A Convenient Synthesis of Ethynyl-*N*-heteroarenes

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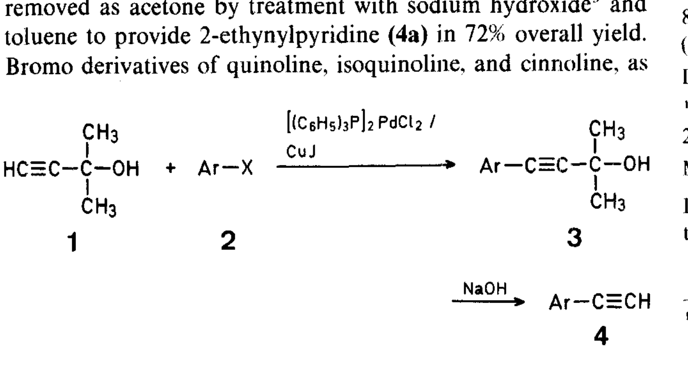
A valuable, efficient method for the condensation of aryl halides with mono-substituted acetylenes in the presence of a palladium complex and a copper(I) salt has been described[1]. This procedure was recently extended[2] to the synthesis of ethynylarenes and diethynylarenes by use of trimethylsilylacetylene with subsequent removal of the trimethylsilyl protecting group by dilute aqueous methanolic potassium hydroxide. 2,6-Diethynylpyridine was prepared by this process in 62% overall yield. We have prepared a number of ethynyl-*N*-heterocycles by an alternative application of the reaction using the commercially available 2-methylbut-3-yn-2-ol (**1**) as the protected acetylene starting material. Condensation of this alkynol with 2-bromopyridine (**2a**) in diethylamine in the presence of catalytic amounts of bis[triphenylphosphine]palladium(II) dichloride and copper(I) iodide gave the heteroarylalkynol **3a**. The protecting group was then removed as acetone by treatment with sodium hydroxide[3] and toluene to provide 2-ethynylpyridine (**4a**) in 72% overall yield. Bromo derivatives of quinoline, isoquinoline, and cinnoline, as well as 3-bromo-4-phenoxycinnoline and 2-chloro-3-phenoxyquinoxaline reacted similarly to give the corresponding ethynyl compounds in moderate to good yields (Table).



2-Methyl-4-(3-quinolyl)-but-3-yn-2-ol (3b):

Bis[triphenylphosphine]palladium(II) dichloride (0.35 g) and copper(I) iodide (50 mg) are added successively to 3-bromoquinoline (10.4 g, 0.05 mol) and 2-methylbut-3-yn-2-ol (5 g, 0.06 mol) in diethylamine (100 ml) under nitrogen at room temperature. The mixture is stirred under nitrogen for 15 h and then evaporated under reduced pressure. Addition of water, and isolation with ether, followed by crystallisation from methanol gives 2-methyl-4-(3-quinolyl)-but-3-yn-2-ol (**3b**) as yellow crystals; yield: 8.3 g (79%); m.p. 115–116 °C.

$C_{14}H_{13}NO$	calc.	C 79.59	H 6.20	N 6.63
(211.3)	found	79.5	5.9	6.4

I.R. (nujol): $\nu = 3420\ cm^{-1}$ (OH).

Raman: $\nu = 2215\ cm^{-1}$ (C≡CH).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.75$ (s, 6 H); 5.0 (s, 1 H, exchanges with D_2O); 7.3–8.3 (m, 5 H); 9.05 ppm (d, 1 H).

3-Ethynylquinoline (4b):

A solution of the alkynol **3b** (7 g) in toluene (125 ml) is heated under reflux with sodium hydroxide (1 g) for 2 h. Decantation, evaporation under reduced pressure, and crystallisation from petroleum ether (b.p. 60–80 °C) gives 3-ethynylquinoline (**4b**); yield: 4.5 g (90%); m.p. 82–83 °C (Lit.[4], m.p. 80–80.5 °C).

I.R. (nujol): $\nu = 3160$; $2090\ cm^{-1}$ (C≡CH).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 3.3$ (s, 1 H); 7.5–8.4 (m, 4 H); 8.95 ppm (s, 2 H).

M.S.: $m/e = 153$ ($M^{+\cdot}$).

In the preparations of **3f** (tetrahydrofuran) and **3g** (dimethyl sulphoxide), the solvent (volume half that of the diethylamine) is added.

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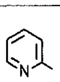
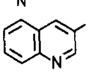
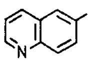
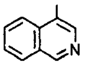
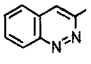
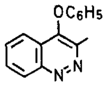
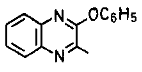
Table. Compounds **3a-g** and **4a-g** prepared

Substrate **2**			Product **3**			Product **4**		
	Ar	X	Yield [%][a]	m.p. [°C][b] (solvent)	Molecular formula[c] or Lit. m.p. [°C]	Yield [%][a]	m.p. [°C][b] (solvent)	Molecular formula[c] or Lit. m.p. [°C]
a		Br	80	61–63° (C_2H_5OAc/PE)	$C_{10}H_{11}NO$[d] (161.2)	90	b.p. 85–86 °C/ 12 torr	b.p. 86–88 °C/ 14 torr[5]
b		Br	79	115–116° (CH_3OH)	$C_{14}H_{13}NO$ (211.3)	90	82–83° (PE)	80–80.5°[4]
c		Br	76	109–110° (C_2H_5OAc/PE)	$C_{14}H_{13}NO$ (211.3)	95	49–50° (hexane)	48.5–49.5°[4]
d		Br	84	128–129° (C_2H_5OAc/PE)	$C_{14}H_{13}NO$ (211.3)	67	72–72.5° (PE)	$C_{11}H_7N$ (153.2)
e		Br	35	119–120° (C_2H_5OAc/PE)	$C_{13}H_{12}N_2O$ (212.2)	50	120–121° (PE)	$C_{10}H_6N_2$ (154.2)
f		Br	43	129–130° (C_2H_5OAc/PE)	$C_{19}H_{16}N_2O_2$ (304.3)	61	109–110° (C_2H_5OAc/PE)	$C_{16}H_{10}N_2O$ (246.3)
g		Cl	63	142–144° (ether)	$C_{19}H_{16}N_2O_2$ (304.3)	49	137–139° (C_2H_5OAc/PE)	$C_{16}H_{10}N_2O$ (246.3)

[a] Yield of pure, isolated product.

[b] Not corrected.

[c] Satisfactory microanalyses obtained: C ±0.4, H ±0.4, N ±0.4.

[d] Lit.[5], m.p. 78.5–79.5 °C, b.p. 120–125 °C/1 torr; Lit.[4], b.p. 120 °C/1.5 torr.

$C_{10}H_{11}NO$	calc.	C 74.51	H 6.88	N 8.69
(161.2)	found	74.1	6.8	8.5

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[1] K. Sonogashira, Y. Tohda, N. Hagihara, *Tetrahedron Lett.* **1975**, 4467.

0039-7881/81/0532-0364 $ 03.00

[2] S. Takahashi, Y. Kuroyama, K. Sonogashira, N. Hagihara, *Synthesis* **1980**, 627.

[3] Cf. H. Meister, *Justus Liebigs Ann. Chem.* **701**, 174 (1967).

[4] U. Haug, H. Fürst, *Chem. Ber.* **93**, 593 (1960).

[5] M. S. Shvartsberg, I. L. Kotlyarevskii, A. N. Kozhevnikova, V. N. Andrievskii, *Izvest. Akad. Nauk SSSR, Ser. Khim.* **5**, 1144 (1970); *C. A.* **73**, 130851 (1970).