), self-determined research funds of CCNU from the colleges' basic research and operation of MOE (Nos. CCNU15A02012).

Notes and references

Published on 11 August 2015. Downloaded by University of Sussex on 15/08/2015 15:40:03

^aKey Laboratory of Pesticide & Chemical Biology, Ministry of Education, Central China Normal University, Wuhan 430079, China. E-Mail: vuguang@mail.ccnu.edu.cn

State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, China

State Key Laboratory of Catalysis, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, China

Electronic supplementary information (ESI) available: CCDC reference numbers 862559-862561 and 913612. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b000000x

- (a) C. G. Oliveri, P. A. Ulmann, M. J. Wiester and C.A. Mirkin, Acc. Chem. Res., 2008, 41, 1618; (b) N. C. Gianneschi, M. S. Masar III and C. A. Mirkin, Acc. Chem. Res., 2005, 38, 825.
- 2 (a) H.J. Yoon, J. P. Kuwabara, J-H. Kim and C. A. Mirkin, Science, 2010, 330, 66; (b) R. Chakrabarty, P. S. Mukherjee and P. J. Stang, Chem. Rev., 2011. 111. 6810.
- (a) D. S. Surry and S. L. Buchwald, Chem. Sci., 2011, 2, 27; (b) D. Maiti, 3 B. P. Fors, J. L. Henderson, Y. Nakamura and S. L. Buchwald, Chem. Sci., 2011, 2, 57; (c) J-H. Xie, S-F. Zhu and Q-L. Zhou, Chem. Rev., 2011, 111, 1713.
- 4 (a) A. J. Saunders, I. R. Crossley, M. P. Coles and S. M. Roe, Chem. Commun., 2012, 48, 5766; (b) Y. Matano and H. Imahori, Acc. Chem. Res., 2009, 42, 1193; (c) C. D. Swor and D. R. Tyler, Coord. Chem. Rev., 2011, 255, 2860; (d) P. G. Edwards and F. E. Hahn, Dalton Trans., 2011, 40, 10278; (e) T. Albers and P. G. Edwards, Chem. Commun., 2007, 858; (f) T. Mizuta, T. Aotani, Y. Imamura, K. Kubo and K. Miyoshi, Organometallics, 2008, 27, 2457; (f) B. P. Friedrichsen, D. R. Powell and H. W. Whitlock, J. Am. Chem. Soc., 1990, 12, 8931; (g) B. J. Whitlock, H. W. Whitlock and H. Alles, J. Am. Chem. Soc., 1974, 96, 3959
- 5 (a) P. G. Edwards, R. Haigh, D. Li and P. D. Newman, J. Am. Chem. Soc., 2006, 128, 3818; (b) P. G. Edwards and M. L. Whatton, Dalton Trans., 2006, 442; (c) P. G. Edwards, K. M. A. Malik, L. Ooi and A. J. Price, Dalton Trans., 2006, 433; (d) A. R. Battle, P. G. Edwards, R. Haigh, D. E. Hibbs, D. Li, S. M. Liddiard and P. D. Newman, Organometallics, 2007, 26, 377; (e) O. Kaufhold, A. Stasch, T. Pape, A. Hepp, P. G. Edwards, P. D. Newman and F. E. Hahn, J. Am. Chem. Soc., 2009, 131, 306; (f) T. Albers, J. Baker, S. J. Coles, P. G. Edwards, B. Kariuki and P. D. Newman, Dalton Trans., 2011, 40, 9525
- B. Koenig, M. Roedel, P. Bubenitschek, P. G. Jones and I. Thondorf, J. 6 Org. Chem., 1995, 60, 7406.
- H. Tsuji, T. Inoue, Y. Kaneta, S. Sase, A. Kawachi and K. Tamao, 7 Organometallics, 2006, 25, 6142.
- 8 (a) T. L. Stott, M. O. Wolf and A. Lam, Dalton Trans., 2005, 652; (b) M. Fessler, G. Czermak, S. Eller, B. Trettenbrein, P. Brüggeller, L. Bettucci, C. Bianchini, A. Meli, A. Lenco and W. Oberhauser, Dalton Trans., 2009,

1859; (c) (h) P. D. Zeits, G. P. Rachiero, F. Hampel, J. H. Reibenspies and J. A. Gladysz, Organometallics, 2012, 31, 2854; (d) M. Stollenz, N. Bhuvanesh, J. H. Reibenspies and J. A. Gladysz, Organometallics, 2011, 30, 6510; (e) M. Stollenz, M. Barbasiewicz, A. J. Nawara-Hultzsch, T. Fiedler, R. M. Laddusaw, N. Bhuvanesh, and J. A. Gladysz, Angew. Chem. Int. Ed., 2011, 50, 6647.

- (a) J-C. Hierso, M. Beaupérin and P. Meunier, Eur. J. Inorg. Chem., 2007, 24, 3767; (b) R. Martin and S. L. Buchwald, Acc. Chem. Res., 2008, 41, 1461
- 10 (a) A. Fihri, D. Luart, C. Len, A. Solhy, C. Chevrin and V. Polshettiwar, Dalton Trans., 2011, 40, 3116; (b) D. Schaarschmidt and H. Lang, ACS Catal., 2011, 1, 411.
- 11 (a)S.-L. Mao, Y. Sun, G-A. Yu, C. Zhao, Z-J. Han, J. Yuan, X-L. Zhu, Q-H. Yang and S-H. Liu, Org. Biomol. Chem., 2012, 10, 9410; (b) M-O, Simon and C-J. Li, Chem. Soc. Rev., 2012, 41, 1415; (c) B. Karimi and P. F. Akhavan, Chem. Commun., 2011, 47, 7686.
- 12 (a) E. Zaborova, J. Deschamp, S. Guieu, Y. Blériot, G. Poli, M. Ménand, D. Madec, G. Prestat and M. Sollogoub, Chem. Commun., 2011, 47, 9206; (b) L. Monnereau, D. Sémeril, D. Matt and L. Toupet, Chem. Eur. J., 2010, 16, 9237.
- 13 R. B. Bedford, S.L. Hazelwood and M. E. Limmert, Chem. Commun., 2002, 2610.

Published on 11 August 2015. Downloaded by University of Sussex on 15/08/2015 15:40:03.

Graphic Abstract

Phenylphosphinacalix[3]trifuran: synthesis, coordination and application in the Suzuki-Miyaura cross-coupling reaction in water

Yue Sun, Meng-Qi Yan, Yan Liu, Ze-Yu Lian, Tong Meng, Sheng-Hua Liu, Jian Chen, Guang-Ao Yu

Phenylphosphinacalix[3]trifuran and supramolecular assemblies with palladium have been synthesized. Phenylphosphinacalix[3]trifuran affords turnover numbers as high as 3.05×10^7 in Suzuki-Miyaura cross-coupling reactions in pure water.

