Pt(0)-Catalyzed Alkynylation of Aryl Iodides with Lithium Alkynyltriisopropoxy Borates

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Abstract: An efficient cross coupling reaction of various lithium alkynyltriiospropoxyborates with a wide array of aryl iodides was catalyzed by $Pt(PPh_3)_4$ -CuI in DMF as a solvent. These cross coupling reactions are general and permit the new sp-sp² carbon-carbon bond formation.

Key words: alkynylation, lithium alkynylborate, Pt-catalyst, Suzuki–Miyaura coupling

Transition metal-catalyzed coupling reactions of metal acetylides are very efficient and reliable methods for constructing new carbon-carbon bonds.¹ In particular, the Sonogoshira reaction has been used extensively over the past three decades for the construction of C(sp²)-C(sp) bonds.² The reaction is a straightforward way to achieve arylalkynes, enynes, and other unsaturated compounds, many of which possess a diverse range of potential applications on such as molecular electronic devices,³ dendrimers,⁴ benzaannulenes,⁵ foldamers or polymers,⁶ pharmaceuticals,⁷ and natural product synthesis.⁸ Therefore there have been extensive efforts to find better catalysts which provide high turnover number, high functional group compatibility, and increased scope of arylalkyne formation.

Of the many organometalloids being used in cross-coupling reactions, the organoboron reagents are the most intriguing since they are stable in air, inexpensive, and environmentally benign.⁹ Utility of alkynylborates in metal-catalyzed reactions have become the subject of intense interest due to their enhanced reactivity. Successful transformations include Suzuki-Miyaura cross coupling,¹⁰ allylic additions to allylic carbonate,¹¹ conjugate addition to enones,¹² Mannich reaction,¹³ and homocoupling reactions.¹⁴ Although we and others have applied the use of these reagents in palladium-catalyzed Suzuki-Miyaura coupling reactions, limitations remain: the conditions often require stoichiometric or excess amount of base, and two equivalents of borate salts are indispensable for smooth transformations. In spite of the synthetic value of organoborates, extensive research is being performed only in the fields of Pd- and Ni-catalyzed reactions whilst the use of Pt catalysts remains mainly unnoticed. Compared to Ni or Pd compounds, Pt compounds have low

reactivity, presumably due to the diffused d-orbital. We imagined that the use of less reactive platinum compounds could provide an interesting alternative for selective cross-coupling reactions of alkynylborates with aryl iodides in the presence of labile organic bromides. To the best of our knowledge, there was no precedent on cross-coupling of alkynylborates with aryl iodides or any other electrophiles by using platinium catalysts. On other hand, platinum-catalyzed Suzuki coupling reaction,¹⁵ Heck reaction,¹⁶ hydrosilylation of terminal alkynes,¹⁷ intramolecular C-H activation,¹⁸ and olefin amination ¹⁹ reactions are known.

On the basis of these promising potentialities, our efforts have been made in developing new synthetic methodologies using organoboron compounds,²⁰ herein we wish to report a new Pt(0)-catalyzed cross-coupling of alkynylborates with aryl iodides with an exquisite chemoselectivity.

To uncover a suitable Pt-catalyst and to search the optimal conditions, we tried to perform the reaction of phenylacetyleneborate (1a) with *p*-iodoanisole (2a). Among PtCl₂, $PtCl_4$, and $Pt(PPh_3)_4$, $Pt(PPh_3)_4$ was shown to be the most effective catalyst. We considered as Cu(I) salt as a potential co-catalyst because of ability to catalyze Sonogashira reaction. To our great delight the use of Pt(PPh₃)₄-CuI system was effective in view of the yield of the product **3aa**. Then, we carried out this reaction in several solvents such as toluene, CH₂Cl₂, MeCN, DME, and DMF. The reaction was found to be very sensitive to DMF as solvent, where significant enhancement of the catalytic activity in DMF was observed. The other solvents CH₂Cl₂, MeCN, and DME were totally ineffective while toluene afforded 3aa only in trace amounts. Gratifyingly, the use of $Pt(PPh_3)_4$ (2.5 mol%) with CuI (5 mol%) in DMF at 120 °C resulted in exclusive formation of 3aa in 82% vield.

Having established the present methodology, we studied this cross-coupling reaction with various aryl iodides (Equation 1 and Table 1). Notably, most of the reactions gave good results. No significant electronic effects were observed for either *para-* or *meta-*substituted aryl iodides. However, the presence of a free hydroxyl group in aryl iodides resulted in some homocoupled products (entries 8 and 9). Even sterically hindered aryl iodides worked well: 2-iodotoluene (**2k**) and 2,6-dimethyliodobenzene (**2l**) showed to have virtually the same reactivity toward phenylacetyleneborate under the present conditions (entries 11 and 12), implying that steric effect is not a sole gover-

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nor in this reaction. It is noteworthy that this Pt-catalyzed alkynylation can be performed in ambient atmosphere without scarifying yield (entries 3 and 4). A wide variety of aryl iodides were found to undergo facile cross-couplings by phenylacetyleneborate (1a). The cross-coupling reaction with 1-iodonaphthalene (2m) gave good yield, without significant loss of yield, heterocyclic iodides 2n and 20 also underwent smooth cross-coupling thereby affording **3an** and **3ao** in acceptable yields of 73% and 71%, respectively (entries 13-15). No coupling product was obtained when bromobenzene or *p*-bromoanisole were used.



Equation 1

Table 1 Platinum-Catalyzed Cross-Coupling of Various Aryl Iodides (2a-o) with Phenylalkynylborate 1a.



^a Isolated yields.

^b Reaction performed in presence of air.

^c Homocoupled product (diphenyl-1,3-butadiyne) was observed.

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It is noteworthy that 4-bromoiodobenzene (2j) underwent chemoselective coupling producing the corresponding bromoarylalkyne derivative (entry 10). As anticipated, the selective coupling with aryl iodide over bromide affording **3aj** is caused by the fast oxidative addition into the $C(sp^2)$ -I bond over the $C(sp^2)$ -Br bond. The electronic properties of the ligand are certainly of importance for this reaction; thus even platinum(0) complexes are not sufficiently electron rich to undergo fast oxidative addition into aryl bromides.²¹ Encouraged by these results, we began to evaluate the general applicability as well as relative reactivity of various alkynylborates (Equation 2).

To this end we have prepared a series of alkynylborates from the commercially available triisopropoxyboarate with alkynyllithiums, which were prepared in situ from

Table 2 Platinum-Catalyzed Cross-Coupling of Various Alkynylborates (1b-p) with Iodobenzene (2b).

Entry	Substrate	Time (h)	Product	Yield (%)
1	0 ₂ N-	12	3bb	72
2	1b Me-	12	3cb	76
3	1с н₃со-√_>—≡	14	3db	80
4	1d tert-C ₄ H ₉	15	3eb	71
5	1e <i>n</i> -C ₄ H ₉	13	3fb	73
6	lf Me₃Si──━	12	3gb	61
7	1g ⊤BSOCH₂───	12	3hb	76
8	1h THPOCH₂─═	10	3ib	62
9	1i TBSO(CH ₂) ₂	12	3jb	74
10	1j ⊤BSO(CH ₂) ₃ ==	12	3kb	71
11	1k BnO(CH ₂) ₄	15	3lb	75
12		12	3mb	69
13	Im OTBS	12	3nb	64
14	1n 1-Np	15	3ob	62
15		12	3pb	71
	1p			



Equation 2

the corresponding terminal alkynes with BuLi at -78 °C in diethyl ether.²²

Most of the alkynylborates were cross-coupled with iodobenzene under the optimized conditions in good to excellent yields as summarized in Table 2. Arylacetyleneborates bearing both an electron-deficient group (**1b**) and electron-rich group (**1c** and **1d**) worked smoothly under these conditions to afford **3bb**, **3cb** and **3db** in 72%, 76%, and 80% yields, respectively (entries 1–3). Alkylsubstituted acetyleneborates such as *tert*-butyl (**1e**) and *n*butyl (**1f**) gave the even more promising results (entries 4, 5). TMS-substituted alkynylborate (**1g**) also underwent effective cross-coupling to afford the product **3gb** in 61% yield (entry 6).

We next employed a series of terminal alkynes bearing an oxy-functionality. The reaction of the TBS ether 1h of propargyl alcohol provided the corresponding arylalkyne 3hb in 76% yield (entry 7). Similarly, THP ether 1i of propargyl alcohol also worked well without any deprotection (entry 8). These reactions with the TBS ethers 1j and ik of 3-butyn-3-ol and 4-pentyn-1-ol afforded the corresponding cross-coupled products 3jb and 3kb in 74% and 71% yields, respectively (entries 9, 10). Benzyl ether 11 of 5hexyn-1-ol was also effective to furnish the product **3lb** in 75% yield (entry 11). The bulky substrates 1m and 1n underwent smooth coupling to give the products 3mb and **3nb** in 69% and 64% yields, respectively (entries 12, 13). Not surprisingly, two more alkynyl substrates 10 and 1p were also effectively coupled under this catalytic system to furnish the products **3ob** and **3pb** in 62% and 71% yields, respectively (entries 14, 15).

The overall process displays good generality as well as good functional group compatibility with regard to the alkyne components as well. Remarkably the catalytic system is equally efficient for an electron donating aryl iodides except substrates bearing free hydroxyl functionality. This offers a significant practical advantage over Pd-catalyzed cross-coupling reaction especially for selective cross-coupling with aryl iodides over aryl bromides.

In conclusion, we have demonstrated a new and efficient platinum-catalyzed alkynylation of aryl iodides under very mild conditions. Especially, selective cross-coupling shown in 4-bromoiodobenzene can make this method useful and attractive strategy for the construction of conjugated aryl alkynes. **Representative Procedure**: To a mixture of lithium alkynyltriisopropoxy borate (**1a**, 0.20200 mmol) and aryl iodide (0.24200 mmol), Pt(PPh₃)₄ (0.00500 mmol, 2.5 mol%), CuI (0.01012 mmol, 5 mol%), DMF (2 mL) was added under argon atmosphere in a round bottomed flask. The resulting suspension was stirred at 120 °C. After heating for the time specified, the reaction mixture was allowed to cool to r.t. The product was extracted into Et₂O (3×10 mL), the solvent was removed by rotary evaporation, and the residue was purified by silica gel chromatography.

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