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Mechanism of the Grignard Reaction in Terms of the Cluster Model of Reaction Center. A Quantum-Chemical Study

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Abstract—Most probable paths of the classical Grignard reaction between ethyl bromide and Mg_{31} cluster simulating the reaction center on the surface of metallic magnesium were analyzed in terms of the density functional theory [B3PW91/6-31G(*d*)]. Principal thermodynamic parameters of the radical reaction path, including the energy of adsorption of oxidant molecules on the cluster, the energy of formation of ethyl radicals, and the energy of their subsequent interaction with the surface, were calculated. The structure corresponding to the true transition state of the Grignard reaction was identified. The low energy of activation of the reaction occurring at the phase boundary (5.1 kcal/mol) indicated that the surface reaction of radical formation cannot be rate-determining.

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The Grignard reaction, i.e., reaction of metallic magnesium with organic halogen compounds in diethyl ether or tetrahydrofuran, is one of the most important processes in organic synthesis. Direct oxidation of zero-valent metals with organic and organoelement compositions is the most accessible method for the synthesis of the majority of coordination and organometallic compounds [1–4].

Despite a long history [4–8], there are no distinct views on the mechanism and rate-determining stage of the Grignard reaction and related processes. At present, the hypothesis developed in [6–15] and implying radical nature of the reaction may be regarded as most substantiated. Here, it is believed that in the initial step an electron is transferred from the metal conduction band to the antibonding orbital of organic halide molecule adsorbed on the metal surface [10, 11]. Organic radicals generated in such a way are very reactive and are major reaction carriers. Radicals are capable of carrying on the transformation sequence both in solution as a result of free diffusion (model D) [12–15] and on the metal surface (model A) [10, 11].

Nowadays, the most fruitful model is believed to be mixed adsorption–diffusion model involving free radicals [16]. Dissociation of organic halide yields free radicals which readily adhere to the metal surface, as follows from their low energy of adsorption on the magnesium surface [17]. According to [12, 13], the concentration of radicals is significant even at a distant of hundreds nanometers from the surface. In keeping with that model, the reaction rate may be determined by the rate of formation of radicals. Taking into account that the concentration of radicals near the metal surface remains approximately constant, it may be presumed that the rate-determining stage is elementary reaction of radical with the surface. On the other hand, abstraction of a magnesium atom requires much energy [18], so that this process is most likely to be rate-determining.

Some authors [19–21] have developed an alternative concept of the Grignard reaction mechanism, namely a ionic–molecular path assuming formation of an activated complex via synchronous rearrangement of valence bonds and change of the spin state of the reacting species. The purely molecular path along the singlet energy surface is the most unfavorable from the viewpoint of energy, and the calculated energy of activation appears to be overestimated several times as compared to the experimental value. In particular, this was reported in [22, 23]. On the other hand, the formation of high-spin intermediates leads to the energy and enthalpy of activation approaching the corresponding experimental values. However, the origin of such states and their relation to the quantitative composition of the reaction mixture and physicochemical factors remain unclear.

Furthermore, the role of solvent in the process is not completely understood. It is only known that solvent considerably affects the energy of active centers in the adsorption on metal surface via redistribution of donated electron density between MOs of the metal [24]. There are data [25–27] indicating the reduction of the work function upon adsorption of various compounds on the metal surface. On the other hand, a solvent can dissolve a film formed by reaction products and transfer Grignard compound to solution as a result of complexation [28]. In any case, the reaction in solution occurs under considerably milder conditions than in the absence of a solvent [29–31].

The concept of surface active centers responsible for the entire cycle of transformations has not been developed in sufficient detail. We previously [18] made an attempt to formulate criteria according to which a part of metal surface (defect) may be regarded as active center. In particular, the most important condition is the low energy of abstraction of an atom from the crystal lattice. As shown in [32], most part of magnesium metal surface is unreactive, and Grignard compounds are formed on relatively small parts of the surface. In fact, about 150 reaction centers per square centimeter of magnesium surface were detected in the developed reaction with ethyl bromide in tetrahydrofuran solution (2.5 M) [33].

Kondin [34] noted high non-uniformity of metal surface etching, and the reaction occurred at the highest rate in the vicinity of maximally deformed areas. According to Teerlinck and Bowyer [35], the Grignard reaction is initiated and proceeds at a finite number of active centers on the metal surface, which grow during the process.

The mechanism of the surface stage of the Grignard reaction remains a matter of extensive discussion [19–23, 36]. Adsorption complexes of magnesium with ethyl bromide, as well as with various aprotic compounds (acetonitrile, THF, Et_2O, DMF, DMSO, pyridine) were studied in detail in [24]. In keeping with the data of [37–41], the chemisorption of organic halides on magnesium, copper, nickel, lead, silver, and palladium surfaces is accompanied by dissociation of the C–Hlg bond. Nuzzo and Dubois [37] revealed formation of Mg–Br bonds upon chemisorption of methyl bromide and its subsequent decomposition on the magnesium surface, whereas C–Mg bonds were not detected even at 120 K. Dissociation of C–Br bond over magnesium surface at 123 K occurs very readily. Taking into account that the pre-exponential factor in this reaction is 10^{13} s^{-1} and that the half-decomposition period is a few seconds, the expected energy of activation of the rate-determining stage should range from 25.7 to 33.5 kJ/mol. It was also noted [37] that the energy of activation of the dissociation of C–Hlg bond in an organic halide molecule near metal surface constitutes about 15% of the corresponding energy in the gas phase. According to the experimental data [42], the energy of activation of Grignard reactions with alkyl bromides is about 6 kcal/mol.

In the present article we consider the mechanism of the reaction of ethyl bromide with magnesium in the gas phase and analyze the most probable transformation paths of the Mg···EtBr adsorption complex. The thermodynamic parameters and energies of activation of particular steps were calculated in terms of the density functional theory at the B3PW91/6-31G (*d*) level. The functional and basis set were selected taking into account that they ensured satisfactory agreement with the experimental data in calculations of analogous systems [24, 43–46].

An active site on the metal surface is represented by Mg_{31} molecular cluster which is a fragment of the crystal lattice of bulk metal. It was assumed that in the Grignard reaction active is the central part of the basal crystallographic plane (0001) including 7 magnesium atoms and that the other atoms exert either an indirect effect or no effect at all. The geometric parameters of ethyl bromide molecule were fully optimized, and the adsorption complexes $Mg_{31}\cdots EtBr$ and intermediates (e.g., $Et\cdots Mg_{31}\cdots Br$, $Mg_{31}\cdots Et$, $Mg_{31}\cdots Br + Et^{\bullet}$) were also calculated after preliminary optimization of their geometries; the atoms belonging to the adsorbate and seven atoms in the outer layer of Mg_{31} cluster were left free, while the other atoms were fixed during the optimization process. The structure of Mg_{31} cluster is shown in Fig. 1.

The thermodynamic parameters of elementary steps were calculated as the difference between the total energies of the final and initial states. Transition states were localized using the Synchronous Transit-Guided Quasi-Newton method (STQN) on the basis of geometric parameters of the reactants and products

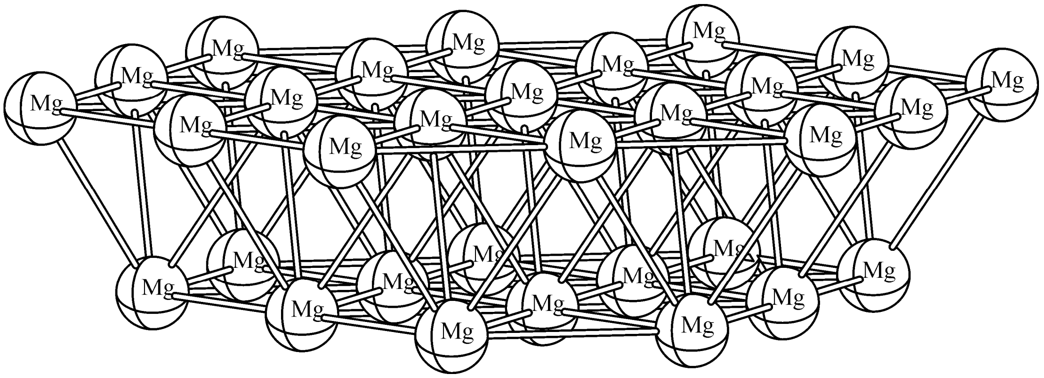

Fig. 1. Structure of Mg_{31} cluster used for the calculation of main Grignard reaction paths.

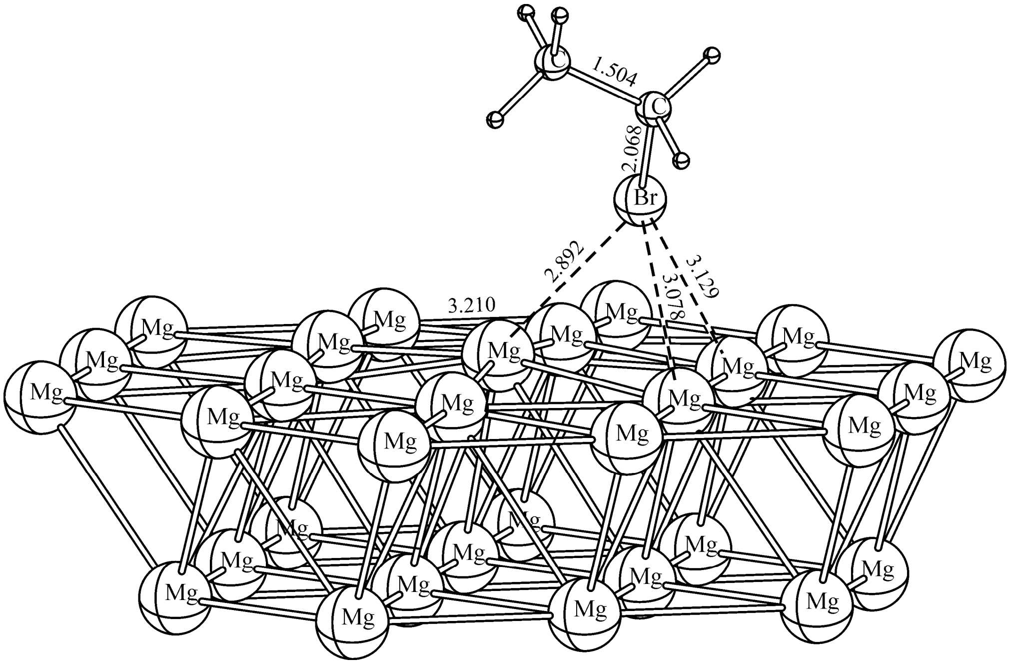

Fig. 2. Structure of the adsorption complex $Mg_{31}\cdots EtBr$ calculated by the B3PW91/6-31G(*d*) method with partial geometry optimization. Interatomic distances are given in Å.

(QST2), as well as on the geometry of probable transition state (QST3). Stationary points were identified as transition states by checking their molecular configurations for the number of imaginary vibration frequencies. The validity of transition states and their correspondence to a given transformation were proved by calculating the internal reaction coordinate. The calculations were performed using GAUSSIAN 09 Rev. A01 software package [47]. The molecular structures were visualized, and the initial geometric parameters were set, using MOLTRAN program [48].

The Grignard reaction begins with adsorption of reactants on the magnesium surface with the formation of adsorption complexes. According to the calculations, the chemisorption of ethyl bromide on Mg_{31} cluster is thermodynamically favorable: its is accompanied by an energy gain of 18.2 kcal/mol. As the initial state of the system we used isolated Mg_{31} cluster and EtBr molecule whose geometries in the ground singlet state were preliminarily optimized as indicated above. Figure 2 shows the structure of the $Mg_{31}\cdots EtBr$ complex.

It was also found that the triplet state of the magnesium cluster is thermodynamically more stable (by 4.4 kcal/mol), presumably due to additional delocalization of electrons over lattice sites.

We previously [17] calculated the energies of the reactions of ethyl bromide with one and two magnesium atoms, which were 3.7 and 7.2 kcal/mol, respectively. When the number of clustered magne-

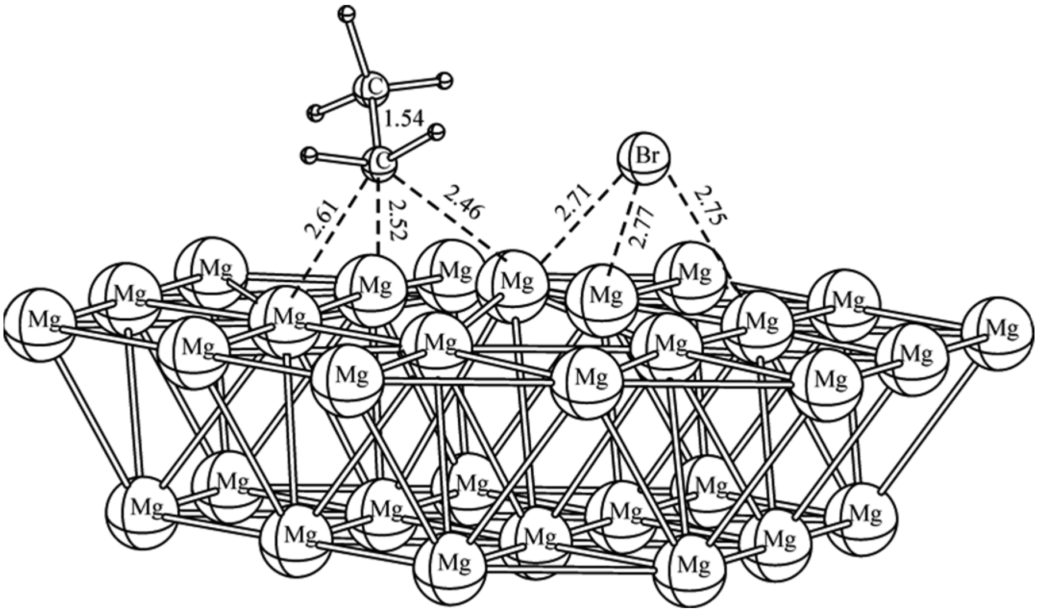

Fig. 3. Structure of the Br$\cdots$Mg$_{31}\cdots$Et intermediate calculated by the B3PW91/6-31G(*d*) method with partial geometry optimization. Interatomic distances are given in Å.

sium atoms reaches 31, the energy of the reaction with ethyl bromide per magnesium atom should be even lower. Likewise, lower energy of chemisorption of EtBr might be expected for an infinitely large cluster, i.e., bulk metal. However, resistometric study on the kinetics in the system Mg–EtBr showed that the enthalpy of adsorption of EtBr on magnesium is very small and is approximately –1.7 kcal/mol. This low adsorption energy was rationalized [4] assuming concurrent interrelated processes, one of which is a proper adsorption, and the second is related to the variation of the energy and geometry of the emerging adsorption complex.

The results of our calculations indicated a strong geo-metry relaxation of the adsorbed ethyl bromide molecule relative to isolated EtBr molecule and a change in the electronic structure of the cluster. Such mode of adsorption may be arbitrarily regarded as non-adiabatic; it leads to essential structural variations of both adsorbate and adsorbent.

In the next step, dissociation of adsorbed ethyl bromide molecule at the C–Br bond gives spatially separated ethyl radical and magnesium surface with bromide ion.

$$\mathrm{Mg_{31}\cdots EtBr \rightarrow Et^{\cdot} + Mg_{31}\text{–}Br.}$$

The process resulting in formation of free bromine atoms is thermodynamically unfavorable: it requires an additional energy of 63.9 kcal/mol. Moreover, molecular bromine has never been detected among the products. Dissociation of the C–Br bond in ethyl bromide molecule is also facilitated by higher polarity of that bond in the adsorbed molecule as compared to isolated.

Free ethyl radicals are very reactive; hypothetically, they are capable of binding to the metal surface. Adsorption of one ethyl radical on Mg$_{31}$ cluster reduces the total energy of the system by 31.2 kcal/mol. The rupture of the C–Br bond in the adsorbed ethyl bromide molecule provide an additional energy gain of 17 kcal/mol. The Grignard compound may be formed both via attack by ethyl radical on the active center possessing a bromine atom and through pre-reaction molecular complex Br$\cdots$Mg$_{31}\cdots$Et generated in the next step by attack by ethyl radical on the magnesium surface. The structure of this intermediate is shown in Fig. 3.

The latter process includes formation of EtMgBr by elimination of a magnesium atom from the outer layer of Mg$_{31}$ cluster. The examined paths of transformations in the system Mg$_{31}$–EtBr are illustrated by Fig. 4.

When adsorption complexes like Mg$_{31}$–EtBr were assumed to be the initial state, and intermediate Br$\cdots$Mg$_{31}\cdots$Et was selected as the final state, we detected a transition state by optimization of the reactants and products to first-order stationary point.

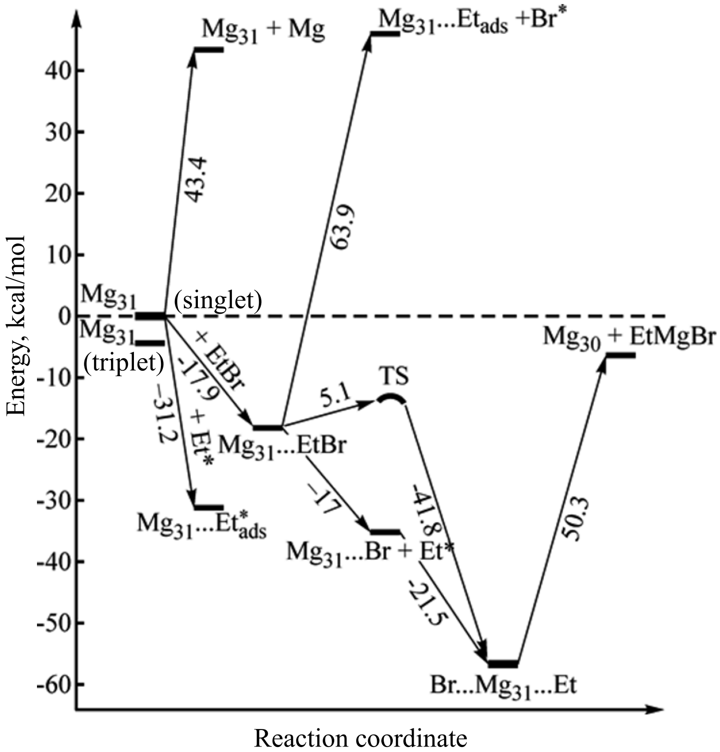

Fig. 4. Principal elementary reactions in the system Mg_{31}–EtBr. Energies of the corresponding transitions are given in kcal/mol (standard conditions); TS stands for transition state, S stands for singlet state, and T stands for triplet state.

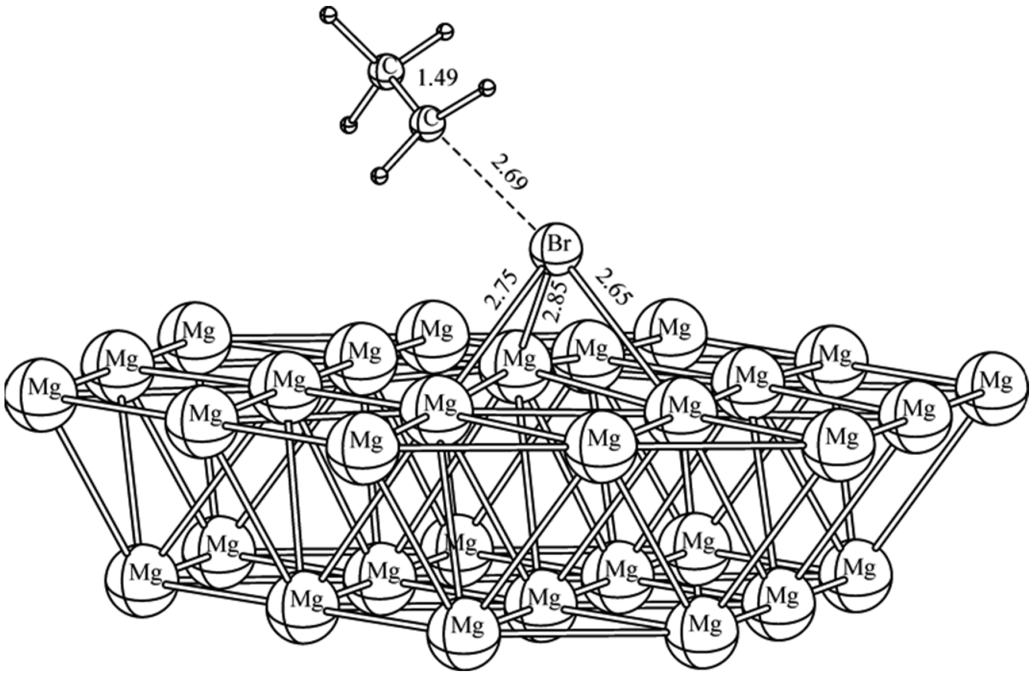

Fig. 5. Calculated structure of the transition state for the reaction $Mg_{31}\cdots EtBr(ads) \rightarrow [Br\cdots Mg_{31}\cdots Et]$. Interatomic distances are given in Å.

Figure 5 shows the structure of the activated complex in the main surface reaction. The distance from the C_2H_5 fragment in this complex to the bromine atom almost rules out the possibility for covalent bonding. This indicates only that the Grignard reaction follows mainly radical mechanism. The calculated energy of activation is 5.1 kcal/mol, which is comparable with the experimental value (6 kcal/mol) and is much lower

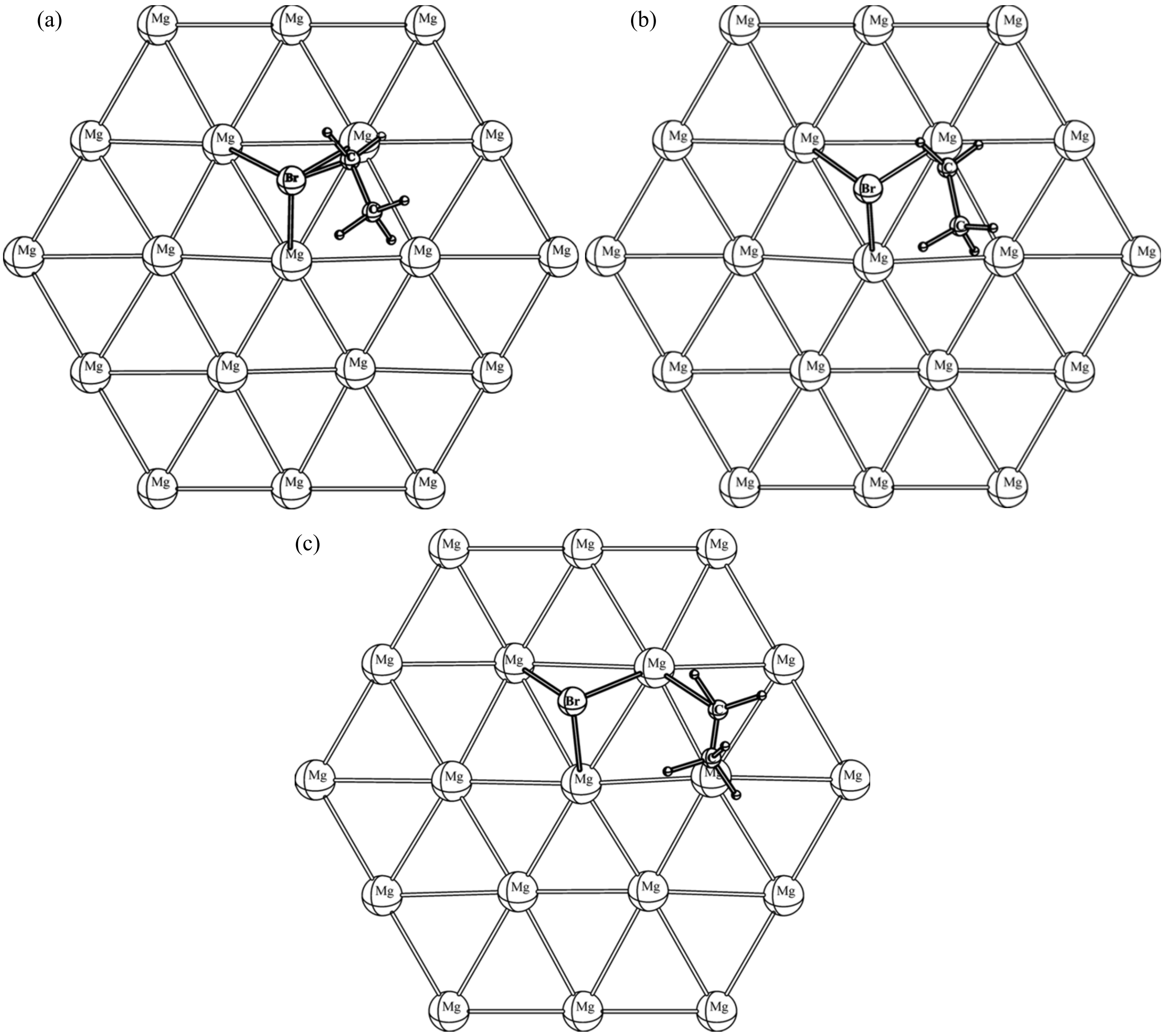

Fig. 6. Calculated structures of the (a) $Mg_{31}\cdots EtBr$ complex, (b) transition state, and (c) $Br\cdots Mg_{31}\cdots Et$ intermediate in the reaction $Mg_{31}\cdots EtBr(ads) \rightarrow [Br\cdots Mg_{31}\cdots Et]$. Top view on the (0001) plane of the cluster.

than the energy of the final step including abstraction of magnesium atom from the cluster with formation of isolated EtMgBr molecule (50.3 kcal/mol). Therefore, the surface reaction involving dissociation of organic halide is unlikely to be rate-determining. Presumably, the rate-determining step is just the transformation of the active surface-bound intermediate into Grignard compound.

All the above stated applies to the singlet ground state. Adsorption of ethyl bromide molecule on Mg_{31} cluster is simulated as coordination to the middle of a triangle formed by three neighboring magnesium atoms (lattice sites). After dissociation, the bromine atom and $Et^{\cdot}$ radical appear coordinated to the middle of two triangles with one common vertex (Fig. 6).

The transition state of the reaction $EtBr + Mg_{31} \rightarrow Et\cdots Mg_{31}\cdots Br$ is in fact a coordinated EtBr molecule with strongly extended C–Br bond (2.67 Å against 2.07 Å in the adsorbed molecule). In keeping with the examined scheme, the formation of a Grignard compound containing several magnesium atoms seems to be improbable, for abstraction of even two magnesium atoms from the active center requires an energy of 20–30 kcal/mol, while an additional energy of 40–80 kcal/mol is necessary to abstract Mg atoms from the crystallographic plane without rupture of the crystal order [18]. Figure 4 completely confirms this hypothesis: the last step of the overall process, i.e., the transformation of intermediate $Br\cdots Mg_{31}\cdots Et$ into isolated molecular product, requires the highest energy, 50.3 kcal/mol. Even though the Grignard compound were formed via direct attack by ethyl radical on the surface center possessing bromide anion residues, a high additional energy of no less than 28.8 kcal/mol per magnesium atom would be necessary. It should be presumed that just this reaction is rate-determining in the gas phase.

Thus the radical path of the Grignard reaction is thermodynamically favorable, and the surface stage cannot be rate-determining because of its very low activation energy (5.1 kcal/mol). The rate-limiting step of the overall process under isolated conditions is the formation of molecular Grignard compound via attack by alkyl radical on the metal surface containing halogen anion fragments or via rearrangement of $Br\cdots Mg_{31}\cdots Et$ intermediate. The role of solvent is likely to be confined to reduction of the activation and/or potential barrier of that step.

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