5014 *J. Org. Chem.* **2000,** *65,* 5014−5015

# Absence of Detectable Freely Diffusing Radicals during the Formation of an Aromatic Grignard Reagent

Robert I. Walter*

*Chemistry Department, University of Illinois at Chicago, Chicago, Illinois 60607*

*mhry@aol.com*

*Received January 25, 2000*

The Grignard reagent has probably been the most widely used intermediate in organic chemistry since its introduction by Victor Grignard in 1900.[1] Despite this wide use, it is not possible to assign a specific structure for a particular reagent. This is because both RMgX and $R_2Mg$ are formed during preparation of the reagent and are connected by the equilibrium described by the Schlenks.[2] The position of this equilibrium depends on the solvent, the structure of the alkyl group, and the nature of the halogen. The mechanisms of reactions that involve RMgX also have been extensively studied, and it has been recognized that the formation of the reagent mixture is a separate problem from its reactions. We are concerned here with the former.

Since the conventional reaction system in which RMgX is formed is heterogeneous, studies by the usual methods of chemical kinetics have been rare prior to the recent extensive investigation by Whitesides and his collaborators.[3] Their results are particularly significant in that they demonstrate directly the presence of a previously hypothetical intermediate free radical during the formation of Grignard reagent from cycloheptyl bromide and magnesium metal. There is agreement among recently active research groups that formation of RMgX is initiated by donation of an electron from magnesium metal to an alkyl halide molecule at the metal surface. The surface radical anion so formed will lose a halide ion to give the initial free radical intermediate in the formation of RMgX. Garst and co-workers[4] have investigated subsequent steps in Grignard reagent formation by examining the equilibrium free radical distribution from this initial radical assumed to be released from the magnesium surface under ether. Subsequent free diffusion of this radical product through the ether solvent while undergoing permissible radical rearrangements gives an equilibrium solution from which solutes return to the Mg to form RMgX and RMgX (rearranged). This equilibrium system can be modeled quantitatively; it would be quenched to product mixtures that correspond well to those observed experimentally. Studies by Walborsky and collaborators[5] on retention of configuration during reactions of chiral cyclopropyl-based halides led them to conclude that RMgX forms on the magnesium surface without migration of any intermediate through the solution. Any free radical intermediate formed is always on the metal surface, and must react there. These systems usually give only partial retention of configuration, together with significant racemization. Walling[6] has compared the abilities of the Garst and the Walborsky models to account for known product mixtures from the reactions of alkyl halides and magnesium. Ashby and Oswald[7] have published Grignard runs under varied conditions; they interpret their data as support for return of radicals from solution to the Mg surface to form RMgX. These studies of RMgX formation based upon observation of changes in stereochemistry or structure of course are limited to aliphatic halides. In fact, we are not aware of any studies of the formation of aromatic Grignard reagents until the 1999 publication by Garst and co-workers. Another such investigation is reported here, based upon the known very fast rearrangement of the *o*-allyloxyphenyl radical (**2** in Scheme 1) reported by Abeywickrema and Beckwith[8] and prepared by them by reduction of *o*-allyloxychlorobenzene with tributyltin hydride. The argument (shown in the scheme) is that the free radical formed by transfer of an electron to halide **1**, followed by loss of the halide ion and subsequent rearrangements, can be trapped by carbonation with $CO_2$, the carboxylic acid so formed isolated and purified, and its structure determined. If at any point in the preparation the free radical **2** is formed and can move away from the metal surface, that radical will undergo very fast rearrangement, and the trapped carboxylic acid will have the structure of 2,3-dihydro-3-benzofuranacetic acid, **5**. If intermediate **2** never leaves the Mg surface, the carbonation product will be unrearranged 2-allyloxybenzoic acid, **4**. The product isolated in a quite pure state is the latter, identified by its proton-decoupled $^{13}C$ NMR spectrum.

## Experimental Section

*o*-Allyloxyiodobenzene **1** was prepared using the modified Williamson synthesis proposed by Goering and Jacobson.[9] We found a significant increase in yield (to 90%) when the mole ratio of potassium carbonate to *o*-iodophenol used in the synthesis was increased above unity.

**Preparation and Carbonation of the Grignard Reagent from 1.** This Grignard was prepared in the conventional manner in ether solution from a small excess of magnesium metal and halide **1**. Reaction generally started easily; a few crystals of iodine helped in stubborn cases. After reaction at the metal surface stopped, the solution was stirred for 60 m at ca. 35°; usually a second straw-colored phase separated. This two-phase mixture was cooled below −5°, and dry $CO_2$ was passed in rapidly until heat evolution stopped. The ether phase was diluted with $CH_2Cl_2$, washed with 1 M HCl, and then extracted twice with molar bicarbonate solution. These alkaline extracts were combined and acidified, and the precipitated solids were filtered and dried. This product gives an NMR spectrum with many relatively weak impurity lines. It was recrystallized by extraction into pentane in a Soxhlet apparatus. Yields of extracted recovered solids were 49−63%, mp 62.7−62.9 °C. $^{13}C$ NMR in $CDCl_3$ (assignments aided by off-resonance decoupling): 165.9 s, $C{=}O$; 157.3 s, $C_2$; 134.7 d, $-C-H$; 133.3 d, $C-H$; 131.1 d, $C-H$; 121.9 d, $C-H$; 119.8 t, $=CH_2$; 118.0 s, $C_1$; 113.1 d, $C-H$; 70.5 t,

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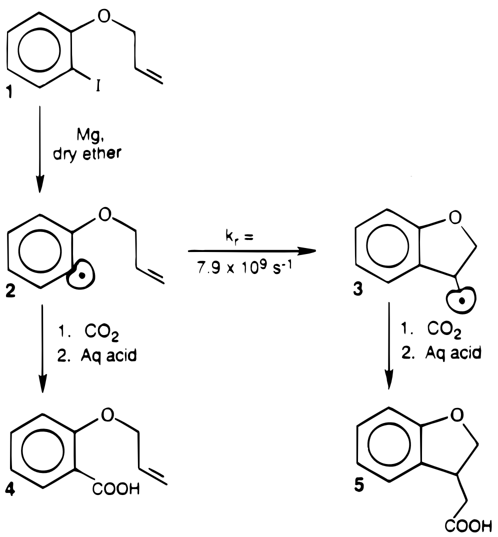
10.1021/jo0001028 CCC: $19.00

**Scheme 1**



OCH$_2$. (The five unassigned C−H shifts are due to carbon atoms which cannot be unambiguously assigned.) These values are identical to the published chemical shifts for the unrearranged acid **4**[10] and significantly different from those for the expected rearrangement product **5**.[11]

Note that the isomerized acid **5** would be expected to carry through the purification sequence with **4**; its absence indicates that little, if any, isomerization occurs. Since radical **2** is known to isomerize very fast in solution, we infer that no freely diffusing radical is present at any stage of the formation of this Grignard reagent from an aromatic halide.

## Discussion

The absence of rearrangement during preparation of the Grignard reagent from halide **1** implies that at no time during the reagent's synthesis is the free radical **2** liberated to move independently in the ether solvent, where it should undergo very fast rearrangement to **3**. We have this result for only one aromatic halide, and this must meet the structural requirements for rearrangement by carrying the halogen atom and an allyloxy group on atoms *ortho* to one another on an aromatic ring. This limits the range of structures which could be tested, but we expect that other aromatic halides that have the necessary structural features would show corresponding behavior. Both phenyl rings and alkenes are known to adsorb on some metal surfaces under high vacuum conditions,[12] so it is possible that both functional groups in **2** adhere to the Mg surface and thus disable this cyclization probe for a radical intermediate during formation of RMgX. The Grignard reagent from **1**, once formed, appears to have normal stability; note that our Grignard reagent solution was stirred for an hour before carbonation. This result cannot apply to preparation of aliphatic Grignard reagents, where rearrangements of the alkyl group are known to be common. Garst and co-workers have recently reported[13] a detailed study of ArMgX formation from aryl halides, including comparisons of product structures in these reactions with those of alkyl halides. They showed that products formed from aliphatic halides by side reactions and successfully predicted by the model proposed earlier by Garst (with different co-workers) generally are absent when an aromatic halide is used. These authors conclude that aromatic free radicals are not intermediates along the major pathway to ArMgX. They probed this point further by observing formation of Grignard reagents from *o*-(3-butenylphenyl) halides, which could ring close by a radical rearrangement analogous to **2** → **3**. This rearrangement has been reported[8] to have a first-order rate constant equal to $7.4 \times 10^7$ sec$^{-1}$, or about 1/16 the value for **2** → **3**. They have observed variable (usually small) amounts of 1-methylindane among the products of these reactions, suggesting variable minor participation by radical intermediates. Their most recent ideas about the mechanisms of Grignard reagent formation are summarized in a recent review.[14]

**Acknowledgment.** The author is much indebted to Professor A. L. J. Beckwith for a discussion some years ago of the use of radical **2** as a mechanistic probe. The research of Ted Field for his senior thesis at UIC (on a different problem) led the author to formulate this investigation. Incorporation of the recent material in refs 13 and 14 was kindly suggested by a referee. This work was supported by the Chemistry Department of the University of Illinois at Chicago.

JO0001028

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