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Abstract: In the presence of the free radical scavenger 2,2,6,6-tetramethylpiperidine-N-oxyl (TMPO*, 0.50 M), cycloheptyl bromide (RBr, 0.001 M) reacts with magnesium metal in a solution containing tert-amyl alcohol (5.0 M), lithium bromide (0.05 M), and diethyl ether at 20 °C and forms N-cycloheptoxy-2,2,6,6-tetramethylpiperidine (TMPOR) as the major product (≥93% yield, based on RBr). In the absence of TMPO[•], cycloheptane (RH) is formed in ≥95% yield. The dependence of the relative yields of TMPOR and RH on the initial concentration of TMPO* suggests that both products share a common precursor-free cycloheptyl radical-and that this radical has a median lifetime of ca. 10-7 s. Cycloheptyl radicals appear to be intermediates on the major path to the Grignard reagent cycloheptylmagnesium bromide. TMPO[•] is reduced by Mg(0) to the anion of the corresponding hydroxylamine, TMPO⁻, at a rate that is competitive with that of the reaction between RBr and Mg(0). Although the magnesium salts of TMPO⁻ are insoluble in diethyl ether, solutions containing TMPO⁻, Mg^{2+} , and Li⁺ remain homogeneous. For systems containing a high concentration of tert-amyl alcohol, a simple mathematical model attributes apparent zero-order kinetic behavior to the dependence of reactive surface area on the extent of reaction between alkyl halide and Mg.

The objective of this work was to confirm the existence of free alkyl radicals as intermediates along the principal reaction pathway between alkyl bromides and alkylmagnesium bromides during formation of Grignard reagents (Scheme I) and to estimate the lifetime of these species. We used trapping with a stable free radical (TMPO[•], 2,2,6,6-tetramethylpiperidine-N-oxyl) to accomplish this objective. Radical trapping with TMPO[•] is normally a straightforward physical organic diagnostic test.²⁻⁶ In this system of reactions, its use was complicated by the fact that reaction of TMPO* with both alkyl Grignard reagents and magnesium metal were rapid. This reaction between Grignard reagent and TMPO[•] (re)generated, at least in part, the alkyl radical R^{•,7} It was, therefore, necessary to destroy any Grignard reagent in situ by protonation with an added alcohol R'OH. This paper details the experiments that defined reaction conditions permitting clear differentiation of the reaction between TMPO* and alkyl radicals R* generated from RBr from reactions between TMPO and RMgBr. Subsequent papers will support the inference of radicals as intermediates in the formation of Grignard reagents by examinations of stereochemistry⁸ and of byproducts.^{9,10} We have published a preliminary account of this work.¹⁰

Current understanding of the mechanism of formation of Grignard reagents by reaction of alkyl halides and magnesium is based on studies of kinetics,¹¹⁻¹⁷ products,¹⁷⁻³⁰ and morphology

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Scheme I. Processes Occurring during Reaction of an Alkyl Bromide with Magnesium Metal in Diethyl Ether in the Presence of TMPO* and an Alcohol R'OHª



^a The transformations of central interest in confirming the existence of R[•] as an intermediate are shown with dark arrows (=); those important in dealing with the reaction of RMgBr with TMPO* use dashed arrows (-+). Competing reduction of TMPO[•] by magnesium is indicated with dotted arrows (.....).

of the magnesium surface after corrosion.³⁰ A molecule of organic halide in solution arrives at the surface of magnesium via a

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combination of convection and diffusion. The first chemical event is a one-electron reduction of the organic halide at the metal surface. Analysis of rate-structure profiles for organic halides^{11,13,14} does not distinguish between a step in which the carbon-halogen bond is broken by halogen abstraction from the alkyl halide by the metal (an inner-sphere process) and a step involving initial electron transfer to the organic halide from the metal (an outer-sphere process). In solution, all alkyl iodides and tertiary alkyl bromides and most secondary alkyl bromides react at mass-transport-limited rates. Several collisions of these alkyl halides and the metallic surface may occur before reaction; diffusion back out into the bulk, stirred solution is, however, not competitive with the electron transfer at or near the magnesium surface. Primary alkyl, neopentyl, cyclopropyl, adamantyl, aryl, and similar organic bromides react in diethyl ether at rates that approach, but are not within, the mass-transport-limited regime. Alkyl chlorides react at rates that are approximately 10^{-2} – 10^{-3} of the mass-transport-limited rates, and thus probably enter and escape the stationary fluid boundary layer close to the metal many times before reaction.

Several pieces of evidence implicate free radicals as the initial products in the reactions between alkyl halides and magnesium metal: First, the byproducts of the reaction are hydrocarbons that are characteristic of disproportionation and combination of alkyl radicals (alkanes, olefins, and alkyl dimers).9,31,32 Second, the reactions of neophyl chloride,²⁵ 6-bromo-1-hexene,^{18,26} and 2chloro-1,1,1-triphenylethane²⁹ with magnesium give the rearranged products that are characteristic of the corresponding free radicals. Third, CIDNP studies¹⁸⁻²¹ establish that alkyl radicals that are formed during the reaction of organic halides with magnesium result from direct electron transfer from the metal to the organic halide and are not due to spurious, unrelated processes, such as reaction between organic halide and Grignard reagent.³³

Steps occurring late in the reaction-as formation of the carbon-magnesium bond and release of magnesium from the metallic lattice-remain incompletely understood. A study of corrosion of the magnesium surface indicated that halide ion is intimately involved in removal of magnesium from the surface, and that the carbon-magnesium bond is not irreversibly formed on collision of the radicals with the surface.³⁰ Magnesium surface alkyls are probably not intermediates, although the evidence against them is inferential.^{34,35} The presence of basic solvents capable of coordinating with magnesium is clearly important in the reaction,^{31,36} but whether it is by virtue of their influence of



Figure 1. Product distribution in the reaction of cycloheptylmagnesium bromide (0.10 mmol, 0.010 M, added dropwise) with TMPO[•] (1.0 mmol, 0.10 M, 10 equiv) and tert-amyl alcohol (R'OH; 0-40 mmol, 0-4.0 M, 0-400 equiv) as a function of $[R'OH]_0/[TMPO^*]_0$ (0.5 M LiBr, Et₂O, 18 °C): (■) cycloheptane (RH), formed by protonation of c-C₇H₁₃MgBr; (•) combined yields of TMPOR, cycloheptene (R(-H)), RH, and bicycloheptyl (RR). Hydrocarbon yields are corrected for amounts present in the stock solution of RMgBr.

coordination on the thermodynamics of the reaction or simply as a result of removing insoluble passivating surface layers is unclear. The role of "Mg(I)"-like species, either in solution or at the magnesium surface, is also incompletely understood.^{34,37}

The choice of stable nitroxyl radicals as trapping agents in this study is based on several considerations: First, the reaction of TMPO[•] with an alkyl radical (R[•]) is very fast, $(k \simeq 1.0 \times 10^9)$ L mol⁻¹ s⁻¹).³⁸ Second, the reaction of TMPO[•] with R[•] proceeds to give only the coupled product, TMPOR; TMPO[•] does not abstract hydrogen atoms that are bound to the carbon adjacent to the radical center in R[•].³⁹ Third, the nitroxyl reacts preferentially with carbon-centered radicals; TMPO[•] is inert toward alkylperoxy radicals $(RO_2^{\bullet})^{40,41}$ and reacts only slowly with alkoxy radicals (RO*): the reaction of tert-butoxy with nitroxyl radicals has a bimolecular rate constant of ca. 10^3 L mol⁻¹ s⁻¹.⁴² Fourth, an extensive body of background information guides the use of nitroxyl radicals in homogeneous organometallic chemistry,43 although heterogeneous reaction systems have been much less thoroughly studied.44

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Mechanism of Formation of Grignard Reagents

The susceptibility of TMPO[•] to reduction by Grignard reagents⁷ and metallic magnesium introduces an undesirable complication to its application as a radical trap in reactions between alkyl halides and magnesium. In this work, experimental conditions were chosen in order to minimize the effects of these side reactions.

This work used cycloheptyl bromide as a representative secondary alkyl halide. It was chosen primarily for ease of analysis of the products of reaction (RH, R(-H), RR, TMPOR) by GLC; other secondary and primary alkyl bromides would be expected to show similar behavior. We elected to examine a secondary rather than primary alkyl bromide because radical-radical reactions are more readily detected with secondary radicals (for which disproportionation is important) than for primary radicals (for which disproportionation is relatively unimportant). We used an alkyl bromide rather than a chloride primarily for convenience: alkyl bromides react cleanly and rapidly; alkyl chlorides tend to give insoluble magnesium(II) chloride containing products that can occlude the magnesium surface and they are much more slowly reacting than alkyl bromides. Most of the experiments reported also included 1,2-bromoethane as a reactive component: this compound helped to keep the magnesium surface clean and to facilitate initiation of reaction.

Results

Use of in Situ Proteolysis in Reactions between RBr and Mg in the Presence of TMPO[•]. The principal difficulty encountered in efforts to trap free radicals during the formation of Grignard reagents has been the rapid reaction of these organometallic species with radical scavengers (dioxygen, halogens, nitroxyls, hydrazyls, nitrones, and others⁴⁵). We have been able to circumvent this problem by carrying out the reactions of alkyl bromides with magnesium in a solution containing both TMPO[•] and *tert*-amyl alcohol (R'OH; Scheme I). Roberts and co-workers have previously demonstrated the use of in situ proteolysis in reactions between alkyl halides and magnesium.⁴⁶

Preformed cycloheptylmagnesium bromide (RMgBr, 1 equiv) in Et₂O was added dropwise to solutions containing TMPO[•] (10 equiv) and varying amounts of R'OH (0-400 equiv) (Figure 1). The Grignard reagent partitions between protonolysis by the alcohol and reaction with TMPO[•] (Scheme I). The reaction of RMgBr with TMPO[•] is an irreversible, one-electron reduction of the nitroxyl to the anion of the corresponding hydroxylamine, TMPO^{-,7} Figure 1 indicates that ratios of R'OH to TMPO[•] that are greater than ca. 35 ensure that any RMgBr formed in reactions between RBr and Mg will hydrolyze exclusively; at [R'OH]/ [TMPO[•]]₀ = 0, less than 5% of any RMgBr formed would be expected to escape hydrolysis and react with TMPO[•], despite the unknown influence of mixing in this control experiment.

Reduction of TMPO' by Mg. Solutions of TMPO' in Et₂O lose their orange color when stirred with magnesium turnings that have been activated by reaction with 1,2-dibromoethane. The resulting colorless, turbid solutions regain the characteristic color of TMPO' upon exposure to air; the corresponding hydroxylamine, 1hydroxy-2,2,6,6-tetramethylpiperidine (TMPOH), can be isolated from such mixtures. These two observations imply that TMPO' is reduced by magnesium to TMPO^{-.44}

By using the "constant-surface" kinetic technique for measuring relative rates of reaction with magnesium,^{11,12} we estimated that the rate of reduction of TMPO[•] was ca. 3 times slower than the rate of reaction of $c-c_7H_{13}Br$ with Mg. Cycloheptyl bromide reacts with Mg only ca. 5% more slowly than does cyclopentyl bromide.¹¹ The reaction of cyclopentyl bromide with Mg is firmly established as mass-transport limited.^{12,15} We infer that cycloheptyl bromide also reacts at a mass-transport-limited rate. The reaction of TMPO[•] with Mg thus apparently occurs at a rate that approaches, but is not quite within the mass-transport-limited regime, since the diffusion coefficients of TMPO[•] and $c-C_7H_{13}Br$ are expected to be similar (within ca. 20%).



Figure 2. Product distribution in the reaction of $c-C_7H_{13}Br$ (0.010 M, 0.10 mmol) with magnesium turnings (25 mg-atom) in the presence of *tert*-amyl alcohol (5.0 M), as a function of time (0.05 M LiBr, Et₂O, 20 °C): (•) total; (•) cycloheptane (RH); (O) bicycloheptyl (RR); (I) cycloheptene (R(-H)). Final yields were as follows: RH, 51%; RR, 34%; R(-H), 15%. The apparent zero-order rate, $k^{obsd} \simeq 2 \times 10^{-5}$ mol L⁻¹ s⁻¹. The estimated range in the absolute yields is ±5%.

Influence of LiBr on Solubilities. Although the magnesium salt of TMPO⁻ is insoluble in Et₂O, ethereal solutions of TMPO[•] containing anhydrous LiBr remain homogeneous when allowed to react with Mg. Solutions containing the Li⁺ salt of TMPO⁻ in Et₂O are clear and colorless, and they seem to be reoxidized by air more slowly than cloudy solutions of the Mg⁺² salt. The presence of Li⁺ does not affect the rate of the reactions of cycloheptyl bromide or of TMPO[•] with Mg. Added LiBr also enhances the solubility of the alkoxide of *tert*-amyl alcohol in diethyl ether containing magnesium salts. We carried out reactions intended to detect the presence of alkyl radicals during the formation of Grignard reagents in solutions containing added LiBr.

Products of the Reaction between Cycloheptyl Bromide and Magnesium in the Presence of LiBr and tert-Amyl Alcohol. The reaction of cycloheptyl bromide with Mg in a solution of diethyl ether containing tert-amyl alcohol, 1,2-dibromoethane and LiBr at 20 °C gave the products shown in Figure 2. We inferred the vield of cycloheptylmagnesium bromide (protonated in situ by R'OH) from these data by taking the difference between the yields of alkane and olefin: %(RH) - %(R(-H)) = 36%. We believe that the byproducts of the reaction (cycloheptene, bicycloheptyl, and the cycloheptane that is not formed by hydrolysis of the Grignard reagent) originate essentially exclusively from radical-radical disproportionation and combination reactions of cycloheptyl free radicals.³² Calculation of the ratio of rate constants for disproportionation and combination from the yields summarized in Figure 2 gives $k_d/k_c = 0.89$. This value agrees closely with the value of 0.95 obtained with authentic cycloheptyl radicals.⁴⁷ Product yields in an experiment without added alcohol were nearly the same: cycloheptane, 59%; bicycloheptyl, 29%; cycloheptene, 12%. The similarity of the product distribution in the absence of added R'OH to that found in the presence of 5.0 M R'OH suggests that the mechanism of the reaction between RBr and Mg is the same in both solvents. This result can be rationalized by assuming that the reactivity of tert-amyl alcohol in this system is restricted to protonation of cycloheptylmagnesium compounds. The alcohol seems to be chemically inert toward other materials in the system: reduction of R'OH by Mg to produce dihydrogen is not observed.

When the initial concentration of cycloheptyl bromide is lowered by a factor of 10 to 0.001 M, its reaction with Mg in a solution containing 1,2-dibromoethane, *tert*-amyl alcohol, and LiBr in Et₂O gives cycloheptane as the major product ($\geq 95\%$): only small amounts of cycloheptene (ca. 3%) and bicycloheptyl (ca. 2%) are formed. We estimate the yield of Grignard reagent before protonolysis (92% RMgBr) as RH – 2R(–H) – RR: this estimation assumes that a quantity of cycloheptane equal to that of cycloheptene is formed by disproportionation of cycloheptyl radicals.

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Figure 3. Plot of $\ln ([c-C_5H_9Br]_t/[c-C_5H_9Br]_0)$ vs t for the reaction of two 2-mmol portions in sequence of cyclopentyl bromide with magnesium turnings (11 mg-atom; Et₂O, °C). tert-Amyl alcohol (0.08 M, 4 mmol) was added to the solution at time A; the second portion of c-C₅H₉Br was added at time B.



Figure 4. Plot of $\ln ([c-C_5H_9Br]_t/[c-C_5H_9Br]_0)$ vs t for the reaction of two 2-mmol portions in sequence of cyclopentyl bromide with magnesium turnings (21 mg-atom; 0.5 M LiBr, Et₂O, 20 °C): (•) first run; (•) second run, $k^{obsd} = (4.30 \pm 0.16) \times 10^{-3} \text{ s}^{-1}$. The uncertainty is expressed at the 95% confidence level.

The rate of reaction of alkyl halides with magnesium is firstorder in alkyl halide in diethyl ether containing no tert-amyl alcohol;^{11,12} in systems containing 5.0 M alcohol, the reaction is approximately zero order $(k^{obsd} \simeq 2 \times 10^{-5} \text{ mol } \text{L}^{-1} \text{ s}^{-1}$ for the example presented in Figure 2). Three data suggest that this change in kinetic behavior reflects chemi- or physisorption of the alcohol on the magnesium surface and not a change in mechanism: First, the reaction between c-C₇H₁₃Br and Mg does not proceed at all in a solvent containing 5.0 M tert-amyl alcohol (ca. 55% by vol) unless 1,2-dibromoethane (≥ 0.005 M) is also present, although reaction proceeds readily without 1,2-dibromoethane in the absence of alcohol. Dibromoethane is commonly added to ethereal mixtures of organic halides and magnesium in order to activate the metal for reaction;⁴⁸ this activation is believed to involve the removal of passivating surface layers on the magnesium. Second, the pseudo-first-order rate constant for the reaction of cyclopentyl bromide with magnesium is unaffected by tert-amyl alcohol, provided that the alcohol is present at a low concentration (0.08 M, Figure 3). Third, we observe pseudo-zero-order kinetics for reactions of alkyl halides with magnesium turnings in diethyl ether alone, under certain experimental conditions (Figure 4). Such kinetic behavior is compatible with a kinetic model that assumes a uniformly increasing surface area for the magnesium and may actually reflect the kinetics of initiation of the reactions of alkyl halides with magnesium. Supplementary material to this paper presents the calculated effect of a regular increase in the



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Figure 5. Product distribution in the reaction of $c-C_7H_{13}Br$ (0.001 M, 0.01 mmol) with magnesium turnings (25 mg-atom) in the presence of TMPO[•] (0.50 M, 5.0 mmol) and *tert*-amyl alcohol (5.0 M), as a function of time (0.05 M LiBr, Et₂O, 20 °C): (•) total; (•) TMPO-c-C₇H₁₃ (TMPOR); (•) cycloheptane (RH); (□) cycloheptane (R(-H)). Final yields were as follows: TMPOR, 95%; RH, 3%; R(-H), 2%. No bicycloheptyl was observed at anytime. The estimated range in the absolute yields is ±5%.



Figure 6. Yields of TMPO-c-C₇H₁₃ (TMPOR, ▲) and cycloheptane (RH, ■) as a function of [TMPO⁺]₀ (M) for the reaction of c-C₇H₁₃Br (0.001 M, 0.01 mmol) with magnesium turnings (25 mg-atom) in a solution containing *tert*-amyl alcohol (5.0 M), LiBr (0.05 M), and Et₂O (20 °C). The combined yields of RH and TMPOR account for ≥93% of the cycloheptyl groups. In all cases, the yields of cycloheptene and bicycloheptyl are ≤5% and ≤2%, respectively. The estimated range in the absolute yields is ±5%.

area of the metallic surface on the pseudo-first-order rate constant for disappearance of RBr.

Products of the Reaction between Cycloheptyl Bromide and Magnesium in the Presence of *tert*-Amyl Alcohol and TMPO[•]. In the presence of a large excess of TMPO[•] (500 equiv), cycloheptyl bromide reacts with magnesium to give the TMPO[•] adduct TMPO-c-C₂H₁₃ (\geq 95%), cycloheptane (3%), and cycloheptene (2%) (Figure 5). No bicycloheptyl was seen at any time.

The reactions of cycloheptyl bromide with magnesium in the presence of lower initial concentrations of TMPO[•] proceed to give cycloheptane and TMPO-c-C₇H₁₃ as the major products—the sum of their yields accounts for >90% of the cycloheptyl moieties. The dependence of the relative yields of RH and TMPOR on the initial concentrations of TMPO[•] (Figure 6) strongly suggests a common precursor (free cycloheptyl radical) for both products. The concentration of TMPO[•] at which this precursor partitions equally between RH and TMPO— $[TMPO[•]]_o = 0.025$ M—combined with the known bimolecular rate constant for the reaction of TMPO[•] with alkyl radicals (1.0×10^9 L mol⁻¹ s⁻¹³⁸) allows an estimation of the median lifetime of intermediate cycloheptyl radicals: $\tau \simeq 10^{-7}$ s.

Figure 7 shows the result of an experiment carried out under the conditions used in Figure 5, with the exception that the initial concentration of cycloheptyl bromide was increased by a factor of 10 (from 0.001 to 0.010 M). The yield of TMPOR is > 80%, which establishes that at least this fraction of the starting RBr is converted to radicals. The production of approximately equal amounts of alkene (ca. 9%) and alkane (ca. 10%) is puzzling.



Figure 7. Product distribution in the reaction of $c-C_7H_{13}Br$ (0.010 M, 0.10 mmol) and magnesium turnings (25 mg-atom) in the presence of TMPO[•] (0.50 M, 5.0 mmol) and *tert*-amyl alcohol (5.0 M), as a function of time (0.05 M LiBr, Et₂O, 20 °C): (•) total; (•) TMPOr- $c-C_7H_{13}$ (TMPOR); (•) cycloheptane (RH); (□) cycloheptene (R(-H)). Final yields were as follows: TMPOR, 81%; RH, 10%; R(-H), 9%. The apparent zero-order rate, k^{obsd} (TMPOR) $\simeq 2 \times 10^{-5}$ mol L⁻¹ s⁻¹. The estimated range in the absolute yields is ±5%.

Their formation cannot be attributed to the disproportionation of cycloheptyl radicals, since very little bicycloheptyl ($\leq 2\%$) is formed. Four types of processes might be responsible for the production of cycloheptane and cycloheptene: reaction of TMPO[•] with RBr, reaction of TMPO⁻ with RBr, reactions involving metallic impurities in the magnesium or transition-metal contaminants from other sources, and decomposition of product TMPO-c-C₇H₁₃. We consider these candidates in turn below.

Reaction of TMPO' with RBr. We find no evidence for S_N^2 type reactivity of TMPO' toward cycloheptyl bromide. Ethereal solutions containing RBr and TMPO' are indefinitely stable at 20 °C. Nucleophilic attack of di-*tert*-butylamine-*N*-oxyl (DTBNO') on methyl trifluoromethanesulfonate has been inferred, but not proven.⁵⁰ Methyl iodide, a good electrophile in S_N^2 reactions, reduces rather than alkylates TMPO' in benzene at 100 °C to give 2,2,6,6-tetramethylpiperidinium iodide.⁵¹

Reaction of TMPO⁻ with RBr. In the presence of TMPO⁻ (0.20 M) (eq 1), cycloheptyl bromide (0.010 M, 0.10 mmol) reacts with magnesium (25 mg-atom) in a solvent containing *tert*-amyl alcohol

(5.0 M) and LiBr (0.05 M) in Et₂O and gives cycloheptane (54%), bicycloheptyl (29%), cycloheptene (14%), and TMPO-c-C₇H₁₃ (\leq 3%). The distribution of the *hydrocarbon* products is within experimental uncertainty (\pm 5%), the same as that in the reaction without added TMPO⁻ (cf. Figure 2). We conclude, therefore, that reaction between TMPO⁻ and RBr is not an important process in this system. The small quantity of TMPO-c-C₇H₁₃ observed in this case can be ascribed to trace amounts of TMPO[•] in the reacting solution, since less than 0.1% of TMPO-c-C₇H₁₃ is produced when a solution containing preformed TMPO⁻ (0.20 M) and c-C₇H₁₃Br (0.010 M) is stirred for 1 h at 20 °C.

Impurities in the Magnesium. Addition of FeCl₃. The substitution of triply sublimed magnesium, magnesium turnings of lesser purity, or a Mg-Fe-Zn alloy for the Mg chips usually employed in these studies (Alfa resublimed⁵²) did not cause experimentally significant changes in the distribution of products (Table I, Experimental Section). The reaction between cycloheptyl bromide and magnesium turnings in the presence of FeCl₃ (1% wt/v) and TMPO[•] gives 76% TMPO-c-C₇H₁₃, 21% cycloheptane, 5% cycloheptene, and <1% bicycloheptyl. Additional cycloheptane



Figure 8. Plot of $[c-C_5H_9Br]_1/[c-C_5H_9Br]_0$ vs t for the reaction of a 2-mmol portion of cyclopentyl bromide with magnesium turnings (21 mg-atom; 0.5 M LiBr, Et₂O, 20 °C): $k^{obsd} \simeq 3 \times 10^{-5}$ mol L⁻¹ s⁻¹. This is a zero-order plot of the data from the first run of Figure 4.

seems to have been formed at the expense of TMPO-c- C_7H_{13} . Transition metals affect the distribution of products of Grignard reactions.^{53–57} The magnitude of the effect on product distribution seen here is sufficiently small that trace metals (from syringe needles and cannulae) probably have little influence on our results.

Decomposition of TMPO-c- C_7H_{13} . We find that approximately 15% of TMPO-c-C₇H₁₃ decomposes within a period of 45 min when added to a stirred, aerated solution of *tert*-amyl alcohol (5.0 M), lithium bromide (0.05 M), and Et₂O at 20 °C. The solution, originally clear and colorless, acquires an orange hue, indicating the reappearance of TMPO[•]. The thermal decomposition of many *N*,*N*,*O*-trialkylhydroxylamines produces equal amounts of *N*,*N*-dialkylhydroxylamine and olefin.⁵⁸ This process is slow in the absence of oxygen: for example, tri-*tert*-butylhydroxylamine has a half-life of ca. 2 years in C₂D₅Br at 20 °C.³⁹ Decomposition is much faster in air-saturated systems.⁵⁸ Traces of oxygen and transition metals may catalyze the decomposition of TMPO-c-C₇H₁₃ to olefin and TMPOH or TMPO[•].

Model for the Apparent Kinetic Behavior. The reaction of c-C₇H₁₃Br with magnesium turnings in a system containing dibromoethane (0.005 M), tert-amyl alcohol (5.0 M), LiBr (0.05 M), and Et₂O proceeds at a rate that appears to be zero-order in cycloheptyl bromide (Figure 2). The observed rates are unaffected by the presence of TMPO[•] (cf. Figures 2 and 7). Previous studies have established that the reaction between organic halides and magnesium is, in the *absence* of dibromoethane, alcohols, and TMPO*, pseudo-first-order in alkyl halide and pseudo-zero-order in magnesium.¹¹ Several observations suggest that the kinetic behavior observed in the studies reported here is artifactual. First, the addition of 1,2-dibromoethane is required to promote the reaction of $c-C_7H_{13}Br$ with Mg in the presence of high concentrations of tert-amyl alcohol. Without dibromoethane, negligible reaction (<2%) occurs between RBr and Mg (or TMPO[•] and Mg) over a 2.5-h period. It is likely that the rate of corrosion of the metal by the dibromide and the resulting increase in reactive metallic surface area is partially reflected in the apparent rate of reaction of cycloheptyl bromide. Second, we have observed similar kinetic phenomena in the reaction of alkyl halides with magnesium in solvents containing neither TMPO[•] nor alcohol. Figure 4 gives the result of an experiment in which two 2-mmol portions of cyclopentyl bromide were allowed to react sequentially with magnesium turnings in a solution of lithium bromide in diethyl ether. In the first run, significant

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curvature is evident in the first-order plot for disappearance of the halide. The same data generate a reasonably straight line in a zero-order plot (Figure 8, $k^{obsd} \simeq 3 \times 10^{-5} \text{ mol } L^{-1} \text{ s}^{-1}$). A more detailed analysis of the kinetic behavior expected in a reaction characterized by increasing reactive magnesium surface area is presented in the supplementary material to this article.

Discussion

This work is compatible with the proposal that free cycloheptyl radicals are bona fide intermediates in the reaction between cycloheptyl bromide and magnesium. Approximately 95% of the cycloheptyl groups are trapped by the radical scavenger TMPO[•] under conditions where, in the absence of the nitroxyl, an equivalent yield of the organometallic species is inferred.

These experiments do not, by themselves, unambiguously establish that the intermediate radical is not "surface-bound": that is, associated in some way with the magnesium surface.^{22,59} The idea of surface-bound radicals has been advanced by Walborsky, primarily to account for one significant but isolated experimental observation that he has held to be incompatible with free-radical intermediates: viz., the substantial retention of stereochemistry observed in conversion of optically active 1-bromo-1-methyl-2,2-diphenylcyclopropane to the corresponding Grignard reagent. We have not applied the test of trapping with TMPO[•] to this system, and thus cannot comment directly on the concept of surface-bound radicals as it applies (or does not apply) to it, but we make several observations concerning this suggestion in the context of aliphatic halides. First, complete loss of stereochemistry is observed in the one representative secondary alkyl system (2norbornyl) that has been examined.⁸ Second, different organic halides may follow different mechanistic paths on conversion to Grignard reagents. A substantial number of observations concerning structural rearrangements and byproducts for the representative aliphatic systems of interest in organic synthesis can, nonetheless, be rationalized without intellectual strain by hypothesizing as intermediates free radicals in solution having normal activity. Third, the phrase "surface-bound radical" may itself be misleading and is certainly ill-defined. Surface magnesium alkyls are plausible (although unproved) intermediates along the path to soluble Grignard reagents, but need not have any of the characteristics in reactivity or magnetic properties that define a free radical. If the chemical reactivity of the hypothetical surface-bound radical is defined to be sufficiently similar to that of a free radical in solution so that the available tests for the structure of reactive intermediates give indistinguishable results when applied to the two, the concept of a surface-bound radical may not be a useful addition to the vocabulary of physical organic chemistry.

In the experiments reported here, the observation that the yield of TMPOR increases at the expense of the yield of Grignard reagent indicates that both are derived from the same precursor, cycloheptyl radical. The concentration of TMPO' diminishes during the course of a reaction as a result of its facile reduction by magnesium; we have not corrected the concentrations of TMPO[•] for occurrence of this reaction. Thus, the value of $\tau \simeq$ 10^{-7} s is an order-of-magnitude estimate for the median lifetime of cycloheptyl radicals. This value, nevertheless, agrees with that inferred from systems in which intermediate radicals undergo competitive unimolecular rearrangements before reduction to organometallic products.^{8,25,29,60} The concordance of the value of τ inferred from the results of two independent sets of experiments further suggests that the contribution from reaction of cycloheptyl radicals with nitroxyl radicals that are physisorbed on or otherwise associated with the magnesium surface is small.⁶¹ We find no evidence that the addition of large quantities of tert-amyl alcohol to systems containing simple alkyl halides and

magnesium in diethyl ether affects the conversion of RBr to radicals, once the reaction has begun. The alcohol primarily affects the rate of the reaction between RBr and magnesium, not the products of the reaction.⁶² Deactivation of the magnesium surface by adsorption of the alcohol or its alcoholate is overcome by adding 1,2-dibromoethane to mixtures containing RBr, alcohol, LiBr, and magnesium in diethyl ether. Many heterogeneous reactions involving metals and alkyl halides will proceed if adsorbed films are not allowed to deactivate the metallic surface, regardless of the method of cleaning. Thus, reports describe the use of ultrasonic irradiation as a method of mechanically scouring the surface of lithium⁶³ and zinc.⁶⁴ Such in situ cleaning promotes the one-step coupling of organic halides with carbonyl compounds, even in wet, technical-grade THF.63

We attribute the apparently anomalous zero-order kinetics in the reaction of cycloheptyl bromide with magnesium to the increase in reactive surface area that accompanies the reaction of 1,2-dibromoethane with magnesium ("initiation"). Such kinetic behavior is consistent with a mathematical model that demonstrates the effect of an increase in area on the observed rate of a process that is intrinsically first-order in reactant. This model, moreover, offers an alternative explanation for the zero-order rates observed in the reactions of 1- and 2-adamantyl bromides with magnesium.⁵⁹ We emphasize that the observation of zero-order kinetic behavior in these complex heterogeneous systems is not unambiguous proof for the existence of a surface-adsorbed "transient species"59 as the sole intermediate that partitions to give products, and we note the difficulties in obtaining mechanistically useful kinetic data when heterogeneous organic reactions are carried out in systems that are hydrodynamically ill-defined.

Experimental Section

General Procedures. All reactions were carried out by using standard inert-atmosphere techniques.⁶⁵ Argon was passed through commercially available oxygen- and water-scrubbing catalysts (Oxisorb). Reagentgrade diethyl ether was distilled under argon from a dark purple solution containing disodium benzophenone dianion directly into a storage flask with a Teflon stopcock (the flask had been previously flame dried and allowed to cool under a stream of argon). tert-Amyl alcohol (Baker) was distilled under argon from calcium hydride, deoxygenated by passing argon through the liquid for ca. 2 h, and transferred to a storage flask (which had been previously flame dried and allowed to cool under a stream of argon). 2,2,6,6-Tetramethylpiperidine-N-oxyl (TMPO*) was purchased from Aldrich (98%) and sublimed before use (26 °C, 0.5 Torr). Cycloheptyl bromide (Aldrich), cyclopentyl bromide (Aldrich), and 1,2-dibromoethane (Baker) were passed through activated alumina and subjected to three freeze-pump-thaw cycles before use. GLC analyses indicated >98% purity for each. Magnesium (Alfa, 99.99%, "Chips for Grignard Resublimed"; Baker turnings "Purified for Grignard Reactions") and hydrocarbons used as internal GLC standards were used as received. A sample of magnesium-4 wt % iron-3 wt % zinc alloy was a gift from Edwin Backman and Professor Merton C. Flemings, MIT Department of Materials Science and Engineering. Triply sublimed magnesium was a gift from Dr. Hal Freedman of Dow Chemical Co.

(62) A dramatic change in the product distribution has been observed on addition of tert-butanol (0.4 M) to systems containing 2-(3-iodopropyl)cyclohexanone and lithium wire in THF (eq i, ii). In each case, the process



that produces tetrahydrochroman probably involves intramolecular alkylation by a magnesium or lithium enolate. This type of reaction is not possible in our system. (Crandall, J. K.; Magaha, H. S. J. Org. Chem. 1982, 47, 5368-5371)

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Mechanism of Formation of Grignard Reagents

Anhydrous ferric chloride (Fisher sublimed) was used as received. Anhydrous lithium bromide (Alfa, 98%) was heated to 150 °C under vacuum (0.5 Torr, 36 h) in order to remove residual water.

Saturated solutions of lithium bromide in diethyl ether were prepared by stirring excess anhydrous LiBr with Et_2O for 24 h at 25 °C. Stirring was stopped, and fine insoluble particles were allowed to settle over a 12-h period. The solution was transferred by cannula to a Schlenk storage flask equipped with a Teflon stopcock (previously flame dried and allowed to cool under an argon stream). The concentration of LiBr in Et_2O was determined by weighing the quantity of salt remaining after removing the solvent and heating the residue to 150 °C under vacuum (0.5 Torr, 2.5 h): [LiBr] = 1.0 M at saturation.

Solutions of cycloheptylmagnesium bromide were prepared by allowing cycloheptyl bromide to react with magnesium turnings in diethyl ether at 0 °C. Concentrations of Grignard reagent were determined by titration with *sec*-butanol in xylenes, using 2,2'-biquinoline⁶⁶ as indicator.

Solutions containing cycloheptane and cycloheptene were analyzed by GLPC on either of two columns: a tandem column of octane on Porasil C connected to either a 10% Carbowax 20 M column or an SE-30 Hi-Plante column. Bicycloheptyl and N-cycloheptoxy-2,2,6,6-tetramethylpiperidine (TMPO-c-C₇H₁₃) were analyzed by GLC on a 3% SE-30 column (12 ft \times 0.125 in.): flow = 40 mL min⁻¹, injector temperature = 200 °C, column temperature = 160 °C.

Reactions of Cycloheptylmagnesium Bromide with TMPO' in the Presence of tert-Amyl Alcohol (Figure 1). A 25-mL round-bottomed flask containing a magnetic stirring bar was capped with a septum, flame dried, and allowed to cool under a stream of argon. TMPO' (0.156 g, 1.0 mmol, 10 equiv) was quickly added to the flask. The septum was replaced and wired down, and the flask was further flushed with argon (ca. 15 min). A 1.0 M solution (5 mL) of lithium bromide in diethyl ether and tert-amyl alcohol (0-2.75 mL, 0-25 mmol) were added to the flask by syringe. Enough Et₂O (3.6-5.0 mL) was added to bring the volume of the solution to 10.0 mL. A cool water bath (18 °C) was placed beneath the flask, and the stirring was begun. The system was vented to the atmosphere through an argon bubbler. A solution of 0.19 M cycloheptylmagnesium bromide (0.52 mI, 0.10 mmol), nonane (11.2 mg, internal GLC standard), and tetradecane (19.7 mg, internal GLC standard) in 0.5 M LiBr/Et₂O was added by cannula, dropwise, over a 60-s period. The resulting solutions were slightly turbid, and the orange color of TMPO* had diminished. The products were analyzed directly by GLC, without further workup of the mixture. The yields of cycloheptene (R(-H)), cycloheptane (RH), and bicycloheptyl (RR) were corrected for the amounts of these hydrocarbons present in the stock solution of Grignard reagent. A response factor of 1.0 was assumed for all hydrocarbons; a response factor of 1.28 was determined for TMPO $c-C_{7}H_{13}$. The yield of RH minus the yield of R(-H) gave the yield of RH due to hydrolysis of RMgBr by the alcohol. The yields of RH and R(-H) (from disproportionation and combination of R^{\bullet}), and RR (from combination of R*) and TMPOR were combined to give the overall yield for the reaction between TMPO' and RMgBr.

Measurement of Relative Rates of Reaction of TMPO' and Cyclopentyl Bromide with Magnesium. Magnesium turnings (0.50 g, 21 mg-atom) and a magnetic stirring bar were placed in a 100-mL, one-necked round-bottomed flask, which was then capped with a rubber septum, flame dried, and allowed to cool under a stream of argon. Fifty milliliters of 0.5 M LiBr in Et₂O was added by cannula. The flask was placed in a cool water bath (20 °C), and the stirring was begun. Dibromoethane (0.05 mL, 0.5 mmol) was injected into the solution. Nonane (0.10 mL, internal GLC standard) and cyclopentyl bromide (0.20 mL, 1.9 mmol) were added after ca. 10 min. Samples were removed (each ≤0.15 mL) by cannula under a slight positive pressure of argon (2-3 psi) and were quenched by addition to small tubes containing ca. 0.5 mL of a cold, saturated aqueous solution of sodium chloride. Following extraction, the ethereal layer of each tube was subjected to GLC analysis. The pseudo-first-order rate constant was obtained by plotting ln ([c-C₅H₉Br]/ $[c-C_5H_9Br]_0$ vs t and evaluating the slope by linear-regression analysis. The solution from the reaction was replaced with ca. 20 mL of 0.5 M LiBr in Et₂O. Dibromoethane (0.05 mL, 0.5 mmol) was injected into the flask. The reaction was allowed to continue for ca. 5 min. The spent solution was replaced with a solution containing TMPO[•] (0.63 g, 4.0 mmol) and 0.5 \dot{M} LiBr in Et₂O. The stirring rate was approximately the same as in the first run. Samples were removed by syringe and injected into 5-mL tubes that had been capped with septa, wired shut, flame dried, and allowed to cool under a stream of argon. The volume of each sample was recorded. Each sample was transferred by cannula into a Pyrex cuvette (1-cm path length) that had been capped with a septum, flame dried, and allowed to cool under argon. The absorbance of each sample was measured at $\lambda = 445$ nm and then multiplied by V_0/V_t to give values

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that were corrected for the change in volume of the reacting solution. Linear regression analysis of the plot of $\ln [(Abs_t - Abs_{\infty})/Abs_0]$ vs t gave the observed pseudo-first-order rate constant. The relative rate of reaction of TMPO[•] and cyclopentyl bromide with magnesium was obtained by comparing the observed rate constants.

A complementary experiment, in which TMPO[•] was allowed to react with magnesium in the first run, was performed similarly. The relative rates measured in the two experiments were averaged.

Preparation of 1-Hydroxy-2,2,6,6-tetramethylpiperidine (TMPOH). TMPO[•] (0.475 g, 3.0 mmol) was allowed to react with magnesium turnings (0.68 g, 28 mg-atom) in 30 mL of a solution containing LiBr (0.3 M) in Et₂O. The solution was turbid and colorless at the end of the reaction. The ethereal solution was removed via a cannula, washed with two 20-mL portions of deoxygenated H₂O, and dried over anhydrous MgSO₄. Solvent was removed by rotary evaporation, leaving a clear, light orange, viscous liquid. TMPOH was purified by sublimation (0.05 Torr, 25 °C): mp 36.5–38.0 °C (lit.⁴⁴ mp 38.5–40.2 °C; lit.⁶⁷ mp 39–40 °C); yield, 0.16 g (33%). Upon exposure to air, the off-white solid was oxidized to TMPO[•].

Reaction of Cycloheptyl Bromide with Magnesium in the Presence of tert-Amyl Alcohol (Figure 2). Magnesium turnings (Alfa; 0.62 g, 26 mg-atom) and a small magnetic stirring bar were placed in a 25-mL one-necked, round-bottomed flask with attached side arm (11 mm o.d.). A Dewar condenser was placed in the neck of the flask; the upper outlet of the condenser and the side arm of the flask were fitted with rubber septa. The apparatus was flushed with argon, flame dried, and allowed to cool under a steady argon stream. Diethyl ether (10 mL), 0.10 mL of 1,2-dibromoethane (1 mmol), and 0.50 mL of a 0.201 M solution of cycloheptyl bromide (0.10 mmol) in Et₂O were added to the flask. Vigorous stirring was begun. The reaction was allowed to proceed for ca. 20 min under an extremely slow stream of argon. The spent solution was removed by cannula, and the magnesium was rinsed with two 10-mL portions of Et₂O. A cool water bath (20 °C) was placed beneath the flask, and powdered dry ice was placed in the condenser. A solution containing tert-amyl alcohol (5.5 mL, 50 mmol) and Et₂O (1.8 mL) was added to the flask by cannula. Vigorous stirring was begun. A solution containing cycloheptyl bromide (0.10 mmol), heptane (5.00 mg, internal GLC standard), pentadecane (4.74 mg, internal GLC standard), and LiBr (5 mmol) in Et_2O was rapidly added to the flask by cannula. The initial volume of the reaction solution was 10.0 mL: $[c-C_7H_{13}Br]_0 =$ 0.010 M; [tert-amyl alcohol]₀ = 5.0 M. Dibromoethane (45 μ L, 0.50 mmol) was injected into the solution, and sampling was begun. Samples (0.30-0.60 mL; the volume of each was recorded) were removed by syringe under a slight positive pressure of argon (4-5 psi) via the side arm; each was added to a small tube containing deoxygenated, saturated NaCl in H₂O (ca. 1 mL). The tubes were stored at -78 °C following extraction. The ethereal layer of each sample was subjected to GLC analysis, and the progress of the reaction was monitored by plotting percent products vs t (t was multiplied by V_0/V_t to give values that were corrected for the change in volume caused by withdrawal of samples). The reaction of 0.001 M cycloheptyl bromide with magnesium in the presence of tert-amyl alcohol and of 0.010 M cycloheptyl bromide with magnesium in the absence of tert-amyl alcohol were performed and analyzed similarly.

Rate of Reaction of Cyclopentyl Bromide with Magnesium after Addition of 0.08 M tert-Amyl Alcohol (Figure 3). A 100-mL round-bottomed flask containing magnesium turnings (0.26 g, 11 mg-atom) and a magnetic stirring bar was capped with a septum, wired shut, flame dried, and allowed to cool under an argon stream. Diethyl ether (50 mL) and 1,2-dibromoethane (20 $\mu L,$ 0.2 mmol) were added to the flask. Vigorous stirring was begun. The solution was cooled to 0 °C, and the flask was placed under a static pressure of ca. 2 psi argon. Cyclopentyl bromide (0.20 mL, 1.9 mmol) and nonane (0.10 mL, internal GLC standard) were injected into the solution, and sampling was begun. Aliquots (each ≤ 0.15 mL) were removed by cannula and quenched with cold, saturated NaCl/H₂O. The ethereal layer of each was analyzed by GLC following extraction. tert-Amyl alcohol (0.42 mL, 3.8 mmol) and another 1.9 mmol portion of cyclopentyl bromide were added at the indicated times. The progress of reaction was determined by plotting ln $([c-C_5H_9Br]/(c-C_5H_9Br]_0)$ vs t.

Data presented in Figures 4 and 8 were obtained in a similar manner. **Reactions of Cycloheptyl Bromide with Magnesium in the Presence of TMPO^{*} and tert**-Amyl Alcohol (Figures 5-7). The same general procedure was employed as in reactions between cycloheptyl bromide and magnesium in the absence of TMPO^{*} (Figure 2). The nitroxyl radical was added to the solution containing c-C₇H₁₃Br either as a solid (for reactions with [TMPO^{*}]₀ \geq 0.10 M), or as a solution in Et₂O (for re-

⁽⁶⁷⁾ Rozantsev, E. G.; Gur'yanova, E. N. Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.) 1966, 936-939.

Table I. Effect of Metallic Purity on the Products of the Reaction between Cycloheptyl Bromide and Magnesium in the Presence of TMPO[•] and *tert*-Amyl Alcohol^a

	% yield ^b				
Mg type ^c	TMPOR	RH	R(-H)	RR	
Alfa, 99.9%	81	10	9	0	
Baker, 99.8%	82	8	9	0	
triply sublimed	87	5	8	0	
Mg-4%Fe-3%Zn	83	8	9	0	
Alfa + FeCl ₃ ^d	72	21	6	<1	

^{*a*} RBr (0.010 M) was allowed to react with Mg turnings (25 mgatom) at 20 °C in a solvent containing TMPO[•] (0.50 M), *tert*-amyl alcohol (5.0 M), and LiBr (0.5 M) in Et₂O; R = c-C₇H₁₃. ^{*b*} Yields were determined by GLC analysis. ^{*c*}Sources of magnesium are given in the General Procedure section. ^{*d*} The solution contained ca. 1% (wt/v) of anhydrous FeCl₃.

actions with $[TMPO^{*}]_{0} \leq 0.10$ M). Addition of reagents, sampling, extraction, and GLC analysis of the aliquots were performed as described above. A survey of the influence of the origin of the magnesium and of added FeCl₃ showed no significant variation (Table I).

Reaction of Cycloheptyl Bromide with Magnesium in the Presence of TMPO⁻ and tert-Amyl Alcohol. After preparation of magnesium turnings (0.61 g, 25 mg-atom) as described above, a solution containing TMPO[•] (0.469 g, 3.0 mmol), tert-amyl alcohol (8.2 mL, 75 mmol), and LiBr (7.5 mmol) in Et_2O was added to the reaction vessel by cannula. The initial volume of the solution was 15.0 mL: $[TMPO^{\circ}]_{0} = 0.20 \text{ M};$ $[tert-amyl alcohol]_0 = 5.0 \text{ M}; [LiBr] = 0.50 \text{ M}. \text{ A cool water bath } (20)$ °C) was placed beneath the flask, and vigorous stirring was begun. Dibromoethane (45 μ L, 0.5 mmol) was injected into the solution after 1 min. The orange color of TMPO' was no longer evident after 20 min, and the solution was slightly turbid. Five milliliters of the solution was removed to another flask and was used to test the reactivity of TMPOtoward $c-C_7H_{13}Br$. To the mixture remaining in the reaction vessel was added 0.50 mL of a solution containing cycloheptyl bromide (0.10 mmol), heptane (3.64 mg, internal GLC standard), and pentadecane (4.35 mg, internal GLC standard) in Et₂O, followed by 1,2-dibromoethane (45 μ L, 0.5 mmol). The reaction was allowed to proceed for 25 min at 20 $^{\circ}$ C. A sample was withdrawn, extracted, and analyzed by GLC, as described above.

Preparation of N-Cycloheptoxy-2,2,6,6-tetramethylpiperidine (TMPO-c- C_7H_{13}). A 300-mL round-bottomed flask was capped with a septum, flame dried, and allowed to cool under a stream of argon. TMPO[•] (3.90 g, 25 mmol) and a magnetic stirring bar were placed in the flask. The septum was replaced and wired down, and the vessel was further flushed with argon. Diethyl ether (50 mL) was added to the flask, an ice bath was placed beneath the flask, and stirring was begun. Cycloheptylmagnesium bromide (1.0 M in Et₂O) was added dropwise until the orange color of TMPO* had disappeared. The colorless, turbid solution was washed with three 50-mL portions of deoxygenated H₂O. The aqueous layers were combined and extracted with Et₂O (50 mL). The organic layers were combined, dried with anhydrous MgSO₄, and concentrated to 5 mL by rotary evaporation. The crude product was distilled through a short-path head at reduced pressure (0.02-0.03 Torr). The fraction having a boiling range of 65-70 °C (0.96 g) was a clear, colorless, viscous liquid and was analyzed by GLC: TMPO-c-C₇H₁₃, 85%; bicycloheptyl, 15%. TMPO-c- C_7H_{13} that remained in the pot (0.3 mL, >98% pure by GLC) was separated from gummy residues by molecular distillation (bath temperature 60-75 °C; 0.04 Torr): ¹H NMR (CDCl₃) § 3.80 (m, 1 H), 1.98 (m, 2 H), 1.75–1.16 (m, 16 H), 1.10 (s, 12 H) ppm; mass spectrum (relative abundance) parent ion m/e 253 (<1), fragments m/e 238 (<1), 157 (11), 142 (100), 69 (9), 55 (11), 41 (16). Anal. $(C_{16}H_{31}NO)$: C, H, N.

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Registry No. TMPO[•], 2564-83-2; TMPOH, 7031-93-8; c- $C_7H_{13}MgBr$, 78378-12-8; c- C_5HgBr , 137-43-9; c- $C_7H_{13}Br$, 2404-35-5; TMPO-*c*- C_7H_{13} , 120881-31-4; Mg, 7439-95-4; *tert*-amyl alcohol, 75-85-4; bi-cycloheptyl, 23183-11-1; cycloheptane, 291-64-5; cycloheptene, 628-92-2.

Supplementary Material Available: A treatment of the influence of changing surface area of the magnesium on the kinetics of disappearance of alkyl halides (6 pages). Ordering information is given on any current masthead page.

Borderline between E1 and E2 Mechanisms. Bimolecular Base-Promoted Elimination via Ion Pairs Competing with Concerted E2 Elimination

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Abstract: The solvolysis of 2-chloro-2-methyl-1-phenylpropane (1) in methanol or in 25 vol % acetonitrile in water at 25 °C yields substitution product 2 (ether or alcohol) and the two elimination products 3 and 4. The olefin fraction in the aqueous solution does not increase significantly in the presence of 0.75 M sodium hydroxide. In methanol, on the other hand, the fraction of 3 and 4, the ratio [3]/[4], and the rate of disappearance of 1 increase with methoxide ion concentration. The kinetic isotope effects $(k_{12}^{H} + k_{13}^{H} + k_{14}^{H})/(k_{12}^{d_2} + k_{13}^{d_2} + k_{14}^{d_2}) = 1.41$ and 1.42, measured for the solvolysis of the dideuterated analogue d_2 -1 in water/acetonitrile and in methanol, respectively, are too large to be secondary effects on a rate-limiting ionization step, but they suggest reaction via a reversibly formed carbocationic intermediate. The solvolysis of the hexadeuterated analogue d_6 -1 exhibits "normal" secondary kinetic isotope effects, $(k_{12}^{H} + k_{13}^{H} + k_{14}^{d_6}) = 1.79$ and 1.81 in water/acetonitrile and methanol, respectively. The presence of 2 M NaOMe increases the isotope effect for d_2 -1 to 2.4 but decreases the effect for d_6 -1 to 1.35. These results indicate that 3 is formed by a parallel methoxide-promoted one-step concerted as $k^H/k^{d_2} = 4.9$ (on the basis of the assumption that the elimination product ratio [3]/[4] for the carbocationic route is not affected by MeO⁻).

It is conceivable that some elimination reactions that have been classified as E2 with carbocationlike transition states consist, in fact, of a mixture of concerted elimination (E2) and elimination from a reversibly formed carbocation ion-pair intermediate (" $E2_{ip}$ "). The measured kinetic deuterium isotope effect for the elimination reaction is then composed of a substantial isotope effect on the E2 route and a small isotope effect on the carbocationic path. A large proportion of the stepwise route, which exhibits