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Diphosphination of Arynes with Diphosphines

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Supporting Information

ABSTRACT: A diphosphination of arynes with diphosphines has been developed. The reaction of stable aryne precursors, 2-(trimethylsilyl)aryl triflates, with tetraaryldiphosphines proceeds in the presence of fluorine- or carbonate-based activators to deliver the corresponding diphosphinated products, sterically and electronically tuned 1,2-bis(diphenylphosphino)benzene (dppbz) derivatives, which can find wide application in transition metal catalysis and material science. Additionally, preliminary computational studies on the reaction mechanism are also reported.



isphosphines are indispensable organic compounds in B modern synthetic chemistry because they are promising bidentate ligands in transition metal catalysis and can greatly affect the selectivity as well as the efficiency of catalytic reactions.¹ Particularly, 1,2-bis(diphenylphosphino)ethanes and -ethenes constitute a prevalent class of ligands, owing to their uniquely rigid chelating nature to the metal center. Thus, rapid and concise synthesis of the above-mentioned chelate-type ligands has been a long-standing research subject in the synthetic community. Among numerous reported procedures, the diphosphination of C-C multiple bonds with diphosphines (R₂P-PR₂) is one of the most attractive and straightforward approaches since the readily available hydrocarbons can be used as the starting substrates.² To date, several reaction systems based on metal catalysts, radicals, and photochemistry have been developed for the diphosphination of alkynes³ and alkenes.⁴ On the other hand, the diphosphination of highly reactive and unstable arynes5 remains undescribed in the literature in spite of the advantage of such an approach.⁶ Given the recent wide application of expected products, that is, 1,2bis(diphenylphosphino)benzenes (dppbzs) in homogeneous catalysis⁷ and material science,⁸ development of new, effective strategies for the diphosphination of arynes is highly desirable. Herein, we report a simple and, thus, practical method for the diphosphination of arynes: TBAT (Bu₄NSiPh₃F₂) or Cs₂CO₃/ 18-crown-6-promoted diphosphination of stable aryne precursors, 2-(trimethylsilyl)phenyl triflates with diphosphines, is described. The newly developed protocol allows for preparation of electronically and sterically diverse dppbz-type ligands, some of which are inaccessible by conventional methods. Although synthesis of phosphorus-substituted arenes via aryne intermediates has been recently developed by several research groups,9 direct introduction of the P(III) group remains

underdeveloped. A related stannylphosphination of arynes with stannylphosphines was reported by Studer, but strongly basic conditions (i-PrMgCl) and careful temperature control (-78 °C) were still necessary, and aryne precursors were limited to 1,2-di(pseudo)halogenated benzenes.¹¹

Our study commenced by identification of an appropriate aryne precursor with tetraphenyldiphosphine (Ph₂P-PPh₂; 2a) as the coupling reagent. After extensive screening of activators and reaction parameters as well as aryne precursors, we were pleased to find that the 2-(trimethylsilyl)phenyl triflate (1a, 0.25 mmol) was the promising substrate, and the desired diphosphination reaction proceeded in the presence of Bu₄NPh₃SiF₂ (TBAT) and MS 4 A in DCE at 60 °C (conditions A; Scheme 1). For ease of handling, the diphosphinated product was analyzed and isolated as the corresponding phosphine sulfide 3aa-S (85% ³¹P{¹H} NMR yield and 79% isolated yield) after treatment with elemental

Scheme 1. Optimal Conditions for Diphosphination of 2-(Trimethylsilyl)phenyl Triflate (1a) with Tetraphenyldiphosphine (2a)





sulfur S₈. The reaction could be easily conducted on a 1.0 mmol scale, and a 350 mg quantity of the product was obtained (68% isolated yield), thus indicating the good reproducibility and practicality of this process. Additionally, the Cs₂CO₃/18-crown-6/THF-promoted conditions (conditions B)¹¹ were also good candidates to deliver **3aa-S** in a comparable yield (71% ³¹P{¹H} NMR yield).¹²

With the optimal conditions in hand, we performed the diphosphination of a variety of 2-(trimethylsilyl)aryl triflates 1 with 2a. Representative products are illustrated in Scheme 2.



^{*a*}Conditions: see Scheme 1. Conditions employed (A or B) in parentheses. Isolated yields are given. ^{*b*}Modified conditions B: $Cs_2CO_3/18$ -crown-6 (2.4 equiv), **2a** (3.0 equiv), B_2pin_2 (1.0 equiv), THF, 60°C, 39 h

The reaction was compatible with electron-donating (methyl, tert-butyl, methoxy) and -withdrawing (trifluoromethyl, chloro) groups at the ortho and meta positions and the corresponding backbone-modified dppbz-type ligands 3ba-S-3ha-S in good yields (46-79%). The more sterically demanding doubly orthosubstituted substrate was also tolerated under identical conditions (3ia-S). Additionally, the fused ring systems, including methylenedioxy and naphthyl groups, could be converted into the desired diphosphines 3ja-S-3la-S in synthetically useful yields. The heteroaromatic pyridine derivative also underwent the diphosphination (3ma-S). Notably, the present strategy accommodated the potentially reactive Bpin moiety (3na-S), which can be a good handle for further modifications toward new ligand design. In this case, the addition of pinB-Bpin improved the yield to some extent: although the detailed role is unclear at this stage, it can be a scavenger of excess fluoride anions to avoid the undesired

decomposition of the aryl-Bpin bond. Conditions A generally showed better results, but conditions B were specifically effective in the case of **3da-S**, **3ea-S**, and **3na-S**.

Owing to the ready availability of functionalized diaryldiphosphines, we then focused our attention toward synthesis of dppbz-type ligands with electronically modified aryl substituents on phosphorus (Figure 1). Pleasingly, conditions



Figure 1. Structure and yields of diphosphinated products 3-S from substituted tetraaryldiphosphines 2 under Conditions A.

A were applicable to electron-rich and -deficient tetraaryldiphosphines, giving electronically diverse dppbz derivatives **3hb-S-3hd-S** in acceptable yields (formed C–P bonds are illustrated with bold lines). To the best of our knowledge, they are novel dppbz ligands that are otherwise difficult to synthesize by other means.¹³ Additionally, the chiral bisphosphine ligand with point chirality on phosphorus was also accessible (**3je-S**), albeit as a 1:1 diastereomixture.

As mentioned above, the diphosphinated products were isolated in the more stable phosphine sulfides, but the direct isolation of P(III) products without S_8 quenching was also feasible (Scheme 3, 3aa and 3ma). Furthermore, the

Scheme 3. Direct Isolation of P(III) Products 3 and Desulfidation of Phosphine Sulfide Products 3-S



desulfidation of **3ga-S** to **3ga** could be easily conducted by using a Schwartz reagent.^{3g,14} Thus, the present diphosphination reaction can provide new and facile access to bidentate ligands.

Reaction mechanisms of arynes with some nucleophiles have been studied experimentally⁵ and theoretically,^{10,15} but details about diphosphination with diphosphines still remains elusive. Thus, to gain some mechanistic insight, we performed computational studies with DFT calculations. Three plausible reaction paths were assumed, as shown in Figure S3: (a) the formation of a zwitterionic intermediate by addition of Ph₂P– PPh₂ to benzyne, (b) (2 + 1) addition of benzyne with Ph₂P– PPh₂, (c) radical addition of PPh₂–PPh₂ to benzyne. The results of the reaction path search for the three paths show that

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the path (a) is the most kinetically and thermodynamically favorable mechanism for the diphosphination. 16

The energy diagram of the path (a) is shown in Figure 2. The relative enthalpy is based on benzyne and Ph_2P-PPh_2 at 0 kcal



Figure 2. Energy profile of the zwitterionic mechanism at the ω B97X-D/6-311+G(d,p) in DCE solvent treated as IEFPCM.

mol⁻¹. The reaction enthalpy (ΔH) in the process where Ph₂P–PPh₂ is added to benzyne and the zwitterionic intermediate is formed was -32.5 kcal mol⁻¹. In this process, no transition state was found, although we searched carefully. The activation enthalpy (ΔH^{\ddagger}) in the process from the zwitterionic intermediate to the diphosphinated product was 2.7 kcal mol⁻¹, and ΔH was -84.3 kcal mol⁻¹. This low ΔH^{\ddagger} value indicates that the zwitterionic intermediate rapidly isomerizes to the diphosphinated product. Therefore, the diphosphination of benzyne by the path (a) is thought to proceed rapidly.

Finally, we focused on recent advances in the hexadehydro-Diels–Alder (HDDA) reaction^{15a,17} and attempted to combine this chemistry with the diphosphination. Gratifyingly, upon simple heating of a mixture of tetrayne 4 and tetraphenyldiphosphine (2a) in THF- d_8 , the expected dppbz derivative 5-O was formed in 29% yield (Scheme 4a). Additionally, the

Scheme 4. Diphosphination of Additional Strained Molecules

a) combination with HDDA reaction



diphosphination could be extended to 2-[(trimethylsilyl)methyl]benzyl phenyl carbonate **6**, a well-known *ortho*quinodimethane precursor, which is among the representative strained and highly reactive molecules similar to arynes (Scheme 4b).¹⁸ In this case, condition-dependent unique divergent reactivity was observed: a combination of KF and 18crown-6 promoted the usual 1:1 coupling reaction to furnish the 1,2-bis{(diphenylphosphino)methyl}benzene 7-S in 51% yield, while the 2:1 diphosphinated product 8-S (CCDC 1827236) was selectively formed under TBAT/MS 4 A-mediated conditions.

In conclusion, we have developed simple and practical strategies for diphosphination of arynes with diphosphines. The reaction of stable and readily prepared aryne precursors, 2-(trimethylsilyl)aryl triflates, proceeds in the presence of fluorine- or carbonate-based activators to form the sterically and electronically tuned 1,2-bis(diphenylphosphino)benzene-type bidentate ligands of great potential in transition metal catalysis and material science. Additionally, the present work can provide new insight into the reactivity of arynes with heteroatom nucleophiles. More detailed mechanistic studies and further development of related phosphination chemistry are ongoing in our laboratory.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.or-glett.8b01470.

Procedures, characterization data, and details of DFT studies (PDF)

Accession Codes

CCDC 1827236 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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