Tetrahedron Letters,Vol.27,No.37,pp 4427-4430,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

COPPER AND ZINC MIXED GEM-DIMETALLIC ORGANIC COMPOUNDS SYNTHESIS AND REACTIVITY. Part 3[1]

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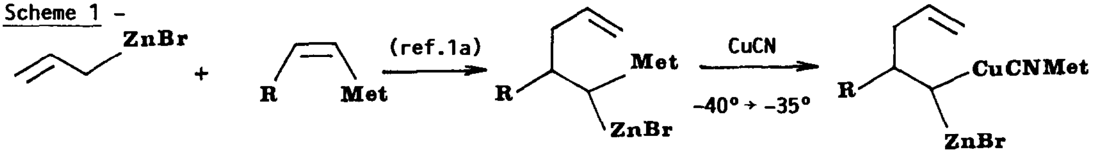
Summary – *The 1-magnesia- and 1-lithia-1-zincaalkenes of type* 1a *and* 1b *give a transmetallation reaction with copper cyanide to the corresponding 1-zinca-cyanocuprates* 2a *and* 2b*. These new organometallics react efficiently with various alkylating or allylating agents to give gem-bis-alkylated or gem-bis-allylated compounds in good to excellent yields. By reaction with acyl chlorides the reagents* 2a *and* 2b *allow a new regiospecific synthesis of enol acylates.*

Scheme 1 -



Met = Li,MgBr (or AlR$_2$)

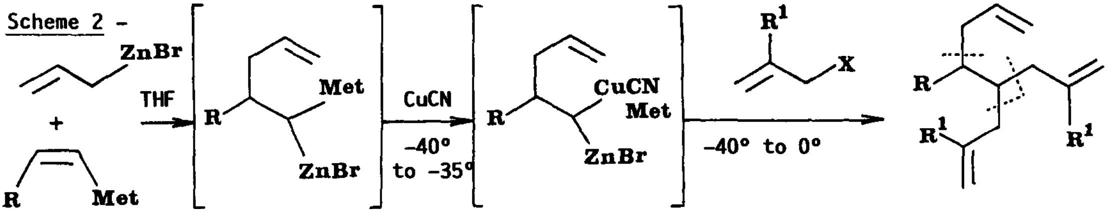
1a : Met = MgBr
1b : Met = Li

2a : Met = MgBr
2b : Met = Li

We have recently reported[1] the synthesis of the mixed dimetallic compounds of type 1 (Met=MgBr[2], Li or AlR$_2$) obtained by the reaction of an allylic zinc bromide with an alkenyl organometallic derivative (see scheme 1) as well as the reactivity of these dimetallic reagents toward various organic substrates.

We report now that the 1-magnesia- and 1-lithia-1-zincaalkenes of type 1a and 1b react with copper cyanide in THF at -40° to -35° (0.25hr) to give soluble organometallic species to which we tentatively assign respectively formulas 2a and 2b. The reactivity of these new dimetallic species is very different from that of their precursors 1. For example whereas compound 1a does not react with any carbon alkylating agents and 1-lithia-1-zincaalkene reacts only slowly with methyl iodide[1b], we have found that the addition of an excess of allyl bromide at -40° to a THF solution of 2a or 2b ($R=C_6H_{13}$) leads to a very exothermic reaction (the temperature rises to +30° !) and the single bis-allylated product 3a is isolated in 88-93% yield (see scheme 2 and entries 1 and 2 of table 1). This bis-allylation reaction is rather general and proceeds with allylic bromides between -40° and -20° and with an allylic chloride (entry 3 of table 1) between +10° and +30°.Allylic acetates and benzyl chloride do not react, even under forcing conditions (+50°) or in the

Scheme 2 -



1a : Met = MgBr ; R = C_6H_{13}
1b : Met = Li ; R = C_6H_{13}
1c : Met = MgBr ; R = H

2a : Met = MgBr ; R = C_6H_{13}
2b : Met = Li ; R = C_6H_{13}
2c : Met = MgBr ; R = H

3a - 3e
overall yields:
(52-93%)

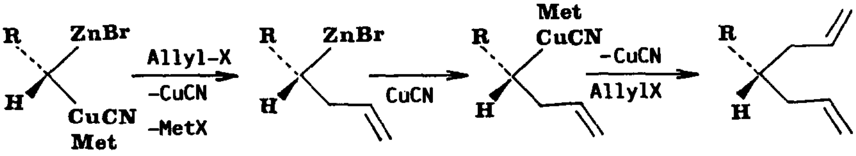
Table 1[3] - Synthesis of the bis-allylated trienes 3a-3e by the reaction of an allylic halide with the in situ generated 1-zinca cyanocuprates 2a-2c

Entry	allylic reagent		1-zinca cyanocuprate	Product	Yield %
	R^1	X			
1	H	Br	2a	3a	93
2	H	Br	2b	3a	88
3	Me	Cl	2a	3b	76[a]
4	H	Br	2c	3c	78
5	Br	Br	2a	3d	52
6	CO_2tert-Bu	Br	2a	3e	73

a/ In this case, the reaction mixture has to be warmed up to +25°.

presence of a catalytic amount of $Pd(PPh_3)_4$; propargylic chloride or bromide gives a complex mixture of products. A remarquable aspect of this reaction is that under our reaction conditions (temperature near or superior to 0°), no decomposition of the cyanocuprate is observed. Functionalized allylic bromides can also be used (entries 5 and 6) and lead to the highly functionalized dibromide 3d and diester 3e in fair yields. We interpret the only formation of the bis-allylated product of type 3 by the following reactions : the dimetallic species 4 reacts first with the allylic halide to give the zinc derivative 5 which, by a transmetallation reaction with copper cyanide, furnishes the new cyanocuprate 6 which again reacts with the allylic halide leading to the product of type 7 (see scheme 3).

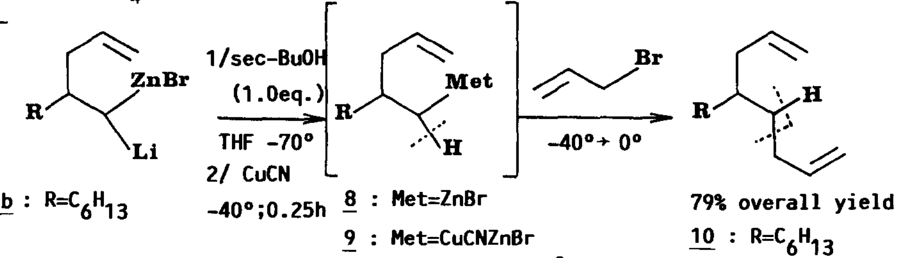
Scheme 3 -



4 5 6 7

To prove the unusual transmetallation reaction from 5 to 6, a THF solution of the bimetallic reagent 1b is treated with one equivalent of sec-butanol at -70° to produce the alkenyl zinc bromide 8 (see scheme 4) ; then one equivalent of copper cyanide is added and the reaction mixture is stirred over 0.25hr at -40° to give a red solution of the zinc cyanocuprate 9. After addition of five equivalents of allyl bromide and 10min of stirring at 0°, an aqueous NH_4Cl solution is added. After work-up and distillation (bp=94°/12mmHg) the mono-allylated compound 10 is isolated in 79% yield[3]. This result demonstrates :

Scheme 4[3] -



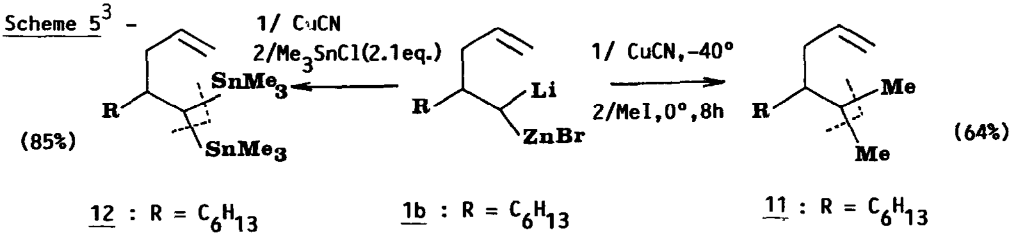
i/ that an organo-zinc compound of type 8 can be transmetallated with copper cyanide to the corresponding zinc cyanocuprate of type 9 (this transmetallation should have important preparative consequences which are currently studied in our laboratory) ;

ii/ that a chemoselective monoprotonation of a dimetallic compound of type 1b is possible[4].

iii/ that mono allylated products[4] of type 10 can also be obtained from dimetallic compounds of type 1b .

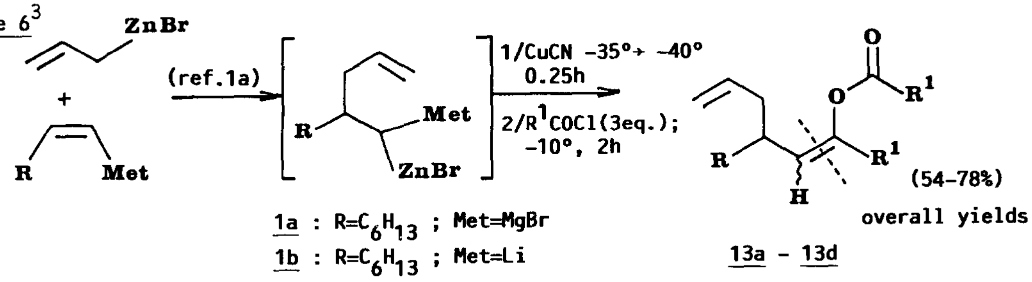
A bis-alkylation reaction is also possible in some cases. Thus with an excess of methyl iodide the gem-dimethylated alkene 11 is obtained in 64% yield (8hr ; 0°) from the 1-lithia-1-zincaalkene 1b . Treatment of the same dimetallic reagent with 2.1 equiv. of trimethyltin chloride (0.5hr ; -20°) furnishes the gem-bis(trimethyltin)-alkene[5] 12 in 85% yield[3] (see scheme 5).

Scheme 5[3] -



We have also found that the new copper reagents 2a and 2b react significantly better with acyl chlorides than the dimetallic derivatives 1a and 1b[6]. Thus the addition of 3 equiv. of an acyl chloride at -10° to -15° to the in situ generated 1-zinca cyanocuprates of type 2 from the corresponding gem-dimetallic compounds of type 1 gives after 2hr at -10° the enol acylates of type 13 in fair yields (see table 2 and scheme 6). The 1-lithia-

Scheme 6[3]



dimetallic 1b gives better yields than the corresponding 1-magnesia reagent 1a (compare entries 2 and 3 of table 2) and a sterically hindered acyl chloride like iso-butyryl chloride gives a lower yield (see entry 4 of table 2). This reaction allows thus a new regiospecific[7] synthesis of the useful enol acylates which are obtained as E:Z mixtures (generally 20:80) ; see table 2.

Table 2[3] - Synthesis of the enol acylates 13a-d by the reaction of an acyl chloride with the in situ generated 1-zinca cyanocuprates 2a and 2b.

Entry	Dimetallic reagent	R^1COCl	Product	E:Z	Yield %
1	1a	CH_3COCl	13a	17:83	78
2	1a	EtCOCl	13b	18:83	63
3	1b	EtCOCl	13b	20:80	74
4	1b	$(CH_3)_2CHCOCl$	13c	20:80	54
5	1b	$(CH_3)_2CH_2CH_2COCl$	13d	23:77	67

In conclusion, the transmetallation with copper cyanide enhances considerably the scope of the 1-magnesia- and 1-lithia-1-zinca alkenes of type 1. Other transmetallation reactions are currently studied in our laboratory, particularly with transition metal salts L_nMetX_2 which should allow the synthesis of carbene complexes and μ-alkylidene complexes[8].

Acknowledgements :

We thank Madame Monique Baudry for the synthesis of various starting materials, the Vieille Montagne Company for a generous gift of zinc of high purity and the C.N.R.S. for financial support (U.A. 473).

References and Notes -

1. a/ P. Knochel and J.F. Normant, Tetrahedron Lett. 27, 1039 (1986) ;
   b/ P. Knochel and J.F. Normant, Tetrahedron Lett. 27, 1043 (1986)
2. This reaction has been discovered by M. Gaudemar in the case of vinyl Grignards : M. Gaudemar, Compt. Rend. Acad. Sc. Paris, Serie C, 273, 1669 (1971) ; see also Y. Frangin and M. Gaudemar, Compt. Rend. Acad. Sc. Paris, Serie C, 278, 885 (1974) ; M. Bellasoued Y. Frangin and M. Gaudemar, Synthesis, 205 (1977)
3. The yields indicated include the preparation of the dimetallic reagent, the transmetallation step and the reactions with the electrophiles. All the compounds obtained show correct spectroscopic data (I.R., ^{1}H-NMR and ^{13}C-NMR). All the reactions were performed on a 10mmol scale.
4. see the following publication
5. For an easy access to the corresponding mono-trimethyltin alkene, see ref. 1b.
6. P. Knochel and J.F. Normant, unpublished results
7. Other regiospecific synthesis of enolates with carbon-carbon bond formation are known : Y. Yamamoto, K. Ohdoi, M. Nakatani and K. Akiba, Chem. Lett. 1967 (1984) ; L.M. Baigrie, D. Lenoir, H.R. Seikaly and T.T. Tidwell, J. Org. Chem. 50, 2105 (1985) ; L.M. Baigrie, H.R. Seiklay and T.T. Tidwell, J. Am. Chem. Soc. 107, 5391 (1985) ; R. Häner, T. Laube and D. Seebach, J. Am. Chem. Soc. 107, 5396 (1985)
8. For example, treatment of a 1-diethylalumina-1-zincaalkene with Cp_2TiCl_2 in THF gives a red solution which reacts with aldehydes ; similar red solutions are obtained by reaction of the 1-magnesia-1-zincaalkene 1a with $TiCl_2(OisPr)_2$. We assume that "Tebbe-like reagents" have been formed during theses reactions[6] (compare with J.J. Eisch and P. Piotrowski, Tetrahedron Lett. 24, 2043 (1983)).

(Received in France 17 June 1986)