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A PALLADIUM-PROMOTED ROUTE TO 3-ALKYL-4-(I-ALKYNYL)-HEXA-I,5-DYN-3-ENES AND/OR I,3-DIYNES

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Summary: Reaction of benzene solutions of arylacetylenes with I equiv. of chloroacetone and 2 equiv. of Et_3N, using a mixture of $(PPh_3)_4Pd$ and CuJ as catalyst, affords I,4-diarylbutadiynes in very good yields. Under similar reaction conditions aliphatic I-alkynes yield mixtures of simmetrically disubstituted I,4-dialkyl-I,3-butadiynes and of 3-alkyl-4-(I-alkynyl)-hexa-I,5-diyn-3-enes.

Coupling reactions of terminal alkynes with aryl and vinyl halides in the presence of catalytic amounts of palladium(II) or palladium(0) complexes and CuJ, are receiving considerable attention from a synthetic standpoint[I]. It has been reported[Ia,b] that when such reactions are carried out using catalytic amounts of $(PPh_3)_2PdCl_2$ and CuJ the reaction mixtures contain small quantities of I,4-disubstituted-I,3-butadiynes (I), in addition to the expected arylacetylenes or I,3-enynes. Such diynes (I), which according to our observations are present in molar amounts identical to those of the palladium(II) complex used when the terminal alkynes are aromatic, and in molar defect when such alkynes are aliphatic, very probably derive from a reductive elimination reaction of an intermediate palladium complex of type 2[Ia].

$$R-C\equiv C-C\equiv C-R$$

1

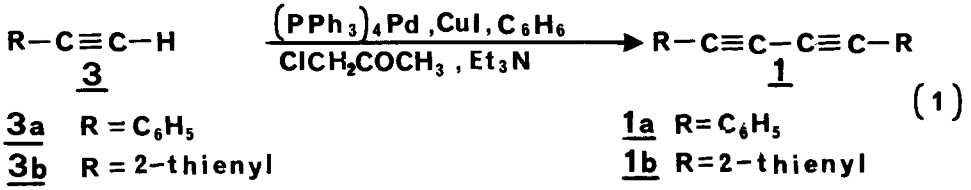
(R=alkyl,aryl)

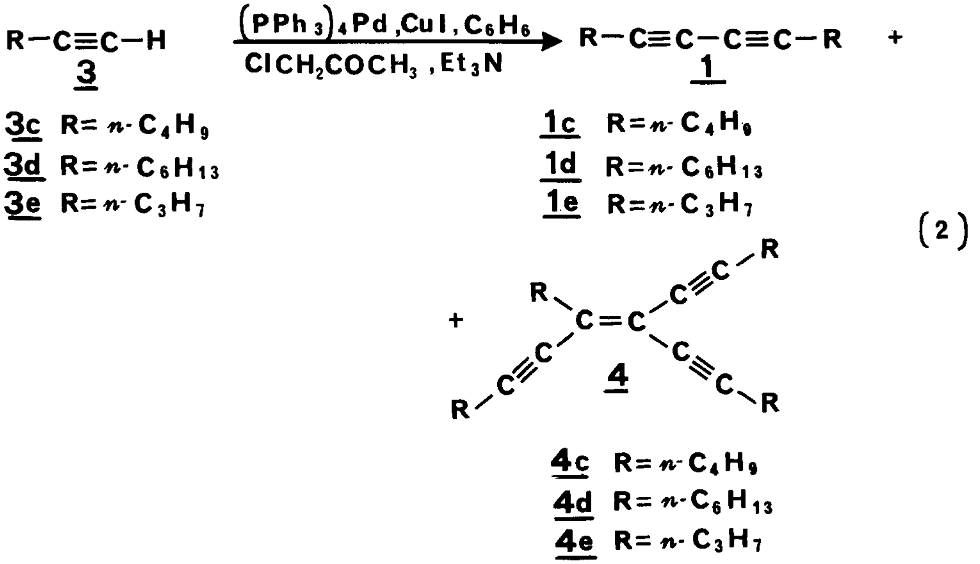
$$(PPh_3)_2Pd\left(C\equiv C-R\right)_2$$

2

In order to explain these results and owing to our interest in the synthesis of I,4-diheteroaryl-I,3-butadiynes as precursors of mixed heteroarene oligomers with potential bioactivity[2], we undertook the study of the reactivity of aromatic and aliphatic I-alkynes with a bimetallic Pd-Cu catalyst system which, on the basis of our knowledge, seemed qualified to produce the desired diynes in good yields[3].

We now report that I,4-diarylbutadiynes (e.g. Ia,b) can be prepared in very good yields by reacting benzene solutions of arylacetylenes with chloroacetone (I equiv.) and Et_3N (2 equiv.), in the presence of a mixture of $(PPh_3)_4Pd$ and CuJ as catalyst (eq. I). Under similar reaction conditions, aliphatic I-alkynes afford mixtures of I,4-dialkyl-I,3-butadiynes (e.g. Ic-e) and of 3-alkyl-4-(I-alkynyl)-hexa-I,5-diyn-3-enes (e.g. 4c-e)(eq.2). The following two typical examples show this different behaviour of aromatic and aliphatic I-alkynes.





Triethylamine (0.I0 mol) was added under a nitrogen atmosphere to a stirred mixture of $(PPh_3)_4Pd$ (I.0I mmol) and CuJ (3.79 mmol) in benzene (20 ml). This mixture was then sequentially treated with chloroacetone (50 mmol) and phenylacetylene (3a)(50 mmol). After stirring for I6 h at room temperature, a NH_4Cl saturated aqueous solution was added and the mixture was extracted with benzene. The filtrated extract was concentrated and the residue was purified by chromatography on a silica gel column to afford I,4-diphenyl-I,3-butadiyne (Ia) in 94% yield[4].

On the other hand, reaction of I-pentyne (3e)(88 mmol) with a solution of chloroacetone (88 mmol) and Et_3N (0.I76 mol) in benzene (45 ml), in the presence of $(PPh_3)_4Pd$ (2.4 mmol) and CuJ (4.88 mmol), afforded after 2 h a reaction mixture containing acetone, 4,6-decadiyne (Ie) and a compound 4e of formula $C_{20}H_{28}$[5]. Chromatography on a silica gel column allowed to recover Ie [50% yield; b.p. 96°/I5 torr; ^{I3}CNMR ($CDCl_3$): δ I3.I7, 20.93, 2I.63, 65.88, 76.88 ppm] and 4e [28.I% yield; MS: m/e 268 (7.7), I95 (I0.6); I82 (23.9), I79 (I8.6), I78 (I5.9), I67 (42.4), I66 (32.6), I65 (75.0), I55 (27.4), I54 (23.4), I53 (4I.5), I52 (45.9), I4I (37.0), I29 (2I.2), I28 (37.I), II5 (36.9), 9I (3I.8), 77 (32.2), 55 (30.9), 5I (2I.2), 43 (I00), 4I (44); ^{I3}CNMR ($CDCl_3$): δ I3.40, I3.64, 2I.5I, 2I.62, 22.03, 36.59, 77.75, 79.26, 80.94, 92.20, 96.62, I00.59, I09.I7, I37.72 ppm; IR (neat) 2200, I7I0, I670, 875 cm^{-I}]. In order to clarify the structure of 4e a solution of this compound in AcOEt was hydrogenated at 25° and I at, in the presence of PtO_2, to afford an alkane 5 of formula $C_{20}H_{42}$ [b.p. 97-

98°/0.08 torr; MS: m/e 282 (M^+,9.4),239(7.5),2II(24.5),I55(22.7),I27(22.6),57(IOO); ^{I3}CNMR (CDCl$_3$):δ I4.IO, I4.5, 2I.22, 22.72, 27.86, 30.7I, 32.52, 33.I6, 39.33, 39.63 ppm]. The structure of 5, which corresponded to that of 4-propyl-5-pentyldodecane, was unequivocally established by an indipendent synthesis starting from diethyl pentylmalonate[6]. On the basis of all these data, it was possible to assign to 4e the structure of 3-propyl-4-(I-pentynyl)dodeca-4,8-diyn-6-ene. Representative results concerning catalytic reactions carried out using different terminal I-alkynes are summarized in Table I.

In conclusion, the ready availability of the catalyst and the reagents, the simplicity of the procedure, and the mildness of the reaction conditions suggest that the above described synthesis of I,4-diaryl-I,3-butadiynes may represent a good alternative to the Glaser reaction[3a]. Interestingly, this palladium-catalyzed reaction, when carried out on aliphatic I-alkynes, can also allow to obtain in satisfactory yields a new class of organic compounds, the 3-alkyl-4-(I-alkynyl)hexa-I,5-diyn-3-enes (4), which are characterized by a previously undescribed chromophore system[7]. Studies are in progress in order to clarify the detailed mechanism and stereochemistry of this reaction, as well as to establish its scope and utility.

Table I. Reaction of I-Alkynes (3) with Chloroacetone and Et$_3$N, in the Presence of (PPh$_3$)$_4$Pd and CuJ, in Benzene Solution.

I-Alkyne (3) (mmol)		Chloroacetone (mmol)	Benzene (ml)	Et$_3$N (mol)	(PPh$_3$)$_4$Pd (mmol)	CuJ (mmol)	Reaction time (h)	Products	
								I (yield %)	4 (yield %)
3c	65	65	45	0.I3	I.9	3.52	25	Ic (54)	4c (n.d.)
3c	65	65	40	0.I3	2.0	3.99	I5	Ic (52)	4c (n.d.)
3a	50	50	20	0.IO	I.0I	3.79	I8	Ia (94)	--
3b	48	48	20	0.096	I.30	3.60	I8	Ib (87)	--
3c	65	65	25	0.I3	--	3.33	I8	--	--
3d	47	56	20	0.094	2.3	I.96	I8	Id (3)	4d (n.d.)
3d	47	47	20	0.095	I.45	3.90	2	Id (48.4)	4d (5I.0)
3e	88	88	45	0.I76	2.40	4.88	2	Ie (50.0)	4e (28.I)

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4. All new compounds gave the expected microanalytical results and all were fully characterized by IR, ^{I}H NMR, ^{I3}C NMR, and mass spectra. All known compounds had physical properties very similar to those reported in the literature.

5. The reactions carried out on aliphatic I-alkynes were rather exothermic and in general faster than those carried out under similar conditions on aromatic I-alkynes. When such reactions were performed using phenacyl bromide instead of chloroacetone, the reaction mixture after hydrolysis contained acetophenone.

6. Diethyl pentylmalonate was converted into diethyl pentylpropylmalonate and subsequently into 3-propylheptanoic acid. The ethyl ester of this acid was reacted with a large excess of pentylmagnesium chloride in ether, to afford after chromatography on a silica gel column, pure 6-pentyl-6-hydroxy-7-propyldodecane. This alcohol was heated at I60° for 8 h in the presence of an equimolar amount of oxalic acid. Water formed in the reaction was removed by distillation. Fractional distillation of the organic phase gave a mixture of (Z)- and (E)-6-pentyl-7-propyl-5-dodecene which was hydrogenated, in the presence of PtO_2, to afford the corresponding alkane 5.

7. Compound 4d had the following UV spectrum (in hexane): λ_{max} (ε). 303 (2368), 292 (249I4), 285 (23357), 275 (I6505), 250 (5974), 236 (6602), 227 nm (6726).

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