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VINYL-COPPER DERIVATIVES XIII : SYNTHESIS OF CONJUGATED DIENES OF VERY HIGH STEREOISOMERIC PURITY

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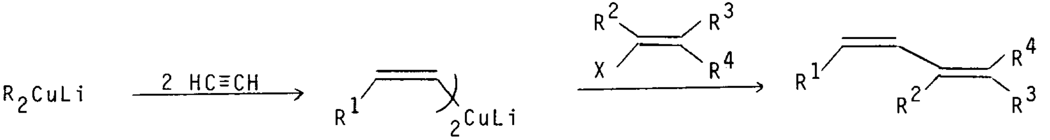
Summary : *Conjugated dienes are obtained by coupling of alkenyl cuprates and alkenyl halides in the presence of* $ZnBr_2$ *and a catalytic amount of* $Pd^{o}L_4$.

Alkyl copper or cuprate reagents couple easily with alkyl as well as alkenyl, aryl and alkynyl halides[1]. Alkenyl copper or cuprate reagents however, only react with alkyl and alkynyl halides[2]. Few examples of alkenyl-alkenyl coupling are reported with low yields and low stereospecificity[3]. On the other hand such alkenyl-alkenyl couplings proceed smoothly with other organometallics derived from Li, Mg, Zn, B, Al, Hg, Zr under Ni or Pd catalysis[4].

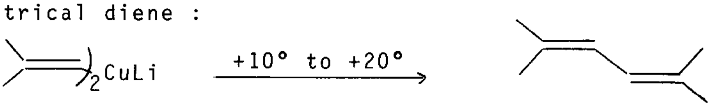
The readily available Z-dialkenyl cuprates **1** obtained by carbometallation of acetylene[5] should be good candidates for a straightforward synthesis of conjugated dienes :



1

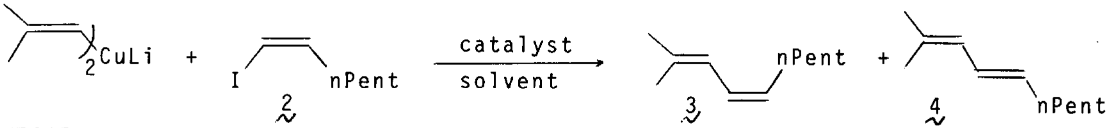
Such dienes of very high stereoisomeric purity are often encountered in the insect sex pheromones, and their synthesis is still a challenge.

This reaction has to be catalysed by $Ni^{\circ}L_2$ or $Pd^{\circ}L_4$ (table I compare entry 1-2-3) but the main difficulty lies in the fact that a low temperature (0,+5°) is necessary to avoid decomposition of the cuprate, leading to the symmetrical diene :



Whereas in many other known cases of alkenyl-alkenyl coupling via Pd° catalysis, room temperature, or even reflux, has to be applied.

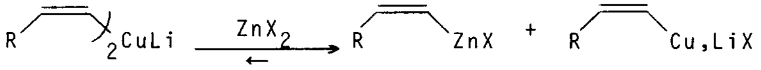
Table I



Entry	Solvent	Temp. °C	Time	Catalyst	Isolated yield	Ratio[6] 3/4
1	Et_2O or THF or HMPT	-10° to +20°	72h	—	Traces	—
2	Et_2O/THF	-10° to +20°	4h	$NiBr_2$,$2PPh_3$(3%)	51%	80/20
3	Et_2O/THF	-10° to +20°	24h	Pd,$4PPh_3$(5%)	50%	91/ 9
4	Et_2O/THF	Inverse add. +15°	0.5h	Pd,$4PPh_3$(5%)	94%	97/ 3
5	Et_2O/THF	-10° to +5°	2h	Pd,$4PPh_3$(5%) + 1eq.$ZnBr_2$	92%	99.6/0.4

The use of $NiBr_2L_2$ as catalyst[7] allows the reaction to proceed, but with low stereoselectivity. With $Pd^{\circ}L_4$, the reaction is slower but the stereoisomeric purity rises to 91/9. Inverse addition proves most rewarding for both yield and purity, but has not been extended successfully to other substrates.

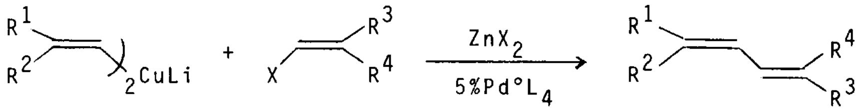
Methyl copper has been obtained from dimethyl zinc and copper halides[8], but conversely, $ZnBr_2$ reacts with some lithium homocuprates to precipitate alkyl copper species. In accordance with a possible equilibrium between zinc and copper species, we anticipated that the vinyl cuprates discussed above might be good precursors of the zinc analogs, whose Pd° catalyzed reaction with vinyl halides represent an elegant way to dienes according to Negishi[9].

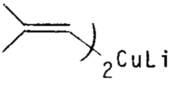
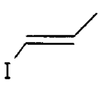
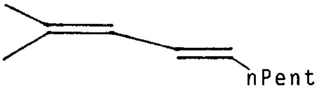
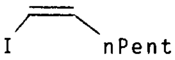
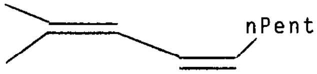
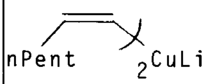
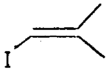
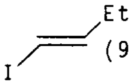
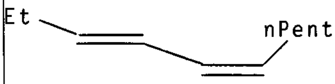
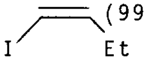
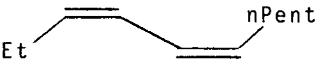
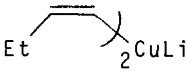
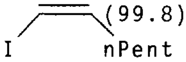
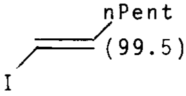
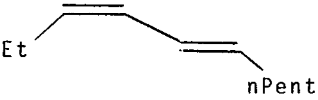
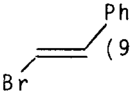
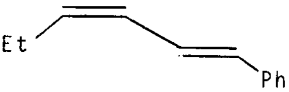


This was indeed the case (see entry 5) and high yields and stereoselectivities are then obtained. Table II summarizes a few typical examples, and the synthesis of 3-5 undecadienes of type EZ or ZZ or ZE which have been compared to the EE isomer[9]. Iodides are generally more reactive than the corresponding bromides. On the other hand, <u>trans</u> halides are more reactive than their <u>cis</u> analogs. Thus, the reaction with the commercial mixture of β-bromostyrene (E : 90.5%) afforded a product of higher isomeric purity (97.5%).

Retention of configuration on the substrate, and organometallics, is the main feature of this approach, that we are extending to trienes, styrenes and various pheromones.

Table II



Cuprate	Halide purity (%)	Product[10]		Isolated yield	Isomeric[6] purity %
	 (99.5)		4	96%	99.5
"	 (99.8)		3	92%	99.6
		"	3	94%	99.8
"	 (99.3)		5	80%	98.9
"	 (99.9)		6	86%	99.5
	 (99.8)	"	6	86%	99.5
"	 (99.5)		7	82%	99.4
"	 (90.5)		8	85%	97.6

Typical procedure :

To an ethereal cuprate solution[5b] (30mmol in 100ml) are added, at -25°C, 30mmol of powdered ZnBr$_2$ and 30ml THF. After 10min,the greenish cuprate solution turns brown and all of the ZnBr$_2$ was dissolved. The mixture of the catalyst (1.5mmol) and the halide (30mmol) in 30ml THF is, then, added. Stirring is continued 2h, while the temperature rose gradually to +5° – +10°. After hydrolysis (50ml NH$_4$Cl sat. sol.) and filtration, the organic layer is dried (MgSO$_4$), the solvents are removed and the crude product is distilled on a 10cm Vigreux column to afford the pure diene.

Aknowledgments :

We thank the C.N.R.S. (Centre National de la Recherche Scientifique, ERA 825) for financial support.

Notes and References -

1. For reviews see
   a/ J.F. Normant : New Applications of Organometallic Reagents in Organic Synthesis (Ed. D. Seyferth) p. 219, Elsevier, Amsterdam (1976)
   b/ G.H. Posner : Org. React. 22 253 (1975)

2. See for example :
   a/ A. Commerçon, J.F. Normant, J. Villieras : Tetrahedron 36 1215 (1980)
   b/ J.F. Normant, G. Cahiez, C. Chuit, J. Villieras : J. Organomet. Chem. 77 269 (1974)
   c/ A. Alexakis, G. Cahiez, J.F. Normant : Synthesis (1979) 826, and references cited therein
3. a/ G. Büchi, J.A. Carlson : J. Amer. Chem. Soc. 91 6470 (1969)
   b/ F. Näf, R. Decorzant, W. Thommen, B. Willhalm, G. Ohloff : Helvetica Chim. Act. 58 1016 (1975)
   c/ H.P. Dang, G. Linstrumelle : Tetrahedron Lett. (1978) 191

4. For reviews :
   a/ E.-I. Negishi : Aspects of Mechanism and Organometallic Chemistry (Ed. J.H. Brewster) p. 285, Plenum, New York (1978)
   b/ M. Kumada : Pure and Appl. Chem. 52 669 (1980)
   See also : N. Miyaura, K. Yamada, A. Suzuki : Tetrahedron Lett.(1979) 3437 and references cited therein

5. a/ A. Alexakis, J.F. Normant, J. Villieras : Tetrahedron Lett.(1976)3461
   b/ A. Alexakis, G. Cahiez, J.F. Normant : J.Organomet.Chem.177 293(1979)

6. The isomeric purity of the products is determined by G.C. (OV 101 capillary glass column, 25m) where all the isomers are clearly distinguished

7. This catalyst is reduced into an Ni° species into the reaction mixture

8. K.H. Thiele, J. Köhler : J. Organomet. Chem. 12 225 (1968)

9. E.-I. Negishi, N. Okukado, A.O. King, D.E. Van Horn, B.I. Spiegel : J. Amer. Chem. Soc. 100 2254 (1978)

10. All compounds gave satisfactory I.R. and NMR (^{1}H and ^{13}C) spectroscopic data. Dienes 5,6 and 7 have been compared with their all trans analog 9 prepared according to ref.9. These four isomers display the following ^{13}C NMR signals for the sp^{2} carbons (δ ppm down field from TMS) :

5	124.7,	128,7,	130.1,	136.0
6	123.1,	123.5,	132.1,	133.5
7	125.5,	126.1,	131.5,	134.7
9	129.5,	130.4,	132.5,	133.8

11. J.B. Stothers, "^{13}C NMR Spectroscopy", Academic Press, 1972, New York. See also E. Breitmaier, G. Haas, W. Voelter "Atlas of ^{13}C NMR data" Heyden and son Ltd, 1975, London.

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