

## The Reaction of Dimesityl Ketone with Grignard Reagents. The Role of Alkyl Radicals, Catalysis by Iron

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After the appearance of several pieces of non-conclusive evidence,<sup>1,2,3</sup> Grignard reagents were shown to react with benzophenone by a rate-determining electron transfer step (SET) followed by fast combination or disproportionation of the alkyl and the magnesium ketyl radicals.<sup>4,5</sup> Information concerning the lifetime of the alkyl radical has been obtained by the use of various 5-hexenyl radical probes.<sup>6</sup>

2,2',4,4',6,6'-Hexamethylbenzophenone (DMK) has been reported<sup>7</sup> to have a SET step which is faster than the radical combination step so that high concentrations of pairs of ketyl radicals and magnesium bound alkyl radicals are allegedly present in the reaction mixture. Since alkyl radicals, either free or magnesium bound, are usually considered extremely reactive, a series of experiments has served to reinvestigate the problem.

Ashby and Goel<sup>7</sup> state that the formation of addition product with Grignard reagents is completely suppressed by the use of DMK, while the reduction is only slowed down. In the present work, however, it was found that conjugate addition to DMK was the normal reaction, when using secondary, tertiary, or benzylic Grignard reagents. With these there was an insignificant build-up only of the blue magnesium ketyl as measured either by the absorption at 579 nm or by bulk susceptibility measurements (see Experimental) of the spin concentration. NMR of the addition products (see Experimental) showed two one proton signals in the vinylic region, which were split by coupling to each other and to a high field and a low field methyl group, respectively. A 1,4- or a 1,6-adduct would comply with these data and the 1,6-adduct was preferred for steric reasons; Fig. 1.

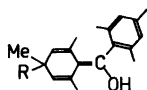


Fig. 1. Structure of products obtained by 1,6-addition of  $\text{RMgX}$  to DMK.

The use of primary Grignard reagents, and especially of ethylmagnesium bromide, apparently led to the build-up of high concentrations of magnesium ketyl, which accounted for more than half of the reaction product before work-up, according to the bulk susceptibility of the solution. When the gas pressure above the reaction mixture was measured it was found that ethane/ethene was formed simultaneously with the ketyl in a ratio of 3:2. Upon work-up the magnesium ketyl is known<sup>8</sup> to disproportionate to form one mol each of ketone and benzhydrol.

The experiments described thus far were carried out using DMK which was purified by recrystallization solely. When the ketone was distilled, however, no color and no spin was produced in the reaction with ethylmagnesium bromide, and reduction product was formed. It was found that the non-distilled DMK was contaminated with traces of iron, which is known to catalyze the formation of ketyl and benzopinacol in the reaction of benzophenone with Grignard reagents.<sup>9</sup> Because of the very low reactivity of DMK, even the smallest traces of iron, e.g.  $10^{-7}$ – $10^{-8}$  g  $\text{ml}^{-1}$  of  $\text{FeCl}_3$ , have a significant effect when using ethylmagnesium bromide. With secondary and tertiary Grignard reagents the addition reaction is rather fast and iron catalysis is less important. With these reagents 5–10% of ketyl is formed as a by-product even in the absence of iron, just like 5–10% of benzopinacol is formed when using unsubstituted benzophenone.<sup>4</sup> The important difference is that the hindered ketyl produced from DMK is rather stable in solution, while the unhindered benzophenone-ketyl dimerizes to form benzopinacol.

Unsuccessful attempts were made to reproduce the EPR spectra presented by Ashby and Goel as evidence for the existence of pairs of radical anion–radical cation.\* Well-resolved spectra were obtained with ethyl- and methylmagnesium bromide reacting with DMK. The spectra were almost identical and very unlike the spectrum obtained by the authors mentioned using methylmagnesium bromide. It was obvious, however, that various coordination equilibria exist in solutions of the ketyl in Grignard reagents. For example, a highly dilute solution of the ketyl absorbs at  $\lambda_{\text{max}}$  579 nm, but not at 640 nm. When a Grignard reagent is added to the solution the absorption at 640 nm appears as a shoulder. The band at 579 nm should therefore be assigned to the magnesium ketyl and not as claimed<sup>7</sup> to the radical ion pair, while the band at

\* Note added in proof. In a recent report<sup>13</sup> the spectra published<sup>7</sup> are interpreted as being those of radical anion–organometal cation complexes, since they have an obvious doublet character.

640 nm arises from a complex and is not typical for the ketyl as such. The presence of complexes may explain that the ESR spectra vary with concentration and also with the presence of different alkylmagnesium compounds in the solution.

In the reaction of DMK with Grignard reagents the rate of spin formation was found by Ashby and Goel to parallel, at least qualitatively, the oxidation potentials of the Grignard reagents as originally observed for the reaction of unsubstituted benzophenone.<sup>5,11,12</sup> Since the spin concentration and the color observed in the reactions of DMK with Grignard reagents concern only the small fraction of ketyl which escapes from the solvent cage during the reaction or is produced by a catalytic process, the rates are not useful for mechanistic interpretations and do not constitute "direct evidence for a single electron transfer in the reduction of ketones by Grignard reagents".<sup>7</sup> As mentioned above, however, such evidence has been obtained earlier for the reaction of unsubstituted benzophenone by correlation of the oxidation potentials of the Grignard reagents with the reaction rates. It seems a reasonable assumption that the substituted benzophenone reacts by an analogous mechanism.

The conclusion of the present experiments is that in the reaction studied the only observable species with an unpaired spin is the magnesium ketyl, while the lifetime of the alkyl radical is probably too short to be measured by available methods.

*Experimental.* NMR spectra were taken on a Bruker HX 90 and a Varian EM 360, UV-visible spectra on a Perkin Elmer 402 and ESR spectra on a JEOL ME 1X.

*Materials.* Dimethyl ketone (DMK) was prepared by acylation of mesitylene with mesityl chloride using aluminum chloride as a catalyst. A sample (A) was recrystallized from benzene-ethanol, m.p. 137.5–138.5 °C. The presence of iron(III) was demonstrated by the reaction with potassium thiocyanate in acidic solution. The ketone was distilled, b.p. 185 °C (2 Pa); this material (B) had m.p. 135–137 °C and gave a negative reaction for iron. Grignard reagents were prepared from sublimed magnesium (Dow Chemical Corp.); THF was distilled from lithium aluminum hydride. Alkyl halides were distilled.

*Addition products.* One mmol of DMK A was added to 10 ml of 0.5 M *t*-butylmagnesium or isopropylmagnesium bromide in THF and kept at room temperature for 2 h during which a blue color developed. For *t*-butyl the work-up procedure was as described.<sup>4</sup> For the isopropyl derivative, the excess Grignard reagent was destroyed by addition of excess of carbon dioxide followed by the addition of cold, saturated ammonium chloride solution. The organic phase was separated and the solvent

removed at 0.25 Pa without heating. The *t*-butyldihydrobenzophenone obtained was crystalline, while the isopropyl derivative was an oil. Upon heating, isobutane and propane were evolved, respectively, and admission of air led to the regeneration of the ketone. Identical reactions were reported for unsubstituted benzophenone.<sup>4</sup> <sup>1</sup>H NMR (CDCl<sub>3</sub>): The spectra were similar, with signals at  $\delta$  6.77 (2 H-arom,s), 5.40 (1 H-vinyl,m), 5.25 (1 H-vinyl,m), 2.06–2.26 (12H,Me,m), 1.11 (3H,Me,d), 0.98 (3H,Me,s), 0.85 (9H,*t*-Bu,s) or the last signal substituted with  $\delta$  0.85 (6H,*i*-Pr,d).

*Bulk susceptibility measurements.* DMK A (100 mg) were mixed with 1 ml of 1 M ethylmagnesium bromide in THF in an NMR sample tube. A sealed glass capillary with a mercury drop was mounted in the rubber stopper and the tube was suspended under a semimicroanalytical balance. The weight of the tube was measured every 30 min to 10<sup>-5</sup> g both directly and after applying a magnetic field of approximately 10 000 gauss to the lower 2 cm of the tube. The difference between the two weighings was 3.49 mg at the time of mixing, but decreased to 2.50 mg after 12 h. By calibration weighings of solutions of dipicyldiphenyl hydrazyl in benzene, this was found to indicate a spin concentration of 0.17 M. The pressure in the tube increased to a final value of 2.8 atm after approximately 20 h. NMR spectroscopy of the gas revealed a ratio between ethane and ethene of 3:2. The weight of the gas escaping by releasing the pressure of the tube after 3 days was 20 mg including 11 mg of solvent vapour. Analogous experiments with DMK A were performed using isopropylmagnesium bromide and *t*-butylmagnesium bromide in THF. No gas pressure was observed and the spin concentrations were below 0.01 M.

When 100 mg of DMK B was reacted with 1 ml of 1 M iron-free ethylmagnesium bromide in THF the solution remained pale greenish yellow for 6 days. The addition of 10<sup>-7</sup>–10<sup>-8</sup> g ml<sup>-1</sup> of FeCl<sub>3</sub> to the reaction mixture caused the development of an intense blue color within 1 h. In the iron-free experiment no spin concentration was detected and a gas pressure of 2.8 atm developed after 40 h. The ratio ethene-ethane was 2:2.3. The product isolated after 6 days was the benzhydrol.

*Visible spectroscopy.* To a solution 0.5 M in THF of ethylmagnesium bromide was added DMK A to a final concentration of 0.0005 M and spectra were taken at room temperature every 5 min in a 10 mm cell. An intense blue color developed with absorption at  $\lambda_{\max}$  579 nm and 640 nm (shoulder). The absorbance at 579 nm after 12 h was  $\approx$  3.0. In an analogous experiment using isopropylmagnesium bromide the same spectrum appeared, but the absorbance at 579 nm reached a maximum of 0.22 after 1 h. Using 0.05 M DMK A and 0.5 M *t*-

butylmagnesium bromide the absorbance at 579 nm reached its final value, 0.95, after 80 min.

*EPR.* Mixtures of Grignard reagents 0.05 M and 0.05 M DMK A were observed at various reaction times. Well-resolved spectra were obtained with methyl- and ethylmagnesium bromide. The spectra were almost identical and very unlike the spectrum reported by Ashby and Goel<sup>7</sup> using methylmagnesium bromide. Quantitative EPR spectroscopy was not attempted.

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