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Ambient arylmagnesiation of alkynes catalysed by ligandless nickel(II)†

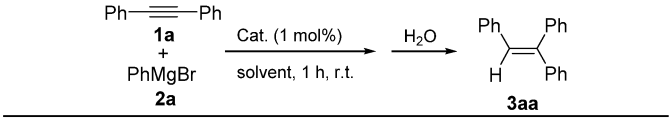
Fei Xue,[a] Jin Zhao*[ab] and T. S. Andy Hor*[ab]

A simple and efficient catalytic arylmagnesiation of diarylacetylenes and aryl(alkyl)acetylenes is accomplished by $NiCl_2{\cdot}6H_2O$ at r.t. in the absence of stabilising ligands. The corresponding tetra-substituted alkenes can be obtained in good yields by subsequent treatment with different electrophiles.

Carbometalation of alkynes is an important method for the synthesis of multi-substituted olefins that exploits the versatile reactivities of alkenylmetals towards various electrophiles.[1] Catalytic and non-catalytic carbometalations proceed readily with alkynes bearing a directing group such as alkoxy and amine[2] but carbometalation of alkynes without heteroatoms has been a long-standing challenge.[3] There have been some recent successes in simple alkynes using organolithium,[4] arylmagnesium,[5] arylboronic acid,[6] arenediazonium tetrafluoroborate[7] and organozinc reagents[8] in the presence of transition metal catalysts. There are however limitations such as high catalytic loading, non-ambient conditions, prolonged reaction duration, or demand for ligand additive, *etc.* For example, $NiCl_2(PPh_3)_2$ (10 mol%) can catalyse the arylmagnesiation of unfunctionalised alkyne giving arylethenes, but only in low yields after up to 70 h.[3d] The carbozincation of arylacetylenes catalysed by $Ni(acac)_2$ (25 mol%) produces tetra-substituted alkenes in high yield but at −35 °C.[3e,f] $Ni(cod)_2$ is effective for the aryl transfer from arylboron substrates to alkynes only in the presence of a proton source.[6a] We herein describe a simple and general method whereby Ni(II) salts are used to catalyse arylmagnesiation of different unfunctionalized diarylacetylenes and aryl(alkyl)acetylenes at r.t. without the need for Ni(II) complexes or the introduction of stabilising ligands. Subsequent treatment with electrophiles conveniently gives tetra-substituted alkenes.

The r.t. reaction between diphenylacetylene (**1a**) and phenylmagnesium bromide (**2a**) followed by hydrolysis was chosen as a model reaction of arylmagnesiation of diarylacetylenes (Table 1). There is negligible reaction without a catalyst (entry 1). A preliminary scan over a range of transition metal salts revealed that common Ni(II) salts (except $NiSO_4{\cdot}6H_2O$ and $Ni(OH)_2$) and their solvent adducts are much more active than Fe(III), Co(II), Cu(I/II) and Pd(II) salts, giving triphenylethylene (*i.e.* 1,2-diphenylethenylbenzene) **3aa** up to 98% yield (entries 2–8) in toluene. $NiCl_2{\cdot}6H_2O$ is nearly as efficient when the reaction is scaled up by 20 times, giving **3aa** in 92% yield (entry 2). In the presence of pavilic acid, $CrCl_2$ catalyses the same reaction giving **3aa** in 70% yield at 110 °C.[5b] Only 44% yield of **3aa** can be obtained from the hydroarylation of **1a** with 2-phenyl-1,3,2-dioxaborinanes

Table 1 Arylmagnesiation of diphenylacetylene followed by hydrolysis[a]



Entry	Catalyst	Yield[b] of **3aa** (%)
1	—	0
2	$NiCl_2{\cdot}6H_2O$	98/92[c]65[d]/23[e]
3	$NiCl_2$	94
4	$NiBr_2$	92
5	$NiCl_2(dme)$	98
6	$NiBr_2(dme)$	98
7	$Ni(acac)_2$	95
8	$Ni(OAc)_2{\cdot}4H_2O$	96
9	Dinickel complex[f]	94
10	$Ni(OH)_2$	13
11	$NiSO_4{\cdot}6H_2O$	4
12	$Fe(acac)_3$	0
13	$Pd(OAc)_2$	0
14	CuCl	0
15	$CuCl_2$	4
16	$CoCl_2{\cdot}6H_2O$	0

[a] Reactions were carried out using 0.5 mmol diphenylacetylene (**1a**) and 0.6 mmol phenylmagnesium bromide (**2a**) in 2.0 mL toluene under N_2. [b] Isolated yield. [c] Using 10 mmol of **1a** and 12 mmol of **2a** in 20 mL toluene. [d] Using MeCN as the solvent. [e] Using THF as the solvent. [f] See ref. 9.

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[a] *Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore 117543, Singapore. E-mail: andyhor@nus.edu.sg, chmzhaoj@nus.edu.sg; Fax: +65 6779 1691; Tel: +65 6516 2675*

[b] *Institute of Materials Research and Engineering, Agency for Science, Technology and Research, 3 Research Link, Singapore 117602, Singapore*

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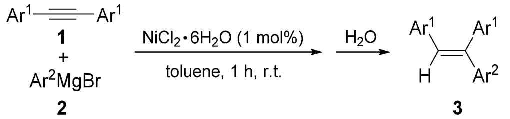
Table 2 Substrate scope for the arylmagnesiation of diarylacetylenes[a]



Entry		Product	Yield[b] (%)	$E:Z$[c]
1	**1a**: Ar^1 = Ph, **2b**: Ar^2 = 4-FPh	**3ab**	92	>99 : 1
2	**1a**: Ar^1 = Ph, **2c**: Ar^2 = 4-MeOPh	**3ac**	89	>99 : 1
3	**1a**: Ar^1 = Ph, **2d**: Ar^2 = 3-MePh	**3ad**	96	97 : 3
4	**1a**: Ar^1 = Ph, **2e**: Ar^2 = 2-MePh	**3ae**	85	98 : 2
5	**1b**: Ar^1 = 4-MePh, **2a**: Ar^2 = Ph	**3ba**	94	<1 : 99
6	**1b**: Ar^1 = 4-MePh, **2b**: Ar^2 = 4-FPh	**3bb**	90	>99 : 1
7	**1b**: Ar^1 = 4-MePh, **2c**: Ar^2 = 4-MeOPh	**3bc**	86	>99 : 1
8	**1c**: Ar^1 = 3-MePh, **2a**: Ar^2 = Ph	**3ca**	92	<1 : 99
9	**1c**: Ar^1 = 3-MePh, **2d**: Ar^2 = 3-MePh	**3cd**	92	—
10[d]	**1d**: Ar^1 = 4-FPh, **2a**: Ar^2 = Ph	**3da**	63	<1 : 99
11[e]	**1e**: Ar^1 = 2-MeOPh, **2a**: Ar^2 = Ph	**3ea**	67	8 : 92
12	**1f**: Ar^1 = 4-^{n}BuPh, **2a**: Ar^2 = Ph	**3fa**	93	8 : 92

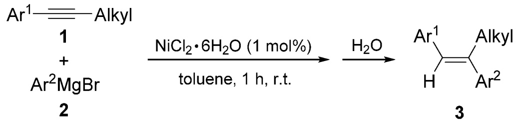
[a] Reactions were carried out using 0.5 mmol diarylacetylenes (**1**) and 0.6 mmol arylmagnesium bromide (**2**) in 2.0 mL toluene under N_2. The conversion of alkyne for all reactions is 100% except in entry 11 which is 77%. [b] Isolated yield. [c] E/Z ratios were calculated by GC-MS and ^{1}H NMR analysis. [d] 60 °C. [e] 60 °C, 4 h.

catalysed by Ni(cod)$_2$ at 80 °C after 24 h.[6a] Use of other solvents such as CH_3CN and THF significantly lowers the yield (entry 2). Tripodal dinuclear complex LClNi(μ-Cl$_2$)NiClL (L = bis[(3,5-dimethyl-1*H*-pyrazolyl)methyl][(2-furanyl)methyl]amine), which is an effective catalyst for the cross-coupling of alkyl halides and Grignard reagents,[9] was also applied to the arylmagnesiation of diphenylacetylene, resulting in high yield of **3aa** (entry 9). Quenching the reaction with D_2O gives **3aa-D** in 97% yield with an exclusive deuteriation at the olefinic methyne, supporting the presence of an alkenylmagnesium intermediate.[5a]

As $NiCl_2{\cdot}6H_2O$ is inexpensive, easy to handle and highly active, it has been chosen as the catalyst for the subsequent syntheses. The scope of the arylmagnesiation of diarylacetylenes catalysed by $NiCl_2{\cdot}6H_2O$ is given in Table 2. The introduction of electron rich or poor substituents on the aryl ring of the Grignard reagent gives similarly high yields (entries 1–4). The method also applies well to diarylacetylenes with electron-donating groups at the *para*- and *meta*-position *viz.* **1b**, **1c** and **1f** (entries 5–9 and 12). Diarylacetylene with an electron-deficient substituent in the *para*-position such as **1d** gives a moderate yield of 63% at 60 °C for 1 h (entry 10). Steric effects have a significant effect on the product yield when there is substitution at the *ortho*-position of the diarylalkyne (entry 11). All the reactions afford high product stereoselectivity without the aid of a directing group. The molecular structures of **3bb** and **3bc** determined using X-ray single-crystal diffraction show that both are *E* isomers. The stereoselectivity of **3bb** was also studied by NOESY measurements (see ESI†). For the other hydroarylation products, the *E*/*Z* ratios were assigned from NMR analysis with literature support.[5c,6e,g,7,10] The ratios of the resulting *E*/*Z* isomers indicate that all the arylmagnesiation reactions proceed by a *syn*-addition across the alkyne. Similar observations were made in similar reactions catalysed by Fe(acac)$_3$–CuBr–PBu$_3$ (ref. 5*a*) and CrCl$_2$–^{t}BuCOOH[5b] systems.

The application of $NiCl_2{\cdot}6H_2O$ in the catalytic arylmagnesiation of aryl(alkyl)alkynes has also been investigated (Table 3). The change of one aryl group in diarylalkyne to the alkyl group ^{n}Bu generally reduces the product yields, but the stereo- and regioselectivity remains similarly high. An array of arylmagnesium bromides with electron-rich or poor substituents react with 1-phenyl-1-hexyne, giving predominantly *E*-tri-substituted alkenes in high yields (entries 1–5). The arylmagnesiation of the *ortho*-substituted 1-(hex-1-yn-1-yl)-2-methylbenzene yields the addition product in 69% at 60 °C (entry 6). Alkynes with an electron-rich group at the *para*- or *meta*-position exhibit high stereo- and regio-selectivity (entries 8, 10 and 11). 1-Naphthalenyl-1-hexyne reacts with phenylmagnesium bromide to form **3ia** in nearly qualitative yield (entry 7). The reaction proceeds efficiently with electro-deficient alkynes (entry 9). 5-Chloro-1-phenyl-hexyne produces the corresponding addition product in 74% yield (entry 12). The product yields are

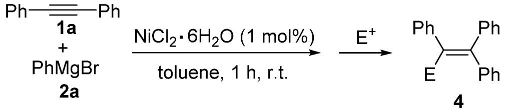
Table 3 Substrate scope for the arylmagnesiation of aryl(alkyl)acetylenes[a]



Entry		Product	Conv.[c] (%)	Yield[b] (%)	$E:Z$[d]
1	**1g**: Ar^1 = Ph, alkyl = ^{n}Bu, **2a**: Ar^2 = Ph	**3ga**	86	81	>99 : 1
2	**1g**: Ar^1 = Ph, alkyl = ^{n}Bu, **2b**: Ar^2 = 4-FPh	**3gb**	100	97	92 : 8
3	**1g**: Ar^1 = Ph, alkyl = ^{n}Bu, **2c**: Ar^2 = 4-MeOPh	**3gc**	92	82	>99 : 1
4	**1g**: Ar^1 = Ph, alkyl = ^{n}Bu, **2d**: Ar^2 = 2-MePh	**3gd**	100	84	98 : 2
5	**1g**: Ar^1 = Ph, alkyl = ^{n}Bu, **2e**: Ar^2 = 3-MePh	**3ge**	100	92	>99 : 1
6[e,f]	**1h**: Ar^1 = 2-MePh, alkyl = ^{n}Bu, **2a**: Ar^2 = Ph	**3ha**	86	69	>99 : 1
7[g]	**1i**: Ar^1 = 1-NapPh, alkyl = ^{n}Bu, **2a**: Ar^2 = Ph	**3ia**	100	99	97 : 3
8	**1j**: Ar^1 = 4-MeOPh, alkyl = ^{n}Bu, **2a**: Ar^2 = Ph	**3ja**	75	66	>99 : 1
9	**1k**: Ar^1 = 4-FPh, alkyl = ^{n}Bu, **2a**: Ar^2 = 4-FPh	**3ka**	100	81	>99 : 1
10	**1l**: Ar^1 = 3-MePh, alkyl = ^{n}Bu, **2a**: Ar^2 = Ph	**3la**	68/90[e]	61/64[e]	>99 : 1
11[g]	**1m**: Ar^1 = 4-BiPh, alkyl = ^{n}Bu, **2a**: Ar^2 = Ph	**3ma**	79/90[e]	68/75[e]	>99 : 1
12	**1n**: Ar^1 = Ph, alkyl = (CH$_2$)$_3$Cl, **2a**: Ar^2 = Ph	**3na**	100[e]	74	98 : 2

[a] Reactions were carried out using 0.5 mmol aryl(alkyl)acetylenes (**1**) and 0.6 mmol arylmagnesium bromide (**2**) in 2.0 mL toluene under N_2. [b] Isolated yield. [c] Based on alkynes. [d] E/Z ratios were calculated by GC-MS and ^{1}H NMR analysis. [e] 60 °C. [f] The regioselective product (*Z*)-1-methyl-2-(1-phenylhex-1-enyl)benzene (in 7% yield) was found from ^{1}H NMR. [g] Nap = naphthalenyl and Biph = biphenyl.

Table 4 Reactions of electrophiles with the arylmagnesiation intermediate[a]



Electrophiles	E	Product	Yield[b] (%)
I_2	I	**4aaa**	84[c]/68[d]
PhCHO	CHPh(OH)	**4aab**	78[c]/70[d]

[a] Reactions were carried out using 0.5 mmol diphenylacetylene (**1a**) and 0.6 mmol phenylmagnesium bromide (**2a**) in 2.0 mL solvent under N_2 for 1 h, then the electrophile was added. [b] Isolated yield. [c] At 0 °C for a further 3 h. [d] At r.t. for a further 3 h.

comparable to those obtained from the reactions catalysed by the Fe(acac)$_3$–iPr (iPr = 1,3-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene) system,[5c] but with higher stereoselectivity.

Reactions of the intermediary alkenylmagnesium with other electrophiles such as iodine and benzaldehyde give the corresponding tetra-substituted alkenes with higher yield at 0 °C than at r.t. (Table 4).

In summary, we have demonstrated a nickel-catalysed arylmagnesiation of diarylacetylenes and aryl(alkyl)acetylenes avoiding the addition of any supporting ligands. The catalytic method is mediated by $NiCl_2{\cdot}6H_2O$ at r.t. and is applicable to a range of substrates. It conveniently generates various tri-substituted alkenes by subsequent hydrolysis with excellent yields and high stereo- and regioselectivity. The process offers facile one-pot access to multi-substituted olefins. We are currently exploring the adoption of similar methods to construct other functional unsaturated systems especially using complex electrophiles.

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