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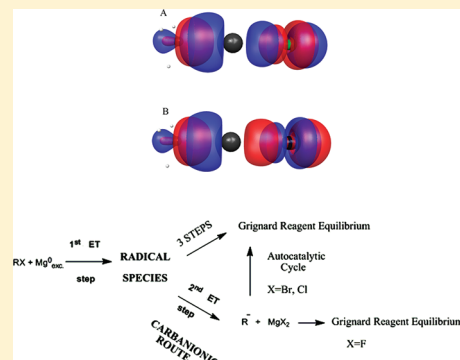
Chemical Bonding and the Equilibrium Composition of Grignard Reagents in Ethereal Solutions

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Supporting Information

ABSTRACT: A thorough analysis of the electronic structure and thermodynamic aspects of Grignard reagents and its associated equilibrium composition in ethereal solutions is performed. Considering methylmagnesium halides containing fluorine, chlorine, and bromine, we studied the neutral, charged, and radical species associated with their chemical equilibrium in solution. The ethereal solvents considered, tetrahydrofuran (THF) and ethyl ether (Et_2O), were modeled using the polarizable continuum model (PCM) and also by explicit coordination to the Mg atoms in a cluster. The chemical bonding of the species that constitute the Grignard reagent is analyzed in detail with generalized valence bond (GVB) wave functions. Equilibrium constants were calculated with the DFT/M06 functional and GVB wave functions, yielding similar results. According to our calculations and existing kinetic and electrochemical evidence, the species R^\bullet , R^- , ^+MgX , and RMgX_2^- must be present in low concentration in the equilibrium. We conclude that depending on the halogen, a different route must be followed to produce the relevant equilibrium species in each case. Chloride and bromide must preferably follow a “radical-based” pathway, and fluoride must follow a “carbanionic-based” pathway. These different mechanisms are contrasted against the available experimental results and are proven to be consistent with the existing thermodynamic data on the Grignard reagent equilibria.

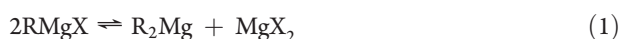


1. INTRODUCTION

The Grignard reaction has been known for more than a century.¹ It is one of the most important C–C bond formation reactions and remains as one of the most widely used reactions in chemical synthesis.² Details on the formation reaction,^{3–7} structure, and reactivity^{8–12} of Grignard reagents have been investigated since then. In spite of its widespread use in organic synthesis during the last 110 years, new applications of Grignard reagents are still being developed, such as Grignard reagent/organic halide cross-coupling and aryl Grignard reagent homocoupling reactions.²

As pointed out by Ashby in his classical 1967 review on the subject,⁸ the study of Grignard reagents is a highly interdisciplinary area. This fact has hampered the development of this subject. Although it is of great interest to organic chemists, it needs physical chemists and its methods to be properly studied. In this work we try to approach the problem of the actual composition of the Grignard reagents from the physicochemical point of view without forgetting its chemical complexity.

One of the first contributions to the understanding of the chemical structure of Grignard reagents was obtained by Schlenk and Schlenk Jr.¹³ They found that the addition of dioxane to ethereal solutions of Grignard compounds RMgX ($\text{X} = \text{halide}$, $\text{R} = \text{alkyl}$, aryl) resulted in precipitation of magnesium halides. On the basis of this information, they suggested the equilibrium (reaction 1) known generally as the Schlenk equilibrium.



Assuming that the equilibrium composition of (1) could be determined by the precipitation of the MgX_2 from the mixture by dioxane, the equilibrium composition values were determined for several Grignard compounds.^{14–16}

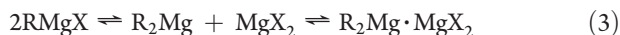
However, the actual chemical structure of Grignard reagents has always been a matter of discussion. Electrolysis experiments were performed reporting that Grignard compounds in ether are electrically conducting. This result indicates that charged species could be present in solution. Species like Mg^{2+} , R^\bullet , X^- , R^- , RMgX^+ , ^+MgX , RMg^+ , RMgX_2^- , MgX_2^- , and several others were proposed.^{17–20} However, we have not found in the literature studies which directly detect these species, the main difficulty being their low concentration in solution. We highlight that the existence of ionic and radical species were indirectly proposed by kinetic and electrochemical approaches, and there is no dispute in the literature on this fact. In the next sections some of these works will be cited and will become reasonable to expect that the presence of radical or carbanion species leads to different equilibrium compositions. Investigations by calorimetric,^{21–23} molecular weight,^{24–26} and ebullioscopic measurements²⁷ and NMR spectroscopy^{28,29} showed that Grignard reagents can exist as dimers and higher aggregates. As a consequence, a modified representation to the solution

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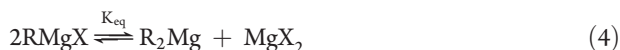
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equilibrium composition was suggested to include that possibility (reactions 2 and 3).



Here, the former is known as the dimerization equilibrium, whereas the latter is the Schlenk one. Although structures in the solid state cannot be directly extrapolated to solution, studies on the solvent–organomagnesium crystallized complex structures on the species of reaction 2 had been performed.^{30–32} It was found that the Mg atoms in Grignard reagents are stable in tetrahedrally coordinated form, and dimeric species are bridged through halide atoms.

The position of the Schlenk equilibrium is considered to be dependent on the nature of the solvent, the nature and steric properties of the organic substituent on the magnesium atom, the type of halogen involved, and the temperature.⁹ In tetrahydrofuran (THF), all alkyl- and arylmagnesium chlorides, bromides, and iodides are found to be monomeric over a wide concentration range. In the same solvent, fluorine compounds were dimeric $[\text{RMgF}]_2$.⁹ In diethyl ether (Et_2O), alkyl- and arylmagnesium bromides and iodides are mostly monomeric at low concentrations and mostly dimeric at higher concentrations (0.5–1.0 M).⁹ In Et_2O the alkylmagnesium chlorides and fluorides are essentially dimeric even at low concentrations.⁹ The measured equilibrium constants (K_{eq}) values for reaction 4



have different magnitude: in Et_2O , values of 10^{-2} – 10^{-3} and in THF values of 0.1–1 are the most common.^{21–23} Another important experimental feature of the Schlenk equilibrium is the value of heat of reaction, ΔH , associated with chemical reaction 4. In diethyl ether the values are positive; in THF the values are negative.³³

This trend is usually associated with the larger coordination number of the magnesium species in THF. The positive value of ΔH in THF leads to smaller values of K , measured by IR³⁴ and NMR.^{28,29} The Schlenk equilibrium constant is usually expressed as²⁸

$$K_s = \frac{[\text{RMgX}]^2}{[\text{R}_2\text{Mg}][\text{MgX}_2]} \quad (5)$$

In the literature it is usually assumed that $[\text{R}_2\text{Mg}] \approx [\text{MgX}_2]$.²⁸ Within this approximation we can calculate the equilibrium constant from the equation

$$\Delta G^0 = -RT \ln K \quad (6)$$

“ R ” is the universal gas constant (8.314 J/(mol·K)) and “ T ” is temperature. These experiments were carried out at 298.15 K and 1 atm.

Theoretical studies on the Schlenk equilibrium and its associated solvent effects have been carried out through semiempirical calculations, using extended Hückel MO,³⁵ ab initio methods (HF^{36,37} and MP2^{38–40} levels), and density functional theory (DFT),^{41,42} with predominant use of the B3LYP functional.^{12,43–49} The stability of possible dimeric structures was studied by Khan and Pratt,⁴¹ and it was observed that the isomers bridged by halide atoms are the most stable. Studies involving the solvent effects have been performed using continuum solvent models^{45,48} and

clusters.^{39,40,44,46,47} The cluster-based studies simulate organomagnesium compounds coordinated through the Mg atom to solvent molecules. It was observed that dimeric species coordinated with more than two solvent molecules were more unstable than those with only two.⁴⁵ It was also noted that in all species involved in equilibrium associated with the Grignard reagent, the Mg atom is stable in the tetrahedrally coordinated form.⁴⁵

The formation of the Grignard reagent itself was also investigated theoretically^{36,50} but ionic species and radical ones were not considered in these studies. On the other hand, detailed mechanistic studies of reactions of Grignard reagents with ketones⁸ and kinetic analyses of Grignard reagent formation^{4–6} provide solid evidence for radical species in the medium. Under the light of these results we wonder whether it would be possible to have useful insights on the nature of the Grignard reagent equilibrium including only polar neutral species.

In the literature it is generally assumed that the most important effects in Grignard reagents composition are due to the solvent and the type of the halogen atom.⁹ Because there is sound evidence of the presence of ionic and radical species in solution of Grignard reagents,^{3–7} it is possible that their relative predominance and effects in the equilibrium could be different depending on the solvent or halogen atom. It is difficult to rationalize the differences between fluorides and the other Grignard reagents considering only the number of solvent coordinated molecules and their basicities. That is, no work in the literature has ever presented a convincing explanation for the observed differences in behavior of the Grignard reagents for different halogens and for different solvents.

A thorough investigation on the chemical and thermodynamic aspects of the equilibrium associated with Grignard reagents is performed in this paper. We also propose an alternative way to understand the electronic structure of Grignard reagents containing fluorine, chlorine, and bromine. We attempt to present a more realistic view of the equilibrium through the consideration of many additional radical and charged species that can possibly occur in THF and Et_2O solutions. In the end we hope to provide useful insights on the chemical equilibrium and the factors that determine the observed properties of the Grignard reagents.

2. COMPUTATIONAL DETAILS

In choosing the computational methods to tackle the problem in question, we need to meet a few criteria. The model used must be able to provide accurate energies for dissociation and association processes. It must also allow the inclusion of a solvent model. Additionally, it must be associated with a definite and sound physical and chemical interpretation. Lastly, the more stringent requirement, it must be able to treat in an equal fashion neutral, charged, and radical species. A computational method that satisfies all these requirements is the generalized-valence-bond-restricted-configuration-interaction (GVB-RCI), with fully optimized orbitals.^{51,52} In spite of the aforementioned desirable qualities, this method has two major drawbacks. First it needs a much larger computational time than, for instance, the widespread used DFT (density functional theory)-based approaches. Second, although it includes all nondynamic and approximates some dynamic electronic correlation effects,⁵² it still lacks part of the dynamic correlation. These drawbacks were managed in the following way. For every closed-shell species involved (monomers, dimers, and other fragments), the results of the GVB-RCI calculations (including geometry optimizations and Hessians) were

checked against MP2 and DFT (M06 functional) results. Possible active spaces for the GVB-RCI calculations were considered to fairly treat the association processes to be studied. The final choices of active space for the GVB-RCI calculations were found to be manageable within our computational resources. No appreciable differences in geometries, relative energies, and zero-point energies were found (Supporting Information). The calculation details are described below.

The GVB-RCI wave functions were emulated as multiconfiguration-self-consistent-field (MCSCF) calculations in the GAMESS⁵³ code using orthogonal orbitals. The core orbitals were fully optimized within the doubly occupation restriction. The GVB-RCI wave functions were calculated with Ivanic's occupation-restricted-multiple-active-space (ORMAS) code as implemented in the GAMESS package.^{54,55} The starting orbitals for the GVB-RCI calculations were taken from localized occupied and virtual HF orbitals. For the methylmagnesium halides, we considered eight electrons in eight orbitals (8,8) in the active space. With each identifiable valence electron pair, we associated a pair of orbitals. The final four pairs chosen were the C–Mg and Mg–halogen bonds and the two “p-like” halogen lone pairs. This choice is in conformity with a previous detailed study on the necessary active space in MCSCF calculations for halogen atoms carried out in ref 51. Although the majority of GVB and most of the MCSCF calculations in the literature consider lone pairs as doubly occupied, their inclusion in the active space is important to properly assess the electronic and conformational properties of the systems considered here.⁵⁶ These calculations are straightforward, comprising the superposition of 454 Slater determinants. Note that the perfect-pairing GVB (GVB-PP) would need only 16 determinants to be emulated as a MCSCF calculation. To maintain consistency, for the dimer we used a doubled active space of sixteen electrons in sixteen orbitals (16, 16). This GVB-RCI calculation is more involved, comprising 411 462 Slater determinants. Although these calculations required larger active spaces, they were feasible within our computational resources. Actually, for the larger active spaces the time limiting steps were the orbital optimization and the molecular geometry derivative calculation steps, not the configuration interaction one.

The resulting GVB-RCI fully optimized wave function was transformed to one configuration of nonorthogonal-singly occupied orbitals to analyze the electronic structure associated with the different chemical bonds involved in these species. It should be remarked that the GVB-RCI wave function is not, strictly speaking, an independent particle model,⁵⁷ such as the more common GVB-PP (perfect-pairing)⁵⁸ or the unrestricted GVB^{59,60} (or spin-coupled, SC^{61–63}) wave functions. Hence, the transformation that takes the GVB-RCI in MCSCF form to one configuration of nonorthogonal-singly occupied orbitals is only approximate. However, it is found out that even with this limitation, the resulting orbitals are still useful to gain insight on the chemical bonding.⁶⁴ Moreover, GVB-PP calculations were performed in the same species and the resulting nonorthogonal-singly occupied orbitals were basically indistinguishable from those obtained in GVB-RCI calculations. The GVB-RCI wave function is particularly suited for dissociation and spin recoupling processes. Even when dealing with nonsinglet states it exactly avoids spin contamination,^{59,65} treating in an equal fashion any spin multiplicity. Hence, the results obtained with this wave function will be used to understand the bonding and the specifics of the singlet and radical species constituting the Schlenk and dimerization equilibria.

Solvent effects were evaluated with the PCM solvent model.^{66–68} The integral equation formalism (IEF)^{69,70} version of PCM was used to describe the effects of the environment with cavities built as a series of interlocking spheres centered on atoms. We considered as solvent the tetrahydrofuran (THF) and ethyl ether (Et₂O) because these two are the preferred media to carry out chemical transformations with Grignard reagents. In the PCM approach, the solvation energy can be decomposed into five different contributions:

$$\Delta G_{\text{solv}} = \Delta G_{\text{electr}} + \Delta G_{\text{cav}} + \Delta G_{\text{rep}} + \Delta G_{\text{disp}} + \Delta G_{\text{Mm}} \quad (7)$$

The electrostatic component to the solvation energy ΔG_{electr} is by far the most important one. One might expect that bulk properties of different ethereal solvents could provide the conditions necessary to mimic the equilibrium profile of different Grignard reagents.⁹

The main GVB-RCI, MP2, and DFT-M06 calculations were performed with the standard aug-cc-pVTZ basis set. This basis set is extensive enough such that qualitative errors in the properties calculated here should not be attributed to its limited size.

Additional calculations were performed to determine the influence of specific interactions of the species considered here with ethereal solvents as clusters in gas phase. This approach was already used in previous computational works in the literature on Grignard reagents. It would be very expensive computationally to perform these calculations at the GVB-RCI or MP2 levels. Instead, they were evaluated at the Hartree–Fock level and DFT level using the M06 functional,⁷¹ to determine stable geometries and equilibrium constants with both solvent molecules coordinated to the Mg atom. In these cluster models calculations we have used the 6-311G* basis set.

As stated above, all DFT type calculations were performed using the M06 functional. The “pure” M06 functional was chosen because the B3LYP functional has a documented poor performance for molecules containing atoms with many valence lone electron pairs.⁷² The M06 functional is also adjusted to describe dispersion effects, which might be important for the systems we are considering.

3. RESULTS AND DISCUSSIONS

We first discuss the chemical bond in magnesium species that take part in Grignard reagents. Afterward, we present our description of the molecular aspects of the Grignard equilibrium with solvent effects.

3.1. Bonding and Molecular Geometries. The species involved in Grignard reagent present chemical bonds between halogens, carbon, and magnesium. Bonds between these atoms should be very polarized. Apart from very limited NBO (natural bond orbital) type studies,^{37,42,44} there is no literature that presents analyses of the type of bonding in these molecules. In this paper we analyze the nonorthogonal-singly occupied GVB orbitals associated with the chemical bonds in the relevant species. Through this approach we are able to characterize the chemical bonds in the species composing the Grignard reagent as covalent, dative or ionic. Particularly, we provide a clear-cut understanding on the differences between fluoride Grignard reagent and the other methylmagnesium halides molecules.

Optimized equilibrium geometries were obtained at the GVB-RCI, MP2, and DFT (M06) levels for all polar neutral species involved in the Schlenk equilibrium. The geometries are

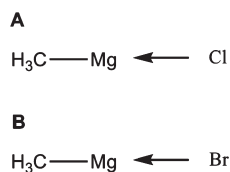


Figure 1. Chemical structures for chlorides and bromides Grignard monomers deduced from the GVB-RCI calculations: (A) CH_3MgCl monomer species; (B) CH_3MgBr monomer species.

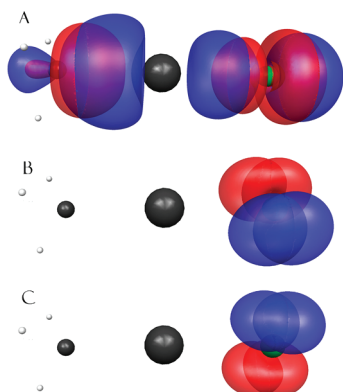


Figure 2. GVB orbitals for the methylmagnesium chloride: (A) for the C–Mg bond; (B) and (C) for “p-like” lone pairs.

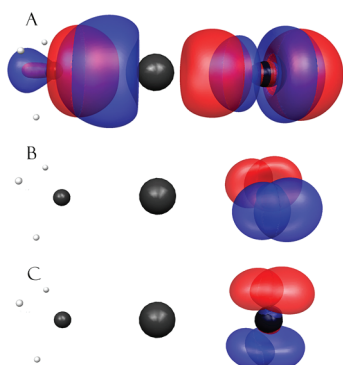


Figure 3. GVB orbitals for the methylmagnesium bromide: (A) for the C–Mg bond; (B) and (C) for “p-like” lone pairs.

summarized in the Supporting Information (Tables S1–6), listing which magnesium compounds were evaluated at different levels of ab initio calculations and different solvents models.

Bond distances and interatomic angles obtained for C–Mg and Mg–X (X: F, Cl, and Br) bonds demonstrated that there are no significant changes in molecular geometries at different levels of calculation in gas phase. The geometries were compared with previous works in the literature,^{36–40} and the values for bond distance and angles are very similar. This is an indication of the lack of unusual electronic effects in these systems and the low sensitivity to correlation, at least concerning molecular geometries and Hessians.

3.1.1. Monomeric Species. First we discuss the bonding in the methylmagnesium halides (F, Cl, and Br). Then we consider the dimeric structures.

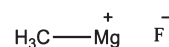


Figure 4. Chemical structure for fluoride methylmagnesium deduced from the GVB-RCI calculations.

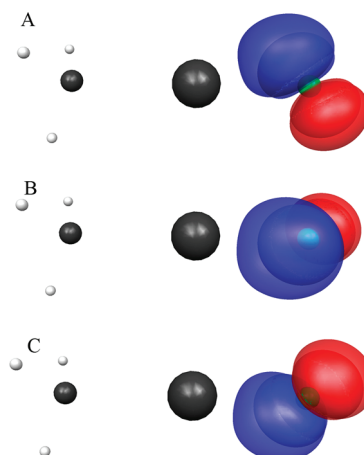


Figure 5. (A)–(C) GVB orbitals for the “p-like” lone pairs in methylmagnesium fluoride.

The methylmagnesium chloride and bromide structures are presented in Figure 1 and the GVB singly occupied-nonorthogonal orbitals for the C–Mg, Mg–Cl, and Mg–Br bonds in the monomer are shown in Figures 2A and 3A. To make visualization easier, the phases of all overlapping orbitals were inverted.

One should note that both orbitals that form the Mg–X bond are clearly centered at the halogen atom. In an ordinary covalent bond, such as the C–H bond in the methyl fragment, each of the GVB orbitals associated with the two electron bonds are approximately centered in different atoms. Thus, the Mg–Cl and Mg–Br bonds are depicting what is qualitatively known as a dative bond, where the two singly occupied orbitals are only slightly dislocated toward the Mg atom along the Mg–halogen axis. The C–Mg bonds in the monomers are somewhat different, being characterized as very polar covalent bonds. This is distinct from the dative Mg–halogen bonds in the sense that the singly occupied bond orbitals are not clearly centered only in one atom, as they are in the Mg–Cl and Mg–Br bonds.

On the other hand, for the methylmagnesium fluoride, the situation of the Mg–F bond is altogether different (Figures 4 and 5).

After both GVB-RCI and GVB-PP calculations, there was no resulting orbital pair collinear with the Mg–F bond axis. After the orbital optimization, the fluorine atom ends up by having three “p-like” lone pairs depicting a F^- ion connected through what seems to be an ionic bond to the Mg atom. One should also note that the singly occupied orbitals are qualitatively different from the “p-like” lone pairs depicted above for chlorine and bromine. For fluorine, the splitting of the doubly occupied lone pair orbital into two singly occupied is radial, whereas for chlorine and bromine, it is angular. This difference is expected and is extensively discussed in ref 48. Thus, the Mg–F bond is fundamentally different from the Mg–Cl and Mg–Br bonds being ionic instead of dative. As can be seen in Table 1, it is also a much stronger bond in the gas phase and in the solvent.

3.1.2. Dimeric Species. The dimeric structures (Figure 6) considered were bridged by the halide atoms, as in the X-ray crystal structures,³¹ and in agreement with a previous theoretical study.⁴¹

Table 1. Mg–X Bond Energies (kcal/mol) in Grignard Monomeric Species, Calculated at the GVB-RCI Level with the aug-cc-pVTZ Basis Set

X	THF	Et ₂ O	Gas Phase
F	151.67	150.72	143.89
Cl	121.41	120.60	115.65
Br	109.49	108.75	104.30

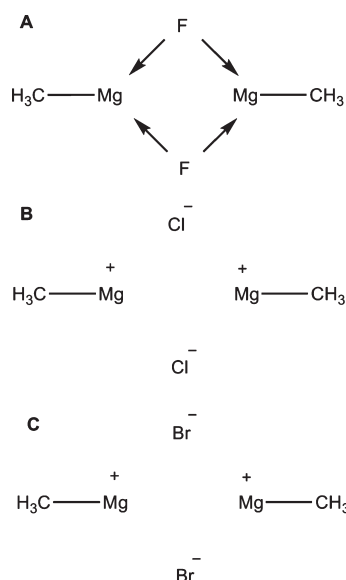


Figure 6. Chemical structures for dimeric species as deduced from GVB-RCI calculations: (A) $(\text{CH}_3\text{MgF})_2$; (B) $(\text{CH}_3\text{MgCl})_2$; (C) $(\text{CH}_3\text{MgBr})_2$.

The different bonding situations that arise in the dimers are the apparent divalence of the halogens and the trivalence of the Mg atom. The bonding picture in these systems can be clearly understood by the same procedure followed in the monomer. The obtained singly occupied orbitals from the GVB-RCI calculations are locally very similar to the ones already presented for the monomers. The C–Mg bonds are essentially identical to the one in the monomers. However, there appears to be an inversion of Mg–X bond character among the halogens. The singly occupied orbitals associated with Mg and the halogens in the dimers are presented below (Figures 7–9).

It was observed that only Mg–F bonds in the dimers are dative. Both singly occupied orbitals are centered in the fluorine and located on the Mg–F bond axis. By the same criteria used above for the monomers, the Mg–Cl and Mg–Br bonds are ionic. Both present orbital pairs are noncollinear with the Mg–X bond axis. As in the fluoride monomer, the bonding can be understood as if a halogen ion ($\text{X}^- = \text{Cl}^-$ or Br^-) and a Mg cation were attached through an ionic bond. How can we understand these results? Our hypothesis is the following. All Mg–X bonds should be very polarized. One can devise a qualitative scale that begins with an ionic bond, next a dative bond, and then a polar covalent bond, all in order of decreasing bond polarity. According to the halogen atom, we could also say that the more polar bonds are those involving fluorine, then chlorine, and then bromine. Up to this point, these considerations account for the observed bonding in the monomers. In the dimer, there are important differences. Now, the halogen atom is subjected to two

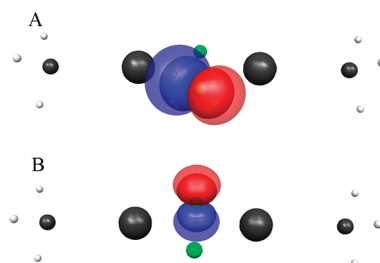


Figure 7. GVB orbitals for the methylmagnesium fluoride dimer: (A) for Mg–F bonds; (B) for “p-like” lone pairs.

positively polarized Mg atoms. This fact may cause a decrease of the bond polarizing ability of the fluorine atom causing the Mg–F bonds of the dimer to be dative instead of ionic. Note that the Mg–F–Mg angle is close to the standard sp^3 hybrid orbitals angle. The Mg–X–Mg angle for chlorine and bromine dimers is approximately the same. It is well-known that the elements on the Li–Ne row of the periodic table are particularly prone to hybridization, whereas the elements on the rows below are not. The reason is that for elements in this row, the valence “s” shell is spatially close from the valence “p” shell allowing efficient hybridization. A great deal of structural and chemical information is successively explained and predicted by this model.^{73,74} Thus, in the case of the chlorine and bromine dimers, because the valence “s” shell is spatially distant from the valence “p” shell, the halogen atoms simply do not have the orbital directionality necessary to perform two covalent or dative bonds to the Mg atom. Note that this is a very general conclusion concerning all halogen bonds with less electronegative elements. Hence, in the chlorine and bromine dimers the Mg–X bonds are ionic.

These chemical bonding results fit nicely within the observed dimerization tendencies in ether solutions. Both THF and Et₂O are low dielectric constant solvents having a low tendency to solvate ions or very polar species. In the case of methylmagnesium fluoride, it is experimentally determined that it is always dimerized in ether solutions. The fact that these solvents have a low tendency to solvate ionic compounds may function as a driving force for the dimerization of the ionic methylmagnesium fluoride to its associated covalent dimer. On the other hand, for chlorine and bromine the situation is more complicated. For chlorine and bromine the solvent driving force may work in the opposite direction, because now the associated dimers are ionic and the monomers are covalent. As the concentration increases, the ability for solvating ions and very polar species also increases, correlating well with the observed concentration dependency on dimerization for methylmagnesium bromide in Et₂O. However, the behavior of methylmagnesium chloride in both solvents and methylmagnesium bromide in THF is more complicated, being discussed at in the end of the next section.

3.1.3. Other Species. As for the other species studied in this work, we pinpoint the $\text{CH}_3\text{MgX}_2^-$ species as a very likely intermediate involved in the dimer formation. Different from dimeric species, all Mg–X bonds in $\text{CH}_3\text{MgX}_2^-$ were dative bonds. This is consistent with the explanations given above for the difference in the Mg–X bonding in the monomers and dimers. Because in the $\text{CH}_3\text{MgX}_2^-$ species, both the Mg–X bonds are the only ones made by the halogen, they are dative bonds. Their singly occupied orbitals are essentially identical to the ones associated with the dative bonds in the monomers, as should be expected. Another important intermediate species

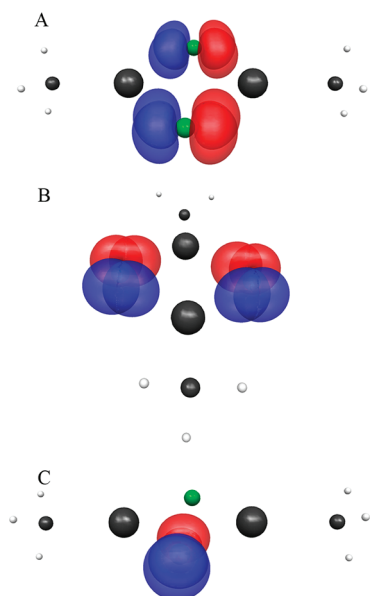


Figure 8. GVB orbitals for the methylmagnesium chloride dimer: (A) and (B) for “p-like” lone pairs in two different views; (C) for the other “p-like” lone pair.

involved in the dimer formation is CH_3Mg^+ , which has a C–Mg bond similar to those of the monomers.

Another chemical bond related issue that we have investigated was the possible specific interaction among solvent molecules and the Mg atom. Many theoretical studies on Grignard reagents published in the literature try to mimic the solvent effects by attaching one or two solvent molecules to the Mg atom in the monomer or dimer of halogen–alkyl–magnesium moieties.^{39,40,44,46,47,49} Those clusters of course do not constitute a solvent model. However, if there is an actual covalent or dative bond between the solvent and the Mg atom, it would be important to consider it in a correct description of the properties of these molecules in solution. The one and only possibility of a specific interaction in this case is a covalent dative bond from the oxygen atom of THF or Et_2O to the Mg atom. We were not able to perform a GVB calculation on this interaction in the cluster because there was no electron density in the Mg–O axis making orbital localization⁷⁵ impossible. Therefore, we are led to conclude that there is no specific interaction between the solvent and the Mg atom. To assign a covalent chemical bond between two fragments, we must have interference among singly occupied orbitals.^{76–79} If there are no orbitals, there is no interference. The cluster is held together only by classical electrostatic forces.

In the next section we discuss the complex equilibrium features of Grignard reagents in solution. It will be clearly shown that polar compounds traditionally identified as present in solution provide no explanation for the experimentally observed thermodynamic profile.⁹ Hence, anion and cation radical species are brought up providing a coherent picture of the details of the equilibria associated with different Grignard reagents, in different ethereal solvents (THF and Et_2O).

3.2. Grignard Equilibrium Constants. *3.2.1. Classical Investigations: Polar Neutral Species.* In the first experimental works and in all theoretical works published in the literature, all characteristics of Grignard reagents are tentatively explained with the Schlenk (reaction 1) and/or the dimerization equilibrium, using

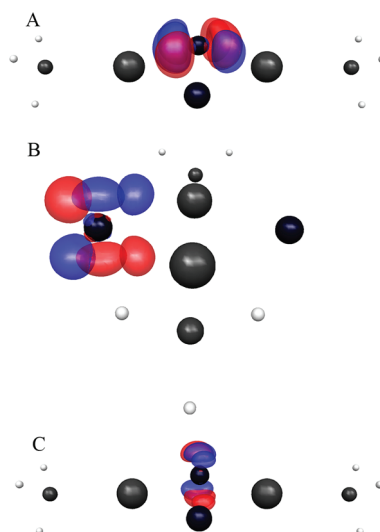
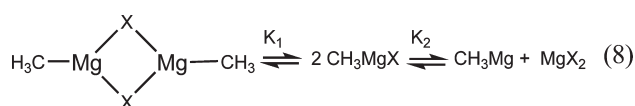


Figure 9. GVB orbitals for the methylmagnesium bromide dimer: (A) for “p-like” lone pairs; (B) and (C) for the other “p-like” lone pair in two different views.

only neutral species. To compare our calculations with previous ones and to validate the adequacy of the electronic structure models used here, we begin by considering only neutral species. We must point out that the assumption that only neutral species are relevant in the calculation of Schlenk or dimerization equilibrium constants has been made in many theoretical papers on the subject. However, in the literature these calculations are always incomplete in the sense that no work treats simultaneously both equilibria and halogen variation. Moreover, no theoretical work even mentions that many observed features of these equilibria are strongly dependent on the concentration. Nevertheless, we consider important to compare our results with those from the literature. This is necessary because it will show that the calculation level and the solvent model are not the important elements in the description of the equilibria. What is really essential is a careful consideration of the possible species present and their possible reaction pathways. In what follows we present our results on the equilibrium constants including only neutral species and compare our findings with other theoretical calculations and experimental results.

Equilibrium constants associated with the Schlenk and dimerization equilibria were calculated in the gas phase, in THF, and in Et_2O solutions with the PCM model (Tables 2 and 3) and with the cluster like model in Table 4. We must remark that no equilibrium constant was measured for the dimerization equilibria, only for the Schlenk equilibria (reaction 4). Clusters of solvent molecules with some neutral species were also calculated to investigate the importance of explicit interactions between solvent and magnesium atom. All Hessian calculations were performed by considering room temperature conditions, $T = 298.15\text{ K}$ and $P = 1\text{ atm}$.

Although our results for the Schlenk equilibrium constant have a qualitative agreement with the experimentally determined values, the simultaneous consideration of the dimerization process complicates the discussion. The results given in Tables 2–4 show that the dimerization energy by far exceeds that for the Schlenk equilibrium. An appropriate interpretation and comparison with the experimental values is crucial. The investigation should pursue the reasons that lead Grignard reagents to present

Table 2. Equilibrium Constants Values of the Dimerization (K_1), and Schlenk Equilibrium (K_2), Performed at the DFT (M-06) Level with the aug-cc-pVTZ Basis Set^a

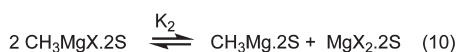
X	gas phase		THF		Et ₂ O	
	K_1 (mol/L)	K_2	K_1 (mol/L)	K_2	K_1 (mol/L)	K_2
F	6.60×10^{-41}	3.54×10^{-2}	8.48×10^{-30}	2.47×10^{-2}	3.34×10^{-31}	2.69×10^{-2}
Cl	4.24×10^{-28}	8.90×10^{-3}	5.67×10^{-19}	4.10×10^{-4}	2.21×10^{-20}	5.02×10^{-4}
Br	4.46×10^{-28}	3.77×10^{-3}	2.53×10^{-17}	2.50×10^{-4}	1.35×10^{-18}	3.65×10^{-4}

^a The constants were evaluated in the gas phase and in ethereal solvents THF and Et₂O with the PCM model. All values include zero-point vibrational energy (ZPVE) correction.

Table 3. Equilibrium Constants Values of the Dimerization (K_1), and Schlenk Equilibrium (K_2), Performed at the GVB-RCI Level with the aug-cc-pVTZ Basis Set^a

X	gas phase		THF		Et ₂ O	
	K_1 (mol/L)	K_2	K_1 (mol/L)	K_2	K_1 (mol/L)	K_2
F	3.65×10^{-36}	4.70×10^{-4}	9.17×10^{-26}	5.17×10^{-3}	1.44×10^{-26}	4.58×10^{-3}
Cl	1.05×10^{-22}	2.04×10^{-4}	2.36×10^{-13}	1.50×10^{-5}	1.22×10^{-14}	2.37×10^{-5}
Br	4.24×10^{-19}	2.87×10^{-4}	3.13×10^{-10}	1.04×10^{-5}	1.49×10^{-11}	1.94×10^{-5}

^a The constants were evaluated in the gas phase and in ethereal solvents THF and Et₂O with the PCM model. All values include zero-point vibrational energy (ZPVE) correction.

Table 4. Equilibrium Constants Values of the Dimerization (K_1), and Schlenk Equilibrium (K_2), of Grignard Reagents Coordinated with Two Solvent Molecules "S" (S: THF and Et₂O), Performed at the DFT (M-06) Level with the 6-311G** Basis Set^a

X	THF		Et ₂ O	
	K_1 (mol/L)	K_2	K_1 (mol/L)	K_2
F	3.16×10^{-40}	2.16×10^{-2}	1.37×10^{-40}	8.39×10^{-3}
Cl	3.10×10^{-27}	4.10×10^{-4}	7.19×10^{-25}	4.95×10^{-4}
Br	6.03×10^{-25}	5.36×10^{-3}	2.84×10^{-23}	1.27×10^{-3}

^a All values include zero-point vibrational energy (ZPVE) correction.

different profiles depending on the solvent, the halogen, and concentration. Theoretical studies are shown below in which we can observe incomplete approaches that do not allow a self-consistent understanding of the equilibrium in solution.

Khan and Pratt have already shown through DFT with a double numeric with polarization function (DNP) basis set that fluoride has the largest dimerization energy of the three in the gas phase.⁴¹ Additionally, Ehlers' group studying $\text{CH}_3\text{MgX} \cdot n\text{Et}_2\text{O}$ (X: Cl and Br), using DFT with the ADF code, showed

that chlorides have dimerization energies larger than that of bromides.⁴⁹ Their results are in agreement with our own. However, the experimental data tell a different story. In ethyl ether solvent, it is experimentally known that chlorides are dimeric even at low concentrations, bromides contain essentially monomeric species at low concentrations (less than 0.5 M) and dimeric species at higher concentrations (0.5–1.0 M).⁹ Hence, both the PCM model that assumes an infinite dilution in the solvent and its cluster model are not able to describe properly Grignard bromides in diethyl ether solution.

Additionally, our results including only neutral species in the gas phase (cluster model) or with the PCM solvent model, fail badly for chlorine and bromine in accounting for the experimental association preferences in THF. Only fluorides are dimeric species in THF.⁹

The documented differences between chlorides and bromides in Et₂O are probably the reasons why Yamazaki and Yamabe⁴⁵ only show the MeMgCl species in their study. They performed DFT/B3LYP/6-31G* calculations of dimers coordinated to the solvent, Me₂O, included together with the SCRF solvent model. They showed that the Grignard addition occurs in a dimeric dichloride bridged form, because chlorides are already experimentally known to be present as dimers in Et₂O. Yousef and co-workers¹² discuss the MeMgBr disproportionation or Schlenk equilibrium in THF and Et₂O with PCM. They have presented results that were already known experimentally. Their investigation did not include dimers. As observed in our PCM results, in Tables 2 and 3, the prevalent species are the dimers. However, they occur only when bromides are in Et₂O in higher concentrations (0.5–1.0 M).

Tables 2–4 indicate that Schlenk equilibrium is shifted toward the formation of the monomeric species, regardless of being in the gas phase or the type of solvent model. Many previous works^{38–41,44,47,49} assessing the disproportionation reaction of methylmagnesium halides have also obtained values of Gibbs energies favoring the formation of monomers.

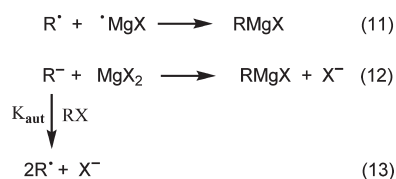
Kato and Mori⁴⁰ found, within their QM/MM approach, that both chlorides and bromides are monomers in Et₂O. This assertion is only correct for bromides below 0.5 M. When they take the bulk solvent out, they showed that the cyclic dimer should not be present. According to their calculations there would be only a linear dimer. Just as in the approaches described above, including our own so far, it does not account for the concentration dependence on the bromides aggregation, once it is experimentally known that CH₃MgBr is a dimer only above 0.5 M. In other words, a model that provides insight on the concentration dependence of the association degree of CH₃MgX species in solution is necessary. It is important to emphasize that the CH₃MgCl is dimeric over a wide concentration range in Et₂O solvent.⁹ Their QM/MM approach was not able to provide a spontaneous profile for dimerization process (cyclic or linear). In their calculations, the formation of the linear dimer of CH₃MgBr is slightly spontaneous (0.5 kcal/mol). It is not clear why this is in contradiction with what is observed in the experimental studies,⁹ which indicates aggregation of RMgBr's. Apparently, in their approach the more stable dimer, the linear one, has the greater coordination number, and without the bulk it is evaluated only as a Grignard ether complex. They do not attempt to explain why only the cyclic dimer appears in crystal structures,^{30–32} once it would be reasonable obtain crystals of structures with a greater number of coordinated solvent molecules.

As can be seen in previous tables, employing a comparative analysis among methylmagnesium halides in solvent, it could possibly indicate the (CH₃MgF)₂ as a dimeric species once it had the highest dimerization energy (*K*₁) and one of lower energies for monomer formation (*K*₂). This is the best that one can do without the inclusion of radical and charged species. It is clear that this type of analysis does not lead to a reasonable explanation for the different forms of aggregation in different solvents (THF and Et₂O) considering chlorides and bromides.

Up to this point, we realize that all previous theoretical approaches, including our own initial results, that consider only polar neutral species offer incomplete descriptions of Grignard reagents equilibria and their aggregation in different ethereal solvents. Hence, it is mandatory to include other species and other pathways that can provide us with better ways to account for the specifics of the different Grignard compositions in solution.

3.2.2. Role of Ionic and Radical Species in Equilibrium. Experimental association⁹ data and X-ray crystal structures^{30–32} consider and depict only neutral polar species. These types of experiments do not provide an accurate picture of the species present in solution. It is certain that ionic and radical species are present in Grignard reagent solutions, as shown by electrochemical studies.^{17–20,80–85} These additional species probably play a pivotal role in the determination of the different degrees of association found experimentally. In the following paragraphs, we briefly review the electrochemically based models for the Grignard reagent formation. Then, on the basis of these models and on our calculations, we propose a model that accounts for both the observed and calculated results.

Scheme 1. Radical Pathway and Carbanionic Pathway for Grignard Formation and Autocatalytic Process



There are different electrochemical models in the literature to examine Grignard reagent formation.^{4,6,80} Most of these studies are based upon observation of stereochemistry changes on structures of Grignard reagents and the related byproduct with which the existence of radicals in solution is directly associated. The conventional view on this question has been that alkyl radicals couple to $\cdot\text{MgX}$ radicals to yield RMgX. In this mechanism, the route of the alkyl radical presents a competition between a set of classical steps for alkyl radical (formation of radical pairs, dimerization, disproportionation, and atom transfer) and a coupling of the radical with $\cdot\text{MgX}$ providing RMgX.⁸¹

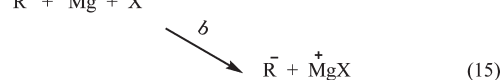
An alternative to this main route was Garst's formulation, which indicated the formation of RMgX via alkyl carbanions.⁸² The radical is reduced by any metallic atom of the surface and/or reduced into carbanion by the radical anions and would react with the MgX₂ species forming RMgX.

Kanoufi et al.⁶ reported electrochemical experiments that yield mixtures of carbanions and radicals at the cathode when alkyl halides are electrolyzed. They suggested that for a given "R" in the alkyl halide, the highest production of radicals (lowest yields in RMgX) should be expected for the iodides and bromides despite the fact that they are the best electron acceptors. This could be caused by two reasons (Scheme 1). The first would be that at the potential where RI and RBr are reductively dissociated, the reduction of the formed radicals into carbanions is relatively slow, and alkyl iodides and bromides would be selectively reduced and not R \cdot . The second reason would be an autocatalytic process, which is favored in the order RI > RBr > RCl. And for the nature of the R group the occurrence of the autocatalytic path would be favored in the order 3° > 2° > 1°. The alkyl chlorides were not examined by the authors because of the large negative potential demanded to carry out the reductive cleavage.⁶ By extrapolation, chlorides would behave just in the opposite way because at the potential at which they accept the electron, the radicals formed by their dissociative reduction would be ready to be transformed into carbanions.⁶ On the other hand, they are less favored than bromine for the autocatalytic process. Hence, iodides and bromides would be reduced easier than R \cdot , and chlorides lead predominantly to the R \cdot because the reduction of the R \cdot radical is easier than that of the starting alkyl halide.⁶ This trend could be observed in the work of Ebersson,⁸⁶ where *E*^o values are estimated for methyl halides in THF solvent. These values are given vs NHE (normal hydrogen electrode) and suggest that CH₃F (−1.59 V) and CH₃Cl (−1.49 V) would be more difficult to reduce than CH₃Br (−1.32 V) and CH₃I (−1.28 V). The extrapolation of this trend indicates that the best candidates for RMgX (alkyl) formation under these conditions would be the alkyl fluorides.

The considerations above give us ground to infer that the formation steps of Grignard reagents may be distinct for different halides. Thus, in a solution containing methylmagnesium bromide

Table 5. Gibbs Energies (ΔG^0 , kcal/mol) for Radical and Ionic Species of Grignard Reagents in Ethereal Solvents Performed at the GVB-RCI Level with the aug-cc-pVTZ Basis Set^a

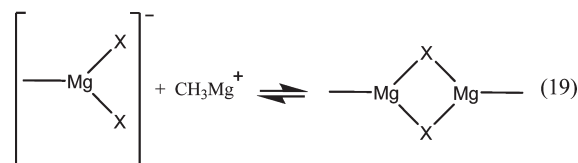
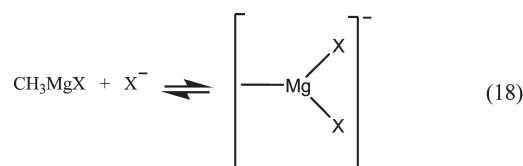
X	THF			Et ₂ O		
	ΔG^0_{11}	ΔG^0_{12}	ΔG^0_{13}	ΔG^0_{11}	ΔG^0_{12}	ΔG^0_{13}
F	−49.37	−7.79	9.91	−49.30	−7.36	11.06
Cl	−49.56	−34.05	−14.50	−49.52	−27.64	−7.77
Br	−49.53	−31.36	−11.49	−49.50	−32.37	−12.45

^a The subscripts on ΔG refer to the reactions depicted in Scheme 1.**Scheme 2.** Possible Species Presented in Grignard Solution via One ET Step (a) and Two ET Steps (b)

the only radical with appreciable lifetime would be the R^\bullet . For fluorides and chlorides, in solution, there could coexist R^\bullet and R^- . These two species are capable of forming $RMgX$ through different reactions, as presented in Scheme 1. Calculated energies for monomeric species formation via radical and carbanion in THF and Et₂O solutions are given in Table 5.

The autocatalytic process is not spontaneous for the alkyl fluoride in THF and Et₂O, as expected, and it is spontaneous for alkyl chloride and bromide.⁶ These results indicate that methylmagnesium fluoride could be the only one that has monomer formation via carbanion and radical species in both solvents. Once it was not possible to access the electrochemical properties of alkyl chlorides, it could not be confirmed whether alkyl chlorides undergo autocatalysis or not, as suggested by the data in Table 5. It seems reasonable at least, on the basis of reduction potentials of the methyl halogens, to expect an intermediate behavior between bromides and fluorides.⁸⁶ A change in radical or carbanionic dominating character could be conceivable depending on the medium employed. The difference on the autocatalytic reaction driving force, ΔG^0_{13} , of alkyl chlorides between THF and Et₂O is also remarkable. As previously proposed, in a solvent of high viscosity as THF, these carbanions would diffuse away more slowly from the metal surface.⁶ A higher concentration of carbanion could accumulate in the close vicinity of the surface, increasing the participation of the autocatalytic route as depicted in Table 5. This discrepancy for alkyl chlorides could be related to the fact that chlorides have a different form of aggregation in THF and Et₂O. Probably, as observed in fluorides, chlorides in Et₂O solvent might suffer a lesser amount of autocatalytic reaction and so it could also experiment some extent of monomer formation via carbanion.

It is well-known that fluoride and chloride Grignard reagents are dimeric species in Et₂O over a wide concentration range. Bromides are dimeric in concentrations greater than 0.5 M. It is

Scheme 3. Intermediate Dimer Species Formation and Dimer Reaction Formation**Table 6.** Gibbs Energies (ΔG^0 , kcal/mol) for a Possible Reaction Pathway To Obtain the Intermediate Species $RMgX_2^-$ in Ethereal Solvents Performed at the GVB-RCI Level with the aug-cc-pVTZ Basis Set

X	THF	Et ₂ O
F	−166.15	−178.55
Cl	−149.77	−167.61
Br	−153.33	−164.38

Table 7. Gibbs Energies (ΔG^0 , kcal/mol) for a Possible Reaction Pathway To Obtain Dimeric Species of Grignard Reagents in Ethereal Solvents Performed at the GVB-RCI Level with the aug-cc-pVTZ Basis Set

X	THF	Et ₂ O
F	−69.16	−82.93
Cl	−47.77	−60.77
Br	−42.10	−54.85

possible that in this concentration the carbanionic via is more prevalent than autocatalytic route providing the necessary conditions for dimer formation.

Regarding the other alkyl groups, a similar picture is experimentally expected.⁶ Within the set of the alkyl groups the methyl carbanion would be the weakest reducing agent and the *tert*-butyl carbanion would be the strongest reductant.⁶ To confirm the presented model, the autocatalytic process was also evaluated for *tert*-butyl radical and ionic species (Supporting Information, Table S8). The resulting values of free energy are as expected. For fluorides the autocatalytic process is still not spontaneous. Chlorides and bromides, which already have a spontaneous profile for autocatalysis, now have an even more favorable profile.⁶

It is experimentally well established that Grignard reagent formation reactions involve a series of electron transfers (ET).^{5,6,83,84} It was remarked⁸³ that in the study of this mechanism, it is essential to consider, for each of the reactive species, the extent of diffusion away from the metal/solution interface. One way to rationalize this very complex chemical landscape is to consider that the possible species presented in the medium are dependent on the predominance of one ET step or two ET steps before reaching the equilibrium. Thus, as

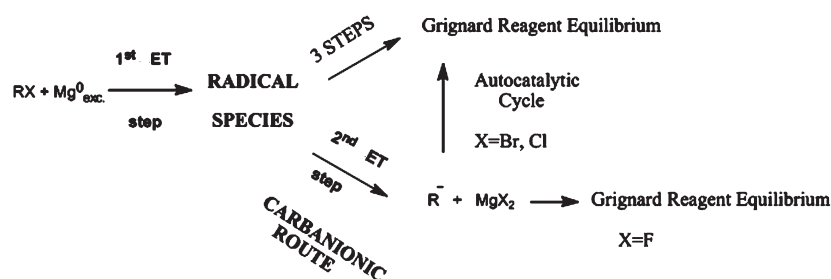


Figure 10. Grignard radical and carbanionic pathways to reach the solution composition at equilibrium.

represented in Scheme 2, the Grignard solution could have predominantly different species according to the number of net ET steps prior to thermodynamic equilibrium.

As indicated in reactions 16 and 17 (Scheme 2), dimeric species could be generated from different pathways; it is necessary to emphasize that the predominant character (radical or carbanionic) is responsible for each species present at equilibrium.

On the basis of our calculations, we propose here a path (Scheme 3) to clarify the mechanism of dimeric species formation. From Table 5 it is reasonable to expect that species RMgX and X^- (reaction 12, Scheme 1) are present in Grignard solutions in different amounts according to the predominance of carbanionic pathway. A possible reaction between these species could yield $\text{CH}_3\text{MgX}_2^-$ as an intermediate species in dimer formation (reaction 18, Scheme 3). This intermediate could react with CH_3Mg^+ yielding the dimeric species (reaction 19, Scheme 3); the Gibbs energies for these reactions are presented in Tables 6 and 7, respectively.

As expected, the intermediate reaction formation (Scheme 3, reaction 18) and dimeric reaction formation (Scheme 3, reaction 19) are spontaneous processes. It is believed that these ionic intermediate species would be in low concentration in solution. No paper in the literature attempts to correlate the participation of ionic and radical species in Grignard formation reactions with the different Grignard composition in solution. Due to the high degree of spontaneity calculated for the reaction of these intermediates to yield the dimers, as suggested in Tables 6 and 7, if these species are really involved in the equilibrium, they are in a very low concentration. The model used assumes that the different Grignard solutions have the same ionic species concentration. However, one expects that chlorides and bromides undergo an autocatalytic process in different degrees. Hence, their radical and carbanionic contributions are not known, so we could estimate that the magnitude of the energies of these reactions cited above are smaller than shown in Tables 6 and 7. In the latter table we could also infer the $\Delta\Delta G^0$ for dimeric species formation in different solvents and Grignard reagents. As previously observed,⁹ only fluoride Grignard is dimeric, and its lowest value is provided in THF solvent as the others. Chlorides are dimeric only in Et_2O solvent, and it is reasonable suggest that values from -60 kcal/mol could yield the dimer. In this way we could anticipate that with the increasing of bromides concentration it would be possible to account for the dimer formation in Et_2O . That is, in higher concentrations we would expect the prevalence of carbanionic route.

Our proposition concerning the equilibrium associated with the Grignard reagents is summarized in Figure 10.

The usual explicit or implicit argument used in theoretical approaches to the subject is that although radical and charged species are important in the formation of the Grignard reagents,

once the equilibrium is reached, these species are not relevant anymore. In the present paper we challenge this view. We show that only by considering radical and charged species, we obtain a cogent picture of the equilibrium composition relevant to account for the features of Grignard reagents.

4. SUMMARY AND CONCLUSIONS

In this paper we have presented a detailed study of the electronic structure and chemical bonding of the components of Grignard reagents. We also have performed a thorough analysis of the complex solution chemical equilibrium that determines the actual components that define the Grignard reagent for three different halogens: fluorine, chlorine, and bromine. It is important to point out that, in spite of the large amount of experimental data that confirms the essential participation of radical and charged species on the Grignard reagents formation, ours is the only theoretical approach to the subject that actually considers the influence of the radical and charged species in the resultant equilibrium. Our most important findings are summarized below.

The chemical bond in methylmagnesium halides was analyzed with singly occupied nonorthogonal orbitals derived from fully optimized GVB-RCI wave functions. We found out that in the neutral methylmagnesium halides the C–Mg bonds are all very similar, being clearly classified as a very polar covalent bond. On the other hand, the Mg–X bond has different characters depending on the halogen. The Mg–Cl and Mg–Br bonds are best viewed as covalent dative bonds, because both singly occupied nonorthogonal orbitals are centered in the halogen atom and are localized in the Mg–X bond axis. Differently, the Mg–F bond is classified as ionic due to the fact that after the GVB-RCI orbital optimization, there was no pair of orbitals located in the Mg–F bond axis. The three pairs considered were centered in the fluorine atom directed away from the Mg–F bond axis. For the dimers of methylmagnesium halides the situation is reversed. The fluorine dimers have covalent dative Mg–F bonds and the chlorine and bromine dimers have ionic Mg–Cl and Mg–Br bonds. The reasons for this curious behavior are explained in detail in the text and are associated with the differences in hybridization tendencies in function of the periodic table row where the halogen atom is located. This model successfully accounts for the chemical bonds in other radical and charged species considered. Additionally, the bonding model is in line with the association tendencies of the methylmagnesium fluoride in ether solutions in relation to the other halides. Finally, we have analyzed the possible specific interaction between solvent molecules and Mg atoms. We have concluded that there is no specific bonding interaction between the solvent and the magnesium,

the system being held together only by classical electrostatic forces.

Equilibrium constants were calculated for the Schlenk equilibrium and dimerization equilibrium, which do not contemplate radical and charged species. These calculations were performed in the gas phase, with the PCM solvent continuum model and with a cluster model where solvent molecules were coordinated to the Mg atom. The solvents used were tetrahydrofuran (THF) and ethyl ether (Et₂O). The qualitative results obtained were very similar regardless of the model for the solvent used, or if the systems were in the gas phase or surrounded by explicit solvent molecules. Although these results are in general agreement with the ones presented in other theoretical works in the literature, they do not yield a consistent picture of the observed features of the Grignard reagents. Hence, we were led to consider alternative radical and charged species to take part in the equilibrium. On the basis of the large body of electrochemical evidence in the literature that points out the importance of charged and radical species in this system, we considered alternative chemical species in the Grignard reagent equilibria. Two possible pathways are proposed in the literature to account for the properties of Grignard reagents. The radical path, and the carbanionic path. We have found that, according to our calculations, depending on the halogen, a different route to equilibrium would be preferably followed. Chlorine and bromine methylmagnesium species would be associated with the radical path, incremented with an autocatalysis path that decreases significantly the formation of carbanions by consuming them to generate radicals. On the other hand, this autocatalysis path would be extremely unfavorable for fluorine methylmagnesium species. Thus fluorine-based Grignard reagents would be mainly produced by the carbanionic route. The consideration of these two possible paths allows an understanding of the observed differences between the equilibrium degrees of association of methylmagnesium halide in ethereal solution. For fluorine the carbanionic route lead to the species involved in dimer reaction formation (Scheme 3, reactions 18 and 19). On the other side bromine and chlorine following the radical route do not lead to these species directly. It would be necessary for the autocatalysis process to obtain the species involved in the reagents in reaction 18. A novel and reasonable pathway that leads to the dimer formation was proposed. Assuming this route, via CH₃MgX₂[−], it is possible to correlate the differences between different halogen-based Grignard reagents, their forms of aggregation, and the relative concentrations of ionic species.

■ ASSOCIATED CONTENT

S Supporting Information. Optimized geometries of magnesium compounds involved in this study, determined at different levels of calculation, spin densities, and Gibbs energies. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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■ REFERENCES

- (1) Grignard, V. C. R. *Hebd. Seances. Acad. Sci.* **1900**, 130, 1322–1325.
- (2) Seyferth, D. *Organometallics* **2009**, 28, 1598–1605.
- (3) Ashby, E. C.; Oswald, J. J. *Org. Chem.* **1988**, 53, 6068–6076.
- (4) Garst, J. F.; Soriaga, M. P. *Coord. Chem. Rev.* **2004**, 248, 623–652.
- (5) Hazimeh, H.; Kanoufi, F.; Combellas, C.; Matallia, J. M.; Marchi-Delapierre, C.; Chanon, M. *J. Phys. Chem. C* **2008**, 112, 2545–2557.
- (6) Kanoufi, F.; Combellas, C.; Hazimeh, H.; Matallia, J. M.; Marchi-Delapierre, C.; Chanon, M. *J. Phys. Org. Chem.* **2006**, 19, 847–866.
- (7) Beal, B. J.; Bello, Z. I.; Cuddihy, K. P.; Healy, E. M.; Koon-Church, S. E.; Owens, J. M.; Teerlinck, C. E.; Bowyer, W. J. *J. Phys. Chem. A* **2002**, 106, 498–503.
- (8) Ashby, E. C. *Quart. Rev.* **1967**, 53, 259–285.
- (9) Ashby, E. C. *Pure Appl. Chem.* **1980**, 52, 545–569.
- (10) Yamakata, H.; Matsuyama, T.; Hanafusa, T. *J. Am. Chem. Soc.* **1989**, 111, 4912–4918.
- (11) Yamakata, H.; Shimizu, M. *Bull. Chem. Soc. Jpn.* **2004**, 77, 1757–1761.
- (12) Yousef, R. I.; Walford, B.; Rüffer, T.; Wagner, C.; Schmidt, H.; Herzog, R.; Steinborn, D. J. *Organomet. Chem.* **2005**, 690, 1178–1191.
- (13) Schlenk, W.; Schlenk, W., Jr. *Chem. Ber.* **1929**, 62 (4), 920–924.
- (14) Schlenk, W., Jr. *Chem. Ber.* **1931**, 64 (4), 739–743.
- (15) Cope, A. C. *J. Am. Chem. Soc.* **1934**, 56, 1578–1581.
- (16) Bartlett, P. D.; Berry, C. M. *J. Am. Chem. Soc.* **1934**, 56, 2683–2685.
- (17) Nelson, J. M.; Evans, W. V. *J. Am. Chem. Soc.* **1917**, 39, 82–83.
- (18) Gadum, L. M.; French, H. E. *J. Am. Chem. Soc.* **1927**, 49, 1925–1299.
- (19) Evans, W. V.; Pearson, R. J. *J. Am. Chem. Soc.* **1942**, 64, 2865–2871.
- (20) Yang, J.; Guo, Y.; Nuli, Y.; Wang, J. *Electrochem. Commun.* **2010**, 12, 1671–1673.
- (21) Smith, M. B.; Becker, W. E. *Tetrahedron Lett.* **1965**, 43, 3843–3847.
- (22) Smith, M. B.; Becker, W. E. *Tetrahedron* **1967**, 23, 4215–4227.
- (23) Holm, T. *Acta Chem. Scand.* **1969**, 23, 579–586.
- (24) Slough, W.; Ubbelohde, A. R. *J. Chem. Soc. Res.* **1955**, 108–114.
- (25) Ashby, E. C.; Smith, M. B. *J. Am. Chem. Soc.* **1964**, 86, 4363–4370.
- (26) Smith, M. B.; Becker, W. E. *Tetrahedron* **1966**, 22, 3027–3036.
- (27) Walker, F. W.; Ashby, E. C. *J. Am. Chem. Soc.* **1969**, 91, 3845–3850.
- (28) Parris, G. E.; Ashby, E. C. *J. Am. Chem. Soc.* **1971**, 93, 1206–1213.
- (29) Evans, D. F.; Fazakerley, V. J. *Chem. Soc. A* **1971**, 184–189.
- (30) Stucky, G. D.; Rundle, R. E. *J. Am. Chem. Soc.* **1963**, 85, 1002–1003.
- (31) Spek, A. L.; Voorbergen, P.; Schat, G.; Blomberg, C.; Bickelhaupt, F. J. *Organomet. Chem.* **1974**, 77, 147–151.
- (32) Richey, H. G., Jr. *Grignard reagents New Developments*; Wiley: Chichester, U.K., 2000.
- (33) Ashby, E. C.; Laemmle, J.; Neumann, H. M. *Acc. Chem. Res.* **1974**, 7, 272–280.
- (34) Salinger, R. M.; Mosher, H. S. *J. Am. Chem. Soc.* **1964**, 86, 1782–1786.
- (35) Ohkubo, K.; Watanabe, F. *Bull. Chem. Soc. Jpn.* **1971**, 44, 2867–2868.
- (36) Sakai, S.; Jordan, K. D. *J. Am. Chem. Soc.* **1982**, 104, 4019–4021.
- (37) Nemukhin, A. V.; Solov'ev, V. N.; Sergeev, G. B.; Topol, I. A. *Mendeleev Commun.* **1996**, 6, 5–7.
- (38) Liu, L.; Davis, S. R. *J. Phys. Chem.* **1991**, 95, 8619–8625.
- (39) Mori, T.; Kato, S. *Chem. Phys. Lett.* **2007**, 437, 159–163.
- (40) Mori, T.; Kato, S. *J. Phys. Chem. A* **2009**, 113, 6158–6165.
- (41) Pratt, L. M.; Khan, I. M. *J. Mol. Struct. (THEOCHEM)* **1995**, 333, 147–152.
- (42) Nemukhin, A. V.; Topol, I. A.; Weinhold, F. *Inorg. Chem.* **1995**, 34, 2980–2983.

- (43) Solov'ev, V. N.; Sergeev, G. B.; Nemukhin, A. V.; Burt, S. K.; Topol, I. A. *J. Phys. Chem. A* **1997**, *101*, 8625–8630.
- (44) Tammiku, J.; Burk, P.; Tuulmets, A. *J. Phys. Chem. A* **2001**, *105*, 8554–8561.
- (45) Yamazaki, S.; Yamabe, S. *J. Org. Chem.* **2002**, *67*, 9346–9353.
- (46) Tammiku, J.; Burk, P.; Tuulmets, A. *J. Phys. Chem. A* **2004**, *108*, 133–139.
- (47) Tammiku, J.; Burk, P.; Tuulmets, A. *J. Mol. Struct.* **2004**, *674*, 233–239.
- (48) Lu, X.; Ye, Jian-Liang; Huang, Pei-Qiang *J. Org. Chem.* **2007**, *72*, 35–42.
- (49) Ehlers, A. W.; Klink, G. P. M.; Eis, M. J.; Bickelhaupt, F.; Nederkoorn, P. H. J.; Lammertsma, K. *J. Mol. Model* **2000**, *6*, 186–194.
- (50) Persev, V. V.; Tulub, A. V. *Dokl. Phys. Chem.* **2006**, *409*, 237–241.
- (51) Faglioni, F.; Goddard, W. A. *Int. J. Quantum Chem.* **1999**, *73*, 1–22.
- (52) Barbosa, A. G. H.; Barcelos, A. M. *Theor. Chem. Acc.* **2009**, *122*, 51–66.
- (53) Schmidt, M. W.; et al. *J. Comput. Chem.* **1993**, *14*, 1347–1363.
- (54) Ivanic, J.; Ruedenberg, K. *Theor. Chem. Acc.* **2001**, *106*, 339–351.
- (55) Ivanic, J. *J. Chem. Phys.* **2003**, *119*, 9364–9376.
- (56) Bitzer, R. S.; Barbosa, A. G. H.; Silva, C. O.; Nascimento, M. A. C. *Carbohydr. Res.* **2005**, *340*, 2171–2184.
- (57) Lödwin, P. O. *Int. J. Quantum Chem.* **1995**, *55*, 77–102.
- (58) Goddard, W. A.; Dunning, T. H.; Hunt, W. J.; Hay, P. J. *Acc. Chem. Res.* **1972**, *6*, 368–376.
- (59) Goddard, W. A. *Phys. Rev.* **1967**, *157*, 81–93.
- (60) Goddard, W. A. *J. Chem. Phys.* **1968**, *48*, 450–461.
- (61) Gerratt, J. *Adv. At. Mol. Phys.* **1971**, *7*, 141–221.
- (62) Gerratt, J.; Cooper, D. L.; Raimondi, M. *Chem. Rev.* **1991**, *91*, 929–964.
- (63) Gerratt, J.; Cooper, D. L.; Raimondi, M.; Karadakov, P. B. *Chem. Soc. Rev.* **1997**, *26*, 87–100.
- (64) Goddard, W. A.; Carter, E. A. *J. Am. Chem. Soc.* **1986**, *108*, 2180–2191.
- (65) Amos, A. T.; Hall, G. G. *Proc. R. Soc. London A* **1961**, *263*, 483–493.
- (66) Tomasi, J.; Persico, M. *Chem. Rev.* **1994**, *94*, 2027–2094.
- (67) Tomasi, J.; Menucci, B.; Cammi, R. *Chem. Rev.* **2005**, *105*, 2999–3093.
- (68) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441–451.
- (69) Cancès, E.; Mennucci, B.; Tomasi, J. *J. Chem. Phys.* **1997**, *107*, 3032–3041.
- (70) Mennucci, B.; Cancès, E.; Tomasi, J. *J. Phys. Chem. B* **1997**, *101*, 10506–10517.
- (71) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215–241.
- (72) Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157–167.
- (73) Goddard, W. A.; Harding, L. B. *Annu. Rev. Phys. Chem.* **1978**, *29*, 363–396.
- (74) Kutzelnigg, W. *Angew. Chem., Int. Ed.* **1984**, *23*, 272–295.
- (75) Pipek, J.; Mezey, P. Z. *J. Phys. Chem.* **1989**, *90*, 4916–4926.
- (76) Ruedenberg, K. *Rev. Phys. Mod.* **1962**, *34*, 326–376.
- (77) Wilson, C. W., Jr.; Goddard, W. A. *Theor. Chim. Acta.* **1972**, *26*, 195–210.
- (78) Goddard, W. A.; Wilson, C. W., Jr. *Theor. Chim. Acta.* **1972**, *26*, 211–230.
- (79) Cardozo, T. M.; Nascimento, M. A. C. *J. Chem. Phys.* **2009**, *130*, 104102-1–104102-8.
- (80) Walborsky, H. M. *Acc. Chem. Res.* **1990**, *23*, 286–293.
- (81) Bodewitz, H. W. H. J.; Blomberg, C.; Bickelhaupt, F. *Tetrahedron* **1973**, *29*, 719–726.
- (82) Garst, J. F.; Ungváry, F. In *Grignard reagents New Developments*; Richey, H. G., Ed.; Wiley: Chichester, U.K., 2000; pp 185–276.
- (83) Hazimeh, H.; Mattalia, J. M.; Marchi-Delapierre, C.; Kanoufi, F.; Combella, C.; Chanon, M. *Eur. J. Org. Chem.* **2009**, *17*, 2775–2787.
- (84) Bodineau, N.; Mattalia, J. M.; Hazimeh, H.; Handoo, K. L.; Timokhin, V.; Négrel, J. C.; Chanon, M. *Eur. J. Org. Chem.* **2010**, *13*, 2476–2486.
- (85) Vegunta, S. S.; Ngunjiri, J. N.; Flake, J. C. *Langmuir* **2009**, *25*, 12750–12756.
- (86) Ebersson, L. *Acta Chem. Scand. B* **1982**, *36*, 533–543.