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# Arenediazonium tetrafluoroborates in palladium-catalyzed C–P bond-forming reactions. Synthesis of arylphosphonates, -phosphine oxides, and -phosphines†

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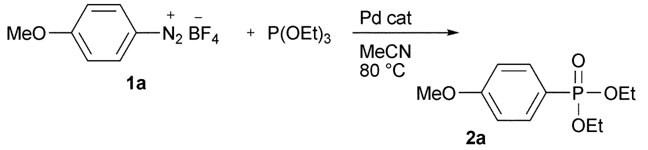
**A novel palladium-catalyzed synthesis of arylphosphonates from arenediazonium tetrafluoroborates and triethylphosphite or diethylphosphite is presented. The reaction tolerates useful substituents including bromo, chloro, nitro, ether, cyano, keto, and ester groups, can be performed as a one-pot process from anilines omitting the isolation of arenediazonium salts, and can be extended to the preparation of arylphosphine oxides and arylphosphines.**

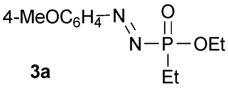
Arylphosphonates and their derivatives have found a wide range of applications in medicinal[1] and polymer[2] chemistry. They have also been used as ligands[3] and synthetic intermediates.[4] Classical syntheses[5] usually involve their preparation from aryl halides and trialkylphosphites *via* photoinduced reactions[5a–c] or under thermal AIBN/$n$-$Bu_3SnH$ conditions.[5d] After the first palladium-catalyzed reaction of aryl halides with hydrogen phosphonates reported by Hirao *et al.*,[6] a large number of transition metal-catalyzed procedures for the conversion of aryl halides into arylphosphonates have been developed based on palladium,[7] copper,[8] and nickel[3c,9] catalysis. Aryl triflates have also been used.[10] Surprisingly, despite their potential as aryl partners in this type of chemistry, there are no examples of arenediazonium salts. Therefore, as part of a program devoted to the development of arenediazonium salt based palladium-catalyzed syntheses,[11] we decided to investigate the feasibility of a palladium-catalyzed approach to aryl phosphonates from arenediazonium tetrafluoroborates.

**Table 1** Optimization studies[a]

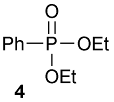


| Entry | [Pd] | Additive | Base | Time/h | Yield% of **2a**[b] |
|---|---|---|---|---|---|
| 1 | — | — | — | 15 | 8 |
| 2 | — | — | $Et_3N$ | 15 | 26[c] |
| 3 | — | — | $Cs_2CO_3$ | 16 | 12[d] |
| 4 | $Pd(PPh_3)_4$ | — | $Et_3N$ | 24 | 18[e] |
| 5 | $Pd(PPh_3)_4$ | NaI | $Et_3N$ | 24 | 19[f] |
| 6 | $Pd(PPh_3)_4$ | — | $Et_3N$ | 24 | —[g,h] |
| 7 | $Pd(PPh_3)_4$ | NaI | $Et_3N$ | 24 | 32[g,i] |
| 8 | $Pd(OAc)_2$ | — | $Cs_2CO_3$ | 15 | 52 |
| 9 | $Pd(OAc)_2$ | NaI | $Cs_2CO_3$ | 18 | 83 |
| 10 | $Pd(OAc)_2$ | KI | $Cs_2CO_3$ | 18 | 82 |
| 11 | $Pd_2(dba)_3$ | NaI | $Cs_2CO_3$ | 24 | 40 |
| 12 | $Pd(OAc)_2$ | NaI | $Et_3N$ | 30 | 68 |
| 13 | $Pd(OAc)_2$ | NaI | $K_2CO_3$ | 24 | 65 |
| 14 | $Pd(OAc)_2$ | KI | $Cs_2CO_3$ | 18 | 84[j] |
| 15 | $Pd(OAc)_2$ | KI | $Cs_2CO_3$ | 20 | 58[k] |
| 16 | $Pd(OAc)_2$ | KI | $Cs_2CO_3$ | 24 | 81[g] |
| 17 | $Pd(OAc)_2$ | KI | $Cs_2CO_3$ | 24 | 7[l] |

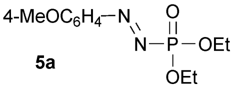
[a] Unless otherwise stated, reactions were carried out on a 0.5 mmol scale at 80 °C using 1 equiv. of **1a**, 2 equiv. of $P(OEt)_3$, 2 equiv. of base (when added), 3 equiv. of NaI or KI (when added) 0.05 equiv. of [Pd] in 3 mL of anhydrous MeCN. [b] Yields are given for isolated products. [c] **3a** was isolated in 17% yield. [d] **3a** was isolated in 7% yield. [e] **3a** and **4** were isolated in 11 and 17% yield, respectively. [f] **3a** and **4** were isolated in 3 and 17% yield. [g] Carried out with $H(O)P(OEt)_2$. [h] **5a** was isolated in 24% yield.[14] [i] **4** was isolated in 23% yield. [j] 1.5 equiv. of $P(OEt)_3$. [k] 2 equiv. of KI and 1.5 equiv. of $P(OEt)_3$. [l] At 50 °C. 4-Iodoanisole was isolated in 58% yield.



**3a**



**4**



**5a**

We started our study by examining the reaction of 4-methoxydiazobenzene tetrafluoroborate **1a** with $P(OEt)_3$ at 80 °C in MeCN. An initial screen showed that **2a** could be isolated in low yield omitting palladium, with ($Et_3N$ or $Cs_2CO_3$) or without bases[12] (Table 1, entries 1–3). The addition of $Pd(PPh_3)_4$ did not change the reaction course significantly. A complex reaction mixture was obtained from which **2a** was isolated in 18% yield along with **3a** and **4**, isolated in 11 and 17% yield, respectively (Table 1, entry 4). Most probably, compound **4** is formed *via* an exchange reaction between the phenyl groups bound to coordinated phosphine and that bound to the palladium center.[13] The addition of NaI gave a similar result (Table 1, entry 5) and the use of $H(O)P(OEt)_2$ revealed unsuccessful as well, leading to the isolation of significant amounts of **5a** in the absence of NaI (Table 1, entries 6) and of **4** when NaI was added (Table 1, entry 7).

Subsequently, we found that the reaction of **1a** with $P(OEt)_3$ in the presence of 5 mol% of $Pd(OAc)_2$ and 2 equiv. of $Cs_2CO_3$ produced **2a** after 18 h in 52% yield (Table 1, entry 8). No evidence of homocoupling product[15] was obtained. However, formation of arylphosphonates under these conditions resulted to be strongly dependent on the nature of the substituents. For example, the reaction of an electron-poor arenediazonium salt such as 4-acetyldiazobenzene tetrafluoroborate with triethylphosphite gave the corresponding phosphonate derivative only in 6% yield after 24 h.

Searching for an appropriate set of conditions that would provide higher yields as well as conversions of a wide variety

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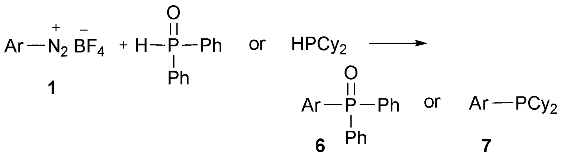
**Table 2** Synthesis of arylphosphonates from arenediazonium tetrafluoroborate and triethylphosphite[a]

| Entry | Arenediazonium salt **1** | Time/h | Yield% of **2**[b] | |
|---|---|---|---|---|
| 1 | $4\text{-MeOC}_6H_4N_2BF_4$ | 18 | 84 | **2a** |
| 2 | $4\text{-MeC}_6H_4N_2BF_4$ | 4 | 84 | **2b** |
| 3 | $3,5\text{-Me}_2C_6H_3N_2BF_4$ | 6 | 65 | **2c** |
| 4 | $3,4,5\text{-(MeO)}_3C_6H_2N_2BF_4$ | 4 | 75 | **2d** |
| 5 | $2\text{-Me},4\text{-MeOC}_6H_3N_2BF_4$ | 26 | 55 | **2e** |
| 6 | $PhN_2BF_4$ | 22 | 81 | **2f** |
| 7 | $4\text{-MeCOC}_6H_4N_2BF_4$ | 4 | 80 | **2g** |
| 8 | $4\text{-EtO}_2CC_6H_4N_2BF_4$ | 5 | 89 | **2h** |
| 9 | $4\text{-NO}_2C_6H_4N_2BF_4$ | 10 | 95 | **2i** |
| 10 | $4\text{-CNC}_6H_4N_2BF_4$ | 8 | 88 | **2j** |
| 11 | $3\text{-CF}_3C_6H_4N_2BF_4$ | 6 | 82 | **2k** |
| 12 | $4\text{-FC}_6H_4N_2BF_4$ | 8 | 81 | **2l** |
| 13 | $4\text{-ClC}_6H_4N_2BF_4$ | 6 | 88 | **2m** |
| 14 | $2\text{-ClC}_6H_4N_2BF_4$ | 24 | 80 | **2n** |
| 15 | $4\text{-BrC}_6H_4N_2BF_4$ | 2.5 | 98 | **2o** |
| 16 | $2\text{-BrC}_6H_4N_2BF_4$ | 26 | 54 | **2p** |

[a] Reactions were carried out on a 0.5 mol scale using 1 equiv. of **1**, 1.5 equiv. of triethylphosphite, 2 equiv. of $Cs_2CO_3$, 3 equiv. of KI, 0.05 equiv. of $Pd(OAc)_2$ in 3 mL of anhydrous MeCN at 80 °C. [b] Yields are given for isolated products.

**Table 3** Synthesis of arylphosphine oxides **6** and arylphosphines **7**[a]



| Entry | Arenediazonium salt **1** | *P*-donor | Time/h | Yield%[b] | |
|---|---|---|---|---|---|
| 1 | $4\text{-MeOC}_6H_4N_2BF_4$ | $HP(O)Ph_2$ | 4 | 90 | **6a** |
| 2 | $PhN_2BF_4$ | $HP(O)Ph_2$ | 6 | 90 | **6b** |
| 3 | $4\text{-EtO}_2CC_6H_4N_2BF_4$ | $HP(O)Ph_2$ | 6 | 60 | **6c** |
| 4 | $4\text{-ClC}_6H_4N_2BF_4$ | $HP(O)Ph_2$ | 24 | 50 | **6d** |
| 5 | $2\text{-Me},4\text{-MeOC}_6H_3N_2BF_4$ | $HP(O)Ph_2$ | 24 | — | **6e** |
| 6 | $2\text{-ClC}_6H_4N_2BF_4$ | $HP(O)Ph_2$ | 26 | 12 | **6f** |
| 7 | $3,4,5\text{-MeO}_3C_6H_2N_2BF_4$ | $HP(O)Ph_2$ | 28 | 82 | **6g** |
| 8 | $3,5\text{-Me}_2C_6H_3N_2BF_4$ | $HP(O)Ph_2$ | 24 | 75 | **6h** |
| 9 | $4\text{-EtO}_2CC_6H_4N_2BF_4$ | $HPCy_2$ | 2 | 70[c] | **7a** |

[a] Reactions were carried out on a 0.5 mol scale using 1 equiv. of **1**, 1.5 equiv. of P-donor, 2 equiv. of $Cs_2CO_3$, 3 equiv. of KI, 0.05 equiv. of $Pd(OAc)_2$ in 3 mL of anhydrous MeCN at 80 °C. [b] Yields are given for isolated products. [c] (4-methoxyphenyl)dicyclohexylphosphine oxide was isolated in 10% yield.

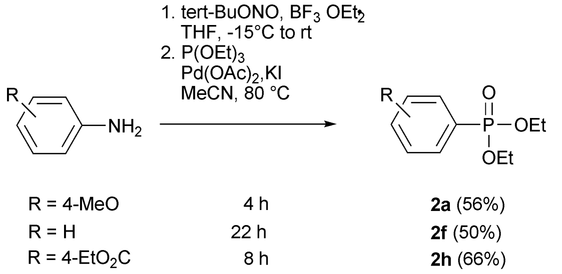
of substrates, we found that adding 3 equiv. of KI and using 1.5 equiv. of $P(OEt)_3$ led to the isolation of **2g** in 80% yield after 4 h. These conditions proved satisfactory with 4-methoxydiazobenzene tetrafluoroborate as well. The phosphonate **2a** was isolated in 84% yield (Table 1, entry 14). $H(O)P(OEt)_2$ can also be employed. The reaction of 4-methoxydiazobenzene tetrafluoroborate with $H(O)P(OEt)_2$ gave **2a** in 81% yield (Table 1, entry 16). The use of $Pd_2(dba)_3$ (Table 1, entry 11) or $Et_3N$ or $K_2CO_3$ (Table 1, entries 12 and 13), decreasing the excess of the additive (Table 1, entry 15) or the reaction temperature (Table 1, entry 17) provided lower yields.

Using the optimized conditions and triethylphosphite as the P-donor, we next explored the scope and generality of the process. As shown in Table 2, a variety of electron-rich and electron-poor arenediazonium tetrafluoroborates give the desired products in good to excellent yields. Ortho substituents are also tolerated (Table 2, entries 5, 14, 16).

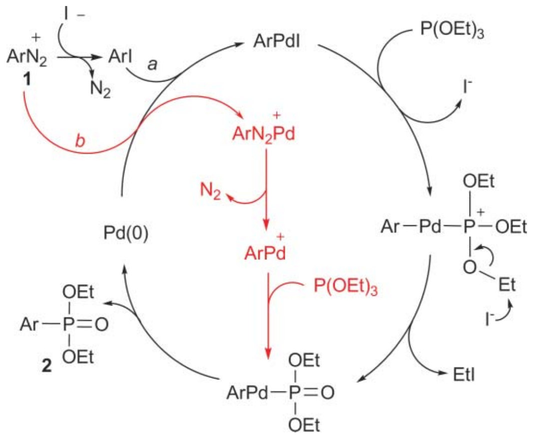
The synthesis of arylphosphine oxides and arylphosphines was also briefly investigated. The results obtained are summarized in Table 3. With *ortho* substituted arenediazonium salts, $H(O)PPh_2$ displayed lower reactivity than $P(OEt)_3$ (compare Table 2, entries 5 and 14 with Table 3, entries 5 and 6).

The entire *diazonium salt synthesis/iododediazoniation/C–P bond forming* sequence can be performed as a one-pot process, without the isolation of the arenediazonium salt intermediate[16] (Scheme 1). The best result was obtained by adding the reagents required for the iododediazoniation/C–P bond forming reaction to the crude mixture resulting from the first step concentrated under reduced pressure. Neglecting the evaporation of the volatile material produced lower yields. For example, 4-anisidine gave the corresponding phosphonate only in 16% yield.

In analogy to related palladium-catalyzed reactions of arenediazonium salts in the presence of iodide anions,[11e] we believe that the reaction proceeds through the mechanism that starts with a iododediazoniation step and that has been depicted for the synthesis of arylphosphonates (Scheme 2, path *a*).



**Scheme 1** One-pot synthesis of arylphosphonates from anilines.



**Scheme 2** Proposed mechanism for the palladium-catalyzed synthesis of arylphosphonates from arenediazonium tetrafluoroborates and $P(OEt)_3$.

Most probably, the alternative catalytic cycle involving the capture of a σ-arylpalladium cation by $P(OEt)_3$ (Scheme 2, path *b*) is operative when KI is not used (Table 1, entry 4). It appears less likely in the presence of iodide anions. Control experiments revealed that arenediazonium salts are quickly converted into the corresponding aryl iodides in the presence of iodide salts. For example, 4-methoxy- and 4-acetyldiazobenzene tetrafluoroborate are converted into the corresponding iodides in 58 and 89% yield after 5 min at room temperature.

In conclusion, we have developed a novel palladium-catalyzed synthesis of arylphosphonates from arenediazonium tetrafluoroborates and triethylphosphite or diethylphosphite. The reaction tolerates a variety of useful substituents including bromo, chloro, nitro, ether, cyano, keto, and ester groups. Ortho substituents such as methyl, bromo, and chloro are also tolerated. The presence of KI pays a key role for the success of the reaction that proceeds through a domino iododediazoniation/C–P bond forming process. Further, the entire *diazonium salt synthesis/iododediazoniation/C–P bond forming* sequence can be performed as a one-pot process from anilines. The method has been extended to the preparation of arylphosphine oxides and arylphosphines.

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