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Iron-catalyzed aryl- and alkenyllithiation of alkynes and its application to benzosilole synthesis[†]

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Phenyl- and vinyllithiums having an alkyl substituent at their *ortho*- and *cis*-position, respectively, readily added to alkynes in the presence of 5 mol% of Fe(acac)₃. The reaction of o-(trimethylsilyl)phenyllithium with alkynes gave benzosiloles through an addition-cyclization sequence.

Carbometalation of internal alkynes gives trisubstituted vinylmetals, which are readily converted to tetrasubstituted alkenes upon reaction with electrophiles.¹ Several methods are available for carbometalation of alkynes with arylmetals but relatively harsh reaction conditions are required, in particular, in the addition to dialkylacetylenes having no heteroatoms.²⁻⁴ Alkenylmetalation is even more difficult and no reports are available for high-yielding alkenylmetalation of unfunctionalized dialkylacetylenes.⁵ Here we report that phenyl- and vinyllithiums having an alkyl substituent at the ortho- or cis-position, respectively, add to alkynes including unfunctionalized dialkylacetylenes under mild conditions in the presence of readily available Fe(acac)₃ as a catalyst without any other additives.⁶⁻⁷ The reaction of o-(trimethylsilyl)phenyllithiums with alkynes leads to the one-pot synthesis of various benzosiloles,⁸ which are known to have a wide application in optoelectronic area.⁹

The reaction of o-tolyllithium (1a: 2 equiv.) with 4-octyne (2m: 1 equiv.) in the presence of Fe(acac)₃ (5 mol%) in Et₂O at 30 °C for 1.5 h followed by methanolysis of the resulting alkenyllithium (3am) stereoselectively gave (E)-4-(o-tolyl)-4-octene (4am) in 84% yield (entry 1 of Table 1).¹⁰ In contrast, no addition product was obtained in the reaction of phenyllithium (1b) under the same conditions (entry 2), showing a marked substituent effect at the ortho position of phenyllithium. The catalyst system consisting of Fe(acac)₃/CuBr/PBu₃, which is effective for arylmagnesiation of dialkylacetylenes^{2a} and aryllithiation of arylalkynes,⁶ also catalyzed the addition of **1a** but not that of **1b** (entries 3 and 4). Other metal complexes including those (Cr,^{2b} Mn,^{3f} Co,^{2c} Ni^{3d}) reported to be effective for any action of any lacetylenes and/or dialkylacetylenes did not catalyze the addition of o-tolyllithium (1a) to alkyne 2m (entries 5-10). No reaction took place in the absence of catalysts (entry 11).

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 Table 1
 Aryllithiation of alkynes followed by methanolysis^a

catalyst (5 mol%) Pr _ Et₂O, 30 °C, 1.5 h 2:1 Pr Pr κ¹ 1a: R1 = Me 2m 3am: Ar = o-tolyl 1b: R¹ = H 3bm: Ar = Ph MeOH 4am: R1 = Me Pr 4bm: R¹ = H

Entry	R^1	Catalyst (mol%)	Conv. $(\%)^b$	Yield $(\%)^c$
1	Me (1a)	$Fe(acac)_3$ (5)	>99	84
2	H (1b)	$Fe(acac)_3(5)$	<2	<2
3	Me (1a)	$Fe(acac)_3 (5)/CuBr (10)/PBu_3 (40)$	>99	73
4	H (1b)	$Fe(acac)_3 (5)/CuBr (10)/PBu_3 (40)$	9	<2
5	Me (1a)	$CrCl_{2}$ (5)/ <i>t</i> -BuCO ₂ H (6.7)	7	<2
6	Me (1a)	$MnCl_2$ (5)	6	<2
7	Me (1a)	$\operatorname{CoBr}_{2}(5)$	28	3
8	Me (1a)	$NiCl_2(PPh_3)_2$ (5)	22	<2
9	Me (1a)	CuBr (5)	<2	<2
10	Me (1a)	$Pd(OAc)_2$ (5)	<2	<2
11	Me (1a)	None	<2	<2

^{*a*} The reaction was carried out in Et₂O (2.0 mL) under a nitrogen atmosphere using an aryllithium (1: 0.80 mmol) and 4-octyne (**2m**: 0.40 mmol) in the presence of a metal complex (0.020 mmol). ^{*b*} Conversion of **2m** determined by GC and/or ¹H NMR. ^{*c*} Yield of isolated product **4** based on **2m**. Stereoselectivities $\geq 98\%$.

Table 2 illustrates the scope of the present carbolithiation of alkynes. Pentyl and isopropyl groups substituted at the orthoposition of phenyllithium also promoted the carbolithiation of 4-octyne (2m) to give the corresponding addition products in high yields (entries 1 and 2). Introduction of an electron-donating group into the para-position of o-tolyllithium did not affect the reaction but an electron-withdrawing group lowered the yield (entries 3 and 4). Phenyllithiums having a methoxy, tert-butyl or phenyl group at the ortho-position did not add to 4-octyne under the same conditions. As well as dialkylacetylenes, aryl(alkyl)- and diarylacetylenes underwent the addition of 1a (entries 5-7). In the aryllithiation of alkyl(phenyl)acetylenes 2n and 2o, lithium was attached predominantly to the carbon having the aryl group. The o-tolyl group of 1a selectively attacked the less hindered carbon of dissymmetrical dialkylacetylene 2q (entry 8). Trimethylvinyllithium (5a), which has a structure similar to 1a, added to 7-tetradecyne (2r) in a high yield (entry 9). It should be noted that the alkenyllithiation does not take place with dimethylvinyllithiums lacking a substituent at the *cis*- or α -position.

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$\begin{array}{cccc} R^2 - Li &+ & R^3 & & & R^4 \\ 2:1 & & & & R^3 & & \\ 1: R^2 = aryl & 2 & & & \\ 5: R^2 = alkenyl & & & & \\ 6: R^2 = alkenyl & & & \\ \end{array}$						
Entry	R ² –Li (1 or 5)	R ³ , R ⁴ in 2	$T/^{\circ}\mathbf{C}$	Time/h	Yield (%) ^b	
1	Li 1c Pent	Pr, Pr (2m)	30	2	86	
2	Li 1d	Pr, Pr (2m)	30	4	89	
3	MeO-Li 1e	Pr, Pr (2m)	30	19	83	
4	CILi 1f	Pr, Pr (2m)	30	6	55	
5	Li 1a	Bu, Ph (2n)	-20	5.5	84 ^{<i>c</i>}	
6	Li 1a	Me, Ph (20)	-20	1	80	
7	Li 1a	Ph, Ph (2p)	-20	2.5	79	
8	Li 1a	Bu, <i>t</i> -Bu (2q)	30	15	80	
9)—(_{⊔i} 5a	Hex, Hex (2r)	0	1.5	81	
10		Hex, Hex (2r)	0	1.5	85	
11	CH Bu Li 5c	Pr, Pr (2m)	0	2	83	
12	Bu Li 5c	Bu, Ph (2n)	-20	1	81 ^{<i>d</i>}	

Table 2 Aryl- and alkenyllithiation of alkynes followed by methanolysis

^{*a*} The reaction was carried out in Et₂O (4.0 mL) under a nitrogen atmosphere using an organolithium (1 or 5: 1.6 mmol) and an alkyne (2: 0.80 mmol) in the presence of Fe(acac)₃ (0.040 mmol). ^{*b*} Yield of isolated product 4 or 6 based on 2. Unless otherwise noted, an isomer was produced with $\geq 97\%$ selectivity. ^{*c*} (*E*)-2-(2-methylphenyl)-1-phenyl-1-hexene (4an): (*E*)-1-(2-methylphenyl)-2-phenyl-1-hexene: (*Z*)-2-(2-methylphenyl)-1-phenyl-1-hexene = 90:8:2. ^{*d*} 6cn: regioisomer = 94:6.

The efficient alkenyllithiation was also observed with cyclic trisubstituted vinyllithiums **5b** and **5c** (entries 10–12).

Treatment of FeCl₃ (0.40 mmol) with phenyllithium (**1b**: 10 equiv.) at -20 °C for 1 h followed by the reaction of 4-octyne (**2m**: 1 equiv.) at 30 °C for 2 h, after methanolysis, gave only a trace amount of **4bm** with a low conversion of **2m** (Scheme 1). Reduction of the amount of **1b** to 6 equiv. increased the yield of **4bm** and conversion of **2m** to 9% and 27%. On the other hand, the same reaction using 10 equiv. of *o*-tolyllithium (**1a**) gave **4am** in 88% yield. The result is rationally understood by the following consideration based on the report that the reaction of FeCl₃ with an excess amount of **1b** gives Li₄[Ph₄Fe].¹¹ The reaction of FeCl₃ with 10 equiv.

FeCl ₃ (0.40 mmol)	Ar- Et ₂	-Li (1) O, –20 °C, 1 ł	→ [Ar–Fe] ^h (+ Ar–Ar)	Pr——— Pr (2m : 0.40 mn 30 °C, 2 h	nol) → MeOH	MeOH Ar H Pr Pr	
		Ar in 1	amount of 1	conv of 2m	yield of 4	4am or 4bm	
		Ph (1b)	4.0 mmol	2%	2%		
		Ph (1b)	2.4 mmol	27%	9%		
		<i>o</i> -tolyl (1a)	4.0 mmol	>99%	88%		





Scheme 2 A plausible catalytic cycle.

of **1b** gives tetraarylferrate **7**′, which does not accept coordination of alkyne **2** (Scheme 2). In contrast, the reaction with 6 equiv. of **1b** gives triarylferrate **7**, which accepts coordination and insertion of **2**, leading to **3**. In the case of **1a**, its bulkiness unstabilizes tetraarylferrate **7**′ and thus relevant triarylferrate **7** (or a less ligated ferrate) readily adds to **2**. After the addition, **8** possibly accepts attack of **1** to be converted to **8**′, from which the most bulky alkenyl group eliminates to give **3** and regenerate **7**.

The carbolithiation products can be readily transformed into tetrasubstituted alkenes. For example, **3am** was treated with benzaldehyde to give the corresponding allylic alcohol in 78% yield (Scheme 3). The bromination product was obtained upon reaction with 1,2-dibromoethane.

The trimethylsilyl group is effective as an *ortho* substituent that promotes the aryllithiation, where the addition was found to be followed by cyclization through nucleophilic substitution at the silicon atom, giving directly benzosiloles.¹² Thus, the reaction of *o*-(trimethylsilyl)phenyllithium (**10a**: 1.6 equiv.) with 4-octyne (**2m**: 1 equiv.) in Et₂O at 30 °C for 2.5 h gave 1,1-dimethyl-2,3-dipropyl-1-silaindene (**11am**) in 92% yield (entry 1 of Table 3). Various benzosiloles were synthesized by this addition–cyclization sequence. Arylalkynes reacted with **10a** at a lower temperature to give the corresponding benzosiloles with high regioselectivities (entries 2–4). Conjugated diyne **2s** underwent regioselective addition at one of the two triple bonds (entry 5). The yield of a silole was high with fluoro-substituted aryllithium **10b** (entry 6). Compounds **13**



Scheme 3 Reaction of aryllithiation product 3am with electrophiles.



Entry	R ⁵ in 10	R ³ , R ⁴ in 2	<i>T/</i> °C	Time/ h	Yield $(\%)^b$	Isomer ratio ^c
1	H (10a)	Pr, Pr (2m)	30	2.5	92	
2	H (10a)	Me, Ph (20)	-20	2	91	97:3
3	H (10a)	Bu, Ph (2n)	-20	2.5	87	94:6
4	H (10a)	Ph, Ph (2p)	-20	2.5	93	
5	H (10a)	Bu, 1-hexynyl (2s)	-20	2	73	>99:1
6	F (10b)	Me, Ph (20)	-20	1.5	95	>99:1

^{*a*} The reaction was carried out in Et₂O (2.0 mL) under a nitrogen atmosphere using an *o*-(trimethylsilyl)phenyllithium (**10**: 0.64 mmol) and an alkyne (**2**: 0.40 mmol) in the presence of Fe(acac)₃ (0.020 mmol). ^{*b*} Yield of isolated product **11** based on **2**. ^{*c*} **11**: regioisomer concerning alkyne **2**.



Scheme 4 Synthesis of compounds having two or three benzosilole units linked by a benzene ring.

having two or three benzosilole units with conjugation through a benzene ring were obtained in high yields by the reaction of polyynes **12** (Scheme 4).

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