Tetrahedron Letters,Vol.25,No.31,pp 3305-3308,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

PRACTICAL PREPARATION AND METALLO-ENE REACTIONS OF (2-ALKENYLALLYL)-MAGNESIUM CHLORIDES: COMPARATIVE STUDY OF MAGNESIUM ACTIVATION[1]

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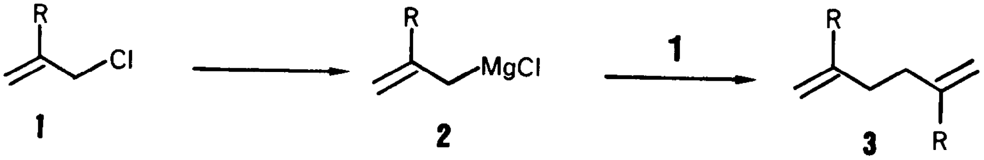
Abstract: Magnesium activated by equilibration with its anthracene adduct in THF metalates smoothly 2-alkenyl chlorides at -65°C without significant coupling. The resulting solutions of Grignard reagents are subjected to thermal (80-130°C) cyclization followed by trapping with electrophiles.

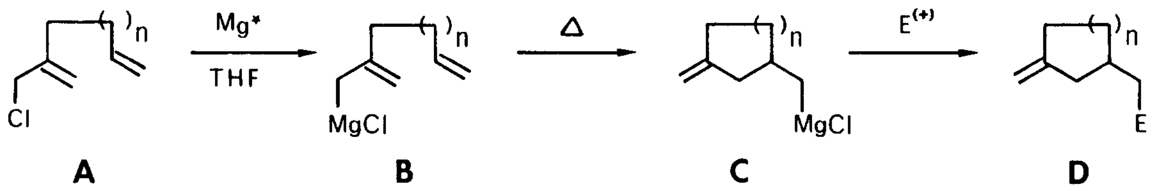
In the course of recent studies[2] and synthetic applications[3] of the magnesium-ene reaction[4] we had initially encountered the problem of preparing reliably and efficiently the starting allyl-Grignard reagents. Conventional metalation of allyl halides 1 (Scheme 1) with Mg powder led frequently (but not always) to the undesired coupling 1 + 2 → 3[5]. Using slurries of highly active, precondensed Mg in THF we have achieved smooth metalation 1 → 2 at -65°C without significant formation of 3[6]. Solutions of the allylmagnesium halides B (Scheme 2) which were cleanly obtained by this method from A could be safely heated under argon at temperatures between 80 to 130°C giving the cyclized Grignard compounds C. Subsequent trapping of C with various electrophiles furnished products D in good overall yield from A[2]. Nevertheless, broad application of this versatile methodology

Scheme 1



was limited by the need for a suitable apparatus to evaporate metallic magnesium despite the description of a relatively simple rotating solution reactor[7].

Scheme 2

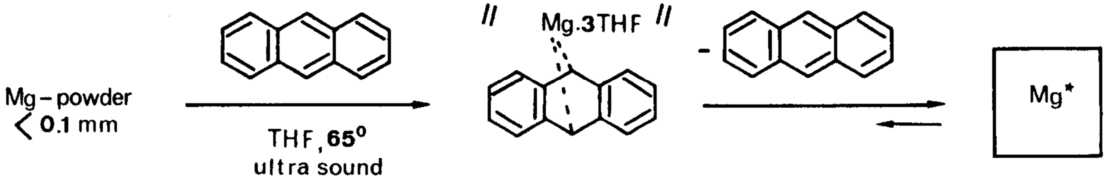


YIELDS OF "TRAPPED" PRODUCTS D

entry	n	E	Evaporated Mg I	"Anthracene-Mg" II	"Rieke-Mg" III
a	1	OH	55	56	55
b	1	C(O)NHPh	71	67	64
c	2	OH	57	51	48
d	2	C(O)NHPh	72	69	64

We wish to present here a practical, facile preparation of solutions of allyl Grignard reagents B which is compatible with a one-pot thermal cyclization and trapping procedure (A → B → C → D). This work was prompted by a recent report describing an exceedingly elegant route to activated magnesium by equilibration of magnesium powder with a catalytic amount of anthracene in THF (Scheme 3)[8].

Scheme 3



ANTHRACENE-MAGNESIUM

Slow addition of halides A to anthracene-activated magnesium in THF led to smooth metalation A → B at -65°C. Heating of the crude reaction mixture followed by *in situ* trapping of C with MoOPh[9] (entries a,c) or with phenylisocyanate (entries b,d) furnished the functionalized products D in yields comparable to those obtained *via* the metal evaporation technique.

Initial attempts to effect the metalation/cyclization/trapping sequence A→ B → C → D using "Rieke-magnesium"[10] gave extensive decomposition. However, careful experimentation showed the compatibility of the Rieke-method with the above reaction sequence giving the final products D with slightly lower yields from A.

The following experimental procedures are representative (all manipulations were carried out under argon):

Method I

Chloride A (0.7 mmol in THF (10 ml) was added over 1.5 h to a rotating slurry of Mg (2-3 mmol) in THF (30 ml) at -65°. Warming up of the reaction mixture to 20°C (1.5h), transfer to a dried Carius tube, heating at 80°C (entries c,d) or at 130°C(entries a,b) for 17 to 23 h furnished solutions of C. Those were oxidized with MoOPH (i: 1.1 eq, -78°C, 1h; ii: H_2O, 0°C → 20°C) to give the alcohols D (entries a,c). Alternatively, trapping of C with phenylisocyanate (i: 1.2 eq, -10° →+20°C; ii: reflux in C_6H_5Br, 12 min:) yielded the corresponding anilides D (entries b,d). The products D were purified by chromatography on SiO_2.

Method II

A mixture of magnesium powder (325 mesh, 2-3 mmol), anthracene (0.06 mmol) and methyl iodide (1 drop) in THF (30 ml) was kept in an ultrasonic bath at 20°C for 14 h. Addition of chloride A (0.7 mmol) at -65°C as well as the remaining operations were carried out as described above.

Method III

Magnesium turnings (4.32 mmol) and 1,2-dibromoethane (4.75 mmol) were heated unde reflux in THF (10 ml) for 50 min. After evaporation of the solvent, drying of the residue (150°C, 1h, 10^{-1} Torr), addition of potassium metal (7.6 mmol) and THF (1 ml) the mixture was heated under reflux for 3 h and then diluted with THF (19 ml). Addition of chlorides A(0.7 mmol) at -65°C as well as the remaining operations were carried out as described above.

We may thus conclude that, in the above context the magnesium evaporation technique offers the advantage of choice of solvent. The use of "Rieke-magnesium" requires tedious, stoichiometrically precise experimentation and is not very attractive for working on a very small or large scale. So far, the simple method of obtaining highly activated magnesium in the presence of a small amount of chemically rather inert and readily removable anthracene appeals to us a the most practical, widely usable approach to allylic Grignard reagents and their reaction products.

Acknowledgements: Financial support of this work by the *Swiss National Science Foundation*, *Sandoz Ltd*, Basel and *Givaudan SA*, Vernier, is gratefully acknowledged. We also thank Dr. *K.M. O'Hagan* for preliminary experiments and Mr. *J.P. Saulnier*, Mr. *A. Pinto* and Mrs. *D. Clément* for NMR and MS measurements.

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(Received in Germany 25 April 1984)