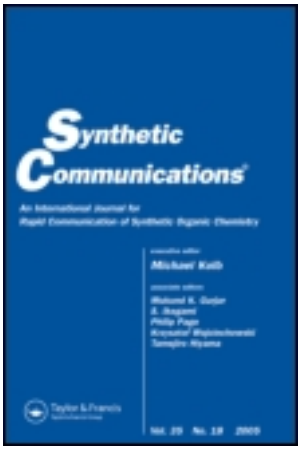

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A Convenient Route to Condensed-Ring Aromatic Acetylenes

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A CONVENIENT ROUTE TO CONDENSED-RING AROMATIC ACETYLENES

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Abstract: Palladium catalysed coupling of aryl halides with 3-methylbut-1-yn-3-ol and a subsequent base-induced retro-Favorsky reaction gave the corresponding ethynyl aromatics in good to excellent yields.

INTRODUCTION

Condensed-ring aromatic acetylenes have found applications in an array of areas including inhibition and modulation of animal microsomes by interactions with specific peptides[1-4], as intermediates in the synthesis of lipoxyenase inhibitors[7-8] and as precursors for the synthesis of nonlinear optical polymers [9-10].

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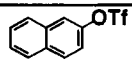
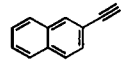
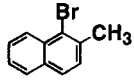
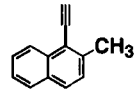
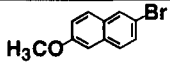
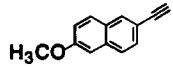
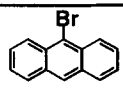
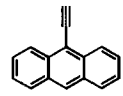
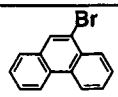
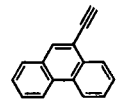
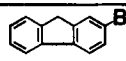
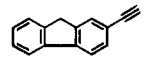
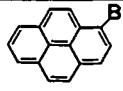
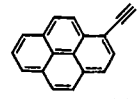
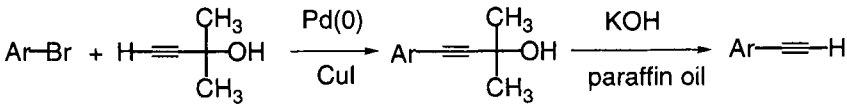
[10]. Arylacetylenes can be prepared by (i) dehydrochlorination of 2-chlorovinyl aromatics with potassium *tert*-butoxide[11], (ii) dehydrochlorination of 1,2-dichloroethyl aromatics with sodium amide[12], (iii) palladium-catalysed coupling of arylhalides with trimethylsilylacetylene with subsequent desilylation[10,13,14] and by (iv) base-catalysed retro-Favorsky elimination of acetone from $ArC{\equiv}CC(CH_3)_2OH$[15]. The use of trimethylsilyacetylene is convenient but expensive whereas the coupling of 3-methylbut-1-yn-3-ol to arylhalides and base-catalysed retro-Favorsky elimination is less expensive but the high temperatures and basic conditions often results in polymerization of the alkyne unless the product can be distilled from the reaction mixture,[15] or a one pot procedure used to generate diarylalkynes[13, 16].

RESULTS AND DISCUSSION

Using a modification to a reported procedure[15] we have prepared condensed aryl acetylenes in good yield by initially coupling the arylhalide with 3-methylbut-1-yn-3-ol and performing the base-catalysed retro-Favorsky elimination using powered potassium hydroxide in paraffin oil at 150°C. The formation of the expected arylacetylene was rapid under these conditions and the reaction was stopped as soon as the visual bubbling from the formation of acetone had ceased. The product was separated by flash chromatography with hexanes as an eluant. The condensed arylacetylenes polymerize on storage so the alkynyl precursor $ArC{\equiv}CC(CH_3)_2OH$ was a convenient means of storing the material and converting as needed. The Table summarises the range of arylacetylenes which can be conveniently prepared by this methodolgy using the procedure outlined below.

Table

Aryl Halide	Product	Mp °C (lit)	M/z	Yield %	^{1}H δ HC≡	^{13}C δ C≡C
		oil (oil)[17]	152	63	3.45	81.8, 82.0
		35-36 (36)[18]	152	86	3.13	77.4, 84.0
		oil	166	63	3.69	80.6, 86.3
		110-111	182	83	3.10	76.7, 84.2
		74-75 (76-76.5)[19]	202	75	3.95	80.4, 88.2
		61-62 (62.5-63)[12]	202	88	3.45	81.7, 81.9
		82-83 (83)[20]	190	89	3.10	77.1, 84.4
		116-117.5 (lit)[21]	226	60	3.59	82.5, 82.8



A typical procedure: To a stirred solution of 2-bromo-6-methoxynaphthalene (0.44g, 1.86 mmol) and 3-methylbut-1-yn-3-ol (0.38ml 3.72 mmol) in piperidine (1ml) under nitrogen was added $Pd(PPh_3)_4$ (5mg, 0.0047 mmol), PPh_3 (2mg, 0.0076 mmol) and the solution of copper bromide (2mg, 0.014 mmol) and lithium bromide (7.8mg, 0.09 mmol) in THF (0.5ml). The clear solution was stirred at 90°C for 2hr. The reaction mixture was diluted with CH_2Cl_2 and washed with 5% HCl to remove piperidine and the residue was chromatographed with (1:1:4, CH_2Cl_2:acetone:hexanes) to give 4-(6-methyoxy-2-naphthyl)-2-methyl-3-butyn-2-ol which was suspended in paraffin oil (1ml) and finely powdered KOH (0.2g) was added then the flask was attached to a vacuum pump at ~ 30mm Hg. The resulted mixture was heated in an oil bath at 150°C. When bubbles ceased to be produced the reaction flask was immediately removed from the oil bath (2-3 min). The resulting mixture was diluted with dichloromethane and washed with water and subjected to flash chromatography with hexanes as eluant. Paraffin oil was eluted initially followed by 2-ethynyl-6-methoxynaphthalene 0.28g (83%). Mp 110-111°C, M/z(M^+): 182. ^1H NMR: δ 3.10(s, ≡C-H); 3.85(s, OCH_3); 7.04(bs, 1H); 7.12(ddd, J = 1.5, 2.7, 8.7Hz, 1H); 7.47(ddd, J = 1.5, 2.8, 8.4Hz, 1H); 7.58-7.66(m, 2H); 7.91(s, H1). ^{13}C NMR: δ 55.2, 76.7, 84.2, 105.8, 117.0, 119.5, 126.9, 128.4, 129.2, 129.4, 132.1, 134.5, 158.6.

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