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ARTICLE TYPE

Novel Bisimidazolium Pincers as Low Loading Ligands for *in situ* Palladium-Catalyzed Suzuki-Miyaura Reaction in Ambient Atmosphere

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A series of novel triazinonide-bridged bisimidazolium pincers were easily synthesized by quaternization of functionalized *N*phenylimidazoles with highly reactive cyanuric chloride under mild conditions. The pincer 3c was proven to be a very 0 efficient ligand for *in situ* Pd-catalyzed Suzuki-Miyaura reaction with ppm-level catalyst loading.

N-heterocyclic carbenes (NHCs) are considered as better σ donors and weaker π -acceptors compared with phosphine ligands.¹ Among them, pyridine-bridged bisimidazolium salts, the 15 precursors of CNC pincers, have attracted much attention because the tridentate rigidity gives metal complexes high stability against air, moisture and heat.² Researches in this field have led to novel complexes,³ organometallic transition metal-catalyzed reactions,^{4,2c,5} soft materials⁶ and luminescent materials.⁷ To date, 20 most reported bisimidazolium pincers are type I bearing alkyl wingtip (R = alkyl group), which are obtained by the quaternization of N-alkylimidazole with 2,6-dibromopyridine^{8a,b} or 2,6-bis(benzimidazolyl)pyridine with alkyl halides.^{8c} **Type II** pincers bearing aryl wingtip (Ar = aryl group) are very limited. 25 Only N-mesitylimidazole and N-2,6-diisopropylphenylimidazole were reported to be directly quaternized with 2.6-dihalopyridine at high temperature for searval days.⁹ However, type II pincers are of particular interest because the steric and electronic properties of the pincers can be subtly tuned by substitutions on 30 the aryl ring. The high reaction temperature obstructs the introduction of functional groups and the long reaction time makes this method less efficient. Therefore, a mild and efficient



³⁵ Cyanuric chloride (2,4,6-trichloro-1,3,5-triazine) 1 is a highly reactive and commonly used reagent, in which three carbons are very electronically deficient and can be easily substituted by nucleophiles such as oxygen and nitrogen, *etc.*¹⁰ Cyanuric chloride even reacted with *N*-methylmorpholine to afford ⁴⁰ trimorpholium salt¹¹ and pyridine to form tripyridinium salts.¹² We envisaged that *N*-arylimidazole may also react with cyanuric chloride to form triimidazolium salts (Scheme 1). We then tried the reaction of cyanuric chloride with 3 equivalents *N*-

phenylimidazole **2a** in dry acetonitrile under reflux. To our ⁴⁵ delight, precipitate formed quickly and the pure compound was easily obtained by column chromatography on silica gel. The ¹H NMR of the product in DMSO- d_6 showed a set of three singlets of the hydrogens on the imidazolium ring, and a set of a typical mono-substituted phenyl ring signals. The singlet at 10.97 ppm ⁵⁰ was attributed to the hydrogen on C-2 of the imidazolium, indicating the successful quaterization of *N*-phenylimidazolium. However, the ¹³C NMR surprisingly showed two signals at 165.4 and 159.9 ppm of the triazine ring, suggesting two different





To determine the structure of the product, the product was firstly converted to hexafluorophosphate (PF_6) salt and the single crystal was grown in MeOH/CH₂Cl₂ (Figure 1). The X-ray 60 diffraction analysis revealed that 3a had crystallographicallyimposed mirror symmetry and the triazine ring was substituted by two imidazoliums and an oxygen atom. The length of the C-O bond (O1-C1) is 1.242(19) Å, which is more likely a C=O double bond (1.230 Å for ureas but 1.362 Å for phenols).¹³ There is only 65 one PF₆ counter anion, suggesting delocalization of another anion within the triazine ring to balance one positively charged imidazolium. So the actual structure of the product is determined to be a triazinonide-bridged bisimidazolium salt **3a** (PF_6^- salt), a type II pincer analogue.¹⁴ The triazinonide is slightly bent as the 70 dihedral angels of N1'-C1-N1-C2 and N1'-C2'-N2-C2 are -4.09(18)° and -3.12(2)°, respectively. The triazinonide, imidazolium and phenyl rings are not coplanar. The imidazolium

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ring twists out of the triazinonide ring -168.27(11)° (N1-C2-N3-C3) and the phenyl ring twists out of the imidazolium ring 154.16(12)° (C3-N4-C6-C7). In addition, the HRMS showed a main peak at 382.1412, which was ascribed to the cationic part of $_{5}$ **3a** with the molecular formula of C₂₁H₁₆N₇O⁺ (382.1411).



Fig. 1 ORTEP drawing of 3a (PF₆) (Ellipsoids are at 50% probability level; PF6 and solvent molecule are omitted for clarity). Symmetry operation: x, 1/2-y, z.

With the defined structure of the product 3a in hand, the reaction was proposed to take place through the substitution of the first two chlorines of cyanuric chloride by N-phenylimidazole followed by the hydrolysis of the third chlorine by water during workup^{12a,15} (Scheme 1). The mild conditions make this reaction 15 a practical method to prepare novel type II imidazolium pincers. Various N-arvl imidazoles with bulky, electron donating, electron-withdrawing groups were then successfully reacted with cyanuric chloride to afford a range of type II pincers (3a-f) in good yields (Scheme 2). Pincers 3a-f were all stable in air and at 20 elevated temperature.



Scheme 2 Synthesis of type II imidazolium pincers 3a-f.

However, N-alkyl imidazoles are much more reactive than Naromatic imidazoles and type I imidazolium pincers could not be 25 obtained by this procedure. Reaction of *n*-butylimidazole 2g and 1 in a 2:1 ratio resulted in a hydrolyzed zwitterionic product 4 after workup, which was characterized by X-ray analysis. Two water molecules and 2g attacked triazine ring to form two carbonyl groups and an imidazolium substituent with the anion 30 delocalizing on N2-C3-N3 to balance the positively charged imidazolium. Type I pincer 3g was finally obtained in 52% yield by the reaction in dry acetonitrile at 0 °C within 20 minutes followed by fast filtration and washes with cold acetonitrile. It needs to point out that pincer 3g is unstable in ambient 35 atmosphere and must be stored under nitrogen in refrigerator, otherwise hydrolysis to 4 occurs rapidly (Scheme 3).¹⁶

The catalytic activities of the bisimidazolium pincers 3a-f were then evaluated by in situ coordination with palladium to catalyze the Suzuki-Miyaura coupling reaction. Although there have been 40 a lot of reports about the CNC-Pd catalyzed Suzuki-Miyaura

View Article Online coupling reaction, the *in situ* catalysis is rare.¹⁷ We chose the coupling between phenylboronic acid with 4-bromo-N,Ndimethylaniline, a relatively less reactive substrate as the model reaction. After screening various conditions (Table S2), the 45 optimized conditions were set to be 0.005 mol% ligand and palladium acetate, 2 equivalents potassium phosphate in a mixed solvent of methanol/water (v/v, 1:1) at 100 °C for 7 hours. In comparison with different ligands, it clearly showed that steric hindered ligand (3b) and electron-rich ligands (3c, 3d and 3e) 50 exhibited better reactivities than electron-deficient ligand 3f (Table S2, entries 9-13). Ligand **3c**, bearing electron-donating 4-N,N-dimethylaminophenyl wingtips, stood out as the best ligand and gave a 94% isolated yield of the target coupling product.



55 Scheme 3 Synthesis of type I imidazolium pincer 3g and hydrolysis of 3g. Inset: ORTEP drawing of hydrolysate 4 (Ellipsoids are at 50% probability level and solvent molecule is omitted for clarity).

For comparison, the pyridine-bridged analogue of pincer 3b, 3b', was synthesized in 70% yield by quaternization of 60 mesitylimidazole with 2,6-dibromopyridine at 150 °C for 3 days, following the literature procedure.9a However, the pyridinebridged analogue of pincer 3c could not be obtained. Using pincer 3b' for the model reaction resulted in only 56% yield of the coupling product, which was much lower than the yield 65 obtained by using pincer 3b (Table S2, entry 14 vs 9). This suggested a positive effect of the triazinonide bridge in this type II pincers over pyridine bridge. In order to illustrate the Pd species involved in the catalysis, the ligand 3a was directed reacted with Pd(OAc)₂ in the presence of ^tBuONa and afforded 70 the Pd complex in 46% yield. ¹H NMR, ¹³C NMR, HRMS and elemental analysis supported the classical 1:1 pincer-Pd $complex^{4a}$ as $Pd(L_{3a})Cl$ (See ESI)

By applying ligand 3c, various bromobenzenes and phenylboronic acids were coupled under the optimized conditions, 75 and the results were summarized in Table 1. Bromobenzene reacted with phenylboronic acid to afford biphenyl in 98% yield (entry 1). Couplings with various arylboronic acids contained both electron donating group and electron withdrawing group gave nice yields, but the results with the later were little lower 80 (entries 2-5). The reactions of less reactive bromobenzenes with electron donating group all gave high yields over 94%, except the slightly decreased yield with ortho-methoxy substitution, probably due to steric hindrance effect (entries 6-9). The cross couplings between both substituted phenylboronic acids and 85 bromobenzenes all exhibited satisfactory results (entries 10-13). Most of the coupling reactions showed turnover numbers (TON) over 18000, indicating this is an efficient catalytic Suzuki-Miyaura reaction.

Table 1 Suzuki couplings between aryl halides and arylboronic acids^a

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| A | .r ₁ —Br + Ar ₂ —B(| Pd(OAc)₂ (0.005 Ligand 3c (0.005 K ₃ PO ₄ , MeOH 100 °C, 7 | mol%) 5 mol%) /H₂O ➤ Ar ₁ h | —Ar ₂ |
|-------|---|--|---|------------------|
| Entry | Ar ₁ Br | $Ar_2B(OH)_2$ | $\mathrm{Yield}^{b}\left(\%\right)$ | TON |
| 1 | ⟨Br | B(OH)2 | 98 | 19600 |
| 2 | ⟨Br | MeO-B(OH)2 | 94 | 18800 |
| 3 | ⟨Br | Ph ₂ N-B(OH) ₂ | 96 | 19200 |
| 4 | Br | F ₃ C B(OH) ₂ | 89 | 17800 |
| 5 | Br | FB(OH)2 | 91 | 18200 |
| 6 | OMe Br | B(OH)2 | 89 | 17800 |
| 7 | MeO | B(OH)2 | 97 | 19400 |
| 8 | MeO-Br | B(OH)2 | 98 | 19600 |
| 9 | NBr | B(OH)2 | 94 | 18800 |
| 10 | NBr | MeO-B(OH)2 | 94 | 18800 |
| 11 | NBr | F-B(OH) ₂ | 92 | 18400 |
| 12 | NCBr | F-B(OH) ₂ | 96 | 19200 |
| 13 | 0 Br | MeO-B(OH)2 | 98 | 19600 |

^{*a*} Conditions: arylbromides (1.0 mmol), arylboronic acid (1.1 mmol), $Pd(OAc)_2$ (0.005 mol%), ligand **3c** (0.005 mol%), K_3PO_4 (2.0 mmol), $H_2O/MeOH$ (v/v 1:1, 1 mL) at 100 °C for 7 h. ^{*b*} Isolated yield.

- ⁵ In summary, we disclose here a facile and mild method to synthesize bisimidazolium pincers of **type II** analogue by using highly reactive cyanuric chloride to quaternize arylimidazoles. This method provides access to various functionalized bisimidzolium pincers, which could not be obtained by traditional
- ¹⁰ synthesis. The *in situ* Pd-catalyzed Suzuki-Miyaura reaction using these pincers showed that pincer **3c**, which bears 4-*N*,*N*dimethylaminophenyl wingtips is a highly efficient ligand with Pd-**3c** loading as low as 0.005 mol%. The high efficiency of the ligand was demonstrated to take advantage of the unusual
- ¹⁵ triazinonide bridge over the traditional pyridine bridge and the electron-donating 4-*N*,*N*-dimethylaminophenyl wingtips which could not be obtained before. The strategy presented here provides an easy way to prepare functional NHC pincer precursors.
- ²⁰ We thank the financial support from the NSFC (Nos 20902063, 21172159 and 21021001) and the SRF for ROCS, SEM (No 20111568-8-2). We also thank the Centre of Testing & Analysis, Sichuan University for NMR measurements and X-ray analyses.

Notes and references

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| 30 | † Electronic | Supplementary | Information | (ESI) | available: | Detailed | |
| | experimental procedures, analytical data and the crystallographic data of | | | | | | |
| | $3a (PF_6)$ and | 4. CCDC 898254 | , 898255. See | DOI: 10 | 0.1039/b000 | 000x/ | |

- 3a (PF₆) and 4. CCDC 898254, 898255. See DOI: 10.1039/b000000x/
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