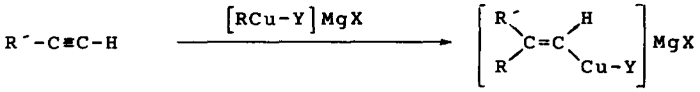
Tetrahedron Letters No. 10, pp 869 - 872, 1977. Pergamon Press. Printed in Great Britain.

STEREOSPECIFIC FORMATION OF CONJUGATED DIENES FROM 3-ALKEN-1-YNES AND ORGANOCUPRATES.APPLICATION IN THE SYNTHESIS OF MYRCENE.

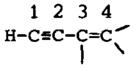
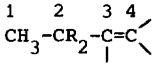
Hans Westmijze , Henk Kleijn , John Meijer and Peter Vermeer.
(Department of Organic Chemistry of the State University ,
Croesestraat 79 , Utrecht ,The Netherlands)

(Received in UK 12 January 1977; accepted for publication 2 February 1977)

Stereospecifically generated vinylcopper(I) compounds are very easily accessible by addition of *organoheterocuprates* [RCuBr] MgX to 1-alkynes in diethyl ether [1,2] or tetrahydrofuran (THF)[3]. Also *organohomocuprates* [RCuR] MgX are suitable reagents for the stereospecific conversion of 1-alkynes into vinylic cuprates in the solvent THF [4] :



Y = R or Br
X = Cl or Br

Recently it was reported that reactive organometallic compounds such as allyl-zinc , - magnesium, -lithium and saturated lithium compounds undergo addition reactions with conjugated enynes  $H-\overset{1}{C}\equiv\overset{2}{C}-\underset{|}{\overset{3}{C}}=\overset{4}{C}\langle$ (1) [5]. It was found that the organolithium and organomagnesium compounds RM (M = Li or MgX) transferred the R radical to C(4) in 1 , giving rise to 3,4 - and 1,4 - addition products. On the other hand, the organozinc compounds RZnBr added to the triple bond in 1 under introduction of R on C(2) , but generally bis addition products of the type  $\overset{1}{C}H_3-\overset{2}{C}R_2-\underset{|}{\overset{3}{C}}=\overset{4}{C}\langle$ were formed in considerable amounts also.

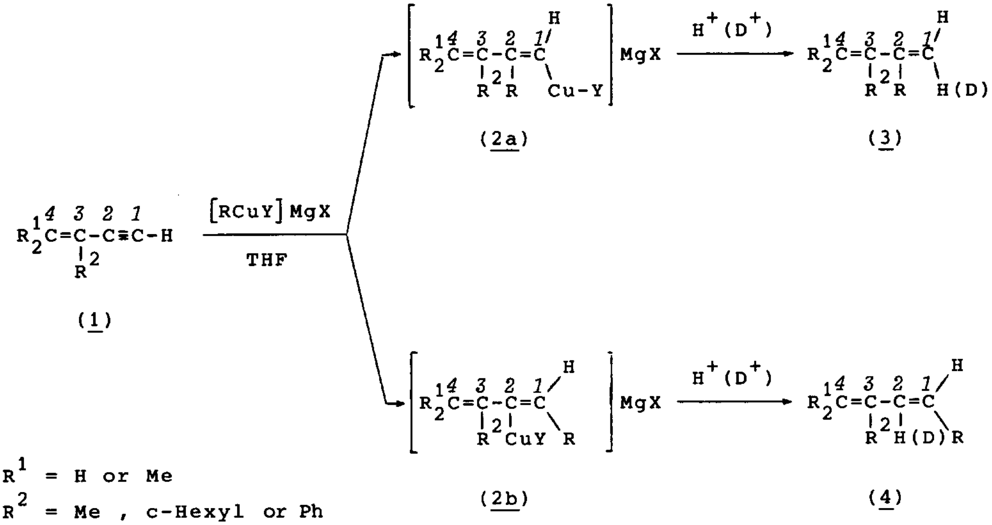
Hitherto no report in the literature deals with a study of the behaviour of 1 towards organocopper(I) compounds.

Enynes like 1 posses two orthogonal π -systems , *viz.* a 1,3-butadiene system on C(1),C(2),C(3), C(4) and a π -bond on C(1),C(2) .

In principe additions of organocopper(I) reagents to both π - systems are possible : Besides the 1,2 - additions described above also 1,4-additions of organocuprates to $>C=\underset{|}{C}-\underset{|}{C}=C<$ are known[6] .

In order to investigate which π -system is most susceptible for attack by organocuprates , we treated a number of enynes 1 with equivalent amounts of [RCuY]MgX (Y = R or Br)[7] in THF.

In all cases we studied only mixtures of the 1,3 -dienes 3 and 4 were isolated after protonolysis of the assumed vinylic cuprates 2a and 2b :



R^1 = H or Me

R^2 = Me , c-Hexyl or Ph

R = Et , i-Pr , Bu , -Bu.

X = Cl or Br

Y = R or Br

Contrary to what was observed for additions of allylzinc compounds to 1 , no products like $\overset{1}{C}H_3-\overset{2}{C}R_2-\underset{|}{\overset{3}{C}}=\overset{4}{C}<$ were formed in the organocopper(I) reactions.

The fact that we never found products resulting from 1,4 - and 3,4 - addition , makes formation of 2a and 2b by direct attack of the cuprate on the C(1),C(2) π -system , which is perpendicular to the 1,3 - butadiene system , very likely.

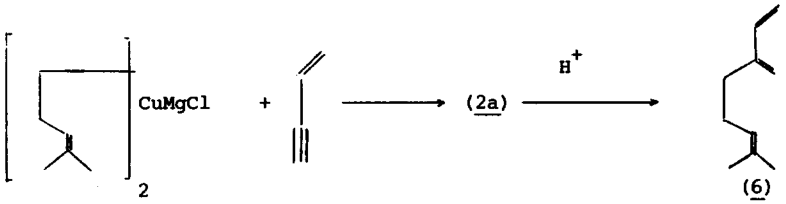
The ratio 3 : 4 appeared to be strongly dependent on the nature of the introduced group R. Adducts 3 were formed almost exclusively ($\gg$ 95 %) upon interaction of 1 and [RCuY]MgX with R = *prim.* alkyl.

On the other hand , the formation of 4 competed effectively with that of 3 for R = *sec.* - or *tert.* - alkyl.

For instance : Interaction of *t* - $Bu_2CuMgCl$ with $CH_2{=}C(c\text{-hexyl}){-}C{\equiv}C{-}H$ gave a mixture of 3 and 4 in a ratio 50 : 50 , while for the reaction of [i-PrCuBr] MgCl with $CH_2{=}C(CH_3){-}C{\equiv}C{-}H$ 3 and 4 were obtained with a ratio 60 : 40 .
These findings are similar to what we observed for additions of organocuprates to Ph-C≡C-H (Compare ref. 3 and 4).

As was observed for other additions of organocopper compounds to C(sp)-C(sp) systems (cf[1-4]) adducts 2a and 2b (and consequently 3 and 4) were formed stereospecifically by *cis* - addition of [RCuY] MgX to the C(1)-C(2) triple bond.
For adducts 4 this stereochemistry could easily be concluded from the ^3J (H,H) coupling constant (≈ 15 Hz) in the C(1)-C(2) double bond.
In the case of 3 the *cis* -addition was proved on the base of ^3J(C,H) coupling constants , e.g. $^3J(C^a , H^b)$ in $H_2C{=}C\ (CH_3){-}C(C^aH_2{-}CH_3){=}CD(H^b)$ was 10.3 ± 0.1 ,which value is characteristic for a *trans* orientation of C^a and H^b [8] .

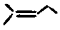
The applicability of our method for R =*prim*.alkyl, can be illustrated by the very simple one-step synthesis of the natural compound Myrcene (6) from ($Me_2C{=}CH{-}CH_2{-}CH_2)_2CuMgCl$ and $CH_2{=}CH{-}C{\equiv}C{-}H$ (purity of 6 : > 96 %).



(6)

(Yield : 90 %.)

Further work in this field is in progress.Physical constants and yields of the obtained compounds are compiled in Table :

Starting compound 1 R^1	 R^2	R in cuprate [a]	Yields of 3 [b] (%)	B.p. of 3 (°C/mmHg)	n_D^{20} of 3	remarks
H	Me	Et	85	96-98/760	1.4440	c
H	Me	Bu	95	37-38/ 15	1.4490	c
H	c-Hexyl	Et	88	90-91/ 15	1.4810	c
Me	Ph	Et	80	52-53/ 0.1	1.5280	d , e
Me	Ph	Bu	85	70-71/ 0.1	1.5183	d , e
H	H		90	50-52/ 15	1.4692	c

Remarks to the Table.

a. For the preparation of [RCuBr]MgX and [RCuR]MgX and concentrations of the reactants see references 3 and 4 .

b. The amount of 4 was $<$ 5 % .

c. One equivalent of 1 was reacted during 20 minutes at -25 °C with 1.10 equivalent of R_2CuMgX or [RCuBr]MgCl . The use of $R_2CuMgX.LiBr$ gave comparable results (compare reference 4). In the reaction of e.g. [BuCuBr]MgBr with $CH_2=C(Me)-C\equiv C-H$ the amount of 4 was 5 - 10 % .

d. The highest conversion of 1 (80 - 85 %) was obtained with $R_2CuMgCl.2LiBr$.

e. One equivalent of 1 was reacted during two hours with two mole equivalents of $R_2CuMgCl.2LiBr$ at + 20 °C.

Acknowledgement.

The authors are indebted to T.Spoormaker for measuring $^{3}J(C,H)$ coupling constants. This investigation was supported by the Netherlands Foundation for Chemical Research (SON).

References.

1. J.F.Normant and M.Bourgain ,Tetrahedron Lett. , 1971 , 2583 .

2. J.F.Normant ,G.Cahiez,M.Bourgain,C.Chuit and J.Villieras , Bull. Soc.Chim.Fr.,1974 ,1656.

3. H.Westmijze,J.Meijer,H.J.T.Bos and P.Vermeer , Recl. Trav. Chim. Pays-Bas, 95 ,299 (1976).

4. H.Westmijze,J.Meijer,H.J.T.Bos and P.Vermeer , Recl. Trav. Chim. Pays-Bas, 95 ,304 (1976).

5. D.Mesnard and L.Miginiac , J.Organometal . Chem. 117 , 99 (1976).

6. J.F.Normant,G.Cahiez and J.Villieras , J.Organometal.Chem., 92 , C 28 (1975).

7. It must be stated that also one mole equivalent of MgBrX was present when the homocuprates R_2CuMgX were used , which is due to the manner of preparation from 2 RMgX and CuBr.

8 U.Vogeli and W.von Philipsborn, Org.Magn.Reson. , 7 , 617 (1975).