

## Theoretical Study of Ene-Reaction of Allylic Grignard Reagents

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**Abstract:** The allyl compounds of Mg, react with an olefin by inversion of the allyl group via a six center transition state. These precyclic reactions may be one of the most important classes of organic reactions. The reactions of propenyl magnesium halides with ethylene were studied using *ab initio* calculations. The methods used for calculations are RHF, B3LYP and MP2 with 6-31G\* basis set. Researchers have investigated the structural properties, theoretical thermodynamic and kinetic data, i.e., rate constants of the reactions.

**Key words:** Mg-ene reaction, Grignard reagents, organometal molecules, *ab initio* calculations, molecular modeling

### INTRODUCTION

Grignard reagents are used as versatile chemical tools for C-C coupling during synthesis of live science or electronic molecules. The Grignard reaction is the addition of an organomagnesium halide to an electrophile. Mg-ene reaction in which transfers of “Mg” from the less-substituted allylic carbon to a carbon of the alkene function occurs simultaneously. Intermolecular Mg-ene reaction as the key step in synthesis of some important natural products has been achieved by Oppolzer *et al.* (1982), Oppolzer and Battig (1982), Oppolzer and Jacobsen (1986), Lemkuhl (1987) and Zuckerman and Breunig (2007). Also, he was studied about the potential energy surfaces of the methalo-ene reactions of allyl-MgH and allyl-Mg-Cl with ethylene using *ab initio* Molecular-Orbital (MO) Methods (Oppolzer, 1989). The insertion of an olefinic C=C bond into a metal-carbon bond is of potential interest as a preparative route to new products and as results of C-C coupling reactions to organic compounds. The allyl compounds of Mg react with the olefin by inversion of the allyl group via a six center transition state. These precyclic reactions may be one of the most important classes of organic reactions. The formal ene-reaction of allylic grignard reagents to olefins has been studied by <sup>1</sup>H-nmr spectroscopy and were applied for synthesis of complex molecules such as monoterpen alkaloids, irridoids,  $\Delta^{9(12)}$ -capnellene and polymers (Oppolzer *et al.*, 1982; Oppolzer and Battig, 1982; Oppolzer and Jacobsen, 1986; Lemkuhl, 1987; Zuckerman and Breunig, 2007; Houk *et al.*, 1995; Lehmkühl *et al.*, 1984). If the Mg-C bond at the beginning is much more reactive than the

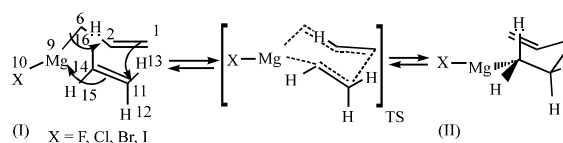


Fig. 1: The Mg-ene reaction of ethylene and Grignard reagent (X = F, Cl, Br, I)

Mg-C bond of the first insertion product, the reaction would terminate after the first step (Lemkuhl, 1987). Researchers studied the free energies ( $\Delta G^\ddagger$  and  $\Delta_r G$ ) of the reactants, transition states and products in the reactions of  $C_3H_5MgX$  (X = F, Cl, Br, I) with ethylene (Fig. 1) are recorded by using *ab initio* calculations. This reaction show the combination of the ethylene with  $C_3H_5MgX$  for reaching to a Mg- $\Delta^{9(12)}$ -capnellene (II) derivative as the favored product of the exothermic reaction are the main motive forces of these Mg-ene reaction.

### MATERIALS AND METHODS

**Computational details and calculations:** The *ab initio* molecular orbital calculations were performed with the Gaussian 98 Program. Geometries for all structures were fully optimized by means of analytical energy gradients in RHF, B3LYP and MP2 levels with the 6-31G\* basis set. Figure 2 shows optimized structures of  $C_3H_5MgX$  and  $C_3H_5MgX$ . The Synchronous Transit-guided Quasi-Newton (STQN) Method was used to locate reactants, products and transition states which were confirmed to have zero and one imaginary frequency,

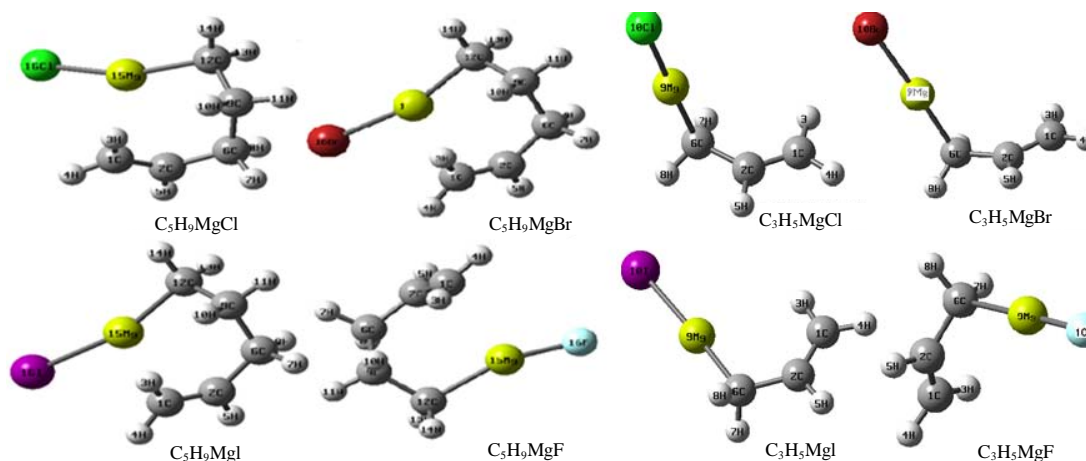


Fig. 2: The optimized structures of  $C_3H_5MgX$  and  $C_3H_9MgX$

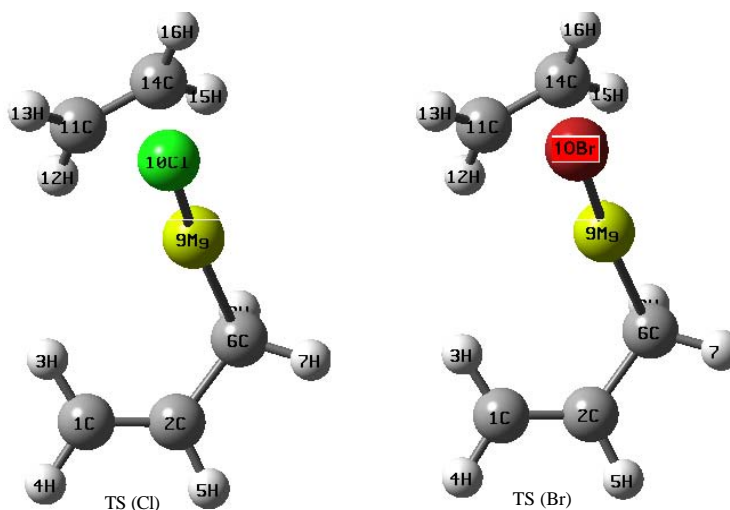


Fig. 3: The transition state of the Mg-ene Grignard reactions of  $C_3H_5MgX$  ( $X = Cl, Br$ ) with ethylene

respectively. Figure 3 shows some of optimized structures of transition state. The frequencies were scaled by a factor of 0.8929 and used to compute the free energies at 298°K. Then, the activation free energies ( $\Delta G^\ddagger$ ) and the free energies changes of reaction ( $\Delta_r G$ ) were calculated.  $\Delta G^\ddagger$  is the free energy difference between transition state and reactants.  $\Delta_r G$  is the free energy difference between products and reactants. Also, rate constants were calculated with the Eyring equation, derived from Transition State Theory (McQuarrie and Simon, 1997):

$$k = k_B T/h \exp\left(\frac{-\Delta G^\ddagger}{RT}\right)$$

In this study, the most conformations of the simple cycloalkynes (I) were investigated in the 1,3-dipolar cycloaddition reactions with ethylene.

## RESULTS AND DISCUSSION

The selected structural parameters for  $C_3H_5MgX$  ( $X = F, Cl, Br, I$ ), transition states and products are summarized in Table 1-3. These results were similar for Hartree Fock (HF), Density Function Theory (DFT) and Moller Plesset (MP2). Therefore, results are recorded only RHF Method. The energies in hartree for reactants, transition states and products by three methods are summarized in Table 4. The energy surface and the barrier energy for the reactions were investigated in detail by changing the position and distances between appropriate atoms in the reaction pathway. The diagram of the activation free energies ( $\Delta G^\ddagger$ ) and the free energies changes of reaction ( $\Delta_r G$ ) at 298°K for in the intermolecular Mg-ene reactions of  $C_3H_5MgX$  ( $X = F, Cl, Br, I$ ) with ethylene for producing the product

Table 1: Selected structural parameters of  $C_3H_5MgX$  (X = F, Cl, Br, I)

Parameters	X = F	X = Cl	X = Br	X = I
<b>Bond length (°A)</b>				
1C-2C	1.325	1.325	1.325	1.321
2C-6C	1.490	1.490	1.490	1.500
6C-9Mg	2.100	2.090	2.080	2.060
9Mg-10X	1.770	2.210	2.380	2.570
<b>Bond angle (°)</b>				
1-2-6C	127.090	127.070	126.960	126.560
2C-6C-9Mg	108.840	107.020	108.250	113.790
6C-9Mg-10X	178.860	179.020	177.770	177.520
<b>Dihedral (°)</b>				
1C-2C-6C-9Mg	-95.880	-92.740	-93.210	0.000
2C-6C-9Mg-10X	23.460	33.100	-177.840	180.000

Table 2: Selected structural parameters of transition states in the intermolecular Mg-ene reactions of  $C_3H_5MgX$  (X = F, Cl, Br, I) with ethylene

Parameters	TS (X = F)	TS (X = Cl)	TS (X = Br)	TS (X = I)
<b>Bond length (°A)</b>				
1C-2C	1.32	1.32	1.32	1.320
2C-6C	1.50	1.50	1.50	1.500
11C-14C	1.32	1.32	1.32	1.320
1C-11C	4.44	4.30	4.29	4.210
9Mg-14C	2.79	2.83	2.84	2.870
6C-9Mg	2.11	2.11	2.09	2.080
9Mg-10X	1.79	2.23	2.41	2.600
<b>Bond angle (°)</b>				
1C-2C-6C	126.74	126.29	126.27	126.150
2C-6C-9Mg	113.16	110.55	110.35	109.100
6C-9Mg-10X	155.05	161.42	161.32	161.840
<b>Dihedral (°)</b>				
1C-2C-6C-9Mg	88.28	78.47	78.02	74.820
2C-6C-9Mg-10X	23.24	33.54	33.61	35.821

Table 3: Selected structural parameters of products in the intermolecular Mg-ene reactions of  $C_3H_5MgX$  (X = F, Cl, Br, I) with ethylene

Parameters	Products ( $C_3H_5MgX$ )			
	X = F	X = Cl	X = Br	X = I
<b>Bond length (°A)</b>				
1C-2C	1.33	1.33	1.33	1.33
2C-6C	1.51	1.51	1.51	1.51
6C-9C	1.53	1.53	1.53	1.53
9C-12C	1.54	1.54	1.54	1.54
12C-15Mg	2.11	2.10	2.09	2.09
15Mg-16X	1.78	2.23	2.40	2.60
<b>Bond angle (°)</b>				
1C-2C-6C	127.10	127.19	127.05	127.09
2C-6C-9C	116.15	116.16	109.84	99.15
6C-9C-12C	113.11	112.95	115.92	112.74
9C-12C-15Mg	110.39	110.41	112.98	110.47
12C-15Mg-16X	161.58	159.71	162.97	162.04
<b>Dihedral (°)</b>				
1C-2C-6C-9C	-31.29	-29.00	-30.49	-29.99
2C-6C-9C10C	-64.52	-64.98	-64.68	-64.81
6C-9C10C-15Mg	49.78	48.19	49.05	49.48
9C10C-15Mg-16X	176.68	179.99	174.34	172.35

$C_3H_5MgX$  by RHF Method are shown in Fig. 4-7. The results show the treatment the electron correlation gives more stable energies. Also, kinetic data, i.e., rate constants of reactions and relative rate constants shown in Table 5. Structures for the synchronous transition state are obtained with mean bond length values of C-Mg and

Table 4: The free energies (G) in hartree of the reactants, transition states and products in reactions of ethylene (I) with  $C_3H_5Mg-X$  (II)

Species	G <sup>a</sup>	G <sup>b</sup>	G <sup>c</sup>
Ethylene	-77.998440	-78.5577600	-78.254520
$C_3H_5Mg-F$	-413.284333	-414.9419847	-413.832461
$C_3H_5Mg-Cl$	-768.659491	-770.5400890	-769.109119
$C_3H_5Mg-Br$	-2858.936629	-2861.5621420	-2859.407230
$C_3H_5Mg-I$	-7165.037650	-7168.4510920	-7165.479140
TS (F)	-491.277549	-493.4951310	-492.085928
TS (Cl)	-846.653277	-849.0940100	-847.362831
TS (Br)	-2936.930492	-2940.1166970	-2937.661730
TS (I)	-7243.033450	-7247.0048840	-7243.733650
Product (F)	-491.297313	-493.5172430	-492.115090
Product (Cl)	-846.674541	-849.1173540	-847.392951
Product (Br)	-2936.952095	-2940.1400110	-2937.692480
Product (I)	-7243.056491	-7247.0293140	-7243.764560

<sup>a</sup>RHF/6-31G\*, <sup>b</sup>B3LYP/6-31G\*, <sup>c</sup>MP2/6-31G\*

Table 5: The free activation energies, the free energies changes in reactions of ethylene (I) with  $C_3H_5Mg-X$  (II) in kcal/mol, rate constants in M/sec relative rate constants (K') calculated by methods of RHF and B3LYP and MP2

X in $C_3H_5Mg-X$	Methods	$\Delta G^\ddagger$	$\Delta_r G$	$K \times 10^{-10}$	K'
F	RHF	3.276	-9.124	2.453	1.000
	B3LYP	2.895	-10.980	4.682	1.000
	MP2	0.660	-17.640	203.660	1.000
Cl	RHF	2.990	-10.420	4.489	1.830
	B3LYP	2.409	-12.239	10.670	3.295
	MP2	0.507	-18.390	263.670	1.290
Br	RHF	2.872	-10.680	4.868	1.984
	B3LYP	2.011	-12.618	20.822	4.447
	MP2	0.013	-19.280	607.030	2.970
I	RHF	1.657	-12.800	37.841	15.429
	B3LYP	1.940	-12.840	23.590	5.039
	MP2	0.005	-19.390	635.419	3.170

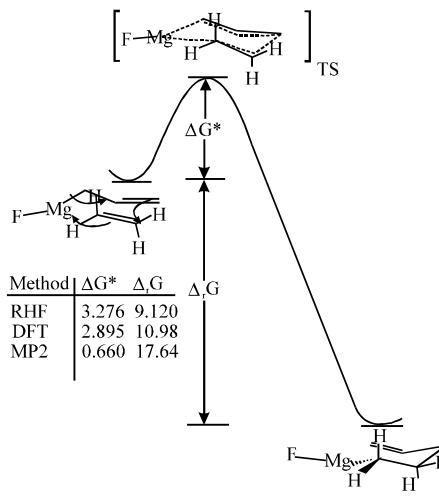


Fig. 4: The diagram of the free energies ( $\Delta G^\ddagger$ ) and the free energies changes of reaction ( $\Delta_r G$ ) at 298°K for the intermolecular Mg-ene reaction (I) of  $C_3H_5MgF$  with ethylene by using RHF/6-31G\*//RHF/6-31G\* Method

C-C bonds in transition states of  $C_3H_5MgX$  (X = F, Cl, Br, I) with ethylene. The bond length values of C6-Mg for

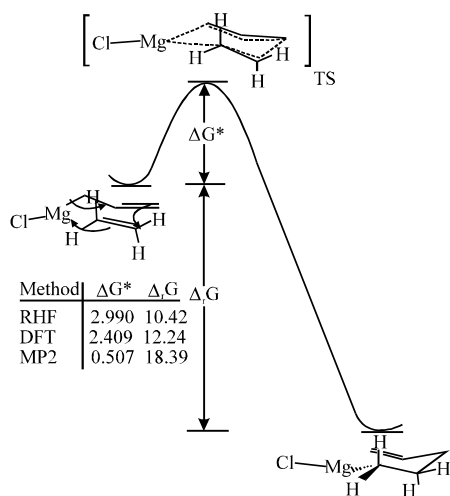


Fig. 5: The diagram of the free energies ( $\Delta G^\ddagger$ ) and the free energies changes of reaction ( $\Delta_r G$ ) at 298°K for the intermolecular Mg-ene reaction (I) of  $C_3H_5MgCl$  with ethylene by using RHF/6-31G\*\*/RHF/6-31G\* Method

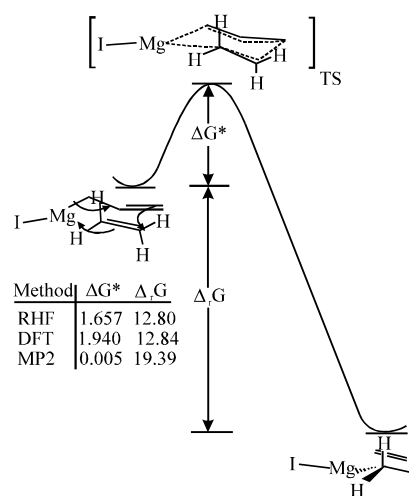


Fig. 7: The diagram of the free energies ( $\Delta G^\ddagger$ ) and the free energies changes of reaction ( $\Delta_r G$ ) at 298°K for the intermolecular Mg-ene reaction (I) of  $C_3H_5MgI$  with ethylene by using RHF/6-31G\*\*/RHF/6-31G\* Method

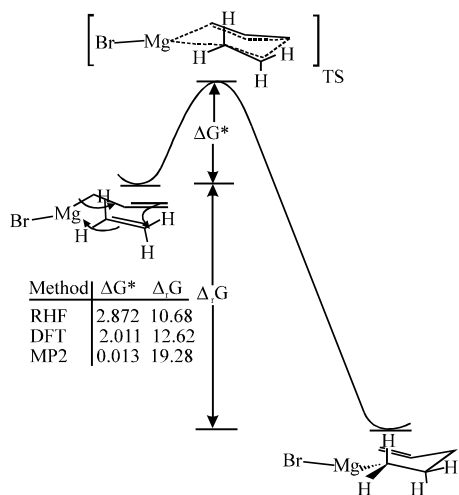


Fig. 6: The diagram of the free energies ( $\Delta G^\ddagger$ ) and the free energies changes of reaction ( $\Delta_r G$ ) at 298°K for the intermolecular Mg-ene reaction (I) of  $C_3H_5MgBr$  with ethylene by using RHF/6-31G\*\*/RHF/6-31G\* Method

the transition states are 2.11, 2.11, 2.09 and 2.08 in Å for the reactions of  $C_3H_5MgX$  ( $X = F, Cl, Br, I$ ) with ethylene, respectively. The calculated Mg-X bonds for  $C_3H_5MgX$  ( $X = F, Cl, Br, I$ ), the transition states and the product  $C_3H_5MgX$  are: ( $X = F$ : 1.77, 1.79, 1.78), ( $X = Cl$ : 2.21, 2.23, 2.23), ( $X = Br$ : 2.38, 2.41, 2.40) and ( $X = I$ : 2.57, 2.60, 2.60), respectively. Table 1-3 show the selected structural parameters of the reactions and the changes of the bond

lengths, bond angles and the dihedral angles of I, TS and II of the reactions. By increasing the size of halogen ( $X$ ) the bond lengths of Mg-X for I, TS and II have increased. For each intermolecular Mg-ene reactions of  $C_3H_5MgX$  ( $X = F, Cl, Br, I$ ) with ethylene (I), the thermodynamic and kinetic stabilities of are related to the character of the halogen, Mg-X ( $X = F, Cl, Br, I$ ) bond lengths and the structural characters particularly around the ( $C_6...Mg_9$  ( $X, 10$ )... $C_{14}C_{11}$ ) of the transition states. The kinetic stabilities were decreased by increasing the size of halogens, subsequently increasing the bond length strain of Mg-X in I and TS. Table 4 shows the calculated rate constants ( $K$ , in M/sec) by utilizing the RHF, DFT, MP2 Methods and basis set 6-31G\* and the Eyring equation.

The chemical affinity and the calculated rate constants in the method increased by the size of halogen in the Mg-X in I. The rate constants with RHF/6-31G\* method for the reactions of  $C_3H_5MgX$  ( $X = F, Cl, Br, I$ ) with ethylene (I) are 2.45E-10, 4.49E-10, 4.87E-10 and 37.84E-10, respectively. Also, the rate constants with DFT/6-31G\* Method for the reactions of  $C_3H_5MgX$  ( $X = F, Cl, Br, I$ ) with ethylene (I) are 4.68E-10, 10.67E-10, 20.82E-10 and 23.59E-10, respectively and the rate constants with MP2/6-31G\* for the reactions of  $C_3H_5MgX$  ( $X = F, Cl, Br, I$ ) with ethylene (I) are 203.66E-10, 263.67E-607.03E-10 and 635.429E-10, respectively. The results demonstrated that the rate constant show a grate different when the halogen was Iodide ( $X = I$ ). The rate constant in this condition is almost 10 times more than the other halogens  $X = F, Cl$

and Br in Mg-X bonds. The free energy differences between transition states and reactants ( $\Delta G^\ddagger$  in kcal/mol) by RHF Method for the reactions I are 3.28, 2.99, 2.87 and 1.66, respectively. The results show decrease in the  $\Delta G^\ddagger$  of the reactions of I by increasing the atomic number of halogen. The free energy changes of reactions ( $\Delta_r G$ ) are shown in Table 5. The values of  $\Delta_r G$  were obtained by the use of three methods. The values of  $\Delta_r G$  by RHF Method for the exothermic reactions of I are -9.12, -10.42, -10.68 and -12.80, respectively. The gaps in the free energies between reactants and products have been increased by the thermodynamic stability of bigger halogen (Table 4 and 5, Fig. 4-7). The results of the calculations show just a difference in the Mg-ene reactions of  $C_3H_5MgX$  (X = F, Cl, Br and I) with ethylene, in comparison with the other reactions in this group. See the results of X = I. The calculated data of relative constants ( $K'$ ) were shown in Table 5. These results suggest that the relative constants of reaction rates decreased by increasing the size of the halogen and increasing the bond length of Mg-X and also chemical affinity of reactants to take part in the Mg-ene reactions of I to produce of the Mg- $\Delta^{9(12)}$ -capnellene (II) derivatives.

### CONCLUSION

Comparing results show that in the Mg-ene Grignard reactions of  $C_3H_5MgX$  (X = F, Cl, Br, I) with ethylene (I) to producing the Mg- $\Delta^{9(12)}$ -capnellene (II) derivatives, the rate constant increases as increasing the size of the halogen and the free energies changes in reactions decreases. The comparison of the thermodynamic and kinetic data of the reactions I showed that the chemical affinity of I increases by increasing the bond length of Mg-X in RHF, DFT and MP2 Methods. The free energies ( $\Delta G^\ddagger$  and  $\Delta_r G$ ) of the reactants, transition states and products in the reactions of the Mg-ene reactions are recorded with three methods at 298°K. The kinetic data (rate constants = K in M/sec and relative constants =  $K'$ ) were calculated by the Eyring equation which is derived from Transition State Theory. In these exothermic reactions, the K and  $K'$  of the reactions increased by increasing the size of X and the bond length of metal-halogen bond for producing the Mg- $\Delta^{9(12)}$ -capnellene (II) derivatives.

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