

# Quantum-Chemical Calculations of the Reaction of Haloalkynes with Grignard Compounds

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**Abstract**—Two pathways of the reactions of methylmagnesium bromide with 1-chloro- and 1-bromo-3-methoxymethyl-1-propynes were simulated by the MNDO quantum-chemical method. The calculations predict initial coordination of magnesium to the C<sup>β</sup> atom of the triple bond, which determines predominant nucleophilic substitution of the halogen atom according to the addition–elimination pattern.

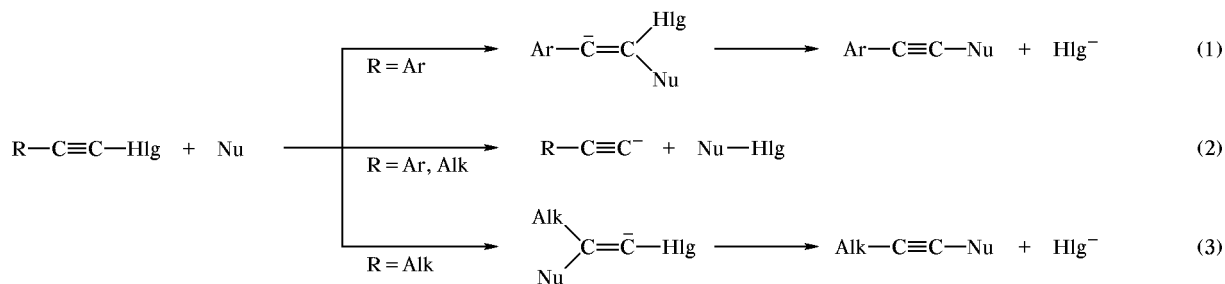
Experimental studies of the reaction of haloacetylenes with various nucleophilic reagents [1–4] gave rise to three main mechanisms of nucleophilic substitution of the halogen atom [2] (Scheme 1). The reaction pathway is determined by the halogen nature, nucleophilicity of the reagent, and stability of intermediate carbanion. The latter depends in turn on the substituent at the β-carbon atom [2]. Path (2) involves nucleophilic attack on the halogen atom; it is preferred for Hlg = Br or I. When Hlg = Cl, such nucleophilic species as OH<sup>−</sup>, HS<sup>−</sup>, SO<sub>3</sub><sup>2−</sup>, S<sup>2−</sup>, and C<sub>2</sub>H<sub>5</sub>S<sup>−</sup> attack carbon atom of the triple bond, following paths (1) and (3) [2]. Reactions of organomagnesium compounds with chloroacetylene derivatives, e.g., with chloropropynal diethyl and dibutyl acetals [5] or 4-chloro-2-methyl-3-butyn-3-ol [6], also give products of paths (1) and (3). Path (2) predominates in the reaction of methylmagnesium bromide with 1-bromo-2-phenylethyne [7]. Presumably, in these reactions halogen replacement follows the same mechanisms as those proposed for other nucleophilic reagents. However, organomagnesium compounds have some

specific features arising from the presence of magnesium atom as electrophilic center.

The present work was aimed at studying specific behavior of organomagnesium reagents in the reactions with haloalkynes and fine details of the mechanism of the process with regard to the halogen nature. The calculations were performed in terms of the MNDO semiempirical approximation [8] (AMPAC 3.00 software package) using magnesium parametrization from [9]. As model process we considered the reaction of methylmagnesium bromide with 1-halo-3-methoxy-1-propynes **I** (Hlg = Cl, Br).

**Electronic structure of initial reactants.** Solutions of alkylmagnesium halides may have very complex composition and structure, which depend on a number of factors (for review, see, e.g., [10]). In our calculations we used monomeric structure of methylmagnesium bromide solvated by two dimethyl ether molecules via coordination of magnesium to lone electron pairs of the ether oxygen atoms: CH<sub>3</sub>MgBr · 2O(CH<sub>3</sub>)<sub>2</sub> (**II**). The Mg–O bonds are fairly strong, the Mg–O distance is 2.105 Å. According to the

Scheme 1.





**Table 2.** Enthalpies of formation ( $\Delta H_f$ , kcal/mol) of  $C^\beta$ -coordinated complexes and lengths of the  $Mg \cdots C^\beta$  and  $Mg \cdots O$  dative bonds therein (Å)

Halogen	Complex	<i>cis</i> -Structure <b>A</b>			<i>trans</i> -Structure <b>B</b>	
		$-\Delta H_f$	$R(Mg \cdots C^\beta)$	$R(Mg \cdots O)$	$-\Delta H_f$	$R(Mg \cdots C^\beta)$
Cl		—	—	—	308.06	2.27
	⊥, 1	312.35	2.49	2.18	310.69	2.24
	⊥, 2	320.88	2.29	2.22	309.47	2.25
Br		—	—	—	297.85	2.27
	⊥, 1	305.03	2.48	2.17	301.10	2.25
	⊥, 2	313.77	2.28	2.22	299.49	2.23

**Table 3.** Stabilization energies of the complexes and energy parameters of the reactions (kcal/mol)

Halogen	Reaction no.	Hlg	$-\Delta E_1^a$	$\Delta E_2^{\neq b}$	$-\Delta E_2^c$	$-\Delta H_1^d$
Cl	4	<b>B</b> <sub>  </sub> , C <sup>α</sup>	63.09	16.95	47.60	80.69
		<b>B</b> <sub>⊥, 1</sub> , C <sup>α</sup>	65.72	22.40	45.24	
		C <sup>β</sup>		32.09		
Br	5	<b>B</b> <sub>  </sub> , Cl	63.09	29.19	3.07	72.52
		<b>B</b> <sub>⊥, 1</sub> , Cl	65.72	33.71	4.63	
	4	<b>B</b> <sub>  </sub> , C <sup>α</sup>	60.03	15.08	44.39	64.08
		<b>B</b> <sub>⊥, 1</sub> , C <sup>α</sup>	63.29	23.58	40.89	
	5	C <sup>β</sup>		32.32	35.33	
		<b>B</b> <sub>  </sub> , Br	60.03	27.60	4.07	63.84
<b>B</b> <sub>⊥, 1</sub> , Br	63.29	31.84	2.53			

<sup>a</sup>  $-\Delta E_1$  is the energy released upon formation of coordination complexes.

<sup>b</sup>  $\Delta E_2^{\neq}$  is the energy barrier to attack by nucleophile in the second stage of the process.

<sup>c</sup>  $\Delta E_2$  is the energy difference between the postreaction complex (or intermediate) formed in the second stage of the process and the prereaction complex.

<sup>d</sup>  $\Delta H_1$  is the enthalpy of the reaction, which is equal to the difference in the energy of the products and initial reactants **I** and **II**.

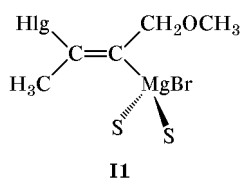
Complexes in which the magnesium atom coordinates only to the oxygen atom appear even less stable than complexes **B** with magnesium coordination at the  $C^\beta$  atom. A possible reason is that the MO including lone electron pair of the oxygen atom has higher energy than the  $\pi$ -MO including the triple bond. Among complexes **A**, the most stable are those in which the dative  $Mg-C^\beta$  bond is appreciably shorter (Table 2).

We calculated different steric structures of  $C^\beta$ -coordinated complexes **A** and **B** with coplanar (||) and orthogonal (⊥) arrangement of the  $CH_3MgBr$  molecule with respect to the  $Hlg-C \equiv C-$  axis. The  $CH_3$  group in complexes **A**<sub>⊥, 1</sub> and **A**<sub>⊥, 2</sub> is oriented upward and downward, respectively. *cis*-Complexes **A**<sub>||</sub> are unstable. The subsequent analysis and calculation of

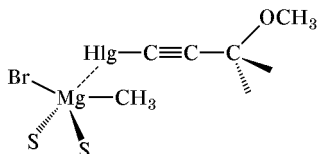
the reaction paths were performed using complexes **B**<sub>||</sub> and **B**<sub>⊥</sub> as examples. Charge distributions in these complexes are given in Table 1. It is seen that electron density transfer to the magnesium atom leads to slight increase of a partial positive charge on the halogen and decrease of negative charge on the  $\alpha$ -carbon atom. Such charge distribution is favorable for the subsequent nucleophilic attack by the  $CH_3$  group of the Grignard compound on both the halogen atom and  $C^\alpha$  in molecule **I**. Structures with coplanar arrangement of the  $CH_3MgBr$  molecule are polarized to a greater extent.

**Reaction mechanisms.** Reactions (4) and (5) were calculated, assuming the distance between the methyl carbon atom of the Grignard compound and electrophilic center in **II** or **I2** ( $C^\alpha$ ,  $C^\beta$ , and halogen atom)

as reaction coordinate. The transition structures were refined by repeated traversal over the transition state (TS) area through a reduced step (0.01 Å), followed by refinement of the TS geometry by minimization of the gradient norm. The principal energy parameters of reactions (4) and (5) thus obtained are given in Table 3. The formation of initial C<sup>β</sup>-coordinated complexes **B**<sub>||</sub> and **B**<sub>⊥,1</sub> in reactions (4) and (5) can be considered as the first stage of the reaction between reagents **I** and **II**. The data in Table 3 show that the activation barrier to reaction (4) is the lowest when nucleophilic attack by the methyl carbon atom of the Grignard compound is directed toward C<sup>α</sup>. This path consists of two steps following the addition–elimination pattern and results in formation of stable intermediate **II** with transoid arrangement of the halogen atom and MgBr group.



The energy of intermediate **II** is considerably lower than those of initial complexes **B**<sub>||</sub> and **B**<sub>⊥,1</sub> (see  $\Delta E_2$  in Table 3), and it approaches the energy level of the postreaction complex in reaction (4). For this direction of nucleophilic attack (from complex **B**<sub>⊥,1</sub>) we also performed calculations of a single-step mechanism with respect to two reaction coordinates: concerted addition of the CH<sub>3</sub> group to the  $\alpha$ -carbon atom and departure of the halogen atom to MgBr. The calculated activation barriers were 24.45 and 27.80 kcal/mol for Hlg = Cl and Br, respectively. These values are slightly greater than those obtained for single reaction coordinate. Presumably, halogen replacement by CH<sub>3</sub> group should occur without formation of intermediate **II** provided that there are factors favoring halogen abstraction. Such a factor may be primary coordination of the Grignard compound to the halogen.

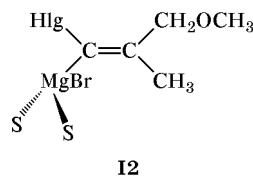


Such coordination complex is more stable than that formed by coordination to the  $\alpha$ -carbon atom; it was also obtained by control calculations for Hlg = F.

Another factor may be participation in reaction (4) of two CH<sub>3</sub>MgBr molecules or Mg(CH<sub>3</sub>)<sub>2</sub> + MgBr<sub>2</sub>; in this case a six-membered transition state could be formed. The calculations performed for the reaction system involving two nonsolvated molecules of methylmagnesium bromide showed formation of different bridged structures in which the magnesium atom coordinates to the  $\beta$ -carbon and oxygen atoms of initial haloalkyne; attack by the methyl group on the  $\alpha$ -carbon atom also gives intermediate **II**. Hence the formation of **II** in reaction (4) is determined by primary coordination of the Grignard compound to the  $\beta$ -carbon atom, in keeping with the MNDO predictions. On the other hand, intermediate **II** could also be formed as a result of primary nucleophilic attack by the methyl group on the  $\alpha$ -carbon atom, which leads to increase of the negative charge on the  $\beta$ -carbon atom and favors addition of MgBr. Obviously, more reliable data could be obtained by precise nonempirical methods and by studying Grignard compounds of various structures. However, this task remains so far fairly laborious.

Decomposition of intermediate **II** having *trans* configuration is characterized by an energy barrier of 21.61 kcal/mol (Hlg = Cl). This barrier is slightly lower than the barrier to formation of **II** and lower than that found for competing reaction (5) (Table 3). It should be noted that such *trans* elimination is favorable, e.g., for dehydrohalogenation of vinyl halides of the general formula CH<sub>2</sub>=CHHlg [13]. Therefore, in terms of the MNDO calculations, the formation of methylacetylenes in reaction (4) by the addition–elimination scheme (i.e., through intermediate **II**) seems to be feasible.

Nucleophilic attack by the CH<sub>3</sub> group on the  $\beta$ -carbon atom gives intermediate **I2** with a different structure:



From the viewpoint of thermodynamics, intermediate **I2** is less stable than **II**. Moreover, its formation requires a higher activation barrier to be overcome (Table 3). Taking into account that this path of the reaction between **I** and **II** is less probable, further decomposition of intermediate **I2** was not considered.

In reaction (5) nucleophilic attack on the halogen atom directly leads to formation of products or, more

precisely, of postreaction complexes in which the halogen atom in  $\text{CH}_3\text{Hlg}$  is still linked to magnesium through a dative bond. The transition structures are four-membered rings with the following bond lengths (the calculations were performed for complex **B**<sub>II</sub>):

Halogen	Cl	Br
$R(\text{Mg}-\text{C}^\alpha)$ , Å	2.285	2.253
$R(\text{Mg}-\text{CH}_3)$ , Å	2.236	2.227
$R(\text{CH}_3-\text{Br})$ , Å	2.191	2.246
$R(\text{Br}-\text{C}^\alpha)$ , Å	1.697	1.768

The energy barriers corresponding to the above transition states exceed by 12–13 kcal/mol (Table 3) those found for reaction (4) involving attack on the  $\alpha$ -carbon atom. Presumably, attack on the halogen atom in primary  $\text{C}^\beta$ -coordinated complexes is sterically hindered, for the halogen atom is a more distant center than  $\text{C}^\alpha$ .

The results obtained for  $\text{Hlg} = \text{Cl}$  are quite consistent with the experimental enthalpies of the two reaction paths (Table 3). The same also applies to the energies of activation, which indicate the least kinetic hindrance for reaction (4). As concerns  $\text{Hlg} = \text{Br}$  [in this case path (5) is preferred in experiments], the reaction enthalpies suggest comparable yields of the products even when the greatest kinetic hindrances for reaction (5) are assumed. Probably, in a real system this reaction pathway follows a different mechanism involving, e.g., primary attack by nucleophilic reagent. The calculations give almost similar mechanisms for  $\text{Hlg} = \text{Cl}$  and  $\text{Hlg} = \text{Br}$  owing to incorrect description of partial electron charges on atoms in the  $\text{Hlg}-\text{C}\equiv\text{C}$  fragment of initial haloalkynes in terms of the MNDO approximation. Another possible reason is overestimation of the interaction between the magnesium atom and  $\pi$ -MO of the triple bond.

Thus, the MNDO calculations of reactions (4) and (5) confirm the predominant contribution of path (4) for  $\text{Hlg} = \text{Cl}$  and predict three-step mechanism of the process: initial coordination of magnesium to the  $\beta$ -carbon atom, formation of stable intermediate **II**,

and formation of the products. Obviously, the case of  $\text{Hlg} = \text{Br}$  requires further study involving more accurate quantum-chemical methods.

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