Pinacol Formation and Reduction of Aromatic Carbonyls with Magnesium–Methanol at Ambient Temperature

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Summary. A simple and inexpensive procedure for the pinacol formation of aromatic aldehydes and reduction of aromatic ketones to the corresponding alcohols with magnesium in dry methanol at ambient temperature is reported. The pinacol formation and reduction are proposed to be proceeding by SET from magnesium.

Keywords. Aldehydes; Ketones; Pinacol formation; Reduction; Magnesium.
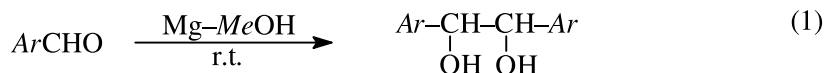
Introduction

Reduction of aldehydes and ketones is one of the useful organic transformations. The carbonyl compounds can be reduced to alcohols or methylene groups and can also be reductively coupled to pinacols or olefins depending on the reducing agent. Reduction of carbonyls to alcohols can be achieved by a variety of reagents, *e.g.*, catalytic reduction, hydride transfer reagents, *Meerwein-Ponndorff-Verley* reduction, sodium–ethanol, borane, *etc.* [1]. Pinacol formation is invariably brought about by one electron reductants, *e.g.*, Zn–ZnCl$_2$ [2], Mg–MgI$_2$ [3], Mg-aq. NH$_4$Cl [4], Al–KOH [5], silole and germole dianions [6], Sm–HCl [7], Mn [8], cerium catalysts [9], other transition metals, lanthanides and actinides [1, 10], *etc.* Ti^{II} and Ti^{III} reagents have received considerable attention for pinacol formation of aldehydes and ketones although formation of olefins is a competing reaction with these reagents [11]. Magnesium in methanol has been reported as an inexpensive reagent for a variety of useful organic transformations, *e.g.*, chemoselective reduction of carbon–carbon double bonds in α,β-unsaturated nitriles [12], esters [13], amides [14], and carbonyls [15], chemoselective reduction of carbon–carbon triple bonds in α,β-unsaturated esters [16], deoxygenation of *N*-oxides [17], reduction of azides

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[18], reductive coupling of nitroarenes [19], dehalogenation of bromides and iodides [20], *etc*. It has been reported as a single electron transfer reagent in the reduction of carbon–carbon double bonds [13], carbon–carbon triple bonds [16], coupling of nitroarenes [19], and dehalogenation of aryl halides in methanol [20]. In view of its versatility as a reducing agent, it was inconceivable to believe that it will be inert to carbonyl groups. Therefore, with its ease of handling and inexpensive nature in mind, we decided to investigate the reactions of magnesium–methanol with a variety of carbonyl compounds.

Results and Discussion

We report herein a simple, convenient, and inexpensive method for the pinacol formation of aromatic aldehydes and reduction of aromatic ketones with magnesium in dry methanol at ambient temperature. The coupling/reductions were complete in reasonable time using a 1:5 molar ratio of substrate to magnesium. With lower molar ratios of substrate to magnesium, the reactions were either incomplete or required much longer reaction times. The progress of the reactions was monitored by thin-layer chromatography using petroleum ether/benzene as eluent. All the reactions were induced by a crystal of iodine and an exothermic reaction (induction) ensued after $\sim$15–30 min. The induction times were longer in the absence of iodine but did not affect the product(s). The aromatic aldehydes formed pinacols whereas aromatic ketones were reduced to the corresponding alcohols in high yields (Eqs. 1 and 2). Methanol has been found to be the solvent of choice. No reduction and/or pinacol formation was observed in ethanol, benzene, *THF*, or dioxane with magnesium under identical reaction conditions. Our results are tabulated in Table 1.

$$Ar\text{CHO} \quad \xrightarrow[\text{r.t.}]{\text{Mg–}Me\text{OH}} \quad \underset{\underset{\text{OH}}{|}}{Ar\text{–CH}}\text{–}\underset{\underset{\text{OH}}{|}}{\text{CH}}\text{–}Ar \qquad (1)$$

$$Ar\text{COR} \quad \xrightarrow[\text{r.t.}]{\text{Mg–}Me\text{OH}} \quad ArR\text{CHOH} \qquad (2)$$

$$Ar = \text{Aryl}; R = \text{Aryl}, Me$$

It is obvious from Table 1 that aromatic aldehydes containing alkyl, alkoxy, or halo groups give pinacols in high yields. No products corresponding to *Cannizzaro* reaction were obtained. 2-Chlorobenzaldehyde and 2,4-dichlorobenzaldehyde gave 2-chlorobenzyl alcohol and 2,4-dichlorobenzyl alcohol, respectively, whereas 4-bromobenzaldehyde yielded a mixture of the corresponding alcohol and pinacol. The pinocols formed in all cases were found to be a mixture of *dl*- and *meso*-compounds in nearly 50:50 ratios as determined by NMR spectra. The reaction of 4-nitrobenzaldehyde gave a mixture of products due to competing reductive coupling of nitroaromatics [15] and reactions of 2- and 4-hydroxybenzaldehydes were incomplete even after prolonged reaction times. The reactions of aliphatic aldehydes were also not complete and yielded mixtures probably due to competing aldol condensations.

Diaryl ketones and aryl methyl ketones, however, underwent complete reduction to the corresponding alcohols in high yields with magnesium-methanol at

**Table 1.** Reactions of aromatic aldehydes and ketones with magnesium–methanol[a] at ambient temperature

Run no.	Substrate ArCHO/ArCOR	Molar ratio Substrate:Mg	Reaction Time[b]/min	Yield/%[c]	
				ArRCHOH	(ArCHOH)$_2$
1.	4-Anisaldehyde	1:5	30	–	90
2.	4-Tolualdehyde	1:5	45	–	89
3.	4-Chlorobenzaldehyde	1:5	30	–	74
4.	Piperonal	1:5	30	–	79
5.	Veratraldehyde	1:5	30	–	92
6.	4-Bromobenzaldehyde	1:5	10	38	32
7.	2-Chlorobenzaldehyde	1:5	60	86	–
8.	2,4-Dichlorobenzaldehyde	1:5	15	87	–
9.	Benzophenone	1:5	30	84[d]	–
10.	4,4′-Dichlorobenzophenone	1:5	30	93	–
11.	4-Bromobenzophenone	1:5	30	96	–
12.	4,4′-Dimethoxybenzophenone	1:5	120	84	–
13.	2-Amino-5-chlorobenzophenone	1:5	180	96	–
14.	Acetophenone	1:5	30	82	–
15.	4′-Methylacetophenone	1:5	30	85	–
16.	4′-Bromoacetophenone	1:5	30	88	–
17.	4′-Methoxyacetophenone	1:5	30	83	–
18.	3′,4′,5′-Trimethoxyacetophenone	1:5	30	95	–
19.	Benzoin	1:10	120	–	83
20.	Benzil	1:10	120	–	81
21.	9-Fluorenone	1:5	150	84	(16)[e]
22.	9-Fluorenone	1:20	120	–	(88)[f]
23.	2,7-Dichloro-9-fluorenone	1:20	60	–	(85)[g]
24.	2,7-Dibromo-9-fluorenone	1:20	120	–	(82)[h]
25.	9-Xanthone	1:10	150	33	(22)[i]
26.	9-Acridone	1:20	180	–	(80)[j]
27.	Anthrone	1:5	210	–	(94)[k]

a: All reactions were induced by a crystal of iodine; b: Time for complete disappearance of starting material; c: Isolated yields; d: Benzopinacol (4%) was also isolated by column chromatography; e: The other product was identified to be fluorene, NMR spectra showed the presence of 16% fluorene; f: Isolated product is fluorene; g: Isolated product is 2,7-dichlorofluorene; h: Isolated product is 2,7-dibromofluorene; i: 22% of xanthene was also isolated; j: The product was identified to be 9,10-dihydroacridine; k: The isolated product was identified to be anthracene
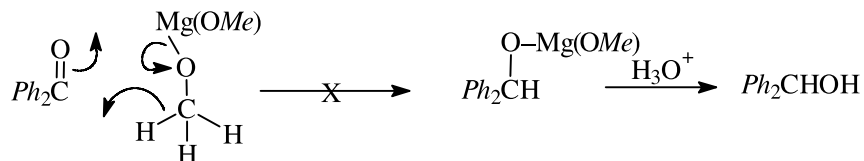
ambient temperature unlike the reductive coupling of aromatic aldehydes. A careful investigation of products showed the formation of a small amount of benzopinacol (1,1,2,2-tetraphenyl-1,2-ethanediol) besides benzhydrol in the reaction of benzophenone with magnesium in methanol (run 9). The electron-releasing groups slowed down the rate of reduction of ketones (runs 12, 13, 25, 26, *etc.*). Reactions of alkyl (other than methyl) aryl and dialkyl ketones with magnesium–methanol were incomplete and indicated the presence of a mixture of products probably due to competing aldol type condensations.

Reduction of 9-fluorenone with magnesium in methanol (1:5 molar ratio of substrate:Mg) gave 9-fluorenol predominantly as expected besides small amounts of 9-fluorene (run 21). Reduction of 9-fluorenone, with a higher molar ratio of substrate:Mg (1:20) yielded 9-fluorene predominantly (run 22). Similarly, reductions of 2,7-dichloro-9-fluorenone and 2,7-dibromo-9-fluorenone with higher molar ratios of substrate:Mg (1:20) also yielded 2,7-dichloro-9-fluorene and 2,7-dibromo-9-fluorene, respectively (runs 23 and 24). Whereas xanthone underwent reduction (1:10 molar ratio) to give a mixture of 9-xanthenol and xanthene (run 25), 9,10-dihydroacridine and anthracene were obtained as the only products (runs 26 and 27) during the reduction of 9-acridone and anthrone, respectively. In independent experiments, it has been shown that 9-fluorenol and 9-xanthenol react with magnesium in dry methanol to give fluorene and xanthene, respectively, unlike the reaction of benzhydrol with magnesium–methanol from which the starting material was recovered quantitatively.
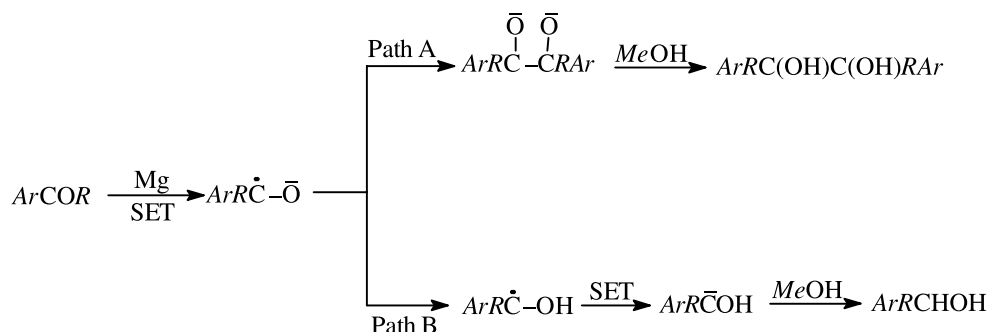
We believed initially that pinacol formation and reduction are proceeding by different pathways. Pinacol formation obviously appears to involve single electron transfer from magnesium to the carbonyl group followed by rapid dimerization. The reduction could be proceeding *via* a 6-membered cyclic transition state (with magnesium methoxide formed *in situ*) similar to the *Meerwein-Ponndorff-Verley* reduction (Scheme 1). The possibility of such a pathway for reduction of carbonyls to give alcohols was, however, eliminated by carrying out a reaction of benzophenone with preformed magnesium methoxide in methanol, when the starting benzophenone was recovered unchanged after 24 h (Scheme 1). It can also be conceived that the alcohols are obtained from ketones by subsequent bond cleavage of the initially formed 1,2-diols. Therefore, a reaction of benzopinacol was carried out with magnesium–methanol under similar reaction conditions. The reaction showed the presence of only the starting benzopinacol even after overnight stirring (Eq. 3), whereas benzophenone undergoes complete reduction to benzhydrol in 30 min. Therefore, this pathway for the formation of alcohols can also be ruled out.

$$ArCOR \xrightarrow{\quad X \quad} ArRC(OH)C(OH)RAr \xrightarrow{\quad X \quad} ArRCHOH \qquad (3)$$
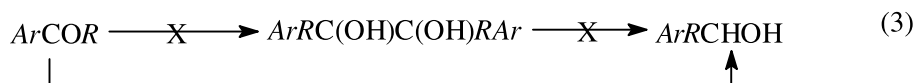
Since magnesium is known to react by single electron transfer during the reduction of carbon–carbon double bonds [9], carbon–carbon triple bonds [12], coupling of nitroarenes [15], and dehalogenation of aryl halides in methanol [16], we conclude that the pinacol formation and reduction of carbonyls are proceeding by single electron transfer (SET) from magnesium to the HOMO of the substrate as

Scheme 1

$$ArCOR \xrightarrow[\text{SET}]{\text{Mg}} Ar R\overset{\bullet}{C}-\bar{O}$$

Path A → $ArR\overset{\bar{O}}{\underset{|}{C}}-\overset{\bar{O}}{\underset{|}{C}}RAr$ $\xrightarrow{MeOH}$ $ArRC(OH)C(OH)RAr$

Path B → $ArR\overset{\bullet}{C}-OH$ $\xrightarrow{\text{SET}}$ $ArR\bar{C}OH$ $\xrightarrow{MeOH}$ $ArRCHOH$

Scheme 2

shown in Scheme 2. Whereas *Path A* involves the rapid dimerization of ketyl radical-anions in the case of aldehydes, *Path B* involves a second electron transfer in case of aryl ketones to give resonance-stabilized carbanions, thus leading to the formation of alcohols. The formation of small amounts of benzopinacol in the reaction of benzophenone is due to competing coupling of the ketyl radical-anion. The reduction of benzophenone with magnesium–methanol slowed down significantly when the reaction was carried out in the presence of diethyl ether–boron trifluoride (1/1) or by bubbling oxygen into the reaction mixture. These observations support the above proposed reaction pathway. When the reaction of 4-methoxybenzaldehyde was carried out with magnesium–methanol in the presence of a 20 molar excess of cumene (a well known hydrogen atom donor), it resulted in the formation of ~12% of 4-methoxybenzyl alcohol unlike traces of alcohol formed in run 1. This is also in agreement with the proposed pathway. The slowdown in the reductions of aromatic ketones containing electron-releasing groups could be due to the higher HOMO-LUMO difference.

Experimental

Methanol (E-Merck) and Mg turnings (S.D. Fine) were used in all the reactions. Methanol was dried by the known procedure [21]. Mg turnings were washed with 1% hydrochloric acid, water, and methanol and finally dried. The starting carbonyls were used after crystallization or distillation. The products were identified by mp, mixed mp, IR and NMR spectra.

General Procedure

To a $100\,cm^3$ conical flask mounted over a magnetic stirrer, fitted with a reflux condenser and a $CaCl_2$ guard tube, was placed a mixture of 1 g of starting carbonyl, magnesium turnings (according to Table 1), and $20\,cm^3$ of dry methanol. Two-three crystals of iodine were added while stirring the solution vigorously at room temperature. A vigorous reaction ensued after a short while. The progress of the reaction was monitored by TLC using petroleum ether:benzene = 25:75 as eluent. After complete disappearance of the starting material, the reaction mixture was quenched with $\sim60\,cm^3$ of $2\,M$ acetic acid. The product obtained, if a solid, was filtered, washed with water, dried, and finally recrystallized. In other cases where an oil separated, the product mixture was extracted with ethyl acetate ($3 \times 10\,cm^3$). The combined extracts were dried over anhyd. $MgSO_4$, filtered, and concentrated on a rotary vacuum evaporator to afford the products. The NMR spectra of the pinacols showed these to be a mixture of *dl*- and *meso*-compounds in nearly 50:50 ratio. The product mixtures in runs 6, 20, and 25 were separated

by column chromatography over silica gel (100–200 mesh) using petroleum ether:benzene $=50{:}50$ as eluent. The product mixture from run 21 was subjected to NMR spectroscopy and the ratio of the two products was calculated from C-9 protons (fluorene, $\delta^{9H} = 3.80$; 9-fluorenol, $\delta^{9H} = 5.44$).

Reaction of Benzophenone with Magnesium Methoxide

Magnesium methoxide was prepared by stirring a mixture of magnesium turnings (2.4 g, 100 mmol), iodine (2–3 crystals), and dry MeOH (48 cm^3) until all the magnesium dissolved to give a white suspension. Benzophenone (0.91 g, 5 mmol) was added to this solution. The reaction mixture was stirred at ambient temperature and the progress of the reaction was monitored by TLC. No reaction was observed to have taken place by TLC using benzene as eluent even after 24 h and benzophenone was recovered quantitatively after work up.

Reaction of Benzopinacol with Mg–Methanol

Magnesium (0.66 g, 27 mmol) and iodine (2–3 crystals) were added to a solution of benzopinacol (1 g, 2.7 mmol) in 20 cm^3 of dry methanol. The reaction mixture was stirred at ambient temperature. The progress of the reaction was monitored by TLC using petroleum ether:benzene $= 25{:}75$ as eluent. No reaction was observed to have taken place by TLC even after 24 h and benzopinacol was recovered quantitatively after work up.

Reaction of 9-Fluorenol with Mg–Methanol

A mixture of 9-fluorenol (1 g, 5.5 mmol), 20 cm^3 of dry methanol, and magnesium turnings (1.33 g, 55 mmol) was stirred at ambient temperature. Iodine (2–3 crystals) was added and the progress of the reaction was monitored by TLC using petroleum ether:benzene $= 40{:}60$ as eluent. The reaction mixture showed the presence of fluorene after 40 min. The reaction was worked up as described in the general procedure. Fluorene was obtained as confirmed by its mp and NMR spectra.

Reaction of 9-Xanthenol with Mg–Methanol

A mixture of 9-Xanthenol (1 g, 5.05 mmol), 20 cm^3 of dry methanol, and magnesium turnings (1.21 g, 50.5 mmol) was stirred at ambient temperature. Iodine (2–3 crystals) was added and the progress of the reaction was monitored by TLC using petroleum ether:benzene $= 25{:}75$ as eluent. The reaction mixture showed the presence of xanthene after 45 min. The reaction was worked up as described in the general procedure. Xanthene was obtained as confirmed by its mp and NMR spectra.

Acknowledgement

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