VINYL-COPPER DERIVATIVES 15¹ : AN EFFICIENT SYNTHESIS OF POLYSUBSTITUTED CONJUGATED DIENES

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Summary :

Magnesium vinyl-copper derivatives, obtained by carbocupration of terminal alkynes, couple with 1-halo-1-alkenes, in the presence of Pd(PPh₃)₄ catalyst, to afford polysubstituted conjugated dienes in high yield and excellent stereoisomeric purity.

We recently reported the Zn^{II} (stoechiometric) and Pd° (catalytic) mediated coupling reaction of lithium (Z)-dialkenyl cuprates 1 with 1-halo-1-alkenes² and with iodo-arenes¹. In these reactions <u>only one</u> alkenyl group is efficiently transferred :



Thus, this procedure can hardly be extended to other carbocupration systems, where the obtained vinylic species are magnesium vinyl-copper reagents 2 and not lithium ate complexes such as 1 :

$$RMgX + CuX \longrightarrow RCu, MgX_2 \xrightarrow{R'C=CH} \xrightarrow{R} Cu, MgX_2 \xrightarrow{2} Cu, MgX_2$$

We anticipated that the less reactive and less stable reagent 2 (as compared to 1) had to be transformed <u>in situ</u> into a more reactive and more stable magnesium <u>ate</u> complex which should also permit the exchange with zinc halides². Indeed, a preliminary experiment with the model reagent 3 indicated that here again zinc halides were necessary to obtain efficiently the coupling reaction:



Moreover, in this case <u>both</u> vinylic groups are transferred (compare with the analogous <u>lithium</u> cuprate 1). Unfortunately, $\beta_{\beta}\beta_{\beta}$ -disubstituted magnesium <u>di</u>-alkenyl cuprates, such as 3, are unavailable via carbocupration³, contrary to reagents 2 or 4 ($\stackrel{R}{R} \leftarrow Cu-R MgX$). We therefore transformed reagents 2 to the corresponding <u>ate</u> complexes by addition of a "non-transferable" Grignard reagent, before the coupling reaction :



It turns out that the presence of zinc halide completely changes the order of transfering ability of alkenyl versus other organic groups, usually observed in organo-copper chemistry. For example, if the reaction with 4b is run without zinc halide the ratio 5/6 is inversed $(15/85)^4$. Only the phenylthio and the t.butoxy groups behave normally and are almost not transferred. We rapidly discovered that in the two latter cases the presence of zinc halide was not necessary. Moreover, since in several cases magnesium t.butoxide is a very poor cuprating agent, we also checked that its presence was also unnecessary. Thus, the reaction procedure became much more simple than earlier expected



leading to polysubstituted conjugated dienes of given geometry in good isolated yields and excellent stereoisomeric purity (see table). It is hard to explain why reagent 2 is able to couple under those conditions whereas reagent 3 does

1.3	$2 \text{ eq} \xrightarrow{R^1}_{R^2}$	Cu,MgX ₂	\prec	$\frac{3}{\sqrt{4}}$ F $\frac{5\% \text{ Pd}(\text{PPh}_3)}{4}$ F		$\prec_{R^4}^{R^3}$
Entry	Vinyl-copper ⁵	Halide	Pur. %	Product ⁶	Isolated yield	Isomeric ⁷ purity
1	tBu Cu	I	99.5	tBunPent	55%	98.9
2	"	InPent	99.8	tBu nPent	53%	98.2 ⁸
3	Ph Et Cu	IEt	99.9	Et Et	52%	99.2
4	Me iPr Cu	InPent	99.5	MenPent	70%	99.5
5	"	InPent	99.8	MenPent	64%	99.8
6	Et Cu	InPent	99.5	MenPent	78%	99.5
7	"	InPent	99.8	MenPent	70%	99.8
8	"	Br	90.5	Me Ph	74%	99.0 ⁹
9	"	I nBu Me	99.9	Me nBu Et Me	55%	99.8
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not. However, as shown above, zinc halides restore the reactivity of 3 and even more, allow the transfer of <u>both</u> its vinylic groups. The prominent importance of magnesium salts in this reaction stems from the fact that the analogous lithium reagent Me Cu,LiX, with or without zinc halides, does not couple efficiently. These considerations gave us the key for the efficient use of both alkenyl groups when starting from a <u>lithium</u> dialkenyl cuprate 1:



by a simple use of a molar equivalent of magnesium chloride.

We are, presently, applying this new procedure to the synthesis of some insect sex pheromones where the stereoisomeric purity is of crucial importance.

Typical procedure : To a solution (Et₂0 or THF) of vinyl-copper 2 (30 mmol in 100 ml) is added at -15°C a solution of 25 mmol alkenyl halide and 1.2 mmol Pd (PPh₃)₄, in 50 ml THF. The stirred mixture is allowed to reach gradually (30-40 min) room temperature, and after 30 min is hydrolysed with 80 ml NH₄Cl sat. sol. The organic salts are precipitated by addition of 150 ml pentane, then filtered off and the organic phase washed once again with NH₄Cl sat. sol. The organic layer is dried (MgSO₄), the solvents are removed under vacuum and the residue is distilled through a 10 cm Vigreux column to afford the pure diene.

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REFERENCES and NOTES

- Part 14 : N. Jabri, A. Alexakis, J.F. Normant : Tetrahedron Lett. <u>22</u> 3851 (1981)
- 2. N. Jabri, A. Alexakis, J.F. Normant : Tetrahedron Lett. 22 959 (1981)
- 3. For a review see : J.F. Normant, A. Alexakis : Synthesis 841 (1981)
- Isopropyl group is known to be much more reactive than alkenyl group in organo-copper chemistry
- Vinyl-copper listed in entries 1-5 are prepared according to : H. Westmijze, J. Meyer, H.J.T. Bos, P. Vermeer : Rec. Tr. Chim. Pays-Bas <u>95</u> 299 (1976). Vinyl-copper listed in entries 5-9 are prepared in ether according to J.F. Normant, G. Cahiez, M. Bourgain, C. Chuit, J. Villieras : Bull. Soc. Chim. Fr.(1974) 1656
- 6. All compounds gave satisfactory I.R. and N.M.R. (1 H and 13 C) spectroscopic data
- The isomeric purity of the products is determined by g.l.c. on a capillary glass column (<u>0y 1.</u> 25 m)
- 8. Upon distillation this product isomerises to an extent of 40%
- 9. As shown in ref. 2, <u>trans</u> alkenyl halides react faster than their <u>cis</u> counterpart. Thus, β -bromo styrene afforded a product of higher isomeric purity.

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