

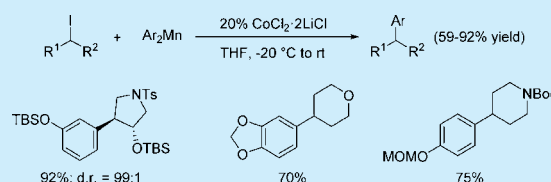
Cobalt-Catalyzed C(sp²)–C(sp³) Cross-Coupling Reactions of Diarylmanganese Reagents with Secondary Alkyl Iodides

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S Supporting Information

ABSTRACT: A cobalt-catalyzed cross-coupling of diarylmanganese reagents with secondary alkyl iodides using the THF-soluble salt CoCl₂·2LiCl, which leads to the cross-coupling products in up to 92% yield, is reported. High diastereoselectivities can be reached in these cross-couplings (dr up to 99:1). Remarkably, rearrangement of secondary alkyl iodides to unbranched products was not observed in these C–C forming reactions.

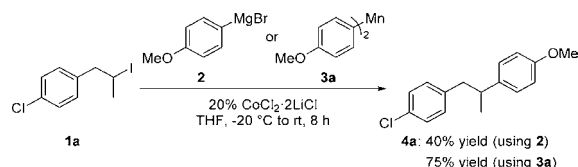


Palladium-catalyzed cross-couplings have widely been used.¹ However, cost² and toxicity³ considerations led to the search of alternative transition metal catalysts for cross-coupling reactions. Especially cobalt-catalyzed transformations have shown their synthetic utility.⁴ Pioneering work of Oshima,⁵ Cahiez,⁶ Gosmini,⁷ and Cossy⁸ demonstrated the broad field of applications of cobalt salt catalysis for forming new carbon–carbon bonds. Ackermann⁹ and Yoshikai¹⁰ also used cobalt complexes for direct C–H activation of various unsaturated systems. Recently, we have shown that cobalt halides are excellent catalysts for the cross-couplings between C(sp³)–C(sp²),¹¹ C(sp³)–C(sp),¹² and C(sp²)–C(sp²)¹³ centers using magnesium or zinc organometallics. However, these organometallic reagents are not always the best choice for performing C–C bond formations since homocouplings are often observed side-reactions.

Herein, we report a new cobalt-catalyzed cross-coupling between secondary alkyl iodides and diarylmanganese reagents catalyzed by CoCl₂·2LiCl and performed in the absence of any additional ligand. Thus, preliminary experiments have shown that the cross-coupling between the secondary alkyl iodide **1a** and *p*-anisylmagnesium bromide (**2**) proceeds in the presence of 20 mol% CoCl₂·2LiCl in THF at –20 to 25 °C (8 h) to produce the substitution product **4a** in only 40% yield due to extensive homocoupling side reactions.

However, we found that by replacing **2** with the corresponding dianisylmanganese reagent (**3a**) prepared by the transmetalation of **2** with MnCl₂·2LiCl¹⁴ (0.5 equiv), the same cross-coupling now produces **4a** in 75% isolated yield (Scheme 1). Remarkably, we did not observe rearrangement products (branched to unbranched) during these couplings.¹⁵

Scheme 1. Cobalt-Catalyzed Cross-Coupling Reactions of Various Metal Reagents with Alkyl Iodide 1a



This encouraging result led us to examine the scope of this cross-coupling more extensively (Table 1). CoCl₂·2LiCl was the

Table 1. Reaction Condition Optimization of the Cross-Coupling of Alkyl Iodide 1a with the Manganese Reagent 3a

entry	catalyst	ligand ^a	yield (%) ^b
1	Co(acac) ₂	–	54
2	Co(acac) ₃	–	82
3	CoBr ₂	–	73
4	CoCl ₂	–	79
5	CoCl ₂ ·2LiCl	–	83 (75) ^c
6	CoCl ₂ ·2LiCl ^d	–	64
7	CoCl ₂ ·2LiCl	L1	32
8	CoCl ₂ ·2LiCl	L2	32
9	CoCl ₂ ·2LiCl	L3	11
10	CoCl ₂ ·2LiCl	L4	69
11	CoCl ₂ ·2LiCl	L5	77
12	PdCl ₂	–	2
13	CuCl ₂	–	3
14	CrCl ₂	–	3
15	NiCl ₂	–	7
16	FeCl ₂	–	26

L1

L2

L3

L4

L5

^aUsing 40% of the ligand. ^bCalibrated GC-yield using undecane as internal standard. ^cIsolated yield. ^dUsing 10% CoCl₂·2LiCl.

preferred catalyst since Co(acac)₂, Co(acac)₃, CoBr₂, and CoCl₂ gave inferior yields (entries 1–4). The use of 10% CoCl₂·2LiCl instead of 20% reduced the yield of **4a** to 64% (compare entries 5

Received: November 9, 2016

Published: December 5, 2016

and 6). Attempts to improve the reaction by adding ligands such as TMEDA (**L1**),¹⁶ 4-fluorostyrene (**L2**),¹⁷ or neocuproine (**L3**)^{12,18} did not improve the reaction yield (entries 7–9). Using NHC ligands **L4** or **L5** did not improve the reaction outcome (entries 10 and 11). Also alternative transition metal salts such as PdCl₂, CuCl₂, CrCl₂, NiCl₂, or FeCl₂ were inefficient (entries 12–16). A solvent screening showed that THF was the best solvent when compared to NMP, DMPU, DME, 1,4-dioxane, and *t*BuOMe.

These cobalt-catalyzed alkylations proved to be general, and the cross-coupling between the dianisylmanganese reagent (**3a**) and various secondary alkyl iodides has been successfully performed (Table 2).¹⁹ Thus, various secondary alkyl iodides

Table 2. Cobalt-Catalyzed Cross-Coupling Reactions between Various Secondary Alkyl Iodides of Type 1 and the Dianisylmanganese Reagent 3a

entry	electrophile	product	yield
1			73% (63%) ^a
2			77%
3			75%
4			84% (81%) ^a
5			75% ^b
6			83% dr = 99:1
7			70%
8			59% dr = 95:5

^a20% CoCl₂ was used instead of CoCl₂·2LiCl. ^bdr ca. 70:30.

bearing a range of various functional groups (OTBS, CF₃, OAc; **1b–d**) reacted with the dianisylmanganese reagent (**3a**) providing the expected products **4b–d** in 73–77% yield (entries 1–3). Also, various cyclohexyl iodides underwent the cross-coupling with **3a** yielding the desired arylated products **4e–g** in 75–84% yield. Additionally, this cross-coupling can also be performed with cyclopentyl iodides **1h–i**, leading to the expected products **4h** and **4i** in 59–70% yield (entries 7 and 8). When a TBSO substituent was present in position 2 to the carbon-iodide bond, excellent diastereoselectivities were observed (dr up to 99:1, see entries 6 and 8).²⁰

Furthermore, a range of functionalized diarylmanganese reagents could also be readily used in this reaction (Table 3). (*p*-MOMO-C₆H₄)₂Mn (**3b**) reacted smoothly with the alkyl

Table 3. Cobalt-Catalyzed Cross-Couplings of Diaryl Manganese Reagents of Type 3 with Secondary Alkyl Iodides of Type 1

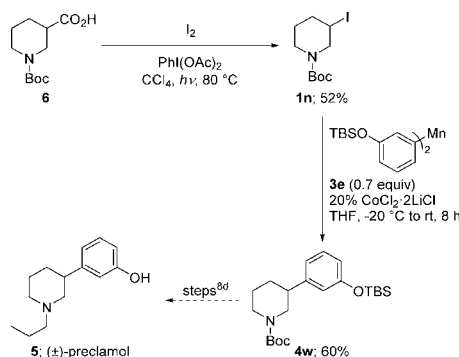
entry	manganese reagent	substrate	product; yield
1			4j ; 76%
2			4k ; 75%
3			4l ; 81%
4			4m ; 87%
5			4n ; 76%
6			4o ; 74%
7			4p ; 92%; dr = 99:1
8			4q ; 80% (48%) ^a
9			4r ; 60% (19%) ^a
10			4s ; 66%
11			4t ; 70%
12			4u ; 63%
13			4v ; 82%; dr = 99:1

^a20% CoCl₂ was used instead of CoCl₂·2LiCl.

iodides **1c** and **1j**, leading to the arylated products **4j–k** in 75–76% yield (entries 1 and 2). The coupling of the electron-poor manganese reagent **3c** with **1a** or **1k** afforded the cross-coupling products **4l–m** in 81–87% yield (entries 3 and 4). Interestingly, the manganese reagents bearing an OBoc (**3d**) or an OTBS group (**3e**) were well tolerated, and the cross-coupling with **1h** and **1i** (dr = 99:1) led to the desired products **4n–p** in 74–92% yield (entries 5–7). Moreover, the electron-rich diarylmanganese reagent **3f** was readily coupled with the cyclic alkyl iodides **1e** and **1b** to provide the corresponding arylated products **4q–r** in 60–80% yield. The cross-coupling of **1l** or **1m** with the di(1,3-benzodioxol-5-yl) manganese reagent (**3g**) afforded the arylated compounds **4s–t** in 66–70% yield (entries 10 and 11). Also, the di(4-methoxy-3,5-dimethylphenyl)manganese reagent (**3h**) was successfully coupled with **1h** and **1i** (dr = 99:1), leading to the desired products **4u–v** in 63–82% yield (entries 12 and 13). For the diarylmanganese reagents **3e** and **3h** using the protected heterocyclic iodohydrine **1i** (dr = 99:1), we also observed excellent diastereoselectivities (dr = 99:1, see entries 7 and 13).

In order to demonstrate the synthetic utility of this method, we prepared the protected iodopiperidine **1n**, which is a key intermediate for the synthesis of (±)-preclamol (**5**). Thus, the commercially available carboxylic acid **6** was converted into the iodide **1n** according to the procedure of Boto and co-workers (Scheme 2).^{8d,21} The cobalt-catalyzed cross-coupling with the

Scheme 2. Formal Synthesis of (±)-Preclamol (**5**)



diarylmanganese reagent **3e** furnished the desired product **4w** in 60% yield.

In summary, we have reported a new cobalt-catalyzed cross-coupling of polyfunctional diarylmanganese reagents with secondary alkyl iodides using the highly soluble cobalt salt $\text{CoCl}_2 \cdot 2\text{LiCl}$ in the absence of any additional ligand. Remarkably, no rearrangement of the secondary alkyl group is observed. Also, this cross-coupling was applied to the preparation of a key intermediate for the synthesis of (±)-preclamol. Further extension of this method as well as mechanistic studies are currently underway.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03349.

Full experimental details; ^1H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the DFG (SFB749), the LMU Munich, and the International Associated Laboratory IrMaCaR between the research groups of P. Knochel and G. Cahiez for financial support. We also thank Albemarle (Hoechst, Germany) for the generous gift of chemicals. M.S.H. thanks the Richard-Winter Foundation for a fellowship.

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