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Iron-Catalyzed Chemo- and Stereoselective Hydromagnesiation of Diarylalkynes and Diynes

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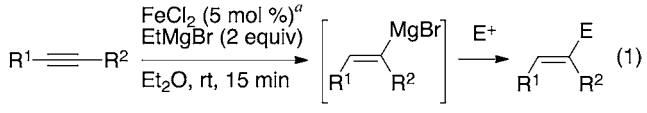
Supporting Information

ABSTRACT: Diarylalkynes are chemo- and stereoselectively hydromagnesiated in high yields at room temperature with an iron species generated in situ from $FeCl_2$ and EtMgBr. Functional groups such as bromide, iodide, amine, phenoxide, and alkene are well tolerated. Under similar conditions, diynes are chemo-, regio-, and stereoselectively hydromagnesiated. The resulting alkenylmagnesium compounds are a platform for further functionalization as a one-pot reaction.

Catalytic hydrometalation, such as hydromagnesiation, of an alkyne via a transient metal hydride species was established in the 1980s for titanium[1] and nickel[2] but has been hardly developed since then. We[3] and others[4−6] have noticed that the iron species generated from the reaction of an iron salt with an alkylmagnesium halide[7] may be a viable catalytic species for hydromagnesiation of C−C double bonds. There have also been recent reports on iron-catalyzed hydrosilylation[8] and hydroboration[9] of C−C multiple bonds. We report here the chemo- and stereoselective preparation of alkenylmagnesium compounds via *cis*-selective hydromagnesiation of diarylalkynes and diynes with EtMgBr as a hydride source and $FeCl_2$ as a catalyst. The reaction typically completes within 15 min at room temperature in the presence of 5 mol % of $FeCl_2$ in diethyl ether without the need for any added ligand. Notably, the conditions tolerate the presence of functional groups such as bromide, iodide, amine, phenoxide, and alkene, which are known to be sensitive to reductive conditions. The reaction regioselectively reduces only one of the two acetylenic bonds in a diyne with good *cis*-selectivity. Hydromagnesiation of a conjugated diyne has seldom been recorded in the literature, and hydrometalation of an internal diyne, only rarely.[10]

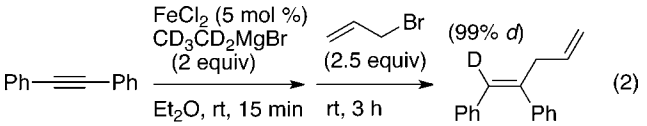
The hydromagnesiation of diphenylacetylene (1.03 g, 5.6 mmol) with EtMgBr (9.66 mL, 1.16 M in diethyl ether, 11.2 mmol) and $FeCl_2$ (36 mg, 0.28 mmol) in diethyl ether (20 mL) at room temperature for 15 min, followed by trapping with 1 M hydrochloric acid (30 mL) or allyl bromide (1.2 mL, 14 mmol), gave (*Z*)-stilbene (**2**, 0.97 g, 94% yield) and 1,2-diphenyl-1,4-pentadiene (**3**, 0.88 g, 72%), respectively, with high (*Z*)-stereoselectivity (eq 1, E = H or allyl). The allylation reaction may have taken place under the influence of an iron catalyst that was still present after the hydromagnesiation reaction.[11] We did not observe the formation of overreduction products such as 1,2-diphenylethane. Alkenes were largely unreactive under these conditions.



$R^1 = R^2$ = Ph (**1**, 1.03 g), E = H[b] **2**: 94% (*E*/*Z* = 2:98)
$R^1 = R^2$ = Ph (**1**, 0.99 g), E = allyl[c] **3**: 72% (*E*/*Z* = 3:97)

[a]Reaction conditions: diphenylacetylene (**1**, 1.03 or 0.99 g), $FeCl_2$ (5 mol %), EtMgBr (2 equiv) in Et_2O, rt (25 °C), 15 min. [b]Hydrochloric acid. [c]Allyl bromide (2.5 equiv), rt, 3 h.

The reaction did not proceed at all in the absence of the iron catalyst (see the Supporting Information for details). Iron salts other than $FeCl_2$, such as $Fe(acac)_2$, $Fe(acac)_3$, or $FeCl_3$, afforded **2** with slightly lower yields (76−79%). Other primary alkyl (e.g., hexyl) magnesium reagents performed equally well, but bulky (isobutyl) or secondary alkyl (cyclohexyl, cyclopentyl) reagents were greatly inferior. Because the reaction does need a ligand, we could consider that the olefin generated by β-elimination and the acetylenic substrate may act as ligands on the iron intermediate.[6] The presence of added 1-hexene did not affect the yield. Addition of bi- or terpyridine-type ligands did not affect the yield either, whereas mono- or diphosphine ligands shut off the reaction. The use of a smaller amount of EtMgBr resulted in lower conversion of the starting material, but the necessity for 2 equiv of this reagent is unclear. 1 equiv is used as a hydrogen source and can be traced at the end of the reaction as the alkene product, and the excess EtMgBr is not consumed during the reaction (Supporting Information). The hydrogen on the product originates from EtMgBr, as unequivocally demonstrated by the deuterium-labeling experiment shown in eq 2.



1 **3**-*d*: 73% (*E*/*Z* = 6:94)

A variety of diarylalkynes undergo the hydromagnesiation reaction, as shown in Table 1. Electron-rich (entries 4 and 9) and electron-deficient (entries 5 and 6) alkynes reacted equally well. Steric hindrance did not affect the yield, and the stereoselectivity was excellent (entry 4). An important feature of this reaction is the tolerance of halides, including bromide

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Table 1. Iron-Catalyzed Hydromagnesiation of Various Diarylalkynes and Subsequent Functionalization[a]

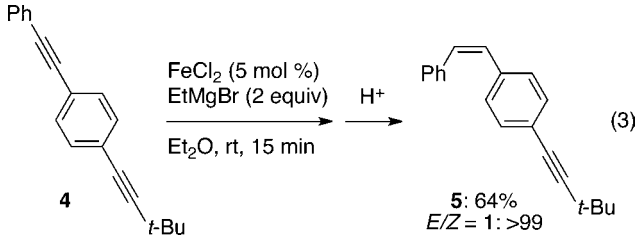
entry	alkyne	electrophile	product	yield (%)[b] (*E*/*Z*)[c]
1[d]	Ph—≡—Ph	H^+	Ph, Ph **2**	94 (2:98)
2	Ph—≡ (1-naphthyl)	H^+	Ph (1-naphthyl)	90 (3:97)
3	Ph—≡—Mes	H^+	Ph, Mes	92 (1:99)
4	Ph—≡—C$_6$H$_4$—X	H^+	Ph, C$_6$H$_4$—X	89 (4:96) (X = Me)
5				81 (6:94) (X = F)
6				78 (7:93) (X = Cl)
7[e]				70 (8:92)[f] (X = Br)
8				64 (6:94)[g] (X = I)
9				89 (11:89) (X = OMe)
10[h]				73 (14:86) (X = NMe_2)
11				75 (11:89) (X = OH)
12	Ph—≡—CH=CH—Ph	H^+	Ph, CH=CH—Ph	42 (18:82)
13[d]	Ph—≡—Ph	Br	Ph, Ph **3**	72 (3:97)
14	Ph—≡—Ph	O, NMe_2	Ph, Ph, O	67 (98:2)
15	Ph—≡—Ph	PhCHO	Ph, Ph, OH	73 (>99:1)
16	S—≡ (2-thienyl)	Ph_2SiHCl	$SiHPh_2$, S, S	38 (>99:1)
17	Ph—≡—Ph	PhI[i]	Ph, Ph	80

[a]Reaction conditions: diarylalkyne (0.30 mmol), $FeCl_2$ (5 mol %), EtMgBr (0.60 mmol) in Et_2O stirred at rt (25 °C) for 15 min. See the Supporting Information for details. [b]Isolated yield. [c]Determined by GC. [d]Reaction with 1 g of substrate. [e]$Fe(acac)_3$ (2.5 mol %) was used as a catalyst. [f](*Z*)-Stilbene was obtained in 3% yield. [g](*Z*)-Stilbene was obtained in 4% yield. [h]$FeCl_2$ (10 mol %) and EtMgBr (1.2 mmol) were used. [i]$NiCl_2(PPh_3)_2$ (5 mol %) was used as a catalyst.

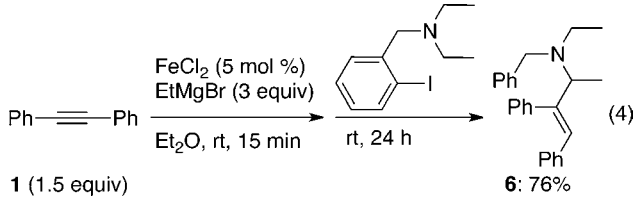
(entry 7) and iodide (entry 8), where only a trace amount of dehalogenated material was observed. This is surprising in light of the previous reports on the iron-mediated reduction of aryl halides[5] and suggests an extremely high affinity of the iron species for the alkyne. A dimethylamino group (entry 10) and a deprotonated hydroxyl group (entry 11) were also tolerated. We note that when substrates containing O or N atoms were used, the stereoselectivity slightly decreased, perhaps because coordination of these atoms to the iron species accelerates the isomerization process.[12] An enyne (entry 12) was selectively hydromagnesiated at the alkyne site to chemoselectively produce a 1,3-diene in moderate yield. The lower stereoselectivity may suggest coordination of the alkene site to the iron species. We note that the reaction of these asymmetrical alkynes proceeded without regioselectivity (Supporting Information).

The alkenylmagnesium intermediate can be further reacted with electrophiles in a one-pot reaction (entries 13−17). The reaction with allyl bromide (entry 13 and eq 1) stereoselectively gave a 1,4-diene. The reaction with *N*,*N*-dimethylformamide (DMF, entry 14) produced an (*E*)-*β*-unsaturated aldehyde, and the reaction with benzaldehyde (entry 15) gave an allylic alcohol, both with high stereoselectivity. Notably, a dithienylacetylene (entry 16) also participated in the hydrometalation reaction stereoselectively to give an (*E*)-alkenylsilane after trapping with the corresponding chlorosilane. Iron-catalyzed hydromagnesiation of diphenylacetylene, following a one-pot nickel-catalyzed cross-coupling with aryl iodides, gave triarylalkenes (entry 17).

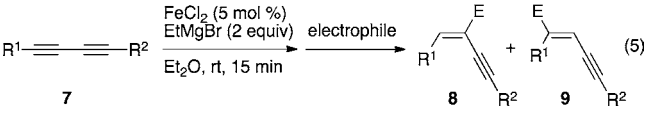
Alkylalkynes reacted poorly under these reaction conditions (data not shown). This allowed site-selective hydrometalation of diyne compound **4** at the diarylalkyne site to produce enyne **5** with high stereoselectivity (eq 3), together with a small amount of diene (7%).



The alkenylmagnesium intermediate can be functionalized in a one-pot sequence involving iron catalysis. This was illustrated by a signature reaction of iron catalysis that we reported some time ago.[13] The vinyl Grignard reagent generated in situ reacts with an *o*-iodobenzylamine to produce first the corresponding aryl radical and then afford an *α*-alkenylation of the amine via 1,5-hydrogen transfer (eq 4).



Under similar reaction conditions, 1,3-diynes (**7**) can be chemo-, regio-, and stereoselectively hydromagnesiated at one of the triple bonds, leaving another intact (eq 5 and Table 2).



Both electron-deficient (entry 2) and electron-rich substrates (entries 3 and 4) reacted with high chemo- and regioselectivity,

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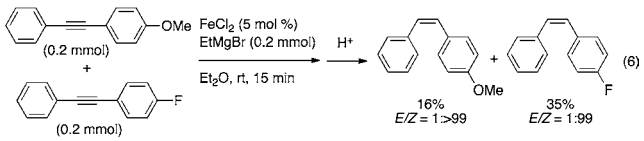
Table 2. Iron-Catalyzed Hydromagnesiation of 1,3-Diynes[a]

entry	R^1	R^2	electrophile	E	yield (%)[b]	E/Z[c]	8:9[d]
1	Ph	Ph	D^+	D	63	14:86	>99:1
2	4-FC_6H_4	4-FC_6H_4	D^+	D	63	11:89	97:3
3	4-MeC_6H_4	4-MeC_6H_4	D^+	D	55	25:75	97:3
4	4-$MeOC_6H_4$	4-$MeOC_6H_4$	D^+	D	65	22:78	97:3
5	Ph	Me_3Si	D^+	D	55	17:83	98:2
6	Ph	Ph	DMF	CHO	50	97:3	>99:1

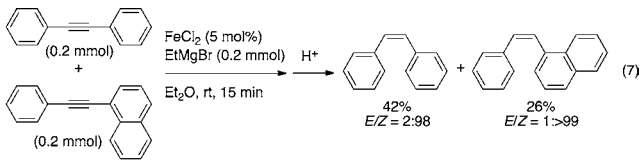
[a]Reaction conditions: 1,3-diyne (0.30 mmol), $FeCl_2$ (5 mol %), EtMgBr (0.60 mmol), in Et_2O stirred at rt (25 °C) for 15 min. See the Supporting Information for details. [b]Isolated yield. [c]Determined by GC. [d]Determined by ^1H NMR.

while the stereoselectivity was lower for electron-rich substrates. An asymmetric diyne (1-phenyl-4-trimethylsilylbutadiyne, entry 5) reacted selectively at the phenyl-substituted triple bond. The resulting magnesium intermediate further reacted with an electrophile such as DMF (entry 6) to selectively produce an α-ynylpropenal in a one-pot reaction.

At this stage, we can only speculate on the reaction pathway to transfer a magnesium and a hydrogen atom from EtMgBr to the alkyne. Decomposition of an alkyliron through β-hydrogen elimination to generate a putative iron hydride species has often been proposed in the literature.[3,4,7] In light of the mechanism of organometallic addition to an unsaturated C−C bond which exhibits high sensitivity to electronic and steric effects,[14] the poor selectivity illustrated in eqs 6 and 7 may suggest a radical mechanism[13] instead of a pure organometallic mechanism.



*Yields and E/Z ratios were estimated by GC in the precence of n-tridecane as an internal standard. Yields were calculated based on the conversion of the corresponding alkyne.



*Yields and E/Z ratios were estimated by GC in the precence of n-tridecane as an internal standard. Yields were calculated based on the conversion of the corresponding alkyne.

In conclusion, an iron species generated from an iron salt and an alkylmagnesium halide can hydromagnesiate a diarylalkyne in high yield with high stereoselectivity, and a diyne, with high chemo-, regio-, and stereoselectivity. This reaction allows facile preparation of alkenylmagnesium compounds[15] from simple starting materials and can be exploited for further functionalization in one pot to synthesize polysubstituted olefins[16] and 1,3-enyne derivatives.[17] We expect that this reaction will open a new horizon for iron catalysis, the repertoire of which is rapidly expanding[18] because of the concern over an expected decrease in the supply of rare metals in the future.[19]

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and physical properties of the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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