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THE PREPARATION OF THF SOLUBLE ROMgH AND $ROMg_2H_3$ COMPOUNDS AND THEIR UNUSUAL STEREOSELECTIVITY IN THE REDUCTION OF CYCLOHEXANONES

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In recent years the use of metal hydrides as stereoselective reducing agents in organic chemistry has attracted considerable attention.[1,2] Although numerous reports have appeared in the literature concerning the reduction of cyclohexanones by hydrides of boron and aluminum, nothing is known about reductions with MgH_2 presumably because of its insolubility in all solvents studied.[3] Recently, we reported the first examples of soluble magnesium-hydride compounds in the form of HMgCl, HMgBr[4] and RMgH.[5] These compounds exhibit considerable solubility in THF; however, unfortunately, they do not exhibit any unusual selectivity as reducing agents. We would now like to report, for the first time, the preparation of HMgOR and H_3Mg_2OR compounds (where R = methyl, 2,6-dimethylphenyl and 2,6-diisopropylphenyl), all of which (except $HMgOCH_3$) exhibit solubility in THF and unusual stereoselectivity as reducing agents toward cyclohexanones.

We have found that alkoxy- and aryloxymagnesium hydrides (HMgOR and H_3Mg_2OR compounds) can be prepared conveniently and quantitatively by the reaction of $Mg(OR)_2$ with an active form of MgH_2 in the appropriate stoichiometric ratio in THF at room temperature (eqs. 1 and 2). When the mole ratio of $Mg(OR)_2$ to MgH_2 is 1:1, the HMgOR compound is formed and

$$Mg(OR)_2 + MgH_2 \xrightarrow{THF} 2HMgOR \qquad (1)$$

$$Mg(OR)_2 + 3MgH_2 \xrightarrow{THF} 2H_3Mg_2OR \qquad (2)$$

when the ratio is 1:3, the H_3Mg_2OR compound is formed. The compounds are formed in quantitative yield. Although MgH_2 was found to be very insoluble in THF, a clear solution results within 15 minutes when these compounds are allowed to react (except in the case of $HMgOCH_3$). Gas evolution and magnesium analysis show H:Mg ratios of 1:1 or 3:2 depending on whether the compound is an HMgOR or H_3Mg_2OR compound (Table I). All compounds were isolated as solids by removal of the THF under vacuum and the X-ray diffraction patterns recorded.

It is clear from these X-ray powder patterns and those of MgH_2 and the $Mg(OR)_2$ compounds, that the HMgOR and H_3Mg_2OR compounds are not physical mixtures containing MgH_2 or $Mg(OR)_2$ and that the HMgOR and H_3Mg_2OR diffraction patterns are quite different from each other. Reference to Table I shows that three HMgOR and three H_3Mg_2OR compounds have been prepared and characterized, all of which are soluble in THF except $HMgOCH_3$ and $H_3Mg_2OCH_3$.

The active form of MgH_2 was prepared by the reaction of $LiAlH_4$ with Et_2Mg in ether solution at room temperature.^{6}

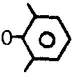
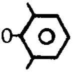
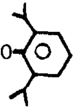
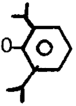
$$Et_2Mg + LiAlH_4 \xrightarrow{Et_2O} MgH_2 + LiAlEt_2H_2 \qquad (3)$$

Compounds 5 and 7 were also prepared by the reaction of MgH_2 with an equalmolar amount of the appropriate alcohol in THF. The reagents were allowed to react at -78°C and then allowed to warm to room temperature at which time a clear solution was observed. The infrared spectra of these solutions were identical to the spectra observed for the preparation of the same compounds by the reaction of MgH_2 and $Mg(OR)_2$ in THF.

$$MgH_2 + ROH \xrightarrow{THF} HMgOR + H_2 \qquad (4)$$

Both the HMgOR and H_3Mg_2OR compounds were allowed to react with 4-*tert*-butylcyclohexanone, 3,3,5-trimethylcyclohexanone, 2-methylcyclohexanone and camphor in order to study the stereoselectivity of these new hydrides. These results are also summarized in Table I. The first important observation is that MgH_2, in spite of previous reports to the contrary, is quite a good reducing agent giving 100% reduction of 4-*tert*-butylcyclohexanone in THF within one hour at room temperature. Also it is interesting to note that MgH_2 behaves very much like $LiAlH_4$ towards the four ketones studied in spite of its insolubility in THF. This is somewhat surprising since most other hydrides attack 4-*tert*-butylcyclohexanone predominantly from the equatorial side. More importantly, it can be seen that all of the HMgOR and H_3Mg_2OR compounds react with all four ketones with high stereoselectivity especially in those cases where some group is close enough to the carbonyl group to provide some steric hindrance For example, hydride (8) reduces the three such ketones in this study in nearly 100% yield and 100% stereoselectivity as a result of equatorial attack. The ease of preparation of these new hydrides and the ease of work up of the reaction mixtures in addition to the unusual stereochemistry observed suggests that these hydrides should have considerable potential as stereoselective reducing agents.

Table I. Relative Yields of Cis or Exo Alcohol in the Reduction of Cyclic and Bicyclic Ketones by ROMgH and $ROMg_2H_3$ Compounds in THF at RT for 24 Hours.[a]

Hydride	Solubility in THF	Analysis (Ratio) Mg:H	4-*tert*-Butyl-cyclohexanone	3,3,5-Trimethyl-cyclohexanone	2-Methyl-cyclohexanone	Camphor
1. $LiAlH_4$	soluble	-	10	80	24	91
2. MgH_2	insoluble	1.00:2.02	24 (56)[c]	85	35	92
3. $HMgOCH_3$	insoluble	1.00:0.95	70	99	98	95
4. $H_3Mg_2OCH_3$	insoluble	1.00:1.45	71	99.5	99.5	99.5
5. HMgO 	soluble	1.00:1.01	68	98.5	98	98.5
6. H_3Mg_2O 	soluble	1.00:1.48	72	99.5	99	99
7. HMgO 	soluble	1.00:0.98	83	99.5	99	99
8. H_3Mg_2O 	soluble	1.00:1.47	78 (91)[d]	100	>99.5	>99.5

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[a] Yields were determined by glc using an internal standard; total yields were 95-100%. [b] The molar ratio of hydride reagent to ketone was 1.5:1.0 for $LiAlH_4$, 4.0:1.0 for MgH_2 and HMgOR, and 1:1 for H_3Mg_2OR. [c] Ratio of MgH_2:ketone = 1.00:1.0. [d] Reaction temperature was 0°C.

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