

A Convenient Synthesis of Ethynylarenes and Diethynylarenes

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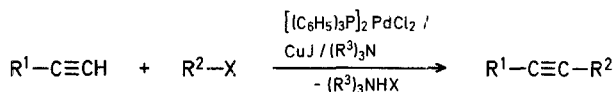
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Acetylenic compounds, especially terminal acetylenes, are valuable synthetic intermediates and there is great interest in the development of methods for introducing an ethynyl group into organic structures. Although recently much at-

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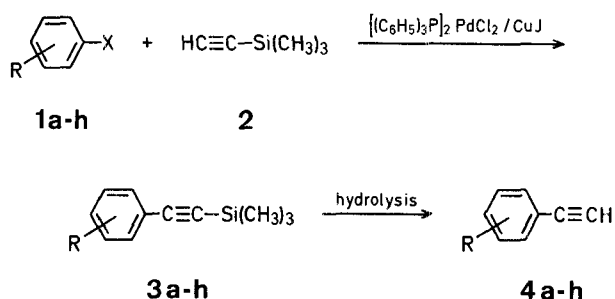
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tention has been paid to the convenient synthesis of acetylenic compounds¹, little work has been done on the synthesis of terminal acetylenes. Previously we have reported that acetylenic hydrogen atoms can be readily substituted by organic halides such as alkenyl², aryl², acyl³, and aminocarbonyl³ halides in the presence of copper(I) iodide/bis(triphenylphosphine)palladium dichloride catalyst in amines (Scheme A).



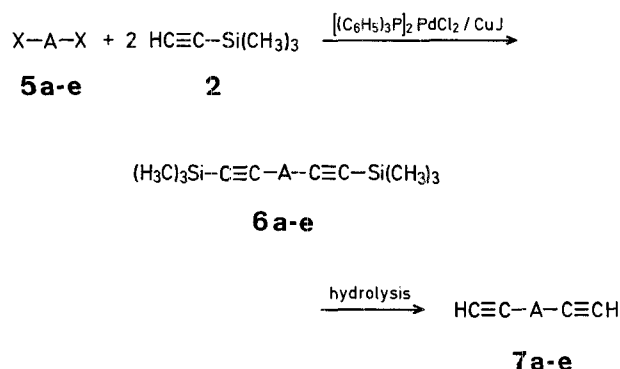
Scheme A

In an attempt to apply this method to preparation of terminal acetylenic compounds, aryl iodides were reacted with a large excess of acetylene gas, but the major product was in each case the disubstituted acetylenic compound. We attempted, therefore, to protect one end of acetylene and then to couple the unprotected end to a suitable halide. We



Scheme B

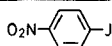
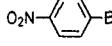
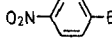
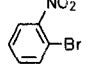
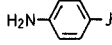
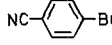
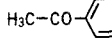
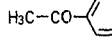
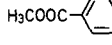
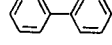
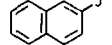
have chosen the trimethylsilyl group as protecting group because it can be quantitatively removed by treatment with dilute alkali⁴. This modification gave satisfactory results for the preparation of not only ethynylarenes **4** (Scheme B), but also of diethynylarene derivatives **7** (Scheme C).



Scheme C

The procedure simply involves mixing of the halide **1** or **5** and a slight excess of trimethylsilylacetylene (**2**) in the presence of catalytic amounts of bis(triphenylphosphine)palladium dichloride and copper(I) iodide in amines such as diethylamine and piperidine (step 1). Removal of the silyl group from the product **3** or **6** can be accomplished simply by treatment with dilute aqueous potassium hydroxide in methanol (step 2). Representative examples are shown in Tables 1 and 2. Among the halides, iodides reacted smoothly with the silylacetylene at room temperature to give the expected products. Bromides and chlorides such as bromobenzene, bromotoluene, and chlorobenzene are

Table 1. Trimethylsilyl ethynylarenes **3a-h** and Ethynylarenes **4a-h** from Aryl Halides **1** (Scheme B)

Aryl halide 1a-h	Reaction conditions amine/temperature	Product 3				Product 4			
		No.	Yield [%] ^a	m.p. [°C] ^b	Molecular formula ^c	No.	Yield [%] ^a	m.p. [°C] ^b	Lit. m.p. [°C]
1a 	C ₂ H ₁₁ N/r.t.	3a	90	96–97°	C ₁₁ H ₁₃ NO ₂ Si (219.3)	4a	91	150–151°	149–150° ⁸
	(C ₂ H ₅) ₃ N/r.t.	3a	92	—	—	—	—	—	—
	(C ₂ H ₅) ₃ N/r.t.	—	—	—	—	4a	88 ^d	—	—
1b 	(C ₂ H ₅) ₃ N/r.t.	3b	70	oil	C ₁₁ H ₁₃ NO ₂ Si (219.3)	4b	87	82–83°	81° ⁸
1c 	(C ₂ H ₅) ₃ N/40°C	3c	83	95–96°	C ₁₁ H ₁₅ NSi (189.3)	4c	79	104–105°	99–100° ⁸
1d 	(C ₂ H ₅) ₃ N/r.t.	3d	82	111–112°	C ₁₂ H ₁₃ NSi (199.3)	4d	92	156–157°	153–154° ⁹
1e 	(C ₂ H ₅) ₃ N/r.t.	3e	80	36–37°	C ₁₃ H ₁₆ OSi (216.4)	4e	85	69–70°	— ^f
	(C ₂ H ₅) ₃ N/r.t.	—	—	—	—	4e	82 ^d	—	—
1f 	(C ₂ H ₅) ₃ N/r.t.	3f	89	57–59°	C ₁₃ H ₁₆ O ₂ Si (232.4)	4f ^e	—	—	—
1g 	(C ₂ H ₅) ₃ N/r.t.	3g	86	65–66°	C ₁₇ H ₁₈ Si (250.4)	4g	94	86–87°	85.5° ¹⁰
1h 	(C ₂ H ₅) ₃ N/r.t.	3h	85	44–44.5°	C ₁₅ H ₁₆ Si (224.4)	4h	94	41°	b.p. 110°/1 torr ¹¹

^a Yield of pure, isolated product.

^b Not corrected.




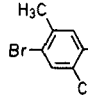


^c The microanalyses were in good agreement with the calculated values (C ± 0.35, H ± 0.20, N ± 0.25).

^d Yield of product from **1** without isolation of **3**.

^e 4-Ethynylbenzoic acid; treatment of **3f** with alkali results in hydrolysis of the ester group to give this acid.

^f C₁₀H₈O calc. C 83.31 H 5.59 (144.2) found 83.08 5.46

Table 2. Bis[trimethylsilylethynyl]arenes **6a-e** and Diethynylarenes **7a-e** from Dihalides **5a-e** (Scheme C)

Dihalide 5a-e	Reaction conditions amine/ temperature	Product 6				Product 7			
		No.	Yield [%] ^a	m.p. [°C] ^b	Molecular formula ^c	No.	Yield [%] ^a	m.p. [°C] ^b	Lit. m.p. [°C]
5a 	(C ₂ H ₅) ₂ NH/r.t.	6a	80	122°	C ₁₆ H ₂₂ Si ₂ (270.5)	7a	88	95-96°	95° ¹²
	C ₃ H ₁₁ N/50°C	6a	77	—	—	—	—	—	—
5b 	(C ₂ H ₅) ₂ NH/ C ₆ H ₆ /r.t.	6b	85	166-167°	C ₂₂ H ₂₆ Si ₂ (346.6)	7b	97	169-170°	165.5-166.5° ¹⁰
5c 	C ₃ H ₁₁ N/60°C	6c	88	98-99°	C ₁₈ H ₂₆ Si ₂ (298.6)	7c	90	113-114°	— ^d
5d 	C ₃ H ₁₁ N/60°C	6d	85	49.5-50°	C ₁₆ H ₂₂ Si ₂ (270.5)	7d	74	n _D ²⁰ : 1.5880	n _D ²⁰ : 1.5900 ¹³
5e 	(C ₂ H ₅) ₂ NH/r.t.	6e	83	106-108°	C ₁₅ H ₂₁ NSi ₂ (271.5)	7e	75	70°	— ^e

^a Yield of pure, isolated product.^b Not corrected.^c The microanalyses were in good agreement with the calculated values (C ± 0.35, H ± 0.20, N ± 0.25).^d C₁₂H₁₀

calc. C 93.46 H 6.54

(154.2) found 93.23 6.42

^e C₉H₅N

calc. C 85.02 H 3.96 N 11.02

(127.2) found 85.18 3.82 10.87

Table 3. Spectral Data for Products **3**, **4**, **6**, and **7**

Prod- uct	I.R. (nujol) [cm ⁻¹]		¹ H-N.M.R. (CDCl ₃) δ _{CH} [ppm]	M.S. m/e (M ⁺)
	ν _{≡CH}	ν _{C≡C}		
3a	—	2160	—	219
3b	—	2165	—	219
3c	—	2150	—	189
3d	—	2160	—	199
3e	—	2155	—	216
3f	—	2162	—	232
3g	—	2163	—	250
3h	—	2155	—	224
4a	3260	2012	3.35	147
4b	3265	2105	3.51	147
4c	3270	2100	2.95	117
4d	3250	2105	3.30	127
4e	3220	2105	3.24	144
4f	3285	— ^a	3.26	146
4g	3285	2105	3.12	178
4h	3285	2105	3.14	152
6a	—	2155	—	270
6b	—	2155	—	346
6c	—	2155	—	298
6d	—	2160	—	270
6e	—	2150	—	271
7a	3270	2100	3.16	126
7b	3290	2110	3.14	202
7c	3275	2095	3.31	154
7d	3300	2070	3.37	126
7e	3280	2100, 2015	3.15	127

^a Overlap with broad COOH absorption.

inactive as is generally seen in ene-yne cross coupling reactions catalyzed by palladium complexes¹. However, activated bromides such as bromoacetophenone and bromonitrobenzene reacted exothermally and gave the expected products.

In order to obtain terminal acetylenic compounds (**4** and **7**), isolation of the silyl derivatives (**3** and **6**) is unnecessary. Thus, after the reaction (step 1) was complete, the solvent amine was evaporated and the resultant residue was treated directly with dilute alkali to give the ethynyl compounds **4** and **7** in good yields.

For the synthesis of the ethynyl- and diethynylarenes, the present method offers some distinct advantages over methods using a copper acetylenides⁵, alkynylzinc⁶, and aryl-copper reagents⁷ in terms of simple procedure, efficiency, and wide application.

p-Nitrotrimethylsilylethynylbenzene (**3a**) and *p*-Nitroethynylbenzene (**4a**):

To a mixture of trimethylsilylacetylene (**2**; 1.18 g, 12 mmol) and *p*-bromonitrobenzene (2.02 g, 10 mmol) in diethylamine (40 ml) are added bis[triphenylphosphine]palladium dichloride (140 mg, 0.2 mmol) and copper(I) iodide (10 mg, 0.1 mmol). The reaction mixture is stirred at room temperature for 4 h under nitrogen and then the solvent is removed under reduced pressure. The residue is extracted into benzene (100 ml) and purified by chromatography on alumina using hexane/benzene (3/2) as an eluent. The pale yellow product is recrystallized from hexane to afford colorless needles of **3a**; yield: 92%.

To a solution of **3a** (2.2 g, 10 mmol) in methanol, 1 normal aqueous potassium hydroxide solution (10 ml) is added and the mixture is stirred at room temperature for 1 h. After removal of methanol, the product is extracted with ether (2 × 100 ml) and purified by chromatography on alumina using benzene/hexane (1/1) to afford a yellow solid. Recrystallization from ethanol or sublimation (60°C/2 torr) gives pale yellow crystals of **4a**; yield: 88%.

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¹ See, for example, E. Negishi in: *Aspects on Mechanisms and Organometallic Chemistry*, J. H. Brewster, Ed., Plenum Press, New York-London, 1978, p. 285.

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