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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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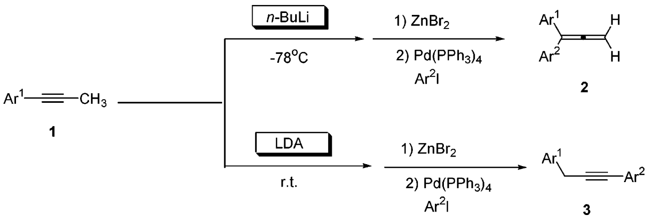
Received January 28, 2005



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/allenylic 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 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).

SCHEME 1

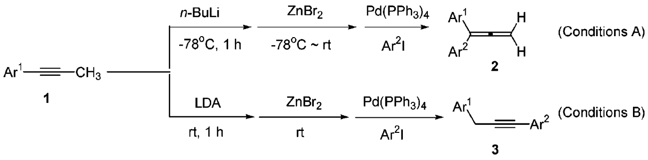
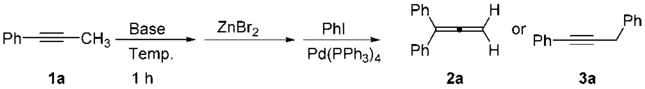


TABLE 1. Effect of Lithiation Reagents and Temperature on the Lithiation of 1-Phenyl-1-propyne, Transmetalation, and Pd-Catalyzed Cross-Coupling with Phenyl Iodide



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

[a] Yields are based on 1-phenyl-1-propyne and were detemined by 300 MHz ^{1}HNMR analysis with CH_2Br_2 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.

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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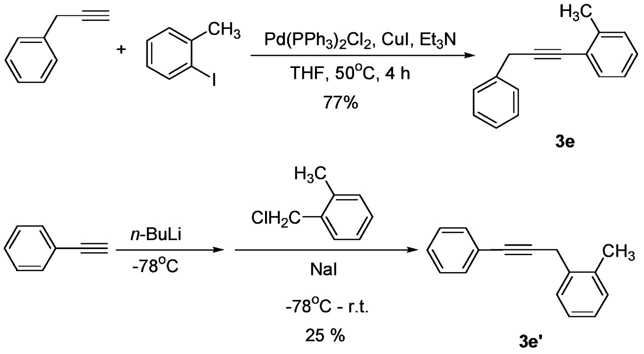
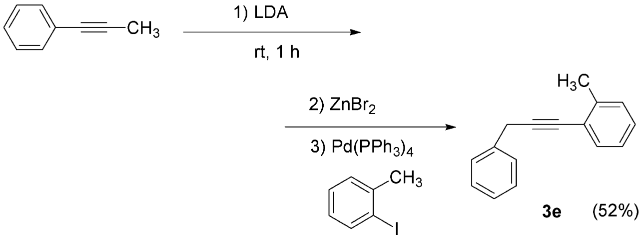
10.1021/jo050183d CCC: $30.25

SCHEME 2



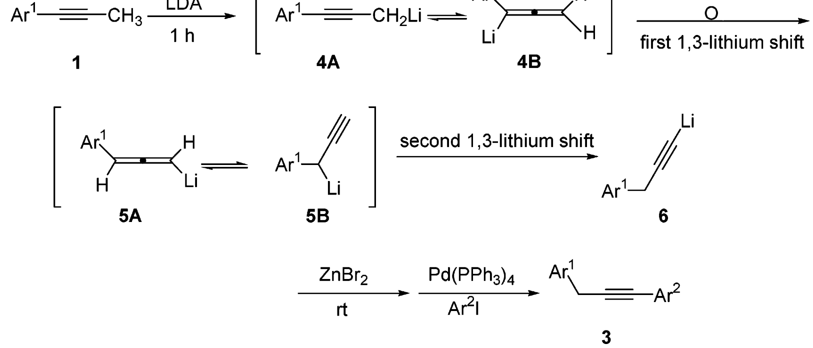
SCHEME 3



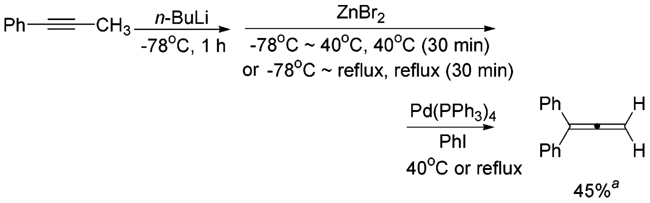
benzene using conditions B would afford either 1,3-diarylpropyne **3e** or **3e′**. To clarify this matter, 1-(*o*-methylphenyl)-3-phenyl-1-propyne **3e** and 1-phenyl-3-(*o*-methylphenyl)-1-propyne **3e′** were prepared by the Sonogashira coupling of 3-phenyl-1-propyne with *o*-methylphenyl iodide and 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 KOBu-*t*,[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 coupling[9] would form product **3**, in which the carbon−carbon triple bond is conjugated with Ar^2 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**.

SCHEME 4



SCHEME 5



[a] Yields are based on 1-phenyl-1-propyne and were determined by 300 MHz ^{1}HNMR analysis with CH_2Br_2 as the internal standard.

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]

			yield[b] (%)	
entry	Ar^1	Ar^2	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	p-$CH_3OC_6H_4$	85 (**2c**)	94 (**3c**)
4	Ph	p-$CH_3OOCC_6H_4$	99 (**2d**)	99 (**3d**)
5	Ph	o-$CH_3C_6H_4$	47 (**2e**)	52 (**3e**)
6	Ph	p-CNC_6H_4	96[c] (**2f**)	92 (**3f**)
7	PhC_6H_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 ZnBr$_2$ in THF was added at −78 °C, and the mixture was allowed to warm to room temperature naturally. Pd(PPh$_3$)$_4$ 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 ZnBr$_2$ in THF was added at room temperature. After 20 min, Pd(PPh$_3$)$_4$ 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(PPh$_3$)$_4$ (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 °C)), it was quenched with saturated NH$_4$Cl and extracted with ether. Drying over MgSO$_4$, rotary evaporation, and flash chromatography on silica gel (petroleum ether) afforded **2a**[3c] (44 mg, 85%) as a liquid: ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.40−7.20 (m, 10H), 5.27 (s, 2 H); ^{13}C NMR (75.4 MHz, CDCl$_3$) 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 N$_2$. After the mixture was warmed and stirred for 1 h at room temperature, a solution of dry ZnBr$_2$ (180 mg, 0.80 mmol) in THF (4 mL) was added. After 25 min at this temperature, Pd(PPh$_3$)$_4$ (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 °C)), it was quenched with saturated NH$_4$Cl and extracted with ether. Drying over MgSO$_4$, rotary evaporation and flash chromatography on silica gel (petroleum ether) afforded **3a**[10] (50 mg, 96%) as a solid: mp 68−70 °C (petroleum ether); ^{1}HNMR (300 MHz, CDCl$_3$) δ 7.50−7.19 (m, 10 H), 3.86 (s, 2 H); ^{13}C NMR (75.4 MHz, CDCl$_3$) 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.

Acknowledgment. Financial support from the National Natural Science Foundation of China, the Major State Basic Research Development Program (Grant No. G2000077500), and Shanghai Municipal Committee of Science and Technology is greatly appreciated.

Supporting Information Available: Analytical data and ^{1}H NMR and ^{13}C 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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