

## A Valence Bond Description of the Grignard Addition Reactions to a Ketone

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### INTRODUCTION

With over a 100-year-old history, the Grignard reaction is one of the most versatile methods for C-C bond formation.<sup>1</sup> The complexity of the mechanism arises from the wide number of possibilities depending on the solvents used, alkyl group of the Grignard reagent, and several others factors. It is well known that the reaction of an allyl Grignard is faster than a methyl one with the same ketone.<sup>2</sup> Our goal here is to establish the rate controlling factors for the alkyl transfer mechanism in the reaction of the methyl and allyl Grignard reagents with acetone.

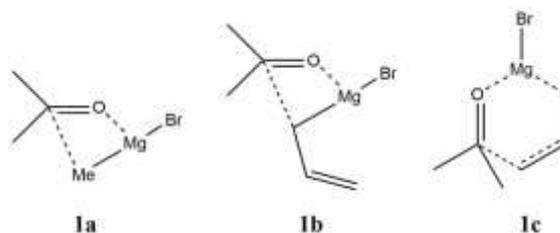
### METHODS

All geometry optimizations and stationary point characterizations were obtained through DFT/M06 functional and the 6-311G\*\* basis set using the polarizable continuum model (PCM) to mimic some of the solvent effects. The reaction path from the transition states (TS's) was followed both in reverse and forward direction to verify that the correct transition states, which connects the reactants and products, were obtained. Liquid-phase rate constants were calculated by equilibrium solvation path approximation with the GAMESSPLUSRATE interface using the SM8 solvation model. A multi-structure Valence Bond description of the TS's were obtained at the Multi-Configuration-Spin-Coupled, MC-SC/6-31G\*\* level with the VB2000/GAMESS package.

### RESULTS AND DISCUSSION

During the simulations, we found two type of TS's in the addition reactions: (i) A 4 - membered Cyclic TS (Fig.1a,b) that presents a considerable barrier reactions; (ii) A 6 – membered Cyclic TS with a barrierless path (Fig. 1c). The calculated rate constants (Table 1) demonstrated that the first type (i) is under thermodynamic control and the second is type (ii) is the kinetic reaction path. These results are consistent with the simple allyl

Grignard reagent tendency; they are often far too reactive to undergo to 1,3 - shifts.<sup>3,4</sup>



**Figure 1.** Possible transition states structures for Grignard addition reaction to the acetone: a) and b) 4-membered TS's, c) 6-membered TS.

| T (K)  | k <sub>1a</sub> | k <sub>1b</sub> | k <sub>1c</sub> |
|--------|-----------------|-----------------|-----------------|
| 273.15 | 4.91E-11        | 4.31E-03        | 3.81E+06        |
| 298.15 | 4.16E-09        | 4.19E-01        | 7.97E+06        |

**Table 1.** The forward rate constants (k) calculated at DFT/M06 level with the 6-311G\*\* basis set in Et<sub>2</sub>O. All evaluated with the SM8 model.

### CONCLUSIONS

The calculations performed in this work reveal the 6 – membered cyclic TS as the responsible path for the great reactivity in the allylation reaction. The 4 – membered cyclic TS's pathways for the addition reactions have a larger  $\Delta G^{0\ddagger}$  and present temperature dependence.

### ACKNOWLEDGMENTS

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<sup>1</sup> Handbook of Grignard Reagents: G. S. Silverman, P. E. Rakita, Eds; Marcel Dekker: New York, NY, (1996).

<sup>2</sup> T. Holm, G. Osztrovsky, R. Madsen, Org. Biomol. Chem., 8, 3402, (2010).

<sup>3</sup> R. W. Hoffman, Pure Appl. Chem., 60, 123, (1988).

<sup>4</sup> S. Yamazaki, S. Yamabe, J. Org. Chem., 67, 9346, (2002).