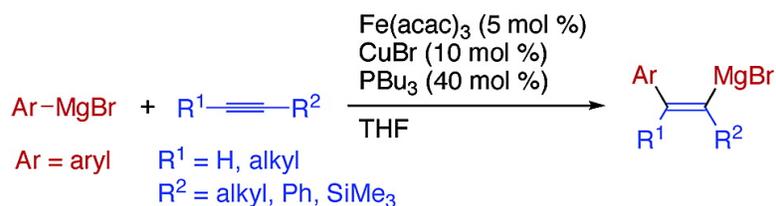


Arylmagnesiation of Alkynes Catalyzed Cooperatively by Iron and Copper Complexes

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Ar = 2-Me-1-Nap, R¹ = R² = Pr: 91% (Fe&Cu), 2% (Fe), 0% (Cu).

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Arylmagnesiation of Alkynes Catalyzed Cooperatively by Iron and Copper Complexes

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Carbometalation of alkynes is one of the most useful methods for olefin synthesis, since the resulting alkenylmetals can be transformed to various multisubstituted ethenes in a stereoselective manner.¹ Although heteroatom-containing alkynes undergo carbometalation with diverse organometallic compounds in the presence or absence of a transition metal catalyst,² unfunctionalized alkynes are poor substrates, in particular for the addition of arylmetals.³ Here we report that iron^{4–8} and copper⁹ complexes cooperatively catalyze the arylmagnesiation of alkynes including dialkylacetylenes that do not contain a heteroatom.³ This presents a rare example of efficient cooperative catalysis.¹⁰ It is also remarkable that the metals (Fe, Cu, and Mg) used in the present catalytic reaction are all inexpensive.

The reaction of 3,5-dimethylphenylmagnesium bromide (**1a**) with 4-octyne (**2a**) in the presence of Fe(acac)₃ (5 mol %), CuBr (10 mol %), and PBU₃ (40 mol %) in THF at 60 °C for 24 h followed by hydrolysis gave 74% yield of 4-(3,5-dimethylphenyl)-4-octene (**3a**), where the ratio of *E/Z* isomers is 95/5 (entry 1 in Table 1).^{11–13} The *E* geometry indicates that arylmagnesiation took place with *syn*-selectivity. The presence of both iron and copper catalysts is essential for the high yield of arylmagnesiation. Thus, the reaction without Fe(acac)₃ did not give **3a** at all, with all the alkyne (**2a**) remaining (entry 2), and the yield of **3a** was much lower (26%) in the reaction without CuBr (entry 3). The cooperative catalysis by the iron and copper is more obvious in the addition of 2-methyl-1-naphthylmagnesium bromide (**1b**) to **2a** (entries 4–6). The yield of arylation product **3b** was 91% in the presence of both Fe(acac)₃ and CuBr catalysts, whereas the yield was very low (0% or 2%) in the absence of either iron or copper catalyst.

Table 2 illustrates the scope of the present arylmagnesiation of alkynes catalyzed by the iron/copper cooperation. Various arylmagnesium bromides added to aliphatic and aromatic unfunctionalized alkynes in stereoselectivities higher than 90% except for the addition to 1-(trimethylsilyl)propyne (entry 11). Regioselectivities over 95% were observed in the reaction of unsymmetrical aryl- and silylacetylenes (entries 8–11).¹⁴ A terminal acetylene, though in a low yield, participated in the reaction despite the intrinsic reactivity of its acidic methyne proton toward basic **1a** (entry 10).

Addition of D₂O to the reaction mixture resulting from addition of **1b** to **2a** gave arylalkene **3b** that is deuterated at its olefinic methyne, indicating that the arylmagnesiation forming alkenylmagnesium actually took place (Scheme 1). Synthetic utility of the arylmagnesiation products was demonstrated by their further transformation through one-pot reactions with an electrophile. Thus, the reaction mixture of the arylmagnesiation of **2a** with **1b** was treated with benzaldehyde or benzyl bromide to give allylic alcohol **4**¹⁵ or tetrasubstituted ethene **5**, respectively.

Reactions examined with a stoichiometric amount of Fe(acac)₃ or CuBr gave us significant insight into the reaction mechanism. Thus, an aryliron species,¹⁶ generated from Fe(acac)₃, PBU₃, and an excess amount (4.0 equiv to Fe) of Grignard reagent **1b** in THF,

Table 1. Arylmagnesiation of 4-Octyne Followed by Hydrolysis^a

entry	Ar	amount (mol %)		conv (%) ^b	yield (%) ^c	<i>E:Z</i> ^d
		Fe(acac) ₃	CuBr			
1	3,5-Me ₂ C ₆ H ₃ (1a)	5	10	>99	74	95:5
2		0	10	<1	0	—
3		5	0	57	26	87:13
4	2-Me-1-Nap (1b)	5	10	>99	91	98:2
5		0	10	<1	0	—
6		5	0	14	2 ^d	>99:1

^a The reaction was carried out in THF (1.7 mL) at 60 °C for 24 h under a nitrogen atmosphere using an arylmagnesium bromide (0.90 mmol), 4-octyne (0.45 mmol) and PBU₃ (0.18 mmol) in the presence of Fe(acac)₃ (22 μmol) and/or CuBr (45 μmol). ^b Determined by GC. ^c Isolated yield based on the alkyne. ^d Determined by GC, GC-MS and ¹H NMR.

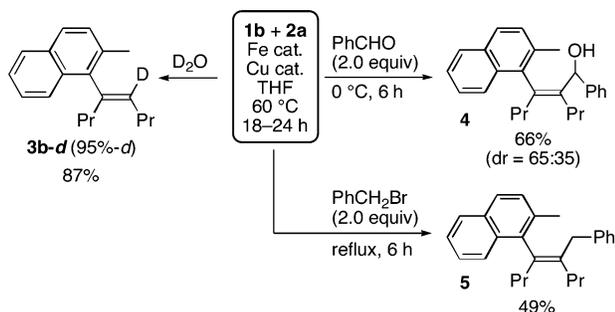
Table 2. Hydroarylation of Alkynes Catalyzed by Iron–Copper^a

entry	Ar	R ¹	R ²	time (h)	yield (%) ^b	<i>E:Z</i> ^c
1	Ph	Pr	Pr	24	62	97:3
2	4-MeC ₆ H ₄	Pr	Pr	43	66	97:3
3	3-MeC ₆ H ₄	Pr	Pr	24	70	95:5
4	2-MeC ₆ H ₄	Pr	Pr	48	61	93:7
5	3-MeOC ₆ H ₄	Pr	Pr	24	56	97:3
6	4-FC ₆ H ₄	Pr	Pr	24	40	95:5
7	3,5-Me ₂ C ₆ H ₃	Bu	Bu	24	67	96:4
8	3,5-Me ₂ C ₆ H ₃	Hex	Ph	24	76	94.5:(:1)
9	2-Me-1-Nap	Me	Ph	24	90	99:1
10	3,5-Me ₂ C ₆ H ₃	H	Ph	24	36	91.5:(:4)
11	3,5-Me ₂ C ₆ H ₃	Me	SiMe ₃	24	56	72:26(:2)

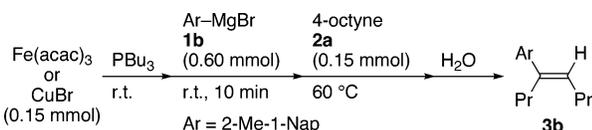
^a The reaction was carried out in THF (1.7 mL) at 60 °C under a nitrogen atmosphere using an arylmagnesium bromide (0.90 mmol) and an alkyne (0.45 mmol) in the presence of Fe(acac)₃ (22 μmol), CuBr (45 μmol) and PBU₃ (0.18 mmol). ^b Isolated yield based on the alkyne. ^c Determined by GC, GC-MS and ¹H NMR. The values in parentheses shows the ratio of a regioisomer to (*E*)- and (*Z*)-**3**.

was treated with 4-octyne (**2a**) (1.0 equiv to Fe) at 60 °C for 20 min. Hydrolysis of the reaction mixture gave hydroarylation product **3b** in 85% yield (Scheme 2). It follows that the addition of an aryliron to the alkyne forming an alkenyliron took place with high selectivity. Considering that the reaction of **1b** with **2a** in the presence of a catalytic amount (5 mol %) of iron gave only a low yield (2%) of **3b** (entry 6 in Table 1), the alkenyliron species generated by the arylironation of the alkyne is not reactive toward further transformations such as transmetalation or polymerization, keeping its alkenyliron structure under the reaction conditions

Scheme 1

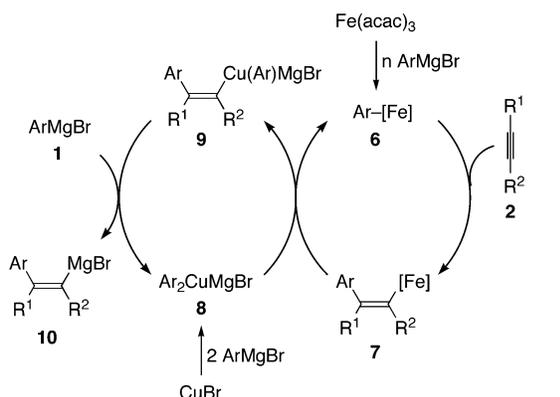


Scheme 2



complex	PBU ₃	time	conv. of 2a	yield	<i>E</i> : <i>Z</i>
Fe(acac) ₃	1.2 mmol	20 min	>99%	85%	96:4
CuBr	0.60 mmol	24 h	<5%	<1%	—

Scheme 3



lacking the copper catalyst. On the other hand, alkyne **2a** did not undergo any reactions with the diarylcuprate¹⁷ derived from **CuBr** and Grignard reagent **1b** (4.0 equiv to **Cu**), indicating that the copper does not participate in the step of arylmetalation of the alkyne forming an alkenylmetal species. It is most likely that the main role of the copper catalyst is to promote the metal exchange between the alkenyliron and the aryl Grignard reagent. The catalytic cycle consistent with the experimental results is shown in Scheme 3. Addition of aryliron **6** to alkyne **2** forms alkenyliron **7**. The alkenyl group on iron transfers to copper by the transmetalation¹⁸ with diarylcuprate **8** to give alkenyl(aryl)cuprate **9** and to regenerate aryliron **6**. Alkenylmagnesium bromide **10** is released as the arylmagnesium product by the transmetalation between alkenylcuprate **9** and aryl Grignard reagent **1**¹⁹ to complete the catalytic cycle.

In conclusion, we have disclosed the arylation of alkynes effectively catalyzed by a catalyst system consisting of iron and copper. The most striking feature is that the cooperative catalysis enables us to conduct otherwise hardly attainable arylation of dialkylacetylenes.

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Supporting Information Available: Experimental procedures and spectral analyses of all reaction products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (11) Configuration of (*E*)-**3a** was determined by NOE experiment in ¹H NMR. The ratio of *E* to *Z* was determined by GC, GC–MS and ¹H NMR.
- (12) The reaction in the absence of PBU₃ gave less than 3% yield of **3a** with 46% conversion of **2a**. The amount of PBU₃ can be reduced to 10 mol % (Fe: 3 mol %; Cu: 6 mol %) without significant loss of the yield (61%, *E*:*Z* = 91:9). For the experimental conditions, see Supporting Information.
- (13) The use of FeCl₃, CuCl, CuI, and CuBr₂ gave similar results. The yields were low with other phosphine ligands (PPh₃, PhPMe₂, PCy₃, and dppp) and with nitrogen ligands (pyridine and substituted pyridines).
- (14) High regioselectivities for aryl(alkyl)alkynes were also reported in the arylmetalations. See refs 3a, d–f.
- (15) A mixture of two diastereomeric isomers, both of which have (*Z*)-configuration, due to the central chirality at the α-carbon of the allylic alcohol and the axial chirality based on the restricted rotation about the naphthyl–alkenyl bond.
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