Palladium-Catalysed Carbonylative Cross-Coupling Reactions of Aryl Iodides and Vinyl Boron Derivatives as a Straightforward Route to Aryl Vinyl Ketones

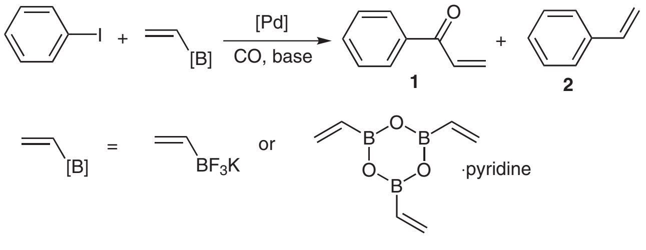
Cyril Pirez, Julien Dheur, Mathieu Sauthier,* Yves Castanet,* André Mortreux

Université des Sciences et Technologies de Lille 1, Unité de Catalyse et Chimie du Solide, UMR CNRS 8181, ENSCL,
B.P. 90108, 59652 Villeneuve dAscq Cedex, France
Fax +33(3)20436585; E-mail: mathieu.sauthier@univ-lille1.fr; E-mail: yves.castanet@ensc-lille.fr

Received 11 February 2009

Abstract: The carbonylative cross-coupling of potassium vinyl trifluoroborate or 2,4,6-trivinyltricycloboroxane with aryl iodides under mild conditions affords aryl vinyl ketones. The optimisation of the reaction conditions leads to the targeted enones in good yields in the case of the aryl substrates bearing donor substituents in *meta* or *para* position. Much more moderate yields were observed with aryl substrates bearing withdrawing substituents.

Key words: carbonylation, cross-coupling, palladium, vinyl boron derivatives, enones.



Scheme 1

Among the methods to produce oxygenated compounds with high efficiency, carbonylation that leads to the introduction of a carbonyl functionality in the final product represents a straightforward method accessing this class of compounds.[1] Transition-metal-catalysed carbonylation reactions have thus become an important tool in modern organic synthesis allowing the formation of a wide range of functionalities such as aldehydes, ketones, and carboxylic acid derivatives.[1]

For our part, we recently reported the rhodium-catalysed carbonylative 1,4-addition of aryl boronic acids to vinyl ketones giving 1,4-diketones.[2] To expand the scope of this new reaction, we had to synthesise various aryl vinyl ketones, which are in addition useful reagents in various metal-catalysed reactions such as Heck,[3] Diels–Alder, or Michael-type reactions.[4,5] They can also be used as monomers in polymerisation reactions for the synthesis of functionalised polymers.[6] Unfortunately, the synthetic strategies reported for the preparation of aryl vinyl ketones is quite limited, and the procedures are often tedious. In view of our current interest in the palladium-catalyzed carbonylative Suzuki cross-coupling reaction between halogenated substrates, carbon monoxide and aryl boronic acids,[7] we envisioned one such reaction involving an aryl halide and a vinyl boron derivative as a general, straightforward route toward the targeted compounds. However, due to the lack of stability of vinyl boronic acid under the reaction conditions,[8] we focused our attention toward more stable synthetic equivalents such as potassium vinyltrifluoroborate or 2,4,6-trivinyltricycloboroxane-pyridine complex which can be easily obtained in a pure form[9,10] and have been recently used in noncarbonylative Suzuki reactions.[10,11]

Preliminary investigations were carried out using potassium vinyl trifluoroborate and iodobenzene as an aryl halide model (see Scheme 1). Table 1 shows that under the conditions classically used in carbonylative Suzuki reactions, the expected enone **1** was obtained but with modest yields (32%, entry 1). Moreover, styrene **2** resulting from the noncarbonylative process was also formed.

The feasibility of the reaction having been established, we have tried to optimize the reaction conditions. Various monodentate and bidentate phosphines [P(*o*-Tol)$_3$, PPh$_2$(*o*-MeOPh), dppe, dppp, dppb, dppf][12] have been tested (although the results are not reported here). It appeared that no significant improvement in terms of conversion or selectivity was observed in comparison with Ph$_3$P. The influence of the nature of the solvent and the base was much more marked. When the reaction was carried out in toluene (entry 2) no reaction occurred and in DMF (entry 3) or dioxane (entry 4) the yields significantly dropped. Using Na$_2$CO$_3$ instead of K$_2$CO$_3$ led to an important increase of the yield (entry 5) whereas others bases such NaOAc, KF, or KO*t*-Bu were less efficient. It should also be noted that when Na$_2$CO$_3$ was used as a base, the yield passed through a maximum for about 1 to 1.2 equivalents of base per PhI and dramatically dropped for higher ratios (compare entries 12, 15, and 16). As this finding could be due to the decomposition of the boron derivative (or its polymerisation), we checked the influence of the amount of this compound on the reaction. The best results were obtained for a vinyltrifluoroborate/PhI ratio of about 1.4. Increasing this ratio had only a slight effect on the yield but a decrease of about 20% is observed for a ratio going from 1.4 to 1.

SYNLETT 2009, No. x, pp 000A–000D
Advanced online publication: xx.xx.2009
DOI: 10.1055/s-0029-1217379 ; Art ID: D05009ST

Table 1 Carbonylative Cross-Coupling of Iodobenzene and Potassium Vinyl Trifluoroborate[a]

Entry	Solvent	Base	VinylBF$_3$K vs PhI (equiv)	PCO (bar)	Temp (°C)	Conversion (%)[b]	Yield (%)[c] of **1**	Yield (%)[c] of **2**
1	THF	K_2CO_3	1.2	20	80	100	32	2
2	toluene	K_2CO_3	1.2	20	80	0	–	–
3	DMF	K_2CO_3	1.2	20	80	100	22	2
4	dioxane	K_2CO_3	1.2	20	80	100	21	2
5	THF	Na_2CO_3	1.2	20	80	100	59	2
6	THF	NaOAc	1.2	20	80	52	34	5
7	THF	KF	1.2	20	80	10	8	2
8	THF	KO*t*-Bu	1.2	20	80	100	0	9
9	THF	Na_2CO_3	1.4	20	80	100	69	3
10	THF	Na_2CO_3	1.2	40	80	100	62	2
11	THF	Na_2CO_3	1.2	5	80	89	86	1
12	THF	Na_2CO_3	1.2	2	80	90	88	1
13	THF	Na_2CO_3	1.2	20	100	100	62	2[d]
14	THF	Na_2CO_3	1.2	20	120	98	41	3[d]
15	THF	Na_2CO_3	1.2	5	80	96	57	2
16	THF	Na_2CO_3	1.2	5	80	96	38	4
17	THF	Na_2CO_3	1.2	5	80	80	78	1

[a] Conditions: PhI (1 mmol, 0.204 g), $Pd(OAc)_2$ (0.022 mmol, 5 mg), Ph_3P (0.07 mmol, 18 mg except entry 17: 0.21 mmol, 54 mg), base (1.1 equiv/PhI except entries 15 and 16, respectively, 2 and 3 equiv/PhI), solvent (8 mL), 20 h (the reaction time was not necessarily optimized).

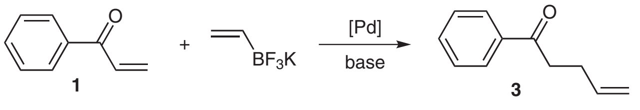
[b] Conversion of PhI determined by GC analysis based on its disappearance.

[c] Determined by quantitative GC analysis.

[d] Yields of compound **3**: 6% and 10% (entries 13 and 14).

Surprisingly, high CO pressure had a rather detrimental effect on the efficiency of the reaction. Indeed the yields increased from 62% to 88% when the CO pressure was lowered from 40 bar to 2 bar (compare entries 10 and 12). This is quite uncommon with this type of reaction, as the selectivities are generally improved in favor of the ketone versus the noncarbonylated product at higher CO pressures.[7]

Higher temperatures than 80 °C induced, as expected, higher activities but at the expense of the selectivity. Above 80 °C the formation of the byproduct **3** resulting from the subsequent noncarbonylative 1,4 addition of the potassium vinyltrifluoroborate on the enone **1** markedly increased (Scheme 2). This addition reaction is known to proceed with arylbronic acids catalysed either by rhodium or palladium but is not reported, to our knowledge, in the case of potassium vinyltrifluoroborate salts with Pd catalysts.[13]



Scheme 2

Varying the Ph_3P/Pd ratio between 3 and 6 had only a slight effect, however, higher ratios led to lower conversions (entry 17).

Moreover, as important differences were found between conversions and yields, and as it is well known that enones are easily polymerised, we checked the stability of the product formed in the reaction mixture. Under the reaction conditions (i.e., in the reaction medium) only moderate degradation was observed at 80 °C after three days (about 30% of the quantity which was present after 24 h). However, if pure phenyl vinyl ketone was dissolved in THF and heated at 80 °C only 25% of the initial quantity remained after three days, showing that the reaction medium is acting as a stabiliser.

It is also noteworthy that no Heck-type reaction occurred between the enone **1** formed at the early stage of the main reaction and the remaining iodobenzene.[3] This is in agreement with the fact that, to our knowledge, no carbonylative Heck reaction has been reported.

Table 2 Carbonylative Cross-Coupling of Various Aryl Halides and Potassium Vinyl Trifluoroborate[a]

Entry	Substrate	Product	Conversion (%)[b]	Yield (%)[b,c] of enone
1	2-iodotoluene	2-methylphenyl vinyl ketone	86	45 (40)
2	3-iodotoluene	3-methylphenyl vinyl ketone	91	76 (70)
3	4-iodotoluene	4-methylphenyl vinyl ketone	80	78 (72)
4	1-bromo-4-iodobenzene	4-bromophenyl vinyl ketone	71	48 (45)
5	1-chloro-4-iodobenzene	4-chlorophenyl vinyl ketone	55	46 (42)
6	1,2-dichloro-4-iodobenzene	3,4-dichlorophenyl vinyl ketone	74	67 (60)
7	4-iodoacetophenone	4′-acetylacrylophenone	85	44 (40)
8	ethyl 4-iodobenzoate	ethyl-4-(2-propenoyl) benzoate	85	72 (68)
9	1-iodonaphtalene	1-(1-naphthalenyl)-2-propen-1-one	90	39 (35)
10	bromobenzene	phenyl vinyl ketone	2	0

[a] Conditions: aryl halide (1 mmol), VinylBF$_3$K (1.2 mmol), Pd(OAc)$_2$ (0.022 mmol, 5 mg), Ph$_3$P (0.07 mmol, 18 mg), Na$_2$CO$_3$ (1.1 mmol, 0.117 g), THF (8 mL), 20 h.

[b] Yield determined by GC analysis.

[c] Numbers in parentheses are isolated yields of >95% pure product.

Table 3 Carbonylative Cross-Coupling of Iodobenzene and 2,4,6-Trivinyltricycloboroxane[a]

Entry	Base	Vinyl[B] (equiv) vs. PhI	P_{CO} (bar)	Conversion (%)(b)	Yield (%)[b] of **1**
1	Na$_2$CO$_3$	0.34	5	25	17
2	K$_2$CO$_3$	0.34	5	95	67
3	K$_2$CO$_3$	0.34	10	94	64
4	K$_2$CO$_3$	0.34	2	96	65
5	K$_2$CO$_3$	1	5	100	53

[a] Conditions: PhI (1 mmol, 0.204 g), Pd(OAc)$_2$ (0.022 mmol, 5 mg), Ph$_3$P (0.07 mmol, 18 mg), base 1.12 mmol, THF (8 mL), 20 h.

[b] Yield determined by GC analysis.

Taking into account the good results obtained with iodobenzene, the study was extended to other aryl halides in order to determine the scope and limitations of the reaction (Table 2). Good results were generally obtained with aryl iodides bearing donor substituents (entries 2, 3) although steric hindrance due to *ortho* substituent can impede the reaction efficiency (entries 1 and 9) as observed in Suzuki coupling.[14] On the other hand, with iodo aryls bearing withdrawing substituents the reaction was less efficient, and the desired ketones were obtained only with moderate yields (entries 4–7). Other aryl halides were ineffective under these reaction conditions.

Finally, 2,4,6-trivinyltricycloboroxane was tested under the similar conditions to the one optimised with potassium vinyltrifluoroborate and the results are reported Table 3. In this case, it was found that K$_2$CO$_3$ was the best base and that the CO pressure had only a slight influence on the results. Interestingly all of the vinyl moieties of 2,4,6-trivinyltricycloboroxane are incorporated in the reaction product.

In summary we have described a facile method for the synthesis of various arylvinyl ketones via a carbonylative Suzuki cross coupling reaction between an aryl iodide and a stable vinyl boron derivative.

Typical Procedure (Table 1, Entry 12)

A suspension of iodobenzene (0.204 g, 1.0 mmol), potassium vinyltrifluoroborate (0.134 g, 1.0 mmol), Na$_2$CO$_3$ (0.120 g, 1.12 mmol), Pd(OAc)$_2$ (0.005 g, 0.022 mmol), and Ph$_3$P (0.018 g, 0.07 mmol) in THF (8 mL) and undecane (0.12 mL as internal standard for GC analyzes) was charged under nitrogen into a 50 mL stainless-steel autoclave equipped with a magnetic stirrer bar. After sealing, the reactor was purged with N$_2$ and pressurized to 5 bar with CO and then heated to 80 °C. At the end of the reaction, the reactor was cooled to r.t. and the reaction mixture was analyzed by GLC to determine conversion and selectivities. The reaction mixture was concentrated under vacuum, and the crude residue was chromatographed on silica using Et$_2$O–PE (1:9) as eluent, to yield analytically pure phenyl vinyl ketone.

All of the reaction products described in this paper were characterized by ^{1}H NMR, ^{13}C NMR, and MS, and gave data in full accordance with the proposed structures.

References and Notes

(1) (a) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. In *Carbonylation, Direct Synthesis of Carbonyl Compounds*; Plenum Press: New York, **1991**. (b) *Topics in Organometallic Chemistry – Catalytic Carbonylation Reactions*, Vol. 18; Beller, M., Ed.; Springer: Berlin/Heidelberg, **2006**.

(2) (a) Sauthier, M.; Castanet, Y.; Mortreux, A. *Chem. Commun.* **2004**, 1520. (b) Chochois, H.; Sauthier, M.; Maerten, E.; Castanet, Y.; Mortreux, A. *Tetrahedron* **2006**, *62*, 11740.

(3) Bianco, A.; Cavarischia, C.; Farina, A.; Guiso, M.; Marra, C. *Tetrahedron Lett.* **2003**, *44*, 9107.

(4) (a) Maruoka, K.; Imoto, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 12115. (b) O'Neill, P. M.; Verissimo, E.; Ward, S. A.; Davies, J.; Korshin, E. E.; Araujo, N.; Pugh, M. D.; Lurdes, S.; Cristiano, M.; Stocks, P. A.; Bachi, M. D. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2991.

(5) (a) Linton, B. R.; Reutershan, M. H.; Aderman, C. M.; Richarson, E. A.; Brownell, K. R.; Ashley, C. W.; Evans, C. A.; Miller, S. J. *Tetrahedron Lett.* **2007**, *48*, 1993. (b) Liu, T.-Y.; Li, R.; Chai, Q.; Long, J.; Li, B.-J.; Wu, Y.; Ding, L.-S.; Chen, Y.-C. *Chem. Eur. J.* **2007**, *13*, 319.

(6) (a) Rodriguez-Castro, M.; Cesteros, L. C.; Katime, I.; Nuno-Donlucas, S. M. *J. Polym. Sci., Part B: Polym. Phys.* **2006**, *44*, 2404. (b) Cheng, C.; Sun, G.; Khoshdel, E.; Wooley, K. L. *J. Am. Chem. Soc.* **2007**, *129*, 10086.

(7) (a) Couve-Bonnaire, S.; Carpentier, J.-F.; Mortreux, A.; Castanet, Y. *Tetrahedron Lett.* **2001**, *42*, 3689. (b) Couve-Bonnaire, S.; Carpentier, J.-F.; Mortreux, A.; Castanet, Y. *Tetrahedron* **2003**, *59*, 2793. (c) Maerten, E.; Hassouna, F.; Couve-Bonnaire, S.; Mortreux, A.; Carpentier, J.-F.; Castanet, Y. *Synlett* **2003**, 1874. (d) Maerten, E.; Sauthier, M.; Castanet, Y.; Mortreux, A. *Tetrahedron* **2007**, *63*, 682.

(8) Matteson, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 4228.

(9) (a) Darses, S.; Michaud, G.; Genêt, J.-P. *Tetrahedron Lett.* **1998**, *39*, 5045. (b) Murphy, J. M.; Tzschucke, C. C.; Hartwig, J. F. *Org. Lett.* **2007**, *9*, 757.

(10) Kerins, F.; O'Shea, D. F. *J. Org. Chem.* **2002**, *67*, 4968.

(11) (a) Molander, G. A.; Rivero, M. R. *Org. Lett.* **2002**, *4*, 107. (b) Molander, G. A.; Brown, A. R. *J. Org. Chem.* **2006**, *71*, 9681.

(12) Abbreviations: dppe = 1,2-bis(diphenylphosphino)ethane, ddpp = 1,2-bis(diphenylphosphino)propane, dppb = 1,2-bis(diphenylphosphino)butane, dppf = 1,2-bis(diphenylphosphino) ferrocene.

(13) (a) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829. (b) Pucheault, M.; Daeses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2002**, 3552.

(14) See, for example : Miyaura, N. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; De Meijere, A.; Diederich, F., Eds.; Wiley-VCH: Weinheim, **2004**.