

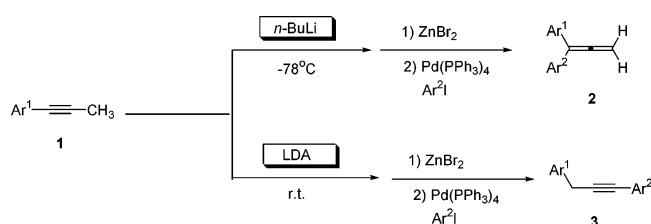
Pd(0)-Catalyzed Highly Selective Synthesis of 1,1-Diarylpropadienes and 1,3-Diarylpropynes from 1-Aryl-1-propynes and Aryl Halides

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Under different reaction conditions, 1,1-diarylpropadienes and 1,3-diarylpropynes can be prepared respectively by the sequential lithiation of 1-aryl-1-propynes, transmetalation, and the corresponding Pd(0)-catalyzed cross-coupling with aryl halides. A rationale for the formation of 1,3-diarylpropynes is proposed.

Tuning the selectivity of reactions remains a challenge in organic synthesis.¹ Recently, much attention have been paid to the regioselectivity of the coupling reactions involving propargylic/allenyl species.² We observed that the regioselectivity of these reactions can be influenced by the electronic and steric effects as well as the ligand effect.³ A clear-cut 1,3-lithium shift was also observed

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SCHEME 1

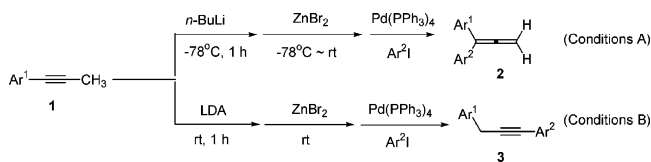


TABLE 1. Effect of Lithiation Reagents and Temperature on the Lithiation of 1-Phenyl-1-propyne, Transmetalation, and Pd-Catalyzed Cross-Coupling with Phenyl Iodide

entry	lithiation reagent	temp	yield ^a of 2a	yield ^a of 3a
1	<i>n</i> -BuLi	−78 °C	65	0
2	LDA	−78 °C	33	0
3	<i>n</i> -BuLi	−40 °C	49	0
4	LDA	−40 °C	19	0
5	<i>n</i> -BuLi	−20 °C	57	0
6	LDA	−20 °C	0	trace
7	<i>n</i> -BuLi	0 °C	28	13
8	LDA	0 °C	0	14
9	<i>n</i> -BuLi	15 °C	0	39
10	LDA	15 °C	0	43
11	<i>n</i> -BuLi	reflux	0	39
12	LDA	reflux	0	41
13	<i>n</i> -BuLi ^b	90 °C	0	0
14	LDA ^b	90 °C	0	20
15	<i>n</i> -BuLi ^c	−78 °C	0	0
16	LDA ^c	17 °C	0	0

^a Yields are based on 1-phenyl-1-propyne and were determined by 300 MHz ¹H NMR analysis with CH₂Br₂ as the internal standard. ^b Reaction was carried out in 1,4-dioxane. ^c After 1-phenyl-1-propyne was lithiated for 1 h, 2 equiv of HMPA was added. Then, the mixture was allowed to stir at room temperature for an additional 1 h and undergo transmetalation and the Pd(0)-catalyzed cross-coupling.

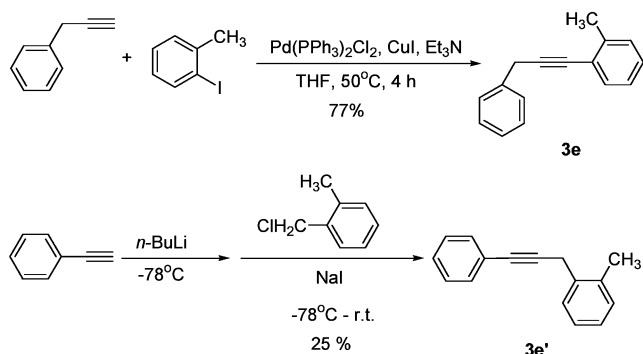
with 1-aryl-1-alkyn-3-yl/1-aryl-1,2-alkadienyl lithium.⁴ Herein, we report our recent observation of a double 1,3-lithium shift of 1-aryl-1-propyn-3-yl/1-aryl-1,2-propadienyllithium and the highly selective synthesis of either 1,1-diaryl allenes **2** or 1,2-diaryl propynes **3** (Scheme 1).

After observing the 1,3-lithium shift reaction in substituted 1-aryl-1-alkyn-3-yl/1-aryl-1,2-alkadienyl lithium, we tried to extend this chemistry to 1-aryl-1-propyne. In this study, two products **2a** and **3a** were identified. Some results are summarized in Table 1: (1) At a higher lithiation temperature, the yield of **3a** was higher. (2) The two lithiation reagents (*n*-BuLi and LDA) showed different results. Lithiation of 1-phenyl-1-propyne using *n*-BuLi at −78 °C formed 1,3-diphenylallene **2a** exclusively (Table 1, entry 1) (conditions A), while using LDA at room temperature the reaction yielded 1,3-diphenylpropyne **3a** as the only product (Table 1, entry 10) (conditions B). (3) Additives such as HMPA showed little effect on the yields and ratios of products **2a** and **3a** (Table 1, entries 15 and 16).

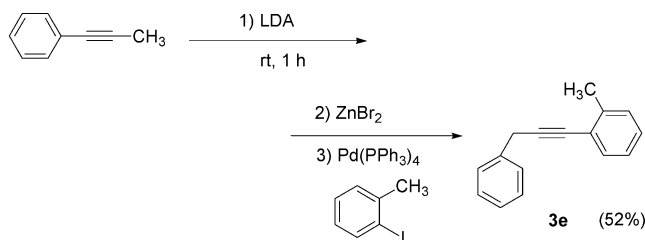
However, there is a puzzle that needs further attention. The reaction of 1-phenyl-1-propyne and *o*-methyliodo-

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SCHEME 2



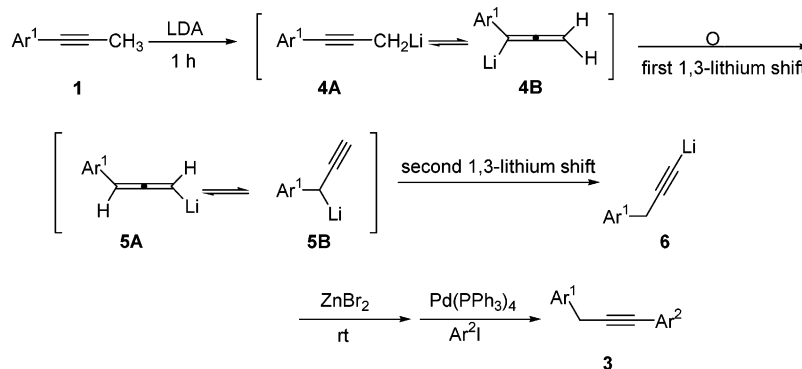
SCHEME 3



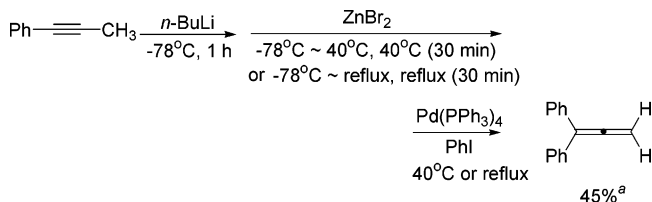
benzene using conditions B would afford either 1,3-diarylpropyne **3e** or **3e'**. To clarify this matter, 1-(*o*-methylphenyl)-3-phenyl-1-propyne **3e** and 1-phenyl-3-(*o*-methylphenyl)-1-propyne **3e'** were prepared by the Sonogashira coupling of 3-phenyl-1-propyne with *o*-methylphenyl iodide and the benzylation of 2-phenylacetylenyl lithium, respectively (Scheme 2). With these two authentic samples in hand, we studied the lithiation–transmetalation–coupling reaction of 1-phenyl-1-propyne with *o*-methylphenyl iodide. It turned out that the product under conditions B was 1-(*o*-methylphenyl)-3-phenyl-1-propyne **3e** (Scheme 3).

It has been reported that carbon–carbon triple bonds can migrate in the presence of a strong base such as KO^tBu ,⁵ KNH_2 ,⁵ potassium 3-aminopropylamide (KAPA),⁶ or alcoholic KOH.⁷ On the basis of these results, it was reasoned that the lithiation of 1-aryl-1-propyne may yield propargylic lithium **4A** or 1,2-allenylic lithium **4B**,⁸ which would undergo the first 1,3-lithium shift to afford intermediates **5A** or **5B**.⁴ **5A** or **5B** would then undergo the second 1,3-lithium shift to afford 3-aryl-1-propynyllithium **6**. Subsequent transmetalation and Pd(0)-catalyzed Negishi coupling⁹ would form product **3**, in which the carbon–carbon triple bond is conjugated with Ar^2

SCHEME 4



SCHEME 5



^a Yields are based on 1-phenyl-1-propyne and were determined by 300 MHz ^1H NMR analysis with CH_2Br_2 as the internal standard.

instead of Ar^1 (Scheme 4). It should be noted that the *i*- Pr_2NH formed after deprotonation may act as the proton source to induce the lithium shift. For the formation of 1,3-diaryl alkynes in Table 1 with *n*-BuLi as the base, deprotonation of THF with the in situ-formed propargyl/1,2-allenyllithium **4A** or **4B** may be involved in the migration of the carbon–carbon triple bond. The second 1,3-lithium shift may be due to the presence of the acidic terminal alkynic proton in intermediate **5B**.

The possibility of the propargyl zinc intermediate being the precursor of the final acetylenic products at the higher temperature has been excluded, since the coupling reaction under conditions A at 40 and 100°C afforded 1,1-diaryl allenes highly selectively (Scheme 5).

Some typical results are summarized in Table 2, indicating that: (1) the reaction is general for differently substituted 1-aryl-1-propyne and aryl halides; (2) the selectivity of the reactions is excellent, and the yields are from good to excellent; and (3) the isolated yields in Table 2 are based on aryl halides. In this reaction, HgCl_2^{3c} was not used.

In summary, a double 1,3-lithium shift was observed in the LDA-induced lithiation of 1-aryl-1-propynes. With conditions A or B, we can easily prepare 1,1-diarylpropadiene or 1,3-diarylpropyne from the same starting materials. Further studies in this area are being carried out in our laboratory.

Experimental Section

General Procedure For Synthesis of 1,1-Diphenyl Propadiene (**2a**) and 1,3-Diphenyl-1-propyne (**3a**): Conditions A.

To a solution of 1-phenyl-1-propyne (46 mg, 0.40 mmol) in THF (3 mL) in a dry Schlenk tube was added *n*-BuLi (0.30 mL, 1.6 M in hexanes, 0.48 mmol) at -78°C under N_2 . After the mixture was stirred at -78°C for 1 h, a solution of dry ZnBr_2 (180 mg, 0.80 mmol) in THF (4 mL) was added. After 10 min at

TABLE 2. Reactions under Conditions A and B (See Scheme 1)^a

entry	Ar ¹	Ar ²	yield ^b (%)	
			conditions A yield (%) of 2	conditions B yield (%) of 3
1	Ph	Ph	85 (2a)	96 (3a)
2	Ph	α -C ₁₀ H ₈	77 (2b)	67 (3b)
3	Ph	<i>p</i> -CH ₃ OC ₆ H ₄	85 (2c)	94 (3c)
4	Ph	<i>p</i> -CH ₃ OOC ₆ H ₄	99 (2d)	99 (3d)
5	Ph	<i>o</i> -CH ₃ C ₆ H ₄	47 (2e)	52 (3e)
6	Ph	<i>p</i> -CNC ₆ H ₄	96 ^c (2f)	92 (3f)
7	PhC ₆ H ₄	Ph	79 ^d (2g)	66 (3g)

^a Conditions A: 1-Aryl-1-propyne was lithiated by *n*-BuLi (1.2 equiv) for 1 h at -78°C . Then, 2 equiv of ZnBr₂ in THF was added at -78°C , and the mixture was allowed to warm to room temperature naturally. Pd(PPh₃)₄ and aryl halides were added subsequently at room temperature. Conditions B: 1-Aryl-1-propyne was lithiated by the addition of LDA (2 equiv) at -78°C and stirred for 1 h at room temperature. Then, 2 equiv of ZnBr₂ in THF was added at room temperature. After 20 min, Pd(PPh₃)₄ and aryl halides were added subsequently at room temperature. ^b Isolated yields are based on the amount of aryl halides used. ^c Also formed was <4% of 1-phenyl-3-(4'-cyanophenyl)-1-propyne (**3f'**). ^d Isolated yields are based on the amount of 1-(4'-biphenyl)-1-propyne used.

this temperature, the reaction mixture was warmed to room temperature for 20 min, which was followed by the addition of Pd(PPh₃)₄ (16 mg, 5 mol %) and iodobenzene (30 μL , 0.27 mmol) subsequently at room temperature with stirring. After the

reaction was complete as monitored by TLC (eluent: petroleum ether (60–90 $^\circ\text{C}$)), it was quenched with saturated NH₄Cl and extracted with ether. Drying over MgSO₄, rotary evaporation, and flash chromatography on silica gel (petroleum ether) afforded **2a**^{3c} (44 mg, 85%) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.40–7.20 (m, 10H), 5.27 (s, 2 H); ¹³C NMR (75.4 MHz, CDCl₃) δ 209.9, 136.2, 128.7, 128.4, 127.2, 109.1, 78.1; MS (70 eV) *m/z* (%) 192 (M⁺, 100.00); IR (neat) 1934 cm⁻¹. **Conditions B.** To a solution of 1-phenyl-1-propyne (46 mg, 0.40 mmol) in THF (3 mL) in a dry Schlenk tube was added LDA (0.40 mL, 2.0 M in pentane/THF/ethyl benzene, 0.80 mmol) at -78°C under N₂. After the mixture was warmed and stirred for 1 h at room temperature, a solution of dry ZnBr₂ (180 mg, 0.80 mmol) in THF (4 mL) was added. After 25 min at this temperature, Pd(PPh₃)₄ (16 mg, 5 mol %) and iodobenzene (30 μL , 0.27 mmol) were added subsequently at room temperature with stirring. After the reaction was complete as monitored by TLC (eluent: petroleum ether (60–90 $^\circ\text{C}$)), it was quenched with saturated NH₄Cl and extracted with ether. Drying over MgSO₄, rotary evaporation and flash chromatography on silica gel (petroleum ether) afforded **3a**¹⁰ (50 mg, 96%) as a solid: mp 68–70 $^\circ\text{C}$ (petroleum ether); ¹H NMR (300 MHz, CDCl₃) δ 7.50–7.19 (m, 10 H), 3.86 (s, 2 H); ¹³C NMR (75.4 MHz, CDCl₃) δ 136.7, 131.6, 128.5, 128.2, 127.9, 127.8, 126.6, 123.6, 87.5, 82.6, 25.7; MS (70 eV) *m/z* (%) 192 (M⁺, 100.00); IR (neat) 1598, 1490 cm⁻¹; Raman 2236 cm⁻¹. Anal. Calcd: C, 93.71; H, 6.29. Found: C, 93.42; H, 6.23.

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Supporting Information Available: Analytical data and ¹H NMR and ¹³C NMR spectra for compounds **2** and **3**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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