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AN AB INITIO APPROACH TO THE MECHANISM OF THE GRIGNARD REACTION

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Summary. The mechanism of the Grignard reaction is investigated for the first time in the light of ab initio SCF MO theory. The possible advantage of a single-electron transfer over a polar mechanism is discussed.

Although the reaction of Grignard reagents, RMgX, with ketones is of great importance in synthetic organic chemistry, the mechanistic details are still in considerable dispute[1]. The most significant question that remains to be answered is whether the reaction proceeds by a polar or a single-electron transfer(SET) mechanism. In past several years this mechanistic problem has been extensively explored by several authors[2]. Despite a number of accumulated experimental data, the topic has not yet been subjected to any theoretical investigations.

In an effort to outline a general mechanistic feature, we first examined the reaction of HMgH with H_2CO using the ab initio SCF MO method at the split-valence 3-21G level[3]. The reaction was considered in the anticipation that it would provide rather favorable conditions for detailed, theoretical treatments. The stationary points on the potential energy surface were carefully determined with the analytic gradient technique[4] and then identified as the equilibrium or the transition state(saddle point) by calculating normal vibrational frequencies.

Figure 1 Optimized geometries in Å and deg. for intermediates (A and B) and transition states (TS1 and TS2).

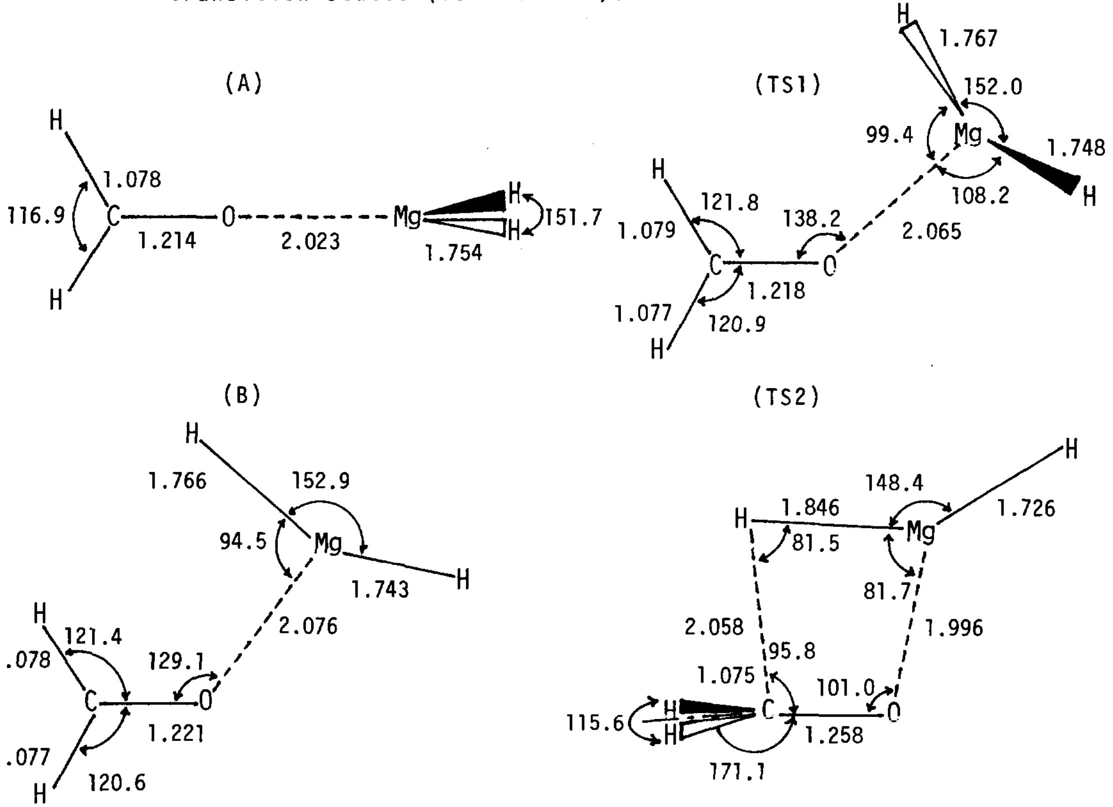
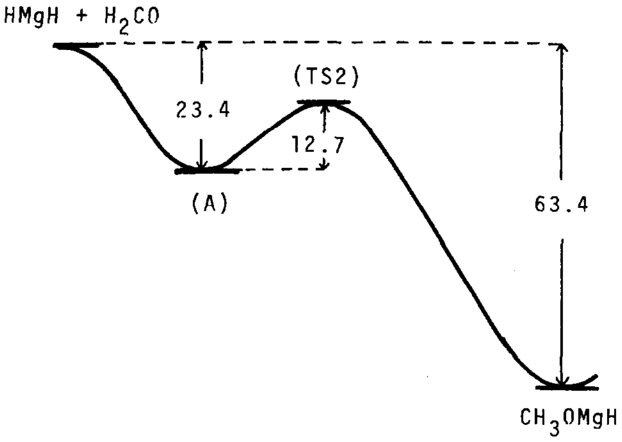


Figure 2 The energy profile (Kcal/mol) for the HMgH + H_2CO reaction along a polar pathway.



Upon going from the reactant, HMgH + H_2CO, to the product, CH_3OMgH, we found two intermediate σ complexes and two transition states, as shown in Fig.1. The complexes (A) and (B), separated with a small energy barrier[5] by a transition state (TS1), are held together with nearly the same stability: 23.4 for (A) and 23.8 kcal/mol for (B). In both complexes, the stabilization is due to the dominant contribution of the electrostatic interaction.[6] There existed no complexation to the π bond of H_2CO which might be expected in a polar mechanism.[7] The complex (A) is transformed via the rotation of HMgH about the carbonyl oxygen in a vertical bisector plane of H_2CO to a four-memberd ring transition state (TS2), resulting in the product.

The calculated energy profile in Fig.2 shows that the reaction is 63.4 kcal/mol exothermic. There is no energy barrier to the formation of the complex (A). The σ complex has to pass over an energy barrier of 12.7 kcal/mol to complete the reaction, this being the rate-determining step. A Mulliken population analysis reveals that HMgH acts as an electrophile. No significant apparent electron transfer between the reactant molecules takes places throughout the reaction, indicative of a polar mechanism.

An interesting finding is that the HOMO of the complex (A) is exclusively localized over HMgH while the LUMO over H_2CO. This means that a radical anion-radical cation pair ($H_2CO^{\overline{\cdot}}$ $MgH_2^{\overset{+}{\cdot}}$), a SET state, is formed just by exciting an electron from the HOMO to the LUMO. Naturally, the SET state could be substantially stabilized by using Grignard reagents with the higher HOMO energy level or ketones with the lower LUMO. An example of the latter is seen in the reaction of HMgH with dimesityl ketone where a SET pathway is suggested.[8]

The alkyl group of RMgX also can influence the advantage of a SET over a polar mechanism. For RMgH, the calculated HOMO energy levels (in eV) rise in the manner of R = H(-10.4), Me(-9.3), Et(-8.9), i-Pr(-8.5), and t-Bu(-8.3), while the LUMO energy levels are essentially unchanged by substitution. The same trends were also calculated for RMgCl. These agree with the experimental fact that a primary Grignard reagent generally prefers a polar mechanism while a tertiary one a SET mechanism. For a substrate whose LUMO is low enough, however, it is no matter whether a Grignard reagent is primary or tertiary.[9] A critical factor influencing the mechanism is a favorable match between the Grignard reagent's HOMO and the substrate's LUMO energy level, as has been noted in terms of the oxidation and the reduction potential.[2]

Also important in the electron transfer nature of the reaction are the effects of solvents. With solvation of two dimethyl ether molecules[10], for instance, HMgH was not only stabilized by 52.7 kcal/mol, but also its HOMO level was raised by 2.2 eV. A further study is in progress.

All computations were carried out at the computer center of the Institute for Molecular Science. We thank Prof. Morokuma for helpful comments.

References and Notes

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2. E. C. Ashby and J. R. Bowers, J. Am. Chem. Soc., 103, 2242 (1981) and a number of previous papers and references cited in this series.
3. J. S. Binkley, J. A. Pople, and W. J. Hehre, J. Am. Chem. Soc., 102, 939 (1980); M. S. Gordon, J. S. Binkley, J. A. Pople, W. J. Pietro, and W. J. Hehre, ibid., in press. We thank Prof. Gordon for the reference prior to publication.
4. A. Komornicki, K. Ishida, K. Morokuma, R. Ditchfield, and M. Conrad, Chem. Phys. Lett., 45, 595 (1977).
5. The complexes (A) and (B) are more stable by 0.5 and 0.9 kcal/mol, respectively, than the transition state (TS1).
6. This is obtained with the energy component analysis method of K. Morokuma, Acc. Chem. Res., 10, 294 (1977). In the complex (A), for instance, the attractive term consists of 65% electrostatic, 19% polarization, and 16% charge transfer interactions.
7. The paths where Mg lies in a plane perpendicular to the H_2CO plane were all downhill, resulting in the approach of HMgH in the H_2CO plane.
8. E. C. Ashby, A. B. Goel, and R. N. DePriest, J. Am. Chem. Soc., 102, 7779 (1980).
9. E. C. Ashby, J. Bowers, and R. DePriest, Tetrahedron Lett., 21, 3541 (1980); E. C. Ashby, and A. B. Goel, J. Am. Chem. Soc., 103, 4983 (1981).
10. It should be mentioned that the optimized geometry of $HMgH \cdot 2Me_2O$ was in good agreement with the crystal structure of ethylmagnesium bromide diethyrate by an X-ray diffraction study (L. J. Guggenberger and R. E. Rundle, J. Am. Chem. Soc., 90, 5375 (1968)).

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