MASARYK
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FACULTY OF SCIENCE

DEPARTMENT OF CHEMISTRY

Ph.D. Dissertation Proposal

HUGO SEMRÁD

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A Quantum Chemical Study on Mechanisms of *Z*/*E* Isomerization within Acetylene Bromoboration

Ph.D. Dissertation Proposal

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1. ABSTRACT

This work aims at exploring the isomerization step of acetylene bromoboration by means of density functional theory (DFT) and the second order Møller-Plesset perturbation theory (MP2) approaches. The proposed theoretical mechanism is in agreement with the experiment (Polášek et al, *J. Org. Chem.* Articles ASAP, Publication Date (Web): May 21, 2020). Our calculations suggest four pathways, two polar and two radical ones, along which the isomerization of (*Z*)-dibromo(2-bromovinyl)borane can proceed. The first polar mechanism involves a reaction of HBr with the *Z*-adduct, where HBr proton adds to the carbon bearing the dibromoborane group and the bromide anion adds to the boron atom. This addition is followed by an immediate decomposition into boron tribromide and vinyl bromide which was observed experimentally in the reaction mixture. The reaction barrier of ca 26 kcal mol^{-1} is achievable under experimental conditions and can lead to the desired product when a radical is created from vinyl bromide, BBr_3 is bound to the free carbon valence and a redundant Br atom leaves with a solvent molecule The second polar mechanism, well known as hydrobromination, involves same reactants as the first route, with the proton added to the carbon as before, but the bromide anion added to the carbon carrying bromine. After the rotation around the C-C bond and HBr elimination, *E*-adduct is formed. Energetically most demanding are the first addition step (a barrier of ca 30–40 kcal mol^{-1}, depending on method) and the last elimination step (40–50 kcal mol^{-1}). Third and fourth reaction routes were suggested based on radical reactions initiated by bromine radical. This can be formed in the mixture by homolytic cleavage of HBr, whereby the radical can be added to both carbons of (*Z*)-adduct. Thus, the third and fourth mechanism considers bromine radical attack on carbon bearing boron and carbon bearing bromine, respectively. In both cases, attacks are followed by a clockwise or an anticlockwise rotation around C–C bond and bromine radical elimination. Both pathways within the radical mechanism provide much lower reaction

barriers than for the polar mechanism, namely 4.6 and 1.8 kcal mol^{-1} for the bromine radical addition to alkene “bromine end” and “boron end”, respectively. Subsequent clockwise or anticlockwise rotation around the C–C bond must overcome a barrier of ca 6 kcal mol^{-1} for bromine added to alkene “bromine end” and of 2–4 kcal mol^{-1} for bromine attached to the “boron end”. The last, elimination step is associated with between 5 and12 kcal mol^{-1} of energy barrier (DFT and MP2 value) for the bromine radical cleavage from the alkene “bromine end” ca 5 kcal mol^{-1} (MP2) for the alkene “boron end”.

2. KEYWORDS

Addition; Alkene; Bromoboration; DFT; Elimination, Hydrobromination; IRC; Isomerization; MP2; Radical; Rotation; Single Coordinate Driving.

3. INTRODUCTION

Quantum chemical calculations are nowadays one of the most important approaches for understanding the electronic structure and reactivity, as well as the mechanisms of chemical reactions. This work is focused on the application of quantum mechanics in organic chemistry, specifically on the isomerization step within the bromoboration reaction of acetylene. The current chapter summarizes previous knowledge on the problem and the aims of this thesis.

The term alkyne bromoboration refers to an electrophilic addition of BBr_3 or other bromoboranes to alkyne triple bond. The BBr_2 group binds to one carbon atom and the bromine atom to the second carbon atom within one elementary step. The new substituents can be orientated in *syn* position relative to each other, then the (*Z*)-adduct is formed, or in *anti* position which results in the (*E*)-adduct. The first published study of bromoboration is due to Lappert and Prokai and dates back to 1963.[1] Its theoretically most interesting aspect is the observed difference between the stereochemistry of the products in the case of addition to acetylene and to diphenylacetylene. While bromoboration of the latter provided the product expected in the *syn* addition, reaction of the former resulted in the more thermodynamically stable *anti* product. Lappert and Prokai suggested two possible explanations for this phenomenon. The first hypothesis concerned the presence and absence of four-centered transition state (**Fig. 1**) for unsubstituted and substituted acetylene, respectively. The second hypothesis suggested a thermodynamic (instead of a kinetic) reaction control with unsubstituted acetylene.

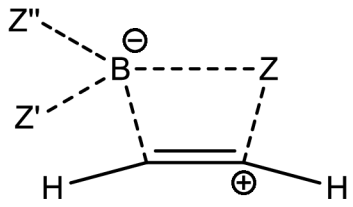


Figure 1: The four-centered transition state.

In 1973, a detailed study reported the bromoboration of phenylacetylene with boron tribromide, resulting in the mixture of (*Z*) and (*E*) adducts.[2] From the relative proportion of the two stereoisomers as a function of a dilution, a reaction temperature and a solvent polarity, the author concluded on different kinetically controlled reaction mechanisms for different adducts, with the *anti* adduct being preferred over the *syn* adduct in solvents that stabilize better polar transition states. The kinetics of bromoboration was then studied in detail

for a series of acetylene derivatives with two ethyl, propyl, and one or two butyl substituents, with the 15:1 *Z*/*E* adducts ratio found 1 hour after preparation and the 1:7 *Z*/*E* ratio after a few days.[3]

In 1994, by the reaction of BBr_3 with acetylene and subsequent esterification with diisopropyl ether, a straightforward stereoselective synthetic route was developed for 1- (dialkoxyboryl)-1,3-dienes.[4] This work inspired bachelor's thesis of J. Polášek from 2014,[5] which focused on the revision of acetylene bromobration mechanism. Stereochemical outcomes of bromoboration experiments raised several questions regarding the isomerization step, whose answer has become the goal of this work. Bromoboration of higher acetylenes provides in most cases *anti* adducts. However, in case of acetylene or 1-haloalk-1-yne, *syn* adduct formation in the first step has been reported. The presence of the *anti* adduct in the reaction mixture for acetylene bromoboration has been explained by the rapid isomerization of the *syn* adduct to the *anti* adduct.[5] The mechanism of this reaction step was studied theoretically in a single study by Wang and Uchyiama.[6] However, the proposed mechanism of isomerization with the participation of BBr_3 contradicted a number of experimental observations by J. Polášek regarding the influence of reactant composition on the kinetics and products stereochemistry.

The theoretical part of the dissertation introduces the basic quantum chemical concepts, important for both the electronic structure calculations and the notion of the reaction mechanism itself. Subsequently, computational methods employed in this thesis are characterized. The following, results part is divided in two chapters, of which the first one concerns the polar isomerization by means of HBr addition while the second one describes the radical isomerization initiated by bromine radical addition.

4. METHODS

The following few pages provide a brief introduction to the methods used in this work, as well as the description of generally available strategies for the localization and identity verification of transition states.

4.1. Density Functional Theory (DFT)

Density Functional Theory (DFT) is one of the key methods in quantum chemistry today. Their popularity is due to the relatively low computational complexity, comparable to the Hartree-Fock method, while achieving significantly higher accuracy for a wide range of systems and molecular properties. The DFT in the so-called Kohn-Sham formulation formally strongly resembles the Hartree-Fock method, but unlike the latter method a priori includes electron correlation through the so-called exchange-correlation functional.

A characteristic and most basic feature of the DFT method is that, unlike the other wavefunction methods, it refers to the electron density $\varrho\ (r)$, which depends on only three spatial coordinates. Pierre Hohenberg and Walter Kohn came up with this groundbreaking idea in 1964.[7] The basis of their approach is the following pair of theorems.

The first Hohenberg – Kohn theorem states that the external potential V_{ex} acting on any system of electrons (in chemical applications V_{ex} is most often a system of atomic nuclei) is a function of only electron density. In other words, while traditional methods of quantum chemistry are based on the knowledge of the external potential, determining Hamiltonian, the wave function and the electron density, the density functional method reverses this construction. Only from the knowledge of the electron density, the external potential can be determined, and thus the wave function and energy as well. From this it can be deduced that energy is a so-called functional of the ground state electron density.

The second Hohenberg - Kohn theorem introduces a variational principle for finding the ground state electron density. The energy corresponding to the exact electron density of the ground state ϱ_0 is always less than the energy calculated for any other physically acceptable density $[\varrho'\ (r)]$. Formally, the energy functional can be decomposed into the contribution of the attraction energy of electrons and nuclei, the kinetic energy $T\ [\varrho\ (r)]$, the classical Coulomb electron-electron repulsion energy $J_{ee}\ [\varrho\ (r)]$ and the non-classical part of repulsion with correlation effects. Kohn-Sham system of non-interacting electrons providing the same resulting density as it has interacting system due to the problems with an expression the kinetic energy from the density. The total functional is then expressed as a sum of kinetic

energy for the non-interacting system, the classical Coulomb repulsion and the so-called exchange-correlation functional $E_{XC}[\varrho(r)]$.[8] Only the latter is necessary to approximate.
The approximation is based then on the so-called exchange-correlation potential acting on the searched Kohn-Sham orbital. One of the most popular approximations of the exchange-correlation functional is the three-parameter potential with the so-called exchange part formulated by Becke (B) and the correlation part formulated by Lee, Yang and Parr (LYP), abbreviated B3LYP.[9,10] The latter potential was used for all DFT calculations performed in this work using the correction for dispersion interactions GD3BJ.[11,12]

4.2. The Second Order Møller-Plesset Perturbation Theory (MP2)

Although DFT is a universal and quite accurate method, it was desirable to use another computational method in this work and then compare the results. The second order Møller-Plesset method (MP2) belongs to the so-called perturbation methods and, like the Hartree-Fock method, is based on the wave function. Unfortunately, the Hartree-Fock method is in most cases not enough to calculate the exact energy of the system. The problem lies in a description of the electron motion. While the Hartree-Fock method considers the motion of electrons to be independent, the motion of electrons is correlated. This correlation can be calculated using perturbation theory, where a perturbation is added to the non-perturbated Hamiltonian for which we know the solution. Mathematically, the Taylor expansion is performed for a new Hamiltonian with a perturbation, where the wave functions are extended into a power series. The calculation then gives HF energy for the first order, while the contributions to the second order (MP2) provide the final energy including correlations.[13,14,15,16,17]

4.3. Potential Energy Surface (PES)

The position of the nuclei, represented by geometric coordinates, can be considered in practical calculations thanks to the Born-Oppenheimer approximation[18] as a parameter determining the electronic energy belonging to a given geometry. Each position of the nuclei then corresponds to a certain value of potential energy, including the potential and kinetic energy of the electrons and the potential energy corresponding to the repulsions of the nuclei. Such a dependence of nuclear and electronic energy on the geometry of molecules is called the Potential Energy Surface (PES). To be precise, it should be noted that this is a hypersurface because energy is not (with the exclusion of diatomic molecules) a function of

only one variable (one bond length) but is a function of several variables. In three-dimensional space, PES can be imagined as a function of two geometric variables (e.g. bond length and bond angle in the H_2O molecule), whose graph is a 3D plot. Each point of the selected plane representing a specific geometry is assigned a specific height by the PES at a coordinate perpendicular to the plane specifying the geometry, and this height corresponds to the electron and nuclear repulsion energy at that point. In practice, PES can be obtained by repeated solutions of the Schrödinger equation for different nuclei configurations on the selected grid. All changes in energy due to a change in the geometry of the system of nuclei and electrons can then be imagined as "traveling" along the PES.

However, not all points on the PES are equally significant.[19,20,21] The most important are the so-called stationary points, where the partial derivatives of energy according to all coordinates are zero. Of the stationary points that meet this condition, local (or global) minima are chemically significant, for which all values of the second energy derivatives are positive with respect to the coordinates and which correspond to stable geometric arrangements of molecules (reactants or products). Furthermore, first-order saddle points are important, for which all but one of the values of the second energy derivatives are positive, and which represent the highest points on the most energy-efficient path between the two minima, i.e. the transition states (TS). It doesn't make much sense to deal with saddle points of higher orders.

The section along the coordinate that corresponds to the path between the two selected minima is called the reaction coordinate. It is of fundamental importance in reaction chemistry. The energy difference between the reactants and the transition state corresponds to the so-called activation energy, which is a measure of the energy intensity of the reaction from a kinetic point of view. In other words, the smaller the value of the activation energy, the easier the reaction will take place. The activation energy also corresponds to the energy that needs to be supplied to realize the reaction at all.

In practical calculation, the localization of the most stable geometric arrangements of molecules takes place through the so-called geometry optimization technique.[19,20] Optimization to a minimum consists in changing the geometry of the molecules so that the gradient (i.e. the vector of energy derivatives according to the coordinates) is zero. The optimized geometry is not obtained in one step. It proceeds iteratively, when we obtain a wave function with its own energy value from the initial geometry, we determine the gradient using the first derivatives, and if it is not zero, the geometry is adjusted in the direction of energy decrease and the whole procedure is repeated until we reach zero gradient. For

completeness, it can be noted that the minimum that has the lowest possible energy on PES is called the global minimum and represents the most thermodynamically stable conformation of a given molecule. However, we do not always find it automatically during optimization, because the optimization takes place only around the minimum closest to the starting geometry.

When searching for a transition state, the situation is even more complicated, because it is necessary to have an approximate estimate of the geometry of this transition state in advance, until this estimate can enter the optimization looking for a first-order saddle point. The question of whether a stationary point is a minimum or a transition state can be decided by performing a vibration analysis, which is described in the following paragraph.

4.4. Vibrational analysis

Each stationary point on the PES corresponds to a total of $3N$-6 vibration degrees of freedom (so-called normal modes) for nonlinear systems and $3N$-5 vibration degrees of freedom for linear systems.[22,23] Vibration analysis is essential in assessing whether it is a local (global) minimum or a first-order saddle point (i.e. a transition state). In vibration analysis, the matrix of the first derivatives of energy with respect to the coordinates of atomic nuclei (so-called gradient) and the matrix of the second derivatives with respect to the same (so-called Hessian) are calculated.[23] During the calculation, the Hessian is diagonalized in order to obtain force constants, and for the purpose of calculating the vibrational frequencies, the Hessian matrix is mass-weighted before diagonalization. The result of diagonalization is a proper vector of force constants, the elements of which are proportional to the squares of the vibrational frequencies.

If all eigenvalues are positive, then all vibration frequencies are real, and it is a local minimum. Similarly, it can be concluded that the acquisition of one negative eigenvalue corresponds to one imaginary vibrational frequency, which belongs to such a stationary point PES, which is the minimum with respect to all coordinates except one, i.e. the transition state. In other words, local minima have all vibrational frequencies positive, transition states have only one imaginary vibrational frequency. One imaginary vibration not only distinguishes the transition state from the local minimum, but also characterizes a pair of local minima, which the given transition state connects by corresponding to the formation and termination of bonds for a given reaction. For completeness, it can be stated that knowledge of vibration

frequencies is also important for the calculation of thermodynamic quantities by statistical methods.[22]

4.5. Single Coordinate Driving method

In this work, the "Single Coordinate Driving" method, abbreviated to "driving", plays a crucial role in finding the transition state of the reaction, which allows searching the PES with knowledge of reactants and / or products of some reaction, characterized by changing some distance, angle or torsion angle.[23] This is the so-called relaxed type of PES surface scan, where the preselected parameter changes and the remaining geometric parameters of the molecule are optimized. We use so-called redundant coordinates[24] entered in the input file immediately below the input geometry, through which we select the type of parameter to be changed (B for the distance between two atoms, A for the bond angle and D for the torsion angle), the number of steps and the size of one step. For example, entering redundant coordinates might look like this:

B 2 8 S 10 0.1

and determines that the distance between atom 2 and 8 (the order given by the input geometry) will be extended in ten steps by a tenth of an Ångström. The extension of the bond is given by the positive value of the step size, the negative value corresponds to the shortening of the selected distance.

Similarly, redundant coordinates can be entered, for example, for rotation around a single bond, with the difference that a torsion angle must be used, which is defined by two planes (i.e. four atoms). However, we often have to do more "drivings" to get an estimate of the transition state that corresponds to the geometry with the highest energy in the reaction path, and then let that geometry be optimized to the transition state. The obtained imaginary vibration must correspond to the given reaction, i.e. it must describe the formation (or breaking) of bonds (see Vibrational analysis), if it does not correspond to the reaction, we must look for other pathways from reactants (or products). For the sake of completeness, it can be noted that vibrational analysis makes sense only when searching for local minima (reactants or products) and transition states, it does not make sense to perform it when "driving" is done. The advantage of "driving" is the exploration of several ways to find the transition state, but at the same time the disadvantage is the complexity of this method for computational time.

4.6. Intrinsic Reaction Coordinate method (IRC)

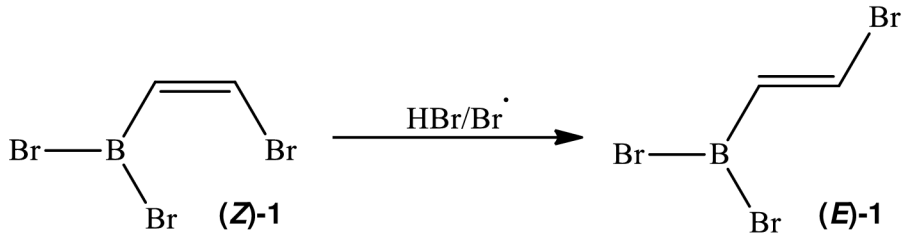
One of the possible verifications whether the found transition state (TS) really belongs to the given reaction is the IRC (Intrinsic Reaction Coordinate) method. When using the IRC method, it is necessary to start from the optimized TS structure, on which the force constants are calculated in the first step. Since these are direction vectors with their own orientation, a gradient in the direction of decreasing energy is calculated in the second step. This process is repeated until the desired convergence criterion is reached in the vicinity of the nearest minimum on the way to the reactants or products, if you like. It is desirable to further optimize the geometries obtained from the IRC to a minimum and to perform a frequency analysis.[25,26]

When we search a transition state, which takes place by driving from an optimized structure of the local minimum, the situation is even more complicated, because it is necessary to have an approximate estimate of the geometry of this transition state before this estimate can enter the first-order saddle point optimization. Subsequently, a vibrational analysis is performed on all obtained optimized structures, which not only fulfils the function of obtaining vibrational values, but thermodynamic quantities (e.g. Gibbs free energy) as well. Verification, of whether the found transition state corresponds to the our studied reaction, is done not only by monitoring the imaginary frequency of vibration but by IRC as well where we find from the found transition state to geometries that lie close to local minima corresponding to reactants on the one hand and products (or intermediates) on the other hand, and therefore it is appropriate to re-optimize these obtained geometries.

Gaussian09[27] was chosen as a computational quantum-chemical program. For the results presented here following the example of Wang a Uchyiama[6] Pople basis set 6-31+G* for boron, carbon and hydrogen atoms and Ahlrich's SVP all-electron basis set for bromine atoms were chosen including the implicit solvent as a dichloromethane. Compared to work of Wang and Uchyiama, however, a solvation model based on density (SMD)[28] was chosen for our purposes. Programs such as Avogadro[29,30] and Molden 5.2[31] were used to visualize molecules, including frequency analysis and PES (driving) scans.

5. RESULTS ACHIEVED

The following paragraphs summarize crucial results obtained, many of them which have been meanwhile presented as conference posters and recently also published in the Journal of Organic Chemistry[32]. The results section is divided into two chapters. The first one is focused on the addition of boron tribromide to acetylene[5,6] and the isomerization of (*Z*)-dibromo(2-bromovinyl)borane, **(*Z*)-1**, to its *E*-counterpart,**(*E*)-1**,through an addition-elimination reaction with HBr.[6] In the second chapter, another possible isomerization pathway initiated by a homolytical bond cleavage, is described. Corresponding radical mechanism is started by an attack of bromine radical on the **(*Z*)-1** carbon binding bromine or on the **(*Z*)-1** carbon binding the dibromoborane group the reaction barrier is lower for the former attack.



Scheme 1: *Z*/*E* isomerization caused by a HBr molecule or a bromine radical.

5.1. Formation of (*Z*)-dibromo(2-bromovinyl)borane

As a first step on the path to understanding the isomerization of **(*Z*)-1**, it is suggested to briefly examine its formation. We know from experiment that this alkene can be formed by the direct addition of boron tribromide to acetylene. The centre of the electron density is the triple bond of acetylene, so it acts as a donor. Boron tribromide, which acts as a Lewis acid, is an acceptor and will want to fill an empty p orbital on a boron atom. The addition of boron tribromide to acetylene is associated with the height of the reaction barrier **12.46 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **22.30 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD). (**Fig. *A*1**)

5.2. Decomposition of (*Z*)-dibromo(2-bromovinyl)borane

In the case of the first pathway of the isomerization step studied, a proton is added to the carbon carrying the dibromoborane group. Based on the calculations performed in this work, the addition results in the decomposition of **(*Z*)-1** to vinyl bromide and boron tribromide, while the amount of both products was observed experimentally depending on the reaction conditions as well. The calculation shows that the reaction barrier to decomposition to vinyl bromide and boron tribromide is in Gibbs free energy **24.8 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **27.7 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD). (**Fig. *A*2**)

Boron tribromide and vinyl bromide can also act as reactants and thus react with each other to give an intermediate (**IM1**) which is analogous to the intermediate after the addition of hydrogen bromide to **(*Z*)-1**. The transition state found for this reaction lies in Gibbs free energy **19.0 kcal mol^{-1}** (B3LYP//6-31+G*/SVP; SMD) or **24.0 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD) above the energy level of the reactants. However, it is an endergonic process, so the intermediate is higher in energy **1.0 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **1.9 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD) than the educts. (**Fig. *A*3**)

5.3. Hydrobromination ("polar" pathway) of (*Z*)-dibromo(2-bromovinyl)borane

The second possible reaction route assumes of the classical addition of a hydrogen halide to an alkene, i.e. it is determined by the addition of a proton to a carbon carrying a dibromoborane group and a bromide anion to a carbon carrying a bromine. The intermediate (**IM1**) is the same as for the reaction of vinyl bromide with boron tribromide. The height of the reaction barrier for the addition of hydrogen bromide to **(*Z*)-1** is **31.3 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **40.9 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD), which is **12.3 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **16.3 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD) higher in energy than in the case of the reaction of vinyl bromide and boron tribromide. This means that a possible intermediate (**IM1**) is more likely to form from the reaction of these reactants than from the addition of hydrogen bromide to **(*Z*)-1**. Because this intermediate is saturated, it can be converted **9.6 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **10.7 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD) lower in energy by rotating around a single carbon bond. The height of the rotation barrier is only **5.1 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **5.3 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD). An

alkene in the trans isomerism, i.e. **(*E*)-1**, can be obtained from the mentioned conformer by back-cleavage of hydrogen bromide. The reaction barrier in the calculations is approximately **37.9 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **50.9 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD), which is a relatively high value and it can be concluded that the trans product is probably formed by a different reaction mechanism than the back cleavage of hydrogen bromide from this conformer. In addition, the product is in Gibbs free energy **8.7 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **9.9 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD) higher than the energy level of the conformer from which cleavage occurred. (**Fig. *A*4**)

5.4. Radical isomerization of (*Z*)-dibromo(2-bromovinyl)borane

The existence of a radical mechanism of isomerization therefore appears to be the most probable interpretation of the results of Jan Polášek's experimental study. The radical mechanism can be represented in two possible ways.

The first way is the addition of a bromine radical to the carbon atom **(*Z*)-1**, which carries bromine. This step is associated with an energy barrier **4.1 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **4.6 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD). Due to the saturation of the bond between the carbons, rotation around this bond is possible and is associated with energy barrier **5.9 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **5.5 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD). The last step of formation of **(*E*)-1** is represented by the cleavage of the bromine atom from this carbon. The energy barrier for this step is related to height **4.9 kcal mol^{-1}** (B3LYP-GD3BJ//6-31+G*/SVP; SMD) or **12.1 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD). Of interest is the different position of products on the energy scale. While in the case of the DFT method the products are lower than the transition state from which the product was created, in the calculations by the MP2 method there is an increase in Gibbs free energy and the products are thus energy higher than the transition state. (**Fig. *A*5**)

The second way is the addition of a bromine radical to the carbon atom **(*Z*)-1**, which carries a dibromoborane group. DFT results are not available for this proposed mechanism, as many structures could not be obtained by this method at all. The height of the energy barrier for the addition of a bromine radical to a carbon carrying a dibromoborane group is **1.8 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD). Since the bond between the carbons has again been saturated, rotation around this bond is also possible. The clockwise rotation barrier is **3.5 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD). (**Fig. *A*6**)

A more interesting alternative is anticlockwise rotation. This path is associated with a higher number of intermediate steps, but with lower energy barriers as well. The last step of formation of **(*E*)-1** is represented by the cleavage of the bromine atom from the carbon carrying the dibromoborane group. The energy barrier for this step is related to height **4.6 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD). Products are higher **7.7 kcal mol^{-1}** (MP2//6-31+G*/SVP; SMD) in energy compared to the intermediate (**IM7**), from which cleavage happened. (**Fig. *A*7**)

6. REFERENCES

1. Lappert, M. F.; Prokai B. *Journal of Organometallic Chemistry*. **1963**, *1*, 384-400.
2. Blackborrow, J. R. *J. Chem. Soc*., Perkin Trans. **1973**, *2*, 1989-1993.
3. Wrackmeyer, B. *Polyhedron*. **1986**, *5*, 1709–1721.
4. Mazal, C.; Vaultier, M. *Tetrahedron Letters*. **1994**, *35*, 3089–3090.
5. Polášek, J. Revize bromoboračních reakce acetylenu. Bakalářská práce, Brno: Masarykova Univerzita, 2014.
6. Wang, Ch.; Uchyiama, M. Mechanistic Understanding of Alkyne Haloboration: An Ab Initio Study. *Eur. J. Org. Chem.* **2012**, 6548-6554.
7. Hohenberg, P.; Kohn, W. Inhomogenous electron gas. *Physical Review*. **1964**, *136*, B864.
8. Kohn, W.; Sham, L. J. Self-Consistent Equations Including Exchange and Correlation Effects. *Physical Review*. **1965**, *140*, A1133.
9. Becke, A. D. Density-functional thermochemistry. III. The role of exact Exchange. *J. Chem. Phys*. **1993**, *98*, 5648-5652.
10. Lee, C.; Yang, W.; Parr, R. G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Physical Review B*. **1988**, *31*, 785-789.
11. Austin, A.; Petersson, G. A.; Frisch, M. J.; Dobek, F. J.; Scalmani, G.; Throssel, K. A density functional with spherical atom dispersion terms. *J. Chem. Theory Comput*. **2012**, *8*, 4989-5007.
12. Grimme, S.; Ehrlich, S.; Goerigk, L. Effect of the damping function in dispersion corrected density functional theory. *J. Comp. Chem*. **2011**, *32*, 1456-65.
13. Frisch, M. J.; Head-Gordon, M.; Pople, J. A. Direct MP2 gradient method. *Chem. Phys. Lett*. **1990**, *166*, 275-80.
14. Frisch, M. J.; Head-Gordon, M.; Pople, J. A. Semi-direct algorithms for the MP2 energy and gradient. *Chem. Phys. Lett*. **1990**, *166*, 281-89.
15. Head-Gordon, M.; Pople, J. A.; Frisch, M. J. MP2 energy evaluation by direct methods. *Chem. Phys. Lett*. **1988**, *153*, 503-06.
16. Saebø, S.; Almlöf, J. Avoiding the integral storage bottleneck in LCAO calculations of electron correlation. *Chem. Phys. Lett*. **1989**, *154*, 83-89.

17. Head-Gordon, M.; Head-Gordon, T. Analytic MP2 Frequencies Without Fifth Order Storage: Theory and Application to Bifurcated Hydrogen Bonds in the Water Hexamer. *Chem. Phys. Lett*. **1994**, *220*, 122-28.

18. Born, M.; Oppenheimer, J. Zur quantentheorie der molekeln. *Annalen der Physik*. **1927**, *84*, 457.

19. Henkelman, G.; Jóhannesson, G.; Jónsson, H. Methods for Finding Saddle Points and Minimum Energy Paths. *Prog. Theo. Chem. Phys*. **2000**, *5*, 269.

20. Schlegel, H. B. Exploring Potential Energy Surfaces for Chemical Reactions: An Overview of Some Practical Methods. *J. Comp. Chemistry*. **2003**, *24*, 1514.

21. Hehre, W. J.; Lathan, W. A.; Pople, J. A.; Radom, L.; Wasserman, E.; Wasserman, Z. Molecular orbital theory of the electronic structure of organic compounds. 28. Geometries and energies of singlet and triplet states of the C_3H_2 hydrocarbons. *J. Am. Chem. Soc*. **1976**, 98, 4378.

22. Waren, J. H.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. Ab Initio Molecular Orbital Theory. Canada: John Wiley & Sons,1986.

23. Jensen, F. Introduction to computational chemistry. 2nd ed. Chichester: John Wiley & Sons, 2007.

24. Peng, C.; Ayala, P. Y.; Schlegel; H. B.; Frisch, M. J. Using Redundant Internal Coordinates to Optimize Equilibrium Geometries and Transition States. *J. Comp. Chem*. **1995**, *16*, 49.

25. Fukui K. The path of chemical-reactions – The IRC approach. *Acc. Chem. Res.* **1981**, *14*, 363-68.

26. H. P. Hratchian and H. B. Schlegel, in Theory and Applications of Computational Chemistry: The First 40 Years, Ed. C. E. Dykstra, G. Frenking, K. S. Kim, and G. Scuseria (Elsevier, Amsterdam, 2005) 195-249.

27. Gaussian 09, Revision D.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.;

Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2013.

28. Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal solvation model based on solute electron density and a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions. *J. Phys. Chem. B*. **2009**, *113*, 6378-96.
29. Avogadro: an open-source molecular builder and visualization tool. Version 1.1.1. http://avogadro.cc/
30. Hanwell, M. D.; Curtis, D. E.; Lonie; D. C.; Vandermeersch, T.; Zurek, E.; Hutchison, G. R. Avogadro: An advanced semantic chemical editor, visualization, and analysis platform. *Journal of Cheminformatics*. **2012**, 4:17.
31. Schaftenaar, G.; Noordik, J. H. Molden: a pre- and post-processing program for molecular and electronic structures. *J. Comput.-Aided Mol. Design*. **2000**, *14*, 123-134.
32. Polášek, J.; Paciorek, J.; Stošek, J.; Semrád, H.; Munzarová, M. and Mazal, C. Stereoselective Bromoboration of Acetylene with Boron Tribromide. A Preparation of (*Z*)-Bromovinylboronates. *Journal of Organic Chemistry*. **2020**. **Articles ASAP (Article) Publication Date (Web):** May 21, 2020.

7. ATTACHMENTS

Key for atom colors: red = bromine; pink = boron; dark grey = carbon; light grey = hydrogen.

Key for line colors: black = MP2 calculations; red = B3LYP-GD3BJ calculations.

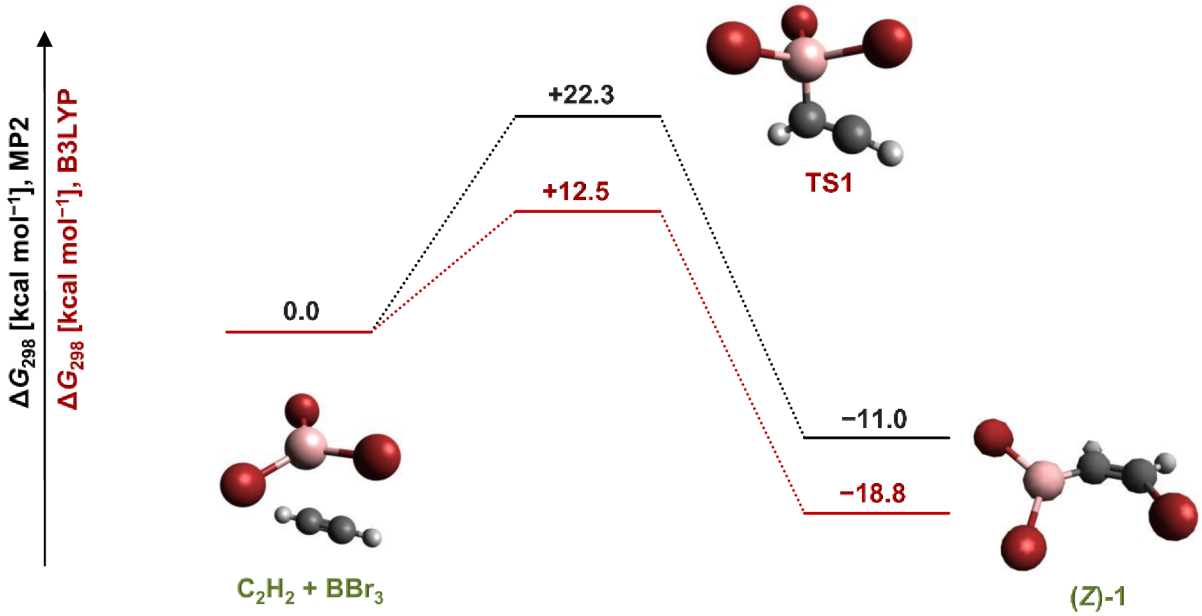


Figure *A*1: BBr_3 addition to acetylene.

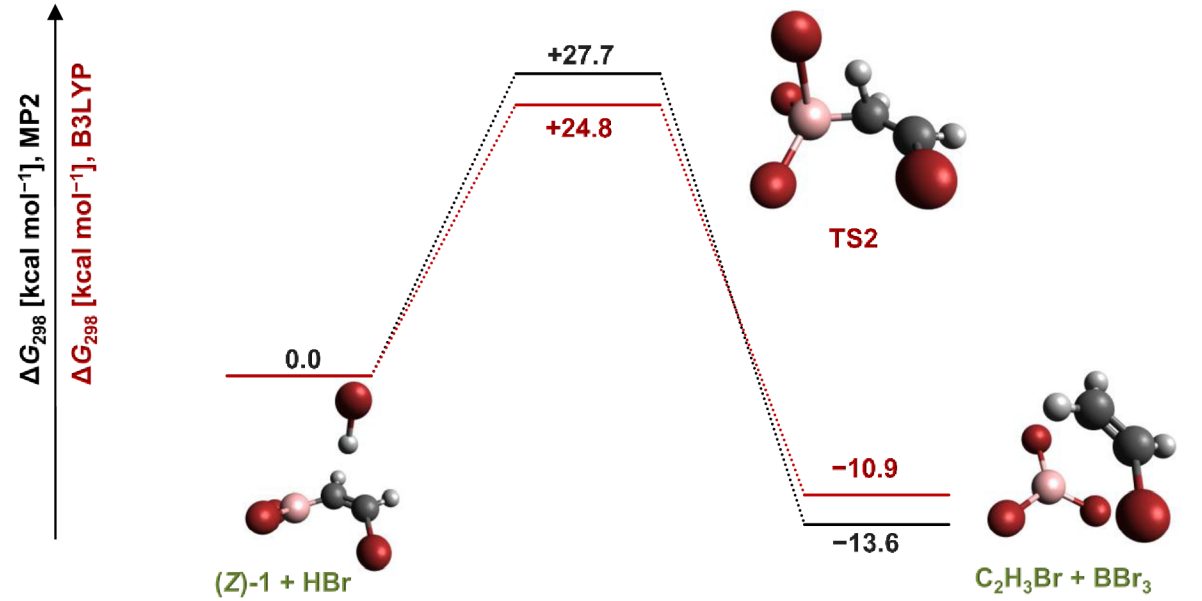


Figure *A*2: Decomposition of **(*Z*)-1** after the hydrogen bromide attack.

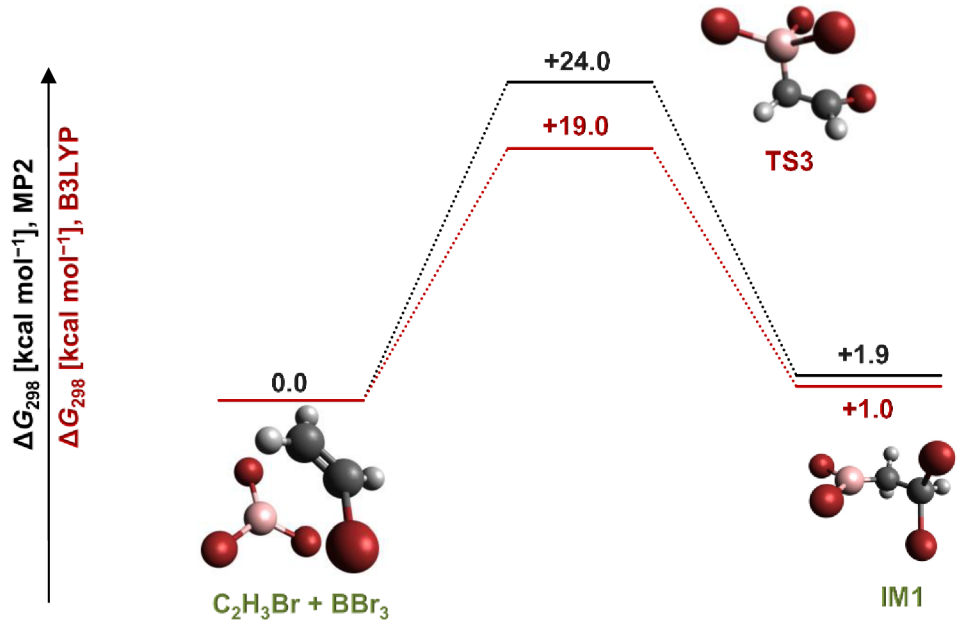


Figure *A*3: Reaction of vinylbromide (observed experimentally in reaction mixture) with BBr_3 provides the same intermediate as results from the hydrobromination of **(*Z*)-1** (see **Fig. *A*4**)

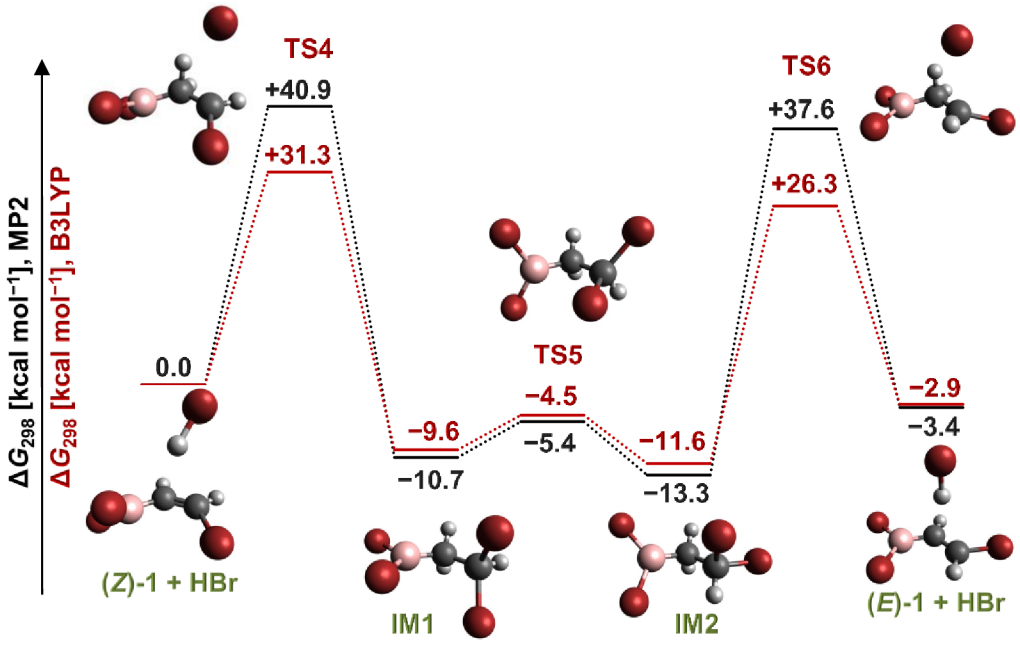


Figure *A*4: Hydrobromination of **(*Z*)-1** provides the same intermediate as shown in Figure *A*3. The energy barrier of the first step is too high to be exceeded under the reaction conditions.

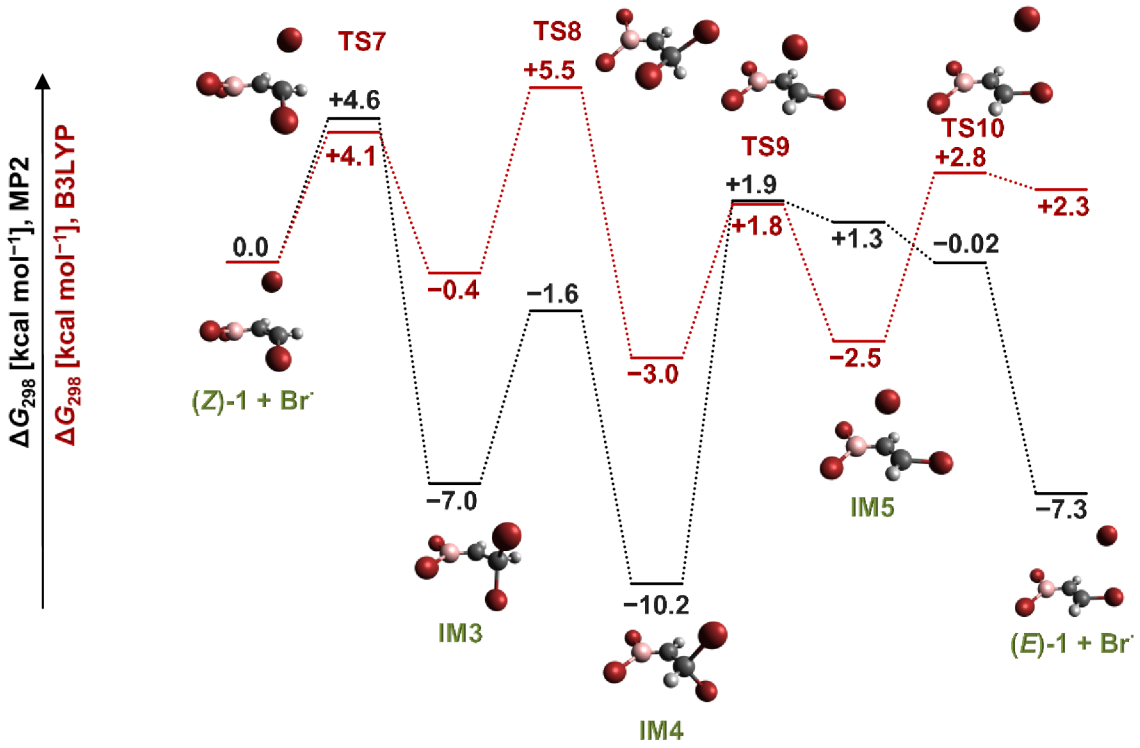


Figure *A*5: Demonstration of a bromine radical attack on bromine-binding carbon of **(*Z*)-1**.

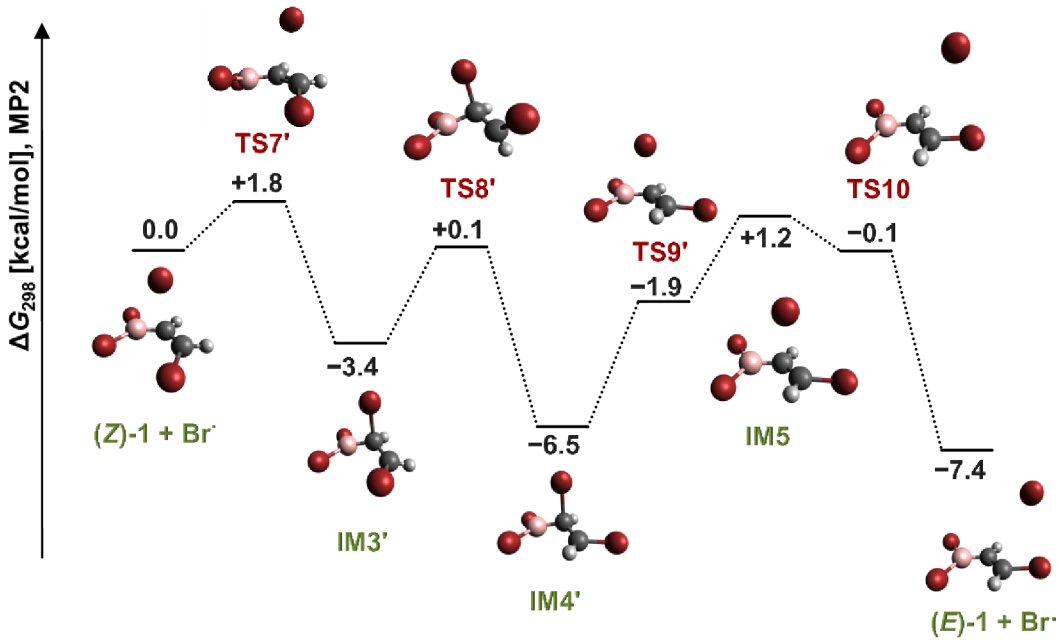


Figure *A*6: A bromine radical attack on the boron-binding carbon of **(*Z*)-1** with subsequent clockwise rotation around the C–C bond.

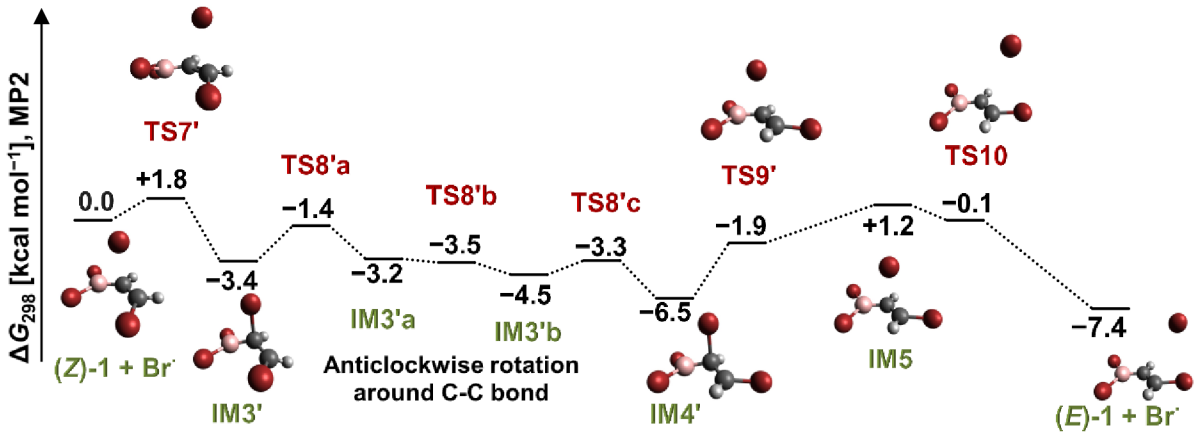


Figure *A*7: Bromine radical attack on the boron-binding carbon of **(*Z*)-1** with subsequent anticlockwise rotation around the C–C bond.

AUTHOR'S PUBLICATIONS

Polášek, J.; Paciorek, J.; Stošek, J.; Semrád, H.; Munzarová, M. and Mazal, C. Stereoselective Bromoboration of Acetylene with Boron Tribromide. A Preparation of (*Z*)-Bromovinylboronates. *Journal of Organic Chemistry*. **2020**. **Articles ASAP (Article) Publication Date (Web):** May 21, 2020.

Overview of Conference Papers

1. SEMRÁD, Hugo, Jakub STOŠEK a Markéta MUNZAROVÁ. Ab initio studies of the acetylene bromoboration mechanism. In 52nd Symposium on Theoretical Chemistry - Chemistry in Solution, Ruhr Universitaet Bochum, Germany, September 26–29, 2016.
2. SEMRÁD, Hugo, Jakub STOŠEK, Pavel KUBÁČEK a Markéta MUNZAROVÁ. Orbital interactions between C_2H_2, BBr_3, and HBr influencing stereospecificity of acetylene bromoboration. In ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY. WASHINGTON: AMER CHEMICAL SOC, 2017. s. "Amer Chem Soc"-"1", 2 s. ISSN 0065-7727
3. STOŠEK, Jakub, Hugo SEMRÁD, Polášek JAN, Ctibor MAZAL a Markéta MUNZAROVÁ. Experimental and quantum chemical studies of alkyne bromoboration. In 9th Barrande-Vltava French-Czech Chemistry Meeting, Strasbourg, France, August 27–28, 2018.
4. SEMRÁD, Hugo a Markéta MUNZAROVÁ. A DFT Study of Radical *Z*/*E* Isomerization of $BBr_2C_2H_2Br$. In 16th Central European Symposium on Theoretical Chemistry, Srní, Czech Republic, September 9–12, 2018.
5. SEMRÁD, Hugo a Markéta MUNZAROVÁ. Reaction Energetics & Diels-Alder Reaction Profiles for Enediones and Decalines by Means of DFT. In 17th Central European Symposium on Theoretical Chemistry, Burg Schlaining, Austria, September 9–12, 2019.
6. POLÁŠEK, Jan, Hugo SEMRÁD, Jakub STOŠEK, Jan PACIOREK, Markéta MUNZAROVÁ a Ctibor MAZAL. Stereoselective Bromoboration of Acetylene with Boron Tribromide. A Simple preparation of (*Z*)-Bromovinylboronates. In XIIIth Workshop on Modern Methods in Quantum Chemistry, Mariapfarr, Austria, March 1–5, 2020.