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Microwave-Assisted Cross-Coupling Reaction of Sodium Tetraphenylborate with Aroyl Chlorides on Palladium-Doped KF/Al_2O_3

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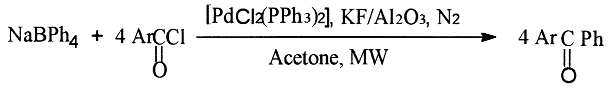
A palladium-catalysed cross-coupling reaction of sodium tetraphenylborate with aroyl chloride using KF/Al_2O_3 as supported reagents in the presence of acetone under microwave-irradiation conditions gives unsymmetrical ketones in good high yield.

The palladium-catalyzed cross-coupling reaction of organoborate compounds with organic electrophiles is a very attractive method for organic synthesis.[1,2] These coupling reactions offer a powerful tool for the formation of carbon-carbon bonds.[3] In the past few years, a number of methods have been devoloped which permit the use of organoboron compounds that are thermally stable and inert to water and oxygen.[3a] Further, these coupling reactions have been successfully used for the synthesis of natural products,[4] pharmaceutical intermediates,[5] and combinatorial libraries of organic compounds.[6]



$$NaBPh_4 + 4\,ArC(=O)Cl \xrightarrow[\text{Acetone, MW}]{[PdCl_2(PPh_3)_2],\ KF/Al_2O_3,\ N_2} 4\,ArC(=O)Ph$$

1 **2a-j** **3a-j**

Scheme 1.

Recently, Bumagin[7] reported that the cross-coupling reaction of $NaBPh_4$ with acyl chlorides in the presence of $Pd(OAc)_2$ and Na_2CO_3 in dry or aqueous acetone gives high yields of unsymmetric ketones. However, the reaction time is long (1–6 h).

In this paper, we wish to report a very simple, fast, econmically viable and general method for palladium-catalyzed cross-coupling reactions of sodium tetraphenylborate with aroyl chlorides in the presence of KF/Al_2O_3 under microwave irradiation conditions.The reactions are show in the Scheme 1.

Microwave-assisted cross-coupling reaction of sodium tetraphenylborate **1** with benzoyl chloride **2a**, affording benzophenone **3a**, was chosen as a model reaction. The effects of catalysts, solvents, supported reagents, and so on were examined (Table 1).

Among several catalysts screend, the best yield was obtained when $[Pd(PPh_3)_4]$ and $[PdCl_2(PPh_3)_2]$ were employed (Table 1, entries 1 and 7). The amount of $[PdCl_2(PPh_3)_2]$ affected the yield and the use of 3 mol% of the catalyst gave the best result (entries 14–16 and 7). Further, the reaction was markedly influenced by the solvents and acetone was the best solvent (entry 4–8). We investigated the effect of bases on the reaction of sodium tetraphenylborate with benzoyl chloride. It was found that the activity of bases is in the following sequence: KF/Al_2O_3 > NaOH/Al_2O_3 > Na_2CO_3/Al_2O_3 > H_3PO_4/Al_2O_3 > Al_2O_3 (entries 9–13 and 7). We also investigated the effects of the power (300–750 W) and time (2–7 min) of microwave irradiation on the formation of **3a**, and found the best yield can be obtained at 525 W for 5 min.

The relative rate of formation of **3a–j** under microwave irra-

Table 1. Effect of Catalysts and Supported Reagents on the Formation of (**3a**)[a)]

Entry	Catalyst (mol%)	Solvent	Supported reagents	Yield/%[b)]
1	$[Pd(PPh_3)_4]$ (3)	Acetone	KF/Al_2O_3	98
2	$PdCl_2$ (3)	Acetone	KF/Al_2O_3	90
3	$[PdCl_2(PPh_3)_2]$ (3)	Benzene	KF/Al_2O_3	34
4	$[PdCl_2(PPh_3)_2]$ (3)	CH_2Cl_2	KF/Al_2O_3	40
5	$[PdCl_2(PPh_3)_2]$ (3)	CH_3CN	KF/Al_2O_3	79
6	$[PdCl_2(PPh_3)_2]$ (3)	THF	KF/Al_2O_3	94
7	$[PdCl_2(PPh_3)_2]$ (3)	Acetone	KF/Al_2O_3	97
8	$[PdCl_2(PPh_3)_2]$ (3)	Acetone/H_2O	KF/Al_2O_3	73
9	$[PdCl_2(PPh_3)_2]$ (3)	Acetone	none	55
10	$[PdCl_2(PPh_3)_2]$ (3)	Acetone	Al_2O_3	64
11	$[PdCl_2(PPh_3)_2]$ (3)	Acetone	H_3PO_4/Al_2O_3	78
12	$[PdCl_2(PPh_3)_2]$ (3)	Acetone	Na_2CO_3/Al_2O_3	82
13	$[PdCl_2(PPh_3)_2]$ (3)	Acetone	NaOH/Al_2O_3	94
14	$[PdCl_2(PPh_3)_2]$ (1)	Acetone	KF/Al_2O_3	86
15	$[PdCl_2(PPh_3)_2]$ (5)	Acetone	KF/Al_2O_3	94
16	$[PdCl_2(PPh_3)_2]$ (7)	Acetone	KF/Al_2O_3	92

a) The reaction was carried out in acetone at a power level of 525 W for 5 min under N_2.
b) Isolated yield.

Table 2. Fast Palladium-Catalyzed Cross-Coupling Reaction of $NaBPh_4$ with Aroyl and Cinnamoyl Chlorides under Microwave Irradiation[a),b)]

Entry	Product		Yield[c)] /%
1	$C_6H_5COC_6H_5$	**(3a)**	97
2	$2\text{-}ClC_6H_4COC_6H_5$	**(3b)**	90
3	$4\text{-}ClC_6H_4COC_6H_5$	**(3c)**	95
4	$3\text{-}BrC_6H_4COC_6H_5$	**(3d)**	92
5	$4\text{-}BrC_6H_4COC_6H_5$	**(3e)**	96
6	$3\text{-}NO_2C_6H_4COC_6H_5$	**(3f)**	91
7	$4\text{-}NO_2C_6H_4COC_6H_5$	**(3g)**	90
8	$4\text{-}CH_3C_6H_4COC_6H_5$	**(3h)**	92
9	$4\text{-}CH_3OC_6H_4COC_6H_5$	**(3i)**	92
10	$C_6H_5CH{=}CHCOC_6H_5$	**(3j)**	90

a) The reactions were carried out in the presence of KF/Al_2O_3 using $[PdCl_2(PPh_3)_2]$ as a catalyst in acetone at 525 W for 5 min under nitrogen. b) Mole ratio: $NaBPh_4$: aroyl chloride : $[PdCl_2(PPh_3)_2]$: KF/Al_2O_3 = 1 : 4.1 : 0.03 : 2.1. c) Isolated yield.

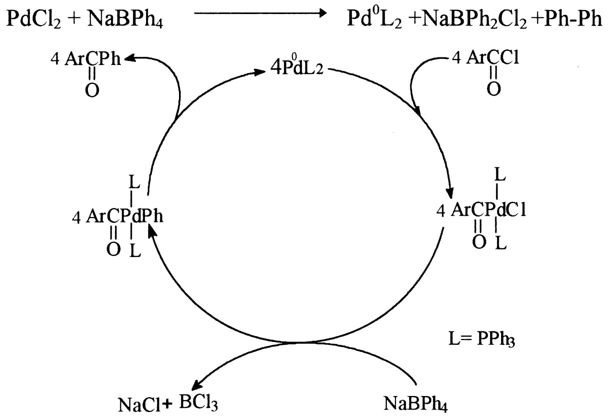
diation and conventional heating was compared, and the results showed that microwave irradiation accelerated the reaction by 156 times over conventinal heating, thus quantifying the microwave heating effect.

In order to define the scope and limitation of this method for unsymmetrical ketone synthesis, the reactions of various acyl chlorides and sodium tetraphenylborate in the presence of KF/Al_2O_3 catalyzed by $[PdCl_2(PPh_3)_2]$ were examined, as shown in Table 2.

The results in Table 2 show that the reaction of aromatic and unsaturated acyl chlorides give the corresponding symmetrical and unsymmetrical ketones in over 90% yield (entry 1–10). In this reaction, the four phenyl groups of sodium tetraphenylborate are available for transfer. The reaction is not sensitive to the structure of acyl chlorides. Various substituents on the phenyl ring, either electron-withdrawing or electron-donating, such as 4-methyl, 4-methoxy, 2- or 4-chloro, 3- or 4-bromo, and 3- or 4-nitro, could be tolerated with little effect on the yields (entry 2–9). Unsaturated acid chloride, such as cinnamoyl chloride, reacted similarly and provided the corresponding unsymmetrical ketone in excellent isolated yield (entry 10).

The reaction may proceed via the catalytic cycle shown in Scheme 2. The oxidative addition of acid chloride to palladium(0) affords acylpalladium(II) chloride. When a palladium(II) catalyst is used, it may be converted into some palladium(0) species, probably via side reactions forming biphenyl.[7] The transfer of the phenyl group from $NaBPh_4$ to palladium with a concomitant elimination of BCl_3, followed by reductive elimination, gives the corresponding phenyl ketones. A similar catalytic cycle was already proposed in the reactions with arylboron[3c] and triphenylbismuth[13] compounds.

In summary, we have developed a simple, efficient and fast procedure for a cross-coupling reaction of sodium tetraphenylborate with aroyl chlorides and cinnamoyl chloride on palladium-doped KF/Al_2O_3 under microwave irradiation conditions. This method is superior to previously reported methods in terms of high yields, purity of products, and short reaction time.



Scheme 2.

Experimental

General Procedure for the Prepartion of Compounds 3a: A mixture of sodium tetraphenylborate (1 mmol), benzoyl chloride (4.1 mmol), $[PdCl_2(PPh_3)_2]$ (0.03 mmol), KF/Al_2O_3 (2.1 mmol) and acetone (10 mL) was irradiated at 525 W for 5 min by microwaves under a nitrogen atmosphere. The precipitate was filtrated and the filtrate was poured into a saturated aqueous sodium chloride (50 mL) and extracted with diethyl ether (3×20 mL), The extracts were washed with water (3×20 mL) and then dried over magnesium sulfate. The solution was concentrated to yield a crude product, which was purified by column chromatography on silica gel (eluent: petroleum/ethyl acetate = 15:1) to afford benzophenone **3a** in 97% yield.

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