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ACTIVATION OF REDUCING AGENTS. SODIUM HYDRIDE CONTAINING COMPLEX REDUCING AGENTS 22. NEW COUPLING REACTION WITH "NICKEL DOPED" COMPLEX REDUCING AGENT.

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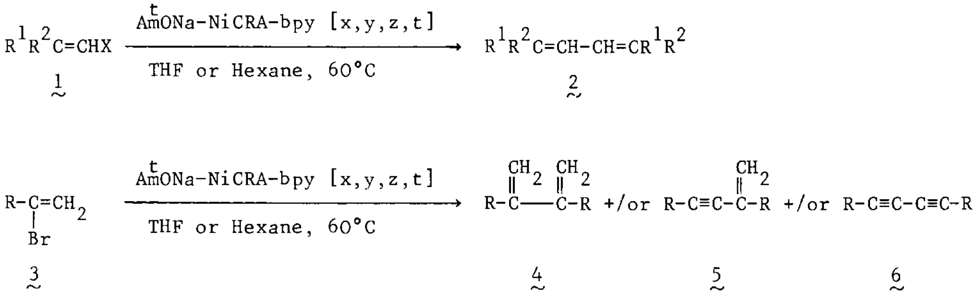
Abstract : Vinyl halides can be coupled by NiCRA-bpy in THF or hexane. Interestingly simply changing the solvent changes the nature of the product : diene in THF, and enyne in hexane.

Metal promoted homocoupling of vinyl halides continues to be actively studied on account of its wide range of synthetic applications.[1] In connection with our investigations on Complex Reducing Agents (CRA)[2], i.e. mixtures prepared in situ of sodium hydride, alkoxide, nickel acetate and 2,2'-bipyridyl, we have previously reported[3] that ^{t}AmONa-NiCRA-bpy (Note) were convenient reagents for coupling aryl and vinyl halides. We found that ^{t}AmONa-NiCRA-bpy [4,2,1,2] could be used with aryl derivatives but that a [2,2,1,2] reagent must be prefered with vinyl halides in order to avoid side reductions. On the other hand, at that time, we were only able to couple halogeno-1-cycloalkenes and α-bromostyrenes.

In the present publication we report that, by a small change in the reagent constitution the coupling reactions may be extended to other vinyl halides. Moreover we also describe an unexpected solvent effect, opening a new field of investigations (Scheme).



$$\underset{\mathbf{1}}{R^1R^2C{=}CHX} \xrightarrow[\text{THF or Hexane, 60°C}]{^{t}\text{AmONa-NiCRA-bpy }[x,y,z,t]} \underset{\mathbf{2}}{R^1R^2C{=}CH{-}CH{=}CR^1R^2}$$

$$\underset{\mathbf{3}}{R{-}\underset{\displaystyle Br}{C}{=}CH_2} \xrightarrow[\text{THF or Hexane, 60°C}]{^{t}\text{AmONa-NiCRA-bpy }[x,y,z,t]} \underset{\mathbf{4}}{R{-}\overset{CH_2}{\overset{\|}{C}}{-}\overset{CH_2}{\overset{\|}{C}}{-}R} \text{ +/or } \underset{\mathbf{5}}{R{-}C{\equiv}C{-}\overset{CH_2}{\overset{\|}{C}}{-}R} \text{ +/or } \underset{\mathbf{6}}{R{-}C{\equiv}C{-}C{\equiv}C{-}R}$$

SCHEME

NOTE : In the present paper we have adopted the convention given in ref.[2a]. Thus a CRA-bpy prepared from NaH, RONa (alkoxide) and nickel acetate in presence of 2,2'-bipyridyl will be abbreviated ^{t}AmONa-NiCRA-bpy [x,y,z,t] where the molar ratio NaH/RONa/Ni(OAc)$_2$/bpy (in that order) is equal to x/y/z/t.

In Table I are gathered the results obtained with 1-halovinyl derivatives 1.

TABLE I : Coupling of $R^1R^2C{=}CHX$ 1 [(a)]

1						
R^1	R^2	X	[x,y,z,t]	Time (h)	2 %[(b)]	Run
Bu	Bu	Br	2,2,1,2	1	81	1
Bu	Bu	Cl	3,2,1,2	1.5	80	2
$(CH_2)_5$		Br	3,2,1,2	1	85	3
$(CH_2)_5$		Cl	3,2,1,2	63	85	4

(a) The molar ratio vinyl halide/metal was always equal to 1

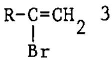
(b) Yields in isolated product.

In agreement with our previous results[3] we found that a [2,2,1,2] reagent could be used when $R^1 = R^2 =$ Bu (run 1). However one equivalent excess of NaH ([3,2,1,2] reagent) was necessary with other halides in order to obtain good yields. A larger excess of NaH led to a large quantity of reduction product. It is noteworthy that contrary to what is known with more conventional reagents[1(b)-(e)], vinyl chlorides are coupled as easily as vinyl bromides. Interestingly, those coupling may be performed in hexane containing THF (THF/Ni = 4) thought reaction times were generally larger.

Very unexpected were the results reported in Table II, dealing with the coupling of 2-bromovinyl derivatives 3. In THF, the main products, formed in very good yields, were the expected dienes 4. Note, however, that run 5 performed in THF, with a [2,2,1,2] reagent led to the formation of 20 % of 5 (R = nC_5H_{11}).

Changing the solvent for hexane (containing 4 equivalents of THF) led to enynes 5 as main products when R = alkyl and to diyne 6 when R = Ph. Note that an increase in the amount of NaH may lead to the formation of the diene in large quantities.

The mechanisms of these reactions are far from being clear. Control experiments aiming at condensing $RC{\equiv}C{-}H$ on $RCBr{=}CH_2$ (R = alkyl) under the conditions presently used led to no enyne 5 formation. Thus, a classical elimination of HBr followed by condensation of the vinyl halide seems to be impossible. Moreover, it would be surprising if CRAL, which are very weak bases, were able to eliminate HBr in hexane but not in THF.

TABLE II : Coupling of  $R-C(Br)=CH_2$ 3 (a)

3, R	[x,y,z,t]	Solvent	Time (h)	4 % (b)	5 % (b)	6 % (b)	Run
n-C_5H_{11}-	3,2,1,2	THF	0,5	75	traces(d)	traces(d)	5
	2,2,1,2	Hexane(c)	4	18	72(e)	-	6
n-C_6H_{13}-	2,2,1,2	THF	1	85	-	-	7
		Hexane(c)	5	5(d)	77(e)	-	8
c.$C_6H_{11}CH_2$-	2,2,1,2	THF	0,75	88	-	-	9
		Hexane(c)	16	-	70(e)	-	10
C_6H_5-	2,2,1,2	THF	1	70	-	-	11
		Hexane(c)	2	-	-	75	12

(a) The molar ratio vinyl halide/metal was always equal to 1

(b) Yields in isolated product, unless otherwise specified

(c) THF was added to the reaction medium in such a way that THF/Ni (mmol) = 4 (see experimental section)

(d) Determined by G.L.C.

(e) 2 were identified by comparison with authentic samples prepared according to [4].

The formation of diyne 6 from α-bromostyrene (run 12) is still more difficult to explain since this reaction corresponds to an actual oxidation !

Finally, ^{t}AmONa-NiCRA-bpy [2,2,1,2] was reacted with PhCH=CBr$_2$. In THF as well as is hexane (containing 4 equivalents of THF), the only product formed was PhC≡C-C≡CPh in 75-80 % yield. PhC≡C-Br was identified as an intermediate, showing that CRAL are also able to couple acetylenic halides.

GENERAL PROCEDURE :

As previously described[3] the NiCRA-bpy are prepared in THF or hexane by addition of ^{t}AmOH in a stirred mixture of NaH, 2,2'-bipyridyl and metallic salt at 60°C.

In hexane, the presence of 40 mmol THF is absolutely necessary : without it, the NiCRA-bpy is inactive and no coupling reaction takes place.

The vinyl halide (10 mmol) and the adequate internal standard (hydrocarbons C$_8$-C$_{14}$) in 10 ml of solvent was then added to the reagent. The reaction was monitored by GC analysis on either CARLO ERBA GI 452 or GIRDEL 330 (flame ionization) equipped with 2 m 10 % OV 101 or 1.5 m 10 % SE 30 columns.

After completion of the reaction the excess of NaH is carefully destroyed by dropwise addition of water. The mixture is then acidified and the organic phase is extracted into diethylether and dried over magnesium sulfate.

After removing of the solvent the products were isolated by chromatography on a silica column or Chromatotron model 7924 T (Harrison Research). They were characterized by their spectroscopic data (IR, ^1H, ^{13}C NMR) or by direct comparison (GC, NMR) with authentic samples.

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