

Trapping of Free Alkyl Radical Intermediates in the Reaction of Alkyl Bromides with Magnesium

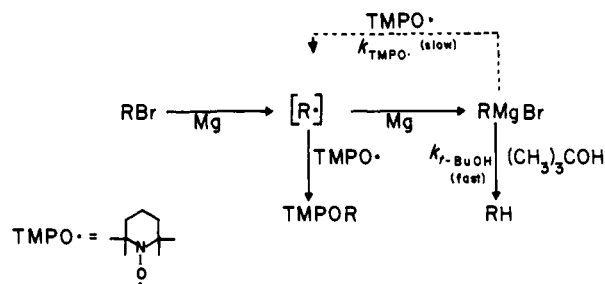
Sir:

Several kinds of evidence have implicated alkyl radicals as intermediates in the reaction of alkyl halides with magnesium.²⁻⁵ CIDNP studies have been especially valuable in establishing that at least some part of the Grignard reagent product derives from radical precursors.⁴ Detailed mechanistic interpretation of these CIDNP studies has been difficult because it has not been clear whether they reflect the major pathway for formation of Grignard reagent or a minor side reaction. Here we describe experiments which indicate that >80% of cyclopentyl bromide (RBr) is converted by reaction with magnesium into a new species, distinct from and a precursor to cyclopentylmagnesium bromide (RMgBr), which reacts with 2,2,6,6-tetramethylpiperidine nitroxyl (TMPO•) in what appears to be an unexceptional radical-radical coupling reaction and forms *O*-cyclopentyl-2,2,6,6-tetramethylhydroxylamine (TMPOR). These studies suggest that free cyclopentyl radicals are precursors of the *major* fraction of this representative Grignard reagent.

The principal difficulty in efforts to trap free radicals during the formation of Grignard reagents has been that these organometallic species themselves react rapidly with all effective radical scavengers which are now known (dioxygen, halogens, nitroxyls, nitrones, and others). We have been able to circumvent this problem by carrying out the reaction of alkyl bromides with magnesium in a solution containing both TMPO• and *tert*-butyl alcohol (*t*-BuOH). The reaction of the Grignard reagent with *t*-BuOH is sufficiently fast that its reaction with TMPO• is entirely suppressed (Scheme I).⁶

Table I summarizes relevant experiments. Reaction of RBr with magnesium, followed by analysis by titration⁷ and GLC, yields the products shown in entry 1. Careful analyses of the yields of hydrocarbons suggest that olefin and dimer are formed almost exclusively by radical-radical combination and disproportionation.⁸ Reaction of a solution of Grignard reagent with 10 equiv of *t*-BuOH, 7 equiv of TMPO•, or a mixture of the two establishes two important facts:⁹ first, in the *absence* of *t*-BuOH, the conversion of RMgBr into TMPOR on reaction with TMPO• is essentially quantitative;¹⁰ second, in the *presence* of *t*-BuOH, this coupling reaction is suppressed and

Scheme I. Reactions Occurring during Reaction of Cyclopentyl Bromide with Magnesium in an Ether Solution Containing TMPO• and (CH₃)₃COH^a



^a Experimental evidence indicates that $k_{\text{BuOH}} > k_{\text{TMPO}}$ (see text).

formation of cyclopentane becomes the major reaction. Entry 4 represents an experiment in which a solution of RMgBr, prepared at the same concentration as those used in entries 2 and 3, was added to a mixture of *t*-BuOH and TMPO• under conditions comparable with those of entries 2 and 3, and over a period of time roughly comparable with the time required to carry out the reactions of entries 6-11. The yields reported in entry 5 (italics) were obtained using slower addition and better stirring to minimize the effects of local depletion of reagents in the volume in which mixing and reaction is taking place. These yields are calculated based on Grignard reagent. For comparison, entry 4 also shows in italics yields based on the concentration of starting Grignard reagent rather than on alkyl bromide. Inspection of entry 5 suggests that, with good mixing, RMgBr reacts with *t*-BuOH to the virtual exclusion of TMPO•, but that with poorer mixing (entry 4) this selectivity is obscured.

Entries 6-11 summarize experiments in which the initial reaction of RBr with magnesium is carried out in solutions containing *t*-BuOH and/or TMPO•.¹¹ These reactions yield insoluble products. The reactions in the presence of *t*-BuOH take approximately twice as long to go to completion as those in its absence, possibly because of insoluble magnesium(II) *tert*-butoxides coating the magnesium surface.¹² When reaction is carried out in the presence of TMPO• (entries 7 and 8), the formation of the olefin and dimer [R(-H) and RR] characteristic of radical-radical reactions is suppressed, and

Table I. Products of Reaction of Cyclopentylmagnesium Bromide, and of Cyclopentyl Bromide and Magnesium, with *tert*-Butyl Alcohol and/or TMPO•^a

entry	step I ^b	step II ^b	yield, % (±2%) ^c					
			RMgBr	RH	R(-H)	RR	TMPOR	total
1	c-C ₅ H ₉ Br + Mg	titration ^d -GLC ^e	73 ^d	84 ^e	4 ^e	8 ^e		96
2	c-C ₅ H ₉ Br + Mg	10 <i>t</i> -BuOH		82	<i>f</i>	7		
3	c-C ₅ H ₉ Br + Mg	+7 TMPO•		11	12	17	59	99
4	c-C ₅ H ₉ Br + Mg	10 <i>t</i> -BuOH + 7 TMPO•		60	6	12	17	95
				<i>84</i>	<i>2</i>	<i>4</i>	<i>13</i>	<i>103</i>
5 ^g	c-C ₅ H ₉ Br + Mg	10 <i>t</i> -BuOH + 7 TMPO•		98	0	0	<i>Tr</i>	98
6	c-C ₅ H ₉ Br + Mg + 10 <i>t</i> -BuOH			47	19	35		101
7	c-C ₅ H ₉ Br + Mg + 5 TMPO•			2	6	6	84	98
8	c-C ₅ H ₉ Br + Mg + 7 TMPO•			Tr	4	2	96	103
9	c-C ₅ H ₉ Br + Mg + 10 <i>t</i> -BuOH + 7 TMPO•			15	Tr	Tr	84	99
10	c-C ₅ H ₉ Br + Mg + 10 <i>t</i> -BuOH + 3 TMPO•			16	3	Tr	72	91
11	c-C ₅ H ₉ Br + Mg + 10 <i>t</i> -BuOH + 2 TMPO•			28	8	<i>h</i>	52	

^a Reactions were carried out at 34 °C in diethyl ether, using [RBr]₀ ≈ 0.09 M. For all entries, 10 *t*-BuOH (e.g., 10 equiv of) corresponds to a concentration of ~0.8 M and 7 TMPO• (e.g., 7 equiv of) to a concentration of ~0.5 M. ^b In entries 2-4, RMgBr was prepared and added slowly (30 min) to an ether solution containing the reagents listed under step II; in entries 6-11, *t*-BuOH and/or TMPO• were present during the reaction of c-C₅H₉Br with magnesium. ^c Yields were estimated by GLC following treatment with concentrated brine solution (0 °C). Tr (trace) means that the compound was detected by GLC, but that the yield was <2%. Yields are based on starting RBr, except for the italicized yields in entries 4 and 5, which are based on RMgBr. ^d Yields were determined by the method of Watson and Eastham.⁷ ^e Yields were measured by GLC using internal standard techniques. ^f R(-H) was obscured by *t*-BuOH in the GLC trace. ^g The values in entry 5 were obtained by slow (30 min) addition to a very vigorously stirred solution of TMPO• and *t*-BuOH, and were thus carried out under conditions which result in better mixing than those used in entries 2-4. ^h Not determined.

TMPOR is the major product formed. The crucial experiment is that in entry 9. The major product of reaction of RBr with magnesium in the presence of both *t*-BuOH and TMPO \cdot is TMPOR, even though entries 4 and 5 indicate that RMgBr, if formed, would react preferentially with the *t*-BuOH under these conditions and yield RH. We rationalize this observation by Scheme I, in which intermediate cyclopentyl radicals are trapped by TMPO \cdot before they can be converted into cyclopentylmagnesium bromide.

We draw four conclusions from the data of Table I. First, reaction of RMgBr is faster with *t*-BuOH than with TMPO \cdot (apparently by a factor of ~ 10). Second, when the reaction of RBr with magnesium is carried out in the presence of *t*-BuOH and TMPO \cdot —conditions in which the Grignard reagent formed would be expected to be converted predominantly into RH—TMPOR is the major product observed. This observation is compatible with a mechanism (Scheme I) in which RBr is converted into R \cdot on reaction with magnesium, and those radicals are trapped by reaction with TMPO \cdot more rapidly than they are converted into RMgBr. Third, accepting Scheme I as a correct description of the mechanism of formation of TMPOR, the fact that the yield of TMPOR is $>80\%$ establishes that at least this fraction of the starting RBr is converted into radicals.¹³ Fourth, the intermolecular trapping reported here,¹⁴ the characteristic intramolecular rearrangements of 5-hexenyl,³ and the CIDNP observed for Grignard products⁴ are all compatible with free (as opposed to "surface-bound") alkyl radicals.¹⁵

References and Notes

- (1) Supported by the National Science Foundation, Grant CHE 7711282.
- (2) Walborsky, H. M.; Aronoff, J. *Organomet. Chem.* **1973**, *51*, 31–53. Walborsky, H. M.; Young, A. E. *J. Am. Chem. Soc.* **1964**, *86*, 3288–3292.
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- (4) Schaart, B. J.; Bodewitz, H. W. H. J.; Blomberg, C.; Bickelhaupt, F. *J. Am. Chem. Soc.* **1976**, *98*, 3712–3713, and references cited therein.
- (5) Barber, J. J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1980**, *102*, 239–243, and references cited therein.
- (6) For an earlier use of fast proteolysis to trap short-lived products in the formation of Grignard reagents, cf. Patel, D. J.; Hamilton, C. L.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 5144–5147.
- (7) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165–168.
- (8) Lawrence, L. M., unpublished work. Hill, C. L, Ph.D. Thesis, Massachusetts Institute of Technology, Cambridge, Mass., 1975.
- (9) The solution of RMgBr was added slowly to a vigorously stirred solution containing *t*-BuOH and/or TMPO \cdot .
- (10) We have not explicitly examined the mechanism of this reaction, but we assume it to be analogous to the electron-transfer process inferred earlier for the reaction of organolithium reagents with TMPO \cdot : Newirth, T.; Whitesides, G. M. *J. Org. Chem.*, **1975**, *40*, 3448–3450. We do not know the rate constant for coupling TMPO \cdot with cyclopentyl radicals, but the reaction of 2,2,6,6-tetramethyl-4-oxopiperidine-*N*-oxyl with cyclopentyl radical is ca. $k = 3.5 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$; Nigam, S.; Asmus, K.-D.; Willson, R. L. *J. Chem. Soc., Faraday Trans. 1* **1976**, 2324–2340.
- (11) TMPO \cdot itself reacts at a clean magnesium surface under these conditions, but more slowly than cyclopentyl bromide (the latter rate is mass transport limited).⁵
- (12) The yield of dimers and olefins is consistently higher in the reactions carried out in the presence of *t*-BuOH than in its absence. The greater importance of radical–radical reactions in systems containing *t*-BuOH may reflect a decrease in the rate of conversion of R \cdot into RMgBr at the alkoxide-obscured magnesium surface.
- (13) Similar studies with *n*-hexyl bromide have succeeded in trapping $\sim 70\%$ of the hexyl moieties as TMPO-*n*-hexyl.
- (14) Bodewitz has described evidence indicating that methyl radicals produced in reaction of methyl iodide with magnesium are trapped by allyl phenyl ether: Bodewitz, H. W. H. J. Ph.D. Thesis, Der Vrije Universiteit, Amsterdam, 1975.
- (15) A referee has suggested that TMPOR might be formed by reaction between surface-bound R \cdot and TMPO \cdot . It is difficult to prove or disprove this suggestion, since the differences between a hypothetical "surface-bound" radical and a free radical in solution have always been so vague as to frustrate experimental distinction. In the experiments reported here, any surface-bound radicals would have to have properties very similar to those of free radicals.

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Received December 3, 1979

Photochemical and Thermal Decomposition of $\text{HCo}(\text{CO})_4$. Evidence for a Radical Pathway Involving $\text{Co}_2(\text{CO})_8$

Sir:

Hydridotetracarbonylcobalt(I), $\text{HCo}(\text{CO})_4$, is presumed to be an active intermediate in several organic reactions catalyzed by cobalt carbonyl compounds. The mechanisms commonly written for these processes embody the well-known 16–18 electron rule.^{2–4} However, evidence has accumulated in recent years that substitution, addition to olefins, oxidative addition, and electron-transfer processes may proceed through, or lead to, 17-electron radical species.^{5–8} We report here upon a study of the thermal and photochemical decomposition reactions of $\text{HCo}(\text{CO})_4$ in hexane solution:



The results are consistent with a radical as opposed to an even-electron mechanistic scheme.

Hexane solutions of $\text{HCo}(\text{CO})_4$ were prepared as described elsewhere.⁹ The $\text{HCo}(\text{CO})_4$ formed was condensed in hexane as solvent. The hexane solutions were vacuum distilled and stored in sealed tubes at liquid nitrogen temperature until used. Careful procedures result in solutions containing very little (but always some) $\text{Co}_2(\text{CO})_8$. [Very small amounts of $\text{HCo}(\text{CO})_4$ may decompose during distillation via a wall reaction.] Solutions with $\text{HCo}(\text{CO})_4$ concentrations up to 0.1 M typically contain concentrations of $\text{Co}_2(\text{CO})_8$ as low as 6×10^{-4} M, as estimated from IR absorbance values. However, solutions of even the lowest concentrations prepared exhibit absorbances $\gg 1$ at 366 nm with the path lengths employed in the photochemical studies.

Our observations regarding the thermal reaction are similar to those reported by others.^{10,11} The rate has been described as second order in $\text{HCo}(\text{CO})_4$. However, as noted by Clark et al.,¹¹ there is a dependence on $[\text{Co}_2(\text{CO})_8]$; the initial rate of decomposition increased with increasing initial $\text{Co}_2(\text{CO})_8$ concentration. In addition, we observe that a second-order plot for disappearance of $\text{HCo}(\text{CO})_4$ is curved upward (Figure 1a), reflecting an increasing reaction rate as $\text{Co}_2(\text{CO})_8$ is formed. This highly reproducible behavior is observed only when the initial $\text{Co}_2(\text{CO})_8$ concentrations are low and the reaction is followed for ~ 2 half-lives or longer. We observe also, in

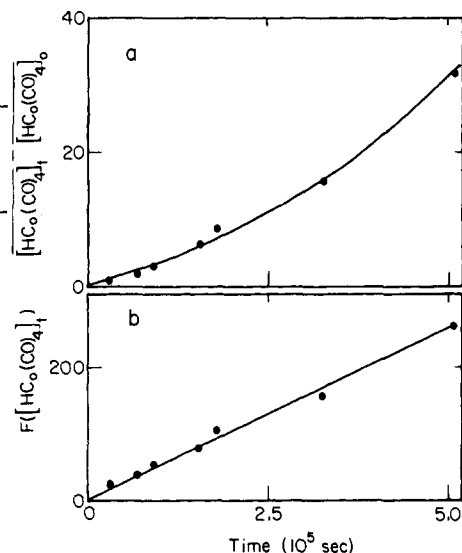


Figure 1. (a) A second-order plot for disappearance of $\text{HCo}(\text{CO})_4$ in the thermal decomposition: $[\text{HCo}(\text{CO})_4]_0 = 5.9 \times 10^{-1} \text{ M}$; $[\text{Co}_2(\text{CO})_8]_0 \sim 1.3 \times 10^{-3} \text{ M}$. (b) Graph of rate data shown in part a, assuming that the rate of $\text{HCo}(\text{CO})_4$ decomposition increases as $[\text{Co}_2(\text{CO})_8]^{1/2}$ (eq 8).