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Preliminary communication

PALLADIUM-CATALYZED CARBONYLATIVE CROSS-COUPLING OF ORGANOBORANES WITH ARYL IODIDES OR BENZYL HALIDES IN THE PRESENCE OF BIS(ACETYLACETONATO)ZINC(II)

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Summary

Carbonylative cross-coupling reactions of organoboranes with aryl iodides and benzyl halides successfully catalyzed by dichlorobis(triphenylphosphine)-palladium(II) in the presence of bis(acetylacetonato)zinc(II) produce unsymmetrical ketones in reasonable yields.

Carbonylative cross-coupling of organometallic compounds with organic halides catalyzed by a transition-metal catalyst is the most straightforward approach to ketone synthesis. Recently, successful bimetallic systems containing palladium catalysts were extensively studied for ketone synthesis [1—5].

As the organometallic reagent, organoboranes are considered to have many advantages for carbonylative coupling with organic halides, since a wide variety of organoborane compounds have so far been reported [6]. Consequently, if organoboranes successfully couple with organic halides with insertion of a carbonyl function into the coupled product, the reaction provides one of the most versatile methods for direct ketone synthesis. However, successful applications of organoborane compounds to carbonylative coupling have not yet been achieved. This is probably due to the difficulty in transmetalation between organoboranes and acylmetal species (e.g., formation of an acylpalladium intermediate) generated in catalytic cycles, which originates from the intrinsically poor nucleophilicity of boron—carbon bonds in organoboranes. Although strong bases such as NaOMe and NaOH proved to be effective for direct coupling of alkenylboranes with organic halides [7], such bases are expected to produce undesirable carbonylated products such as carboxylic

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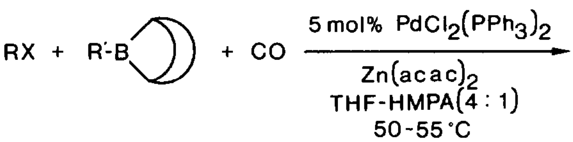
acid derivatives under carbonylation conditions by intercepting the acylmetal species formed.

We have found that bis(acetylacetonato)zinc(II), Zn(acac)$_2$, effectively promoted carbonylative coupling of organoboranes with aryl iodides or benzyl halides in the presence of a palladium catalyst under very mild conditions (50—55°C, 1 atm of CO), producing unsymmetrical ketones in reasonable yields. Here we report the preliminary results of this reaction.

Remarkably the reaction greatly depended on the solvents and zinc salts used. The reaction between iodobenzene and triethylborane (Et_3B) at 50—55°C in tetrahydrofuran (THF)/hexamethylphosphoramide (HMPA) (4/1) proceeded smoothly in the presence of 5 mol% dichlorobis(triphenylphosphine)palladium(II) ($PdCl_2(PPh_3)_2$) and Zn(acac)$_2$, to afford propiophenone (run 1 in Table 1), but the formation of propiophenone was extremely slow or did not take place in benzene, 1,2-dimethoxyethane, or acetonitrile. In THF solution the reaction occurred under similar conditions, but the yield of propiophenone was not satisfactory (43%, as determined by GLC analysis) even with a two-fold excess of Et_3B and longer reaction time (20 h). The presence of HMPA in the solvent is thus essential to force the reaction to completion. The use of zinc(II) acetate, instead of Zn(acac)$_2$, resulted in an extremely slow reaction in which only 10% conversion of the iodobenzene used was achieved after 24 h at 50—55°C, and no reaction occurred in the presence of zinc(II) bromide or in the absence of Zn(acac)$_2$ under these conditions. It is noteworthy that when lithium isopropoxide was used instead of Zn(acac)$_2$, the reaction resulted in quantitative formation of isopropyl benzoate without formation of the desired ketone product.

We also examined other metal acetylacetonate compounds as alternative reagents for Zn(acac)$_2$ in the reaction between iodobenzene and triethylborane. The results are summarized in Table 2. Interestingly, many other metal acetylacetonate compounds examined were found to be ineffective for this reaction, and thus Zn(acac)$_2$ proved to be the most suitable reagent.

Several examples of reactions with trialkylboranes are listed in Table 1 (run 2—5). These reactions usually required a small excess of organoborane reagent for complete consumption of the starting halide. Thus the reaction utilizes only one of the three alkyl groups of the trialkylborane molecule. Fortunately, the use of *B*-alkyl-9-borabicyclo[3.3.1]nonane (*B*-alkyl-9-BBN) derivatives solved this problem, since only the *B*-alkyl groups participated in the reaction (eq. 1, run 6—11 in Table 1):



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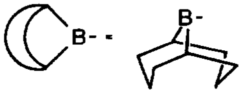
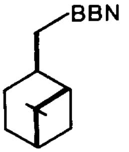
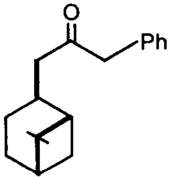


TABLE 1

SYNTHESIS OF KETONES BY CARBONYLATION OF ARYL IODIDES OR BENZYL HALIDES WITH ORGANOBORANES IN THE PRESENCE OF BIS(ACETYLACETONATO)ZINC AND PALLADIUM CATALYST [a]

Run	Halide	Borane reagent [b]	Time (h)	Product [c]	Yield [d] (%)
1	PhI	Et_3B [e]	10.5	$PhCOC_2H_5$	(82)
2	$PhCH_2Br$	Et_3B [e]	3	$PhCH_2COC_2H_5$	72.5(81)
3	p-BrC_6H_4I	Et_3B [e]	21	p-$BrC_6H_4COC_2H_5$	(75)
4	p-$CH_3COC_6H_4I$	Et_3B [e]	10	p-$CH_3COC_6H_4COC_2H_5$	71.5
5	PhI	n-Hex_3B	16	$PhCO(CH_2)_5CH_3$	(70)
6	PhI	$CH_3(CH_2)_5$-BBN	18	$PhCO(CH_2)_5CH_3$	(74)
7	PhI	$PhCH_2CH_2$-BBN	21.5	$PhCOCH_2CH_2Ph$	69
8	PhI	$CH_3OCO(CH_2)_{10}$-BBN	24	$PhCO(CH_2)_{10}CO_2CH_3$	74
9	PhI	$CH_3\overset{CH_3}{CH}CH_2\overset{CH_3}{CH}$-BBN	6	no reaction	
10	$PhCH_2Cl$	$PhCH_2CH_2$-BBN	15	$PhCH_2COCH_2CH_2Ph$	60.5
11	$PhCH_2Br$		3.5		43

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[a] Reactions were carried out in THF/HMPA (10 ml, 4/1) at 50—55° C with 1 atm CO, 1.0 mmol halide, 1.2 mmol borane reagent, 1.1 mmol $Zn(acac)_2$, 0.05 mmol $PdCl_2(PPh_3)_2$, and 0.1 mmol PPh_3. [b] Hex = hexyl; BBN = 9-borabicyclo[3.3.1]nonan-9-yl. [c] Products were characterized by IR, ^1H NMR, and mass spectroscopy, or identified by comparison of spectral data with those for authentic samples. [d] Yields isolated (are based on staring halides); yields in parentheses were determined by GLC. [e] Commercial; 1 *M* solution in n-hexane.

TABLE 2

CARBONYLATION IN THE PRESENCE OF VARIOUS METAL ACETYLACETONATE REAGENTS [a]

Reagent	Yield (%) of propiophenone [b] (Reaction time)
Li(acac)	trace (2 h), 16% (24 h)
$Mg(acac)_2$	trace (20 h)
$Al(acac)_3$	no reaction (20 h)
$Ca(acac)_2$	31% (20 h)
$[Ti(acac)_3]_2\cdot TiCl_6$	no reaction (14 h)
$Mn(acac)_3$	5% (20 h)
$Fe(acac)_3$	no reaction (22 h)
$Co(acac)_3$	no reaction (20 h)
$Cu(acac)_2$	14% (4 h) [c]
$MoO_2(acac)_2$	no reaction (5 h)
$SnCl_2(acac)_2$	no reaction (24 h)

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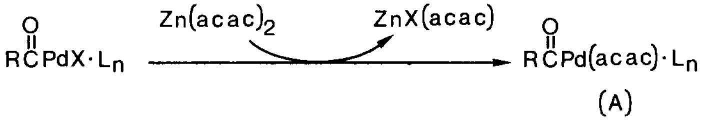
[a] Reactions were carried out at 50° C in THF/HMPA (4/1) with iodobenzene, triethylborane and $PdCl_2(PPh_3)_2$ as catalyst (5 mol%). [b] Determined by GLC. [c] Metallic copper precipitated.

However, the situation proved to be unfavorable for transferring secondary alkyl groups from *B*-alkyl-9-BBN, under our conditions (e.g., run 9 in Table 1), and the transfer reaction occurred readily for primary alkyls only.

The addition of water to the reaction system did not have a crucial effect on the above reactions. This observation excludes a possible pathway of this reaction involving the formation of moisture-sensitive alkylzinc species by transmetalation between $Zn(acac)_2$ and the organoborane reagent [8]. Presumably, $Zn(acac)_2$ acts as a base and participates in the transmetalation process between the organoborane reagent and the acylpalladium intermediate formed in the catalytic cycle. This successful reaction may possibly be ascribed to the acylated acetylacetonatopalladium(II) intermediate (A in eq. 2), which is



$$\mathrm{R\overset{\overset{O}{\|}}{C}PdX\cdot L_n} \xrightarrow{\mathrm{Zn(acac)_2}\ \curvearrowright\ \mathrm{ZnX(acac)}} \underset{\mathrm{(A)}}{\mathrm{R\overset{\overset{O}{\|}}{C}Pd(acac)\cdot L_n}} \qquad (2)$$

formed in the metathetical reaction between $Zn(acac)_2$ and the acylpalladium intermediate and which possibly reacts with the borane reagents as in a related reaction reported recently [7]. However, for this effect supplementary assistance of the zinc cation counterpart could also be assumed from the poor results in Table 2.

Further approaches to solve the problems in applying this reaction to other organoborane compounds and organic halides are now under investigation.

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