removed *in vacuo*, and the remaining solution was lyophilized to produce 0.07 g of material which was submitted to chromatography on a carboxymethylcellulose (CMC) column[21] (0.9 × 56 cm) using a continuous ammonium acetate concentration gradient for elution (Figure 3). The most retarded peak (tubes 237–280) was lyophilized three times and yielded[37] compound XIII in a yield of 0.028 g. Peptide XIII behaved as a single component in paper electrophoresis (mobility relative to L-lysine, 0.95; pH 3.7, 400 v, 5 hr). The amino acid composition of XIII was determined according to the method of Spackman, Stein, and Moore[23] and was found to be in good agreement with the theoretically expected values (Table I); $[\alpha]^{24}_{D}$ −76.7° (*c* 0.4, 0.1 *M* acetic acid). Prolinol content was determined by the dinitrophenylation procedure.

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(37) In several experiments the over-all yield of peptide, calculated on the basis of the starting materials used for the final coupling step, was approximately 10% based on the peptide content (about 75%) as determined by the optical density of a solution of the synthetic product in 0.01 *N* HCl at 280 mμ.

Communications to the Editor

Homogeneous Electron Transfer to Primary Alkyl Halides and Radicals

Sir:

The reactions of sodium naphthalene (0.01–0.1 *M*) with 5-hexenyl and cyclopentylmethyl bromides and chlorides in 1,2-dimethoxyethane at room temperature yield substantial quantities of hydrocarbon products. While the nature of the products indicates that radicals are intermediates in these reactions, the major portion of the product cannot arise in radical–radical or radical–solvent reactions. The evidence indicates that carbanions, instead, are the immediate precursors of the major hydrocarbon products. For the similar reactions of alkyl iodides, evidence that radical–radical reactions, and perhaps radical–solvent reactions, are important has been presented recently.(1)

When sodium naphthalene is used in excess, small quantities of dimeric (C_{12}) hydrocarbons are produced (*ca.* 3% for the chlorides, *ca.* 7% for the bromides), while substantial yields (40–70%) of C_6 hydrocarbons (1-hexene and methylcyclopentane) are obtained.(2) No 1,5-hexadiene, potentially a product, *via* E2 or radical disproportionation reactions, was produced in detectable quantities.

The major product from either of the 5-hexenyl halides is 1-hexene, formed in 40–70% yields. This hydrocarbon cannot arise in a radical–solvent reaction (eq 2) since hydrogen abstraction from solvent does not compete effectively with the cyclization of the 5-hexenyl radical to the cyclopentylmethyl radical (eq 3).(3) The 1-hexene is therefore best interpreted as arising directly from the 5-hexenyl anion.

$$\mathrm{CH_2{=}CHCH_2CH_2CH_2CH_2X + Naph\cdot^- \longrightarrow CH_2{=}CHCH_2CH_2CH_2CH_2\cdot + Naph + X^-} \quad (1)$$

$$\mathrm{CH_2{=}CHCH_2CH_2CH_2CH_2\cdot + SH \longrightarrow CH_2{=}CHCH_2CH_2CH_2CH_3 + S\cdot} \quad (2)$$

$$\mathrm{CH_2{=}CHCH_2CH_2CH_2CH_2\cdot \longrightarrow (cyclo\text{-}C_5H_9)CH_2\cdot} \quad (3)$$

The most reasonable sources of the 5-hexenyl anion are reduction of the 5-hexenyl radical (eq 4) and opening of the cyclopentylmethyl anion. The latter route is excluded by the fact that reductions of cyclopentylmethyl bromide and chloride with sodium naphthalene yield methylcyclopentane as the only C_6 hydrocarbon.(6) Since we have not been able to obtain convincing evidence that C_6 anions persist in solution for times detectable on a laboratory time scale, it is probable that they obtain protons from the solvent before quenching.

$$\mathrm{CH_2{=}CHCH_2CH_2CH_2CH_2\cdot + Naph\cdot^- \longrightarrow CH_2{=}CHCH_2CH_2CH_2CH_2^- + Naph} \quad (4)$$

Methylcyclopentane is formed in reductions of 5-hexenyl bromide and chloride in yields which depend on concentration conditions and method of mixing reagents. Since the yield can be reduced to near zero when large and excess concentrations of sodium naphthalene are used, it cannot be formed through cyclization of the 5-hexenyl anion, but is best viewed as arising through reaction 3 (followed by reduction, as in reaction 4) in a competition with reaction 4.

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(1) G. D. Sargent and S. Bank, Abstracts of the Middle Atlantic Regional Meeting of the American Chemical Society, Feb 3–4, 1966, Philadelphia, Pa., p 120.

(2) Alkyl halides were admitted by means of a breakseal to a solution of sodium naphthalene. Mixing was accomplished by vigorous shaking. The reaction was instantaneous on a laboratory time scale. Reaction mixtures were quenched with acetic acid within 5 min. The products do not isomerize under these conditions. Analyses were by vapor phase chromatography.

(3) This is indicated by considerations of the data of Lamb[4] and Walling,[5] applying reasonable solvent and temperature corrections. As control experiments, however, we have examined the products of decomposition of 6-heptenoyl peroxide in 1,2-dimethoxyethane at 50° in the presence and absence of a scavenger (Koelsch's radical). Methylcyclopentane was the only scavengeable C_6 product (0.44 mole/mole of peroxide in the absence of scavenger). The yield of open-chain C_6 hydrocarbons was 0.05 mole/mole of peroxide, and this was not detectably affected by the presence of a scavenger. Thus, all of the detectable noncage C_6 hydrocarbon product was methylcyclopentane. A reduction of 5-hexenyl bromide with sodium naphthalene at 50° in 1,2-dimethoxyethane gave results similar to those reported above.

(4) R. C. Lamb, P. W. Ayers, and M. K. Toney, *J. Am. Chem. Soc.*, **85**, 3483 (1963).

(5) C. Walling and M. S. Pearson, *ibid.*, **86**, 2226 (1964).

(6) A tacit assumption here is that the cyclopentylmethyl radical does not react with solvent before it is reduced. Since the 5-hexenyl radical does not, and since both radicals are primary alkyl radicals, this assumption is justified by the consideration that both radicals should have similar reactivities.

Sargent and Bank obtained much larger yields of dimeric hydrocarbons in their experiments on the reduction of alkyl iodides with sodium naphthalene in 1,2-dimethoxyethane.[1] In experiments performed since learning of their results, the fact that significant amounts of 2,3-dimethylbutane are formed from isopropyl iodide in this reaction has been confirmed in our laboratories, our conditions being somewhat different from theirs (lower concentrations).[7] It is also our understanding from Professor Sargent that bromides and chlorides give much diminished yields of dimeric hydrocarbons in their hands.[8] We agree with him that a possible source of the difference in behavior may lie in the greater reactivity of the iodides in the first, radical-producing step of the reaction, so that the higher peak transient concentration of radicals may make radical coupling much more favorable in the reactions of the iodides than for the bromides and chlorides. Other alternatives exist, but present data do not permit distinctions among these.

In principle, the relative rate constants for reactions 3 and 4 can be obtained from experiments such as ours. In practice, questions of efficiency of mixing and state of aggregation of sodium naphthalene at these relatively high concentrations render accurate, consistent, and meaningful values difficult to obtain. However, all our experiments thus far suggest that k_4/k_3 is at least 10^3 l. mole^{-1}. Since k_3 is probably at least near 10^5 sec^{-1} (from considerations of rates of reactions like (2) and the fact that (3) is much faster than (2)) k_4 is at least 10^8 l. mole^{-1} sec^{-1}, which is near the diffusion-controlled limit. It would not be unreasonable for a reaction such as (4) to be diffusion controlled.

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(7) Results of Mr. C. D. Smith.

(8) Conversation with Professor Sargent.

(9) We have recently learned of results of S. J. Cristol and R. V. Barbour (*J. Am. Chem. Soc.*, **88**, 4262 (1966)) which parallel those reported here in cholesteryl systems.

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Radical Intermediates in the Oxygenation of a Grignard Reagent

Sir:

The oxygenation of the Grignard reagent prepared from either 1,2,6-tribromohexane or 6-bromo-1-hexene[1] yields both 5-hexen-1-ol and cyclopentylcarbinol in a ratio of about 3:1. In contrast, carbonation[2] and hydrolysis (dilute HCl) of the same Grignard reagent give open-chain and cyclic products in ratios of about 20:1. Neither oxygenation, nor carbonation, nor hydrolysis of the Grignard reagent formed from cyclopentylmethyl bromide results in open-chain products. Table I presents the data.

Table I. Reactions of Grignard Reagents[a]

Process	Products, %	
	From 6-Bromo-1-hexene	
Oxygenation	5-Hexen-1-ol, 74 (75)	Cyclopentylcarbinol, 26 (25)
Carbonation	6-Heptenoic acid, 95 (97)	Cyclopentylacetic acid, 5 (3)
Hydrolysis	1-Hexene, 93 (96)[b]	Methylcyclopentane, 7 (4)[b]
	From Cyclopentylmethyl Bromide	
Oxygenation	5-Hexen-1-ol, 0	Cyclopentylcarbinol, 100
Carbonation	6-Heptenoic acid, 0	Cyclopentylacetic acid, 100
Hydrolysis	1-Hexene, 0	Methylcyclopentane, 100

[a] Reactions carried out as described in ref 3. Yield figures in the table refer in each case to the distribution of products between the two indicated. The absolute yields, based on alkyl halide consumed in the Grignard preparations, were in each case 70–80%. The figures in parentheses refer to nonvacuum-manifold reactions, while the others refer to vacuum-manifold experiments. [b] The Grignard was prepared, in this case, from 1,2,6-tribromohexane. In general, Grignard preparations from this halide gave the same results, within experimental error, as those from 6-bromo-1-hexene.

These facts constitute strong evidence that the oxygenation of these Grignard reagents proceeds through free alkyl radicals.

Clearly, the Grignard preparations from the cyclopentylmethyl and 5-hexenyl bromides do not lead to the same mixture of Grignard reagents. The exclusively cyclic nature of the products derived from the cyclopentylmethyl bromide and the very small quantities of cyclic products obtained from the open-chain halides in the carbonation and hydrolysis of the reagents suggests strongly that the 5-hexenyl and cyclopentylmethyl Grignard reagents do not interconvert at all under our reaction conditions.[3,4] The small amounts of cyclic products obtained from the carbonation and hydrolysis reactions of the Grignard reagent prepared from open-chain materials are presumed to reflect the presence of like quantities of cyclopentylmethylmagnesium bromide in the Grignard reagent as initially prepared.[6]

The formation of cyclic product in the oxygenation therefore requires that some intermediate in the reac-

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(1) R. C. Lamb and P. W. Ayers, *J. Org. Chem.*, **27**, 1441 (1962).

(2) R. C. Lamb, P. W. Ayers, and M. K. Toney, *J. Am. Chem. Soc.*, **85**, 3482 (1963).

(3) Grignard reagents were prepared by direct reaction of magnesium metal with the halides in diethyl ether, with and without moderation of an ice bath. The preparations were carried out in rigorously degassed vessels on a vacuum manifold. Solvent was distilled into the vessels from storage over sodium benzophenone ketyl. The magnesium metal was pretreated by heating with dry iodine, after which the excess iodine was removed by evacuation. In some earlier, nonvacuum-manifold preparations, a nitrogen atmosphere was employed and the magnesium was untreated. Both methods led to the same final results. Gaseous carbon dioxide and oxygen were employed for carbonations and oxygenations, and syringes were employed for introducing dilute HCl in the hydrolyses. Oxygenation, carbonation, and hydrolyses were done both at room temperature (vacuum-manifold experiments) and ice-bath temperatures (earlier experiments). Analyses were by vapor phase chromatography.

(4) The lack of interconversion of the Grignard reagents is consistent with similar findings for the corresponding alkylsodium species in 1,2-dimethoxyethane, although in the latter case the organoalkali compounds were undoubtedly being destroyed quite rapidly, as they were formed, through reaction with the solvent.[5]

(5) J. F. Garst, P. W. Ayers, and R. C. Lamb, *J. Am. Chem. Soc.*, **88**, 4260 (1966).

(6) Cyclization during Grignard preparation would be expected if free radicals are involved in this process, as proposed by others.[7] The present observation constitutes additional evidence on this point.

(7) (a) C. Rüchardt and H. Trautwein, *Ber.*, **95**, 1197 (1962); (b) H. M. Walborsky and A. E. Young, *J. Am. Chem. Soc.*, **86**, 3288 (1964); (c) D. J. Patel, C. L. Hamilton, and J. D. Roberts, *ibid.*, **87**, 5144 (1965).