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Nickel-Catalyzed Synthesis of Phosphonium Salts from Aryl Halides and Triphenylphosphine

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Abstract: An efficient method to synthesize functionalized tetraarylphosphonium salts is described. The nickel-catalyzed coupling reaction between aryl iodides, bromides, chlorides, or triflates and triphenylphosphine generates tetraarylphosphonium salts in high yields. The coupling is wide in scope and tolerates a variety of functional groups such as alcohols, amides, ketones, aldehydes, phenols, phosphines and amines.

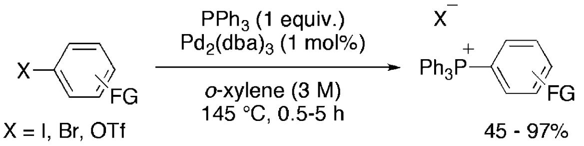
Keywords: coupling; lipophilicity; nickel; phosphorus; soluble support

Introduction

The importance of phosphonium salts is increasing in various fields of chemistry ranging from medicinal chemistry, organic synthesis and material sciences. Examples include their use as catalytic phase-transfer agents,[1] organic reagents,[2] ionic liquids,[3] conducting agents[4] and flame-proofing agents.[5,6] Additionally, the lipophilic properties of aryl-substituted phosphonium salts led to their application in cellular biology.[7] These applications include the treatment of diseases[8] and as drug carriers[9] due to their ability to penetrate cells and accumulate in mitochondria.[10,11]

Recently, we reported that the tetraarylphosphonium (TAP) unit can be used as a solubility control group to modify and predict the solubility properties of supported reagents and synthetic intermediates. A number of TAP-supported reagents derived from triphenylphosphine, diethyl azodicarboxylate,[12] tributyltin chloride,[13] and dialkylcarbodiimide[14] have been prepared and successfully used in various reactions. Furthermore, the reagents' by-products can be removed from the reaction medium by a precipitation/filtration sequence. We have also shown that TAP were effective soluble supports for the synthesis of small molecules to facilitate the isolation of reaction products, thereby avoiding extensive chromatographic purifications.[15] Although functionalized TAP are proving to be valuable compounds with many applications in various areas, to date, there is no simple or general catalytic method for their preparation.[16]

The palladium-catalyzed formation of TAP was first reported using aryl iodides[17] and, more recently, our group has extended this methodology to include aryl bromides and triflates [Eq. (1)].[18] However, the reaction was not highly chemoselective and many substituents on the aryl halide were not tolerated (*vide infra*). Horner's nickel-mediated coupling[19] using nickel(II) salts as reagents also suffers from poor functional group tolerance, and it requires a high nickel loading (50 mol%) as well as high temperature (>250 °C).[20] Although expensive nickel(0) complexes can be used as catalysts, a high loading (>10 mol%) is required. Furthermore, strongly electron-donating substituents (OMe, NMe_2) on the aryl halide moiety are necessary.[1b,c,21] Herein, we report a simple and general nickel-catalyzed method for the coupling of triphenylphosphine and various functionalized aryl halides.



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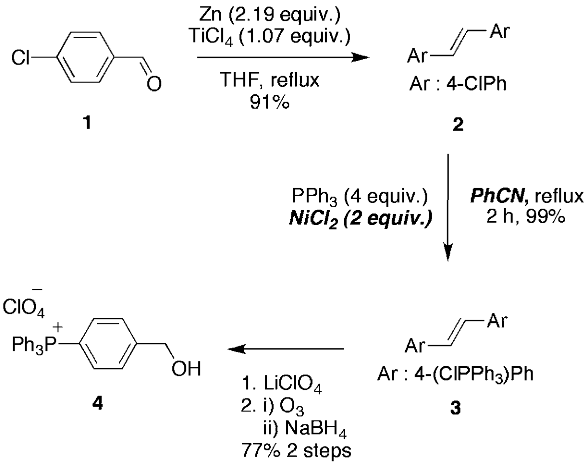
Results and Discussion

Synthesis of Relevant TAP Salts

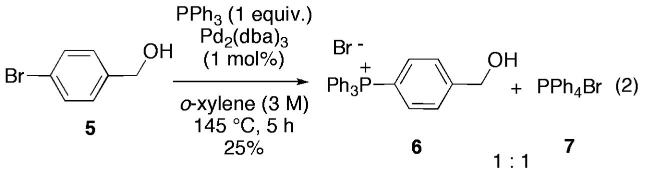
Recognizing the importance of phosphonium-supported benzyl alcohol **4** as a valuable template for drug

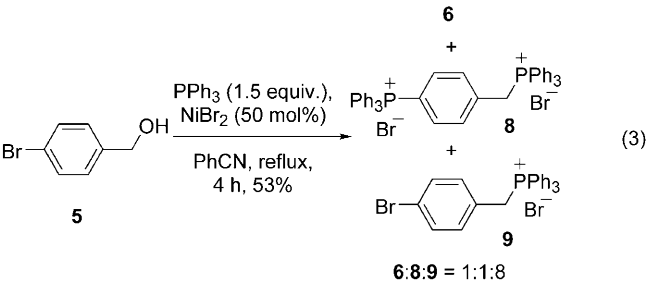


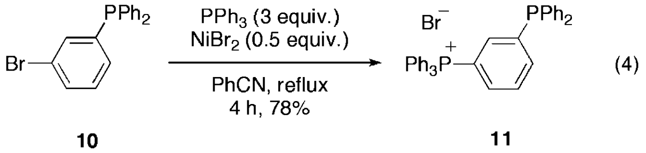
Scheme 1. Previous synthesis of TAP **4**.

carriers or for supported reagents and phosphine **11** as a valuable supported triphenylphosphine, we initially focused on developing new and more efficient reaction conditions for the preparation of these two phosphonium salts. The previous route to access **4** required three steps as shown in Scheme 1. The high loading in nickel chloride (2 equiv.), the low solubility of bis(phosphonium) **3**, and the difficulty to scale up the reaction (>10 g) prompted us to find an alternative and more efficient route to access benzyl alcohol **4**.

The one-step synthesis of **6** from commercially available 4-bromobenzyl alcohol (**5**) using the optimized palladium-catalyzed conditions[18] afforded a black precipitate and low yields of inseparable products **6** and **7** [Eq. (2)]. Furthermore, Horner's conditions using a nickel-mediated coupling provided a complex mixture of various phosphonium salts in which **6** was only a minor by-product [Eq. (3)]. Conversely, although the nickel-mediated coupling of bromophosphine **10** led to TAP **11** in good yield, an excess of triphenylphosphine was necessary to minimize reaction by-products derived from **11** [Eq. (4)]. Furthermore, phosphine **10** was quantitatively recovered under the palladium-catalyzed conditions.







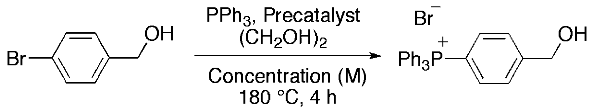
With these results in mind, our goal was to develop a new nickel-catalyzed tetraarylphosphonium salt-forming process that would be compatible with both substrates **5** and **10** as well as with a large number of functional groups.

Optimization and Scope

The first modification investigated was to find an alternative solvent to benzonitrile in the nickel-mediated coupling reaction and, ultimately, to reduce the reaction temperature as well as the catalyst loading. Solvents screened included dimethyl sulfoxide and diethylene glycol diethyl ether (DEGDEE) using 50 mol% of $NiBr_2$, although these led to a complex mixture of TAP salts when **5** was used as the starting material. However, a promising 55% yield of alcohol **6** was obtained when the reaction was carried out in ethanol under microwave irradiation (180 °C). Moreover, the substitution of ethanol by ethylene glycol afforded pure benzyl alcohol **6** in 51% yield when heated to 180 °C in an oil bath (Table 1, entry 1). Lowering the reaction temperature (<150 °C) did not give any of the desired salt while increasing the temperature to 196 °C (refluxing ethylene glycol) also yielded a complex mixture of TAP salts (Table 1).

A decrease in the catalyst loading from 50 to 1 mol% still afforded a 31% yield of the desired product when heated in ethylene glycol at 180 °C (entry 2). Varying the nickel precatalyst (entries 3–7) to nickel(I) bromide tris(triphenylphosphine) complex (entry 3) or nickel tris(triphenylphosphine) (entry 4) led to similar yields, but the air sensitivity and high costs associated with these complexes led to the optimization of the reaction with a cheaper and more stable Ni(II) catalyst precursor. Replacing anhydrous nickel(II) bromide by nickel(II) chloride (entry 5), nickel(II) acetate (entry 6) and nickel(II) bromide hexahydrate (entry 7) led to decreased yields. Gratifyingly, it was found that the concentration of the reaction had an important impact on the yield. The optimal concentration to obtain high catalyst turnover was 3 M (entries 2, 8 vs. 9). Concentrations greater than 3 M gave irreproducible yields, principally due to the partial solubility of the reagents. Finally, the

Table 1. Optimization of the Ni-catalyzed coupling reaction with 4-bromobenzyl alcohol (**5**).



5 **6**

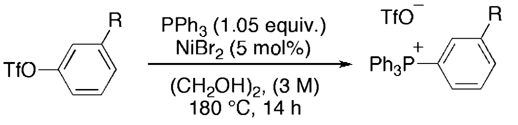
Entry	Precatalyst (mol%)	PPh_3 [equiv.]	(M)[a]	Yield [%][b]
1	$NiBr_2$ (50)[c]	1	1.5	51
2	$NiBr_2$ (1)	1	1.5	31
3	$Ni(PPh_3)_3Br$ (1)	1	1.5	34
4	$Ni(PPh_3)_3$ (1)	1	1.5	35
5	$NiCl_2$ (1)	1	1.5	21
6	$Ni(OAc)_2$ (1)	1	1.5	–[d]
7	$NiBr_2 \cdot 6H_2O$ (1)	1	1.5	27
8	$NiBr_2$ (1)	1	1	22
9	$NiBr_2$ (1)	1	3	56
10	$NiBr_2$ (1)	1	3	37[e]
11	$NiBr_2$ (3)	1	3	75
12	$NiBr_2$ (3)	1.05	3	91
13	$NiBr_2$ (3)	1.10	3	93
14	$NiBr_2$ (3)	1.20	3	97

[a] Concentration of compound **5**.
[b] Isolated yield.
[c] $NiBr_2$ refers to anhydrous $NiBr_2$.
[d] Many side-products are formed.
[e] Reaction time of 2 h.

amount of triphenylphosphine (entries 12–14) had also a large influence on the yield in addition to the rate of the reaction. In fact, increasing the amount of triphenylphosphine from 1 equiv. to 1.05 equiv. using 3 mol% of pre-catalyst increased the yield from 75% to 91% (entry 12). Furthermore, a 94% yield was obtained when the reaction was run on a 0.53-mol scale, affording 226 g of **6**. Although 1.2 equiv. (entry 14) resulted in a slightly improved 97% yield, 1.05 equiv. were used to examine the scope of the reaction (Table 2). Aryl iodides were more reactive and the catalyst loading was reduced to 2 mol% with a reaction time of 4 h giving similar yields [88% for 4-iodobenzyl alcohol (Table 2, entry 1)] to the optimized aryl bromide conditions. However, the reaction was less effective with aryl chlorides as longer reaction times were required and various side products were obtained with 4-chlorobenzyl alcohol. Consequently, chlorobenzene was used to optimize the reaction, and an 86% yield of tetraphenylphosphonium chloride was obtained by increasing both the reaction time to 14 h and the catalyst loading to 5 mol% (Table 2, entry 15).[22]

With these conditions in hand, different functionalized aryl halides were submitted to the reaction conditions as summarized in Table 2. The yields obtained under the palladium-catalyzed condition are also highlighted for comparison purposes.[18] In addition to the low catalyst loading required, it was found that these reaction conditions tolerate a wide range of functional groups when the reactions were performed with aryl bromides and iodides. In most of the cases, yields are similar to those obtained under palladium-catalyzed conditions. The Ni-catalyzed reaction permitted access to many functionalized tetraarylphosphonium salts that could not be prepared directly using palladium catalysis including alcohols (entries 1 and 23), phenols (entries 14 and 20), aldehydes (entry 22), phosphines (entry 21), amides (entries 16 and 22) and tertiary amines (entry 17). Aryl halides possessing electron-donating substituents gave excellent yields of the desired product in much shorter reaction times. In addition, aromatic ketones and aldehydes (entries 4, 10–12) were converted *in situ* to the corresponding cyclic acetals under the reaction conditions, however the subsequent deprotection under acidic conditions proceeded smoothly.[23] Unfortunately, esters were not tolerated while amides required an excess of triphenylphosphine in order to obtain good yields of the corresponding phosphonium salts (entry 16). Unprotected primary amines were not tolerated, although amines bearing acyl protecting groups gave good yields of desired product (entry 22). The synthesis of a monophosphonium salt from a dibromoarene turned out to be less efficient than under palladium catalysis[18] (entries 2 and 26). The solubility of the monophosphonium species in ethylene glycol is presumably responsible for the lack of selectivity of this reaction. The yield of the monophosphonium salt was improved if a slight excess of the corresponding dibromoarene was used. Nonetheless, diphosphonium salts such as **17** that are not accessible under palladium-catalyzed conditions could be prepared in good yields with this procedure (entry 7). *o*-Substituted aryl halides gave lower yields of the corresponding TAP (entries 23 and 24) while such compounds were found to be unreactive under palladium-catalyzed conditions. Although the functional group tolerance was not as good with aryl chlorides, good yields were obtained with ketones (entries 10 and 11) and phenols (entries 14 and 20). These compounds are quite useful since they both bear an anchoring group that allows further functionalization. It should be highlighted that all the phosphonium salts that were prepared above were isolated and purified by a simple precipitation/filtration sequence.[24]

Aryl trifates displayed similar reactivities as aryl chlorides under theses reactions conditions [Eq. (5)].

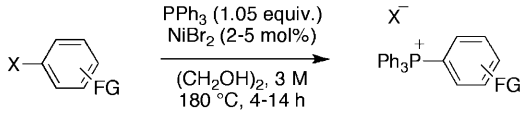


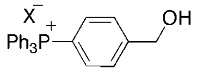
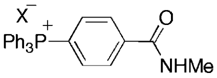
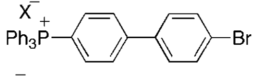
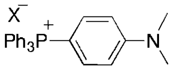
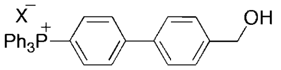
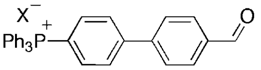
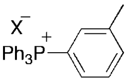
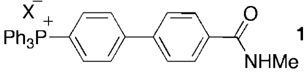
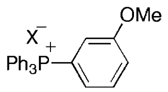
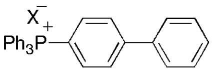
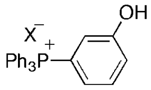
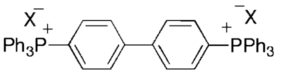
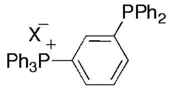
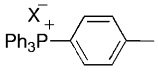
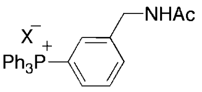
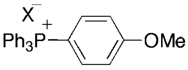
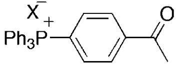
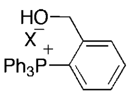
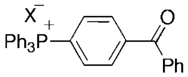
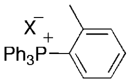
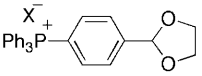
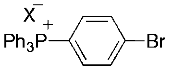
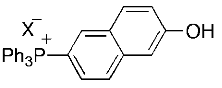
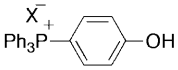
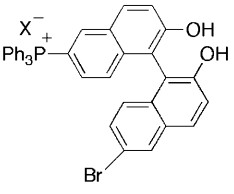
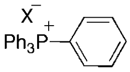
(5)

R = H (**35**)
R = Me (**36**)

R = H : 84% (**37**)
R = Me : 71% (**38**)

Table 2. Scope of the Ni-catalyzed coupling.[a]



Entry	Product		Yield (%)[b]	Entry	Product		Yield (%)[b]
1		**6**	X = Br, 91 (Mix) X = I, 88 (Mix)	16		**25**	X = Br, 53, 79[g] (NR) X = I, 55, 82[g] (NR)
2[c]		**12**	X = Br, 69 (96)	17[d]		**26**	X = Br, 46 (NR) X = I, 48 (NR)
3[f]		**13**	X = Br, 92 (96) X = I, 82 (89)				
4		**14**	X = Br, 96 (95) X = I, 83 (92)	18		**27**	X = Cl, 72 (NR) X = Br, 91 (88) X = I, 90 (80)
5		**15**	X = Br, 85 (80) X = I, 82 (83)	19[d]		**28**	X = Br, 75 (91) X = I, 85 (95)
6		**16**	X = Br, 89 (93)	20[e]		**29**	X = Cl, 73 (NR) X = Br, 85 (Mix) X = I, 85 (Mix)
7[i]		**17**	X = Br, 89 (NR)	21[g]		**11**	X = Br, 91 (NR)
8		**18**	X = Cl, 63 (NR) X = Br, 99 (93) X = I, 98 (92)	22		**30**	X = Br, 82 (Mix) X = I, 85 (Mix)
9[d]		**19**	X = Br, 79 (98) X = I, 92 (94)				
10		**20**	X = Cl, 66 (NR) X = Br, 97 (41) X = I, 82 (40)	23[e]		**31**	X = Br, 67 (Mix) X = I, 75 (Mix)
11		**21**	X = Cl, 82 (NR) X = Br, 96 X = I, 90	24		**32**	X = Br, 61 (NR) X = I, 66 (NR)
12[f]		**22**	X = Br, 67 (Mix) X = I, 72 (Mix)				
13[c]		**23**	X = Br, 69 (Mix) X = I, 83 (Mix)	25		**33**	X = Br, 99 (55)
14[e]		**24**	X = Cl, 87 (NR) X = Br, 93 (Mix) X = I, 85 (Mix)	26[c]		**34**	X = Br, 67 (89)
15		**7**	X = Cl, 86 (NR) X = Br, 88 (95) X = I, 91 (96)				

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[a] *Conditions:* aryl chlorides: 5 mol% of $NiCl_2$, 14 h; aryl bromides: 3 mol%, 4 h; aryl iodides: 2 mol%, 4 h.

[b] Isolated yield. In parenthesis are the yields obtained under the palladium-catalyzed conditions (NR = no reaction; Mix = mixture of products).

[c] 1.5 equiv. of the aryl halide was used.

[d] Reaction time of 15 min.

[e] Reaction time of 2 h.

[f] Reaction time of 3 h.

[g] 3 equiv. of triphenylphospine were used.

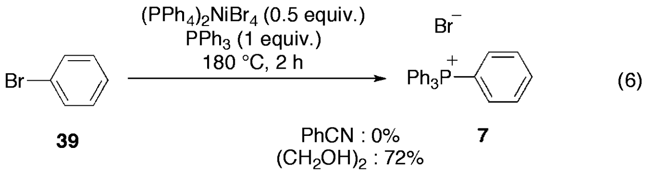
[h] 5 mol% of $NiBr_2$ was used.

[i] 3 equiv. of PPh_3 were used in boiling ethylene glycol for 4 h.

[j] 10 mol% of $NiCl_2$ was used.

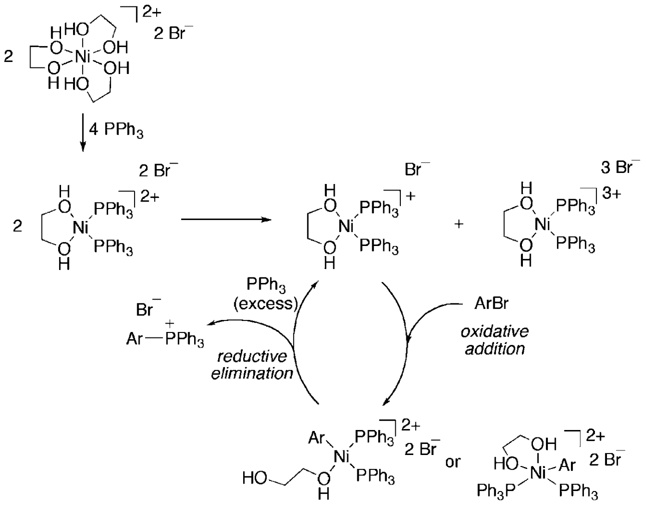
Mechanism

The effect of ethylene glycol in improving the catalytic turnover in this reaction is quite remarkable. By way of contrast, when benzonitrile is used as the solvent the reaction requires a minimum of 0.5 equiv, of nickel bromide. It has been reported that the classical Horner reaction, either neat or in benzonitrile, leads to the nickelate species $[ArPR_3]_2$ $[NiBr_4]$[25,26] that does not regenerate the active catalyst. This was further confirmed when we preformed $[Ph_4P]_2$ $[NiBr_4]$[26] and submitted it as pre-catalyst to a typical Horner reaction in benzonitrile [Eq. (6)]. No new TAP salt was formed[27] which clearly demonstrates that $[Ph_4P]_2$ $[NiBr_4]$ does not catalyze the reaction or does not lead to an active catalyst in benzonitrile. It is believed that the reaction shown in Eq. (3) and Eq. (4) halts at the nickelate species which explains that 50 mol% of $NiBr_2$ is required to get a good yield of TAP.[19] Conversely, when the pre-formed $[Ph_4P]_2$ $[NiBr_4]$ was submitted as pre-catalyst to the reaction in ethylene glycol, a good yield of new tetraphenylphosphonium bromide was isolated. Thus, it seems that alcoholic solvents such as ethanol (which also led to good conversion) and ethylene glycol have the ability to regenerate a catalytically active species in the reaction from $[Ph_4P]_2$ $[NiBr_4]$.



(6)

The proposed catalytic cycle is presented in Scheme 2. When $NiBr_2$ is dissolved in ethylene glycol, it adopts an octahedral complex with two molecules of solvent as exemplified with aqueous $NiBr_2$ that is found under the $[NiBr_2(H_2O)_4]$ octahedral structure.[28] Under heating at 180 °C, we believe that the solvent can displace Br^- to form an octahedral $\{Ni[(CH_2OH)_2]_3\}Br_2$ complex.[29] We cannot rule out the extrusion of HBr to form a Ni–O bond. However, we believe that the generation of HBr is unlikely as we do not observe any of the side reactions that would be expected especially when 50 mol% of $NiBr_2$ is used (Table 1, entry 1). Triphenylphosphine has a greater ligand field than alcohols and will thus displace the solvent ligands to generate a tetracoordinated $\{Ni(CH_2OH)_2(PPh_3)_2\}Br_2$.[29] Mechanistic studies performed in EtOH have demonstrated the disproportionation step that generates the active nickel(I) catalyst that begins the Ni(I)/Ni(III) catalytic cycle.[30] We believe that Ni(I) is also the active catalyst in our case since, though similar yields were obtained when beginning with Ni(0), Ni(I) or Ni(II) species (Table 1, entry 2–4), the reaction using the Ni(I) occurred with the fastest rate. We postulate that ethylene glycol is present as a ligand onto the Ni through the catalytic cycle. This would explains the high catalytic turnover by preventing the formation of $[Ph_4P]_2$ $[NiBr_4]$.



Scheme 2. Proposed catayltic cycle for the coupling reaction.

Conclusions

In conclusion, we have developed an efficient method to synthesize functionalized tetraarylphosphonium salts. This Ni-catalyzed reaction is conducted in ethylene glycol using a readily available and cheap Ni(II) precatalyst. The reaction conditions tolerate many functional groups including alcohols and aldehydes. Lower catalyst loadings are used (as low as 2 mol%) compared to previously reported Ni-catalyzed methods and the reaction is compatible with aryl iodides, bromides, chlorides, and triflates. This reaction has also been successfully run on a relatively large scale (>0.5 mol). Finally, a major advantage of this method is the ease of purification of the products by a simple precipitation/filtration sequence.

Experimental Section

Typical Procedure for the Nickel-Catalyzed Formation of Functionalized TAP Chloride Salts from Functionalized Aryl Chlorides: Triphenyl(*p*-tolyl)phosphonium Chloride (9 Cl)

Commercially available 4-chlorotoluene (380 mg, 355 μL, 3.00 mmol, 1.00 equiv.), $NiCl_2$ (19.4 mg, 0.15 mmol, 5 mol%) and triphenylphosphine (826 mg, 3.15 mmol, 1.05 equiv.) were mixed in a 10-mL tube (without the use of an inert atmosphere). To this mixture were added ethylene glycol (1 mL, 3 M) and a magnetic stir bar and the tube was sealed with a Teflon cap. The sealed tube was heated at 180 °C in an oil bath for 14 h. The reaction mixture became homogeneous within 1–2 h and the colour slightly blue as the reaction proceeded. After 14 h, the tube was cooled to room temperature, and the mixture diluted with 40 mL of DCM. The organic layer was washed 3 times with water, once with brine, dried over anhydrous $MgSO_4$, filtered through Celite and concentrated under reduced pressure. The solid was then diluted in a minimum of DCM (*ca.* 5 mL) and 20 mL of diethyl ether were added while the flask was vigorously shaken. The precipitate was filtered on Celite and washed with 20 mL of diethyl ether. The solid was then redissolved in 100 mL of DCM. The organic layer was concentrated under reduced pressure to afford **9 Cl** as a pure beige solid; yield: 735 mg (63%); mp 200–203 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.87–7.81$ (m, 3 H), 7.76–7.69 (m, 6 H), 7.57–7.49 (m, 8 H), 7.45–7.38 (m, 2 H), 2.46 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 147.4$ (d, $J = 3.0$ Hz, 1 C), 135.7 (d, $J = 3.0$ Hz, 3 C), 134.3 (d, $J = 10.7$ Hz, 2 C), 134.2 (d, $J = 10.3$ Hz, 6 C), 131.6 (d, $J = 13.3$ Hz, 2 C), 130.8 (d, $J = 12.8$ Hz, 6 C), 117.6 (d, $J = 87.7$ Hz, 3 C), 113.5 (d, $J = 92.1$ Hz, 1 C), 21,9 (d, $J = 1.5$ Hz, 1C); ^{31}P NMR (122 MHz, $CDCl_3$): $\delta = 23.6$; IR (film): $\nu = 3052$, 2843, 1598, 1437, 1108, 921, 722 cm^{-1}; HR-MS (ES, pos): $m/z = 343.1459$, calcd. for $C_{25}H_{22}P_1$ [M]$^+$: 353.1459.

Typical Procedure for the Nickel-Catalyzed Formation of Functionalized TAP Bromide Salts from Functionalized Aryl Bromides: [4-(Hydroxymethyl)phenyl]triphenylphosphonium Bromide (2 Br)

Commercially available 4-bromobenzyl alcohol (561 mg, 3.00 mmol, 1.00 equiv.), $NiBr_2$ (20 mg, 0.09 mmol, 3 mol%) and triphenylphosphine (826 mg, 3.15 mmol, 1.05 equiv.) were placed together in a 10-mL tube. To this mixture were added ethylene glycol (1 mL, 3 M) and a magnetic stir bar and the tube was sealed with a Teflon cap. The sealed tube was heated at 180 °C in an oil bath for 4 h. The reaction mixture became homogeneous within an hour and the colour turned slightly green as the reaction proceeded. After 4 h, the tube was cooled to room temperature, uncapped and the mixture diluted with 40 mL of DCM. The organic layer was washed 3 times with water, once with brine, dried over anhydrous $MgSO_4$, filtered thorough Celite and concentrated under reduced pressure. The solid was then diluted in a minimum of DCM (*ca.* 5 mL) and 20 mL of diethyl ether were added while the flask was vigorously shaken. The precipitate was filtered on Celite and washed with an additional 20 mL of diethyl ether. The solid was then redissolved in 100 mL of DCM and concentration under reduced pressure afforded **2 Br** as a pure white solid; yield: 1.23 g (91%); mp 220–223 °C; ^{1}H NMR (300 MHz, CD_2Cl_2): $\delta = 7.89–7.84$ (m, 3 H), 7.82–7.78 (m, 2 H), 7.74–7.68 (m, 6 H), 7.62–7.46 (m, 8 H), 5.42 (t, $J = 7.2$ Hz, 1 H), 6.09–5.93 (br m, 2 H), 5.87 (dd, $J = 5.3$ Hz, 9.3 Hz, 1 H), 5.70 (t, $J = 6.3$ Hz, 1 H), 4.77 (d, $J = 6.3$, 2 H); ^{13}C NMR (75 MHz, CD_2Cl_2): $\delta = 153.4$ (d, $J = 3.0$ Hz, 1 C), 136.4 (d, $J = 3.0$ Hz, 3 C), 135.3 (d, $J = 10.3$, 6 C), 135.0 (d, $J = 10.8$ Hz, 2 C), 131.4 (d, $J = 12.9$ Hz, 6 C), 129.4 (d, $J = 13.3$ Hz, 2 C), 118.8 (d, $J = 89.6$ Hz, 3 C), 115.0 (d, $J = 91.6$ Hz, 1 C), 63.3 (s, 1 C); ^{31}P NMR (122 MHz, CD_2Cl_2): $\delta = 23.7$; IR (film): $\nu = 3251$ (br), 3052, 1600, 1586, 1437, 1108, 1060, 954 cm^{-1}; HR-MS (APCI, pos): $m/z = 369.1403$, calcd for $C_{25}H_{22}O_1P_1$ [M]$^+$: 369.1408, LR-MS (ES, neg): $m/z = 79.0$, calcd. for ^{79}Br [M]$^-$: 78.9, 81.0, calcd. for ^{81}Br [M]$^-$: 80.9.

Typical Procedure for the Nickel-Catalyzed Formation of Functionalized TAP Iodide Salts from Functionalized Aryl Iodides: [4-(Hydroxymethyl)phenyl]triphenylphosphonium Iodide (2 I)

4-Iodobenzyl alcohol (702 mg, 3.00 mmol, 1.00 equiv.), $NiBr_2$ (13.1 mg, 0.06 mmol, 2 mol%) and triphenylphosphine (826 mg, 3.15 mmol, 1.05 equiv.) were mixed together in a 10-mL tube. To this mixture were added ethylene glycol (1 mL, 3 M) and a magnetic stir bar and the tube was sealed with a Teflon cap. The sealed tube was heated at 180 °C in an oil bath for 4 h. The reaction mixture became homogeneous within an hour and the colour turned reddish as the reaction proceeded. After 4 h, the tube was cooled to room temperature, uncapped and the mixture diluted with 40 mL of DCM. The organic layer was washed 3 times with water, once with brine, dried over anhydrous $MgSO_4$, filtered through Celite and concentrated under reduced pressure. The solid was then dissolved in a minimum of DCM (*ca.* 5 mL) and 20 mL of diethyl ether were added while the flask was vigorously shaken. The precipitate was filtered on Celite and washed with 20 mL of diethyl ether. The solid was then redissolved in 100 mL of DCM. The solution was concentrated under reduced pressure to afford **2 I** as a pure white solid; yield: 1.31 g (88%); mp 230–233 °C; ^{1}H NMR (300 MHz, CD_2Cl_2): $\delta = 7.89–7.84$ (m, 3 H), 7.82–7.78 (m, 2 H), 7.74–7.68 (m, 6 H), 7.62–7.46 (m, 8 H), 5.42 (t, $J = 7.2$ Hz, 1 H), 6.09–5.93 (br m, 2 H), 5.87 (dd, $J = 5.3$ Hz, 9.3 Hz, 1 H), 5.70 (t, $J = 6.3$ Hz, 1 H), 4.77 (d, $J = 6.3$, 2 H); ^{13}C NMR (75 MHz, CD_2Cl_2): $\delta = 153.4$ (d, $J = 3.0$ Hz, 1 C), 136.4 (d, $J = 3.0$ Hz, 3 C), 135.3 (d, $J = 10.3$ Hz, 6 C), 135.0 (d, $J = 10.8$ Hz, 2 C), 131.4 (d, $J = 12.9$ Hz, 6 C), 129.4 (d, $J = 13.3$ Hz, 2 C), 118.8 (d, $J = 89.6$ Hz, 3 C), 115.0 (d, $J = 91.6$ Hz, 1 C), 63.3 (s, 1C); ^{31}P NMR (122 MHz, CD_2Cl_2); $\delta = 23.7$; IR (film): $\nu = 3251$ (br), 3052, 1600, 1586, 1437, 1108, 1060, 954 cm^{-1}; HR-MS (APCI, pos): $m/z = 369.1403$, calcd. for $C_{25}H_{22}O_1P_1$ [M]$^+$: 369.1408; HR-MS (ES, neg): $m/z = 126.9050$, calcd. for ^{127}I [M]$^-$: 126.9056.

Typical Procedure for the Nickel-Catalyzed Formation of Functionalized TAP Triflate Salts from Aryl Triflates: Tetraphenylphosphonium Triflate (30)

Phenyl trifluoromethanesulfonate (678 mg, 3.00 mmol, 1.00 equiv.), $NiBr_2$ (33.1 mg, 0.15 mmol, 5 mol%) and triphenylphosphine (826 mg, 3.15 mmol, 1.05 equiv.) were mixed together in a 10-mL tube. To this mixture were added ethylene glycol (1 mL, 3 M) and a magnetic stir bar and the tube was sealed with a Teflon cap. The sealed tube was heated at 180 °C in an oil bath for 14 h. The reaction mixture became homogeneous within one to two hours and the colour turned blue as the reaction proceeded. After 14 h, the tube was cooled to room temperature, uncapped and the mixture diluted with 40 mL of DCM. The organic layer was washed 3 times of water, once with brine, dried over anhydrous $MgSO_4$, filtered through Celite and concentrated under reduced pressure. The solid was then dissolved in a minimum of DCM (*ca.* 5 mL) and 20 mL of diethyl ether while the flask was vigorously shaken. The precipitate was filtered on Celite and washed with 20 mL of diethyl ether. The solid was then redissolved in 100 mL of DCM. The solution was concentrated under reduced pressure to afford **30** as a pure beige solid; yield: 735 mg (63%); mp: 200–203 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.90–7.81$ (m, 4H), 7.76–7.69 (m, 8H), 7.60–7.53 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 135.8 (d, $J = 3.0$ Hz, 4C), 134.4 (d, $J = 10.3$ Hz, 8C), 130.8 (d, $J = 12.9$ Hz, 8C), 117.4 (d, $J = 89.6$ Hz, 4C); ^{31}P NMR (122 MHz, $CDCl_3$): $\delta = 23.3$; ^{19}F NMR (282 MHz, $CDCl_3$): $\delta = -79.5$; IR (film): $\nu = 3065$ (br), 3062, 1585, 1483, 1435, 1262, 1141, 1107, 1030, 995, 905 cm^{-1}; HR-MS (ES, pos): $m/z = 339.1288$, calcd. for $C_{24}H_{20}P_1$ $[M]^+$: 339.1302; HR-MS (ES, neg): $m/z = 148.9525$, calcd. for CF_3SO_3 $[M]^-$: 148.9532.

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