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MIXED GEM-DIMETALLIC ORGANIC COMPOUNDS. A NEW CLASS OF MULTI-COUPLING REAGENTS
PART 2[1]

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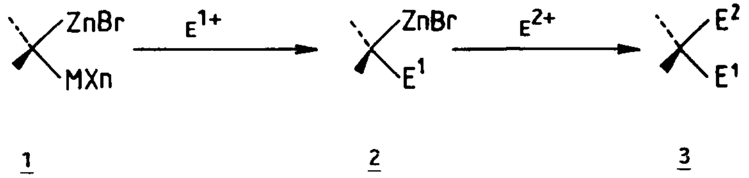
Summary - The 1-magnesia-1-zincaalkene 4 and the 1-lithia-1-zincaalkene 15, easily obtained by a carbometallation reaction, are able to react successively with two different electrophiles to give good yields of various gem-difunctionalized compounds like the α-deuterated- and α-iodo- stannanes 7b-c and the α-allylated thioethers 10a-b. This demonstrates the usefulness of compounds of type 4 and 15 as multi-coupling reagents. A new fragmentation reaction of alkylidene malonates is described.

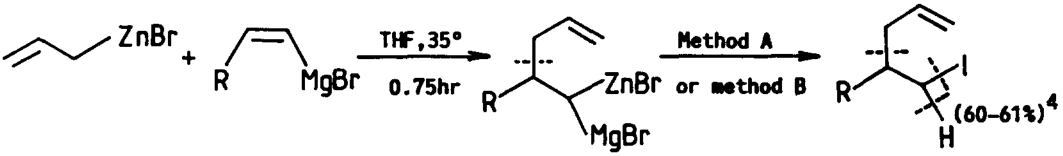
Scheme 1



We have recently[1] shown that various gem-dimetallic compounds of type 1 are easily prepared by carbometallation of an alkenyl metallic derivative of Mg, Li or Al by an allylic zinc bromide. The different nature of the two metals present in compound 1 allows us to hope that a different reactivity of thesetwo metals can be used to make successively two new bonds : first by reaction of the more reactive carbon-metal bond of 1 whith an electrophile E^1 leading to the organo-zinc derivative 2, then by reaction of 2 with a different electrophile E^2 to furnish the gem-disubstituted compounds 3 (see scheme 1). Thus reagents of type 1 are potential multi-coupling[2] reagents.

In fact, we have now found that the 1-magnesia-1-zincaalkene[3] 4 is able to react selectively with two different electrophiles under proper reaction conditions to give products of type 3. First, addition of iodine (1eq.) to a cooled THF solution of the dimetallic reagent 4 (10min, -78°), followed by hydrolysis gives the unsaturated iodide 5 in 61% (method A in scheme 2). The same product 5 is also obtained by treating the reagent 4 first with acetic acid (1eq. ; 15min ; -80° to -40°C), then with iodine (1eq.) to furnish 5 in 60% yield (method B in scheme 2).

Scheme 2

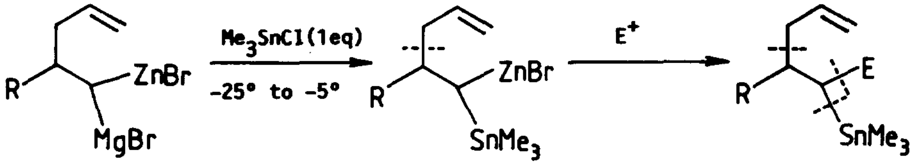


4 : R=C_6H_{13} 5 : R=C_6H_{13}

Method A : 1/ I_2(1eq.),-80°C,10min ; 2/ H_3O^+ - Method B : 1/ AcOH(1eq.),-80° to -40°C,15min; 2/ I_2(1eq.).

In a similar way, a THF solution of the dimetallic derivative 4 reacts readily with trimethyltin chloride[5] (45min,-25° to -5°C) to give an intermediate zinc compound 6 which can then react with a second electrophile (H_3O^+, D_3O^+ or I_2) to give the functionalized stannanes 7a-c in high yields (see scheme 3).

Scheme 3



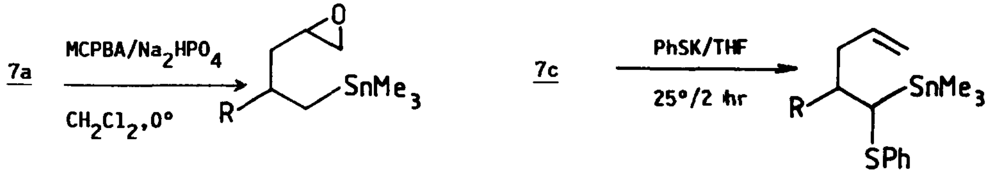
4 : R=C_6H_{13}

6 : R=C_6H_{13}

7a : E=H : 88%
7b : E=D : 94% (100% deuterated)
7c : E=I : 75%

The tin derivatives 7a and 7c are useful for the synthesis of other functionalized stannanes. Thus treatment[6] of 7a with m-chloroperbenzoic acid in CH_2Cl_2 (1,8eq. of MCPBA ; 2eq. of Na_2HPO_4, 0°C, 8hr) gives the epoxide 8 in 91% yield (see scheme 4). The α-iodo stannane 7c reacts[7] smoothly with potassium thiophenolate in THF (2hr, 25°C) to furnish the thioether 9 in 81% yield (see scheme 4).

Scheme 4



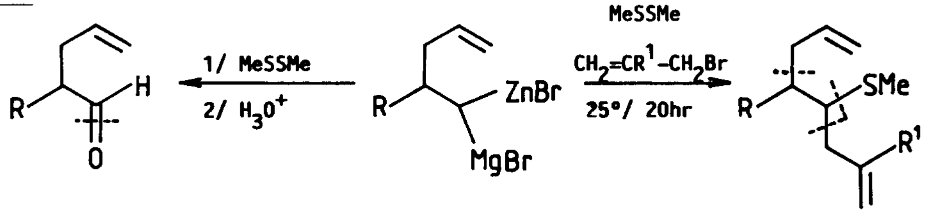
8 : R=C_6H_{13} (91%)

9 : R=C_6H_{13} (81%)

It is also possible to add simultaneously two different electrophiles to the reagent 4. Thus treatment of the dimetallic compound 4 with 5eq. of an allylic bromide and 2.3eq. of dimethyldisulfide (25°C, 20hr) furnishes the α-allylated thioethers 10a and 10b in 76% and

77% yield respectively (see scheme 5). If dimethyldisulfide is added alone to the reagent 4, then the aldehyde 11 is isolated after hydrolysis with 0.01N HCl in 53% yield (see scheme 5).

Scheme 5[4]



11 : $R=C_6H_{13}$ (53%)

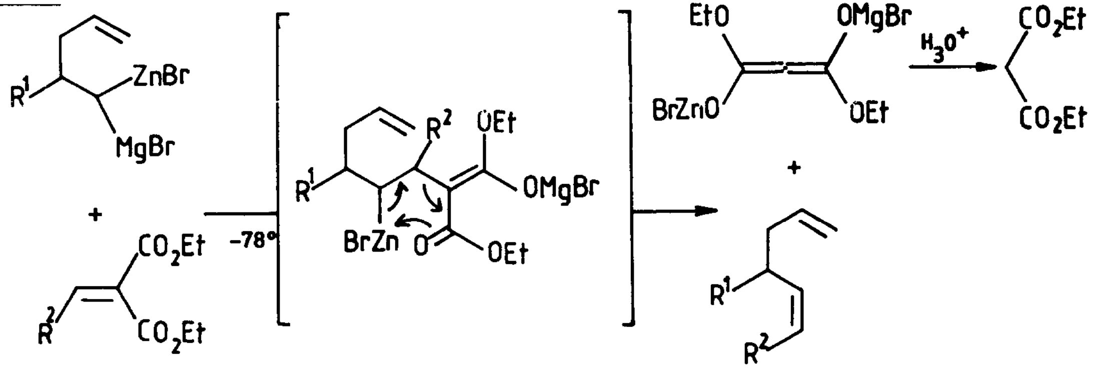
4 : $R=C_6H_{13}$

10a : $R=C_6H_{13}$;R^1=H : 76%

10b : $R=C_6H_{13}$;R^1=Me: 77%

We found also that the addition of various alkylidene malonates of type 12 to the reagent 4 (-78° ; 0.5hr) gives, after the fragmentation of the postulated Michael-adduct 13, the dienes 14a-c and diethyl malonate in good yields. The newly formed double bond is mainly Z (except if R^2=Ph in malonate 12), see scheme 6. This synthesis of 1,5-dienes of type 14 is complementary to a method recently developped (see the preceding publication) which leads to the (E)-1,5-dienes 14 (purity ≫ 90% of (E)-isomer).

Scheme 6[4]



13

4 : $R^1=C_6H_{13}$

12a : R=isoPr

12b : R^2=Pent

12c : R^2=Ph

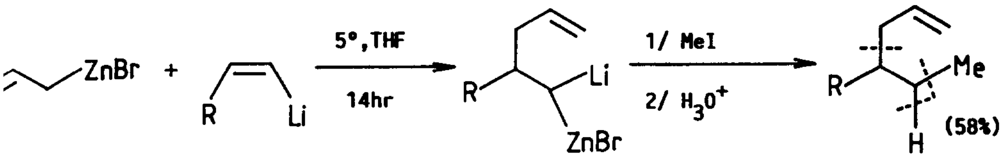
14a: $R^1=C_6H_{13}$;R^2=iso-Pr:67%;(E/Z:16/84)

14b: $R^1=C_6H_{13}$;R^2=Pent : 67%;(E/Z:16/84)

14c: $R^1=C_6H_{13}$;R^2=Ph : 74%;(E/Z:75/25)

The 1-magnesia-1-zincaalkene 4 does not react with methyl iodide under various reaction conditions, however the corresponding 1-lithio-1-zincaalkene 15 furnishes the monomethylated alkene 16 in 58% yield (5eq. of MeI, 12hr, 25°C) ; see scheme 7.

Scheme 7[4]



15 : $R=C_6H_{13}$ 16 : $R=C_6H_{13}$

We have demonstrated that the gem-dimetallic compounds of type 4 or 15 can form two new bonds with two appropriate electrophiles from a same carbon atom (see scheme 1). We continue our study on the reactivity of these 1,1-dimetallic reagents.

Acknoledgements

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References and Notes

1. Synthesis and reactivity of gem-dimetallic organic compounds. Part 1 : preceding publication.
2. For a definition of a multi-coupling reagent see : P. Knochel and D. Seebach, Tetrahedron Lett. 23, 3897 (1982) ; for some recently developped allylic multi-coupling reagents see : D. Seebach and P. Knochel, Helv. Chim. Acta, 67, 261 (1984) ; P. Knochel and J.F. Normant, Tetrahedron Lett. 26, 425 (1985) ; P. Auvray, P. Knochel and J.F. Normant, Tetrahedron Lett. 26, 2329 (1985).
3. The real structure of this reagent can be more complex ; for a discussion see the preceding publication.
4. The yields indicated include the preparation of the dimetallic compound and its reactions with the two electrophiles E^1 and E^2 (see scheme 1). All the compounds obtained show correct spectroscopic data (I.R., ^{1}H-NMR and ^{13}C-NMR).
5. The good reactivity of trimethyltin chloride with the methylene di-Grignard has been reported : J.W. Bruin, G. Schat, O.S. Akkerman and F. Bickelhaupt, J. Organomet. Chem. 288, 13 (1985).
6. For similar transformations on tin derivatives see : R.W. Bott, C. Eaborn and T.W. Swaddle, J. Organometal; Chem. 5, 233 (1966) ; D.J. Peterson, M.D. Robbins and J.R. Hansen, J. Organometal. Chem. 73, 237 (1974).
7. The α-iodo stannane 7c reacts with Bu_2CuLi_2CN in THF (-50° to -20°C) to give, after hydrolysis, the tin derivative 7a in 70% yield. This reaction constitutes one of the rare reactions where a cuprate promotes a halogen-copper exchange in such basic solvent. We investigate the synthetic potential of the intermediate 1-trimethylstannyl alkenyl copper reagent.

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