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NMR EMISSION AND ENHANCED ABSORPTION RESULTING FROM THE RADICAL REACTIONS OF GRIGNARD REAGENTS WITH ALKYL HALIDES.

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The degrees of ionic and radical character in the reactions of Grignard reagents have been a matter of concern for many years (1). Although these reactions are believed to be predominantly ionic, evidence for radical intermediates in selected cases has slowly accumulated (2). For the case of Grignard reactions with alkyl halides, Kharasch (3) concluded that bond homolysis was important only in the presence of certain transition metal salts or when the radicals so formed were particularly stable, as in the benzyl systems. It is the purpose of this communication to report evidence for radical character in the reactions of simple alkyl Grignard reagents with alkyl bromides (4) and iodides, based on the observation of emission and enhanced absorption in nmr spectra taken during the reaction course (5).

The relatively slow reaction ($t_{1/2} \sim$ 10 minutes, 40°) of a four-fold excess of t-butyl bromide with the Grignard reagent* (2M) prepared from t-butyl chloride in tetrahydrofuran under argon gave isobutylene (6%), isobutane (39%) and tetramethylbutane (6%)**. The nmr spectra displayed in Figure 1 were taken during the course of the reaction, and clearly show enhanced absorption and emission (the multiplet effect) (5a) for the vinyl protons of isobutylene and the methyl

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* The terms "t-butyl Grignard" and "n-butyl Grignard" refer to t-butylmagnesium chloride and n-butylmagnesium bromide respectively.

** Analyses are from integrated nmr spectra taken at the end of the reaction. Reported yields based on initial Grignard concentration have been corrected for the amount of isobutane, isobutylene and tetramethylbutane formed during the preparation of the Grignard. The excess of isobutane over isobutylene may result in part from hydrogen atom abstraction by t-butyl radicals from tetrahydrofuran, and in part by reaction of the isobutylene with t-butyl radicals. Diisobutylenes can be detected in the product by gas chromatography and mass spectrometry.

protons of isobutane.* Such polarization ** is clear evidence for the intermediacy of *t*-butyl radicals, presumably formed by a one-electron transfer from the organometallic to the alkyl halide. Polarization** has also been observed in the vinyl protons of 1-butene formed from the reaction of *n*-butyl Grignard and *n*-butyl iodide, demonstrating that the less stable primary radicals also can be formed in this way.

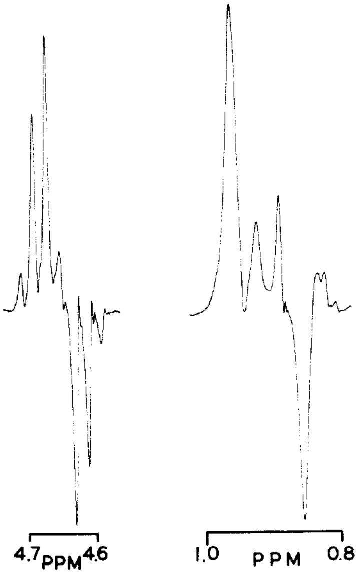

Figure 1. Nmr spectrum taken at 60 MHz approximately one minute after the addition of *t*-butyl bromide to *t*-butyl Grignard reagent in tetrahydrofuran. The vinyl protons of isobutylene (δ 4.6-4.7) were scanned at a sensitivity 2.5 x that of the methyl protons of isobutane (δ 0.8 - 1.0). Absorption for *t*-butyl Grignard (δ 0.93), and tetramethylbutane (δ 0.89) can be seen between the peaks of the isobutane doublet.

For the copper catalyzed reaction of alkyl Grignard reagents and alkyl bromides, it has been proposed that olefins were formed by a non-free radical process and arose only from the Grignard reagent (6). The experiments to support this claim were complicated by the cooper-catalyzed alkyl exchange between Grignard and halide. Reactions conducted without added transition metal salts are free from this difficulty. Mixtures of either *t*-butyl Grignard and *n*-butyl iodide or bromide and *n*-butyl Grignard and *t*-butyl bromide show no evidence of alkyl exchange, within the limits of detectibility by nmr absorption. However, both reactions show strong spectral enhancements and dehancements for the isobutylene formed from the disproportionation of the *t*-butyl radical, indicating that both the halide and the Grignard give rise to olefins by a

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* Polarization of the kind observed in isobutylene and isobutane sums to zero when the emission and absorption for a set of magnetically equivalent protons is combined. Consequently, no polarization is expected or observed in the single line of tetramethylbutane. The absorptions for the methyl protons of isobutylene and the methyl proton of isobutane are obscured by solvent.

** Nuclear polarization is an appropriate description of the effect described here *only* in terms of the positive and negative enhancements of individual nmr lines.

radical reaction*.

Using the approximate rates of the reactions and assuming that radicals are destroyed only by diffusion controlled radical-radical reactions, a maximum radical concentration of 10^{-6} -10^{-7} mole/liter can be calculated. This is at or below the usual detection limit by esr and demonstrates the greater sensitivity of the nmr techniques for the inference of radical intermediates over direct esr detection. Indeed, preliminary esr studies of these systems have failed to detect the presence of free radicals. Further, while esr has detected radicals in Grignard systems, usually in reactions with aryl ketones (7) there is evidence that such radicals represent a side reaction to give ketyl radicals (8) and are not involved in the main product forming reaction. The nmr methods reported here suffer from no such ambiguity, since the evidence of radical intermediacy can be detected directly in the products of the reaction.

Since Grignard-alkyl halide reactions are strongly catalyzed by transition metals, it is important to consider the question of catalysis by impurities, even in the absence of added transition metal salts. This possibility was diminished by the use of triply sublimed magnesium** and carefully purified reagents. Addition of metal salts at about the level of possible impurities** *in the magnesium had little or no effect*** on either the reaction rate or the nmr spectra. However, if the concentration of added metal ion is increased (0.001% Ni, for example), the reaction rate, and consequently the signal enhancements are increased.*

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* While it is not yet possible to differentiate conclusively between free and complexed radicals by nmr observations, it is worth noting that the polarization exemplified here is similar to that observed in cases such as peroxide decomposition where the intermediate radicals are formed in the absence of likely complexing agents.

** a) Kindly supplied by Dr. J. F. Pashak, Dow Chemical Company. Impurities (Cu < 0.001%, Fe < 0.0005%, Mn < 0.0005%, Ni < 0.0005%) are established by the lower detection limits of the analytical method, and constitute only upper limits for impurity levels.

*** Using the time elapsed between mixing the reagents and cancellation of the *isobutylene emission by absorption (18 ± 3 minutes)* as a characteristic rate parameter for the reaction, no change outside of the stated limits was caused by the addition of 0.001% Cu (as Cu_2Br_2), 0.0005% Fe (as $FeCl_2$), 0.0005% Mn (as $MnCl_2$) or 0.0005% Ni (as $NiCO_3$). It should be noted that the effects of metal salt additions to the Grignard *reagent may not be directly* comparable to those of metal impurities in the magnesium because of differences in oxidation state or in aggregation.

The sensitivity of reaction rates fo the presence of minute amounts of transition metals requires that a distinction be made between Grignard reagents (reagents prepared by the reaction of organohalides with magnesium metal) and organomagnesiums or organomagnesium halides. In the first case our results show clearly that Grignard reagents carefully prepared from the best available magnesium react with alkyl halides by a radical route. It is premature to conclude that pure organomagnesium compounds would show the same reaction mode.

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